

Contents

	Page No.
List of Abbreviations and Symbols	i
List of Figures	v
List of Tables	ix
Preface	x
1. Introduction	01- 06
2. Literature review	07- 48
2.1 Overview of Hepatitis	07
2.2 Geographical distribution/epidemiology	08
2.3 The Hepatitis B virus	09
2.4 Hepatitis B virus replication	11
2.5 Hepatitis B virus Transmission	16
2.6 Clinical aspects of Hepatitis B virus	18
2.7 Immune pathogenesis of Hepatitis B virus infection	22
2.8 Mechanisms of Hepatitis B virus clearance	27
2.9 Diagnostics of Hepatitis B virus infection	27
2.10 Polymer-based vaccination	31
2.11 Delivery of therapeutic molecules	33
2.12 Polymeric nanoparticles for antigen delivery & adjuvants	35
2.13 Distribution of polymeric nanoparticles	37
2.14 Aspects of immune response	40
2.15 Nanoparticles: advantages and disadvantages	41
2.16 Route of administration of Hepatitis B vaccine	43
2.17 Animal models for Hepatitis B	46
3. Objective and plan of work	50- 52
4. Materials and methods	53- 99
4.1 Materials	54
4.2 Methods	56
4.2.1 Preformulation study	56
4.2.2 Formulation of antigen HBsAg loaded polymeric nanoparticles	59
4.2.3 <i>In-vitro</i> characterization of polymeric HBsAg loaded nanoparticles	66
4.2.4 Surface characterization	67

4.2.5 <i>In-vitro</i> release of HBsAg from nanoparticles	68
4.2.6 Structural integrity of HBsAg loaded nanoparticles	71
4.2.7 <i>In-vitro</i> cellular uptake study of nanoparticles	72
4.2.8 Haemocompatibility studies	73
4.2.9 Stability study	75
4.2.10 Selection of route of administration in BALB/c mice	76
4.2.11 <i>In-vivo</i> cellular internalization study	79
4.2.12 Immunological characterization and measurement of antibody levels	80
4.2.13 <i>In-vivo</i> lymphocyte and T cells proliferation study	83
4.2.14 Assessment of immunological parameter in Humanized Xenograft model	86
5. Results and discussion	101-157
5.1 Preformulation study	101
5.2 Formulation of antigen HBsAg loaded polymeric nanoparticles	102
5.3 <i>In-vitro</i> characterization of polymeric HBsAg loaded nanoparticles	116
5.4 Surface characterization	118
5.5 <i>In-vitro</i> release of HBsAg from nanoparticles	121
5.6 Structural integrity of HBsAg loaded nanoparticles	124
5.7 <i>In-vitro</i> cellular uptake study of nanoparticles	126
5.8 Haemocompatibility studies	130
5.9 Stability study	134
5.10 Selection of route of administration in BALB/c mice	135
5.11 <i>In-vivo</i> cellular internalization study	139
5.12 Immunological characterization and measurement of antibody levels	140
5.13 <i>In-vivo</i> lymphocyte and T cells proliferation study	145
5.14 Assessment of immunological parameter in Humanized Xenograft model	148
6. Conclusion	159-160
7. References	161-188
8. List of publications	-----

Contents
