

	Page
Acknowledgement	vi
List of Figures	viii
List of Tables	xi
Abstract	xiii
<i>Chapter 1 Introduction</i>	1 – 18
1.1 Cancer	1
1.1.1 Causes of cancer	3
1.1.2 Cancer treatment	3
1.1.3 Chemotherapy	4
1.2 Thioureas	5
1.2.1 Synthesis of thioureas	5
(a) From Cyanamid's	5
(b) From Isothiocynates	6
(c) From Thiophosgene	6
1.2.2 Importance of thioureas	7
1.3 Ureas	7
1.3.1 Synthesis of ureas	7
(a) From Isocynates	7
(b) From carbamates	8
(c) From thioureas	8
1.3.2 Importance of ureas	9
1.4 Thioureas and ureas as anticancer agents	9
1.5 Limitations of thioureas and ureas using as drugs	11
1.6 Ferrocene	11
1.7 Preliminary screening of anti-cancer potency	13
1.8 DNA binding with small molecules	14
1.9 Techniques to study non-covalent interactions	15
1.9.1 UV-visible spectrophotometry in DNA binding	15

	Page
1.9.2 Thermal Melting Assay of DNA	16
1.10 Aims of study	18
Chapter 2 Experimental and Characterization	19 – 51
2.1 Materials	19
2.2 Instrumentation	19
2.3 General description of the work	19
2.4 Synthesis of Nitrophenylferrocenes (a – e)	22
2.4.1 4-nitrophenylferrocene (a)	22
2.4.2 2-methyl-4-nitrophenylferrocene (b)	23
2.4.3 2-methoxy-4-nitrophenylferrocene (c)	23
2.4.4 2-Chloro-4-nitrophenylferrocene (d)	23
2.4.5 3-nitrophenylferrocene (e)	24
2.5 Synthesis of ferrocenylanilines (A – E)	24
2.5.1 4-Ferrocenylaniline (A)	24
2.5.2 3-methyl-4-Ferrocenylaniline (B)	26
2.5.3 3-methoxy-4-Ferrocenylaniline (C)	26
2.5.4 3-Chloro-4-Ferrocenylaniline (D)	26
2.5.5 3-Ferrocenylaniline (E)	27
2.6 Synthesis of ferrocene based thioureas (A_t1 – E_t7)	28
2.6.01 1-(4-(ferrocenyl)phenyl)-3-methylthiourea (A_t1)	28
2.6.02 1-(4-(ferrocenyl)phenyl)-3-ethylthiourea (A_t2)	29
2.6.03 1-(4-(ferrocenyl)phenyl)-3-propylthiourea (A_t3)	29
2.6.04 1-(4-(ferrocenyl)phenyl)-3-allylthiourea (A_t4)	29
2.6.05 1-(4-(ferrocenyl)phenyl)-3-phenylthiourea (A_t5)	30
2.6.06 1-(4-(ferrocenyl)phenyl)-3-(4-nitrophenyl)thiourea (A_t6)	30
2.6.07 1-(4-(ferrocenyl)phenyl)-3-(2,4-dichlorophenyl)thiourea (A_t7)	31
2.6.08 1-(4-(ferrocenyl)-3-methylphenyl)-3-methylthiourea (B_t1)	31
2.6.09 1-(4-(ferrocenyl)-3-methylphenyl)-3-ethylthiourea (B_t2)	31
2.6.10 1-(4-(ferrocenyl)-3-methylphenyl)-3-propylthiourea (B_t3)	32
2.6.11 1-(4-(ferrocenyl)-3-methylphenyl)-3-allylthiourea (B_t4)	32

	Page	
2.6.12	1-(4-(ferrocenyl)-3-methylphenyl)-3-phenylthiourea (B_t5)	33
2.6.13	1-(4-(ferrocenyl)-3-methylphenyl)-3-(4-nitrophenyl)thiourea (B_t6)	33
2.6.14	1-(4-(ferrocenyl)-3-methylphenyl)-3-(2,4-dichlorophenyl)thiourea (B_t7)	33
2.6.15	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-methylthiourea (C_t1)	34
2.6.16	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-ethylthiourea (C_t2)	34
2.6.17	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-propylthiourea (C_t3)	35
2.6.18	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-allylthiourea (C_t4)	35
2.6.19	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-phenylthiourea (C_t5)	35
2.6.20	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-(4-nitrophenyl)thiourea (C_t6)	36
2.6.21	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-(2,4-dichlorophenyl)thiourea (C_t7)	36
2.6.22	1-(3-chloro-4-(ferrocenyl)phenyl)-3-methylthiourea (D_t1)	37
2.6.23	1-(3-chloro-4-(ferrocenyl)phenyl)-3-ethylthiourea (D_t2)	37
2.6.24	1-(3-chloro-4-(ferrocenyl)phenyl)-3-propylthiourea (D_t3)	37
2.6.25	1-(3-chloro-4-(ferrocenyl)phenyl)-3-allylthiourea (D_t4)	38
2.6.26	1-(3-chloro-4-(ferrocenyl)phenyl)-3-phenylthiourea (D_t5)	38
2.6.27	1-(3-chloro-4-(ferrocenyl)phenyl)-3-(4-nitrophenyl)thiourea (D_t6)	39
2.6.28	1-(3-chloro-4-(ferrocenyl)phenyl)-3-(2,4-dichlorophenyl)thiourea (D_t7)	39
2.6.29	1-(3-(ferrocenyl)phenyl)-3-methylthiourea (E_t1)	39
2.6.30	1-(3-(ferrocenyl)phenyl)-3-ethylthiourea (E_t2)	40
2.6.31	1-(3-(ferrocenyl)phenyl)-3-propylthiourea (E_t3)	40
2.6.32	1-(3-(ferrocenyl)phenyl)-3-allylthiourea (E_t4)	41
2.6.33	1-(3-(ferrocenyl)phenyl)-3-phenylthiourea (E_t5)	41
2.6.34	1-(3-(ferrocenyl)phenyl)-3-(4-nitrophenyl)thiourea (E_t6)	41
2.6.35	1-(3-(ferrocenyl)phenyl)-3-(2,4-dichlorophenyl)thiourea (E_t7)	42
2.7	Synthesis of ferrocene based ureas (A_u3 – E_u7)	43
2.7.01	1-(4-(ferrocenyl)phenyl)-3-propylurea (A_u3)	43
2.7.02	1-(4-(ferrocenyl)phenyl)-3-allylurea (A_u4)	43
2.7.03	1-(4-(ferrocenyl)phenyl)-3-phenylurea (A_u5)	44
2.7.04	1-(4-(ferrocenyl)phenyl)-3-(4-nitrophenyl)urea (A_u6)	44
2.7.05	1-(4-(ferrocenyl)-3-methylphenyl)-3-propylurea (B_u3)	45

	Page
2.7.06 1-(4-(ferrocenyl)-3-methylphenyl)-3-(4-nitrophenyl)urea (B_u6)	45
2.7.07 1-(4-(ferrocenyl)-3-methylphenyl)-3-(2,4-dichlorophenyl)urea (B_u7)	45
2.7.08 1-(4-(ferrocenyl)-3-methoxyphenyl)-3-ethylurea (C_u2)	46
2.7.09 1-(4-(ferrocenyl)-3-methoxyphenyl)-3-propylurea (C_u3)	46
2.7.10 1-(4-(ferrocenyl)-3-methoxyphenyl)-3-phenylurea (C_u5)	47
2.7.11 1-(4-(ferrocenyl)-3-methoxyphenyl)-3-(4-nitrophenyl)urea (C_u6)	47
2.7.12 1-(4-(ferrocenyl)-3-methoxyphenyl)-3-(2,4-dichlorophenyl)urea (C_u7)	47
2.7.13 1-(3-chloro-4-(ferrocenyl)phenyl)-3-phenylurea (D_u5)	48
2.7.14 1-(3-chloro-4-(ferrocenyl)phenyl)-3-(4-nitrophenyl)urea (D_u6)	48
2.7.15 1-(3-chloro-4-(ferrocenyl)phenyl)-3-(2,4-dichlorophenyl)urea (D_u7)	49
2.7.16 1-(3-(ferrocenyl)phenyl)-3-phenylurea (E_u5)	49
2.7.17 1-(3-(ferrocenyl)phenyl)-3-(4-nitrophenyl)urea (E_u6)	49
2.7.18 1-(3-(ferrocenyl)phenyl)-3-(2,4-dichlorophenyl)urea (E_u7)	50
2.8 Methods for activity studies	50
2.8.1 DNA binding Studies	50
2.8.2 Anti-Oxidant Studies (DPPH scavenging assay)	51
2.8.3 Modal Membrane Interaction Studies	51
Chapter 3 Results and Discussion	52 – 82
3.1 Synthesis	52
3.2 Elemental Analysis	53
3.3 Infra Red Spectroscopic Characterization	54
3.4 Nuclear Magnetic Resonance Spectroscopic Characterization	56
The ¹ HNMR	56
The ¹³ CNMR	60
3.5 Single crystal X-ray diffraction analysis	66
3.5.1 Crystal structures of nitrophenylferrocenes	66
3.5.1.1 2-methoxy-4-nitrophenyl ferrocene (c)	69
3.5.1.2 2-chloro-4-nitrophenyl ferrocene (d)	70
3.5.1.3 3-nitrophenyl ferrocene (e)	71
3.5.2 Crystal structure of 3-Ferrocenyl aniline (E)	74

	Page	
3.5.3	Crystal structures of Ferrocenyl thioureas	77
3.5.3.1	1-(4-(ferrocenyl)phenyl)-3-allylthiourea (A_t4)	77
3.5.3.2	1-(4-(ferrocenyl)-3-methoxyphenyl)-3-phenylthiourea (C_t5)	80
Chapter 4	Biological Studies	83 – 106
4	Biological Screening	83
4.1	Modal membrane interaction studies	83
	Nitrophenylferrocenes	84
	Ferrocenyl anilines	87
	Ferrocenyl ureas and thioureas	90
4.2	Antioxidant Activity (DPPH Free Radical Scavenging Assay)	95
4.3	DNA binding studies	98
4.3.1	UV-Visible Spectroscopic titration	99
4.3.2	Thermal Denaturing Assay	103
	Conclusions	105
	Future plans	106
	Reference	107
	List of Publications and Presentation	117
	Publications	119
