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PREPARATION AND CHARACTERIZATION OF
NANOPARTICLES FROM MICROEMULSION
SYSTEM FOR TOPICAL DELIVERY OF
COENZYME Q₁₀

Miss Patcharaporn Manopinives

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for the Degree of Master of Sciences Program in Pharmaceutical Technology

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พัชรภรณ์ มโนภินิเวศ : การเตรียมและศึกษาลักษณะเฉพาะของอนุภาคนาโนจากระบบไมโครอิมัลชันเพื่อการนำส่งโคเอนไซม์คิวเทนแบบเฉพาะที่ (PREPARATION AND CHARACTERIZATION OF NANOPARTICLES FROM MICROEMULSION SYSTEM FOR TOPICAL DELIVERY OF COENZYME Q₁₀) อ.ที่ปรึกษา: ผศ.ดร. วราภรณ์ วารีสน้อยเจริญ, 158 หน้า. ISBN 974-14-2441-8

อนุภาคนาโนสามารถเตรียมโดยการทำแม่แบบไมโครอิมัลชันที่เกิดขึ้นขณะร้อนให้เย็นแบบปกติ ในงานศึกษานี้ทำการปรับเปลี่ยนวัฏภาคน้ำมัน (อิมัลซิฟายอิงแวกซ์ หรือ บริจ 72) และวัฏภาคของสารลดแรงตึงผิว (บริจ 78 หรือ ทวิน 80) เพื่อให้ได้ไมโครอิมัลชัน จากการศึกษาพบว่าชนิดของเมทริกซ์ไขมัน และความเข้มข้นของสารลดแรงตึงผิวมีผลต่อขนาดของอนุภาคนาโนที่ได้อรวมทั้งยังพบว่า การทำไมโครอิมัลชันที่เกิดขึ้นขณะร้อนให้เย็นทันทีในอ่างน้ำแข็ง จะมีผลให้เกิดการแยกชั้นของวัฏภาคไขมันและก่อให้เกิดอนุภาคนาโน ที่มีขนาดเล็กกว่าการทำให้เย็นแบบปกติ คำรับไมโครอิมัลชันที่ประกอบด้วยแวกซ์ (ซีโตสเทียริวแอลกอฮอล์ กับ ซีโตแมคโครกอล) และทวิน 80 จะให้อนุภาคนาโนที่มีขนาดเล็ก สม่ำเสมอ และมีความคงตัว โคเอนไซม์คิวเทนจะถูกกักเก็บลงในอนุภาคนาโนที่ได้อ และพบว่า ความเข้มข้นของแวกซ์และทวิน 80 จะมีผลต่อขนาดของอนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทน สูตรคำรับที่ถูกเลือกเพื่อใช้กักเก็บโคเอนไซม์คิวเทนประกอบด้วย แวกซ์ 4 มิลลิกรัมต่อมิลลิลิตร ทวิน 80 48 มิลลิโมลาร์ อนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทนแสดงลักษณะอนุภาคที่กลมและมีขนาดเล็กกว่า 100 นาโนเมตร รวมทั้งมีเปอร์เซ็นต์การกักเก็บที่สูง คือ ร้อยละ 80.19 และ 78.00 สำหรับ อนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทนไว้ 2 และ 4 มิลลิกรัมต่อมิลลิลิตรตามลำดับ จากการวิเคราะห์ดีฟเฟอเรนเชียลสแกนนิ่งแคลลอริเมทรีแสดงให้เห็นว่า โคเอนไซม์คิวเทนที่อยู่ในเมทริกซ์ไขมันกระจายอยู่ในรูปอสัณฐาน และอนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทนนี้ ไม่ได้เกิดจากการผสมทางกายภาพของแต่ละองค์ประกอบ โคเอนไซม์คิวเทนจะถูกปลดปล่อยจากอนุภาคนาโนอย่างรวดเร็วในสิบชั่วโมงแรก จากนั้นจะช้าลงและคงที่ อนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทนที่อยู่ในรูปผงแห้งโดยใช้เมนิทอลร้อยละ 2 เป็นตัวปกป้องอนุภาคขณะทำให้เย็นจะให้ความคงตัวดีกว่าอนุภาคที่ไม่อยู่ในรูปผงแห้ง นอกจากนี้ยังพบว่า ครีมที่ผสมรวมกับอนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทนมีความคงตัวทางกายภาพที่ดีภายใต้สภาวะเร่ง จากผลการทดลองสามารถสรุปได้ว่า อนุภาคนาโนที่กักเก็บโคเอนไซม์คิวเทน เตรียมได้จากแม่แบบไมโครอิมัลชันและสามารถบรรจุลงในสูตรคำรับเฉพาะที่ได้

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PATCHARAPORN MANOPINIVES: PREPARATION AND CHARACTERIZATION OF NANOPARTICLES FROM MICROEMULSION SYSTEM FOR TOPICAL DELIVERY OF COENZYME Q₁₀. THESIS ADVISOR: ASSISTANT PROFESSOR WARANGKANA WARISNOICHAROEN, Ph.D. 158 pp. ISBN 974-14-2441-8

Nanoparticles have been prepared by simple cooling of a warm microemulsion template. In this study, the microemulsion was achieved by varying the oil phase (emulsifying wax or Brij[®] 72) and surfactant phase (Brij[®] 78 or Tween[®] 80). It was found that the type of lipid matrix and concentration of surfactant had an effect on the size of the nanoparticles. The rapid cooling of a warm microemulsion in an ice-bath caused the precipitation of the lipid phase to form the smaller nanoparticles. The systems composed of emulsifying wax (cetostearyl alcohol and cetomacrogol) and Tween[®] 80 offered the small, uniform and stable nanoparticles. Coenzyme Q₁₀ was then incorporated into the nanoparticles and it was shown that the concentration of wax and Tween[®] 80 had influence on the size of Coenzyme Q₁₀-loaded nanoparticles. The formulation which was selected to incorporate Coenzyme Q₁₀ was composed of 4 mg/mL wax and 48 mM Tween[®] 80. The Coenzyme Q₁₀-loaded nanoparticles were spherical and had the size smaller than 100 nm and high percentage entrapment efficiency; 80.19% and 78.00 % for 2 and 4 mg/mL Coenzyme Q₁₀, respectively. The differential scanning calorimetry analysis indicated that Coenzyme Q₁₀ was dispersed in lipid matrix as an amorphous state and the Coenzyme Q₁₀-loaded nanoparticles were not a simple physical mixture of their individual component. The *in vitro* release profile of Coenzyme Q₁₀ from nanoparticles exhibited a rapidly initial release in the first ten hours, followed by a period of slower and extended release. Freeze-dried Coenzyme Q₁₀-loaded nanoparticles using 2% w/w mannitol as a cryoprotectant showed a greater stability than non freeze-dried nanoparticles. Moreover the cream mixed with Coenzyme Q₁₀-loaded nanoparticles offered a good physical stability under accelerated condition. In conclusion, Coenzyme Q₁₀-loaded nanoparticles were prepared from microemulsion template and could be incorporated in to topical preparation.

Field of study Pharmaceutical Technology

Student's signature *Patcharaporn Manopinives*

Academic year.....2005.....

Advisor's signature *Warangkana Warisnoicharoen*

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CONTENTS

	PAGE
ABSTRACT (THAI).....	iv
ABSTRACT (ENGLISH).....	v
ACKNOWLEDGEMENTS.....	vi
CONTENTS.....	vii
LIST OF TABLES.....	ix
LIST OF FIGURES.....	
LIST OF ABBREVIATIONS.....	
CHAPTER I INTRODUCTION.....	1
CHAPTER II LITERATURE REVIEW.....	6
1. NANOPARTICLES.....	6
2. PRODUCTION OF LIPID-BASED NANOPARTICLES.....	7
3. COENZYME Q ₁₀	12
4. PHYSICOCHEMICAL CHARACTERIZATION OF NANOPARTICLES.....	19
5. DRUG INCORPORATION IN NANOPARTICLES.....	22
6. STABILITY OF NANOPARTICULATE SYSTEM.....	26
7. APPLICATION OF NANOPARTICLES.....	32
CHAPTER III MATERIALS AND METHOD.....	39
1. MATERIALS.....	39
2. EQUIPMENT.....	39
3. GLASSWARE AND MISCELLANEOUS.....	40
4. METHODS.....	41
CHAPTER IV RESULTS AND DISCUSSION.....	58
1. PREPARATION OF NANOPARTICLES AND COENZYME Q ₁₀ -LOADED NANOPARTICLES FROM MICROEMULSION SYSTEM.....	58
2. DETERMINATION OF ENTRAPMENT EFFICIENCY.....	74
3. CHARACTERIZATION OF COENZYME Q ₁₀ -LOADED NANOPARTICLES BY TEM.....	77

4. THERMAL ANALYSIS OF COENZYME Q ₁₀ -LOADED NANOPARTICLES BY DSC.....	79
5. <i>IN VITRO</i> RELEASE STUDY.....	82
6. STABILITY STUDY OF COENZYME Q ₁₀ -LOADED NANOPARTICLES.....	84
CHAPTER V CONCLUSION.....	92
REFERENCES.....	94
APPENDICES.....	103
APPENDIX A.....	104
APPENDIX B.....	110
APPENDIX C.....	122
APPENDIX D.....	134
APPENDIX E.....	146
VITA.....	158

LIST OF TABLES

TABLE	PAGE
3-1 The composition of microemulsion.....	42
3-2 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 2 mg/mL wax and 1 mg/mL Coenzyme Q ₁₀	44
3-3 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 2 mg/mL wax and 2 mg/mL Coenzyme Q ₁₀	44
3-4 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 4 mg/mL wax and 1 mg/mL Coenzyme Q ₁₀	45
3-5 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 4 mg/mL wax and 2 mg/mL Coenzyme Q ₁₀	46
3-6 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 6 mg/mL wax and 1 mg/mL Coenzyme Q ₁₀	46
3-7 The composition of 2 mL of Coenzyme Q ₁₀ -loaded nanoparticles consisting of 6 mg/mL wax and 2 mg/mL Coenzyme Q ₁₀	47
3-8 Composition of 2-mL Coenzyme Q ₁₀ -loaded nanoparticles consisting of various amount of Tween [®] 80, wax and Coenzyme Q ₁₀	48
4-1 Average diameter (z-average) and polydispersity index (PI) of nanoparticles consisting of oil (wax) at 2 mg/mL and various concentrations of Brij [®] 78 after 4 and 24 hours (mean ± S.D., n=3).....	61
4-2 Average diameter (z-average) and polydispersity index (PI) of nanoparticles consisting of oil (wax) at 2 mg/mL and various concentrations of Tween [®] 80 (T80) after 4 and 24 hours (mean ± S.D., n=3).....	62

TABLE	PAGE
4-3 Average diameter (z-average) and polydispersity index (PI) of nanoparticles containing cetostearyl alcohol and cetomacrogol at 2 mg/mL and Tween [®] 80 (T80) prepared by 2 different cooling methods (mean \pm S.D., n=3).....	65
4-4 Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q ₁₀ -loaded nanoparticles at 24 hours after preparation (mean \pm S.D., n=3).....	68
4-5 Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q ₁₀ -loaded nanoparticles, consisting of 4 or 6 mg/mL of wax at 24 hours after preparation (mean \pm SD, n=3).....	70
4-6 Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q ₁₀ -loaded nanoparticles with various amount of Coenzyme Q ₁₀ at 24 hours after preparation (mean \pm S.D., n=3).....	72
4-7 Entrapment efficiency (%) and recovery (%) of Coenzyme Q ₁₀ -loaded nanoparticles (mean \pm S.D., n =2).....	76
4-8 Percentage of Coenzyme Q ₁₀ from nanoparticles, Rx D24 and D44 (mean \pm S.D., n=3).....	82
4-9 The size of nanoparticles, Rx D24 and D44 (mean \pm S.D., n = 3) and remaining amount of Coenzyme Q ₁₀ (mean \pm S.D., n = 2).....	85
4-10 The appearance of freeze-dried Coenzyme Q ₁₀ - loaded nanoparticles and the size of reconstituted freeze-dried product after storage at 25°C for 1 week (mean \pm S.D., n=3).....	87
4-11 The stability of Coenzyme Q ₁₀ in freeze-dried nanoparticles, Rx D24 and D44, after storage for 4 week at 4°C and 25°C (mean \pm S.D., n=2).....	89

TABLE	PAGE
4-12 The stability of mixed cream containing the freeze-dried Coenzyme Q ₁₀ -loaded nanoparticles and Coenzyme Q ₁₀ crystal subjected to accelerated test.....	90
4-13 The stability of Coenzyme Q ₁₀ in freeze-dried Coenzyme Q ₁₀ -loaded nanoparticles mixed cream after storage for 4 week at 25°C (mean ± S.D., n = 2).....	91
B1 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol:Tween [®] 20) and different concentrations of Brij [®] 78.....	111
B2 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol:Tween [®] 60) and different concentrations of Brij [®] 78.....	112
B3 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: cetomacrogol) and different concentrations of Brij [®] 78.....	113
B4 The appearance of formulations consisting of 2 mg/mL Brij [®] 72 and different concentrations of Brij [®] 78.....	114
B5 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol:Tween [®] 20) and different concentrations of Tween [®] 80.....	115
B6 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol:Tween [®] 60) and different concentrations of Tween [®] 80.....	116
B7 The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: vetomacrogol) and different concentrations of Tween [®] 80.....	117
B8 The appearance of formulations consisting of 2 mg/mL Brij [®] 72 and different concentrations of Tween [®] 80.....	118

TABLE	PAGE
B9 The appearance of Coenzyme Q ₁₀ -loaded nanoparticles formulation.....	119
C1 Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by simple cooling method using Brij [®] 78 as a surfactant determined at 4 hours and 24 hours.....	123
C2 Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by simple cooling method using Tween [®] 80 as a surfactant determined at 4 hours and 24 hours.....	125
C3 Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by rapid cooling method using Tween [®] 80 as a surfactant.....	128
C4 Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q ₁₀ -loaded nanoparticles prepared by rapid cooling method determined at 24 hours.....	129
C5 The stability data of Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q ₁₀ -loaded nanoparticles (rapid cooling method).....	132
C6 Average diameter (z-average) and polydispersity index (PI) of freeze-dried Coenzyme Q ₁₀ - loaded nanoparticles (Rx D24 and D44), determined after 1-week at 25°C.....	132
D1 Accuracy of Coenzyme Q ₁₀ assayed by HPLC.....	137
D2 The data of within-run precision of Coenzyme Q ₁₀ assayed by HPLC.....	138
D3 The data of between-run precision of Coenzyme Q ₁₀ assayed by HPLC.....	139
D4 The peak area of Coenzyme Q ₁₀ assayed by HPLC.....	140
D5 The amount of entrapped and unentrapped Coenzyme Q ₁₀ in Coenzyme Q ₁₀ -loaded nanoparticles dispersion.....	141
D6 The data of Coenzyme Q ₁₀ released from nanoparticles (Rx D24).....	143
D7 The data of Coenzyme Q ₁₀ released from nanoparticles (Rx D44).....	143
D8 Stability data of Coenzyme Q ₁₀ -loaded nanoparticles (Rx D24 and D44).....	144

TABLE	PAGE
D9 Stability data of freeze-dried Coenzyme Q ₁₀ -loaded nanoparticles (RxD24 and D44) and used 2% mannitol as cryoprotectant.....	145
D10 Stability data of freeze-dried Coenzyme Q ₁₀ -loaded nanoparticles (RxD24 and D44) in cream base.....	145
E1 The statistical analysis of concentration of Brij [®] 78 and nanoparticle size using cetostearyl alcohol and Tween [®] 20 as core material.....	147
E2 The statistical analysis of concentration of Brij [®] 78 and nanoparticle size using cetostearyl alcohol and Tween [®] 60 as core material.....	147
E3 The statistical analysis of concentration of Brij [®] 78 and nanoparticle size using cetostearyl alcohol and cetomacrogol as core material.....	148
E4 The statistical analysis of concentration of Brij [®] 78 and nanoparticle size using Brij [®] 72 as core material.....	148
E5 The statistical analysis of concentration of Tween [®] 80 and nanoparticle size using cetostearyl alcohol and Tween [®] 20 as core material.....	149
E6 The statistical analysis of concentration of Tween [®] 80 and nanoparticle size using cetostearyl alcohol and Tween [®] 60 as core material.....	149
E7 The statistical analysis of concentration of Tween [®] 80 and nanoparticle size using cetostearyl alcohol and cetomacrogol as core material.....	150
E8 The statistical analysis of concentration of Tween [®] 80 and nanoparticle size using Brij [®] 72 as core material.....	150
E9 The statistical analysis of cooling method and nanoparticle size (Rx B50).....	151
E10 The statistical analysis of cooling method and nanoparticle size (Rx B52).....	151
E11 The statistical analysis of cooling method and nanoparticle size (Rx B54).....	152
E12 The statistical analysis of Tween [®] 80 concentration and CoenzymeQ ₁₀ - loaded nanoparticle size (1 mg/mL of CoenzymeQ ₁₀).....	152
E13 The statistical analysis of Tween [®] 80 concentration and CoenzymeQ ₁₀ - loaded nanoparticle size (2 mg/mL of CoenzymeQ ₁₀).....	153

TABLE	PAGE
E14 The statistical analysis of wax concentration and CoenzymeQ ₁₀ -loaded nanoparticle size prepared from 60 mM of Tween 80 and 1 mg/mL of CoenzymeQ ₁₀	153
E15 The statistical analysis of wax concentration and CoenzymeQ ₁₀ -loaded nanoparticle size prepared from 60 mM of Tween 80 and 2 mg/mL of CoenzymeQ ₁₀	154
E16 The statistical analysis of CoenzymeQ ₁₀ concentration and Coenzyme Q ₁₀ -loaded nanoparticle size prepared from 24 mM of Tween [®] 80 and 2 mg/mL of wax.....	154
E17 The statistical analysis of CoenzymeQ ₁₀ concentration and Coenzyme Q ₁₀ -loaded nanoparticle size prepared from 48 mM of Tween [®] 80 and 4 mg/mL of wax.....	155
E18 The statistical analysis of CoenzymeQ ₁₀ concentration and Coenzyme Q ₁₀ -loaded nanoparticle size prepared from 72 mM of Tween [®] 80 and 6 mg/mL of wax.....	155
E19 The statistical analysis of storage time and Coenzyme Q ₁₀ -loaded nanoparticle of Rx D24.....	156
E20 The statistical analysis of storage time and Coenzyme Q ₁₀ -loaded nanoparticle of Rx D44.....	156
E21 The statistical analysis of concentration of mannitol and particle size (Rx D24).....	157
E22 The statistical analysis of concentration of mannitol and particle size (Rx D44).....	157

LIST OF FIGURES

FIGURE	PAGE
2-1 Nanoparticles (a) nanocapsule type and (b) nanosphere or monolithic type.....	7
2-2 Schematic representation of the three most commonly encountered microstructure (a) oil-in-water, (b) bicontinuous and (c) water-in-oil microemulsion.....	10
2-3 The structure of Coenzyme Q ₁₀ , comprising a quinone ring and a side chain of 10 isoprene units.....	13
2-4 The pathway of Coenzyme Q ₁₀ synthesis.....	14
2-5 The role of Coenzyme Q ₁₀ in the electron transport chain of mitochondrial.....	16
2-6 the release of drug from nanoparticles and plot of drug release rate versus time of (a) monolithic device, (b) reservoir device and (c) eroding monolithic device	24
2-7 Schematic curves of the total potential energy (V_T) of the interaction versus distance for two particles, showing the effect of the steric stabilization	28
2-8 Enthalpic stabilization.....	30
2-9 Bridging flocculations.....	31
2-10 Model of occlusive effect depending of size of the particles, 2 μ m (left) and 200 nm (right).....	34
2-11 Illustration of the proposed influence of particle size on cutaneous penetration pathways.....	36
4-1 Average diameter of nanoparticles received from different cooling methods, simple cooling (S) and rapid cooling (R) (mean \pm S.D., n=3).....	66
4-2 Correlation between concentrations of wax and lowest concentrations of Tween [®] 80 for microemulsion formation.....	71
4-3 Mean particle size of Coenzyme Q ₁₀ -loaded nanoparticle using the various amount of Coenzyme Q ₁₀ and wax (mean \pm S.D., n = 3).....	73

FIGURE	PAGE
4-4 The HPLC profile of Coenzyme Q ₁₀	74
4-5 Calibration curve of the standard Coenzyme Q ₁₀	75
4-6 Photograph under transmission electron microscope (TEM) of Coenzyme Q ₁₀ -loaded nanoparticles (a) Rx D24 and (b) Rx D44.....	78
4-7 Photograph under transmission electron microscope (TEM) of Coenzyme Q ₁₀ -loaded nanoparticles containing 2 mg/mL of Coenzyme Q ₁₀ with the different concentration of wax (a) 2mg/mL, (b) 4 mg/mL and (c) 6 mg/mL.....	78
4-8 The DSC thermogram of (1) Coenzyme Q ₁₀ , (2) wax, (3) physical mixture of Coenzyme Q ₁₀ and wax at a weight ratio of 1:1, and (4) nanoparticles containing 4 mg/mL Coenzyme Q ₁₀	80
4-9 The DSC thermogram of (1) Coenzyme Q ₁₀ , (2) wax, (3) physical mixture of Coenzyme Q ₁₀ and wax at a weight ratio of 1:2, and (4) nanoparticles containing 2 mg/mL Coenzyme Q ₁₀	81
4-10 Release patterns of Coenzyme Q ₁₀ from nanoparticles, Rx D24 and D44 (mean ± S.D., n=3).....	83
4-11 Mechanism of Coenzyme Q ₁₀ release from nanoparticle matrix. A.initial rapid desorbtion process (burst release) and B. slow controlled release process.....	83
4-12 The appearance of freeze-dried Coenzyme Q ₁₀ -loaded nanoparticles containing (a) 2 mg/mL Coenzyme Q ₁₀ (pale yellow color), (b) 4 mg/mL Coenzyme Q ₁₀ (yellow color) and of (c) Coenzyme Q ₁₀ powder (orange color).....	88
4-13 The appearance of (a) o/w cream base, mixed-cream containing freeze-dried nanoparticles load with Coenzyme Q ₁₀ (b) 2 mg/mL (Rx D24), (c) 4 mg/mL (Rx D44) and (d) mixed-cream containing Coenzyme Q ₁₀ powder.....	90

FIGURE	PAGE
C1 Particle size distribution of Coenzyme Q ₁₀ - loaded nanoparticles, (a) Rx D24, (b) Rx D44, determined at 24 hours after preparation.....	133
D1 HPLC chromatogram of (a) Coenzyme Q ₁₀ in dioxane (b) dioxane and (c) nanoparticles placebo dispersion.....	136
D2 A representation of calibration curve of Coenzyme Q ₁₀	140

LIST OF ABBREVIATIONS

°C	=	Degree celsius
CV	=	coefficient of variation
DSC	=	differential scanning calorimetry
HLB	=	hydrophilic-lipophilic balance
HPLC	=	high performance liquid chromatography
ME	=	microemulsion
min	=	minute
mL	=	milliliter
mg	=	milligram
mM	=	millimolar
MP	=	melting point
mW	=	molecular weight
nm	=	nanometer
o/w	=	oil-in-water
PCS	=	photon correlation spectroscopy
SD	=	standard deviation
TEM	=	transmission electron microscope
µg	=	microgram
µL	=	microgram
UV	=	ultraviolet
w/v	=	weight by volume
w/w	=	weight by weight