



# INDEX

Chapter No.	Contents	Page No.
1	<b>Introduction</b> .....	1
1.1	Introduction.....	1
1.2	Objectives of the work.....	4
1.3	Materials.....	5
2	<b>Literature Review</b> .....	6
2.1	<b>Cancer</b> .....	6
2.1.1	What is Cancer? .....	6
2.1.2	Growth of solid tumors .....	6
2.1.3	Cancer Therapy .....	8
2.2	<b>Tumor Angiogenesis</b> .....	13
2.2.1	Angiogenesis .....	13
2.2.2	History: Angiogenesis .....	14
2.2.3	Tumour growth is angiogenesis dependant .....	15
2.2.4	Angiogenic Switch .....	15
2.2.5	The Process of Angiogenesis .....	17
2.2.6	Tumour angiogenesis: molecular mechanism .....	19
2.2.7	Angiogenesis regulators: Endogenous factors .....	21
2.2.8	Tumour Vasculature: Morphology and characteristics .....	25
2.2.9	Enhanced Permeation and Retention effect (EPR) .....	26
2.3	<b>Antiangiogenic Therapy</b> .....	31
2.3.1	Antiangiogenesis : History .....	31
2.3.2	Antiangiogenic Therapy .....	32
2.3.3	Antiangiogenesis strategies .....	33
2.3.4	Different classifications for Angiogenesis Inhibitors (AIs) .	34
2.3.5	Combination therapy .....	35
2.3.6	Normalization of Tumor Vasculature .....	37
2.3.7	Criteria for Antiangiogenic Activity .....	39
2.3.8	Natural Antiangiogenic Agents .....	39

<b>Chapter No.</b>	<b>Contents</b>	<b>Page No.</b>
<b>2.4</b>	<b>Nanotechnology in cancer .....</b>	46
2.4.1	Introduction: Cancer Nanotechnology .....	46
2.4.2	Polymeric Nanoparticles .....	47
2.4.3	Clearance mechanism and circulation time .....	48
2.4.4	Mechanisms of targeting: Passive and Active .....	49
2.4.5	Polymeric Nanoparticles .....	52
2.4.6	Preparation methods .....	55
2.4.7	Characterisation of nanoparticles .....	61
<b>2.5</b>	<b><i>In Vitro</i> Studies on Nanoparticles .....</b>	70
2.5.1	<i>In vitro</i> release study .....	70
2.5.2	<i>In vitro</i> cell line studies .....	71
<b>2.6</b>	<b>Plan of work .....</b>	76
<b>3</b>	<b>Drug Profiles .....</b>	78
3.1	Etoposide .....	78
3.2	Quercetin Dihydrate .....	83
<b>4</b>	<b>Analytical methods for drug estimation</b>	92
4.1	Solubility studies .....	92
4.2	Estimation of Etoposide and Quercetin Dihydrate in PLGA nanoparticles .....	92
4.3	Estimation of Etoposide and Quercetin Dihydrate in pH 7.4 phosphate buffer .....	98
4.4	Result and discussion .....	105
<b>5</b>	<b>Preparation and Characterisation of nanoparticles .....</b>	111
5.1	Introduction .....	111
5.2	Preparation of PLGA nanoparticles .....	111
5.3	Optimization of Nanoparticle Formulations .....	112
5.4	Characterization of nanoparticle formulations .....	120
5.5	Stability studies .....	125

<b>Chapter No.</b>	<b>Contents</b>	<b>Page No.</b>
5.6	Results and discussion .....	127
5.7	Conclusion.....	131
<b>6</b>	<b><i>In-Vitro</i> studies on nanoparticles .....</b>	<b>133</b>
6.1	Introduction .....	133
6.2	In vitro drug release from ETN and QDN.....	133
6.3	In vitro cell line studies: Cytotoxicity by MTT assay.....	133
6.4	Result and Discussion.....	135
6.5	Conclusions .....	142
<b>7</b>	<b><i>In-Vivo</i> studies on nanoparticles</b>	<b>144</b>
7.1	Introduction .....	144
7.2	Radiolabeling .....	145
7.3	Tumor growth inhibitory activity .....	154
7.4	Histopathological studies:Tumor microvessel density evaluation .....	154
7.5	Results and Discussion .....	163
7.6	Conclusions .....	166
<b>8</b>	<b>Summary and Conclusions .....</b>	<b>170</b>