

## TABLE OF CONTENTS

S. No.	Title	Page No.
	Declaration	ii
	Abstract	iii-v
	Acknowledgement	vi-viii
	Table of contents	ix-xii
	List of figures	xiii-xx
	List of tables	xxi
	List of publications	xxii
	List of Abbreviations	xxiii-xxiv
<b>Chapter 1</b>	<b>INTRODUCTION</b>	<b>1-30</b>
1.1	Cancer	1-2
1.1.1	Types of cancer	3
1.1.2	Pathogenesis of Cancer	4-5
1.1.3	Treatment strategies against cancer	5-6
1.1.4	Common targets for chemotherapeutic agents	7
1.2	Breast cancer	7
1.2.1	Types of breast cancer	8
1.2.1.1	Non-invasive breast cancer	8
1.2.1.2	Invasive breast cancer	9
1.2.2	Role of estrogens in breast cancer	10-11
1.2.3	Role of aromatase and its inhibitors	12-14
1.2.4	Role of human epidermal growth receptor (HER2)	14-15
1.3	Coumarin	16-17
1.4	Concept of coumarin hybrid molecules	18-19
1.5	Selected pharmacophores for hybridization with coumarin	20
1.5.1	Quinoxaline	20
1.5.2	Dihydropyrimidinone	21
1.5.3	Dihydropyridine	21
1.6	Molecular docking	22-23
1.7	Common softwares for molecular docking	24
1.8	Research envisaged	25-26

1.8.1	Rationale for the designed work	26-28
1.9	Aim and objectives	28
1.10	Plan of work	29-30
<b>Chapter 2</b>	<b>LITERATURE REVIEW</b>	<b>31-56</b>
<b>Chapter 3</b>	<b>EXPERIMENTAL (MATERIAL AND METHODS)</b>	<b>55-92</b>
3.1	Chemicals and equipments	57
3.2	Softwares	57
3.2.1	MOE Software	57
3.2.2	swissADME	57
3.2.3	preADMET	58
3.2.4	PreADME and PROTOX	58
3.3	Molecular docking studies	58
3.3.1	Preparation of protein	58
3.3.2	Preparation of ligand	58
3.3.3	Docking of designed molecules and validation	59
3.4	<i>In silico</i> drug likeliness prediction	59
3.5	<i>In silico</i> ADME prediction	60
3.6	<i>In silico</i> toxicity prediction	60
3.7	Synthesis of coumarin-quinoxaline derivatives	61
3.7.1	Synthesis of (Z)-2-(hydroxyimino)-N-(2-oxo-2H-chromen-7-yl)acetamide derivatives (Intermediate)	61
3.7.2	Synthesis of substituted isatins (pyrano[3,2-f]indole-2,6,7(8H)-triones)	61
3.7.3	Synthesis of coumarin-quinoxaline Hybrids (pyrano[3',2':5,6]indolo[2,3-b]quinoxalin-2(12H)-ones)	62-71
3.8	Synthesis of coumarin-dihydropyrimidinone derivatives	71
3.8.1	Synthesis of substituted 3-acetoacetyl coumarins 4 (1-(2-oxo-2H-chromen-3-yl)butane-1,3-dione)	72
3.8.2	General procedure for synthesis of coumarin-dihydropyrimidinone hybrids (6-methyl-5-(2-oxo-2H-chromene-3-carbonyl)-4-phenyl-3,4-dihydropyrimidin-2(1H)-ones)	72-83
3.9	Synthesis of coumarin-dihydropyridine derivatives	83

3.9.1	General procedure	83-95
3.10	Anticancer activity	95
3.10.1	MTT assay	95-97
3.10.2	Normal cell toxicity	97-98
<b>Chapter 4</b>	<b>RESULTS AND DISCUSSION</b>	<b>99-193</b>
4.1	<i>In silico</i> screening studies	99
4.1.1	Molecular docking of coumarin-quinoxaline hybrids	99-130
4.1.2	Drug likeliness prediction of coumarin-quinoxaline hybrids	130-131
4.1.3	ADME prediction studies of coumarin-quinoxaline hybrids	131-132
4.1.4	Toxicity prediction studies of coumarin-quinoxaline hybrids	132-133
4.1.5	Molecular docking studies of coumarin-dihydropyrimidone hybrids	133-148
4.1.6	Drug likeliness prediction of coumarin-dihydropyrimidone hybrids	148-149
4.1.7	ADME prediction studies of coumarin-dihydropyrimidinone hybrids	149-150
4.1.8	<i>In silico</i> toxicity studies of coumarin-dihydropyrimidone hybrids	150-151
4.1.9	Molecular docking studies of coumarin-dihydropyridine hybrids	151-166
4.1.10	Drug likeliness prediction of coumarin-dihydropyridine hybrids	167
4.1.11	ADME prediction studies of coumarin-dihydropyrimidinone hybrids	168-169
4.1.12	<i>In silico</i> toxicity studies of coumarin-dihydropyrimidone hybrids	169
4.2	Synthesis	169
4.2.1	Synthesis of Coumarin-Quinoxaline Hybrids	169-171
4.2.2	Synthesis of Coumarin-Dihydropyrimidinone Hybrids	171-173
4.2.3	Synthesis of Coumarin-Dihydropyridine Hybrids	173-176
4.3	<i>In vitro</i> antiproliferative activity	177
4.3.1	<i>In vitro</i> antiproliferative evaluation of the synthesized coumarin-quinoxaline hybrids	177-180

4.3.2	<i>In vitro</i> antiproliferative evaluation of the synthesized coumarin-dihydropyrimidinone hybrids	181-184
4.3.3	<i>In vitro</i> antiproliferative evaluation of the synthesized coumarin-dihydropyridine hybrids	185-188
4.3.4	Normal cell toxicity	189
4.4	Structural activity relationship	189
4.4.1	SAR of coumarin-quinoxaline hybrids	189-190
4.4.2	SAR of coumarin-dihydropyrimidinone hybrids	190-191
4.4.3	SAR of coumarin-dihydropyridine hybrids	191-192
<b>Chapter 5</b>	<b>SUMMARY AND CONCLUSION</b>	<b>193-196</b>
	<b>REFERENCES</b>	<b>197-212</b>
	<b>APPENDIX</b>	<b>213-228</b>