STUDIES ON PHARMACOLOGY AND
EFFICACY OF HERBAL DRUGS
USED IN PAKISTAN

THESIS SUBMITTED BY

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خلاصة

الخلاصة

دفنت في العالم كأعمال الروايات كما استُهلت في أمثال قدم ركاب。

رفعت قلب أمثال الأ.LinkedList: إل تدريجًا على السعر، مما تم رفعه إل تدريجًا على السعر.

عند الحاضر في العالم، وما أن عرضت في العالم، وما أن عرضت في العالم.

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SUMMARY
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The use of drugs of plant origin is from time immemorial. Since the birth of man in universe the use of drugs of plant origin was started. The system is known by various names as Ayurvedic system, Unar system, Eastern system or traditional system of medicine. Th fundamental aim is to provide remedy for the certain ailments. In Pakistan economy plays an important role. The drugs are taken in the form of pills containing active principle. It cannot be ascertained to say that synthetic drugs provide such remedy as whole herb can, because during synthesis many drugs are totally or partially destroyed while in whole plant nothing is added or subtracted. The great example of utilizing the traditional system can be seen in China.

*Nigella sativa* belongs to family Ranunculaceae, also called with the name black seeds commonly known in Urdu as Kalongi. It contains yellowish volatile oil, 1.5% and a fixed oil 37.5%, essential oil, albumin sugar, mucilage, organic acids, metarbin, toxic glucosides, melanthin resembling helleborin, ash 5% moisture and arabic acid. Volatile oil is the active constituent. It consists of (1) carvone 45-60%, an unsaturated ketone, (2) terpene or d-limonene also called carvene and (3) cymene.

As mentioned in Nadkarni’s book (1954) seeds are used as a condiment in curries and with other aromatic substances and bitters used to control hiccup, employed to correct purgatives, useful in
indigestion, loss of appetite, fever, diarrhoea, dropsy, puerperal diseases, they have action as a galactagogue. It stimulates uterine contraction. Useful in amenorrhoea and dysmenorrhoea. Seeds are said to be vormicidal, used for various skin eruptions and can stop vomiting.

Herbal medicines as the major remedy in traditional system have been used in medical practice for thousand years. An evaluation have been carried out to find out the effect of the drug on blood, blood pressure and in muscular pain, for this purpose both males and females were divided into groups according to age. Blood examination was done before and after the completion of the treatment i.e. 7 days. Statistical calculation was done to find out the results. It was concluded that there have been no adverse effects of *Nigella sativa* on blood and blood pressure and no remarkable change in liver enzymes was noted.

Safety evaluation studies on oil of *Nigella sativa* were done, for this purpose male and female rats were used. *Nigella sativa* oil was given in different doses. No mortality and behavioural changes were noted 24 hours after administration of *Nigella sativa* oil. Investigations regarding SGOT, bilirubin, total protein, total lipids, cholesterol and triglyceride remained in normal range after administration of *Nigella sativa* oil.
INTRODUCTION
INTRODUCTION

The use of drugs of plant origin is from the immemorial time. Since the birth of man in universe, the use of drugs of plant origin started because the man found around his surroundings the plants and started using them. With the passage of time he found the drugs of plant origin having therapeutic efficacy.

The system is known by different names as Ayurvedic system, Unani system, Eastern system or Traditional Medicine. The fundamental object of all the systems is the same as to provide remedy for certain ailments.

Gradually, with the modern research, more work has been done towards the synthesis of drugs from herbal sources. Needless to say that this system has stood the test of time. Its products for remedies are based on renaissance of wisdom, experience, efficacy, suitability and the absence of serious side effects. The system provides cheap medicines. In Pakistan economy plays an important role. The life saving drugs are becoming costly day by day. Many Afro-Asian countries have adopted this system as an effective, and having relative freedom from problems which are often encountered in other systems.

Eastern system of treatment has motivated a man to take medicines in the form of active principle which is available in the form of a pill and to make a pill special type of devices are adopted and it is
believed that the treatment of certain diseases like diabetes, tuberculosis, cancer and asthma can be possible.

It cannot be ascertained that synthetic drugs provide such remedy as whole herb can, because during synthesis many ingredients are totally or partially destroyed while in whole plant nothing is added or subtracted. Also these synthetic drugs are doing what was accepted from them, at the same time they are also doing or producing which was not derived from them, thus creating more miseries and troubles (Bukhari et al. 1987).

Today more people are returning to traditional medicine for the promotion and propagation of health thus adopting the slogan of W.H.O “Health for all by the year 2000”. The system of traditional medicine is used nowadays for the treatment of many diseases and ailments including wounds, ulcers, intestinal disorders, febrile illnesses, disorders of urinary tract, rheumatic pains, skin disorders, asthma, diabetes, hypertension, cancer and tuberculosis. This system is also beneficial in many deficiency disorders.

Herbal system of treatment plays an important role in uplifting the health of an individual and of nation. This system has provided therapeutic agents for cure of diseases, which were taken as incurable such as vincristine, vinblastin, quinines, emetics, morphine, atropine.
reserpine, scopolamine and artemesinin. Search is still going on to find out the remedy of many more ailments.

The great example of utilizing the traditional system can be seen in China. They utilize 80-90% of their natural products for treatment and cure. Herbal origin drugs have many actions e.g. freeze dried garlic (Allium sativum) has hypotensive effect as demonstrated in the study conducted by Malik and Siddiqui (1981).

Considering the viewpoint of use of medicines of herbal origin a search has been done to assess the efficacy and utility of Nigella sativa.

In view of the ever-growing importance of the herbal medicine, the investigator has conducted a study on the efficacy of Nigella sativa in muscular pains in human.
REVIEW OF LITERATURE
REVIEW OF LITERATURE

NIGELLA SATIVA

Family: Ranunculaceae
Arabic name: Habat-Baraka
Urdu name: Kalongi (Siyah Dana)
English name: Nigella seeds
Parts used: Seeds, oil of seeds

*Nigella sativa* is the botanical name. It is also called with the name black seeds, black cumin. Commonly known in urdu as Kalongi. In Arabic it is called Habba-tus-Sauda/Habb-tul-Burk/Shoneez. In Persian it is called Shoneez. Its parts used are seeds and oil.

This is a small plant having pungent odour, about 30 to 60 cm high having 2.5-5 cm long leaves and pale, blue flowers. Seeds are triangular tubercular, very black in colour and bitter in taste as described by Hasan (1989).

CONSTITUENTS:

Seeds contain a yellowish volatile oil 1.5 percent and a fixed oil 37.5%, essential oil, albumin, sugar, mucilage, organic acids, metarbin, toxic glucosides, melanthin resembling helleborin, ash 5%, moisture and arabic acid. Volatile oil is the active constituent. It consists of carvone 45-60%, an unsaturated ketone, terpene or d-limonene also called carvene and cymene.
USES:

As mentioned by Nadkarni (1954). Seeds are used as a condiment in curries and with other aromatic substances and bitters, seeds about half a drachm are given with butter milk to cure obstinate hiccup, are employed to correct purgatives and other medicines. Also useful in indigestion, loss of appetite, fever, diarrhoea, dropsy, puerperal diseases. They have action as a galactagogue; a decoction of the seeds is given to recently delivered females in combination with a few other medicines, it also stimulates uterine contraction. In doses of 10 to 20 grams, it is useful in amenorrhoea and dysmenorrhoea and in large doses cause abortions. It is also said that seeds are wormicidal.

Akhtar and Aslam (1997) studied the effect of *Nigella sativa* on cestodes and it was suggested that the total glycosides of *N. sativa* seeds possess considerable activity against cestodes in the goats and may be responsible for the anticestodal efficacy of the powdered seeds already reported to be effective against tapeworms of sheep. Similar medicinal use has been described in book by Khan et al. (1997).

Antifasciolic efficacy of indigenous plant drugs (Kalongi) was studied by Kailani et al. (1995) and from the data it was conceivable that the drug was sufficiently potent and safe to treat fasciola infection in buffaloes. However, further chemical and pharmacological studies would decide the exact mechanisms of action, the active principles contained
and the real worth of those indigenous drugs for the treatment of fascioliasis in the ruminants.

**CHEMICAL COMPOSITION OF *NIGELLA SATIVA***:

Al-Jassir (1992) studied the chemical composition of *Nigella sativa* seeds growing in Saudi Arabia.

Proximate analysis of black cumin seeds showed a composition of 20.85% protein, 38.20% fat, 4.64% moisture, 4.37% ash, 7.94% crude fibre, 31.94% total carbohydrates. Potassium, phosphorus, sodium and iron were the predominant elements present. Zinc, calcium, magnesium, manganese and copper were found at lower levels. However, lead, cadmium and arsenic were not detected in the seeds. Linoleic acid and oleic acid were the major unsaturated fatty acids while palmitic acid was the main saturated one. Glutamic acid arginine and aspartic acid were the main amino acid present while cystine and methionine were the minor amino acids. These results indicate the high nutritional potential of Saudi black cumin seeds especially as a source of protein and fat. The total aerobic bacterial count was $7 \times 10^7$ cfu/g and the yeast and mould counts were $4 \times 10^2$ cfu/g. The low number observed for *Staphylococcus aureus* and *Bacillus cereus* make black cumin seeds acceptable without any associated health hazard. According to description by Hassan (1989) fatty composition of *Nigella sativa* comprises as palmitic 12.79%, stearic 7.19%, oleic 7.29%, linoleic 4.09%, arachidic 2.84%, euricic 13.04% and also contains unidentified essential oils (Kumar and Thakur 1989).
**ACTIONS AND USES:**

Seeds are aromatic, digestive, carminative, stomachic, antibilious, diuretic, lithontritic, anthelmintic, emmenagogue and galactagogue. They are used in indigestion, biliousness, dropsy, worm infestation, renal calculi, oligo-galactation, mild puerperal sepsis, amenorrhoea and dysmenorrhoea. In large doses seeds cause abortion (more than 2 g). Seeds are also anti-phlegmatic, expectorant and used in chronic bronchitis and bronchial asthma. They are locally anesthetic especially their oil which is externally used in rheumatic pains, vitiligo, eczema and skin eruptions.

**DOSAGE AND ADMINISTRATION:**

According to literature available the seeds are given in powder form 0.5-1 gm alone or mixed with honey. Seeds are ground in vinegar to make a paste to be applied externally on vitiligo. Seeds are heated in oil (1:10) on slow fire to be used externally.

**ACTIVE CONSTITUENTS OF NIGELLA SATIVA:**

Nigellene (C₁₈H₂₂O₄) a non-carboxyl fraction, nigellone (antiasthmatic) a pharmacologically active principle 2-methyl-4-isopropyl-p-quinone glucoside, melanthin, melanthigenin (1%), fixed oil (approximately 35%), essential oil approximately (1.5%). Fatty acids: palmitic, myristic, stearic, oleic 38-76%, linolenic (1.88%), linoleic acid, β-sitosterol. Seeds contain a phenolic fraction.
The seeds when bruised into vinegar give relief to pityriasis, leucoderma, ring worm, eczema, alopecia, freckles and pimples. It has also been tried in asthma, chronic headache or migraine and in chest congestion. In dysmenorrhoea seed powder is prepared in decoction to administer. Nigella seeds are extensively used as spice.

Description given by Nickolson (1991) about Nigella is as follows:

Nigella niger black, referring to the colour of the seeds. Devil in bush; fennel flower; love in a mist. Including Garidella. ORD Ranunculacea. A genus comprising about half a score species of curious hardy, erect growing annuals inhabiting the Mediterranean region and Western Asia. Flowers white, blue or yellowish; calyx of five petals like deciduous sepals; petals five, two lipped with a hollow, nectariferous claw. Stem leaves alternate, cut into very narrow, subpinnate segments. Nigellas are of the easiest culture in any moderately good garden soil. Seeds should be sown in March or April, in the open border in light soil and the seedlings thinned out to cinapart. The species most generally grown are N. damascena and N. hispanica.

TRIALS OF NIGELLA SATIVA:

Acute and Chronic Metabolic Study of Nigella sativa Linn.:

The study was performed by Khan and Chaudhuri (1998), according to this study mice were used as experimental animal. The food intake was increased but no change was observed on defaecation interestingly though there was no change in water intake but there was a large increase in the amount of urination. though the mouth-lung body weight-gain study was not uniform in choosing initial weight of the experimental animals but it can be safely concluded that Nigella sativa causes a decrease in body weight gain rate of both the sexes. Male rat showed more variation in their gaining of body weight. In the organ weight studies, there was an increase in weight of the liver only in the female rats. The weight of the kidney increased irrespective of the sex of the rat. Adrenal weight increased only in the male rats. Among the male gonads there was an increase in weight in cauda epididymides and seminal vesicles. Gross histopathological changes were noticed in the kidney and testes. Possible histopathological changes were noticed in the liver and small intestine. Abnormal changes were noted in the pancreas, stomach, glomeruli, urinary bladder, testes, adrenal cortex, adrenal medulla and lacrimal gland.

According to study by Agel and Shaheen (1996), the effects of the volatile oil of Nigella sativa seeds were tested on smooth muscles of rats and guinea pigs in vitro using isolated uterine horns. The volatile oil
inhibited the spontaneous movements of rat and guinea pig uterine smooth muscles and also the contractions induced by oxytocin stimulation. These effects were concentration dependent and reversible by tissue washing. This suggests that this volatile oil may have some anti-oxytocic potential.

According to study of Hashim et al. (1994) modulatory effects of essential oils from species on the formation of DNA adduct by aflatoxin B₁ in vitro was tested, the essential oil from common species such as nutmeg, ginger, cardamom, celery, xanthoxylum, black pepper, cumin and coriander were tested for their ability to suppress the formation of DNA adducts by aflatoxin B₁ in vitro in a microsomal enzyme mediated reaction. All oils were found to inhibit adduct formation very significantly and in a dose-dependent manner. The adduct formation appeared to be modulated through the action on microsomal enzymes because an effective inhibition on the formation of activated metabolite was observed with each oil. The enzymatic modulation is perhaps due to the chemical constituents of the oil, and this could form a basis for their potential anticarcinogenic role.

Respiratory effects and mechanism of action of *Nigella sativa* were elucidated by El-Tahir et al. (1993). On urethane-anaesthetized guinea-pig, investigated and compared with those of its constituent thymoquinone. They suggested that volatile oil - induced respiratory effects were mediated via release of histamine with direct involvement of
histaminergic mechanisms and indirect activation of muscarinic cholinergic mechanisms.

According to the studies performed by Salomi et al. (1992), about the antitumour principles from *Nigella sativa* seeds containing fatty acids was studied for antitumour activities against Ehrlich ascites carcinoma, Daltons lymphonia ascites and sarcoma. *In vivo* EAC tumour development was completely inhibited by the active principle at the dose of 2 mg/mouse per day × 10.

Antimicrobial activity of *Nigella sativa* was studied by Hanafy and Hatem (1991), the extract showed antibacterial synergism with streptomycin and gentamicin and showed additive antibacterial action with spectinomycin, erythromycin, tobramycin, doxycycline, chloramphenicol, nalidixic acid, ampicillin, lincomycin and sulphamethoxazole-trimethoprim combination. The extract successfully eradicated a non-fatal subcutaneous staphylococcal infection in mice when injected at the site of injection.

Antimicrobial efficacy of *Saussurea lappa* roots and anticestodal effect of *Nigella sativa* seeds was studied in children by Akhtar and Riffa (1991). It is concluded that these indigenous medicinal plants contain active principles effective against nematodes and cestodes and no adverse effects were produced by these drugs.
*Nigella sativa* has galactagogue action. The study was done by Agrawala et al. (1971). The cardiovascular actions of the volatile oil of the black seed (*Nigella sativa*) in rats were elucidated by Eltahir et al. (1993) the results suggested that volatile oil induced cardiovascular depressant effects were mediated mainly centrally via indirect and direct mechanisms that involved both 5-hydroxytryptaminergic and muscarinic mechanisms. The direct mechanisms may be due to the presence of thymoquinone in the volatile oil. The volatile oil seemed to possess the potential of being a potent centrally acting antihypertensive agent.

The analgesic study in mice revealed *Nigella sativa* Linn. to be analgesic reaching a peak effect in 2 hours time.

The aqueous extracts of the seeds of *Nigella sativa* Linn. can be used as analgesic and anti-inflammatory agent for pain and acute inflammation as studied by Khan et al. (1999). It was suggested that compound responsible for analgesic and anti-inflammatory activity should be isolated and chemically synthesized.

Haq et al. (1995) studied the effect of *Nigella sativa* on human lymphocytes and polymorphonuclear leukocyte phagocytic activity, the effect of *N. sativa* seeds and their soluble fractions were studied *in vitro* on lymphocyte response to different mitogens and on polymorphonuclear leukocyte phagocytic activity. No stimulatory effect of *N. sativa* was detected on lymphocyte response to phytohemagglutinin, concanavalin-A
or pokweed mitogen. A stimulatory effect of *N. sativa* was noticed on the lymphocyte response to pooled allogenic cells, this effect was more pronounced when the low molecular weight fraction was used and varied from one normal individual to another. *N. sativa* enhanced the production of interleukin 3 by human lymphocytes when cultured with pooled allogenic cells or without any added stimulator. *N. sativa* did not however enhance or suppress interleukin-2 secretion by mitogen activated peripheral blood mononuclear cells. *Nigella sativa* increased interleukin-1B, suggesting therefore that it has an effect on macrophages. It also suppressed the leukocyte chemiluminescence activity using phorbol myristate.

The chronic metabolic effect was measured by giving once daily dose of the alcoholic extract to the animals for one month. The extract was administered orally. In case of the control animal saline water was substituted for the extract, animals employed were rats of both sexes of the same age and weighing between 120-150 gm. Both the groups treated and control remained under same environmental condition and were provided with enough food and water throughout the experiment. The body weight of each rat was measured daily and compared with that of control.

The effects of the volatile oil of the black seed (*Nigella sativa*) on the arterial blood pressure and heart of urethane anaesthetized rats were investigated and the effects were compared with those of its
constituents. The results suggested that volatile oil induced cardiovascular depressant effects were mediated mainly centrally via indirect and direct mechanisms that involved both 5-hydroxytryptaminergic and muscarinic mechanisms. The direct mechanisms may be due to the presence of thymoquinone. The volatile oil seemed to possess the potential of being a potent centrally acting antihypertensive agent (el-Tahir et al. 1993).

The effect of a plant mixture extract on liver gluconeogenesis in streptozotocin induced diabetic rats was done and was concluded that the antidiabetic action of the plant extract may, at least partly be mediated through decreased hepatic gluconeogenesis. The extract may prove to be a useful therapeutic agent in the treatment of non-insulin dependent diabetes mellitus (Al-Awadi et al. 1991). In another study an extract of a mixture of *Nigella sativa* seeds and gum (myrrh assafoetida aloe and olibanum) used by Kuwaiti diabetics was found to improve glucose tolerance in both streptozotocin diabetic and normal rats. They have reported that this effect was neither mediated through the stimulation of insulin secretion nor through the suppression of the intestinal absorption of glucose. In this report the blood glucose lowering action of the extracts of individual components of this mixture was studied in order to identify the active components responsible for this effect (Al-Awadi and Guma 1987).
Hepatotoxicity of *Nigella sativa* seeds and *Dregea volubilis*, leaves was studied by administering orally under light ether anaesthesia to male Sprague-Dawley rats for 14 days. Key hepatic enzyme concentration and histopathological changes in the liver in both treatment groups at the end of 14 days were compared with a control group which received distilled water under identical conditions for 30 days and with a group of normal animals. Serum γ-glutamyl transferase concentrations were significantly increased in both extract groups while serum alkaline phosphatase concentrations were significantly increased following administration of only *D. volubilis* when compared with either the control or the normal group, serum alanine aminotransferase concentrations were significantly increased in both extract groups when compared with the normal group but not with the control group. Degenerative changes in hepatocytes were seen following administration of *D. volubilis* while consistent significant histopathological changes were not evident following administration of *N. sativa* (Tennekoon et al. 1991). The effect of *Nigella sativa* was studied on cisplatin induced toxicity in mice, an extract of *Crocus sativus* stigmas partially prevented the decreases in body weight, haemoglobin levels and leucocyte counts caused by 2 mg/kg of cisplatin intraperitoneal for 5 days. Treatment with the *C. sativus* extract also significantly prolonged the life span of cisplatin-treated mice almost three fold. In contrast an extract of *Nigella*
sativa seed only tended to protect from cisplatin-induced falls in hemoglobin levels and leucocyte counts (Nair et al. 1991).

On experiments to find out the toxicity of oil fraction of the Indian spices. The result of the contact toxicity test of oil fraction of the Indian spices, *Nigella sativa* Linn., *Ranunculaceae*, *Trachyospermum roxburghianum* DC, *Umbelliferae* and *Trigonella foenum-graecum* Linn., *Leguminasae*, against stored grain pests, *Callosobruchus chinensis* Linn., *rhizopertha dominica* Fab. and *Stiophilus oryzae* Linn., were reported. The antifeedant effect of three spices with *S. oryzae* were also reported. The oil fraction of *T. foenum-graecum* was found to be most effective (Mohanty et al. 1990).

Studies were carried on antimicrobial activity of *Nigella sativa* seeds, the result of the work shows that microgram concentrations (25-400 µg/disc) of the ether extract of *Nigella sativa* seeds inhibited growth of several species of pathogenic bacteria representing Gram positive bacteria (*Staphylococcus aureus*). *Nigella sativa* evantuates on refrigeration a crystalline substance known as thymohydroquinone, the compound was found to have high antimicrobial effect against Gram positive microorganisms (El-Fatatry 1975). Gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and a pathogenic yeast (*Candida albicans*). *Salmonella typhimurium* was non-sensitive to the range of concentrations of the extract used in that study (25-400 µg/disc). The data suggest that the antibacterial action of the extract
may be more pronounced on Gram positive than on Gram negative bacteria.

*Nigella sativa* extract showed antibacterial synergism with streptomycin and gentamicin. These findings suggest that preparation from that plant if given with those antibacterial drugs would enhance their efficacy. Results of *in vivo* studies show that the ether extract successfully eradicated localized infection with *Staphylococcus aureus* in mice. Thus *Nigella sativa* seeds can possibly provide the basis for a successful antibacterial preparation for the chemotherapy of localized infections.

Other possible application of *Nigella sativa* is in the preservation of food and prevention of food poisoning, since some of the bacterial species inhibited by *Nigella sativa* extract are known to be involved in food poisoning. The odour and taste of the ether extract of *Nigella sativa* are weak and not disagreeable if not pleasant which would favour its use in food technology. The possible use of extracts of *Nigella sativa* seeds in the prevention of dental plaques and caries has been previously suggested (Hanafy and Hatem 1991).

Inhibitory effects of *Nigella sativa* and saffron (*Crocus sativus*) on chemical carcinogenesis in mice was studied by using topical application of *Nigella sativa* and *Crocus sativus* extracts (common food species) inhibited two stage initiation / promotion (dimethyl benz[a]anthracene/
croton oil] skin carcinogenesis in mice. A dose of 100 mg per kg body weight of these extracts delayed the onset of papilloma formation and reduced the mean number of papillomas per mouse respectively. The possibility that these extracts could inhibit the action of 20 methyl cholangithrene induced soft tissue sarcomas was evaluated by studying the effect of these extracts on MCA-induced soft tissue sarcomas in albino mice. Intraperitoneal administration of *Nigella sativa* (100 mg/kg body weight) and oral administration of *Crocus sativus* (100 mg/kg body weight) 30 days after subcutaneous administration of MCA (745 nmol x 2 days) restricted tumour incidence to 33.3% and 10% respectively, compared with 100% in MCA treated controls (Salomi *et al.* 1991).

Histamine release from mast cells has been inhibited by nigellone. Nigellone is the carboxyl polymer of thymoquinone, isolated from *Nigella sativa* L. seeds. The polymer is far less toxic but retains much of the pharmacologic properties of thymoquinone, which is the active principle. The investigations were done on rat peritoneal mast cells in vitro show that nigellone in relatively low concentrations is very effective in inhibiting histamine release induced by the secretagogues: antigen in sensitized cells, compound 48/80 and the calcium ionophore A23187. the mechanism of action seems to be through decreasing intracellular calcium by inhibiting its uptake and stimulating the efflux, and an inhibition on protein kinase C. There is also indication for a mild
inhibition of oxidative energy metabolism contributing to some inhibition of the release (Chakravarty 1993).

Samples of the expressed fixed oil from different sources of *Nigella sativa* seeds were examined by thin layer and gas chromatography for content of fixed oils and thymoquinone and these substances were tested as possible inhibitors and pure thymoquinone both inhibited the cycloxygenase and 5-lipoxygenase pathways of arachidonate metabolism in rat peritoneal leukocytes stimulated with calcium ionophore as shown by dose-dependent inhibition of thromboxane B$_2$ and leukotriens B$_4$, respectively. Thymoquinone was very potent with approximate IC$_{50}$ values against 5-lipoxygenase and cyclooxygenase of <1 microgram and 3.5 microgram/ml respectively. Both substances also inhibited non-enzymatic peroxidation in ox brain phospholipid liposomes but thymoquinone was about ten times more potent however the inhibition of eicosanoid generation and lipid peroxidation by the fixed oil of *N. sativa* is greater than is expected from its content of thymoquinone and it is possible that other components such as the unusual C20:2 unsaturated fatty acids may contribute also to its anticicosanoid and antioxidant activity. These pharmacological properties of the oil support the traditional use of *N. sativa* and its derived products as a treatment for rheumatism and related inflammatory diseases (Houghton *et al.* 1995).
Postcoital contraceptive efficacy of the seeds of *Nigella sativa* in mice was tested to prevent pregnancy in Sprague-Dawley rats treated orally at 2 g/kg, daily dose on days 1-10 postcoitum. Significant antifertility activity was also observed in its column fractions and subfractions. At contraceptive dose, the active hexane extract exhibited only mild uterotrophic activity comparable almost to 0.002 mg/kg dose of 17 varies; is directly proportional to ethinylestradiol, but was devoid of any estrogenicity in immature rat bioassay (Keshri *et al.*, 1995).

Some species inhibit aflatoxin formation, the effect of black pepper, cinnamon, peppermint, cumin, ginger and clove on growth and aflatoxin formation of *Aspergillus flavus* were studied in rice powder corn steep medium. The effects of the first five species were judged to be inhibition of aflatoxin formation rather than of mycelial growth. Clove completely inhibited both mycelial growth and aflatoxin formation at a concentration above 0.1%. No aflatoxin was produced when cumin and mint levels of 5% and 10% were used. Black pepper and ginger levels of 10% decreased aflatoxin formation by 100%. Higher concentrations of cinnamon, mint, cumin and ginger stimulated mycelial growth (Mabrouk and Shayeb 1980).

The possible application of native lipase of *Nigella sativa* seed in the esterification of fatty acids to glycerol was investigated and the effect of process parameters and the enzyme selectivity on the reaction were determined. For this aim the esterification of oleic acid, sunflower oil,
fatty acids and coco oil fatty acids with glycerol were studied (Mert et al. 1995).

Petroleum ether extract of seeds at 1000-62.5 ppm, concentrations were tested for the growth regulating activity against the fifth instar larvae of Dsydercus similis, Semicarpus anacardium, Annona squamosa, Sapindus trifoliatus, Vateria indica, Datura alba, Carica papaya, Butea frondosa, Magnifera indica, Nigella sativa, Polyalthia longifolia seed oils have shown high JH activity. While the seed oils of Hydrocarpus wightiana, Cassia cercia, Leucaena leucocephala, Mallotus philipiensis and Vernonia anthelimittica seed oils showed no activity. The JH is correlated with the structure and composition of fatty acids in the seed oils (Haresh and Thakur 1989).

After continued cytogenetic exploration of inducing mutagenesis in Nigella sativa L., a spice yielding plant of the family Ranunculaceae, it has been possible to recover some mutant limes and two of them (leaf mutants) have been described in the present communication (Datta and Biswas 1986).

The present authors have recovered several mutant lines of Nigella sativa L. belonging to the family Ranunculaceae, seed of which is of commercial importance for yielding their spice black cumin. The mutants having contrasting variations differ from one another. In this communication qualitative and quantitative changes in seed proteins.
have been evaluated by analysing the electrophoretic banding pattern of buffer and acid soluble protein fractions and quantitative assessment of total protein in the control and seven mutant lines of *Nigella sativa* L. [Datta et al. 1987].

Study of mutagenic responsiveness is a pre-requisite for conducting any mutation research programme. During the course of mutation research work following the treatment with X-ray and EMS in *Nigella sativa* L. (black cumin a member of the family Ranunculaceae), cytogenetic consequences of α-irradiation and EMS treatment have been evaluated. In this communication sensitivity of *N. sativa* to γ-irradiation has been embodied (Datta et al. 1986).

*Nigella sativa* L. (black cumin) a member of the family Ranunculaceae is cultivated in India as a spice yielding plant. Medicinal use of this plant is also known. Attempts have been made to induce structural and functional mutations with X-ray irradiations in varieties of plant species. *Nigella sativa* l. is rather unexplored. The present text is a part of a research project entitled cytogenetic investigation in post-irradiated *Nigella* spp. and deals with the effects of X-irradiations on seeds germination, seedling growth, cytological aberration and pollen sterility in x, plants of *Nigella sativa* L. (Datta and Biswas, 1983).

The effects of herbicide 2,4-dinitrophenol on mitosis, DNA, RNA and protein synthesis in *Nigella sativa* L. was studied to note the
changes in mitosis, DNA, RNA and protein synthesis. The chemical affected division frequency considerably and chromosomal abnormalities like sticky bridge fragmentation, micronuclei etc. were recorded. By using precursors of nucleic acid and protein synthesis it was found that DNP also inhibited DNA, RNA and protein synthesis. the decrease in division frequency can be correlated with the DNA synthesis (Chand and Roy 1981).

The extracts of Nigella sativa seeds have some effects on the blood coagulation and fibrinolytic activity (Ghoneim et al. 1982). They claim that the fatty extract was used successfully by the public. In certain cases of epistaxis has a certain degree of reality. The fatty solvent may play a mechanical role in stopping bleeding. Other possible mechanisms may share in this effect. Chemical investigation of the constituents of Nigella should be carried out and other investigations are needed to complete the picture.
PURPOSE OF STUDY
PURPOSE OF STUDY

Herbal medicines as the major remedy in traditional medicinal systems have been used in medical practice for thousands of years and have made a great contribution to maintaining human health. A majority of the world’s population in developing countries still relies on herbal medicines to meet its health needs. The use of these medicines has a particularly rich tradition among the peoples of Pakistan. The herbal medicines are gaining popularity as alternative medicines in developed countries. Herbal medicines can be defined as a plant derived or preparation with therapeutic or other human health benefits which contains either raw or processed ingredients from one or more plants.

There are many reasons for carrying out research. An evaluation may be carried out to prove scientifically the traditional experience on the safety and efficacy of herbal medicines. It may also be conducted to validate a newly found plant material or a new combination of herbal medicines or even a new indication, a new dosage form or a new administrative route for an existing herbal medicine. Purified or semi-purified compounds derived from herbal medicine may also be presented for research.

*NGELLA SATIVA (KALONGI)*:

Kalongi is good for cough, as anthelmintic, increases the menstrual flow and the secretion of milk and diuresis. It is useful for

Purpose of this study is to find out the effects of *Nigella sativa* on different functions of the body. *Nigella sativa* is being used commonly as condiments, it is used in the form of seeds as black cumen and in the form of oil. The oil is prepared from seeds by many local companies and is sold in the market with the name of Kalongi oil (in Urdu the alternative name of *Nigella sativa* is Kalongi). As a traditional edible substance every body is familiar with this substance and is available in kitchens. In some local preparations like Achar, Chatni, (A local preparation) *Nigella sativa* is used.

While searching the literature there have been very little scientific study published. The substance which is so commonly used needs some detailed scientific study. Considering this view point the study was done to find out the effect of *Nigella sativa* on the muscular pain. The effects were investigated on the blood, liver enzymes, haemoglobin and on blood pressure.

*Nigella sativa* was tried in nausea to find out its effects.

It was also tried in alopecia areata because it has been mentioned in many books but no published data is available.
MATERIALS AND METHODS
MATERIAL AND METHODS

MATERIAL:

The oil of *Nigella sativa* (kalongi oil) was purchased from the market, registered Amir Kalongi oil Karachi Pakistan.

METHODS:

It was dispensed to the patients as 5 ml once a day, administered orally, the patient selected were free of any ailment except muscular pains and were not taking any other drug simultaneously. Before the administration of the drug total leucocyte count was done, liver enzyme estimation like SGPT, serum alkaline phosphatase and S-bilirubin were estimated, the drug was administered daily for seven consecutive days and after seven days the same investigations were repeated to find out any change.

For this purpose the grouping of the patients was done according to age as age group 20-30 years, 31-40 years, 41-50 years, 51-60 years and calculations were done as a whole from the age of 20-60 years. In each group ten patients were taken. The same studies were done in both males and females. The patients were collected from Baqai Medical University Hospital and from charitable clinics.

NORMAL VALUES*:

Hematology:

| Total leucocyte count | 4000-11000/cu mm |
**Differential Count:**

- Neutrophil: 40-75%
- Lymphocytes: 20-45%
- Eosinophils: 1-6%
- Monocytes: 2-10%
- Basophils: 0-1%

**Liver Function Tests:**

- Serum bilirubin, total: 0-1.0 mg %
- Serum bilirubin, direct: 0-0.3 mg %
- SGPT: 10 up to 40 units/litre
- Serum alkaline phosphatase: 98-279 units/litre

**Serum Alkaline Phosphatase:**

This normally is derived from liver, bone, placenta and intestine. The main clinical value of serum alkaline phosphatase is its sensitivity in detecting early intrahepatic or extrahepatic bile duct obstruction (often before jaundice develops) and in pointing to the presence of infiltrative disease or space occupying lesions. Serum alkaline phosphatase helps to differentiate hepatocellular from obstructive jaundice. High values (5 times normal) favour obstruction and normal serum alkaline phosphatase virtually excludes this diagnosis (Andrew 1987).
SGPT (Serum Glutamic Pyruvic Transaminase):

Although SGPT is widely distributed in the body, it is predominantly confined to the liver and is therefore more specific for liver disease. In general, levels greater than 10 times the upper limit of normal indicate acute hepatic cellular injury as seen in viral hepatitis. Drugs or toxins induced hepatitis (ischaemic liver disease or transiently cholangitis). Lesser elevations are not specific and may be seen with any other form of liver injury including cholestasis or infiltrative liver disease.

Serum Bilirubin:

An elevated serum bilirubin cannotes either the presence of hepatobiliary disease, over production of bilirubin or both. The direct reacting (conjugated) bilirubin is specific for the presence of hepatobiliary disease and is sensitive index for mild hepatic disease. Elevations are found in more than 30% of patients with liver disease whose total serum bilirubin is normal, a mild increase in serum direct bilirubin results in urinary excretion of bilirubin hence a urine bilirubin determination may prove sensitive in detecting mild hepatic disease.

The height of serum bilirubin is only limited diagnostic value in individual patients. Elevations over 35 mg/100 ml generally indicate the presence of renal insufficiency in addition to hepatobiliary disease,
unconjugated haemolysis seldom causes a total serum bilirubin of more than 5 mg/100 ml unless hepatobiliary disease is also present.

**Leucopaenia:**

It is defined as an absolute neutrophil count less than 1,500/cumm. There are many aetiologic factors, here we are concerned with the drug. The count decreases due to accumulated destruction (immune mechanism as seen with certain drugs and autoimmune diseases and hypersplenism. This mechanism can be of major clinical significance when severe agranulocytosis occurs.

**STATISTICAL ANALYSIS:**

In present study computer software package “Microsoft Excel” for data feeding and analysis. has been used. The results are given in the text as Mean (X̄), standard deviation (S.D.) for continuous variables (blood pressure, Hb%, etc.) and used “paired t-test” for difference between two groups (before and after treatment). Percentages for categorical variables (muscular pain) and used Chi-square test to compare the effects of drug on muscular pain.

In all statistical analysis, only p-values <0.05 are considered significant.
Formula for Paired t-Test:

\[ t = d + \sqrt{SD^2 / n} \]

Where,

\[ d = \Sigma d / n, \text{ and} \]

\[ SD^2 = \frac{\Sigma d^2 - (\Sigma d)^2 / n}{n - 1} \]
GROUPS OF PATIENTS
TO FIND OUT THE EFFECTS OF *NIGELLA SATIVA*

IN PATIENTS

**GROUPS OF PATIENTS:**

For this purpose the patients were categorized as male (Group A) and female (Group B) according to their age as follows:

**GROUP A MALES:**

**Group A₁**

No. of patients 10  Age group 20-30 years

**Group A₂**

No. of patients 10  Age group 31-40 years

**Group A₃**

No. of patients 10  Age group 41-50 years

**Group A₄**

No. of patients 10  Age group 51-60 years

**GROUP B FEMALES:**

**Group B₁**

No. of patients 10  Age group 20-30 years

**Group B₂**

No. of patients 10  Age group 31-40 years

**Group B₃**

No. of patients 10  Age group 41-50 years

**Group B₄**

No. of patients 10  Age group 51-60 years

In all groups A₁, A₂, A₃, A₄, B₁, B₂, B₃, B₄, blood examination was done before and at the completion of treatment (the total
leucocytes, neutrophils and lymphocytes, eosinophils and monocytes) were counted.

In all these groups liver function tests (serum bilirubin, SGPT, serum alkaline phosphatase) were estimated before the start of treatment and at the end.

Muscular pain was scored as mild, moderate and severe at the start of the treatment and the same was assessed at the end.

The patients who failed to follow during the period of treatment were dropped from this study. Only those patients who were not taking any other drug were enrolled and were given Nigella sativa oil.

No patient has shown any symptom of gastric discomfort after taking the drug (Nigella sativa).
OBSERVATION AND RESULTS
RESULTS

TABLE 1 – AGE GROUP 20-30 YEARS (MALE):

The systolic blood pressure before administration of *Nigella sativa* was 117±6.7 mmHg and after the administration it was found to be 118±6.3 mmHg. The diastolic before administration was 73±6.7 mmHg and after administration it was 75±5.3 mmHg. It was concluded that both systolic and diastolic, BP remained under normal range. The haemoglobin was before 13.0±1.8% while after administration it was 12.7±1.5%, it also found to be non-significant. Neutrophil count, lymphocytes, eosinophils, monocytes before and after the drug showed no change and was non-significant.

Regarding liver enzymes and serum bilirubin showed no difference, SGPT and serum alkaline phosphatase decreased after administration of the drug as compared with before administration and it was found significant at P<0.05 but it was within normal range.

TABLE 2 – AGE GROUP 31-40 YEARS (MALE):

The drug was administered to the male patients ranging from 31-40 years of age, systolic and diastolic blood pressure showed no effects. Haemoglobin % remained within normal limits. WBC, neutrophils, lymphocytes, eosinophils, monocytes remained within normal range. The results were non-significant.
Serum bilirubin, SGPT, serum alkaline phosphatase results remained within normal range and were non-significant.

**TABLE 3 - AGE GROUP 41-50 YEARS (MALE):**

Blood pressure both diastolic and systolic showed no variation, the results were non-significant, it means that the drug had no adverse effect on blood pressure.

Estimation of haemoglobin, WBC count, neutrophils, lymphocytes, eosinophils, monocytes were within the normal range the results were non-significant.

Serum bilirubin, SGPT, serum alkaline phosphatase were also in the normal range, this shows that the substance *(Nigella sativa)* given has no adverse effect on liver functions (SGPT statistically decreased with $P<0.05$).

**TABLE 4 - AGE GROUP 51-60 YEARS (MALE):**

Investigations regarding blood pressure both systolic and diastolic remained within normal range, showed no increase or decrease in blood pressure. It was non-significant.

Haemoglobin showed little increase but remained in normal range. WBC, neutrophils, lymphocytes, eosinophils, monocytes remained within the normal range which showed no adverse effects.
Serum bilirubin was non-significant SGPT after administration of the drug was significant with P<0.05. Results of serum alkaline phosphatase were non-significant. Liver enzymes remained within normal range before and after administration of drug.

**TABLE 5 – AGE GROUP 20-60 YEARS [All groups] (MALES):**

Considering the results as a whole in age group ranging from 20-60 years the blood pressure remained within normal range both systolic and diastolic.

Haemoglobin, WBC, neutrophils, lymphocytes, eosinophils, monocytes, were within normal range.

Serum bilirubin, SGPT, were non-significant. Serum alkaline phosphatase was significant at P<0.05, but it is only statistical variation, regarding normal range, serum alkaline phosphatase was normal.

**TABLE 6 – EFFECT OF DRUG ON MUSCULAR PAIN (MALES):**

The effect of *Nigella sativa* was evaluated on the patients complaining of muscular pain.

**Age Group 20-30 Years:**

10% of the patients of this age group after using *Nigella sativa* much improved and had no pain, 90% of the patients improved slightly, at P<0.05.
Age Group 31-40 Years:

In this group 100% of the patients improved slightly. P<0.05.

Age Group 41-50 Years:

In this group 90% of the patients improved slightly and 10% improved moderately in respect of pain. P<0.05.

Age Group 51-60 Years:

In this group 70% of the patients had slight and 30% had moderate improvement in muscular pain with P<0.05.

Overall study signifies that from the age of 20-60 years, 2.5% patients fully recovered from pain, 87.5% slightly recovered and 10% moderately recovered showing P<0.05.

This present study signifies that Nigella sativa has good results in improving the symptoms of muscular pain.

TABLE 7 – AGE GROUP 20-30 YEARS (FEMALE):

Effect of drug on blood pressure, blood and liver function was evaluated in patients after seven days of administration of drug Nigella sativa in female patients. Systolic BP was mean 123±9.5 mm Hg which decreased after drug intake to mean 117±4.8 P<0.05, it was in normal range and diastolic before was mean 76±5.2 mm Hg and decreased mean was 72±6.3 it was non-significant.
Regarding haemoglobin the mean before drug administration was 12.4±0.7 % and later on it was increased to 12.9±0.9 % P<0.05.

Regarding WBC, total count, neutrophils, lymphocytes, eosinophils, monocytes it was non-significant.

Serum bilirubin was non-significant. SGPT before the drug was 25±3.1 U/L and after it was 23±3.7 U/L with P<0.05. Serum alkaline phosphatase was also non-significant after the administration of drug.

It was concluded that *Nigella sativa* had no adverse effects on the blood pressure, blood picture and on liver enzymes in this age group.

**TABLE 8 – AGE GROUP 31-40 YEARS (FEMALE):**

In female patients age group 31-40 years before use of drug blood pressure systolic was mean 121±7.4 mm Hg and after it was mean 121±7.4 mm Hg non-significant, and diastolic was mean 75±5.3 mm Hg and after it was 70±9.4 mm Hg non-significant, it means that there has been no adverse effect on blood pressure in present study.

Haemoglobin percentage increased from 12.6±0.5 % to 12.9±0.6 %, P<0.05. Other readings like WBC total count, neutrophils, lymphocytes, eosinophils, monocytes were within normal range both before and after use of drug. It means that there has been no adverse effect of this drug on blood.
Regarding serum bilirubin, SGPT and serum alkaline phosphatase there has been no increase in the enzyme which signifies that *Nigella sativa* has no adverse effect on liver.

**TABLE 9 – AGE GROUP 41-50 YEARS (FEMALE):**

Blood pressure in this group, systolic was 128±7.9 decrease to 126±7 mm Hg it was within normal range and non-significant and diastolic was 77±4.8 mm Hg decreased to 74±5.2 mm Hg, and it was in normal range non-significant.

Regarding haemoglobin it was 12.8±1.1 % before drug and increased to 13.0±1.1 %, non-significant.

Regarding blood count WBC total were 6400±390/cu mm and after drug 6200±570/cu mm, non-significant. Regarding neutrophils lymphocytes, eosinophils, monocytes they were in normal range before and after the drug and were non-significant.

Serum bilirubin, SGPT, serum alkaline phosphatase they were in normal range before and after and non-significant.

It can be concluded that in this group there have been no adverse effects on blood with the drug.

**TABLE 10 – AGE GROUP 51-60 YEARS (FEMALE):**

In the females age group 51-60 years, the systolic blood pressure was 132±7.9 mm Hg increased to 135±8.5 mm Hg. It was in normal range and non-significant diastolic was 81±7.4 mm Hg and after drug
remained the same 81±7.4 mm Hg, non-significant. There was no adverse effect on blood pressure with the drug.

Haemoglobin percentage before the drug was 12.8±1.2 which increased by 13.3±0.8, non-significant.

WBC total, neutrophils, lymphocytes, eosinophils, monocytes were in the normal range and non-significant.

Regarding serum bilirubin, SGPT, they were in normal range, non-significant. Serum alkaline phosphatase was 108±5.8 U/L decreased to 106±5.7 U/L was at P<0.05 (it was also within normal range).

**TABLE 11 – AGE GROUP 20-60 YEARS [All groups] (FEMALES):**

Effect of drug on blood pressure, blood and liver enzymes was evaluated in female in age group 20-60 years as a whole.

Regarding systolic BP it was 126±9 mm Hg and after drug it was 125±9.6 mm Hg. Non-significant.

Regarding haemoglobin it was 12.6±0.9 % increased to 13.0±0.8 % non-significant remained in normal limits.

Regarding WBC, neutrophils, lymphocytes, eosinophils, monocytes, they were also in the normal range before and after the drug and were non-significant.
Serum bilirubin, SGPT, serum alkaline phosphatase they were also in normal range.

Finally it can be concluded that in females the use of N. sativa he got no adverse effects on blood as well as on liver, sometimes it can increase haemoglobin percentage.

**TABLE 12 – EFFECT ON MUSCULAR PAIN AFTER USING NIGELLA SATIVA IN FEMALE PATIENTS:**

**Age Group 20-30 Years:**

80% patients left with slight symptoms and 20% left with moderate symptoms significant at \( P<0.05 \).

**Age Group 31-40 Years:**

50% patients left with slight symptoms of pain while 50% left with moderate symptoms, the drug was effective at \( P<0.05 \).

**Age Group 41-50 Years:**

80% of the patients after administration of the drug left with slight symptoms of pain and 20% left with moderate symptoms of pain significant at \( P<0.05 \).

**Age Group 51-60 Years:**

30% of the patients were left with no symptoms, 50% left with slight pain and 20% left with moderate pain, there was improvement of pain at \( P<0.05 \).
Overall Assessment for 20-60 Years of Age:

7.5% of the patients left with no symptoms, 65% improved and left with slight muscular pain. 27.5% improved and left with moderate pain at P<0.05.

Inference:

*Nigella sativa* is good analgesic and can be given for this purpose.

**TABLE 13 - TRIAL OF NIGELLA SATIVA OIL IN NAUSEA:**

Age group 15-25, male, n=10. These patients were given *Nigella sativa* oil in nausea in the dose of 5 ml OD orally. Their nausea stopped.

Age group 15-25, female, n=10. These patients were given *Nigella sativa* oil in nausea in the dose of 5 ml once a day orally. Their nausea stopped.

**TABLE 14 - TRIAL OF NIGELLA SATIVA OIL IN ALOPECIA AREATA:**

Age group 18-25, males, n=30. These patients had alopecia areata at face, they applied *Nigella sativa* oil on the lesion of alopecia by rubbing for two weeks twice daily, in 90% of the patients alopecia improved.
TABLE 1

EFFECTS OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN MALE
(AGE GROUP 20-30 YEARS)
(n=10)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Drug administration</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Mean±S.D.</td>
<td>After Mean±S.D.</td>
</tr>
<tr>
<td>Blood pressure (mm Hg):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>117±6.7</td>
<td>118±6.3</td>
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<tr>
<td>Diastolic</td>
<td>73±6.7</td>
<td>75±5.3</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>13.0±1.8</td>
<td>12.7±1.5</td>
</tr>
<tr>
<td>WBC - Total /cu mm</td>
<td>6400±1100</td>
<td>7000±1200</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>62±2.7</td>
<td>66±4.1</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>32±2.5</td>
<td>29±4.7</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>3±0.8</td>
<td>4±1.3</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>2±0.7</td>
<td>2±0.9</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.9±0.1</td>
<td>0.9±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>33±5.4</td>
<td>30±4.2</td>
</tr>
<tr>
<td>Serum alkaline phosphatase</td>
<td>106±10.2</td>
<td>101±8.8</td>
</tr>
</tbody>
</table>
TABLE 2

EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN MALE
(AGE GROUP 31-40 YEARS)
(n=10)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Drug administration</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Mean±S.D.</td>
<td>After Mean±S.D.</td>
</tr>
<tr>
<td>Blood pressure (mm Hg):</td>
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<tr>
<td>Systolic</td>
<td>121±7.4</td>
<td>121±7.4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72±7.9</td>
<td>72±7.9</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>12.5±1.9</td>
<td>125±1.5</td>
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<tr>
<td>WBC – Total/cu mm</td>
<td>7100±560</td>
<td>7000±540</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>67±1.9</td>
<td>66±2.8</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>28±2.4</td>
<td>28±2.8</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>3±0.7</td>
<td>4±1.3</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>2±0.8</td>
<td>2±0.6</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.7±0.3</td>
<td>0.8±0.2</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>35±3.4</td>
<td>36±2.3</td>
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<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>110±3.9</td>
<td>109±6.4</td>
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</table>
TABLE 3
EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD
AND LIVER FUNCTION IN MALE
(AGE GROUP 41-50 YEARS)
(n=10)

<table>
<thead>
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<th>Variables</th>
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<td>Mean±S.D.</td>
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<tr>
<td>Systolic</td>
<td>121±8.8</td>
<td>121±8.8</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76±7.0</td>
<td>76±7.0</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>13.9±0.7</td>
<td>13.7±0.7</td>
</tr>
<tr>
<td>WBC – Total/cu mm</td>
<td>7600±260</td>
<td>7500±300</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>62±2.1</td>
<td>62±5.9</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>31±2.5</td>
<td>30±2.7</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>4±1.5</td>
<td>3±1.5</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>4±0.9</td>
<td>3±1.4</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.7±0.2</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>31±3.8</td>
<td>28±5.4</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>111±3.9</td>
<td>111±1.3</td>
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TABLE 3

EFFECT OF *NIGELLA SATIVA* ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN MALE

(AGE GROUP 41-50 YEARS)

(n=10)

<table>
<thead>
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<th>P-value</th>
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<td>After Mean±S.D.</td>
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<tr>
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<td>121±8.8</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76±7.0</td>
<td>76±7.0</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>13.9±0.7</td>
<td>13.7±0.7</td>
</tr>
<tr>
<td>WBC - Total/cu mm</td>
<td>7600±260</td>
<td>7500±300</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>62±2.1</td>
<td>62±5.9</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>31±2.5</td>
<td>30±2.7</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>4±1.5</td>
<td>3±1.5</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>4±0.9</td>
<td>3±1.4</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.7±0.2</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>31±3.8</td>
<td>28±5.4</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>111±3.9</td>
<td>111±1.3</td>
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</table>
### TABLE 4

**EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN MALE**

*(AGE GROUP 51-60 YEARS)*

*(n=10)*

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<th>P-value</th>
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<td>130±8.2</td>
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<tr>
<td>Diastolic</td>
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<td>80±6.7</td>
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<tr>
<td>Haemoglobin gm %</td>
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<td>13.9±0.9</td>
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<td>WBC - Total/cu mm</td>
<td>7500±660</td>
<td>7600±510</td>
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<td>Neutrophils %</td>
<td>62±2.7</td>
<td>63±2.4</td>
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<tr>
<td>Lymphocytes %</td>
<td>30±2.7</td>
<td>30±2.1</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>3±0.7</td>
<td>3±1.0</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>5±1.6</td>
<td>5±1.8</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.8±0.2</td>
<td>0.8±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>33±3.3</td>
<td>35±1.2</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>112±1.5</td>
<td>112±1.6</td>
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TABLE 5

EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN MALE
(AGE GROUP 20-60 YEARS)
(n=40)

<table>
<thead>
<tr>
<th>Variables</th>
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<th>P-value</th>
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<td>Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td>Mean±S.D.</td>
<td>Mean±S.D.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood pressure (mm Hg):</th>
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</thead>
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<tr>
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<tr>
<td>Diastolic</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
</tr>
<tr>
<td>WBC – Total/cu mm</td>
</tr>
<tr>
<td>Neutrophils %</td>
</tr>
<tr>
<td>Lymphocytes %</td>
</tr>
<tr>
<td>Eosinophils %</td>
</tr>
<tr>
<td>Monocytes %</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
</tr>
<tr>
<td>SGPT U/L</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
</tr>
</tbody>
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**TABLE 6**

**EFFECT OF NIGELLA SATIVA ON MUSCULAR PAIN IN MALES**

<table>
<thead>
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<th>P-value</th>
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<td>Before No. (%)</td>
<td>After No. (%)</td>
</tr>
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<tr>
<td>None</td>
<td>– –</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Slight</td>
<td>– –</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (40)</td>
<td>– –</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (60)</td>
<td>– –</td>
</tr>
<tr>
<td>Age group 31-40 years (n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>– –</td>
<td>– –</td>
</tr>
<tr>
<td>Slight</td>
<td>1 (10)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (60)</td>
<td>– –</td>
</tr>
<tr>
<td>Severe</td>
<td>3 (30)</td>
<td>– –</td>
</tr>
<tr>
<td>Age group 41-50 years (n=10)</td>
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<td></td>
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<td>None</td>
<td>– –</td>
<td>– –</td>
</tr>
<tr>
<td>Slight</td>
<td>– –</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (60)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (40)</td>
<td>– –</td>
</tr>
<tr>
<td>Age group 51-60 years (n=10)</td>
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<td></td>
</tr>
<tr>
<td>None</td>
<td>– –</td>
<td>– –</td>
</tr>
<tr>
<td>Slight</td>
<td>– –</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (30)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Severe</td>
<td>7 (70)</td>
<td>– –</td>
</tr>
<tr>
<td>Age group 20-60 years (n=40)</td>
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<tr>
<td>None</td>
<td>– –</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>Slight</td>
<td>1 (2.5)</td>
<td>35 (87.5)</td>
</tr>
<tr>
<td>Moderate</td>
<td>19 (47.5)</td>
<td>4 (10.0)</td>
</tr>
<tr>
<td>Severe</td>
<td>20 (50.0)</td>
<td>– –</td>
</tr>
</tbody>
</table>
TABLE 7

EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN FEMALE
(AGE GROUP 20-30 YEARS)
(n=10)

<table>
<thead>
<tr>
<th>Variables</th>
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<td>After Mean±S.D.</td>
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<tr>
<td>Blood pressure (mm Hg):</td>
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<tr>
<td>Systolic</td>
<td>123±9.5</td>
<td>117±4.8</td>
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<tr>
<td>Diastolic</td>
<td>76±5.2</td>
<td>72±6.3</td>
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<tr>
<td>Haemoglobin gm %</td>
<td>12.4±0.7</td>
<td>12.9±0.9</td>
</tr>
<tr>
<td>WBC - Total/cu mm</td>
<td>4600±330</td>
<td>4700±200</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>59±1.9</td>
<td>60±1.8</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>30±1.3</td>
<td>30±1.9</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>5±1.1</td>
<td>5±0.9</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>6±1.7</td>
<td>5±1.6</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.6±0.1</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>25±3.1</td>
<td>23±3.7</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>103±7.4</td>
<td>101±6.7</td>
</tr>
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</table>
## TABLE 8

**EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN FEMALE**

**(AGE GROUP 31-40 YEARS)**

**(n=10)**

<table>
<thead>
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<th>Variables</th>
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<td>121±7.4</td>
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<tr>
<td>Diastolic</td>
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<td>70±9.4</td>
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<tr>
<td>Haemoglobin gm %</td>
<td>12.6±0.5</td>
<td>12.9±0.6</td>
</tr>
<tr>
<td>WBC – Total/cu mm</td>
<td>6300±330</td>
<td>6400±380</td>
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<tr>
<td>Neutrophils %</td>
<td>60±1.7</td>
<td>60±1.8</td>
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<td>Lymphocytes %</td>
<td>30±1.1</td>
<td>29±1.4</td>
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<tr>
<td>Eosinophils %</td>
<td>5±1.2</td>
<td>5±1.2</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>6±1.4</td>
<td>6±1.2</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.6±0.1</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>26±2.3</td>
<td>25±1.7</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>108±4.5</td>
<td>106±6.4</td>
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</table>
TABLE 9

EFFECT OF NIGELLA SATIVA ON BLOOD PRESSURE, BLOOD
AND LIVER FUNCTION IN FEMALE
(AGE GROUP 41-50 YEARS)
(n=10)

<table>
<thead>
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<th>Variables</th>
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<td>After Mean±S.D.</td>
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<td>126±7.0</td>
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<tr>
<td>Diastolic</td>
<td>77±4.8</td>
<td>74±5.2</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>12.8±1.1</td>
<td>13.0±1.1</td>
</tr>
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<td>WBC – Total/cu mm</td>
<td>6400±390</td>
<td>6200±570</td>
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<td>61±1.9</td>
<td>61±1.9</td>
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<tr>
<td>Lymphocytes %</td>
<td>30±1.9</td>
<td>30±1.8</td>
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<tr>
<td>Eosinophils %</td>
<td>5±0.8</td>
<td>5±0.6</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>5±0.7</td>
<td>5±0.9</td>
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<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.7±0.1</td>
<td>0.7±0.2</td>
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<tr>
<td>SGPT U/L</td>
<td>27±3.3</td>
<td>28±3.9</td>
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<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>106±4.7</td>
<td>106±4.8</td>
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TABLE 10

EFFECT OF *NIGELLA SATIVA* ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN FEMALE
(AGE GROUP 51-60 YEARS)
(n=10)

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<td>After</td>
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<td>Mean±S.D.</td>
</tr>
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<tr>
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<td>132±7.9</td>
<td>135±8.5</td>
</tr>
<tr>
<td>Diastolic</td>
<td>81±7.4</td>
<td>81±7.4</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>12.8±1.2</td>
<td>13.3±0.8</td>
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<td>WBC – Total/cu mm</td>
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<td>6100±230</td>
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<td>Neutrophils %</td>
<td>61±2.5</td>
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<tr>
<td>Lymphocytes %</td>
<td>30±1.7</td>
<td>29±1.4</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>5±0.9</td>
<td>5±0.9</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>5±1.4</td>
<td>5±1.2</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.6±0.1</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>27±2.8</td>
<td>27±2.8</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>108±5.8</td>
<td>106±5.7</td>
</tr>
</tbody>
</table>
**TABLE 11**

EFFECT OF *NIGELLA SATIVA* ON BLOOD PRESSURE, BLOOD AND LIVER FUNCTION IN FEMALE
(AGE GROUP 20-60 YEARS)
(n=40)

<table>
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<td>After Mean±S.D.</td>
</tr>
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<td>125±9.6</td>
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<tr>
<td>Diastolic</td>
<td>77±6.0</td>
<td>74±8.1</td>
</tr>
<tr>
<td>Haemoglobin gm %</td>
<td>12.6±0.9</td>
<td>13.0±0.8</td>
</tr>
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<td>WBC - Total/cu mm</td>
<td>5800±820</td>
<td>5800±780</td>
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<td>Neutrophils %</td>
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</tr>
<tr>
<td>Lymphocytes %</td>
<td>29±1.5</td>
<td>29±1.6</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>5±1.0</td>
<td>5±0.9</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>5±1.5</td>
<td>5±1.3</td>
</tr>
<tr>
<td>Serum bilirubin mg/dL</td>
<td>0.6±0.1</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>SGPT U/L</td>
<td>26±3.0</td>
<td>26±3.4</td>
</tr>
<tr>
<td>Serum alkaline phosphatase U/L</td>
<td>106±5.9</td>
<td>105±6.2</td>
</tr>
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<td>Muscular pain</td>
<td>Drug administration</td>
<td>P-value</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>(%)</td>
</tr>
<tr>
<td>Age group 20-30 years (n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Slight</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>(50)</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>(50)</td>
</tr>
<tr>
<td>Age group 31-40 years (n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Slight</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>(60)</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>(40)</td>
</tr>
<tr>
<td>Age group 41-50 years (n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Slight</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>(60)</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>(40)</td>
</tr>
<tr>
<td>Age group 51-60 years (n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
<td>(10)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>(20)</td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>(70)</td>
</tr>
<tr>
<td>Age group 20-60 years (n=40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
<td>(2.5)</td>
</tr>
<tr>
<td>Moderate</td>
<td>19</td>
<td>(47.5)</td>
</tr>
<tr>
<td>Severe</td>
<td>20</td>
<td>(50.0)</td>
</tr>
</tbody>
</table>
### TABLE 13

**TRIAL OF NIGELLA SATIVA OIL IN NAUSEA**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Sex</th>
<th>No. of patients</th>
<th>Duration of treatment</th>
<th>Dose</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-25</td>
<td>Male</td>
<td>n=10</td>
<td>One day</td>
<td>5 ml OD orally</td>
<td>Nausea stopped</td>
</tr>
<tr>
<td>15-25</td>
<td>Female</td>
<td>n=10</td>
<td>One day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 14

**TRIAL OF NIGELLA SATIVA OIL IN ALOPECIA AERATA**

**TOPICAL APPLICATION**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Sex</th>
<th>No. of patients</th>
<th>Duration of treatment</th>
<th>Site</th>
<th>Administration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25</td>
<td>Male</td>
<td>n=30</td>
<td>Two weeks</td>
<td>Face</td>
<td>Local twice daily</td>
<td>Alopecia improved in 90% of patients</td>
</tr>
</tbody>
</table>
SAFETY EVALUATION STUDIES ON OIL OF
NIGELLA SATIVA

INTRODUCTION:

Herbal preparations are being used commonly in Pakistan for the treatment of various ailments. However, no study has been carried out to confirm the efficacy using sensitive scientific technique.

PURPOSE OF STUDY:

The literature regarding safety evaluation of Nigella sativa is very scanty rather not available so it has been planned to do the same experiments on animals.

MATERIALS AND METHODS:

Nigella sativa (Kalongi) oil was purchased from local market (Amir's kalongi oil). Total lipids, cholesterol, triglyceride, bilirubin, total protein and SGOT were estimated. Kits of E. Merck were used for biochemical estimation. Pentothal sodium was used as anaesthetic.

EXPERIMENTAL ANIMALS:

Rats Sprague-Dawley animals male and female were used in the study, they were kept under observation before experiment for one week.

Animals were anaesthetized with pentothal sodium 10 mg/kg intraperitoneally, 24 hours after the last dose of treatment, blood samples approximately (3-4 ml) were withdrawn from cardiac puncture and investigations were done.
SAFETY EVALUATION STUDIES:

Acute Toxicity Test:

Animals were divided into four groups. Each group had 10 rats of both sexes (5 male and 5 female). *Nigella sativa* (Kalongi) oil was administered orally for seven consecutive days at the dose of 2.5 ml/100 G body weight, 5 ml/100 G, and 10 ml/100 G of body weight and one group served as a control whom 0.9% NaCl was given.

No mortality and behavioural changes were noted 2 hours after administration and animals were kept under observations for one week.

Effect of Kalongi Oil in Rats:

The protective effect of *Nigella sativa* (Kalongi) oil was evaluated by assessing serum glutamate oxaloacetate transaminase (SGOT), bilirubin, total protein, total lipids, cholesterol and triglyceride. Sprague Dawley rats weighing between 210 to 240 Gm of either sex were divided into four groups, each group consisting of 10 rats.

Group I animals were given 0.9% sodium chloride solution (normal saline) for seven days. 10 ml/100 G served as control (Table 2 & 3).

Group II animals were given 2.5 ml per 100 G of body weight *Nigella sativa* (Kalongi oil) orally for seven consecutive days (Table 1).

Group III animals were given 5 ml per 100 G of *Nigella sativa* (Kalongi oil) orally for seven consecutive days (Table 1).
Group IV animals were given 10 ml per 100 G of body weight *Nigella sativa* (Kalongi oil) for seven consecutive days (Table 1).

After administration of different doses of *Nigella sativa* oil at autopsy no change or abnormality was found in organs; liver, spleen, heart and kidney (Table 1).

The investigations regarding serum bilirubin, total proteins and SGOT (Table 2) and total lipids, serum cholesterol, triglycerides (Table 3) were done and were compared with the control group.

**TABLE 1**

**EFFECTS OF *NIGELLA SATIVA* (KALONGI) OIL IN RATS AFTER ORAL ADMINISTRATION OF DIFFERENT DOSAGES FOR 7 DAYS**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Dose (ml/100G)</th>
<th>n</th>
<th>Weight of rats (\bar{x} \pm \text{SEM(G)})</th>
<th>Mortality</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>2.5</td>
<td>10</td>
<td>311.9(\pm)6.5</td>
<td>NIL</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>5.0</td>
<td>10</td>
<td>223.6(\pm)4.8</td>
<td>NIL</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IV</td>
<td>10.0</td>
<td>10</td>
<td>243.4(\pm)8.0</td>
<td>NIL</td>
<td></td>
</tr>
</tbody>
</table>

Weight of rats significantly lowered (P<0.001) as compared to 2.5 ml/100G dose.

**Autopsy:**

At autopsy no change or abnormality found in organs; liver, spleen, heart and kidney.
## TABLE 2

**EFFECT OF **NIGELLA SATIVA (KALONGI)** OIL ON BILIRUBIN, TOTAL PROTEIN AND SGOT AFTER ORAL ADMINISTRATION FOR 7 DAYS IN RATS**

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>n</th>
<th>Bilirubin (mg/dl) $\bar{x}$±SEM</th>
<th>Total protein (g/dl) $\bar{x}$±SEM</th>
<th>SGOT (IU/L) $\bar{x}$±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>*I</td>
<td>0.9% NaCl</td>
<td>10</td>
<td>2.81±0.44</td>
<td>10.41±0.09</td>
<td>1146±3.05</td>
</tr>
<tr>
<td>**IV</td>
<td><em>Nigella sativa oil (10 ml/100G body weight)</em></td>
<td>10</td>
<td>2.40±0.11</td>
<td>6.50±0.14</td>
<td>1139.6±6.0</td>
</tr>
</tbody>
</table>

| P     | N.S                                      | <0.001 | N.S                           |

*Control group.
**Test group

## TABLE 3

**EFFECT OF **NIGELLA SATIVA (KALONGI)** OIL ON TOTAL LIPIDS, CHOLESTEROL AND TRIGLYCERIDE AFTER ORAL ADMINISTRATION FOR 7 DAYS IN RATS**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>n</th>
<th>Total lipids (mg/dl) $\bar{x}$±SEM</th>
<th>Cholesterol (mg/dl) $\bar{x}$±SEM</th>
<th>Triglyceride (mg/dl) $\bar{x}$±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>*I</td>
<td>0.9% NaCl</td>
<td>10</td>
<td>557.91±0.44</td>
<td>192.08±0.9</td>
<td>338±3.05</td>
</tr>
<tr>
<td>**IV</td>
<td><em>Nigella sativa oil (10 ml/100G body weight)</em></td>
<td>10</td>
<td>554.6±0.36</td>
<td>152.1±1.24</td>
<td>291±10.6</td>
</tr>
</tbody>
</table>

| P     | <0.001                                    | <0.001 | <0.001                           |

*Control group.
** Test group
Histopathological Studies:

Liver and kidney were taken immediately after the blood was collected. They were fixed in 10% formalin, dehydrated in graded (80-100%) alcohol, cleared in xylene and embedded in paraffin. Six \( \mu \)m sections were prepared, then deparaffinated in xylene, passed through 80% to 100% alcohol and stained with hematoxylin and eosin (H&E) for assessment of liver and kidney histology.

RESULTS AND DISCUSSION:

Acute Toxicity:

As shown in Table 1 the drug was administered in different doses for seven consecutive days in different groups of rats did not show any mortality at the end of the treatment. Only the weight of the animals (rats) significantly lowered \( (P<0.01) \) as compared to 2.5 ml/100G dose.

It coincides the studies performed by Khan and Chaudhari (1998) in which they have also noted decrease on gain of body weight in rats.

Autopsy:

At autopsy no gross changes in the organs viz. liver, spleen, heart and kidney were observed.

Regarding effects on bilirubin, total proteins and SGOT after oral administration was investigated after one week of the drug administration (Group IV) and it was compared with the control.
Serum bilirubin in control group was 2.81±0.44 and in test group it was 2.40±0.11 it was non-significant (Table 2).

Serum total proteins (g/dl) was 10.41±0.09 in control group, in test group it was 6.50±0.14 with P<0.001 as shown in Table 2.

SGOT in control group (IU/L) was 1146±3.05 and in test group it was 1139.6±6.0, non-significant (Table 2).

Regarding effect of Nigella sativa (kalongi) oil on total lipids, cholesterol, and triglycerides in rats after oral administration.

Total lipids (mg/dl) was 557.91±0.44 in control group and in test group it was 554.6±0.36 with P<0.001 (Table 3).

Serum cholesterol (mg/dl) was 192.08±0.9 in control group and it was 152.1±1.24 in test group with P<0.001 (Table 3).

Triglycerides (mg/dl) was 338±3.05 in control group which was 291±10.6 in test group with P<0.001 (Table 3).

From the above study it can be said that Nigella sativa had no adverse effects on the serum bilirubin, total proteins, SGOT, total lipids, serum cholesterol and triglycerides. The statistical difference was not in such a way to ascertain any adverse effect.
HISTOLOGY OF THE LIVER:

Histologically the liver consists of stroma and parenchyma.

Stroma:

The liver is surrounded beneath its peritoneal covering by a connective tissue capsule, called Glisson's capsule from the capsule septae radiate into the substance of the gland dividing each lobe into polyhedral units called hepatic lobules. In addition to the interlobular connective tissue concentrated in the portal area, there is a framework of reticular connective tissue fibers within each lobule.

Parenchyma:

Parenchyma of the liver consists of very large number of polyhedral hepatic lobules. These are considered the physiological and anatomical units of liver. In the centre of each hepatic lobule there is a small circular vein, central vein. Hepatic lobules are separated from each other by triangular spaces, portal triads.

Hepatic Lobule:

Each hepatic lobule is composed of two main components:

1. Hepatic cells
2. Anastomosing blood vessels (hepatic sinusoids)

(i) Around the central vein hepatic cells are arranged in the form of radiating anastomosing cords. These cords of cells in turn branch
and anastomose with each other. Each hepatic cell is polygonal in shape, having one nucleus with one or two nucleoli. The cell may be binucleated. The cytoplasm of the cell have lipid granules and basophilic material. It is a secretary material so it gives a spong appearance. There is no basement membrane but the cells are supported by reticular fibres.

(ii) **Hepatic Sinusoids:**

These are potential spaces between the anastomosing cords of hepatic cells. They make up the intralobular system of blood vessels. These sinusoids are lined by a discontinuous sheet of cells which separate the blood from hepatic cells. These cells are of two types:

(I) Flat endothelial cells

(II) Large irregular cells with large nuclei, called Kupffer cells.

Both types of cells are phagocyte in nature. They engulf any foreign particles entering the liver via blood stream. Between the Kupffer’s cells small spaces are present causing the blood of the sinusoids to come in direct contact with hepatic cells.

**Portal Triad:**

This is a potential space between the lobules of liver. Each portal triad contains a branch of hepatic artery and an interlobular bile duct.
All these structures are surrounded by a connective tissue sheath, i.e., perivascular fibrous capsule.

**Duct System:**

Hepatic bile duct system is divided into two parts:

1. **Intrahepatic Ducts:**

   In each hepatic lobule between the adjacent hepatic cells are small passages called bile canaliculi. Bile secreted by the hepatic cells is poured into these canaliculi. From these canaliculi branches are given which go deep into the adjacent sinusoids between the cell plates. These branches form a network and radiate outward to the periphery of the hepatic lobule where they are joined by bigger canals, the interlobular bile canals. Each interlobular bile canal drains the hepatic lobules which surround it. The portions of the hepatic lobules that are drained by the same interlobar bile ducts.

2. **Extrahepatic Ducts:**

   The interlobar bile ducts unite to form right and left hepatic ducts which join to form common hepatic duct. The bile canaliculi are lined by cuboidal cells. As the duct increases in size towards the porta of the liver the epithelium becomes high columnar.

**Blood Vessels:**

They are hepatic artery carrying oxygenated blood to liver. Portal vein carrying absorbed material from GIT to liver.
Structure of Liver after *Nigella sativa* Administration:

There have been no change in the structure, liver structures were quite normal in test group treated with *Nigella sativa* oil (Fig. 2). But possible histopathological changes were noticed in the liver studied by Khan and Chaudhari (1998).

**Kidney:**

Kidney is a compound tubular gland consisting of stroma and parenchyma.

**Stroma:**

The renal capsule is formed of dense fibrous connective tissue with few scattered smooth muscle fibres and is loosely attached to the kidneys.

Remaining of the stroma form a very fine reticular network between the tubules, so no trabeculae and septae are present.

**Parenchyma:**

The whole of the parenchyma is made up of about one million uriniferous tubules. Each uriniferous tubule consists of a secretary part; the nephron and a collecting part, the collecting duct.

**(a) Nephron:**

It is the structural and functional unit of the kidney. Each nephron is formed of:
(i) Malphigian renal corpuscle
(ii) Proximal convoluted tubule
(iii) Loop of Henle
(iv) Distal convoluted tubule

**Juxta Glomerular Apparatus:**

A portion of the convoluted tubule comes in very close contact with the arterioles entering and leaving the Bowman’s capsule. Both the tubule and the artery show modifications at this point.

**Collecting Tubules:**

At the termination of the distal convoluted tubule, a short connecting tubule is present which is continuous with the arched collecting tubule that passes into collecting tubules.

**Structure of Kidney after *Nigella sativa* (Kalongi) Oil Administration:**

There has been no pathological changes seen microscopically in transverse sections of kidney tissues in test group treated with *Nigella sativa* oil (Fig. 4). But histopathological changes were observed in structure of kidney by Khan and Chaudhari (1998).

Since there has been a very scanty literature available about *Nigella sativa*. The references regarding safety evaluation are not available.
CONCLUSION:

*Nigella sativa* (kalongi) oil did not produce any morphological and structural changes in liver and kidney in experimental animals. It is recommended to do long-term experiments for further studies.
Fig. 1: T.S. of rat liver (control).

Fig. 2: T.S. of rat liver (treated).
Fig. 3: T.S. of rat kidney (control).

Fig. 4: T.S. of rat kidney (treated).
DISCUSSION
DISCUSSION

*Nigella sativa* Linn. (family Ranunculaceae) a cultivated herb is commonly known as Kalagira or Kalongi. Seeds are used in the indigenous system of medicine and possess carminative, digestive, diuretic and antiseptic properties. Seeds have been reported beneficial in uterine ailments. They have been found useful in dysmenorrhoea. *Nigella sativa* has been found having antimicrobial, antifertility activity.

Synthetic drugs cannot provide a remedy, while a whole herb can, because during synthesis many things are totally or partially destroyed while in a whole plant nothing is added or subtracted. And these synthetic drugs are doing what was accepted from them that is why today more and more people and more and more nations are returning to traditional medicine for the promotion and propagation of health thus achieving the slogan of WHO "Health for all by 2000". Thus traditional medicine is therefore now no more an orthodox system of treatment.

This system is being used for the treatment of many diseases or ailments e.g. wounds, ulcers, intestinal complaints, to allay fever, for disorders of urinary tract, rheumatic pains, heart complaints, various types of skin disorders/diseases, asthma, diabetes, hypertension, cancer, tuberculosis. This system is also beneficial in many deficiency and nutritive deficiency diseases. Most of our rural population is
benefited by seeking treatment of various ailments through this system of treatment by local drug vendors.

The state of research on plants used in traditional medicine and its development in Egypt is indicated by the number of scientific institutions devoted to this problem, universities, the natural research centre, the Desert Institute and Horticulture Departments. The use of certain medicinal plants has been industrialized e.g. Ammi visnaga, Cymbopogon proximus, Nigella sativa and Aloe vera. Other plants are under investigation: Urginea maritima, Phytolacca americana and euphorbia sp. Glycyrrhiza glabra, Cynara scolymus and Solanum laciniatum (Sayed 1980).

In present study there have been no effects on lymphocytes due to Nigella sativa before and after administration the number of lymphocytes remained the same. In a study (Haq et al. 1995), the effects of Nigella sativa seeds and their soluble fractions were studied in vitro on lymphocyte response to different mitogens and on polymorphonuclear leukocyte phagocytic activity. No stimulatory effect of N. sativa was detected on lymphocyte response to phytohemagglutinin concavalin A or pokeweeds mitogen. A stimulatory effect of N. sativa was noticed on the lymphocyte response to pooled allogeneic cells. This effect was more pronounced when the low molecular weight (<10 kDa) fraction was used and varied from one normal individual to another. No effect of N. sativa or its fractions was, however noticed on bacterial phagocytosis or killing
when *Staphylococcus aureus* was used, indicating that the decrease in chemiluminescence activity in the presence of *N. sativa* is not relevant to the bactericidal activity.

*Nigella sativa* is commonly used component of spices in Indo-Pakistan, they are considered to be having some nutritive value. In present study in some females there have been increase in haemoglobin with P<0.05 (Table 7) in age group 20-30 years in females. Similarly in age group 31-40 years of female P<0.05 (Table 8) and also in age group 51-60 years with P<0.05) (Table 10). According to study (Pradeep *et al.* 1993), spices analysed were red chillies (*Capsicum annum*), black pepper, coriander seeds, cumin seeds, garlic, dry ginger and ajowan (*Carum copticum*).

In present study *N. sativa* was prescribed to the individuals having normal blood pressure, there have been no effect on blood pressure. In some cases, statistically there have been some change in systolic BP with P<0.05 (Table 7) and in some cases there have been change in diastolic BP with P<0.05 (Table 11). In a study performed by El-Tahir *et al.* (1993) the results suggested that volatile oil induced cardiovascular depressant effects were mediated mainly centrally via indirect and direct mechanisms that involved both 5-hydroxytryptaminergic and muscarinic mechanisms. The direct mechanisms may be due to the presence of thymoquinone in the volatile oil. The volatile oil seemed to possess the potential of being a potent centrally acting antihypertensive agent.
In present study there have been no changes in liver enzymes after administration of *Nigella sativa*, studies were done by Tennekoon et al. (1991), serum alanine aminotransferase concentrations were significantly increased in both extract groups when compared with the normal group but not with the control group. Histological changes were not evident following administration of *N. sativa*.

Oil fraction toxicity of Indian spices was assessed by Mohanty et al. (1990). The results of contact toxicity of *Nigella sativa* Linn. against stored grain pests have been reported.

Regarding literature about this commonly used substance is still scanty and it needs further and detailed studies, both on human and animals.

*Nigella sativa* was given in the form of oil once a day, 5 ml for one week to relieve muscular pain. In all age groups from 20-60 years both in males and females there have been P<0.05. There have been much improvement as has been shown in Table 6 and 12. According to the literature available in Pakistan, it is said that *Nigella sativa* is a wonderful remedy to relieve muscular pain (Khan et al., 1997), but there is very little published data on scientific grounds.

*Nigella sativa* was also tried in patients developing nausea and vomiting. The drug was given to patients both male and female from age group 15-25 years. In all the patients nausea stopped, it means that
Nigella is also having antinauseating and antiemetic properties (Table 13). The similar effect has also been mentioned by Nadkarni (1954).

Nigella sativa oil was topically applied on the Alopecia areata on face for two weeks (Table 14) twice daily in twenty cases. There have been good response in these patients and hair growth started in all patients, it is also manifested in literature (Khan et al. 1997) but scientific published data is not so far available.

According to the topical use of this oil there have been no contact sensitivity in any patient but according to the study by Steinmann et al. (1997) contact sensitivity has been reported.
CONCLUSION

The results obtained from present study demonstrated that *Nigella sativa* is an effective drug in relieving muscular pain, relieving nausea and also curing alopecia areata. It does not produce contact sensitivity.

Regarding liver it does not produce any adverse effect on the liver. Regarding blood picture, it does not produce any adverse effect on blood.

According to the literature available it is extensively used as spice and as a medicine with other aromatics. The herb has been regarded as a valuable remedy in hepatic and digestive disorders as well as stimulant in a variety of conditions which are ascribed to cold humours. In its external use it has been given locally on pityriasis, leucoderma, ringworm, eczema, alopecia, freckles and pimples. It has been given in asthma, chronic headache, migraine and chest congestion. There are many preparations, however it can be tried in all the mentioned diseases in literature including hepatic disorders.

It has also been shown in literature to be effective in cancers for which it is recommended that it should be tried in treatment of cancers.

*Nigella sativa* oil did not produce any morphological and structural changes in liver and kidney in experimental animals on safety evaluation studies.
Fig. 2: Effects of drug on muscular pain in males (n=40)
2. STUDIES OF THE EFFECTS OF OLIVE OIL
ON LICHEN SIMPLEX CHRONICUS
AND PRURITUS SENILIS
# TABLES

**Table 1:** Effect of olive oil three times a day on signs, dryness of the skin (*Lichen simplex chronicus*) according to age group in male (*n=40*). ......................................................... 129

**Table 2:** Effect of olive oil three times a day on symptoms, pruritus (*Lichen simplex chronicus*) according to age group in male (*n=40*). ......................................................... 130

**Table 3:** Effect of olive oil three times a day on signs, dryness of the skin (*Lichen simplex chronicus*) according to age group in female (*n=40*). ......................................................... 131

**Table 4:** Effect of olive oil three times a day on symptoms, pruritus (*Lichen simplex chronicus*) according to age group in female (*n=40*). ......................................................... 132

**Table 5:** Effect of olive oil three times a day on clinical signs, dryness of skin (pruritus senilis) in male (*n=10*) and female (*n=10*) age group 65-75 years ........................................... 133

**Table 6:** Effect of olive oil three times a day on symptoms, pruritus (pruritus senilis) in male (*n=10*) and female (*n=10*) age group 65-75 years ........................................... 134
SUMMARY
SUMMARY

Olive oil is obtained from a tree fruit known as olive. It is commonly used in medicine as an emollient. It is an effective medicine to relieve dryness of the skin. It is free of cholesterol and contains vitamin E. It is also used as preservative. Can also be administered orally to give nourishment to the body. Olive oil has been used for thousand years. It is used to cure debility. It is also used as a vehicle. Its nutritive value is remarkable. It has been used in paralysis and rheumatic pain. Considering its value it has been tried in pruritus senilis and lichen simplex chronicus, for this purpose 40 male and 40 female patients were taken. The signs of drynesss and symptoms of pruritus have been noted down weekly as has been shown in Tables 1-4. Study was done on pruritus senilis in which both male and female patients from the age of 65-75 were enrolled 10 males and 10 females. Dryness and pruritus was observed before treatment and at one week, two weeks, three weeks and at fourth week. In all these conditions there have been good response.

Adverse cutaneous reactions to topical use has not been observed in any patient in this study. No contact sensitization has been observed in any patient.
INTRODUCTION
INTRODUCTION

OLIVE OIL:

Olive oil is obtained from a tree fruit known as olive. It is commonly used in medicine as an emollient. It is an effective medicine to relieve dryness of the skin. It is free of cholesterol and contains vitamin E. It is also used as a preservative and edible things can be kept for longer time if kept in olive oil. This oil can be taken orally where it functions and gives nourishment to the body. For the last four thousand years olive oil in civilizations of Africa, Europe and Asia, has been used as medicine. In the present century it has gained widespread utility throughout the world. It has been included by many research aspects that the nations using olive oil has less chances of coronary diseases as compared to other nations. The olive oil has gained popularity in European countries too. During 1982-83 America has imported 10 million gallons of olive oil and in 1997-98 the imported quantity of olive oil increased by five times. Olive is cultured lavishly in Italy, the farms are full of cultivated trees bearing bunches of olive fruit. To pick up olive fruit from the branches of trees is not so easy task, the fruit is small and to snatch each fruit one by one seems to be difficult. The fruits are collected and are carried at storage. As a crude method the olive fruit is crushed and olive is separated from the liquid contents and is then packed in bottles is ready for market. The places where farmers cultivate olive, they take a typical sort of breakfast by applying garlic on the bread and then olive and sprinkle powdered pepper and salt.
Thousand years back olive oil had gained an important place and was considered pious. Egyptians were having the believe that goddess of cultivation introduced olive cultivation to human. According to Greek mythology goddess of wisdom Athena presented this to human and it was considered a useful present for mankind. It was used to lit the lamps. It was also used as an ointment.

The eastern banks have been using for the last two thousand years. The cultivation of olive extended upto Greek and Dutch and carried it from Greek to Italy and at least 74% quantity of olive oil is supplied by these nations. In Andhalsia olive oil is having importance of trade. In Arabian countries olive oil is used as edible and also to beautify hair. In Indo-Pakistan it is used for massage. Majority of the peoples consider that all varieties of oil have the same quality, some is bitter. Americans use very light oil which should be tasteless and having no smell. Arabs are fond of green and sweet oil so that they could apply it on the bread. The oil which is extracted by machines is considered purified. The Greek olive oil (Kokoneiki) is popular and is commonly used with vegetable, meat, fruits and cheese. It has been estimated that the women who use some quantity of olive oil with their food have less chances of breast cancer, therapeutic effects are also produced on gastric ulcer and kidney stones. It is also effective in burns.
REVIEW OF LITERATURE
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OLEA EUROPaea LINN.:  

It belongs to the family Oleaceae. English name is olive, Urdu name is Zaitun. According to Khan et al. (1997), the olive is nutritive, emollient, demulcent, laxative, allays the irritation of digestive organs and alimentary canal, on long-term use resolves the obstructions and fatty depositions or stones in liver, gall bladder, kidneys and urinary bladder. Experimentally it has most emollient, resolvent and sedative actions and its massage imparts strength to whole body.

MEDICINAL USES:

Olive oil much used in Middle East for edible purpose relieves general debility and weakness in all age groups and is administered as aphrodisiac. About 12-60 ml of the oil has desirable anticonstipative action, in anal fistula or swellings and ulcers as well as anal fissures. Proves useful in unidentified cause of colic and given as enema it helps control the pain. In case of liver obstructions continuous use for recommended duration assists resolution of the depositions (or stones) and slowly purges out of the body without notice. Being nervine stimulant and sedative acts usefully against rheumatic pains, paralysis, sciatica to resolve the malhumorous deposited to relieve pain. Softens the body when massaged and is useful in alopecia, psoriasis, and burns
when applied as ointment. Useful massage for aging individuals and lean children as corrective vulnerary for wounds. It is also used as vehicle.

The plant is 3 meter long has shining leaves having small round fruit, the colour of which is violet. The tree is present in Asiae Kochak, Palestine, Greek, Portugal, Spain, Turkey, Italy, North Africa, Aljazira, Tunis and in California, Mexico, Peru and South Australia. The olive oil is imported from France, Italy, Spain, Turkey, Aljazira, Tunis and Greek and also from Balochistan.

It is said that tree olive is the oldest. The tree has become the sign of peace. In ancient Egypt the olive oil was used in edible things and was also kept for preservation of food.

The fruit is full of nutrition but due to its taste it is not used as fruit. The sardine fishes are kept in boxes with olive oil. It is full of wealth of usefulness.

CHEMICAL CONTENTS:

It is included in Official Pharmacopoeia of U.S.A. According to BPC Pharmacopoeia Codex it is useful for the treatment. The physical property of olive oil should be that greenish or greenish yellow. Should not have any perfume, should be lighter than water at 4°C if condensed. It contains oleic acid, palmitic acid, Arachis oil, linoleic acid, stearic acid, myristic acid and glycerides. It is not soluble in water. Soluble in alcohol, ether, chloroform and liquid paraffin.
The oil is obtained from the ripe fruit. The unripe fruit contains less quantity of oil. The fruit is crushed in crushing machines and the oil obtained is virgin oil. In second round the water is mixed and again crushed and water is removed. In Italy during this process tannic oil is also added and the oil obtained from 2nd and 3rd round is called table oil. Previously it was considered not to have phytosterol but now some kinds of oil contain cholesterol.

It was considered a remedy of haemorrhoids, skin diseases, plurisy and leprosy. According to Ibn-ul-Qim a smentioned by Ghaznavi (1992) the olive oil produces freshness, keeps alertness, removes the worms from gut, gives luster to the hair, gives vigor in old age. It is effective in burns. It is aphrodisiac, tonic to stomach and keeps the chest away from disease. The leaves of olive are boiled with water and mouthwash is done. It heals the ulcers of mouth.

Ghaznavi (1992) in his book has written the observations of old physicians about olive oil, says that the exudate of fruit of olive if boiled to become dense then applied on the teeth, removes the insects. If rinsed it relieves the ulcers of the mouth. The oil of olive if applied on the scalp regularly it prevents from baldness. It is also effective in seborrhoea capitis. If it is massaged, it gives relief to the muscles, it is effective in osteoarthritis and sciatica. It is anti-infective. It also relieves constipation, effective in dysentery. Kills the intestinal worms, removes the stone from the kidney. Also effective in gallstones. It is diuretic.
Association of olive oil intake with cancer risk in humans have been reviewed on two grounds: (1) olive oil has been directly examined in context of an extensive food frequency questionnaire or have evaluated the role of monounsaturated fat in populations of Mediterranean countries where a large fraction of monounsaturated fat originate from olive oil and (2) they have analyzed the data with explicit or implicit control for energy intake to accommodate the likely confounding influence of caloric consumption and to account to a certain extent for differential completeness of reporting between cases and controls. Ecologic studies were also considered and relevant experimental data were invoked, the results were with respect to breast cancer, there is converging evidence for a protective effect, although the data are not definite. For other cancer types, the overall epidemiologic evidence, although promising, is quantitatively limited and qualitatively suboptimal. It was concluded that the issue is a major public health importance and deserves additional study (Morgan et al., 1997). The mortality from coronary heart disease is much lower in Italy and the Mediterranean countries than in northern Europe and United States. Diet is one of the major environmental factors playing an important etiological role in different coronary heart disease rates in these areas. The seven countries study demonstrated that the average consumption of saturated fatty acids and cholesterol was directly related to coronary heart disease (CHD) death rates, these being higher in northern Europe
and United States and lower in the Mediterranean countries and the far East. Olive oil particularly rich in oleic acid, could play a beneficial role in CHD prevention as reported in the Italian Nine Communities Study carried out in the early eighties. Another multicentre study, the Inter-Salt Study has clearly shown lower blood pressure in participants with lower intake of both sodium and alcohol and higher intake of potassium. Recent findings have also shown that two helping of fish per week and antioxidant vitamins, particularly vitamin E and β-carotene are related to low CHD incidence rate in the Mediterranean area compared to other countries. It was concluded that Mediterranean diet represents a useful and effective mean for the prevention of CHD (Jossa and Mancini, 1996).

In a study the effects of replacing hard fat with olive oil or starchy foods on blood lipoprotein concentrations were reviewed. The saturated fatty acids lauric, myristic and palmitic acid raise both low density lipoprotein and high density lipoprotein, somewhat compared with oleic acid. If any fat is replaced by carbohydrates, fasting triglycerides values rise and concentration fall, effect on LDL depend on the type of fat that is being replaced. Trans-isomers of oleic acid lower HDL and raise LDL and lipoproteins. When body weight is forcibly kept constant, substitution of unsaturated oils such as olive oil for hard fats rich in saturated or trans-fatty acids will produce a more favourable lipoprotein profile than replacement of fat by carbohydrate. However high-oil diets
might lead to obesity, which would undo their favourable effects (Katan et al., 1995).

Effects of two types of fish oil supplements as serum lipids and plasma phospholipid fatty acids in coronary heart disease. The data of the study suggest that fish oil administration is associated with an increase in LDL cholesterol level in a diverse group of patients with coronary artery disease. This change appears to be correlated with n-3 fatty acid absorption. The impact of this increase in LDL is unknown but should be considered as potentially adverse (Reis et al., 1990).

In a randomized double blind crossover study the effect of dietary fish oil or olive oil was examined on supplementation of blood pressure, intracellular free platelet, calcium, plasma lipoproteins and circulating vasoactive substances such as norepinephrine, epinephrine and renin in patients with essential hypertension. Ten hypertensive patients were randomly assigned to receive 9G fish oil or 9G olive oil daily for 6 weeks after a four week baseline period. The 6-week treatment period were separated by a 4-week washout. During treatment with fish oil diastolic blood pressure decreased from 103±1 to 98±2 mm Hg (P<0.05) but did not change significantly during olive oil intake. Systolic blood pressure was not affected by either treatment. Intracellular free platelet calcium decreased in patients receiving fish oil (from 102±8 nM to 86±6 nM (P<0.05) but not significantly altered by olive oil treatment. In contrast, the dose-response curve for thrombin-induced intracellular free platelet
calcium was not altered by the fish oil enriched diet, plasma triglycerides decreased by approximately 4% in the fish oil group while low density lipoprotein cholesterol, high density lipoprotein cholesterol and total cholesterol were not altered. Renin activity, norepinephrine and epinephrine in plasma were not influenced by fish oil supplementation. It was concluded that a moderate increase in dietary fish oil reduces diastolic blood pressure, intracellular free platelet calcium and plasma triglycerides in patients with essential hypertension (Passfall, 1993). A double blind crossover trial was conducted with 18 healthy, untreated mildly hypertensive subjects to test the effect on blood pressure of 6 or 12 G fish oil/d (50% n-3 fatty acids) as compared with an olive oil placebo. Blood pressure was measured every 6 week in the clinic and three times daily by subjects using a semi-automated device in their homes. Complication was determined biochemically. No significant changes in home or clinic blood pressure measurements were noted for either dose after 6 or 12 weeks of treatment. Blood pressure changes were not correlated with compliance, baseline dietary fish consumption or blood pressure. Moderate doses of fish oil did not have a substantial effect on blood pressure. It was concluded that fish oil was not a practical treatment for mild hypertension (Morris et al., 1993). Fish and fish oils have been reported to reduce blood pressure in normotensive and untreated hypertensives. The study was conducted to find out the effect of dietary supplementation with fish oil on blood pressure in 20
treated hypertensives with controlled blood pressure who continued their usual antihypertensive drug treatment throughout. A double blind randomized crossover design was used with two phases each of 8 weeks duration. In one phase subjects took fifteen 1G fish oil capsules daily and in other 15 capsules of identical appearance containing 1G olive oil daily. There was no difference between the treatment phases for any blood pressure parameter, heart rate or body weight, but blood pressure was lowered in both phases compared with pretreatment values. The fasting plasma triglycerides concentration was 30% lower in the fish oil phase (P<0.001), but there was no difference between the phases for plasma concentrations of total or high density lipoprotein (HDL) cholesterol. It was concluded that in treated hypertensives with controlled blood pressure any additional fall in blood pressure produced by dietary supplementation with fish oil is so small that the requirement for antihypertensive drug therapy is unlikely to be reduced (Wing et al., 1990).

The effect of minor constituent of olive oil on cardiovascular disease were evaluated and the findings suggest that polyphenolic compounds found in olive oil are endowed with several biologic activities that may contribute to the lower incidence of coronary heart disease in the Mediterranean area (Visioli and Galli, 1998). Dietary changes are important hundred years ago in Europe, America and Australia were needed to feed their growing industrial populations by 1909 margarins
were first made by the hydrogenation of marine oils and later vegetable oils as a substitute for butter thereby introducing saturated fats. The Japanese escaped such changes to their rice diet by the influence of the inevitable annual monsoon while southern Europe's CHD immunity may hinge on its permanent olive oil and vitamin C antioxidant staples. Britains angina pectoris probably arose following the enclosures which changed arable into animal farming in the middle ages but cases rose only slowly from Heberden’s 100 in 1802 to McKenzie’s 200 by 1923. It seems, likely therefore that much of the sudden increase to 2000 reported by Maurice Cassidy in 1945 despite the impact of this century's increased longevity on CHD, will be due to dietary changes together with smoking increasing impact (Walsh, 1990).

The usefulness of olive oil was investigated in a standard hypolipidemic diet suitable for the secondary prevention of atherosclerosis some patients who had received a diet with a P/S value of 1.3 were turned to a diet rich in olive oil, with a P/S ratio of 0.52; the same number of patients were fed on with the initial diet. The main differences found were a decrease of LDL cholesterol parallel to an increase of HDL cholesterol in the patients fed on the diet rich in olive oil. No modifications were found in these patients as far as hemostatic function and liver functional tests are concerned (Zoppi et al., 1985).

Greek man have a longer life expectancy than men from other European countries or from North America. Several aspects of the
traditional Greek diet may contribute to its beneficial role in countering the development of coronary heart disease. They include the high intake of olive oil that tends to increase the ratio of high to low density lipoprotein cholesterol, the regular consumption of fiber rich legumes and vegetables in males cooked using olive oil, the high intake of moderate consumption of wine with meals that tends to increase high density lipoprotein cholesterol without posing major risk of intoxication (Trichopoulou et al., 1994).

Prevention of coronary heart disease and hypertension was tried by using cholestyramine or gemfibrozil, the best dietary intervention for cholesterol lowering are still unresolved with recent interests in fish oil and olive oil (Sleight, 1988). There is a controversy in determining the effects of olive oil in the lipidic metabolism. Studies were done to find out the changes produced in the lipid profile after substituting sunflower dietic oil within virgin olive oil. The improvement of the lipidic parameters can only be explained by the use of olive oil in the diet of Agemza cadets (Casasnovas et al., 1997).

A case control study was carried out to elucidate the role of recent diet, specially in the influence of food groups, in the development of cancer of the breast. The result was a significant trend of increasing risk with increasing intake emerged for the following food groups. It was concluded that consumption of tomatoes, mainly consumption of eggs
and olive oil and primarily exhibited a statistically significant relationship (P<0.05) with BC stage in Valencia (Morales et al., 1998).

The lipid-altering effects of an almond based diet with an olive oil based diet were compared against a cheese and butter based control diet. Results suggested that the more favourable lipid-altering effects induced by the almond group may be due to interactive or additive effects of the numerous bioactive constituents found in almonds (Spiller et al., 1998).

The metabolic effects of co-ingestion of saturated and monounsaturated fat with potato were compared, 12 NIDDM subjects received 300G mashed potato alone or in combination with 40G olive oil, 50G butter or 100G butter respectively. It was concluded that butter increased the insulin response in patients with NIDDM more than olive oil, and large amounts also increased FFA and triglyceride levels (Rasmussen et al., 1998).

Epidemiological studies of breast and pancreatic cancer in several Mediterranean populations have demonstrated that increased dietary intake of olive oil is associated with a small decreased risk or no increased risk of cancer, despite a higher proportion of overall lipid intake. Experimental animal model studies of high dietary fat and cancer also indicate that olive oil has either no effect or a protective effect on the prevention of a variety of chemically induced tumours. It is proposed
that the high squalene content of olive oil as compared to human food is a major factor in the cancer risk reducing effect of olive oil (Newmark, 1997). Epidemiological investigations and laboratory experimentation with animal models suggest that relatively high intakes of long chain n-3 fatty acids and n-9 fatty acids present in olive oil, reduce breast cancer risk by mechanisms that may involve modification of the biosynthesis of eicosanoids from n-6 polyunsaturated fatty acids although there is limited support for the hypothesis that total, intake affects breast cancer risk (Rose, 1997). In a study the experimental animal studies were performed and it was suggested that olive oil consumption as contrasted to consumption of other fat types does not enhance. The occurrence of chemically induced mammary tumours but human data are sparse. Furthermore, evidence is inconclusive concerning the role of food groups, as distinct from that of major nutrient, in the etiology of breast cancer in women. Although major categories of macronutrients do not show significant associations with breast cancer risk in most studies, including the present one vegetables and fruits are inversely significantly and strongly associated with this risk. There is evidence that olive oil consumption may reduce the risk of breast cancer whereas margarine intake appears to be associated with an elevated risk for the disease (Trichopoulou et al., 1995). An association between fats and colorectal carcinoma has been suggested, but the epidemiologic evidence by type of dietary fat is less clear. Colorectal carcinoma rates have been relatively
low in Mediterranean countries compared with most other western
countries, but the components of the Mediterranean diet responsible for
this favourable pattern are unclear and according to the studies
seasoning fats did not appear to increase the risk of colorectal carcinoma
and there was little evidence for a differential effect by fat type. If such a
differential effect exists, it is minor and could favour olive oil (Biaga,
1998).

In a randomized double blind placebo controlled study, patients
were given 10 olive oil or fish oil capsules daily TDS in addition to
betamethasone dipropionate was applied. Most patients gradually
worsened upon discontinuation of corticosteroids. Using survival
analysis methods no significant difference was found between the fish
and olive oil groups. The fish oil in the therapy of psoriasis was put with
prospective and discuss the efficacy of fish oil when used alone versus in
combination therapy (Gupta et al., 1990). In a double blind block
randomized, the effect of dietary supplementation was investigated with
eicosapentaenoic acid in patients with psoriasis. The experimental group
received 10G of fish oil daily containing approximately 1.8G
eicosapentaenoic acid while the controls were given an isoenergetic
amount of olive oil, there have been no significant change in the clinical
manifestations of psoriasis in either group after 8 weeks of treatment
(Bjorneboe et al., 1988). Another study shows similar effects that olive oil
after using as control and active medicaments cyclosporin A [Duncan et al., 1993].

It is suggested that dietary modification with additional marine oil may be useful way of modifying disease activity in systemic lupus erythematosus (Walton et al., 1991).

The effect of olive oil and fish consumption on rheumatoid arthritis – a case control study was done and it was concluded that olive oil consumption and adherence to orthodox lent may have a protective effect on the development and/or the severity of rheumatoid arthritis. This is a hypothesis generated by the present study that needs verification (Linos et al., 1991).

Dietary fish oil and olive oil supplementation was done in a patient with rheumatoid arthritis. The clinical benefits of dietary supplementation with omega-3 fatty acids were more commonly observed in patients consuming higher dosages of fish oil for time intervals that are longer than those previously studied. Dietary supplementation with olive oil is also associated with certain changes in immune function which require further investigation (Kremer et al., 1990). Evening primrose and olive oil has been tried in the treatment of rheumatoid arthritis, it was administered as 10 ml twice daily for 12 weeks. Laboratory investigations were done and PGE$_2$ was found
decreased and TxB₂ increased in both treatment groups, but no
significant improvement could be seen in either groups (Jantti, 1989).

Effect of olive oil on immune system in middle aged man was
consumption of diet rich in monounsaturated fatty acids has been linked
with a low prevalence of atherosclerosis and there has been great
interest in the effect of MUFA's on lipoproteins metabolism. Consumption
of the MUFA diet did not affect natural killer cell activity or proliferation
of nitrogen-stimulated leukocytes. The effect of a MUFA-rich diet on
adhesion molecule expression may have implications for the influence of
dietary fat on inflammatory disease (Yaqoob et al., 1998).

Abnormal fatty acid metabolism may contribute to clinical
problems such as itching, abnormal perspiration, susceptibility to
infection, delayed wound healing, anaemia and increased hemolysis, as
seen in patients with chronic renal failure. A double blind study of
patients on haemodialysis who received either fish oil, olive oil, or
sunflower oil documented that patients may have increased levels of the
proinflammatory prostaglandin PGE₂ and that fish oil intervention may
decrease these levels, change the fatty acid profile, improve hematocrit
levels of the proinflammatory prostaglandin PGE₂ and that fish oil
intervention may decrease these levels, change the fatty acid profile,
 improve hematocrit levels and improve patient perception of symptoms
of pruritus (Pock, 1997).
In end stage disease management of constipation was done in intractable cases by Clezy enema (a large volume enema that is prepared by a hospital pharmacist and contains the softeners: paraffin oil 30 ml, glycerine 30 ml, Enema soap 30 ml and olive oil 60 ml, made upto 400 ml with water). If manual evaluation is contemplated, a premedication with midazolam 5 mg subcutaneously will give short sedation for this procedure (Burke, 1994).

Fish oil improves arterial compliance in non-insulin-dependent diabetes mellitus, in a double blind, placebo controlled study the effects of dietary fish oil were investigated after dietary supplementation on arterial wall charateristics in 20 patients with non-insulin-dependent diabetes mellitus, the results support the hypothesis that fish oils alter vascular reactivity and favourably influence arterial wall characteristics in patients with non-insulin dependent diabetes mellitus. This vascular effects may contribute to the cardioprotective actions of fish oil in humans (McVeigh et al., 1994).

Influence of fish oil on serum lipoprotein levels was studied in endogenous hypertriglyceridemia, men were evaluated. The observation was performed in two groups of patients, 10 cases each in the group 1. Subjects received fish oil first in the dose of 12 grams daily for 3 weeks and then for the next 3 weeks olive oil in the same dose. Patients from group II received the same oil but in the inverse order. Results after olive oil were a control for fish oil. Marked decreases in the serum and VLDL
triglycerides and also VLDL-cholesterol level after fish oil was shown. Increases in LDL and HDL cholesterol were observed. In a patient fish oil was given for 6 weeks. No differences in the serum lipid levels after this period of time in comparison with results after three weeks were observed (Szostak and Nowicka 1994).

Various dietary marine oils and olive oil on fatty acid composition of serum and platelets and effects on platelets and serum lipids were investigated as part of an extensive study of the effects. The combination of cod liver oil and olive oil may produce better effects than these oils given separately. The changes in platelet functions are directly associated with alterations of fatty acid composition in platelet membrane (Vognild et al., 1998).

To relieve nasal congestion somewhere olive oil is instilled in the nose, aspiration of olive oil results in lipoid pneumonia resistant to antimicrobial treatment. It developed in five cases who presented as persistent cough, tachypnoea, recurrent febrile illness and chest infections (Annobil et al., 1997).

The essential fatty acids, in dietary supplementation among children play an essential role, as studied the results suggested that n-3 and n-6 polyunsaturated fatty acids may play a favourable role in the defence mechanism of these subjects (Venuta et al., 1996).
Low density lipoprotein in oxidation is inhibited in vitro by olive oil constituents, the low density lipoprotein oxidation may be a factor in the development of atherosclerosis. The Mediterranean diet rich in vegetables, grain, legumes, fruits and oils mainly olive oil has been suggested to reduce the incidence of coronary heart disease because of its low saturated and high monounsaturated fatty acid content (Visioli et al., 1995). Since it has been observed that monounsaturated fatty acids enriched diet modifies red cell membrane lipids and cation transport system in normotensive subjects similarly a hypertensive group of patients have been evaluated. In a group of 18 moderately hypertensive women the diet was supplemented for two months with olive oil which replaced an equal amount of seasoning fats. Before and after this period, red cell fatty acid composition was evaluated by gas chromatography in order to verify diet compliance. Although the reduction in maximal rate of the Li-Na CT after olive oil was not significant, it was the only cation transport parameter being correlated with the variations of membrane lipids (Corrocher et al., 1992).

In a study the techniques to assess the day long reduction in oral malodor of a novel 2-phase oil: water mouth rinse, as compared to a corresponding placebo rinse and to a commercial 0.2% chlorhexidine mouth rinse. Sixty dental students were divided randomly into 3 groups and instructed to use one of the rinses prior to bed time and the following morning measurements carried out in the late afternoon about
8-10 hours following rinsing, were compared with baseline measurements carried out in the late afternoon of the previous day. Volatile sulphide levels were measured using a portable industrial sulphide monitor. Microbial levels were estimated. Both two phase mouth rinse and chlorhexidine brought about significant decreases in volatile sulphides as compared to the placebo group. These results were corroborated by the organoleptic data. Similarly both chlorhexidine and two phase mouth rinse were highly effective in reducing microbial levels as measured by the rinsing technique in comparison to placebo group (Rosenberg et al., 1992). Another study regarding effects of two phase oil-water mouth wash on halitosis was done to remove such oral microorganisms causing. The oil phase consists of olive oil and other essential oils. The aqueous phase includes cetylpyridinium chloride which is a disinfectant that promotes the adhesion of microorganisms to oil droplets. This study determined the effects of this mouth wash on the production of volatile sulfide in vivo and in vitro. Neither rinsing with water nor brushing teeth decreased the concentration of sulfide in mouth air at 3.5h after treatment. A reduction of only 30% sulfide was observed when a commercial mouthwash was used. However, this study demonstrated that the use of the two phase mouthwash led to approximately 80% reduction of sulfide and saliva putrefaction system were completely inhibited by the two phase mouthwash. It was
concluded that two phase mouthwash strongly inhibited the production of volatile sulfide (Yaegaki and Sanda, 1992).

Calcium hydroxide with olive oil has been used as an apical barrier in debunted teeth with periapical lesions (Pereira et al., 1988).

Spontaneous pneumothorax is rare among Nigerians, the experience of investigators of this article of olive oil confirms its advantages as a good agent for chemical pleurodesis. The experiments were performed on rabbits, it was concluded that in high risk patients with poor respiratory reserve including some who have bronchopleural fistulas and are unfit for surgery, chemical pleurodesis offers an alternative method for maintaining reexpansion and preventing recurrence (Ofoegbu, 1980).

The influence of dietary saturated and unsaturated fat on hepatic cholesterol metabolism and the biliary excretion of chylomicron cholesterol in the rat were assessed and it was found that biliary cholesterol secretion was higher in corn oil fed rats than in those fed olive or palm oil or a low fat diet, and this was associated with a markedly increased lithogenic index in these animals. The activity of cholesterol 7-α-hydroxylase was higher in the olive and corn oil-fed than in palm oil fed animals (Bravo et al., 1998).

Pilot study was done on n-3 polyunsaturated fatty acids in the treatment of human experimental gingivitis. This human experimental
gingivitis study demonstrated that n-3 polyunsaturated induced a tendency towards reduced inflammation but it was not possible to conclude significant efficacy (Campan et al., 1997).

Cyclosporin A is a selective T-cell immunosuppressant and does not inhibit the phagocytic system to the same degree as also steroids. Significant nephrotoxicity has been associated with its systemic use for solid organ transplantation or chronic idiopathic uveitis. Topical administration of CsA 2% in olive oil reduces the risk of systemic side effects and appears to be well tolerated without local toxicity. Ocular penetration currently limits its indications for corne-scleral immune diseases or high risk corneal grafts (Rakic, 1993). A new vehicle for delivery of cyclosporin A to the eye, collagen shields were tested as a means of delivering the immunosuppressive drug, cyclosporin A to the cornea and aqueous humor in rabbit eye. Both the corneal and aqueous humor concentrations of cyclosporin A achieved with the shield delivery system were 10 fold higher than those obtained with topical cyclosporin A, olive oil drops. The cyclosporin A levels achieved in the cornea using the collagen shield are sufficient to inhibit cellular immune reactions in vivo. These results demonstrate that collagen shields may be useful as an ocular delivery system for the drug cyclosporin A (Reidy et al., 1990). Cyclosporin containing collagen shields suppress corneal allograft rejection delivered in collagen shields or olive oil drops treatment was begun either immediately after grafting or at the first sign of immune
graft reaction. The results indicate that the collagen shield is an effective delivery system for cyclosporin and the topically administered cyclosporin is effective in suppressing the initiation of graft rejection and in reversing a graft reaction in progress (Chen et al., 1990). Olive oil drops containing an equivalent concentration of cyclosporin A drops were administered at 15 minutes intervals with the first hour and then one hourly over a 6 hour period, in addition collagen shields soaked for 30 minutes in the liposome preparation were tested in vitro and in vivo as a new drug delivery approach. There have been better absorption and cyclosporin with olive oil (Pleyer et al., 1994).

Influence of topically applied cyclosporin A in olive oil on corneal epithelium permeability 24 hours after instillation of 2% cyclosporin A olive oil increased (P<0.001) and that of the solvent alone increased 6.68 times (P<0.001). No differences in corneal permeability were found between cyclosporin A – olive oil and the vehicle (P=0.651). It was concluded that the olive oil used to dissolve cyclosporin A is responsible for the increased epithelial permeability (Benitez del Castillo et al., 1994).

Thygeson’s superficial punctate keratitis is a distinct clinical entity characterized by round conglomerates of discrete granular white gray, fine intraepithelial dots without conjunctival involvement. The only effective treatment with regards to relieving symptoms and diminishing lesions have been topical corticosteroids, but their prolonged use can be associated with severe side effects. This study was done to present the
long-term results of the use of 2% topical cyclosporin A in olive oil in Thygeson's SPK. Eight patients diagnosed as having Thygeson's SPK were included. All patients were treated with 2% cyclosporin is dissolved in olive oil four times a day for three months and two times a day for one month before withdrawing therapy. The followup period ranged from twelve to twenty five months. The number of corneal lesions varied between 5 and 15 before treatment. After cyclosporin treatment no corneal lesion was observed and the cornea remained clear after the follow up period. In conclusion 2% cyclosporin in olive oil is a safe alternative to corticosteroids in the treatment of Thygeson's SPK, and resulted in satisfactory control of the condition (Delcastillo et al., 1996-97).

Stability of cyclosporin 1% in artificial tears prior to the manufacturers recommendations of using a lipid soluble vehicle such as olive oil. Patients preferred the artificial tears preparation over the oil based cyclosporin product. Because of the good clinical response and the reluctance of patients to change to the oil vehicle product, the stability of cyclosporin 1% was determined in artificial tears. Cyclosporin 1% was prepared in artificial tears (polyvinyl alcohol 1.4% and povidone 0.6%) by adding 1 ml of the injectable (50 mg/ml) cyclosporin into 4 ml of the artificial tears solutions. Cyclosporin 1% in artificial is stable for upto 28 days in the refrigerator or at least 7 days at room temperature because of the ease of preparation, the proven clinical effectiveness of the product
and better patient acceptance, the product making continued (Fiscella et al., 1996).

According to a study at present corn oil, castor oil, and olive oil and the three most commonly used vehicles. The aim of this study was to determine the effect that topically applied cyclosporin A dissolved in different oils has on corneal epithelial permeability measured by fluorophotometry. Forty healthy volunteers with absence of ocular or systemic disease and not receiving topical or systemic drugs were enrolled. Measurements were taken before and 45 minutes after the instillation of 40 microlitres of a 2% aqueous solution of sodium fluorescein without preservatives. Basal corneal permeability and the permeability 24 hours after the instillation of 2% cyclosporin A – olive oil, olive oil alone, 2% cyclosporin A – castor oil, castor oil alone, 2% cyclosporin A – corn oil and corn oil alone, were calculated to prepare the topical 2% cyclosporin A, a sandimum oral solution was employed under sterile conditions.

It was found that epithelial permeability 24 hours after the instillation of any cyclosporin A formulations or solvents increased more than 6.62 times (P<0.001). No differences in corneal permeability values were found between any of the cyclosporin A formulations and the vehicles. It was concluded that oils used to dissolve cyclosporin A are mainly responsible for the increased corneal epithelial permeability. No
differences were observed of the tested solvents on corneal epithelial permeability (Benitz et al., 1995).

Topical cyclosporin treatment of keratoconjunctivitis sicca in secondary Sjörgren's syndrome was assessed. The study was a randomized double masked placebo-controlled trial. Thirty eyes of 15 patients were randomized to undergo treatment with topical cyclosporin in olive oil and 30 eyes of the other 15 patients received a placebo which was the sterile olive oil used as a vehicle for the cyclosporin. The effect of the 2 months long treatment with either medication on the status of the dry eye state was measured by Schirmer-1 test, tear film break up time and rose bengal staining. There was a significant increase in the breakup time and significant decrease in rose bengal staining. Score between the cyclosporin and control groups at the end of the 2 months study period (P<0.01) Schirner-1 test remained unaffected (P>0.05). These results probably indicate that topical cyclosporin modulates the goblet cell function in secondary Sjörgren's associated keratoconjunctivitis sicca and through this mucous enhancing action of some other mechanism not yet known helps to maintain the structural integrity of the epithelium (Gunduz and Ozdemir, 1994).

According to the study penetration of cyclosporin A into the rabbit cornea and aqueous humor after topical drop and collagen shield administration, the amounts of cyclosporin A in corneal and aqueous samples from eyes treated with cyclosporin A castor oil and cyclosporin
A olive oil were compared with each other and with collagen shield treated eyes. Cyclosporin A concentration were measured by radioimmunoassay. After total dose of 6 mg cyclosporin A, the results show that the cyclosporin A of castor oil drops were higher than those obtained with olive oil drops. In eyes with collagen shields, cyclosporin A levels were higher than olive oil drops but nearly equal to the castor oil drops. Collagen shields may be useful as an ocular delivery system for cyclosporin A (Kanpolat et al., 1994).
PURPOSE OF STUDY
PURPOSE OF THE STUDY

The effectiveness of methods of treating diseases of the skin have improved greatly as compared to past. Selection of a method of treatment which will have excellent curative or palliative effect is not difficult in most patients. The usual restraints of fear of systemic toxicity have been lacking in topical therapheusis. Considering the sensitization and adverse effect of systemic therapy there have been inclination of physicians towards topical therapy. Hydrocortisone and other steroid preparations are commonly used. This therapy is considered to produce excellent results but on the other side there are certain adverse effects produced. These adverse effects included absorption of drugs and treatment seems to be expensive.

Therapeutic environment change is also important, air conditioning is important to produce sweat retention. A more equable (subtropical) climate is the best single treatment for skin diseases like congenital ichthyosis and dry senile skin.

STANDARD TOPICAL THERAPY:

The number of local medicaments varieties of compresses, paints, lotions, emulsions, pastes and ointments.

The exact mode of action of many of the agents is uncertain and often glossed over with meaningless. The human skin in common with
other body tissues has an enormous inherent capacity for self restoration. To take advantage of this it must have rest and protection from the usual bombardment of noxious stimuli which it normally fends off with ease. Simple local medicaments selected with reasonable care promote the self restoration of the skin by protecting it the best selection of the medicaments must be made primarily on the basis i.e. not in terms of positive effects on the skin itself but in reducing not adding to the strains on the skin during convalescence.

There are many diseases of the skin for which no clear cut effective therapy is available. Pruritus is one of them. The methods relieving pruritus are less satisfactory. Use of topical corticosteroids is increasing day by day and is rather misused and is creating many adverse effects. There is no rationalization in the use of this drug. The remedies of herbal origin are still gaining importance because they are not producing many adverse effects. For this purpose the topical remedy for two diseases i.e., Lichen simplex chronicus (neurodermatitis) and pruritus senilis have been selected to be treated with application of olive oil.
MATERIALS AND METHODS
MATERIALS AND METHODS

First the skin conditions on which olive oil was applied are described.

LICHEN SIMPLEX CHRONICUS:

The condition may be defined as the lichenification process resulting from chronic scratching and rubbing of the skin under stress and anxiety. Any emotional conflicts particularly those arising from sex, financial and social problems may initiate itching, scratching produces further irritation and a vicious cycle is established resulting in lichenification.

The skin becomes thickened infiltrated and pigmented. The criss cross markings become more prominent. Margins are irregular but usually well defined. There may be one or several localized patches. The sites commonly affected are nape of the neck, arms, angogenital area, scrotum back of the knee, legs and ankle.

PRURITUS SENILIS:

The term implies to generalized itching in elderly peoples usually past the age 50 or 60. With senile atrophic, dry skin, itching is precipitated by rough or woolen clothings, sudden changes in temperature, bath are the other known causes of pruritus and itching dermatoses are absent, though the itching becomes generalized but sooner or later it may be confined to trunk or the lower extremities. The
course is usually progressive. Treatment consists of application of oil, cream, animal fat and avoidance from exciting causes.

MATERIALS AND METHODS:

The study was conducted on a group of patients suffering from lichen simplex chronicus and pruritus senilis. The patients were collected from Baqai Medical University Hospital and charitable clinics.

LICHEN SIMPLEX CHRONICUS:

40 male patients were taken suffering from lichen simplex chronicus and were divided in groups. They were given olive oil to apply on the affected part three times a day regularly and signs, dryness and symptoms of pruritus were noted down after one week, two weeks, three weeks and four weeks.

The assessment score was assigned qualitatively as none, slight, moderate and severe. The patients having qualitative symptoms were assessed weekly.

Similar study was conducted on 40 female patients according to same age group.

In the same way the symptoms of pruritus were noted down in both male and female patients.
STUDY ON PRURITUS SENILIS:

Since the disease occurs in old age group, the patients for this study were selected from the age of 65 to 75 both male and female. The signs-dryness of the skin and symptoms of pruritus were scored as slight moderate and severe, the assessment was done every week upto four weeks and olive oil was applied daily one time for the whole duration of treatment.
GROUPS OF PATIENTS
GROUPING OF PATIENTS

LICHERN SIMPLEX CHRONICUS:

For this purpose the patients were divided into eight groups according to age and sex.

MALES:

Group A:

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Age group</th>
<th>10-20 years</th>
</tr>
</thead>
</table>

Group A1:

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<th>No. of patients</th>
<th>Age group</th>
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Group A2:

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<th>Age group</th>
<th>31-40 years</th>
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Group A3:

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<th>Age group</th>
<th>41-50 years</th>
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</thead>
</table>

FEMALES:

Group B:

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<th>Age group</th>
<th>10-20 years</th>
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Group B1:

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<th>21-30 years</th>
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Group B2:

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<th>No. of patients</th>
<th>Age group</th>
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</table>

Group B3:

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<thead>
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<th>No. of patients</th>
<th>Age group</th>
<th>41-50 years</th>
</tr>
</thead>
</table>
PRURITUS SENILIS:

Group C:

No. of patients  10  Males  Age group  65-75 years

Group C1:

No. of patients  10  Females  Age group  65-75 years

The signs - dryness and symptoms pruritus were assessed in pruritus senilis in 10 male and 10 female patients.
OBSERVATION AND RESULTS
RESULTS AND OBSERVATIONS

STUDY ON LICHEN SIMPLEX CHRONICUS DRYNESS OF THE SKIN:

TABLE 1 – MALES:

Table 1 – Group A:

In age group 10-20 years, patients suffering from lichen simplex chronicus, before treatment the signs of dryness were in 40% of the patients moderate and in 60% severe.

After application of olive oil at one week 70% had moderate signs and 30% had severe signs. After two weeks 90% of the patients were left with moderate signs and 10% with severe signs. At three weeks 60% remained with slight signs and 40% remained with moderate signs, at four weeks 70% remained with slight signs and 30% with moderate signs. The results were significant at P<0.05.

Table 1 – Group A1:

In age group 21-30 years male 10% of the patients were having moderate dryness of the skin while 90% were having severe dryness before treatment.

At one week after treatment 30% were having moderate dryness while 70% were having severe dryness of the skin, at two weeks 30% were having slight dryness and 50% of the patients were having
moderate dryness while 20% were having severe dryness, at three weeks interval 40% were having slight dryness while 60% were having moderate dryness, at four weeks 50% were having slight dryness and 50% were having moderate dryness. The results were significant at P<0.05.

Table 1 - Group A₂:

Age group 30-40 years before treatment 10% of the patients were having slight dryness, 40% were having moderate dryness while 50% were having severe dryness.

After treatment at one week 10% of the patients were having slight dryness, 60% were having moderate dryness and 30% were having severe dryness, at two weeks 40% were having slight dryness, 50% were having moderate dryness while 10% were having severe dryness, at three weeks 60% were having slight dryness and 40% were having moderate dryness, at four weeks 80% were having slight dryness and 20% were having moderate dryness. The end results were that 80% of the patients turned to slight dryness while 20% to moderate dryness, the results were significant at P<0.05.

Table 1 - Group A₃:

Age group 41-50 years, before treatment 10% of the patients were having slight sign of dryness, 40% were having moderate and 50% were having severe dryness.
At one week after treatment 10% turned to slight 60% to moderate and 30% to severe, at two weeks 20% turned to slight while 80% turned to moderate, at three weeks 60% turned to slight while 40% turned to moderate, at the end of four weeks 60% turned to slight while 40% turned to moderate, the end result was that 60% patients turned to slight signs and 40% to moderate signs the results were significant at P<0.05.

In All Age Group – Overall Result:

Before start of the treatment 5% of the patients were having slight signs of dryness, 32.5% were having moderate and 62.5% were having severe signs.

At one week after treatment 5% were having slight, 55% were having moderate and 40% were having severe dryness, at the end of two weeks 22.5% were having slight, 67.5% were having moderate and 10% were having severe signs of dryness, at the end of 3 weeks 55% were having slight and 45% were having moderate signs of dryness. At the end of therapy 2.5% of the patients had no dryness, 65% were having slight dryness, 32.5% were having moderate dryness. None of the patients was having severe dryness. The results were significant at P<0.05.
STUDY ON LICHEN SIMPLEX CHRONICUS "PRURITUS":

TABLE 2 – MALES:

Table 2 – Group A:

In age group A, from 10-20 years of age before treatment 40% of the patients were having moderate symptoms and 60% severe.

After one week 70% of the patients turned to moderate while 30% remained severe. After two weeks 90% remained moderate and 10% severe. After three weeks 100% became moderate at the end of treatment 70% remained slight and 30% remained moderate. The results were significant at P<0.05.

Table 2 – Group A1:

In age group 21-30 years before treatment 10% were having moderate symptoms and 90% were having severe symptoms.

After one week 30% were having moderate symptoms while 70% were having severe symptoms. After two weeks treatment 30% were having slight symptoms, 60% were having moderate symptoms and 10% were having severe symptoms at the end of 3 weeks 40% were having slight symptoms and 60% were having moderate symptoms while at the end of 4 weeks 50% of the patients were having slight symptoms, 50% were having moderate symptoms only. Results were significant at P<0.05.
Table 2 – Group A2:

Age group 31-40 years, 10% patients had slight symptoms of pruritus before treatment, 50% of the patients had moderate symptoms while 40% had severe symptoms.

After one week 10% patients had slight, 60% moderate and 30% had severe symptoms. At the end of two weeks 40% patients had slight symptoms, 50% moderate and 10% severe. At the end of three weeks 60% patients had slight symptoms, 40% moderate. At the end of 4 weeks 10% of the patients were symptom free, 80% were having slight symptoms and 10% moderate symptoms. The results were significant at P<0.05.

Table 2 – Group A3:

Age group 41-50 years males, before treatment 10% of the patients had slight symptoms of pruritus, 40% moderate and 50% had severe.

At the end of one week of treatment 10% had slight symptoms, 60% moderate and 30% severe, at the end of two weeks 20% had slight symptoms, 80% had moderate at the end of three weeks 10% patients were left with no symptoms, 50% had slight symptoms and 40% with moderate symptoms. At the end of 4 weeks 20% patients left with no symptoms, 70% left with slight symptoms and 10% with moderate symptoms. The results were significant at P<0.05.
Overall Groups – Age 10-50 Years:

Before the start of treatment 5% patients had slight symptoms, 35% had moderate symptoms and 60% had severe symptoms.

At one week 5% had slight, 55% had moderate and 40% had severe symptoms. At two weeks 22.5% turned to slight symptoms, 72.5% to moderate and 5% to severe. At three weeks 2.5% had no symptoms, 52.5% had slight while 45% had moderate symptoms. At four weeks 7.5% were totally symptom free, 67.5% slight, 25% moderate. The results were significant at P<0.05.

STUDY ON LICHEN SIMPLEX CHRONICUS “DRYNESS” OF THE SKIN:

TABLE 3 – FEMALES:

Table 3 – Group B:

In age group 10-20 years before treatment 20% of the patients had moderate signs of dryness in lichen simplex chronicus and 80% had severe signs.

At one week treatment 20% had moderate and 80% had severe signs, at two weeks interval 100% had moderate signs, at three weeks 10% had slight signs and 90% had moderate signs, at four weeks 20% had slight signs and 80% had moderate signs with P<0.05.
Table 3 – Group B₁:

In age group B₁ (21-30 years) 30% patients had moderate and 70% had severe signs before application of olive oil.

At one week treatment 50% had moderate signs and 50% severe signs, at two weeks 90% had moderate signs and 10% had severe signs of dryness, at 3 weeks 90% had moderate signs while 10% had severe signs. At four weeks 20% had slight signs, 70% had moderate signs and 10% had severe signs at P<0.05.

Table 3 – Group B₂:

In age group 31-40 years, before treatment the patients had 10% slight signs, 30% moderate and 60% severe.

At one week treatment 10% had slight signs, 80% had moderate signs and 10% had severe signs. At two weeks 10% had slight signs and 90% had moderate signs. At three weeks 60% had slight signs and 40% had moderate signs, at four weeks 20% had slight signs while 80% had moderate signs, significant at P<0.05.

Table 3 – Group B₃:

Age group 41-50 years, 50% of the patients had moderate signs, while 50% had severe signs.

After treatment at one week moderate signs had 70% and severe signs had 30% of the patients, at two weeks 90% had moderate and 10%
had severe signs, at 3 weeks 20% had slight signs, 70% had moderate signs, 10% had severe signs. At four weeks 60% had slight signs while 40% remained with moderate signs the results were significant at P<0.05.

**Overall Age Groups – 10-50 Years:**

Before treatment 2.5% patients had slight signs, 32.5% had moderate and 65.0% had severe signs.

After treatment at one week 2.5% had slight signs, 55% moderate and 42.5% severe signs, at two weeks 2.5% had slight signs, 92.5% had moderate signs and 5% had severe signs. At three weeks 7.5% had slight signs, 87.5% had moderate signs and 5% had severe signs. At four weeks 2.5% had no signs, 35% had slight signs, 60% had moderate signs, 2.5% had severe signs, at P<0.05.

**STUDY ON LICHEN SIMPLEX CHRONICUS PRURITUS:**

**TABLE 4 – FEMALES:**

Table 4 – Female: Pruritus in Lichen Simplex Chronicus:

In age group, group B 10-20 years before treatment the symptoms of pruritus were in 20% of the patients of moderate type, while 80% had severe symptoms.

At one week after treatment 20% had moderate and 80% had severe symptoms, at two weeks 40% had slight and 60% had moderate
symptoms, at three weeks 70% had slight and 30% had moderate symptoms, at four weeks 80% had slight symptoms while 20% had moderate symptoms at P<0.05.

**In Age Group B1 – Age 21-30 Years:**

Before treatment the symptoms of pruritus were moderate in 40% of patients and severe in 60% of patients.

At one week after treatment they were in 20% slight, in 40% moderate and in 40% severe, at two weeks in 20% were slight and in 80% were moderate, at 3rd week the symptoms of pruritus were slight in 50% of the patients and moderate in 50% of the patients at four weeks 60% of the patients had slight symptoms while 40% had moderate symptoms, it was concluded to be improvement and significant at P<0.05.

**In Age Group B2 – Age 31-40 Years:**

Before treatment the symptoms in 10% of the patients were slight, in 30% moderate and in 60% severe.

After treatment at one week the symptoms were slight in 10% of the patients and moderate in 90% of the patients, at two weeks 50% of the patients had slight symptoms while 50% had moderate symptoms of pruritus, at three weeks 90% had slight symptoms and 10% had moderate symptoms while at four weeks 10% left with no symptoms of
pruritus, 80% left with slight symptoms and 10% with severe symptoms. The results were significant at P<0.05.

In Age Group B3 – Age 41-50 Years:

Before start of the treatment 50% of the patients had moderate symptoms of pruritus while other 50% had severe symptoms of pruritus.

After treatment at one week 10% had slight symptoms, 60% had moderate symptoms and 30% had severe symptoms, at two weeks 50% had slight symptoms and another 50% had moderate symptoms, at three weeks 70% left with slight symptoms and 30% left with moderate symptoms. At four weeks 90% patients remained with slight symptoms and 10% remained with moderate symptoms. The results were significant at P<0.05.

The Overall Assessment in All Age Groups – 10-50 Years Female:

Before treatment 2.5% had slight symptoms, 35% had moderate symptoms and 62.5% had severe symptoms.

At one week after treatment 10% of the patients left with slight symptoms, 52.5% with moderate symptoms and 37.5% with severe symptoms. At two weeks 40% of the patients left with slight symptoms and 60% of the patients left with moderate symptoms, at three weeks the 70% patients left with slight symptoms and 30% left with moderate symptoms, at four weeks 2.5% of the patients left with no symptoms,
77.5% left with slight symptoms and 20% left with severe symptoms of pruritus, the results were significant at \( P<0.05 \).

**STUDY ON PRURITUS SENILIS DRYNESS OF THE SKIN:**

**TABLE 5 – MALES:**

The study was done on 10 male patients to assess the effects of olive oil in age group 65-75 years.

Before treatment 60% of the patients had moderate signs while 40% had severe signs of dryness before application of olive oil.

After treatment 30% left with slight signs and 70% left with moderate signs, at two weeks 40% left with slight signs and 60% left with moderate signs, at three weeks 70% left with slight signs and 30% with moderate signs, at four weeks 100% left with slight signs only. The results were significant at \( P<0.05 \).

**TABLE 5 – FEMALES:**

The study was done on 10 female patients to assess the effects of olive oil application in age group 65-75 years.

Before treatment 20% of the patients had moderate signs of dryness of the skin and 80% of the patients had severe signs of dryness. After application of olive oil at one week 70% left with moderate signs while 30% left with severe signs, at two weeks 10% left with slight, 70% with moderate and 20% with severe signs of dryness, at three weeks 30%
left with slight signs of dryness and 70% left with moderate signs of dryness, at four weeks 90% left with slight signs and 10% left with moderate signs of dryness. The results were significant at P<0.05.

**STUDY ON PRURITUS SENILIS PRURITUS:**

**TABLE 6 – MALES:**

The study was conducted on 10 male patients to assess the effects of olive oil in pruritus in pruritus senilis age group 65-75 years.

Before treatment 60% of the patients had moderate symptoms of pruritus and 40% had severe symptoms of pruritus. After application of olive oil at one week 30% of the patients were left with slight symptoms and 70% were left with moderate symptoms, at two weeks 60% left with slight symptoms and 40% with moderate symptoms, at three weeks 70% were left with slight symptoms and 30% with moderate symptoms, at four weeks 100% of the patients were left with only slight symptoms, the results were significant at P<0.05.

**TABLE 6 – FEMALES:**

The study was conducted on 10 female patients age group 65-75 years, on pruritus in pruritus senilis.

Before application of olive oil 20% of the patients had moderate symptoms of pruritus while 80% had severe symptoms. At one week of application of olive oil 70% left with moderate symptoms and 30% with
severe symptoms, at two weeks 10% of the patients left with slight symptoms, 70% with moderate symptoms and 20 with severe symptoms, at three weeks 30% of the patients left with slight symptoms and 70% with moderate symptoms, at four weeks 90% left with slight symptoms, while 10% with moderate symptoms, the results were significant at P<0.05.
TABLE 1
EFFECT OF OLIVE OIL THREE TIMES A DAY ON SIGNS
DRYNESS OF THE SKIN (LICHEN SIMPLEX CHRONICUS)
ACCORDING TO AGE GROUP IN MALE (n=40)

<table>
<thead>
<tr>
<th>Age group and severity of clinical signs</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>One week</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Group A</td>
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</tr>
<tr>
<td>10-20 years n=10</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (40)</td>
<td>7 (70)</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (50)</td>
<td>3 (30)</td>
<td>1 (10)</td>
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<tr>
<td>Slight</td>
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<tr>
<td>Moderate</td>
<td>1 (10)</td>
<td>3 (30)</td>
<td>5 (50)</td>
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<tr>
<td>Severe</td>
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<tr>
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<tr>
<td>Slight</td>
<td>1 (10)</td>
<td>1 (10)</td>
<td>4 (40)</td>
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<tr>
<td>Moderate</td>
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<td>6 (60)</td>
<td>5 (50)</td>
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<tr>
<td>Severe</td>
<td>5 (50)</td>
<td>3 (30)</td>
<td>1 (10)</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
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<td>1 (10)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (40)</td>
<td>6 (60)</td>
<td>8 (80)</td>
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<td>5 (50)</td>
<td>3 (30)</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>Slight</td>
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<td>22 (55)</td>
<td>27 (67.5)</td>
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<tr>
<td>Severe</td>
<td>25 (62.5)</td>
<td>16 (40)</td>
<td>4 (10)</td>
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TABLE 2
EFFECT OF OLIVE OIL THREE TIMES A DAY ON SYMPTOMS
PRURITUS (LICHEN SIMPLEX CHRONICUS) ACCORDING
TO AGE GROUP IN MALE (n=40)

<table>
<thead>
<tr>
<th>Age group and severity of symptoms</th>
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<th>After treatment</th>
<th>P-value</th>
</tr>
</thead>
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<td>No. (%)</td>
<td>One week</td>
<td>Two weeks</td>
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<tr>
<td>Slight</td>
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<td>Moderate</td>
<td>4 (40)</td>
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<td>9 (90)</td>
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<tr>
<td>Severe</td>
<td>6 (50)</td>
<td>3 (30)</td>
<td>1 (10)</td>
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<tr>
<td>Group A1</td>
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<tr>
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</tr>
<tr>
<td>Moderate</td>
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<td>3 (30)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Severe</td>
<td>9 (90)</td>
<td>7 (70)</td>
<td>1 (10)</td>
</tr>
<tr>
<td></td>
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<tr>
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</tr>
<tr>
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<td></td>
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</tr>
<tr>
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<td>1 (10)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (50)</td>
<td>6 (60)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (40)</td>
<td>3 (30)</td>
<td>1 (10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Group A3</td>
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</tr>
<tr>
<td>41-50 years n=10</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
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<td>1 (10)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (40)</td>
<td>6 (60)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (50)</td>
<td>3 (30)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-50 years n=40</td>
<td></td>
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<tr>
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</tr>
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<td>2 (5)</td>
<td>89 (22.5)</td>
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<td>Moderate</td>
<td>14 (35)</td>
<td>22 (55)</td>
<td>29 (72.5)</td>
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<tr>
<td>Severe</td>
<td>24 (60)</td>
<td>16 (40)</td>
<td>2 (5)</td>
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</table>
TABLE 3

EFFECT OF OLIVE OIL THREE TIMES A DAY ON SIGNS
DRYNESS (LICHEN SIMPLEX CHRONICUS) ACCORDING
TO AGE GROUP IN FEMALE (n=40)

<table>
<thead>
<tr>
<th>Age group and severity of clinical signs</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>One week No. (%)</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-20 years (n=10)</td>
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<td></td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (20)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Severe</td>
<td>8 (80)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Group B1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30 years (n=10)</td>
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<td></td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (30)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Severe</td>
<td>7 (70)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Group B2</td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>1 (10)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (30)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (60)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Group B3</td>
<td></td>
<td></td>
</tr>
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</tr>
<tr>
<td>None</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (50)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (50)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-50 years (n=40)</td>
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</tr>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
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<td>1 (2.5)</td>
</tr>
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<td>22 (55)</td>
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<tr>
<td>Severe</td>
<td>26 (65)</td>
<td>17 (42.5)</td>
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### TABLE 4

**EFFECT OF OLIVE OIL THREE TIMES A DAY ON SYMPTOMS**

**PRURITUS (LICHEN SIMPLEX CHRONICUS) ACCORDING TO AGE GROUP IN FEMALE (n=40)**

<table>
<thead>
<tr>
<th>Age group and severity of symptoms</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>One week (%)</td>
<td>Two weeks (%)</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-20 years (n=10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (20)</td>
<td>2 (20)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Severe</td>
<td>8 (80)</td>
<td>8 (80)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Group B1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30 years (n=10)</td>
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<td></td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>2 (20)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (40)</td>
<td>4 (40)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (50)</td>
<td>4 (40)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Group B2</strong></td>
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<td></td>
<td></td>
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<tr>
<td>31-40 years (n=10)</td>
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<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>1 (10)</td>
<td>1 (10)</td>
<td>5 (50)</td>
</tr>
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<td>9 (90)</td>
<td>5 (50)</td>
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</tr>
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<td><strong>Group B3</strong></td>
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<td>41-50 years (n=10)</td>
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</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>1 (10)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (50)</td>
<td>6 (60)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (50)</td>
<td>3 (30)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
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</tr>
<tr>
<td>10-50 years (n=40)</td>
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<tr>
<td>None</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>1 (2.5)</td>
<td>4 (10)</td>
<td>16 (40)</td>
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<td>25 (62.5)</td>
<td>15 (37.5)</td>
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TABLE 5

EFFECT OF OLIVE OIL THREE TIMES A DAY ON CLINICAL SIGNS

DRYNESS OF SKIN (PRURITUS SENILIS) IN MALE (n=10) AND

FEMALE (n=10) AGE GROUP 65-75 YEARS

<table>
<thead>
<tr>
<th>Severity of clinical signs</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>One week</td>
<td>Two weeks</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>No. (%)</td>
</tr>
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<td>Group C</td>
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<tr>
<td>Male</td>
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<td></td>
</tr>
<tr>
<td>None</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>3 (30)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (60)</td>
<td>7 (70)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (40)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Group C₁</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
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<td></td>
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<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (20)</td>
<td>7 (70)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Severe</td>
<td>8 (80)</td>
<td>3 (30)</td>
<td>2 (20)</td>
</tr>
</tbody>
</table>
### TABLE 6

**EFFECT OF OLIVE OIL THREE TIMES A DAY ON SYMPTOMS**

**PRURITUS (PRURITUS SENILIS) IN MALE (n=10) AND FEMALE (n=10) AGE GROUP 65-75 YEARS**

<table>
<thead>
<tr>
<th>Severity of clinical signs</th>
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<th>After treatment</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>One week</td>
<td>Two weeks</td>
</tr>
<tr>
<td>Group C</td>
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</tr>
<tr>
<td>Male</td>
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<td>-</td>
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</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>3 (30)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (60)</td>
<td>7 (70)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (40)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Group C₁</td>
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</tr>
<tr>
<td>Female</td>
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<td></td>
<td></td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slight</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (20)</td>
<td>7 (70)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Severe</td>
<td>8 (80)</td>
<td>3 (30)</td>
<td>2 (20)</td>
</tr>
</tbody>
</table>
DISCUSSION
DISCUSSION

According to study it has been shown that adverse cutaneous reactions to topically applied olive oil are seldom reported, 77 females and 23 males have been patch tested out of them 5 patients showed positive test reactions. It is concluded that olive oil is very weak irritant (Kranke et al., 1997), whereas in present study there have been no contact sensitization in any patient given topical treatment. For elicitation of skin reactions topical challenge with the compounds in olive oil or intradermal challenge with saline as the solvent was necessary. Topical challenge with the methacrylates in ethanol failed to elicit any allergic skin reactions because of their volatility. Since methyl methacrylate has been reported to be a potent sensitizer in humans, the guinea pig model described here may be useful for scoring products before marketing (Chung and Giles, 1977). Since in the present study olive oil was applied topically which showed good results in dryness and pruritus, olive oil has been used in rheumatoid arthritis may have a protective effect on the severity of rheumatoid arthritis, this hypothesis needs verification (Linos et al., 1991). Sensitization to olive oil has not yet been reported in the German literature. A lady developed eczematous reaction after treatment of her leg with a boric acid/zinc oxide preparation in an oil vehicle. On testing olive oil proved to be positive (Jung and Holzegel, 1987).
CONCLUSION

Olive oil is a commonly used oil, as emollient, it has not been undergone to a scientific study on topical use. The present study produces an importance of this substance to control pruritus and dryness particularly in old peoples. There is a saying from every corner of this country. There is no published literature about the topical efficacy of olive oil. Excessive use of topical corticosteroids are creating problems and they cannot be used for a prolonged time. However, further investigations and development of compounds based on herbal medicines may be beneficial.
3. STUDIES OF SERUM CHOLESTEROL LEVEL AFTER ADMINISTRATION OF ISPAGHULA HUSK
# TABLES

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Group B₃ female age 61-70 years. ............................................... 179
SUMMARY
SUMMARY

Ispaghula husk belongs to the family Plantaginaceae. In Urdu it is called Isphagula, in English it is called Spogel, parts used are seeds and husk, it is mucilaginous, laxative, cooling, demulcent, emollient, it is used in the treatment of chronic constipation, amoebic and bacillary dysentery and diarrhoea due to irritable conditions of gastrointestinal tract. It also decreases serum cholesterol. It has been tried in various conditions as chronic constipation, irritable bowel, azotemia, electrolytes and bowel regulations in patients, has been tried in patients with haemorrhoids, in ulcerative colitis. It has been claimed to decrease serum cholesterol.

It was tried in hypercholesterolemia, for this purpose patients who had increased serum cholesterol level were selected both male and female from the age of 40-70 years. Males were labeled as A₁, A₂, A₃ and females were labelled as B₁, B₂, B₃ groups. In all the groups serum cholesterol level was estimated before the start of treatment and Ispaghula husk was given once daily in the dose of 5 G with a glass of water the serum cholesterol was again estimated at the end of six weeks in all the patients who completed six weeks period. In each group ten patients were placed and there were thirty males and thirty females. After investigation of the serum cholesterol it was concluded that serum cholesterol decreased in all groups showing P<0.05. It can be concluded
that this study determines that Ispaghula husk has the capability of decreasing serum cholesterol level. The results are comparable with studies performed by other investigators. Regarding published studies in Pakistan, are rare only in books it has been highlighted to have efficacy of decreasing cholesterol level.

The patients who were kept on Ispaghula husk improved their bowel habits. The same is also comparable with other studies highlighting this quality of Ispaghula husk.
INTRODUCTION
INTRODUCTION

ISPAGHULA HUSK:

Ispaghula belongs to family Plantaginaceae. In Urdu it is called Ispaghul. In English it is called Spogel. Parts used are seeds and husk.

FUNCTIONS AND ACTIONS:

They have been described by Khan et al (1997) as it is mucilaginous, laxative, cooling, demulcent, emollient, some microstatic effects on intestinal microorganisms are also attributed to the seeds and husk. As simple decoction seeds and husk are referred abundantly, as refrigerant and mildly astringent. Generally the plants are also regarded as lubricating, resolvent, local anaesthetic and anti-inflammatory.

SPECIFIC ACTION:

Glutinous, laxative.

MEDICINAL USES:

The chief use of Ispaghula husk is in the treatment of chronic constipation; amoebic and bacillary dysentery and diarrhoea due to irritable conditions of gastrointestinal tract. Crushed seeds are made into poultice applied to rheumatic and glandular swellings. It relieves constipation mechanically by forming bland mucilage which possess the mucilaginous properties, therefore during its passage through intestine, exerts soothing and protective action as demulcent, emollient and lubricant. It also decreases serum cholesterol.
REVIEW OF LITERATURE
REVIEW OF LITERATURE

Ispaghol husk has been used from a long time for bowel movements, for constipation and indigestion. Frequency of defaecation, faecal form, straining at the start and end of defaecation, feelings of incomplete evacuation of faeces and urgency of defaecation were recorded in 69 healthy volunteers during three distinct 28 day study phases: Pretreatment, treatment with ispaghula husk and post-treatment. During treatment there was a significant increase (P<0.01) in stool frequency and significant decreases in straining at the start (P<0.001) and end (P<0.001) of defaecation and in feelings of incomplete evacuation (P<0.001). There was evidence of a beneficial residual effect after treatment had stopped. There are indications that ispaghula husk (Fybogel orange) is of benefit in relieving constipation symptoms in apparently healthy people (Davies et al 1998).

Treatment of chronic constipation by a bulk-forming laxative (Fibrolax), this study was done on seventy-five patients affected by chronic constipation. They were treated for 4 weeks with an Ispaghula husk preparation, a bulk forming laxative. After treatment frequency, stool consistency, abdominal pain and signs of venous stasis improved after treatment and no important side effect was recorded. Cholesterol, HDL, HDL-cholesterol and triglycerides did not show significant changes (Borgia et al 1983). An open multicentre study was done in general
practice for comparison of ispaghula husk with lactulose and other laxatives in treatment of simple constipation efficacy, speed of action and acceptability of ispaghula husk, lactulose and other laxatives in the treatment of patients with simple constipation. A total of 65 GPs recruited 394 patients of whom 224 (56.9%) were assigned to treatment with ispaghula and 170 (43.1%) to other laxatives (mainly lactulose) for up to four weeks. Thirteen patients withdrew before treatment started, so that 381 entered the study. Patients were assessed by their GP before entry and after two and four weeks treatment. Patients also kept daily record of their bowel movement. After four weeks treatment, ispaghula husk was assessed by the GPs to be superior to other treatments in improving bowel function and in overall effectiveness, palatability and acceptability. Patients' reports of time to first bowel movement showed little difference between the treatment. Over 60% of patients in each treatment group passed a first motion within 24 hours and over 80% within 36 hours. Ispaghula husk produced a higher percentage of normal, well formed stools and fewer hard stools than other laxatives. Incidence of soiling, diarrhoea and abdominal pain were lower in the group receiving Ispaghula husk. Overall, Ispaghula husk was an effective treatment for simple constipation, and was associated with better stool consistency and a lower incidence of adverse events compared with lactulose or with other laxatives (Dettmar and Sykes 1998).
According to a study the efficacy and acceptability of mebeverine and high fibre dietary advice versus mebeverine and Ispaghula in fixed combination in the treatment of irritable bowel syndrome in adults, the study was conducted on one hundred and eleven patients with irritable bowel syndrome diagnosed by symptom profile or negative investigations between the ages of 18 and 75 years. All patients had a history of abdominal pain occurring at least once a week for a period of three months or more. Details of abdominal pain severity and frequency, bowel frequency and stool consistency were recorded by means of clinicians, assessments and patient diaries. Both treatment groups demonstrate highly significant improvements in the numbers of pain attacks and their severity no statistically significant differences between the two groups were demonstrated. Five patients in the mebeverine / dietary advice group reported five concurrent effects and nine patients in the mebeverine / Ispaghula group reported 13 concurrent effects. All of the mebeverine / dietary advice group found their treatment acceptable but upto 28% of the mebeverine / ispaghula group found their treatment impalatable. It was concluded that both treatments are effective in the treatment of irritable bowel syndrome in adults. The fixed combination of mebeverine / ispaghula, however was found to be impalatable by upto 28% of the patient in that group. These does not therefore appear to be any advantage in using fixed combination therapy in this condition (Chapman et al 1990). A placebo controlled, double blind, crossover trial
involving 20 patients was conducted to assess the effect of Ispaghula husk on the major bowel symptoms and the whole gut transit time in irritable bowel syndrome (IBS) and to determine if changes in these parameters were related to global improvement. All 20 patients were interviewed at the end of the treatment periods and 14 patients kept concurrent daily records. Ispaghula therapy resulted in improvement in global symptoms and satisfying bowel movements (p<0.001) but produced no change in abdominal pain or flatulence. There was a correlation between the improvement of well being and the number of days of satisfying bowel movements (P<0.001) but not with the indexes of pain, stool frequency or changes in the transit time. The easing of bowel dissatisfaction appears to be a major reason for the therapeutic success of ispaghula in irritable bowel syndrome (Jalihal and Kurian 1990). To examine the long-term management of irritable bowel syndrome conducted a two-part controlled therapeutic trial on 28 patients who had recovered completely after four to six weeks of treatment with Ispaghula husk and propantheline. In Part I, patient were randomly divided into two groups. Group A received a placebo capsule while group B continued with treatment as before. After six months the response to treatment was assessed according to a scoring system. The overall relapse rate in group B was 46 percent compared to 82% in group A. With continued treatment patients in group B became asymptomatic from the fourth month while patients in group A continued to deteriorate. In Part II,
patients who had relapsed whilst on placebo received active treatment. Six of the seven who agreed to continue with the study became asymptomatic within four weeks. However, all patients who were asymptomatic while an active treatment relapsed on discontinuation and again recovered on reinstitution of active treatment. It was concluded that irritable bowel syndrome is a chronic relapsing disorder and that treatment with a combination of ispaghula husk and propantheline is effective both in relieving symptoms and in the maintenance of remission (Misra et al 1989).

Treatment of chronic diarrhoea was done with loperamide versus ispaghula husk, twenty five patients with chronic diarrhoea were included in an open randomized crossover trial comparing the effect of loperamide with ispaghula and calcium. Nineteen patients completed both treatments. Before treatment the median number of daily stools was 7 (range 4-13) stool consistency ispaghula and calcium was significantly better. A combination of ispaghula and calcium seems to be a cheap and effective alternative to conventional treatment of chronic diarrhoea. Moreover side effects were minimized (Qvitzau et al 1988).

Diarrhoea is a common complication of central feeding in critically ill patients. This placebo controlled clinical trial assessed the effect of adding fibre in the form of ‘Gybobel’ (Ispaghula husk), one sachet twice daily, on the occurrence of diarrhoea during enteral feeding. Sixty eight patients without prospectively defined exclusion criteria were enterally
fed with osmotic in the intensive care unit during the study period, 35 receiving 'Fybogel' and 33 placebo. Nineteen patients in each group had diarrhea on at least 1 day during enteral feeding, with 66 (23%) feeding days complicated by diarrhea in the 'Fybogel' group and 68 (23%) in the placebo group. Narcotic infusions, thiopentone infusions, Mylanta, H₂ antagonists and Nystatin suspension did not significantly affect the incidence of diarrhea. Weak correlations were found between diarrhea and the number of antibiotics each patient received (r=0.2, P<0.05) and also the number of positive non-ental bacterial cultures (r=0.2, P<0.05) the addition of fiber in the form of 'Fybogel' to enteral feeds did not affect the occurrence of diarrhea (Hart and Dobb 1998).

Decomposition of dietary fibers in the stomach and small bowel was studied in 13 healthy male volunteers. Liquid control meals were compared with test meals in addition contained a source of fibre in random order. Aspirations were collected from the stomach, the proximal jejunum, the mid gut and the terminal ileum. Radiolabelled polyethylene glycol-4000 was used as non-absorbate water-phase marker, and the formation of free arabinose was used to quantify the hydrolysis of dietary fibres. Ingested fibers, aspirates and urine specimens were analyzed for monosaccharides, either free or fiber bound, by gas-liquid chromatography. Both types of fibers were hydrolyzed in the stomach but not in the small bowel. Of ispaghula husk, 1-6% was hydrolyzed, as was 5-8% of wheat bran. Intestinal absorption of free arabinose was 85-
93%, but excretion of arabinose in the urine was not greater than after control meals. For further evaluation of gastric hydrolysis six additional healthy male volunteers were studied by serial aspirations from the central part of the stomach. Hydrolysis was instantaneous for both fibers and was significantly more pronounced for wheat bran that for ispaghula husk (Anderson et al. 1988).

A double blind placebo controlled trial of ispaghula husk is 80 patients with irritable bowel syndrome is reported. Global assessment judged treatment to be satisfactory in 82% of patients receiving ispaghula and 53% of the placebo group (P less than 0.02). Bowel habit was unchanged in the placebo group, while constipation significantly improved in patients taking ispaghula (P=0.026). Transit time decreased significantly in those taking ispaghula compared with placebo (P=0.001) especially in patients with initially high transit times. Abdominal pain and bloating improved in both groups, with no significant differences between ispaghula and placebo. Four of the eight withdrawals on ispaghula and 10 of the 15 withdrawals on placebo were because of treatment failure. Ispaghula significantly improves overall well being in patients with irritable bowel syndrome, and in those with constipation favourably affects bowel habit and transit time (Prior and Whorwell 1987). The optimum dose of ispaghula husk was determined in the irritable bowel syndrome and was corelated relief of symptoms with whole gut transit time and stool weight in part I, 14 male patients were
given ispaghula husk in increasing doses of 10G, 20G, and 30G per day for a duration of 17 days each (14 days of study period + three days of stool collection). Ten patients completed the trial. The symptom score improved significantly with all the three doses of ispaghula. Both 20G and 30G doses of ispaghula were superior to the 10G dose but there was no significant (P less than 0.001) increase in daily stool weight with 10G dose of fiber with further significant increases with the 20G and 30G doses. A positive correlation was seen between the improvement in the symptom score and the increase in stool weight. With the 10G dose of ispaghula but not with the 20G and 30G doses. Whole gut transit time remained fairly constant throughout the study period and there was no relationship with either the dose of ispaghula, the alteration in stool weight, or the improvement in the patients symptoms (Kumar et al 1987).

Studies were done to find out the dietary fiber composition, degradation and faecal bulking capacity in rat were investigated by means of balance experiments on rats. Nitrogen fat and mineral excretion in faeces was also studied. The dietary fiber content of the various bulk laxatives was quite different: ACO fiber tablets, barley and citrus pulp, 451; Fiberform (wheat bran based) 817; Inolaxol (Sterkulia gum), 696; and Vi-Siblin (ispaghula husk), 533. The increase in faecal dry matter per 1G dietary fiber was similar with ACO fiber tablets, fiberform and Vi-Siblin. Inolaxol gave a significantly (P less than 0.001)
higher faecal dry weight increment, mainly due to an increased mineral excretion. Of the dry weight increment, 59-82% constituted undergraded dietary fiber. Thus 68.97% of the fiber passed through the gastrointestinal tract without being degraded. All the bulk laxatives caused a similar increase in faecal N content, whereas the increase in faecal lipids was most pronounced with Vi-Siblin. The water holding capacity of faeces was more pronounced with Inolaxol and Vi-Siblin than with ACO fiber tablets and Fiberform (Snyman and Asp 1985).

1. Four human subjects on strictly controlled diets were given a fiber supplement, 25G Ispaghula husk (Isogel)/day for 3 weeks.

2. Replicate diets and faeces were collected during two 5 days balance periods. The first period served as control for the second, which occurred after the supplement had been fed for 2 weeks.

3. Diets and faeces were analysed for total solids, gross energy, total nitrogen, fat, available and unavailable carbohydrates.

4. Three of the four subjects showed a considerable increase in faecal bulk. Total faecal weight was more than doubled in two subjects. In two subjects the increase was brought about mainly by extra fiber in the faeces accompanied by a higher proportion of faecal water whereas in one subject it was also an increased excretion of nutrients. One subject showed very little change in faecal bulk.
5. High values for the apparent digestibility of fiber were found during the control period from 0.70 to 0.80. There was more variation during the experimental period when apparent digestibility of total fiber ranged from 0.47 to 0.82. Values arrived at for the minimum apparent digestibility of the fiber supplement were generally high; one subject appeared to digest Isogel completely. Isogel was degraded preferentially to the food derived fiber, in particular, cellulose in the faeces was increased during the experimental period.

6. Only one subject showed distinct decreases in the apparent digestibility of energy, N and fat in diet. The results do not therefore agree with the generally held view that increased fiber in the diet decreases the apparent digestibility of the other nutrients (Prynne and Southgate 1979).

Irritable bowel syndrome was treated with lorazepam, hyoscine butylbromide and Ispaghula husk. In this regard, a double blind controlled therapeutic trial of factorial design was used to study the therapeutic effects of lorazepam, hyoscine butylbromide and Ispaghula husk in 12 randomized blocks of eight patients with the irritable bowel syndrome. Each of the three agents caused a sustained symptomatic improvement in some of the patients, although only with ispaghula was the difference between the real and dummy preparation statistically significant. When the eight possible combinations of treatment were
analysed none of the 12 patients who received only dummy preparations of the three agents had maintained any improvement over the three months of trial seven patients improved among the 12 who received potent preparations of all three agents, and between four and six patients improved in the groups receiving one or two of the potent preparations. These therapeutic results are not promising but Ispaghula husk used for irritable bowel syndrome is effective (Ritchie and Truelove 1979).

A fiber made psyllium husk was given to 12 elderly patients for 4 months in order to investigate their faecal output and selected serum parameters. The fiber significantly improved bowel function and faecal output confirming its values as a non-irritant, harmless bulk forming laxative. Serum cholesterol was decreased by 20% while triglycerides remained unchanged. There was a significant reduction in serum calcium after withdrawal of the fiber supplement. No significant changes in the serum iron present, and in total iron binding capacity, fibrinogen or in the haematological parameters, attributable to the fiber. The high phytate content of the fiber does not appear to have any clinically significant effect on mineral absorption. It is suggested that dietary fiber may have significant cholesterol lowering capacity due to the binding of bile-acids in the intestine (Burton and Manninen 1982).

Animal experiments were performed to find out the effect of dietary psyllium hydrochloride and lignin on bile. The experiments suggest that
supplementing the diet with either psyllium seed husk or lignin alters the ratio of deoxycholic acid to chenodeoxycholic in bile. In the study dosages of psyllium seed husk or lignin acceptable to patients with gallstones do not appear to alter the relative amounts of cholesterol or individual bile acids in bile (Brydon et al 1979).

In patients with haemorrhoids the bulk evacuant have been used, to perform experiments. Fifty three patients with symptomatic haemorrhoids have been studied in a double blind cross-over trial of a bulk forming agent (Ispaghula husk) against a placebo. Although only 11 percent of patients complained of constipation a significant benefit in symptoms and improved bowel habit was demonstrated (Webster 1978).

Fourteen out of 18 patients (78%) had abnormal function 32 months after the modified soave pull-through procedure for Hirschsprung's disease. The abnormalities were loose stools perianal excoriation, sibiling and retal prolapse. Excoriation was caused by stools containing an excess of water, particularly in the extractable, phase with raised Na+ and chloride (Postuma and Corkery 1976).

After doing a clinical trial of effect of acute dietary fibre supplementation on colonic pH in healthy volunteers and it was demonstrated the ability of dietary fibre to lower right colonic pH and to increase breath hydrogen excretion. The changes were greater with
soluble fibre than with insoluble fibre but the change in luminal pH was persistent all round the colon with insoluble fibre (Naedder et al 1998).

The effect of psyllium on mucin secretion was determined by comparing water soluble and insoluble fractions of excreta from germ free rats fed a fibre free (FF) diet or a diet containing pyrillium seed husk. Excreta from the same rats after colonization with a rat mixed cecal culture were separated with water soluble, plant and bacterial fractions to compare to the remaining carbohydrate and the mass of bacteria. The sugar composition and water solubility of carbohydrate in excreta from germ-free rats fed fiber-free diets indicated that a primary fermentable substrate was mucin ptylin seed husk increased fecal excretion of mucin derived sugars almost three fold in germ-free rats. Fecal carbohydrate was reduced from 619 to 237 μmol/g of dry feces and mostly in the bacterial fraction when rats fed on faecal free diet were colonized. The total sugar content and the amount of muramic acid, but not bacterial counts and mass, indicated that psyllin seed husk increased faecal bacteria. Fractionation of excreta from PS-fed rats was complicated by a gel which based on sugar composition was psyllium seed. Sugar composition of the water soluble fraction from excreta from PS-fed rats suggested that it contained some bacterial component, possibly exopolysaccharides and some of the PS but not mucin. PS digestibility ranged from 60-80% depending on what faecal fraction was used for output. Because of the presence of PS-derived sugars in the gel
and soluble fractions. It was not possible to determine which if any, of
the PS digestibilities was correct (Cabotaje et al 1994).

A high intake of dietary fiber has been hypothesized to decrease
the risk of colorectal cancer. This hypothesis has been tested by
performing experiments. This study evaluated the effect of fiber on
adenoma size in patients with familial polyposis and an intact rectum
and the other four studies are focusing on the recurrence of adenoma in
patients with previous adenomas. The results available so far provide
some evidence for the inhibition of adenoma growth through a high fiber
and/or low fat diet. Further results are expected within a year. If there is
sufficient evidence for a protective effect of dietary fiber on colorectal
carcinogenesis, a simple, safe and expensive prophylaxis for a very
common cancer will be indicated (Faivre and Giacosa 1998).

Taurocholic acid adsorption during non-starch polysaccharide was
done *in vitro* study. A human faecal inoculum was incubated with 24-
14C taurocolic acid and several non-starch polysaccharide sources,
glucose or a substrate free control. Portions of fermentation mixture
were taken at 0, 3, 6, 21 and 24h and centrifuged to acquire a
supernatant fraction and a pellet containing the fermentation residue.
14C was measured in supernatant fraction and pellets at all time points.
Volatile, fatty acids were measured at 0 and 24h to confirm bacterial
growth. Radioactivity in the pellet increased overtime for all substrates.
Glucose resulted in the greatest incorporation of taurocholic acid into
the pellet, followed by pectin. At 24h the proportion of the total radioactivity found in the pellet was 92% for glucose, 79% for pectin, 60% for wheat bran, 59% for ispaghula seed, 53% for ispaghula husk and 26% for the control (mean of duplicates). Glucose and pectin produced the greatest quantity of VFA (volatile fatty acid) at 24h. VFA production was highly correlated with radioactivity in the pellet (r=0.976, P<0.005). These results suggest that the bile binding capacity of a faecal culture mixture may be strongly influenced by the fermentability of the available substrate and hence related to bacterial metabolic activity (Gelissen and Eastwood 1995).

According to a cecal model fermentation in ileorectal and ileal pouch, the fecal concentrations of total short chain fatty acids were normal in 16 patients with ileorectal anastomoses (mean ±SEM, 99.7±10.3 mmol/L) and 28 patients with ileal pouch anal anastomoses (138.8±8.5 mmol/L) and did not differ from those in 14 healthy non-colectomized controls (130.7±12.6 mmol/L). Acetate : propionate : butyrate : isobutyrate + valerate + isovalerate ratios were similar in the ileorectum (71:12:12:5%) and in the colorectum (66:14:13:7%) of healthy non-colectomized controls, whereas the concentration of acetate was increased at the expense of the polypeptide-derived isobutyrate, valerate, and isovalerate in the ileal pouch (77:12:11:1%). Ammonia was accordingly significantly diminished in ileal pouch contents (28.8±3.2 mmol/L vs 45.2±4.1 mmol/L) concentrations of lactate were normal and
low. Twenty four hours productions of total short-chain fatty acids in 16.6% fecal homogenates from both groups of patients were normal. Addition of saccharides (e.g. glucose, starch, pectin, ispaghula husk) increased the production of acetate propionate, and butyrate and decreased the production of ammonia and isobutyrate, valerate and isovalerate, which was increased in homogenates with allumin added. This pattern of substrate fermentation was similar in homogenates from ileal pouch, ileorectum, and control colorectum. In conclusion, the concentrations of short chain fatty acids, lactate and ammonia indicate that ileorectal fermentation resembles normal colorectal fermentation in non-colectomized healthy individuals, whereas the fermentation in ileal pouch contents seems to be more carbohydrate predominated (Nordgaard-Andersen et al 1993).

Intestinal structure of male adult African green monkeys (Cercopithecus aethiops ssp. vervets) was studied after 3½ years of consuming diets containing 10% psyllium husk of cellulose. Scanning electron microscopy (SEM) identified mild damage (cellular swelling and disarray, and microvillar denudation and disarray) at villous tips throughout the small intestine in the psyllium-fed monkeys. The cellulose group had similar duodenal damage. Differences were not found in colons by SEM. By light microscopy, jejunum had shorter villi with psyllium feeding based upon villous height (P less than 0.05) and length around a sectioned villus (P less than 0.1) but not based upon the
number of enterocytes per villus. Jejunal and ileal circular and longitudinal muscle layer thickness were increased in psyllium-fed monkeys. Colonic mucosal height was significantly (P less than 0.05) reduced and muscle layer thickness was mildly reduced in the psyllium-fed monkeys. Group differences were not found in intestinal weight or length or in the weight of small intestinal mucosal scrapings. Psyllium husk may cause epithelial cell loss and muscle layer hypertrophy in jejunum and ileum and thinning of the colonic wall after prolonged feeding (Panlini et al 1987).

According to a study, tumors were induced in one-half of the rats fed each diet by the gastric intubation of 1,2-dimethylhydrazine (DMH) during weeks 3-11. In terms of the number of animals with tumors in each group, psyllium strongly reduced the tumorigenicity of DMH and cellulose moderately reduced tumorigenicity, whereas the two fibers did not differ significantly from each other with respect to tumorigenicity. Psyllium-fed rats had the highest fecal aerobic counts, lowest β-glucuronidase, and highest 7-α-dehydroxylase activities. The psyllium diet also resulted in increased fecal output and percent moisture. Rats fed cellulose tended to have greater fecal bulk and lower β-glucoronidase activity compared with rats fed on fiber and lower 7-α-dehydroxylase activity compared with rats fed psyllium husk (Roberts-Anderson et al 1987).
In a study the effect of ispaghula husk on colonic motility of the right and left side was examined in 10 patients with left sided diverticular disease using an untethered pressure sensitive radiotelemetry capsule. After treatment ispaghula husk reduced mouth to rectum transit by a median of 8.8 hours and the time to mid transverse colon by five hours. In the right colon there was an increase in the median percentage activity of 7% and the median number of pressure waves greater than 5 mm Hg/hour rose by 35.3. Motility changes in the left colon were less pronounced. Five of the seven patients with abdominal pain and six of the nine patients with altered bowel habit responded to treatment. These results suggest that it is ispaghula husk's action on the right unaffected colon which alleviates the symptoms of left sided diverticular disease [Thorburn et al 1992]. In metachronous adenomas of the large bowel randomized trial of calcium and fiber was done at European multicentric intervention study, it was done to test the efficacy of oral calcium supplementation with 2G calcium per day and oral dietary supplementation with mucilaginous substances on adenoma recurrence, secondary aims were to study the treatment efficacy on colonic cell proliferation and on stool bile acid and sterol concentration. Serum and plasma samples were also collected. To better interpret the effect of the intervention, a diet history questionnaire and an aspirin and anti-inflammatory drug questionnaire are administered. The aim will be achieved through a randomized placebo-
controlled clinical trial using a parallel design in patient aged 35 to 75 at entry with a complete colonoscopy and a clean colon. Overall, 655 subjects have been included. All randomized patients were followed up every six months for 3 years. If one of the evaluated interventions proves efficient, the benefits of a simple, safe and inexpensive prophylaxis for a very common cancer will be clear [Faivre et al 1997].

The efficacy of ispaghula husk in relieving gastrointestinal symptoms in patients with ulcerative colitis in remission was studied in a placebo-controlled trial running for 4 months. Twenty-nine patients (81%) completed the trial, four withdrew after colitis relapse (three while receiving placebo). Grading of symptoms judged ispaghula to be consistently superior to placebo (P less than 0.001) and associated with a significantly higher rate of improvement (69%) than placebo (24%) (P less than 0.001). The results show that ispaghula can be helpful in the management of gastrointestinal symptoms in quiescent ulcerative colitis (Hallert et al 1991).

The fermentation of carbohydrate in rat ileal excreta is enhanced with cecal inocula compared with fecal inocula. The differential fermentative capacities of microflora from two regions of the large bowel and how fermentation was altered by prior exposure of the microflora to the substrate to be fermented were studied using an in vitro fermentation system. It was concluded that using cecal microflora as the inoculum source provides a more accurate index of fermentation during transit
through the large bowel and that non-cellulosic and storage polysaccharides of the plant cell wall are utilized before cellulose (Monsma and Marlett 1996).

In a study urea kinetics were measured by using prime/intermittent oral doses [15N15N] urea in five healthy men taking formula diets adequate in energy and containing either 70 or 35 G of protein/day.

1. In some studies the low-protein diet was supplemented with non-starch polysaccharides in the form of ispaghula husk or ripe bananas.

2. On the 70G of protein/day diet urea production was 132% of intake. Only 54% of the urea produced was excreted in the urine with 46% being salvaged in the colon; 90% of the salvaged nitrogen was retained in the metabolic nitrogen pool.

3. On the 35G of protein/day diet the small decrease in urea production rate compared with that on the 70G of protein/day diet was not significant, but only 36% of the urea produced was excreted in urine, with the majority, 64% being salvaged.

4. The extent of urea-nitrogen salvaging on the 35G of protein/day diet was similar in magnitude to the decrease in nitrogen intake, with the effect that the sum of intake and salvaged nitrogen did
not differ between the 35 and the 70G of protein/day diets. This implies that quantitative control is exerted over the rate at which urea nitrogen is salvaged.

5. The addition of non-starch polysaccharides to the 35G of protein/day diet had a demonstrable effect upon fecal weight and composition but did not exert any significant influence upon urea kinetics (Langran et al 1992).

Studies were done to compare the effects on colon function caused by feeding ispaghula husk and polydextrose, polydextrose is a new soluble food ingredient which cannot be digested by intestinal enzymes and so may affect colonic function. Studies in healthy volunteers compared the effects of diet supplementation with 30G/day polydextrose, a standard dose of 7G/day ispaghula and two mixtures containing 2G/day ispaghula with either 30G/day polydextrose or polydextrose with a control period. During the 10-day periods, the mass, frequency and consistency of faeces were assessed as well as the whole gut transit time. Ease of defaecation, flatulence and palatability of the preparations. All preparations significantly increased the weekly faecal mass above control values (P less than 0.05) but there were no significant differences between the preparations. Transit time and stool frequency were not affected significantly by any of the preparations. Both preparations supplying 30G/day polydextrose softened stool frequency were not affected significantly by any of the preparations (P greater than
0.05). Both preparations supplying 30G/day polydextrose softened stool consistency equally but the other preparations had no effect.

The studies done on the diet of six normal and five ileostomy subjects was supplemented with 10G/day plantago ovata psyllium husk for 3 weeks while six normal and four ileostomy subjects received 10G/day psyllium seed. Fecal and ileostomy output sterol excretion, serum cholesterol and triglycerides were measured before and after supplementation. The husk had no effect on cholesterol or triglyceride concentration in either normal or ileostomy subjects. Total and high density-lipoprotein-cholesterol concentrations were reduced on average by 6.4% and 9.3% respectively, in the normal group after seed supplementation. No effect on fecal bile acid excretion in normal subjects was found after both regimes. Ileostomy bile acids were increased after seed supplementation, whereas no effect on cholesterol concentration was found. According to this study it was concluded that psyllium seed might be more effective than the husk in reducing serum cholesterol, that this cholesterol-lowering effect is not mediated by increased fecal bile acid losses, and increased ileal losses of bile acids might be compensated for enhanced reabsorption in the colon (Gelissen et al 1994).

Colonic fermentation of ispaghula, wheat bran, glucose and albumin to short chain fatty acids and ammonia evaluated in vitro in 50 subjects and it was concluded that different colonic flora from a large
number of subjects share general biochemical characteristics, which metabolize different substrates to specific patterns of ammonia and short-chain fatty acids (Mortensen and Nogard-Andersone 1993).
DISORDERS OF LIPID METABOLISM:

Cholesterol and triglycerides are insoluble and are transported between the intestine, liver and periphery in the form of soluble complexes known as lipoproteins. These circulate as spherical particles with an envelop of phospholipid and apoproteins and at non-polar lipid core. They can be divided by density, configuration and electrophoretic mobility into chylomicrons. Very low-density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs) and high-density lipoproteins (HDLs).

Chylomicrons are large particles composed mainly of triglycerides. They are synthesized in the small intestinal mucosa and provide the main form of transport for dietary fat. They also contain phospholipid, a small amount of cholesterol, apoprotein B-48 (apo B-48) and apo A-I, A-II, and acquire apo C-II and apoE, transferred from HDLs. Chylomicrons give the post-prandial plasma a lactescent appearance that normally clears within a few hours. The chylomicrons are catabolized to form chylomicron remnants by lipoprotein lipase (activated by apo C-II) in peripheral tissues as well as by hepatic lipase. Triglyceride is progressively removed by lipolysis to remove free fatty acids. Some apo A-I, A-II and apo C are transferred to HDLs, chylomicron remnants are eventually taken up by specific apo B and apo E receptors in the liver.
VLDLs are synthesized mainly in the liver and represent endogenous triglyceride synthesis. They contain apo B100 and apo. VLDLs are also catabolized by lipoprotein lipase in the peripheral tissues. The breakdown of VLDLs and transfer of some apoproteins HDLs give rise to smaller, denser remnant particles some of which can be identified as IDLs.

IDLs are taken up by the hepatocyte LDL receptors by binding to the apo E on the IDL surface. Alternatively, IDLs are converted by further hydrolysis of triglycerides (probably by hepatic lipase) to LDLs.

LDLs are the major cholesterol-carrying lipoprotein in normal plasma, their main protein being (as for VLDLs) apo B-100. The majority of LDLs enter the liver cells after binding to high-affinity receptors found in the coated pit region that recognize apo B-100. After binding, the LDL is internalized and metabolized, releasing free cholesterol that partly contributes to endogenous cholesterol.

A 'scavenger pathway' is also available to clear LDLs. An acetyl-LDL receptor is available in many tissues including macrophages and sinusoidal endothelial cells in the liver. These specifically take up LDLs that have been modified by oxidation. It is this mechanism that seems to convert macrophages to foam cells found in the fatty streak, the earliest lesion in atherosclerosis.
HDLs are produced in the liver and intestine and contain 20-50% of circulating cholesterol. HDLs are the substrate for lecithin cholesterol acyl transferase (LCAT) which catalyses the conversion of free cholesterol to cholesterol ester and also lecithin to lysolecithin. Apo A-I and A-II are the major proteins. This heterogenous group of particle may be involved in reverse cholesterol transport (i.e. from the periphery back to the liver).

The enzyme lipoprotein lipase (LPL) is situated in the capillary endothelium of most tissues and is formed as a precursor. It is activated by apo C-II on the surface of chylomicrons and VLDLs. The activity of this enzyme regulates the hydrolysis of all triglyceride-rich proteins.

GENETIC CONTROL:

So far genes for 10 apolipoproteins and 4 lipoprotein processing proteins have been isolated, sequenced and mapped on chromosomes 1, 2, 3, 6, 8, 11, 15, 16 and 19. The gene for the LDL receptor is on the short arm of chromosome 19. Hyperlipidaemias can be divided into a group of rare but relatively well-defined single gene disorders and a larger group, presumably polygenic in which genetic and environmental factors overlap.

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS:

There is a well-established association between atherosclerosis and plasma cholesterol, but even stronger associations appear when the cholesterol carrying LDL and HDL lipoprotein fractions are considered.
LDL cholesterol levels are predictive of coronary heart disease, but an inverse relationship is seen with HDL-cholesterol, so that high levels appear to be protective.

Cholesterol deposited in atheromatous lesions is derived from LDL and enters the lesion at a rate-dependent upon the plasma concentrations. The protective role of HDL may be in mediating hepatic cholesterol excretion by reverse transport of cholesterol from the periphery.

The atherogenecity of triglyceride-rich lipoprotein is less clear but these are strong epidemiological associations with ischaemic heart disease and peripheral vascular disease. Marked hypertriglyceridaemia carries a risk of pancreatitis and is another indication for treatment.

In males the incidence of coronary heart disease is least in those with cholesterol values below 5.2 mmol-L\(^{-1}\), rises linearly to a level of 6.5 mmol-L\(^{-1}\), and rises even more steeply above this point. Since the population mean lies around 5.6 mmol-L\(^{-1}\). The inference is that most people in western societies might benefit from having a lower cholesterol, especially since there is now evidence that lowering cholesterol does indeed reduce the incidence of coronary heart disease. These observations have profound social implications, while incidentally generating an enormously profitable market for the pharmaceutical industry.
Some benefit might be derived from dietary modification and attention to other potential coronary risk factors. There is at present little evidence to support routine screening for cholesterol in the healthy population.

Modification of diet reduces cholesterol by 15-25% and triglyceride by 20-40%. Diet modification alone is therefore appropriate for those in the cholesterol range from 5.2-6.4 mmol L\(^{-1}\) and is usually adequate from 5.2-6.4 mmol L\(^{-1}\) and is usually adequate for those in the range from 6.8-8 mmol L\(^{-1}\). Above 8 mmol L\(^{-1}\), further investigation for underlying disease (e.g. hypothyroidism) and to characterize the lipoprotein disorder is called for. Diet remains the basis of therapy and lipid lowering agents are an adjunct. Advice should be geared to the individual patient rather than to the biochemistry report. For example, obesity and other coronary risk factors need to be taken in to account and a more aggressive approach is called for if the patient is young, has established arterial disease or has a strong family history of this. Conversely the relative risk of hypercholesterolemia is reduced in women and diminishes with increasing age.

**THE HYPERLIPIDEMIAS:**

**CLINICAL FEATURES:**

Features associated with hyperlipidemia include:

- Xanthelasma (cholesterol deposit on the eyelid).
- Premature arcus in the cornea.
• Xanthomas (cholesterol deposits in the skin).
• Rarely, lipaemia retinalis (turbid blood in the retinal vessels).

**INVESTIGATION:**

Initial investigation involves measurement of the fasting cholesterol and triglyceride levels.

The patient follows his normal diet for the preceding 2 weeks and drugs that may affect lipid metabolism are withdrawn. The results may be influenced by acute illness, but the test may be performed soon after myocardial infarction and any high levels confirmed before treatment is started.

Values should be assessed according to the age of the patient. Results over the 95 percent should be investigated further, including measurement of HDL-cholesterol and lipoprotein electrophoresis.

Examination of stored serum provides useful information, a diffuse milky appearance usually means raised VLDL, whereas a creamy upper layer with clear plasma beneath indicates chyomicronaemia. Family members should be investigated when a primary hyperlipidaemia is suspected.

**GENERAL MANAGEMENT OF HYPERLIPIDAEMIAS:**

**General Principles:**

• The maintenance of a lean body weight.
• A low fat diet.
• Avoidance of alcohol.
• Avoidance of oestrogens and thiazides.
• Avoidance of smoking.
• The treatment of diabetes and hypertension when present.
• Moderate exercise.

**Lipid Lowering Agents:**

• Reduced synthesis of VLDLs and LDLs.
• Enhanced VLDL clearance.
• Enhanced LDL catabolism (e.g. cholestyramine, which is a non-absorbable anion exchange resin that binds bile acids in the gut lumen, thus reducing the enterohepatic circulation and enhancing cholesterol conversion to bile acids).
• HMG-Co-A reductase inhibition.

Drugs such as simvastatin inhibit this rate-limiting enzyme in cholesterol synthesis and consequently there is an increase in LDL receptor expression.

Cholestyramine reduced the incidence and progression of coronary disease in a large cohort of American men with raised cholesterol levels. Until wider clinical experience has been obtained, simvastatin should be reserved for resistant hypercholesterolaemia.
CLASSIFICATION OF HEREDITARY HYPERLIPIDAEMIAS:

This is complex and many find it confusing. This is because the standard Fredrickson/WHO classification is based on patterns found during laboratory analysis rather than on disease entities. These patterns may result from a variety of disease processes and sometimes overlap. Familial hypercholesterolaemia is characterized by hypercholesterolaemia due to raised LDL levels, there can be mild elevation in triglycerides and VLDLs. It is autosomal dominant in inheritance with an incidence of 1:500 heterozygotes in the population. The metabolic defect is related to binding and internalization of LDL to its receptor protein. A familial apo B-100 defect giving raised LDLs has recently been described.

Heterozygotes often develop coronary artery disease between the third and fourth decade of life and account for 5% of survivors of myocardial infarction under the age of 60. Premature arcus and xanthomas may be present and cholesterol levels are markedly elevated. Homozygotes have grossly elevated cholesterol and marked xanthomatosis and develop coronary artery disease whilst in their teens.

Treatment is with a low cholesterol diet, cholestryramine and nicotinic acid and can be very effective if this regimen is followed conscientiously. In refractory cases simvastatin should be used.
FAMILIAL DYS-β-LIPOPROTEINAEMIA:

This is characterized by raised cholesterol and triglyceride levels due to raised IDLs and chylomicrons remnants. The defect is due to an abnormal form of apoprotein E-Apo E₂ which fails to bind to specific receptors, so that lipoproteins are not cleared. The disease develops in adult life and is often associated with obesity, glucose intolerance and hyperuricaemia. Palmar xanthomas may be present and are diagnostic. The risk of coronary artery and peripheral vascular disease is increased.

Treatment is by weight reduction and reduced dietary cholesterol and fat. Nicotinic acid may also be necessary.

Familial hypertriglyceridaemia is an autosomal dominant disorder associated with raised VLDLs. The exact mechanism is unclear. There is an association with diabetes. It is exacerbated by a number of environmental factors including obesity, alcohol diuretics (thiazides) and contraceptive pill and glucocorticoids. Treatment is with weight reduction, low fat diet, alcohol avoidance, careful control of diabetes and oral gemfibrozil for patients with very high triglyceride levels. The risk of coronary disease is small.

FAMILIAL COMBINED HYPERLIPIDAEMIA:

This common disorder has raised cholesterol and triglyceride levels and has an increased risk of coronary artery disease. The precise mechanism is unclear but it is probably related to dysfunction of apo B.
Lipoprotein lipase or apo C-II deficiency is a rare autosomal recessive condition and is characterized by the presence of chylomicrons in fasting plasma. Chylomicrons cannot be metabolized due to deficiency of extrahepatic, LDL or its co-factor apo C-II.

Patients present in childhood with hepatosplenomegaly, eruptive xanthomas and lipaemia retinitis; some experience recurrent pancreatitis. Despite the raised triglyceride levels there is little evidence of premature vascular disease. Treatment is with a strict low fat diet. Fish oils, containing polyunsaturated ω-3 fatty acids are also used.

**HYPOLIPIDAEMIA:**

Low lipid levels can be found in severe protein energy malnutrition. They are also seen occasionally with severe malabsorption and in intestinal lymphangiectasia.

**FAMILIAL α-LIPOPROTEIN DEFICIENCY:**

One of the two HDL apoproteins, apo A-1, is deficient in homozygotes with this very rare disease so that there is little HDL in plasma. Tangier disease is inherited as an autosomal recessive The serum cholesterol is low but serum triglycerides are normal or high. Cholesterol accumulates in reticuloendothelial tissue. Although the mechanism is uncertain, producing enlarged and orange coloured tonsils and hepatosplenomegaly. There are also corneal opacities and a polyneutropathy.
# LIPIDS - LOWERING AGENTS:

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ion exchange resins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>12-24 G daily</td>
<td>Gastrointestinal side effects e.g. constipation, indigestion, nausea. Increased VLDL unsuitable for hypertriglyceridaemia.</td>
</tr>
<tr>
<td><strong>Fibrates</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bezafibrate</td>
<td>200 mg three times a day with food</td>
<td>Well tolerated</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>600 mg twice daily</td>
<td></td>
</tr>
<tr>
<td><strong>Nicotinic acid derivatives</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid</td>
<td>100-200 mg initially</td>
<td>Flushing and GIT upset</td>
</tr>
<tr>
<td></td>
<td>1-2 G TDS maximum</td>
<td>Limit tolerance</td>
</tr>
<tr>
<td>Probufol</td>
<td>500 mg BD (with food)</td>
<td></td>
</tr>
<tr>
<td><strong>HMG CoA reductase inhibition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>10-40 mg taken in the evening</td>
<td>Not fully evaluated. Resistant cases only. Caution with liver disease</td>
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</table>
PURPOSE OF STUDY

Ispaghula husk is the commonly available plant origin drug. It is commonly used in Pakistan, the main purpose of its use is to relieve constipation or to give it to the individuals to improve bowel habits. In Pakistan the land is full of useful plants, they can be used as medicines. A large number of drugs of plant origin are available. The villages of Pakistan have more population than the cities. Some plant origin drugs are easily approachable for them. The changes in the weather, changes in environment are very important for the treatment of ailing man. Aspaghol has been used for many ailments and hyperpyrexia to relieve thirst, dysentery, to relieve constipation.

This drug is known almost to every individual. It has been observed that the individuals who take this drug their cholesterol level becomes normal. The review of literature also points out its use, in hypercholesteorlemia. The literature regarding research on Ispaghol is very scanty rather not available. In the locally published books its usefulness has been highlighted but no research has been recorded about this useful medicine. Research publications are not available though some practitioners claim its efficacy, considering this viewpoint a study has been performed to determine its efficacy on hypercholesterolemia.
MATERIALS AND METHODS
MATERIAL AND METHODS

The study was performed on the male and female subjects having hypercholesterolemia, for this purpose patients from the age group of 40 to 70, both males and females were placed in groups like:

**MALES***:

- $A_1$ age group 40-50 years.
- $A_2$ age group 51-60 years.
- $A_3$ age group 61-70 years.

**FEMALES***:

- $B_1$ age group 40-50 years.
- $B_2$ age group 51-60 years.
- $B_3$ age group 61-70 years.

In each group there were ten patients.

The patients suffering from hypercholesterolemia were registered for this study. The patients were collected from Baqai Medical University Hospital and from charitable clinics. Serum cholesterol level was estimated before the start of the treatment and after six weeks. Ispaghula husk was given once daily in dose of 5G orally with a glass of water. The patients were instructed to continue the treatment for six weeks, those patients who did not cooperate were dropped out from this study. The serum cholesterol was again estimated at the end of six weeks and comparison was noted down.

* Normal range of serum cholesterol = upto 220 mg/dL
RESULTS AND OBSERVATION
RESULTS AND OBSERVATIONS

TABLE 1 – MALES:

In age group A₁ (40-50 years) serum cholesterol was measured and it was 243±4.9 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 228±3.8 with P<0.05.

In age group A₂ (51-60 years) serum cholesterol was measured and it was 258±5.5 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 248±5.3 with P<0.05.

In age group A₃ (61-70 years), serum cholesterol was measured and it was 260±2.7 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 246±5.2 with P<0.05.

In total number of patients i.e. 30, the calculation was done and before treatment it was found 254±8.8 mg/dL and after treatment it decreased to 240±10.1 with P<0.05.

TABLE 2 – FEMALES:

In age group B₁ (40-50 years) serum cholesterol was measured and it was 257±7.4 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 242±6.1 with P<0.05.
In age group B2 (51-60 years) serum cholesterol was measured and it was 258±5.2 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 248±5.0 with P<0.05.

In age group B3 (61-70 years), serum cholesterol was measured and it was 255±8.7 mg/dL before the start of the treatment and after treatment with Ispaghula husk it decreased to 247±7.7 with P<0.05.

The calculation was done in total number of patients i.e. 30. The serum cholesterol was 255±9.4 mg/dL before the start of treatment and after treatment with Ispaghula husk it decreased to 244±7.8 with P<0.05.

Patients who were kept on Ispaghula husk have also improved their bowel habits (an additional benefit).
TABLE 1

EFFECT OF ISPAGHULA HUSK ON SERUM CHOLESTEROL
ACCORDING TO AGE IN MALES (n=30)

EACH GROUP (n=10)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age group (years)</th>
<th>n</th>
<th>Serum cholesterol mg/dL</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before treatment (Mean±S.D.)</td>
<td>After 6 weeks treatment (Mean±S.D.)</td>
</tr>
<tr>
<td>A₁</td>
<td>40-50</td>
<td>10</td>
<td>243±4.9</td>
<td>228±3.8</td>
</tr>
<tr>
<td>A₂</td>
<td>51-60</td>
<td>10</td>
<td>258±5.5</td>
<td>248±5.3</td>
</tr>
<tr>
<td>A₃</td>
<td>61-70</td>
<td>10</td>
<td>260±2.7</td>
<td>246±5.2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>30</td>
<td>254±8.8</td>
<td>240±10.1</td>
</tr>
</tbody>
</table>
TABLE 2

EFFECT OF ISPAGHULA HUSK ON SERUM CHOLESTEROL

ACCORDING TO AGE IN FEMALES (n=30)

EACH GROUP (n=10)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age group (years)</th>
<th>n</th>
<th>Serum cholesterol mg/dL Before treatment (Mean±S.D.)</th>
<th>After 6 weeks treatment (Mean±S.D.)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B₁</td>
<td>40-50</td>
<td>10</td>
<td>257±7.4</td>
<td>242±6.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>B₂</td>
<td>51-60</td>
<td>10</td>
<td>258±5.2</td>
<td>248±5.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>B₃</td>
<td>61-70</td>
<td>10</td>
<td>255±8.7</td>
<td>247±7.7</td>
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</tr>
<tr>
<td>Total</td>
<td></td>
<td>30</td>
<td>255±9.4</td>
<td>244±7.8</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
DISCUSSION
DISCUSSION

Lowering cholesterol levels by natural dietary modification is an attractive first line option for the treatment of mild to moderate hypercholesterolaemia. The addition of soluble fibers for example, psyllium to the modified diet has produced better results. In this study the cholesterol-level lowering effect of Ispaghula husk was compared before the start of the treatment and after completion of treatment for six weeks. Ispaghula treatment was given in the dose of 5G/day for six weeks. According to this study the serum cholesterol level in all groups of the patients fell down in males and also in females. Ispaghula produced reduction in serum cholesterol level with P<0.05. According to the studies performed by MacMahon and Charles (1998) similar observations have been made. According to the study performed by Davidson et al (1998), serum lipid profiles were assessed in a randomized, double-blind controlled study it was indicated potential for long-term benefit. The effects of psyllium husk fiber supplementation to the diets were studied and was concluded that reduction of serum cholesterol was due to reduction of LDL cholesterol. Psyllium fiber supplementation lowered serum cholesterol regardless of saturation level of dietary fat (Ganji and Kies 1996). Study was performed by Abraham and Mehta (1998) to determine the effect of psyllium husk on plasma total and lipoprotein cholesterol in healthy human subjects. Fecal steroid excretion, determined from 5 day collections was not affected by
psyllium supplementation. Although psyllium tended to delay lipid absorption, plasma triglycerides, retinyl esters, glucose, insulin and glucagon quantitated during meal tolerance tests given on the last day of each diet period were not different. Thus the cholesterol-lowering mechanism of psyllium may not involve increased bile acids excretion or decrease in nutrient absorption.

The patients who were given Ispaghula husk for hypercholesterolaemia proved their bowel habits improved the study correlates with the study performed by Borgia et al (1983), the study was performed on seventy five patients affected by chronic constipation, frequency, stool consistency, abdominal pain and signs of venous stasis improved after treatment. Ispaghula husk improved the bowel habits in haemorrhoidal patients, it clarifies the efficacy of Ispaghula husk in constipation (Webster et al., 1978).

From this study it could be concluded that Ispaghula husk has got the efficacy to decrease serum cholesterol and it also improves the bowel habits as well as it is better remedy for constipation.
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ACKNOWLEDGEMENTS

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