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## **APPENDICES**

## **APPENDIX A**

The data of chemical substance used in formulation

The properties of surfactants used are as follows (Wade and Weller, 1994)

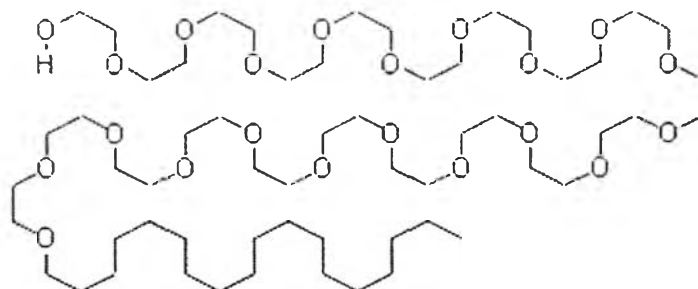
### 1. Brij<sup>®</sup> 72

Chemical name:	Polyoxyethylene (2) stearyl ether
Molecular formula:	C <sub>22</sub> H <sub>46</sub> O <sub>3</sub>
Molecular weight:	359
HLB:	4.9
Melting point:	43 °C
Specific gravity:	1.09
Solubility:	Soluble in ethanol. Dispersible in cottonseed oil Insoluble in mineral oil, propylene glycol and water
Appearance:	White waxy solid
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent and wetting agent

### 2. Brij<sup>®</sup> 78

Chemical name:	Polyoxyethylene (20) stearyl ether
Molecular formula:	C <sub>38</sub> H <sub>118</sub> O <sub>21</sub>
Molecular weight:	1151.56
HLB:	15.3
Melting point:	38 °C
Specific gravity:	1.09
Solubility:	Soluble in ethanol and water. Dispersible in cottonseed oil Insoluble in mineral oil, propylene glycol
Appearance:	White waxy solid
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent and wetting agent

Structural formula:



### 3. Cetostearyl alcohol (Laurex<sup>®</sup>)

Chemical name:	Cetostearyl alcohol
Definition:	A mixture of solid aliphatic alcohols. It contains not less than 40% of stearyl alcohol (C <sub>18</sub> H <sub>38</sub> O; MW 270.5) and the sum of the contents of cetyl alcohol (C <sub>16</sub> H <sub>34</sub> O; MW 242.4) and of stearyl alcohol is not less than 90.0%
HLB:	13-14
Melting point:	48-53 °C
Density:	0.4 g/cm <sup>3</sup>
Solubility:	Soluble in ethanol (95%), ether and oil Practically insoluble in water
Appearance:	White flakes or granules. On heating, it melts to a clear, colorless liquid free of suspended matter.
Functional category:	Emollient, emulsifying agent, viscosity-increasing agent

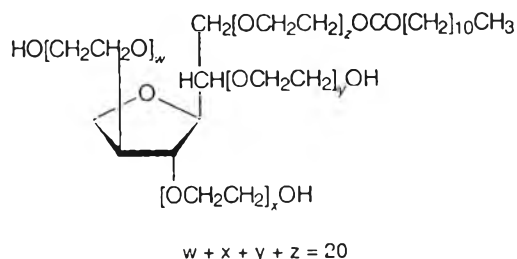
#### 4. Cetomacrogol 1000 (Cresmer<sup>®</sup> 1000)

Chemical name:	Polyoxyethylene glycol 1000
Molecular formula:	$\text{CH}_3 (\text{CH}_2)_m (\text{OCH}_2\text{CH}_2)_n \text{OH}$ where $m = 15-17$ and $n = 20-24$
Molecular weight:	1125-1326
HLB:	15.8
Melting point:	38 °C
Specific gravity:	0.949
Refractive index:	1.448-1.452
Solubility:	Soluble in water, toluene and ethanol upon warming
Appearance:	White waxy solid at room temperature
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent and wetting agent

#### 5. Polysorbate 20 (Tween<sup>®</sup> 20)

Chemical name:	Polyoxyethylene (20) sorbitan monolaurate
Molecular formula:	$\text{C}_{58}\text{H}_{114}\text{O}_{26}$
Molecular weight:	1128
HLB:	16.7
Relative density:	1.1
Solubility:	Miscible with ethanol, water, ethyl acetate and methanol Insoluble in mineral oil and vegetable oil
Appearance:	Yellow oily liquid at 25 °C
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent, wetting agent and dispersing/suspending agent

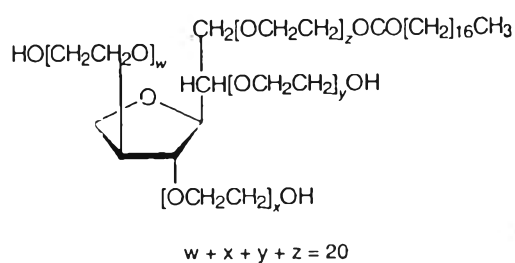
Structural formula:



## 6. Polysorbate 60 (Tween<sup>®</sup> 60)

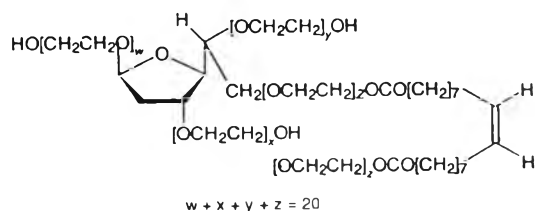
Chemical name:	Polyoxyethylene (20) sorbitan monostearate
Molecular formula:	$C_{64}H_{126}O_{26}$
Molecular Weight:	1312
HLB:	14.9
Relative density:	1.08
Solubility:	Miscible with ethanol, water, ethyl acetate and methanol Practically insoluble in fatty oils and in liquid paraffin
Appearance:	Yellow gelatinous mass at 25°C
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent, wetting agent and dispersing/suspending agent

Structural formula:



## 7. Polysorbate 80 (Tween<sup>®</sup> 80)

Chemical name:	Polyoxyethylene (20) sorbitan monooleate
Molecular formula:	$C_{64}H_{124}O_{26}$
Molecular Weight:	1310
HLB:	15.0
Relative density:	1.1
Solubility:	Miscible with water, alcohol, dehydrate alcohol, ethylacetate, and methyl alcohol Pratically insoluble in liquid paraffin and fixed oils
Appearance:	Yellowish or brownish-yellow oily liquid with a faint characteristic odor,
Functional category:	Non-ionic surfactant, emulsifying agent, solubilizing agent, wetting agent and dispersing/suspending agent
Structural formula	





## **APPENDIX B**

The details of microemulsion formation and appearance of nanoparticles and CoenzymeQ<sub>10</sub> – loaded nanoparticles.

All of formulations were prepared to the final volume of 2 mL. The appearance of the samples was recored as seen in Tables B1-B9 and the following symbols were used.

ME = microemulsion; C = clear; ST = slightly turbid; T = turbid; M = milky; P = precipitation or formulation unstable; PY = pale yellow color; YY = yellow color; SY= strong yellow color; N = microemulsion not formed at  $60 \pm 2$  °C; Y = microemulsion formed at  $60 \pm 2$  °C. \*mL = milliliter of 100 mM stock solution of 100 mM Brij<sup>®</sup> 78 or 10% Tween<sup>®</sup> 80.

**Table B1** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol:Tween<sup>®</sup> 20 and different concentrations of Brij<sup>®</sup> 78.

Rx	Brij <sup>®</sup> 78			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
A1	0	0	0	1.996	99.8	N	M	M	P
A2	1	0.02	1	1.976	98.8	N	M	M	M
A3	2	0.04	2	1.956	97.8	N	T	M	M
A4	3	0.06	3	1.936	96.8	N	T	T	M
A5	4	0.08	4	1.916	95.8	N	T	T	M
A6	5	0.10	5	1.896	94.8	N	T	T	M
A7	6	0.12	6	1.876	93.8	N	ST	M	M
A8	7	0.14	7	1.856	92.8	N	ST	M	M
A9	8	0.16	8	1.836	91.8	N	ST	M	P
A10	9	0.18	9	1.816	90.8	N	ST	P	P
A11	10	0.2	10	1.796	89.8	Y	ST	P	P
A12	11	0.22	11	1.776	88.8	Y	ST	P	P
A13	12	0.24	12	1.756	87.8	Y	ST	P	P
A14	13	0.26	13	1.736	86.8	Y	ST	P	P
A15	14	0.28	14	1.716	85.8	Y	ST	P	P
A16	15	0.3	15	1.696	84.8	Y	ST	P	P

**Table B2** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: Tween<sup>®</sup> 60 and different concentrations of Brij<sup>®</sup> 78.

Rx	Brij <sup>®</sup> 78			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
A17	0	0	0	1.996	99.8	N	M	M	P
A18	1	0.02	1	1.976	98.8	N	T	T	M
A19	2	0.04	2	1.956	97.8	N	T	T	M
A20	3	0.06	3	1.936	96.8	N	ST	T	M
A21	4	0.08	4	1.916	95.8	N	ST	T	M
A22	5	0.10	5	1.896	94.8	N	ST	T	M
A23	6	0.12	6	1.876	93.8	N	ST	T	M
A24	7	0.14	7	1.856	92.8	N	ST	M	P
A25	8	0.16	8	1.836	91.8	N	ST	M	P
A26	9	0.18	9	1.816	90.8	Y	ST	P	P
A27	10	0.20	10	1.796	89.8	Y	ST	P	P
A28	11	0.22	11	1.776	88.8	Y	ST	P	P
A29	12	0.24	12	1.756	87.8	Y	ST	P	P
A30	13	0.26	13	1.736	86.8	Y	ST	P	P
A31	14	0.28	14	1.716	85.8	Y	ST	P	P
A32	15	0.30	15	1.696	84.8	Y	ST	P	P

**Table B3** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: cetomacrogol) and different concentrations of Brij® 78.

Rx	Brij® 78			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
A33	0	0	0	1.996	99.8	N	M	M	P
A34	1	0.02	1	1.976	98.8	N	M	M	M
A35	2	0.04	2	1.956	97.8	N	T	T	M
A36	3	0.06	3	1.936	96.8	N	T	T	M
A37	4	0.08	4	1.916	95.8	N	T	T	M
A38	5	0.10	5	1.896	94.8	N	ST	T	M
A39	6	0.12	6	1.876	93.8	N	ST	M	P
A40	7	0.14	7	1.856	92.8	N	ST	M	P
A41	8	0.16	8	1.836	91.8	N	ST	M	P
A42	9	0.18	9	1.816	90.8	Y	ST	P	P
A43	10	0.20	10	1.796	89.8	Y	ST	P	P
A44	11	0.22	11	1.776	88.8	Y	ST	P	P
A45	12	0.24	12	1.756	87.8	Y	ST	P	P
A46	13	0.26	13	1.736	86.8	Y	ST	P	P
A47	14	0.28	14	1.716	85.8	Y	ST	P	P
A48	15	0.30	15	1.696	84.8	Y	ST	P	P

**Table B4** The appearance of formulations consisting of 2 mg/mL Brij 72<sup>®</sup> and different concentrations of Brij<sup>®</sup> 78.

Rx	Brij <sup>®</sup> 78			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
A49	0	0	0	1.996	99.8	N	M	M	P
A50	1	0.02	1	1.976	98.8	N	T	T	M
A51	2	0.04	2	1.956	97.8	N	T	T	M
A52	3	0.06	3	1.936	96.8	N	T	T	M
A53	4	0.08	4	1.916	95.8	N	T	T	M
A54	5	0.10	5	1.896	94.8	N	ST	T	M
A55	6	0.12	6	1.876	93.8	Y	ST	ST	P
A56	7	0.14	7	1.856	92.8	Y	ST	ST	P
A57	8	0.16	8	1.836	91.8	Y	ST	ST	P
A58	9	0.18	9	1.816	90.8	Y	ST	ST	P
A59	10	0.20	10	1.796	89.8	Y	ST	T	P
A60	11	0.22	11	1.776	88.8	Y	ST	T	P
A61	12	0.24	12	1.756	87.8	Y	ST	T	P
A62	13	0.26	13	1.736	86.8	Y	ST	P	P
A63	14	0.28	14	1.716	85.8	Y	ST	P	P
A64	15	0.30	15	1.696	84.8	Y	ST	P	P

**Table B5** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: Tween<sup>®</sup> 20) and different concentrations of Tween<sup>®</sup> 80.

Rx	Tween <sup>®</sup> 80			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
B1	0	0	0	1.996	99.80	N	M	M	P
B2	2	0.052	2.62	1.944	97.18	N	ST	T	T
B3	4	0.105	5.24	1.891	94.56	N	ST	ST	ST
B4	6	0.157	7.86	1.839	91.94	N	ST	ST	ST
B5	8	0.210	10.48	1.786	89.32	N	ST	ST	ST
B6	10	0.262	13.10	1.734	86.70	N	ST	ST	ST
B7	12	0.314	15.72	1.682	84.08	N	ST	ST	ST
B8	14	0.367	18.34	1.629	81.46	N	ST	ST	ST
B9	16	0.419	20.96	1.577	78.84	N	ST	ST	ST
B10	18	0.472	23.58	1.524	76.22	N	ST	ST	ST
B11	20	0.524	26.20	1.472	73.60	N	ST	ST	ST
B12	22	0.577	28.82	1.420	70.98	N	ST	ST	ST
B13	24	0.629	31.44	1.367	68.36	N	C	ST	ST
B14	26	0.681	34.06	1.315	65.74	N	C	ST	ST
B15	27	0.707	35.37	1.289	64.43	N	C	ST	ST
B16	28	0.734	36.68	1.262	63.12	Y	C	ST	T
B17	29	0.760	37.99	1.236	61.81	Y	C	T	T
B18	30	0.786	39.30	1.210	60.50	Y	C	T	T

**Table B6** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: Tween<sup>®</sup> 60) and different concentrations of Tween<sup>®</sup> 80.

Rx	Tween <sup>®</sup> 80			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
B19	0	0	0	1.996	99.80	N	M	M	P
B20	2	0	0	1.996	99.80	N	ST	T	T
B21	4	0.052	2.62	1.944	97.18	N	ST	ST	ST
B22	6	0.105	5.24	1.891	94.56	N	ST	ST	ST
B23	8	0.157	7.86	1.839	91.94	N	ST	ST	ST
B24	10	0.210	10.48	1.786	89.32	N	ST	ST	ST
B25	12	0.262	13.10	1.734	86.70	N	ST	ST	ST
B26	14	0.314	15.72	1.682	84.08	N	ST	ST	ST
B27	16	0.367	18.34	1.629	81.46	N	ST	ST	ST
B28	18	0.419	20.96	1.577	78.84	N	ST	ST	ST
B29	20	0.472	23.58	1.524	76.22	N	ST	ST	ST
B30	22	0.524	26.20	1.472	73.60	N	ST	ST	ST
B31	24	0.577	28.82	1.420	70.98	N	C	ST	ST
B32	25	0.655	32.75	1.341	67.05	N	C	ST	ST
B33	26	0.681	34.06	1.315	65.74	N	C	ST	ST
B34	27	0.707	35.37	1.289	64.43	Y	C	ST	ST
B35	28	0.734	36.68	1.262	63.12	Y	C	ST	ST
B36	29	0.760	37.99	1.236	61.81	Y	C	ST	ST
B37	30	0.786	39.30	1.210	60.50	Y	C	ST	ST

**Table B7** The appearance of formulations consisting of 2 mg/mL wax (4:1 cetostearyl alcohol: cetomacrogol) and different concentrations of Tween<sup>®</sup> 80.

Rx	Tween <sup>®</sup> 80			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
B38	0	0	0	1.996	99.80	N	M	M	P
B39	2	0.052	2.62	1.944	97.18	N	ST	T	T
B40	4	0.105	5.24	1.891	94.56	N	ST	ST	ST
B41	6	0.157	7.86	1.839	91.94	N	ST	ST	ST
B42	8	0.210	10.48	1.786	89.32	N	ST	ST	ST
B43	10	0.262	13.10	1.734	86.70	N	ST	ST	ST
B44	12	0.314	15.72	1.682	84.08	N	ST	ST	ST
B45	14	0.367	18.34	1.629	81.46	N	ST	ST	ST
B46	16	0.419	20.96	1.577	78.84	N	ST	ST	ST
B47	18	0.472	23.58	1.524	76.22	N	ST	ST	ST
B48	20	0.524	26.20	1.472	73.60	N	ST	ST	ST
B49	22	0.577	28.82	1.420	70.98	N	C	ST	ST
B50	23	0.603	30.13	1.393	69.67	N	C	ST	ST
B51	24	0.629	31.44	1.367	68.36	N	C	ST	ST
B52	25	0.655	32.75	1.341	67.05	Y	C	ST	ST
B53	26	0.6812	34.06	1.315	65.74	Y	C	ST	ST
B54	27	0.707	35.37	1.289	64.43	Y	C	ST	ST
B55	28	0.734	36.68	1.262	63.12	Y	C	ST	ST
B56	30	0.786	39.30	1.210	60.5	Y	C	ST	T



**Table B8** The appearance of formulations consisting of 2 mg/mL Brij<sup>®</sup> 72 and different concentrations of Tween<sup>®</sup> 80.

Rx	Tween <sup>®</sup> 80			Water		ME formation	Appearance		
	mM	*mL	%w/w	mL	%w/w		10 min	24 hours	1 week
B57	0	0	0	1.996	99.80	N	M	M	P
B58	2	0.052	2.62	1.944	97.18	N	ST	ST	T
B59	4	0.105	5.24	1.891	94.56	N	ST	ST	T
B60	6	0.1572	7.86	1.839	91.94	N	ST	ST	ST
B61	8	0.210	10.48	1.786	89.32	N	ST	ST	ST
B62	10	0.262	13.10	1.734	86.70	N	ST	ST	ST
B63	12	0.314	15.72	1.682	84.08	N	ST	ST	ST
B64	14	0.367	18.34	1.629	81.46	N	ST	ST	ST
B65	16	0.419	20.96	1.577	78.84	N	C	ST	ST
B66	17	0.445	22.27	1.551	77.53	N	C	ST	ST
B67	18	0.472	23.58	1.524	76.22	N	C	ST	ST
B68	19	0.498	24.89	1.498	74.91	Y	C	ST	ST
B69	20	0.524	26.20	1.472	73.60	Y	C	ST	ST
B70	21	0.550	27.51	1.446	72.29	Y	C	ST	ST
B71	22	0.576	28.82	1.420	70.98	Y	C	ST	ST
B73	24	0.629	31.44	1.367	68.36	Y	C	ST	ST
B75	26	0.681	34.06	1.315	65.74	Y	C	ST	ST
B77	28	0.734	36.68	1.262	63.12	Y	C	T	T
B78	30	0.786	39.30	1.210	60.50	Y	C	T	T

**Table B9** The appearance of Coenzyme Q<sub>10</sub>-loaded nanoparticles formulation.

Rx	wax (%w/w)	Co- Q <sub>10</sub> (%w/w)	20% Tween <sup>®</sup> 80		Water (%w/w)	ME formation (at 60 ± 2°C)	Appearance	
			mM	%w/w			10 min	24 hours
C11	0.2	0.1	20	13.10	86.60	N	ST, PY	ST, PY
C12	0.2	0.1	24	15.72	83.98	Y	C, PY	ST, PY
C13	0.2	0.1	30	19.65	80.05	Y	C, PY	C, PY
C14	0.2	0.1	35	22.93	76.78	Y	C, PY	C, PY
C15	0.2	0.1	40	26.20	73.50	Y	C, PY	C, PY
C16	0.2	0.1	45	29.48	70.26	Y	C, PY	C, PY
C17	0.2	0.1	50	32.75	66.95	Y	C, PY	C, PY
C18	0.2	0.1	60	39.30	60.40	Y	C, PY	C, PY
C21	0.2	0.2	20	13.10	86.50	N	ST, PY	ST, PY
C22	0.2	0.2	24	15.72	83.88	Y	C, PY	ST, PY
C23	0.2	0.2	30	19.65	79.95	Y	ST, PY	ST, PY
C24	0.2	0.2	35	22.93	76.68	Y	C, PY	ST, PY
C25	0.2	0.2	40	26.20	73.40	Y	C, PY	ST, PY
C26	0.2	0.2	45	29.48	70.13	Y	C, PY	C, PY
C27	0.2	0.2	50	32.75	66.85	Y	C, PY	C, PY
C28	0.2	0.2	60	39.30	60.30	Y	C, PY	C, PY
C32	0.2	0.3	24	15.72	83.78	N	C, YY	ST, YY
C42	0.2	0.4	24	15.72	83.68	N	ST, SY	ST, SY
D11	0.4	0.1	35	22.93	76.58	N	ST, PY	ST, PY
D12	0.4	0.1	40	26.20	73.30	N	ST, PY	ST, PY
D13	0.4	0.1	45	29.48	70.03	N	ST, PY	ST, PY
D14	0.4	0.1	48	31.44	68.06	Y	ST, PY	ST, PY
D15	0.4	0.1	50	32.75	66.75	Y	C, PY	ST, PY
D16	0.4	0.1	55	36.03	63.48	Y	C, PY	ST, PY

Table B9 (Continued)

Rx	wax (%w/w)	Co- Q <sub>10</sub> (%w/w)	20% Tween <sup>®</sup> 80		Water (%w/w)	ME formation (at 60 ± 2°C )	Appearance	
			mM	%w/w			10 min	24 hours
D17	0.4	0.1	60	39.30	60.20	Y	C,PY	ST,PY
D18	0.4	0.1	70	45.85	53.65	Y	C,PY	ST,PY
D21	0.4	0.2	35	22.93	76.48	N	ST,YY	ST,YY
D22	0.4	0.2	40	26.20	73.20	N	ST,YY	ST,YY
D23	0.4	0.2	45	29.48	69.93	N	ST,YY	ST,YY
D24	0.4	0.2	48	31.44	67.96	Y	ST,YY	ST,YY
D25	0.4	0.2	50	32.75	66.65	Y	C,YY	ST,YY
D26	0.4	0.2	55	36.03	63.38	Y	C,YY	ST,YY
D27	0.4	0.2	60	39.30	60.10	Y	C,YY	ST,YY
D28	0.4	0.2	70	45.85	53.55	Y	C,YY	ST,YY
D34	0.4	0.3	48	31.44	67.86	Y	ST, YY	ST, YY
D44	0.4	0.4	48	31.44	67.76	Y	ST, SY	ST, SY
E11	0.6	0.1	35	22.93	76.38	N	T,PY	T,PY
E12	0.6	0.1	40	26.20	73.10	N	ST,PY	T,PY
E13	0.6	0.1	45	29.48	69.83	N	ST,PY	T,PY
E14	0.6	0.1	50	32.75	66.55	N	C,PY	T,PY
E15	0.6	0.1	60	39.30	60.00	N	C,PY	T,PY
E16	0.6	0.1	72	47.16	52.14	Y	C,PY	ST,PY
E17	0.6	0.1	80	52.40	46.90	Y	C,PY	ST,PY
E18	0.6	0.1	90	58.95	40.35	Y	C,PY	ST,PY
E21	0.6	0.2	35	22.93	76.28	N	T,YY	T,YY
E22	0.6	0.2	40	26.20	73.00	N	T,YY	T,YY

**Table B9** (continued)

Rx	wax (%w/w)	Co- Q <sub>10</sub> (%w/w)	20% Tween <sup>®</sup> 80		Water (%w/w)	ME formation at 60 ± 2°C	Appearance	
			mM <sub>i</sub>	%w/w			10 min	24 hours
E23	0.6	0.2	45	29.48	69.73	N	T,YY	T,YY
E24	0.6	0.2	50	32.75	66.45	N	ST,YY	ST,YY
E25	0.6	0.2	60	39.30	59.90	N	C,YY	ST,YY
E26	0.6	0.2	72	47.16	52.04	Y	C,YY	ST,YY
E27	0.6	0.2	80	52.40	46.80	N	C,YY	ST,YY
E28	0.6	0.2	90	58.95	40.25	N	C,YY	ST,YY
E36	0.6	0.3	72	47.16	51.94	Y	ST, YY	ST, YY
E46	0.6	0.4	72	47.16	51.84	Y	ST, SY	ST, SY

## **APPENDIX C**

The data and graph of particle size and size distribution of nanoparticles and CoenzymeQ<sub>10</sub> –loaded nanoparticles

The data of nanoparticle sizes (average diameter or z-average) and size distribution (Polydispersity Index; PI) were reported as mean  $\pm$  SD (n=3). The data are in Tables C1-C6 and Figure C1.

**Table C1** Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by simple cooling method using Brij<sup>®</sup> 78 as a surfactant determined at 4 hours and 24 hours.

Rx	Time (hrs)	Z-average (nm)				PI			
		1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
A9	4	94.60	92.0	91.60	92.73 $\pm$ 1.63	0.193	0.192	0.200	0.318 $\pm$ 0.004
	24	861.90	341.30	454.60	552.60 $\pm$ 273.79	1	1	1	1
A11	4	56.50	53.70	54.10	54.77 $\pm$ 1.51	0.307	0.338	0.310	0.318 $\pm$ 0.020
	24	1682.40	2097.10	1008.00	1595.83 $\pm$ 549.69	1	1	1	1
A13	4	55.80	54.30	54.90	55.00 $\pm$ 0.75	0.387	0.350	0.304	0.347 $\pm$ 0.040
	24	663.00	1622.60	835.10	1040.23 $\pm$ 511.63	1	1	1	1
A24	4	106.40	102.20	102.30	103.63 $\pm$ 2.40	0.255	0.227	0.237	0.240 $\pm$ 0.010
	24	365.20	336.70	286.80	329.57 $\pm$ 39.68	1	1	1	1
A26	4	72.40	73.60	71.10	72.37 $\pm$ 1.25	0.360	0.355	0.340	0.35 $\pm$ 0.010
	24	743.40	325.90	345.30	471.53 $\pm$ 235.64	1	0.955	0.903	0.95 $\pm$ 0.450
A28	4	60.90	68.80	63.80	64.50 $\pm$ 3.40	0.410	0.434	0.379	0.408 $\pm$ 0.028
	24	837.40	605.00	409.30	617.23 $\pm$ 214.31	1	1	1	1

Table C1 (Continued)

Rx	Time (hrs)	Z-average (nm)				PI			
		1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
A40	4	93.10	91.50	91.90	92.17 $\pm$ 0.83	0.168	0.175	0.158	0.167 $\pm$ 0.010
	24	119.20	121.10	121.80	120.70 $\pm$ 1.35	0.256	0.342	0.333	0.310 $\pm$ 0.050
A42	4	60.50	59.40	58.60	59.50 $\pm$ 0.95	0.307	0.240	0.228	0.258 $\pm$ 0.040
	24	149.10	119.20	161.80	143.37 $\pm$ 21.87	0.633	0.531	0.572	0.579 $\pm$ 0.050
A44	4	51.90	52.80	50.10	51.60 $\pm$ 1.37	0.298	0.253	0.217	0.256 $\pm$ 0.041
	24	175.70	167.20	151.40	164.77 $\pm$ 12.33	0.663	0.589	0.754	0.669 $\pm$ 0.083
A53	4	468.10	488.30	446.20	467.53 $\pm$ 21.06	0.378	0.366	0.380	0.375 $\pm$ 0.008
	24	592.80	578.40	595.00	588.73 $\pm$ 9.016	0.471	0.501	0.486	0.486 $\pm$ 0.015
A55	4	550.50	545.50	549.80	548.60 $\pm$ 2.71	0.399	0.382	0.367	0.383 $\pm$ 0.017
	24	609.00	621.10	582.40	604.17 $\pm$ 19.80	0.522	0.554	0.469	0.515 $\pm$ 0.043
A57	4	416.50	410.20	402.30	409.67 $\pm$ 7.12	0.262	0.200	0.187	0.211 $\pm$ 0.040
	24	489.00	472.40	465.70	475.70 $\pm$ 12.0	0.356	0.363	0.352	0.357 $\pm$ 0.006

**Table C2** Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by simple cooling method using Tween<sup>®</sup>80 as a surfactant determined at 4 hours and 24 hours.

Rx	Time (hrs)	Z-average (nm)				PI			
		1	2	3	Mean ± SD	1	2	3	Mean ± SD
B14	4	178.60	170.40	165.10	171.37 ± 6.80	0.429	0.457	0.476	0.454 ± 0.024
	24	200.90	180.40	172.40	184.57 ± 14.70	0.366	0.416	0.437	0.406 ± 0.036
B16	4	255.60	223.60	213.30	230.83 ± 2.06	0.389	0.449	0.479	0.439 ± 0.046
	24	242.90	231.00	216.40	230.10 ± 13.27	0.405	0.430	0.440	0.425 ± 0.018
B18	4	988.50	1067.60	957.80	1004.60 ± 56.65	0.607	0.568	0.578	0.584 ± 0.020
	24	1602.20	1723.20	1614.40	1646.60 ± 66.62	0.881	1	1	0.96 ± 0.069
B32	4	108.30	100.80	96.90	102.00 ± 5.79	0.378	0.448	0.434	0.42 ± 0.037
	24	109.90	97.70	98.10	101.90 ± 6.93	0.366	0.414	0.399	0.393 ± 0.026
B34	4	135.60	117.30	111.90	121.60 ± 12.42	0.364	0.457	0.487	0.436 ± 0.064
	24	135.70	122.20	115.80	124.57 ± 10.16	0.369	0.412	0.435	0.405 ± 0.034
B36	4	220.60	195.30	184.60	200.17 ± 18.49	0.412	0.491	0.505	0.469 ± 0.050
	24	213.30	197.90	186.40	199.20 ± 13.50	0.441	0.437	0.484	0.424 ± 0.026



Table C2 (Continued)

Rx	Time	Z-average (nm)				PI			
		1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
B50	4 hrs	79.00	72.40	70.40	73.93 $\pm$ 4.50	0.358	0.408	0.412	0.393 $\pm$ 0.030
	24 hrs	88.20	82.00	80.80	83.67 $\pm$ 3.97	0.357	0.393	0.386	0.362 $\pm$ 0.019
	48 hrs	124.00	116.30	112.80	117.70 $\pm$ 5.73	0.386	0.388	0.429	0.401 $\pm$ 0.020
	1 wk	125.60	122.00	119.20	122.27 $\pm$ 3.20	0.385	0.394	0.419	0.399 $\pm$ 0.018
B52	4 hrs	89.40	79.50	76.80	81.90 $\pm$ 6.63	0.373	0.425	0.420	0.406 $\pm$ 0.029
	24 hrs	97.40	86.50	84.20	89.37 $\pm$ 7.05	0.340	0.397	0.406	0.381 $\pm$ 0.036
	48 hrs	109.90	105.60	102.90	106.13 $\pm$ 3.53	0.439	0.464	0.458	0.454 $\pm$ 0.013
	1 wk	120.40	111.90	110.50	114.27 $\pm$ 5.36	0.399	0.450	0.466	0.438 $\pm$ 0.035
B54	4 hrs	76.60	71.30	68.90	72.3 $\pm$ 3.93	0.356	0.375	0.393	0.375 $\pm$ 0.019
	24 hrs	90.70	83.00	81.80	85.20 $\pm$ 4.83	0.319	0.351	0.343	0.338 $\pm$ 0.017
	48 hrs	111.50	98.20	92.50	100.73 $\pm$ 9.75	0.369	0.429	0.452	0.417 $\pm$ 0.043
	1 wk	118.00	114.10	112.70	114.93 $\pm$ 2.75	0.370	0.401	0.392	0.388 $\pm$ 0.016

Table C2 (Continued)

Rx	Time (hrs)	Z-average (nm)				PI			
		1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
B66	4	76.60	71.60	71.30	73.20 $\pm$ 2.98	0.335	0.365	0.347	0.349 $\pm$ 0.015
	24	102.00	96.60	77.80	92.10 $\pm$ 12.70	0.303	0.339	0.533	0.392 $\pm$ 0.124
B68	4	79.30	69.90	67.70	72.30 $\pm$ 6.16	0.400	0.409	0.425	0.411 $\pm$ 0.012
	24	106.80	96.30	94.30	99.10 $\pm$ 6.71	0.386	0.425	0.423	0.412 $\pm$ 0.022
B70	4	134.60	125.30	119.30	126.40 $\pm$ 7.71	0.458	0.472	0.499	0.476 $\pm$ 0.021
	24	160.20	141.80	137.20	146.40 $\pm$ 12.17	0.438	0.459	0.484	0.460 $\pm$ 0.023



**Table C3** Average diameter (z-average) and polydispersity index (PI) of drug-free nanoparticles prepared by rapid cooling method using Tween<sup>®</sup>80 as a surfactant.

Rx	Time	Z-average (nm)				PI			
		1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
B50	4 hrs	59.40	54.40	53.50	55.77 $\pm$ 3.18	0.455	0.496	0.499	0.483 $\pm$ 0.025
	24 hrs	77.40	73.50	72.90	74.60 $\pm$ 2.44	0.421	0.440	0.429	0.430 $\pm$ 0.010
	48 hrs	87.80	78.70	75.60	80.70 $\pm$ 6.34	0.377	0.432	0.445	0.418 $\pm$ 0.036
	1 wk	98.20	90.40	86.50	91.70 $\pm$ 5.96	0.356	0.399	0.418	0.391 $\pm$ 0.032
B52	4 hrs	55.10	52.00	51.60	52.90 $\pm$ 1.92	0.550	0.550	0.564	0.555 $\pm$ 0.008
	24 hrs	93.00	92.80	91.60	92.47 $\pm$ 0.76	0.499	0.485	0.380	0.455 $\pm$ 0.065
	48 hrs	102.20	95.50	94.00	97.23 $\pm$ 4.37	0.359	0.389	0.404	0.384 $\pm$ 0.023
	1 wk	113.20	107.20	102.80	107.73 $\pm$ 5.22	0.367	0.396	0.415	0.393 $\pm$ 0.024
B54	4 hrs	20.90	23.30	19.40	21.20 $\pm$ 1.97	0.448	0.416	0.409	0.424 $\pm$ 0.021
	24 hrs	51.50	47.50	42.30	47.10 $\pm$ 4.61	0.500	0.517	0.522	0.513 $\pm$ 0.012
	48 hrs	70.10	59.50	56.40	62.00 $\pm$ 7.18	0.449	0.515	0.537	0.500 $\pm$ 0.046
	1 wk	104.70	91.30	94.50	96.83 $\pm$ 7.00	0.446	0.502	0.419	0.456 $\pm$ 0.042

**Table C4** Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q<sub>10</sub>-loaded nanoparticles prepared by rapid cooling method determined at 24 hours.

Rx	Z-average (nm)				PI			
	1	2	3	Mean ± SD	1	2	3	Mean ± SD
C11	73.90	71.20	67.60	70.90 ± 3.16	0.460	0.490	0.495	0.482 ± 0.019
C12	65.30	62.70	61.50	63.17 ± 1.94	0.491	0.506	0.507	0.501 ± 0.009
C13	35.30	30.60	29.00	31.63 ± 3.27	0.556	0.544	0.544	0.548 ± 0.007
C14	55.90	48.30	44.30	49.50 ± 5.89	0.568	0.570	0.568	0.569 ± 0.001
C15	55.10	40.30	30.90	42.10 ± 12.20	0.622	0.631	0.612	0.622 ± 0.010
C16	53.50	37.70	27.60	39.60 ± 13.05	0.614	0.629	0.587	0.610 ± 0.021
C17	40.40	29.40	24.60	31.47 ± 8.10	0.623	0.604	0.520	0.582 ± 0.055
C18	35.50	26.60	22.40	28.17 ± 6.69	0.623	0.574	0.546	0.581 ± 0.039
C21	93.80	90.70	88.80	91.10 ± 2.52	0.455	0.473	0.481	0.470 ± 0.013
C22	64.10	55.50	51.40	57.00 ± 6.48	0.549	0.552	0.556	0.552 ± 0.004
C23	49.40	42.90	38.90	43.73 ± 5.30	0.537	0.538	0.527	0.534 ± 0.006
C24	77.10	63.50	60.50	67.03 ± 8.85	0.489	0.524	0.522	0.512 ± 0.020
C25	53.70	39.10	32.50	41.77 ± 10.85	0.605	0.595	0.584	0.595 ± 0.011
C26	51.00	35.50	26.10	37.53 ± 12.57	0.627	0.624	0.579	0.610 ± 0.027
C27	52.70	35.20	25.60	37.83 ± 13.74	0.619	0.601	0.577	0.599 ± 0.021
C28	41.10	28.40	38.10	35.87 ± 6.64	0.629	0.596	0.340	0.522 ± 0.158
C32	50.80	44.80	41.10	45.57 ± 4.90	0.590	0.584	0.573	0.582 ± 0.009
C42	89.00	83.50	79.70	84.07 ± 4.68	0.672	0.668	0.661	0.667 ± 0.005

Table C4 (Continued)

Rx	Z-average (nm)				PI			
	1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
D11	113.20	107.50	105.00	108.57 $\pm$ 4.20	0.312	0.320	0.320	0.317 $\pm$ 0.005
D12	102.30	96.60	94.70	97.87 $\pm$ 3.96	0.382	0.399	0.422	0.401 $\pm$ 0.020
D13	112.40	98.20	92.20	100.93 $\pm$ 10.37	0.353	0.382	0.416	0.384 $\pm$ 0.032
D14	94.80	88.90	86.50	90.07 $\pm$ 4.27	0.364	0.377	0.381	0.374 $\pm$ 0.009
D15	90.80	79.10	78.80	82.90 $\pm$ 6.84	0.336	0.410	0.425	0.390 $\pm$ 0.048
D16	83.70	80.99	77.30	80.60 $\pm$ 3.20	0.391	0.381	0.400	0.391 $\pm$ 0.009
D17	68.40	60.80	57.10	62.10 $\pm$ 5.76	0.479	0.516	0.542	0.512 $\pm$ 0.032
D18	76.00	68.20	64.80	69.67 $\pm$ 5.74	0.543	0.557	0.563	0.554 $\pm$ 0.010
D21	107.10	100.30	99.20	102.20 $\pm$ 4.28	0.336	0.358	0.347	0.347 $\pm$ 0.011
D22	127.30	118.70	118.70	121.57 $\pm$ 4.97	0.415	0.419	0.423	0.419 $\pm$ 0.004
D23	86.20	75.80	73.20	78.40 $\pm$ 6.88	0.423	0.473	0.481	0.459 $\pm$ 0.031
D24	91.60	85.70	83.00	86.77 $\pm$ 4.40	0.460	0.471	0.474	0.469 $\pm$ 0.007
D25	85.20	75.00	71.20	77.13 $\pm$ 7.24	0.424	0.470	0.478	0.457 $\pm$ 0.029
D26	73.80	67.00	64.40	68.40 $\pm$ 4.85	0.533	0.559	0.557	0.550 $\pm$ 0.015
D27	70.50	60.70	57.00	62.73 $\pm$ 6.98	0.488	0.541	0.555	0.528 $\pm$ 0.035
D28	69.30	59.20	54.00	60.83 $\pm$ 7.78	0.604	0.602	0.596	0.601 $\pm$ 0.004
D34	91.80	84.40	80.90	85.70 $\pm$ 5.57	0.469	0.501	0.504	0.491 $\pm$ 0.020
D44	96.80	84.40	77.80	86.33 $\pm$ 9.65	0.496	0.516	0.533	0.515 $\pm$ 0.018

**Table C4** (Continued)

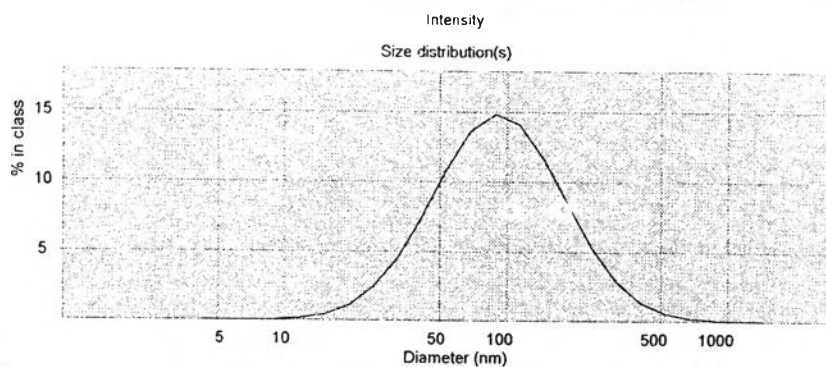
Rx	Z-average (nm)				PI			
	1	2	3	Mean $\pm$ SD	1	2	3	Mean $\pm$ SD
E11	124.40	117.50	116.30	119.40 $\pm$ 4.37	0.323	0.327	0.321	0.323 $\pm$ 0.003
E12	105.90	99.30	98.50	101.23 $\pm$ 4.06	0.229	0.251	0.248	0.243 $\pm$ 0.012
E13	112.90	106.00	104.80	107.90 $\pm$ 4.37	0.252	0.269	0.27	0.262 $\pm$ 0.009
E14	125.10	117.70	113.40	118.73 $\pm$ 5.92	0.314	0.338	0.347	0.333 $\pm$ 0.017
E15	129.90	120.10	117.90	122.73 $\pm$ 6.39	0.283	0.307	0.311	0.300 $\pm$ 0.015
E16	128.30	126.90	123.10	126.10 $\pm$ 2.69	0.490	0.477	0.483	0.483 $\pm$ 0.006
E17	94.00	89.70	87.20	90.30 $\pm$ 3.44	0.417	0.452	0.456	0.442 $\pm$ 0.021
E18	104.10	91.80	86.30	94.07 $\pm$ 9.11	0.491	0.515	0.523	0.510 $\pm$ 0.017
E21	116.40	110.40	107.40	111.40 $\pm$ 4.58	0.274	0.275	0.282	0.277 $\pm$ 0.004
E22	121.50	112.00	109.80	114.43 $\pm$ 6.22	0.282	0.312	0.329	0.308 $\pm$ 0.024
E23	125.20	119.00	118.40	120.87 $\pm$ 3.76	0.305	0.327	0.326	0.319 $\pm$ 0.013
E24	117.40	109.10	107.50	111.33 $\pm$ 5.31	0.298	0.330	0.339	0.322 $\pm$ 0.021
E25	113.70	106.20	104.40	108.10 $\pm$ 4.93	0.356	0.387	0.392	0.378 $\pm$ 0.019
E26	95.90	89.20	85.40	90.17 $\pm$ 5.32	0.462	0.474	0.501	0.479 $\pm$ 0.020
E27	95.40	88.40	85.30	89.70 $\pm$ 5.17	0.450	0.469	0.477	0.465 $\pm$ 0.014
E28	103.50	95.30	89.10	95.97 $\pm$ 7.22	0.468	0.479	0.500	0.483 $\pm$ 0.016
E36	92.40	87.60	86.30	88.77 $\pm$ 3.21	0.474	0.504	0.514	0.497 $\pm$ 0.020
E46	126.5	116.00	113.70	118.73 $\pm$ 6.82	0.435	0.462	0.467	0.455 $\pm$ 0.017

**Table C5** The stability data of Average diameter (z-average) and polydispersity index (PI) of Coenzyme Q<sub>10</sub>-loaded nanoparticles (rapid cooling method).

Rx	Time	Z-average (nm)				PI			
		1	2	3	Mean ± SD	1	2	3	Mean ± SD
D24	24 hrs	108.30	95.30	90.10	97.90 ± 9.37	0.388	0.411	0.429	0.409 ± 0.020
	1 wk	106.40	94.90	93.40	98.23 ± 7.11	0.406	0.437	0.428	0.424 ± 0.016
	4 wks	102.10	98.30	95.50	98.63 ± 3.31	0.431	0.423	0.438	0.431 ± 0.008
	8 wks	102.80	95.80	92.70	97.10 ± 5.17	0.433	0.443	0.458	0.444 ± 0.013
D44	24 hrs	96.80	84.40	77.80	86.33 ± 9.65	0.496	0.516	0.533	0.515 ± 0.018
	1 wk	103.30	89.90	82.40	91.87 ± 10.59	0.513	0.532	0.527	0.524 ± 0.010
	4 wks	95.80	86.30	82.00	88.03 ± 7.06	0.517	0.523	0.524	0.522 ± 0.004
	8 wks	100.00	90.10	84.20	91.43 ± 7.98	0.509	0.531	0.526	0.522 ± 0.012

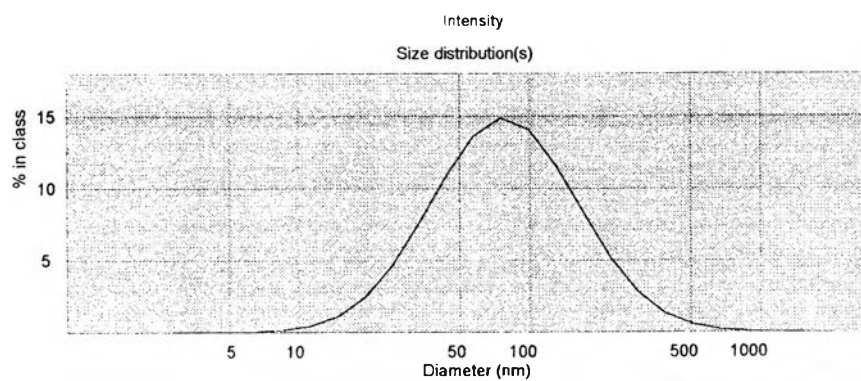
**Table C6** Average diameter (z-average) and polydispersity index (PI) of freeze-dried Coenzyme Q<sub>10</sub>- loaded nanoparticles (Rx D24 and D44), determined after 1-week at 25°C.

Rx	Manitol (%)	Z-average (nm)				PI			
		1	2	3	Mean ± SD	1	2	3	Mean ± SD
D24	1	85.2	83.2	83.9	84.10 ± 1.06	0.061	0.580	0.573	0.587 ± 0.018
	2	87.6	84.4	85.9	85.97 ± 1.60	0.611	0.602	0.586	0.600 ± 0.013
	4	93.3	90.0	92.0	91.77 ± 1.66	0.527	0.516	0.483	0.508 ± 0.023
D44	1	81.0	79.5	79.6	80.03 ± 0.84	0.552	0.551	0.565	0.556 ± 0.008
	2	74.0	73.2	72.2	73.13 ± 0.90	0.523	0.513	0.519	0.518 ± 0.005
	4	84.3	84.1	82.9	83.77 ± 0.76	0.480	0.461	0.460	0.467 ± 0.012



Size (nm)	% Intensity	Size (nm)	% Intensity	Size (nm)	% Intensity
4.3	0.0	32.3	4.6	244.5	5.2
5.5	0.0	41.6	7.6	314.8	2.8
7.1	0.0	53.6	10.9	405.3	1.3
9.1	0.0	69.1	13.6	521.9	0.6
11.8	0.2	88.9	14.9	672.0	0.2
15.1	0.4	114.5	14.1	865.4	0.1
19.5	1.1	147.4	11.6	1114.3	0.0
25.1	2.4	189.8	8.3	1434.8	0.0

(a)



Size (nm)	% Intensity	Size (nm)	% Intensity	Size (nm)	% Intensity
2.9	0.0	25.5	4.6	224.2	5.2
3.8	0.0	33.4	7.6	294.3	2.8
5.0	0.0	43.8	10.9	386.3	1.3
6.5	0.0	57.6	13.7	507.0	0.5
8.6	0.2	75.5	14.9	665.5	0.2
11.3	0.4	99.2	14.1	873.5	0.1
14.8	1.1	130.1	11.6	1146.5	0.0
19.4	2.4	170.8	8.3	1504.9	0.0

(b)

**Figure C1** Particle size distribution of Coenzyme Q<sub>10</sub>- loaded nanoparticles, a) Rx D24, b) Rx D44, determined at 24 hours after preparation.



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## **APPENDIX E**

Statistical analysis data using SPSS program

**Table E1** The statistical analysis of concentration of Brij® 78 and nanoparticle size using cetostearyl alcohol and Tween® 20 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	6096274.423	5	1219254.885	11.450	.000
Within Groups	1277774.907	12	106481.242		
Total	7374049.329	17			

Tukey HSD				
Brij 78 concentration	N	Subset for alpha = .05		
		1	2	3
10 mM 4 hours	3	54.7667		
12 mM 4 hours	3	55.0000		
8 mM 4 hours	3	92.7333		
8 mM 24 hours	3	552.6000	552.6000	
12 mM 24 hours	3		1040.2333	1040.2333
10 mM 24 hours	3			1595.8333
Sig.		.463	.484	.355

**Table E2** The statistical analysis of concentration of Brij® 78 and nanoparticle size using cetostearyl alcohol and Tween® 60 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	820351.723	5	164070.345	9.552	.001
Within Groups	206110.853	12	17175.904		
Total	1026462.576	17			

Tukey HSD			
Brij 78 concentration	N	Subset for alpha = .05	
		1	2
11 mM 4 hours	3	64.5000	
9 mM 4 hours	3	72.3667	
7 mM 4 hours	3	103.6333	
7 mM 24 hours	3	329.5667	329.5667
9 mM 24 hours	3		471.5333
11 mM 24 hours	3		617.2333
Sig.		.205	.149

**Table E3** The statistical analysis of concentration of Brij<sup>®</sup> 78 and nanoparticle size using cetostearyl alcohol and cetomacrogol as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	31128.945	5	6225.789	58.761	.000
Within Groups	1271.420	12	105.952		
Total	32400.365	17			

Tukey HSD					
Brij 78 concentration	N	Subset for alpha = .05			
		1	2	3	4
11 mM 4 hours	3	51.6000			
9 mM 4 hours	3	59.5000			
7 mM 4 hours	3		92.1667		
7 mM 24 hours	3			120.7000	
9 mM 24 hours	3			143.3667	143.3667
11 mM 24 hours	3				164.7667
Sig.		.928	1.000	.147	.185

**Table E4** The statistical analysis of concentration of Brij<sup>®</sup> 78 and nanoparticle size using Brij<sup>®</sup> 72 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	88217.153	5	17643.431	94.652	.000
Within Groups	2236.847	12	186.404		
Total	90454.000	17			

Tukey HSD					
Brij 78 concentration	N	Subset for alpha = .05			
		1	2	3	4
8 mM 4 hours	3	409.6667			
4 mM 4 hours	3		467.5333		
8 mM 24 hours	3		475.7000		
6 mM 4 hours	3			548.6000	
4 mM 24 hours	3				588.7333
6 mM 24 hours	3				604.1667
Sig.		1.000	.974	1.000	.735

**Table E5** The statistical analysis of concentration of Tween® 80 and nanoparticle size using cetostearyl alcohol and Tween® 20 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5656864.558	5	1131372.912	791.891	.000
Within Groups	17144.367	12	1428.697		
Total	5674008.925	17			

Tukey HSD				
Tween 80 concentration	N	Subset for alpha = .05		
		1	2	3
26 mM 4 hours	3	171.3667		
26 mM 24 hours	3	184.5667		
28 mM 24 hours	3	230.1000		
28 mM 4 hours	3	230.8333		
30 mM 4 hours	3		1004.6333	
30 mM 24 hours	3			1646.6000
Sig.		.432	1.000	1.000

**Table E6** The statistical analysis of concentration of Tween® 80 and nanoparticle size using cetostearyl alcohol and Tween® 60 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	31746.583	5	6349.317	44.142	.000
Within Groups	1726.073	12	143.839		
Total	33472.656	17			

Tukey HSD			
Tween 80 concentration	N	Subset for alpha = .05	
		1	2
25 mM 24 hours	3	101.9000	
25 mM 4 hours	3	102.0000	
27 mM 4 hours	3	121.6000	
27 mM 24 hours	3	124.5667	
29 mM 24 hours	3		199.2000
29 mM 4 hours	3		200.1667
Sig.		.260	1.000



**Table E7** The statistical analysis of concentration of Tween® 80 and nanoparticle size using cetostearyl alcohol and cetostearyl alcohol as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	664.432	5	132.886	4.729	.013
Within Groups	337.213	12	28.101		
Total	1001.645	17			

Tukey HSD			
Tween 80 concentration	N	Subset for alpha = .05	
		1	2
27 mM 4 hours	3	72.2667	
23 mM 4 hours	3	73.9333	
25 mM 4 hours	3	81.9000	81.9000
23 mM 24 hours	3	83.6667	83.6667
27 mM 24 hours	3	85.1667	85.1667
25 mM 24 hours	3		89.3667
Sig.		.093	.542

**Table E8** The statistical analysis of concentration of Tween® 80 and nanoparticle size using Brij® 72 as core material.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	13154.178	5	2630.836	34.253	.000
Within Groups	921.660	12	76.805		
Total	14075.838	17			

Tukey HSD				
Tween 80 concentration	N	Subset for alpha = .05		
		1	2	3
19 mM 4 hours	3	72.3000		
17 mM 4 hours	3	73.1667		
17 mM 24 hours	3	92.1333	92.1333	
19 mM 24 hours	3		99.1333	
21 mM 4 hours	3			126.4000
21 mM 24 hours	3			146.4000
Sig.		.131	.916	.126

**Table E9** The statistical analysis of cooling method and nanoparticle size (Rx B50).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	10670.372	7	1524.339	71.346	.000
Within Groups	341.847	16	21.365		
Total	11012.218	23			

Tukey HSD

Cooling method	N	Subset for alpha = .05			
		1	2	3	4
rapid cooling 4 hours	3	55.7667			
simple cooling 4 hours	3		73.9333		
rapid cooling 24 hours	3		74.6000		
rapid cooling 48 hours	3		80.7000	80.7000	
simple cooling 24 hours	3		83.6667	83.6667	
rapid cooling 1 week	3			91.7000	
simple cooling 48 hours	3				117.7000
simple cooling 1 week	3				122.2667
Sig.		1.000	.232	.134	.917

**Table E10** The statistical analysis of cooling method and nanoparticle size (Rx B52).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	7811.860	7	1115.980	48.139	.000
Within Groups	370.920	16	23.183		
Total	8182.780	23			

Tukey HSD

Cooling method	N	Subset for alpha = .05				
		1	2	3	4	5
rapid cooling 4 hours	3	52.9000				
simple cooling 4 hours	3		81.9000			
simple cooling 24 hours	3		89.3667	89.3667		
rapid cooling 24 hours	3		92.4667	92.4667		
rapid cooling 48 hours	3			97.2333	97.2333	
simple cooling 48 hours	3				106.1333	106.1333
rapid cooling 1 week	3				107.7333	107.7333
simple cooling 1 week	3					114.2667
Sig.		1.000	.196	.510	.201	.471

**Table E11** The statistical analysis of cooling method and nanoparticle size (Rx B54).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	20058.736	7	2865.534	85.759	.000
Within Groups	534.373	16	33.398		
Total	20593.110	23			

Tukey HSD

Cooling method	N	Subset for alpha = .05					
		1	2	3	4	5	6
rapid cooling 4 hours	3	21.2000					
rapid cooling 24 hours	3		47.1000				
rapid cooling 48 hours	3		62.0000	62.0000			
simple cooling 4 hours	3			72.2667	72.2667		
simple cooling 24 hours	3				85.1667	85.1667	
rapid cooling 1 week	3					96.8333	
simple cooling 48 hours	3					100.7333	100.7333
simple cooling 1 week	3						114.9333
Sig.		1.000	.087	.413	.182	.068	.114

**Table E12** The statistical analysis of Tween® 80 concentration and CoenzymeQ<sub>10</sub>-loaded nanoparticle size (1 mg/mL of CoenzymeQ<sub>10</sub>).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5107.007	7	729.572	11.940	.000
Within Groups	977.627	16	61.102		
Total	6084.633	23			

Tukey HSD

Tween 80 concentration	N	Subset for alpha = .05		
		1	2	3
60 mM	3	28.1667		
50 mM	3	31.4667		
30 mM	3	31.6333		
45 mM	3	39.6000		
40 mM	3	42.1000	42.1000	
35 mM	3	49.5000	49.5000	49.5000
24 mM	3		63.1667	63.1667
20 mM	3			70.9000
Sig.		.062	.067	.061

**Table E13** The statistical analysis of Tween® 80 concentration and CoenzymeQ<sub>10</sub>-loaded nanoparticle size (2 mg/mL of CoenzymeQ<sub>10</sub>).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	7862.993	7	1123.285	13.546	.000
Within Groups	1326.760	16	82.923		
Total	9189.753	23			

Tukey HSD				
Tween 80 concentration	N	Subset for alpha = .05		
		1	2	3
60 mM	3	35.8667		
45 mM	3	37.5333		
50 mM	3	37.8333		
40 mM	3	41.7667	41.7667	
30 mM	3	43.7333	43.7333	
24 mM	3	57.0000	57.0000	
35 mM	3		67.0333	67.0333
20 mM	3			91.1000
Sig.		.152	.056	.076

**Table E14** The statistical analysis of wax concentration and CoenzymeQ<sub>10</sub>-loaded nanoparticle size prepared from 60 mM of Tween 80 and 1 mg/mL of CoenzymeQ<sub>10</sub>.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	13739.707	2	6869.853	173.559	.000
Within Groups	237.493	6	39.582		
Total	13977.200	8			

Tukey HSD				
wax concentration	N	Subset for alpha = .05		
		1	2	3
2 mg/mL	3	28.1667		
4 mg/mL	3		62.1000	
6 mg/mL	3			122.6333
Sig.		1.000	1.000	1.000

**Table E15** The statistical analysis of wax concentration and CoenzymeQ<sub>10</sub>-loaded nanoparticle size prepared from 60 mM of Tween 80 and 2 mg/mL of CoenzymeQ<sub>10</sub>.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	7997.607	2	3998.803	102.484	.000
Within Groups	234.113	6	39.019		
Total	8231.720	8			

Tukey HSD				
wax concentration	N	Subset for alpha = .05		
		1	2	3
2 mg/mL	3	35.8667		
4 mg/mL	3		62.7333	
6 mg/mL	3			108.1000
Sig.		1.000	1.000	1.000

**Table E16** The statistical analysis of CoenzymeQ<sub>10</sub> concentration and CoenzymeQ<sub>10</sub>-loaded nanoparticle size prepared from 24 mM of Tween<sup>®</sup> 80 and 2 mg/mL of wax.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	2356.756	4	589.189	27.247	.000
Within Groups	216.240	10	21.624		
Total	2572.996	14			

Tukey HSD				
Co Q10 concentration	N	Subset for alpha = .05		
		1	2	3
3 mg/mL	3	45.5667		
2 mg/mL	3	57.0000	57.0000	
no Q10	3		60.5000	
1 mg/mL	3		63.1667	
4 mg/mL	3			84.0667
Sig.		.077	.516	1.000

**Table E17** The statistical analysis of CoenzymeQ<sub>10</sub> concentration and CoenzymeQ<sub>10</sub>- loaded nanoparticle size prepared from 48 mM of Tween<sup>®</sup> 80 and 4 mg/mL of wax.

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	89.129	4	22.282	.608	.666
Within Groups	366.660	10	36.666		
Total	455.789	14			

Tukey HSD		
		Subset for alpha = .05
Co Q10 concentration	N	1
3 mg/mL	3	85.7000
4 mg/mL	3	86.3333
2 mg/mL	3	86.7667
1 mg/mL	3	90.0667
no Q10	3	92.0000
Sig.		.712

**Table E18** The statistical analysis of CoenzymeQ<sub>10</sub> concentration and CoenzymeQ<sub>10</sub>- loaded nanoparticle size prepared from 72 mM of Tween<sup>®</sup> 80 and 6 mg/mL of wax.

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	3376.563	4	844.141	27.419	.000
Within Groups	307.867	10	30.787		
Total	3684.429	14			

Tukey HSD				
Co Q10 concentration	N	Subset for alpha = .05		
		1	2	3
3 mg/mL	3	88.7667		
2 mg/mL	3	90.1667		
no Q10	3		109.7667	
4 mg/mL	3		118.7333	118.7333
1 mg/mL	3			126.1000
Sig.		.998	.341	.515

**Table E19** The statistical analysis of storage time and Coenzyme Q<sub>10</sub>-loaded nanoparticle of Rx D24

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	3.796	2	1.898	.064	.938
Within Groups	176.653	6	29.442		
Total	180.449	8			

Tukey HSD		
Storage time	N	Subset for alpha = .05
		I
8 weeks	3	97.1000
0 week	3	98.2333
4 weeks	3	98.6333
Sig.		.937

**Table E20** The statistical analysis of storage time and Coenzyme Q<sub>10</sub>-loaded nanoparticle of Rx D44

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	40.460	2	20.230	.294	.756
Within Groups	413.320	6	68.887		
Total	453.780	8			

Particle size		
Tukey HSD		
Storage time	N	Subset for alpha = .05
		I
0 week	3	86.3333
4 weeks	3	88.0333
8 weeks	3	91.4333
Sig.		.743

**Table E21** The statistical analysis of concentration of mannitol and particle size (RxD24).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	96.490	3	32.163	5.006	.030
Within Groups	51.400	8	6.425		
Total	147.890	11			

Tukey HSD			
Mannitol concentration	N	Subset for alpha = .05	
		1	2
1%	3	84.1000	
2%	3	85.9667	85.9667
0%	3	86.7667	86.7667
4%	3		91.7667
Sig.		.594	.088

**Table E22** The statistical analysis of concentration of mannitol and particle size (RxD44).

One way ANOVA

Particle size					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	296.350	3	98.783	4.153	.048
Within Groups	190.287	8	23.786		
Total	486.637	11			

Tukey HSD			
Manitol concentration	N	Subset for alpha = .05	
		1	2
2%	3	73.1333	
1%	3	80.0333	80.0333
4%	3	83.7667	83.7667
0%	3		86.3333
Sig.		.106	.439



## VITA

Miss Patcharaporn Manopinives was born on May 12, 1979 in Bangkok, Thailand. She graduated with a Bachelor's Degree in pharmaceutical sciences in 2001, from Faculty of Pharmaceutical Sciences, Chulalongkorn University. She worked at Siriraj hospital as Pharmacist for 3 years, during 2001-2004.

