Table of Contents

1 Introduction ...................................................................................................... 1

1.1 Need of Vesicular drug delivery systems .................................................. 3

1.2 Niosomes .................................................................................................... 3

1.2.1 Mechanism of niosomes formation ...................................................... 4

1.2.2 Types of niosomes ................................................................................. 5

1.2.3 Salient features of niosomes ................................................................ 5

1.2.4 Materials used for niosomes preparation ............................................ 6

1.2.5 Methods of niosomes preparation ....................................................... 10

1.2.6 Methods of separation of unentrapped drug ....................................... 14

1.2.7 Characterization of niosomes .............................................................. 15

1.2.8 Stability of niosomes ........................................................................... 16

1.3 Proniosomes ............................................................................................... 18

1.3.1 Materials used for the proniosomes preparation .................................. 21

1.3.2 Methods of proniosomes preparation ................................................ 22

1.4 Transdermal drug delivery systems ............................................................ 24

1.4.1 Routes of penetration .......................................................................... 25

1.4.2 Vesicles as a transdermal and dermal delivery .................................... 26

1.4.3 Niosomes as a tool for transdermal drug delivery ................................ 30

1.5 Inflammation ............................................................................................... 32

1.5.1 Inflammatory diseases ......................................................................... 35

1.5.2 Nonsteroidal anti-inflammatory drugs ................................................ 41

1.5.3 Experimental evaluation of anti-inflammatory activity ....................... 44

1.6 References .................................................................................................. 46
2 Literature review ............................................................................................ 52

2.1 Factors affecting characteristics of niosomes 53

2.1.1 Factors affecting vesicle size 53

2.1.2 Factors affecting entrapment efficiency 53

2.1.3 Factors affecting entrapment efficiency and solute release rates 54

2.1.4 Factors affecting solute release profile 60

2.2 Findings reported on niosomes for topical or transdermal applications 61

2.3 Findings reported on dry proniosomes 64

2.4 Finding reported on proniosomes for transdermal applications 65

2.5 References 67

3 Aim of present study ..................................................................................... 72

4 Preparation and characterization of niosomes ............................................ 75

4.1 Materials and equipments 75

4.2 Preliminary experimental work 76

4.2.1 Selection of the method for the preparation of niosomes 76

4.2.2 Selection of the surfactant for the preparation of niosomes 80

4.3 Characterization of niosomes 82

4.3.1 Microscopic evaluation 82

4.3.2 Percentage Drug Entrapment 82

4.3.3 Determination of vesicles size 82

4.4 Optimization of niosome formulations 83

4.4.1 Factorial Design 83
4.4.2 Method of preparation of Niosomes 84
4.4.3 Multiple regression 84
4.4.4 Optimization of piroxicam niosomes 85
4.4.5 Optimization of ketoprofen niosomes 92
4.4.6 Optimization of aceclofenac niosomes 101
4.4.7 Stability studies of the optimized batches of the niosomes 109
4.4.8 Comparisons 111
4.4.9 Conclusion 112
4.5 References 113

5 Preparation and characterization of proniosomes ......................... 115

5.1 Materials and equipments 115

5.2 Preliminary experimental work 116

5.2.1 Comparison of proniosome-derived niosomes with conventional niosomes 116

5.2.2 Selection of the carriers for the preparation of proniosomes 118

5.3 Characterization of proniosomes 124

5.3.1 Scanning Electron Microscopy 124

5.3.2 Flow properties 124

5.3.3 Microscopic evaluation 124

5.3.4 Percentage Drug Entrapment 124

5.3.5 Determination of vesicles size 124

5.4 Optimization of proniosomes 125

5.4.1 Method of preparation of proniosomes 125

III
5.4.2 Preparation of proniosome-derived niosomes
5.4.3 Lack of fit
5.4.4 Checkpoint analysis
5.4.5 Optimum formula
5.4.6 Optimization of piroxicam proniosomes
5.4.7 Optimization of ketoprofen proniosomes
5.4.8 Optimization of aceclofenac proniosomes
5.4.9 Stability studies of the optimized batches of proniosomes
5.4.10 Comparisons
5.4.11 Conclusion

5.5 References

6 Preparation and evaluation of niosome-based gel formulations

6.1 Materials and Equipments
6.2 Preparation of Niosome-based gel formulations
   6.2.1 Preparation of polymeric gel dispersion
   6.2.2 Preparation of niosomal gel
   6.2.3 Preparation of Proniosomal gel (Pro'vesicular surfactant gel)
6.3 Characterization of niosomes and provesicles
6.4 In vitro evaluation of niosome-based gel formulations
   6.4.1 In vitro release studies
   6.4.2 Animal Selection
   6.4.3 Skin membrane preparation
   6.4.4 In vitro skin permeation studies
   6.4.5 Pharmacological response
6.4.6 Statistical analysis .......................... 177
6.5 Niosome-based gel formulations of Piroxicam .......... 178
6.6 Niosome-based gel formulations of ketoprofen .......... 188
6.7 Niosome-based gel formulations of Aceclofenac ......... 194
6.8 Comparisons .................................. 199
6.9 Conclusion .................................. 200
6.10 References ................................... 201

7 Summary and conclusion ........................................ 203

8 Annexures ................................................................... 213
1 Drug Profile .................................................................. 213
   A Piroxicam .................................................. 213
   B Ketoprofen ................................................. 217
   C Aceclofenac ................................................ 221
2 Standard curve for U V Spectrophotometric analysis .... 226
   A Standard curve of piroxicam in phosphate buffer saline pH 7.4 226
   B Standard curve of ketoprofen in phosphate buffer saline pH 7.4 227
   C Standard curve of aceclofenac in phosphate buffer saline pH 7.4 228
3 Profiles of formulation components ............................ 229
   A Sorbitan Esters (Sorbitan Fatty Acid esters) ............. 229
   B Cholesterol .............................................. 231
   C Maltodextrin ......................................... 232
   D Directly compressible lactose ............................ 234
   E Carbopol .............................................. 237
4 Presentations and Publications .................................. 241