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APPENDICES

APPENDIX A

DETAIL OF SOME SUBSTANCES

1. Isopropyl myristate (IPM) (Wade and Weller, 1994)

1.1 Chemical name

1-Methylethyl tetradecanoate

1.2 Empirical formula

$C_{17}H_{34}O_2$

1.3 Structure formula

$$CH_3(CH_2)_{12}\overset{\overset{\displaystyle O}{\|}}{C}{-}OCH(CH_3)_2$$

1.4 Appearance

IPM is a clear, colorless, practically odorless, mobile liquid with a bland taste.

1.5 Typical properties

Boiling point: 140.2^{0}C at 266 Pa (2 mmHg)

Freezing point: $\approx$ 3^{0}C

Solubility: miscible with acetone, chloroform, ethanol, ethyl acetate, fats, fatty alcohols, fixed oil, liquid hydrocarbons, toluene and waxes. Practically insoluble in glycerin, propylene glycol and water.

Viscosity: 5-7 mPa s (5-7 cP) at 25 ^{0}C

1.6 Stability

IPM is resistant to oxidation and hydrolysis and dose not become rancid. It should be storage

1.7 Safety

IPM is widely used in cosmetics and topical pharmaceutical formulation and is generally regarded as a nontoxic and nonirritant material.

2. Propylene glycol (Wade and Weller, 1994)

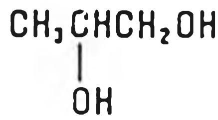
2.1 Chemical name

1, 2-Propanediol

2.2 Empirical formula

$C_3 H_8 O_2$

2.3 Structure formula



2.4 Appearance

Propylene glycol is a clear, colorless, viscous, practically odorless liquid with slightly acrid taste resembling glycerin.

2.5 Typical properties

Boiling point: 188 ^{0}C

Melting point: -59^{0}C

Solubility: miscible with acetone, chloroform, ethanol (95%), glycerin and water; soluble 1 in 6 parts of ether; not miscible with light mineral oil or fixed oils but will dissolve some essential oils.

2.6 Stability

Propylene glycol is stable in well closed container at cool temperature, but at high temperatures, in the open, it tends to oxidize, giving rise to products such as propionaldehyde, lactic acid, pyruvic acid and acetic acid.

2.7 Safety

Propylene glycol is widely used in a variety of pharmaceutical formulations and is generally regarded as a nontoxic material.

3. Polysorbate 20 (Tween® 20) (Wade and Weller, 1994)

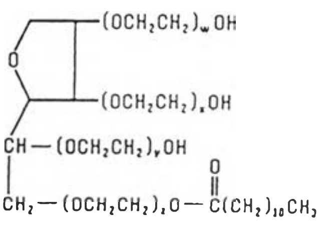
3.1 Chemical name

Polyoxyethylene sorbitan monolaurate

3.2 Empirical formula

$C_{58} H_{114} O_{26}$

3.3 Structure formula



3.4 Appearance

Tween® 20 is yellow oily liquid at $25^{0}C$

3.5 typical properties

HLB: 16.7

Solubility: soluble in ethanol and water, insoluble in mineral oil and vegetable oil.

3.6 Stability

Tween® 20 is stable to electrolytes and weak acids and bases.

3.7 Safety

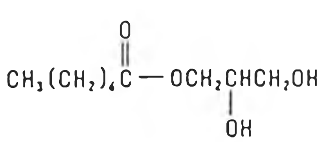
Tween® 20 is widely used in cosmetics, food products and oral, parenteral and topical pharmaceutical formulations and generally regarded as nontoxic and nonirritant material.

4. Glycerylmonocaprylate (Imwitor® 308)

4.1 Chemical name

Glyceryl Monocaprylate

4.2 Formula and structure



4.3 Appearance

Imwitor® 308 is white, solid, crystalline mass with a faint fatty odor and a very bitter, scratching taste.

4.4 Typical properties

Solubility: soluble in ether, n-hexane and ethanol, insoluble in water

4.5 Safety

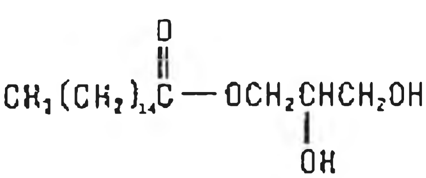
Imwitor® 308 is generally recognized as safe (GRAS). According the Code of Federal Regulations (CFR) of the FDA (21 CFR 184.1505).

5. Glyceryl monopalmitate (Palsgaard® 0093)

5.1 Chemical name

Glycerin monopalmitate

5.2 Formula and structure



5.3 Appearance

Palsgaard® is white powder.

5.4 Safety

Palsgaard® is generally used in wide range products such as bakery, dairy and ice cream.

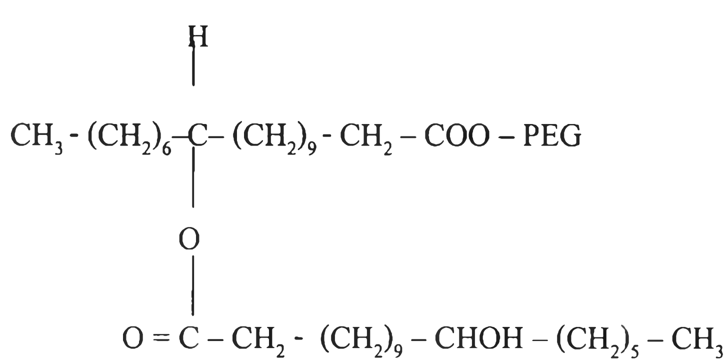
6. **Polyethylene glycol 660 –(12)- hydroxystearate (Solutol ® HS15)** (Wade and Weller, 1994)

6.1 Chemical name

Polyethylene glycol-660-(12)- hydroxystearate

6.2 Chemical structure

Apart from free polyethylene glycol and its mono-esters, diesters are also detectable. NMR analysis has provided clues to one possible structure of the di-ester.



6.3 Composition

Solutol®HS15 is composed of polyglycolester of 12- hydroxystrearic acid (70%) as hydrophobic part and polyethylene glycol (30%) as hydrophilic part.

6.4 Appearance

This substance is a while-yellowish paste at room temperature that becomes liquid at 30 °C.

6.5 Solubility

Solutol®HS15 dissolves in water, ethanol and 2-propanol to form clear solutions.

6.6 Typical properties

Solidification point	: 25-30 °C.
Saponification number	: 53-63
PH (10% in water)	: 6-7

6.7 Safety

The acute toxicity data are determined on different species of animals

LD_{50} (mouse, IV)	: >= 3.16 ml/kg
LD_{50} (rabbit, IV)	: > 1.0 g/kg, < 1.4 g/kg
LD_{50} (dog, IV)	: >= 3.1 g/kg
LD_{50} (rat, IV)	: > 1.0 g/kg, < 1.47 g/kg

7. Polyoxyl 35 caster oil (Cremophor ® EL) (Wade and Weller, 1994)

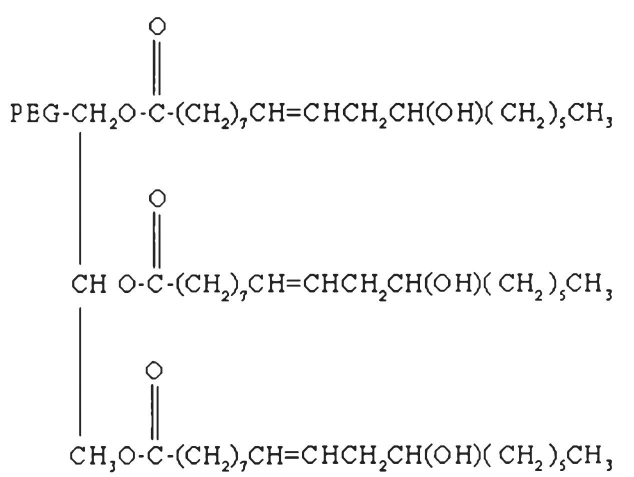
7.1 Chemical name

Polyoxyl 35 castor oil; Polyoxyethylene glycerol triricinoleat 35.

7.2 Empirical formula

Polyoxyl 35 castor oil has hydrophobic constituents comprised of about 83% of the total mixture. The main component is polyethylene glycol ricinoleate. Other hydrophobic constituents include fatty acid esters of polyethylene glycol along with some unchanged castor oil. The hydrophilic part (17%) consists of polyethylene glycols and glycerol ethoxylates.

The possible chemical structure according to the constituents reported from maufacture is shown below.



7.3 Appearance

Cremophor ® EL is a pale yellow, oily liquid that is clear at temperatures above 30 °C. It has a slight but characteristic odor and can be completely liquefied by heating to 26 °C.

7.4 Solubility

Cremophor® EL forms clear solutions in water. It is also soluble in ethyl alcohol, n-propyl alcohol, isopropyl alcohol, ethyl acetate, chloroform, carbon tetrachloride, trichloroethylene and xylene.

7.5 Typical properties

Cloud point	: 72.5 °C (at 1% solution)
Density	: 1.05-1.06 g/cm^3 at 25 °C
HLB value	: 12-14
pH value	: 6-8 (10% aqueous solution)
Melting point	: residual solids liquefy at 19-20°C

7.6 Safety

There have been reports of anaphylactic reactions in animals and humans after parenteral administration of pharmaceutical products containing Cremophor® EL.

8. Tween® 80 (Wade and Weller, 1994)

8.1 Chemical name

Polyoxyethylene 20 sorbitan monooleate

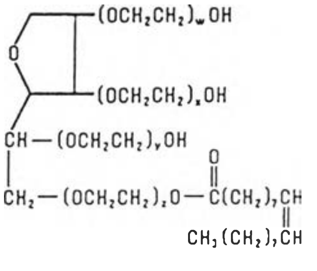
8.2 Molecular formula

$C_{64}H_{124}O_{26}$

8.3 Molecular weight

1310 g/mole

8.4 Chemical structure



8.5 Appearance

Tween® 80 is a clear yellowish or brownish-yellow oily liquid with a faint characteristic odor, somewhat bitter taste. It has a HLB value of 15.0

8.6 Solubility

Tween® 80 is miscible with water, alcohol, dehydrate alcohol, ethylacetate, and methyl alcohol; pratically insoluble in liquid paraffin and fixed oils.

8.7 Safety

Tween® 80 is widely used in cosmetics, food products, parenteral and topical pharmaceutical formulations and is generally well tolerated, practically non-irritating and of very low toxicity. The WHO has set an estimated acceptable daily intake for tween® 80, calculated as total polysorbate esters, at up to 25 mg/kg.

9. Glycerin (Louie and Niemiec, 1996; Wade and Weller, 1994)

9.1 Chemical name

Glycerol, 1, 2, 3-propanetriol; propane-1, 2, 3-triol; trihydroxypropane.

9.2 Molecular formula

$C_3 H_8O_3$

9.3 Molecular weight

92.09 g/mole

9.4 Chemical structure

$HOCH_2CHCH_2OH$

(with OH on the central carbon)

9.5 Appearance

Glycerin is a clear, colorless, odorless, syrupy and hygroscopic liquid.

9.6 Solubility

Glycerin is miscible with water, alcohol and methanol. One part of glycerin dissolves in 11 part of ethyl acetate and in 500 parts of ethylether. It is insoluble in benzene, chloroform, ether, mineral oil, fixed and volatile oils, halogenated hydrocarbons and aromatic hydrocarbons.

9.7 Typical properties

Energy provide	: 4.32 Cal/g
Melting point	: 17.9 $^{\circ}$C
Hygroscopicity	: medium to high
Relative density	: 1.258-1.263 g/cm
Surface tension	: 63.4 mN/m at 20 $^{\circ}$C
Viscosity	: 1,490 mPa s at 20 $^{\circ}$C
	954 mPa s at 25 $^{\circ}$C
Osmolarity	: 2.6% v/v solution is iso-osmotic with serum

9.8 Safety

Glycerin in very large oral doses can exert systemic effects, such as headache, thirst and nausea. Injection of large doses may induce convulsions, paralysis and hemolysis. The oral LD_{50} in mice is 31.5 g/kg and intravenous LD_{50} in mice is 7.45 g/kg. Glycerin can be used as solvent for parenteral formulations in concentration up to 50% w/v

APPENDIX B

Phase diagram of Microemulsion

The appearance of micelle system shows in Tables b1. — b48. (C=clear; T=turbid; V=viscous; M=milky; G=gel; U=unstable). Phase behaviors of microemulsions investigated after storage for 24 hrs and one week are shown in Figures b1. — b14. and b15. — b28., respectively.

Table b1. The appearance of micelle at 1:1 weight ratio of T80 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b2. The appearance of micelle at 2:1 weight ratio of T80 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b3. The appearance of micelle at 4:1 weight ratio of T 80 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b4. The appearance of micelle at 1:1 weight ratio of T80 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C,V
80	C,V
90	C,V

Table b5. The appearance of micelle at 2:1 weight ratio of T80 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b6. The appearance of micelle at 4:1 weight ratio of T80 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b7. The appearance of micelle at 1:1 weight ratio of T80 to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G
50	M,G
60	M,G
70	M,G
80	M,G
90	M,G

Table b8. The appearance of micelle at 2:1 weight ratio of T80 to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G
50	M,G
60	M,G
70	M,G
80	M,G
90	M,G

Table b9. The appearance of micelle at 4:1 weight ratio of T80 to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G
50	M,G
60	M,G
70	M,G
80	M,G
90	M,G

Table b10. The appearance of micelle at 1:1 weight ratio of T20 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C,V
80	C,V
90	C,V

Table b11. The appearance of micelle at 2:1 weight ratio of T20 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b12. The appearance of micelle at 4:1 weight ratio of T20 to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C,V
80	C,V
90	C,V

Table b13. The appearance of micelle at 1:1 weight ratio of T 20 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C,V
80	C,V
90	C,V

Table b14. The appearance of micelle at 2:1 weight ratio of T20 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b15. The appearance of micelle at 4:1 weight ratio of T20 to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C
70	C
80	C
90	C,V

Table b16. The appearance of micelle at 1:1 weight ratio of Sol to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b17. The appearance of micelle at 2:1 weight ratio of Sol to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b18. The appearance of micelle at 4:1 weight ratio of Sol to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b19. The appearance of micelle at 1:1 weight ratio of Sol to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C
80	C,V
90	C,V

Table b20. The appearance of micelle at 2:1 weight ratio of Sol to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b21. The appearance of micelle at 4:1 weight ratio of Sol to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b22. The appearance of micelle at 1:1 weight ratio of Cre to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C
70	C,V
80	C,V
90	C,V

Table b23. The appearance of micelle at 2:1 weight ratio of Cre to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b24. The appearance of micelle at 4:1 weight ratio of Cre to Gly

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b25. The appearance of micelle at 1:1 weight ratio of Cre to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b26. The appearance of micelle at 2:1 weight ratio of Cre to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b27. The appearance of micelle at 4:1 weight ratio of Cre to PG

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b28. The appearance of micelle at 1:1 weight ratio of T20 to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T
40	C
50	C
60	C
70	C
80	C
90	C,V

Table b29. The appearance of micelle at 2:1 weight ratio of T20 to Im

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b30. The appearance of micelle at 4:1 weight ratio of T20 to Im

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C,V
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b31. The appearance of micelle at 1:1 weight ratio of T 80 to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T
40	T
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b32. The appearance of micelle at 2:1 weight ratio of T80 to Im

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C
40	C,V
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b33. The appearance of micelle at 4:1 weight ratio of T80 to Im

% Surfactant + Cosurfactant	Appearance
10	C
20	C,V
30	C,V
40	C,V
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b34. The appearance of micelle at 1:1 weight ratio of Sol to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T
40	T
50	U
60	U
70	U
80	C
90	C,V

Table b35. The appearance of micelle at 2:1 weight ratio of Sol to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T
40	T
50	T
60	T
70	C,V
80	C,V
90	C,V

Table b36. The apperance of micelle at 4:1 weight ratio of Sol to Im

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C,V
40	C,V
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b37. The appearance of micelle at 1:1 weight ratio of Cre to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T,V
40	T,V
50	T
60	T,V
70	C,V
80	C,V
90	C,V

Table b38. The appearance of micelle at 2:1 weight ratio of Cre to Im

% Surfactant + Cosurfactant	Appearance
10	T
20	T
30	T
40	C
50	C
60	C,V
70	C,V
80	C,V
90	C,V

Table b39. The appearance of micelle at 4:1 weight ratio of Cremophor to Imwitor

% Surfactant + Cosurfactant	Appearance
10	C
20	C
30	C,V
40	C,V
50	C,V
60	C,V
70	C,V
80	C,V
90	C,V

Table b40. The apperance of micelle at 1:1 weight ratio of T20 to Pal

% Surfactant + Cosurfactant	Appearance
10	M
20	M
30	M,G
40	M,G

Table b41. The apperance of micelle at 2:1 weight ratio of T20 to Pal

% Surfactant + Cosurfactant	Appearance
10	G
20	G
30	G
40	M,G

Table b42. The apperance of micelle at 4:1 weight ratio of T20 to Pal

% Surfactant + Cosurfactant	Appearance
10	M
20	M
30	M,V
40	M,G

Table b43. The appearance of micelle at 1:1 weight ratio of Sol to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

Table b44. The appearance of micelle at 2:1 weight ratio of Sol to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

Table b45. The appearance of micelle at 4:1 weight ratio of Sol to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

Table b46. The apperance of micelle at 1:1 weight ratio of Cre to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

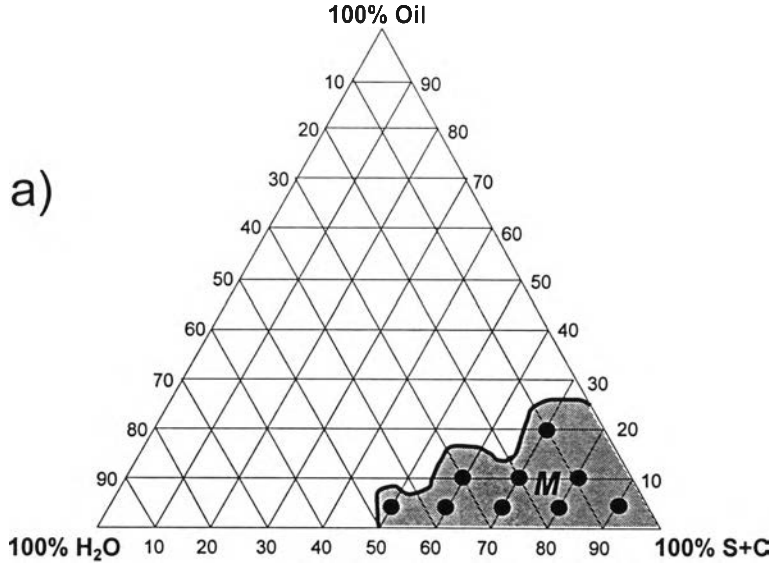
Table b47. The apperance of micelle at 2:1 weight ratio of Cre to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

Table b48. The apperance of micelle at 4:1 weight ratio of Cre to Pal

% Surfactant + Cosurfactant	Appearance
10	M,G
20	M,G
30	M,G
40	M,G

a)



b)

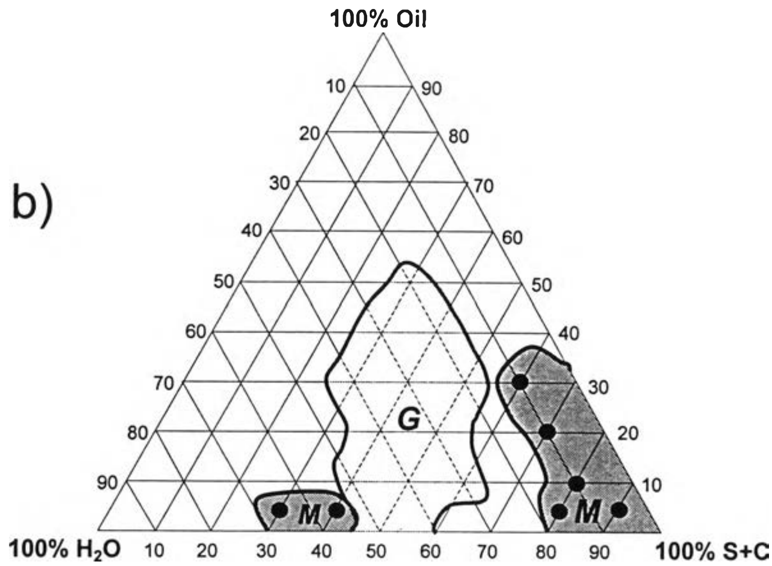


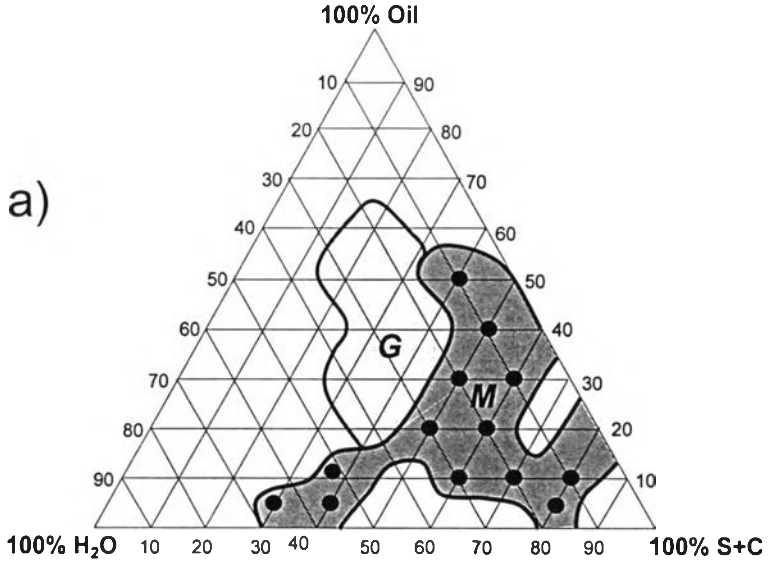
Figure b1. Pseudo-ternary phase diagram of surfactant / IPM / water microemulsion (24 hrs)

a) IPM / T20 / water **b) IPM / T80 / water**

G = Gel, M = Microemulsion

● **Represented the clear solution**

a)



b)

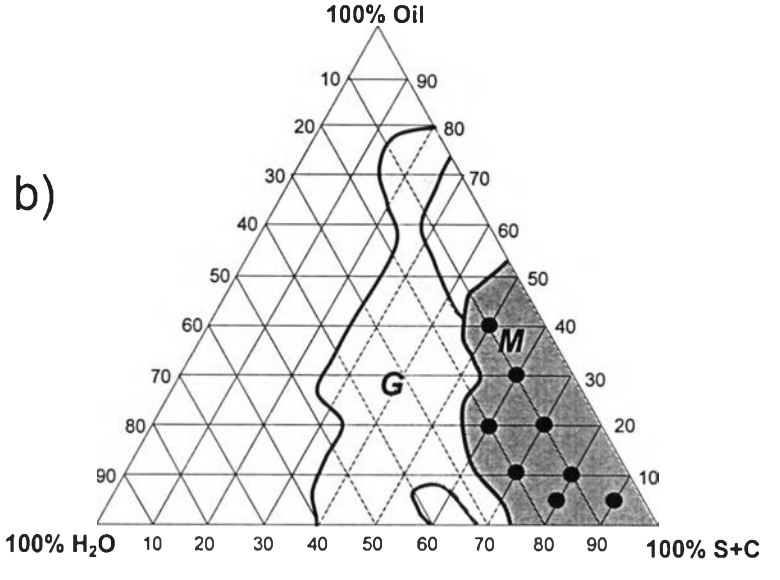


Figure b2. Pseudo-ternary phase diagram of surfactant / IPM / water microemulsion (24 hrs)

a) IPM / Sol / water **b) IPM / Cre/ water**

G = Gel, M = Microemulsion

● **Represented the clear solution**

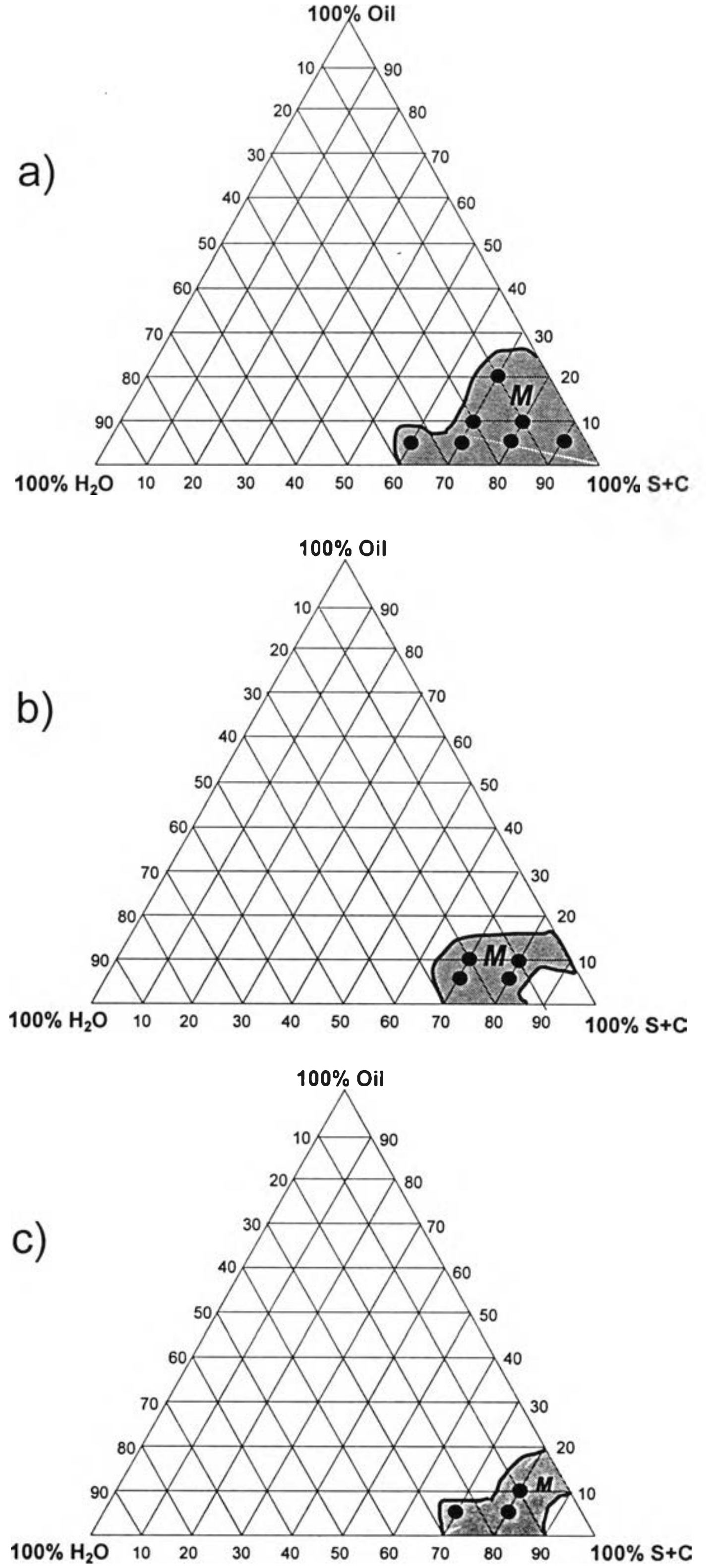


Figure b3. Pseudo-ternary phase diagram of IPM / T20 / Gly/ water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

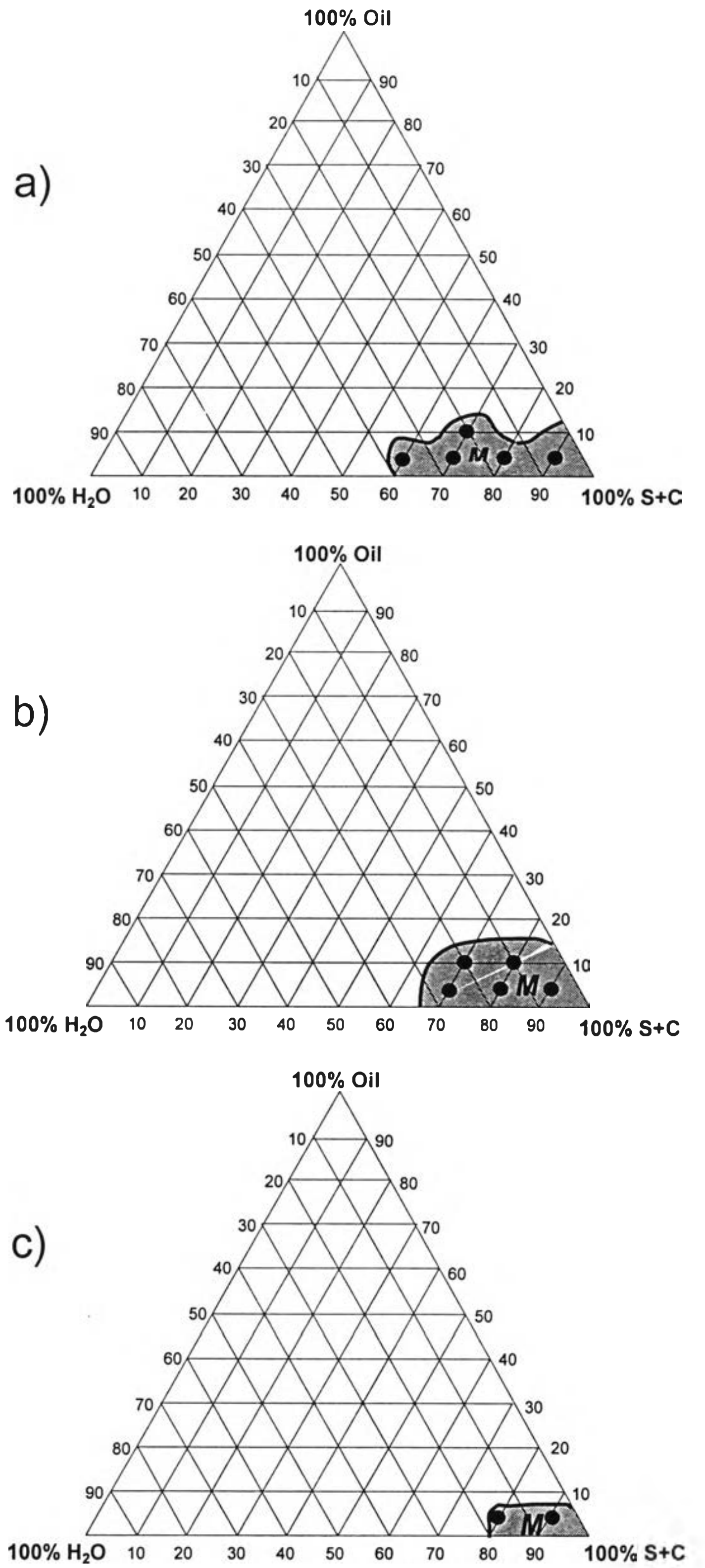


Figure b4. Pseudo-ternary phase diagram of IPM/ T20/ PG/ water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

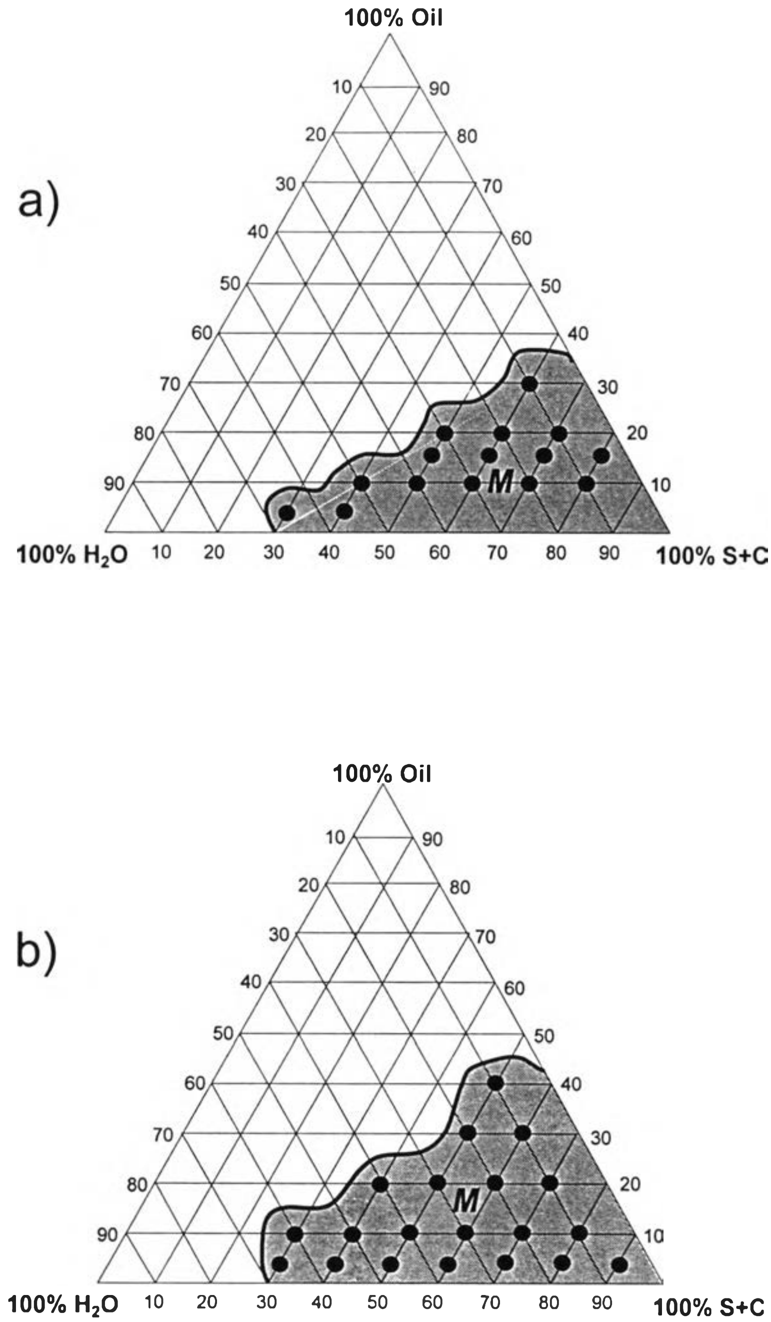


Figure b5. Pseudo-ternary phase diagram of IPM / T20 / Im / water (24 hrs) system at 4:1(a) and 2:1(b) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

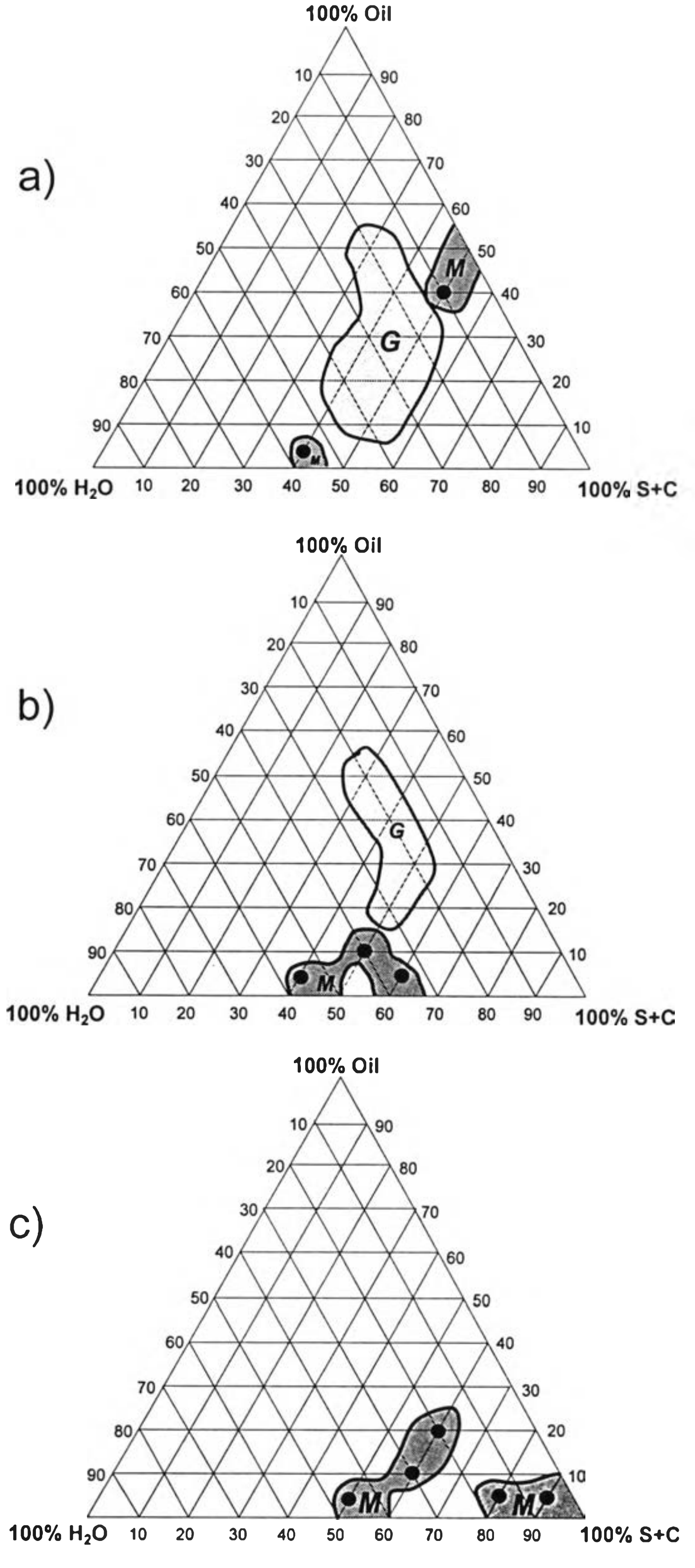


Figure b6. **Pseudo-ternary phase diagram of IPM / T80 / Gly / water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant**

G = Gel, M = Microemulsion

● **Represented the clear solution**

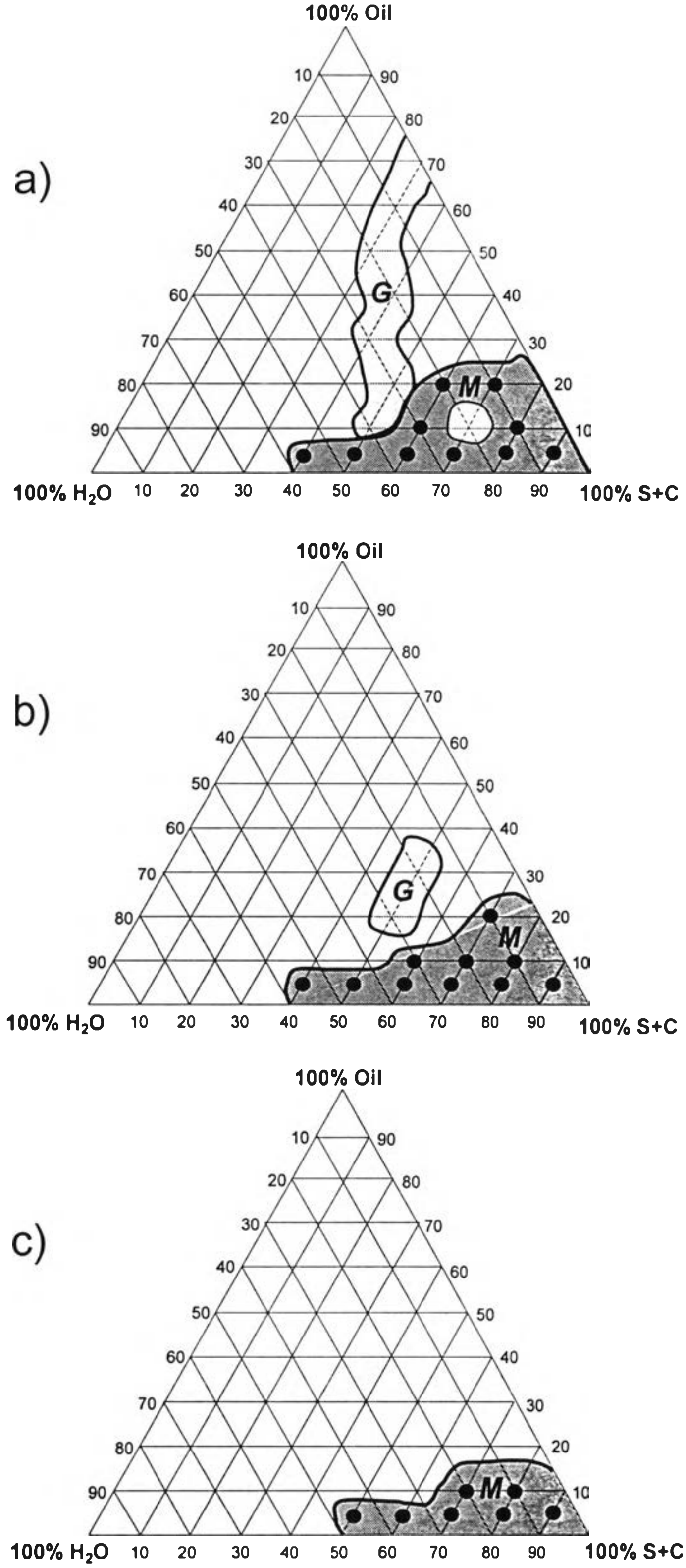


Figure b7. Pseudo-ternary phase diagram of IPM / T80 / PG/ water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

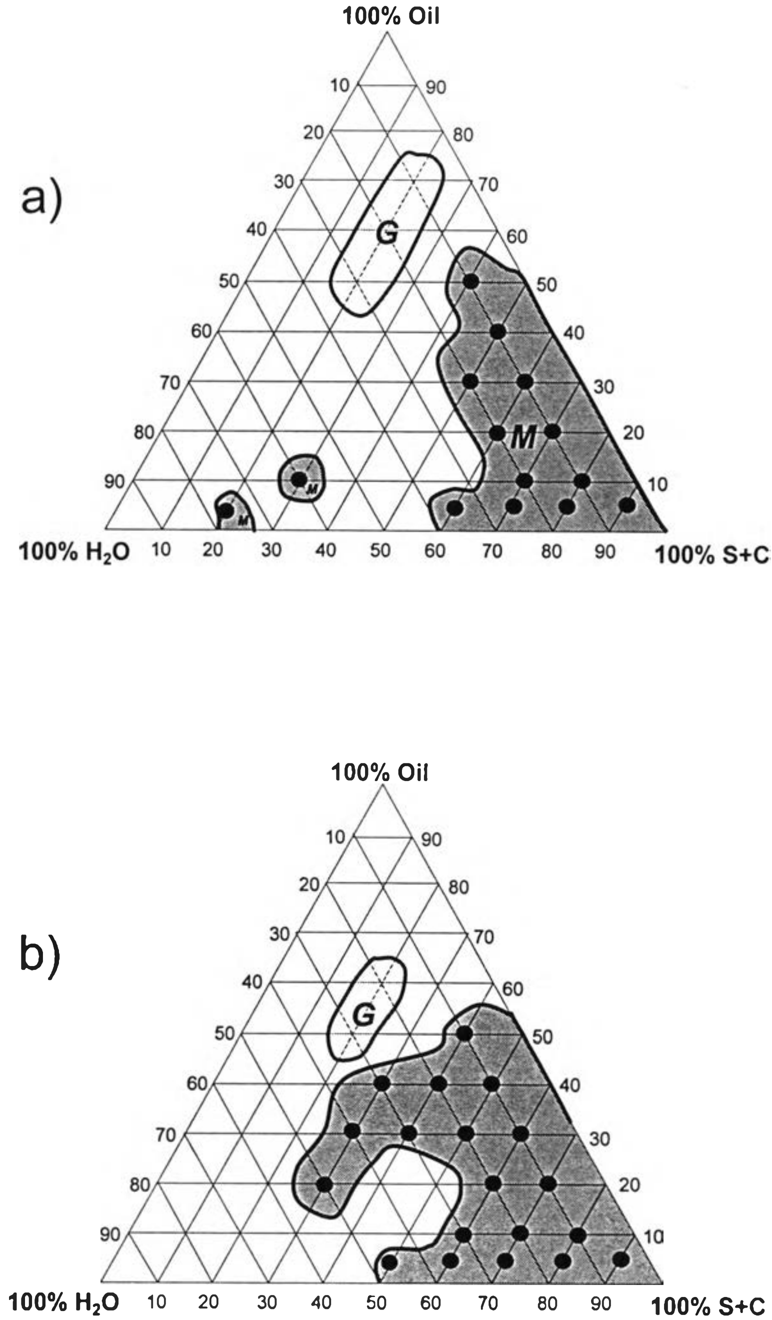


Figure b8. **Pseudo-ternary phase diagram of IPM / T80 / Im/ water (24 hrs) system at 4:1(a) and 2:1(b) weight ratio of surfactant to cosurfactant**

G = Gel, M = Microemulsion

● **Represented the clear solution**

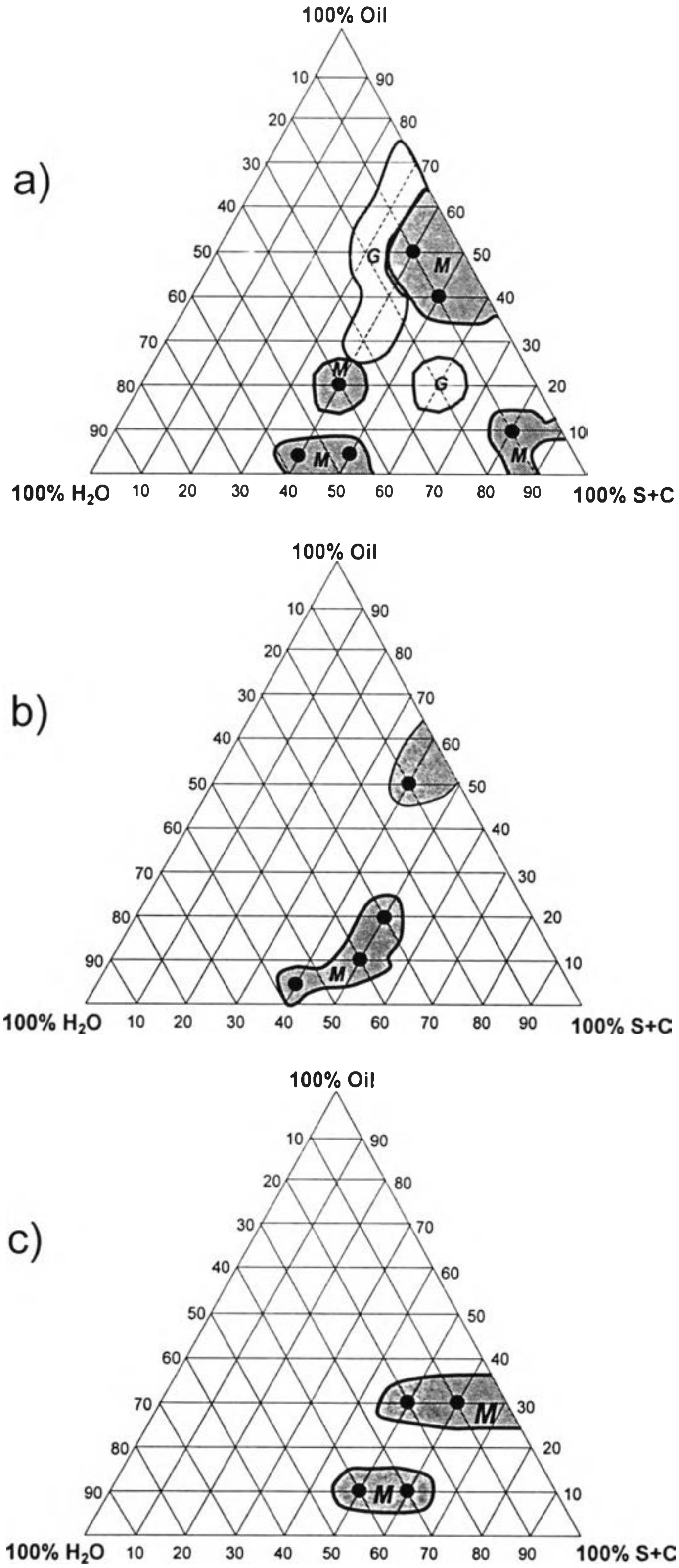


Figure b9. **Pseudo-ternary phase diagram of IPM / Sol/ Gly / water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant**

G = Gel, M = Microemulsion

● <u>**Represented the clear solution**</u>

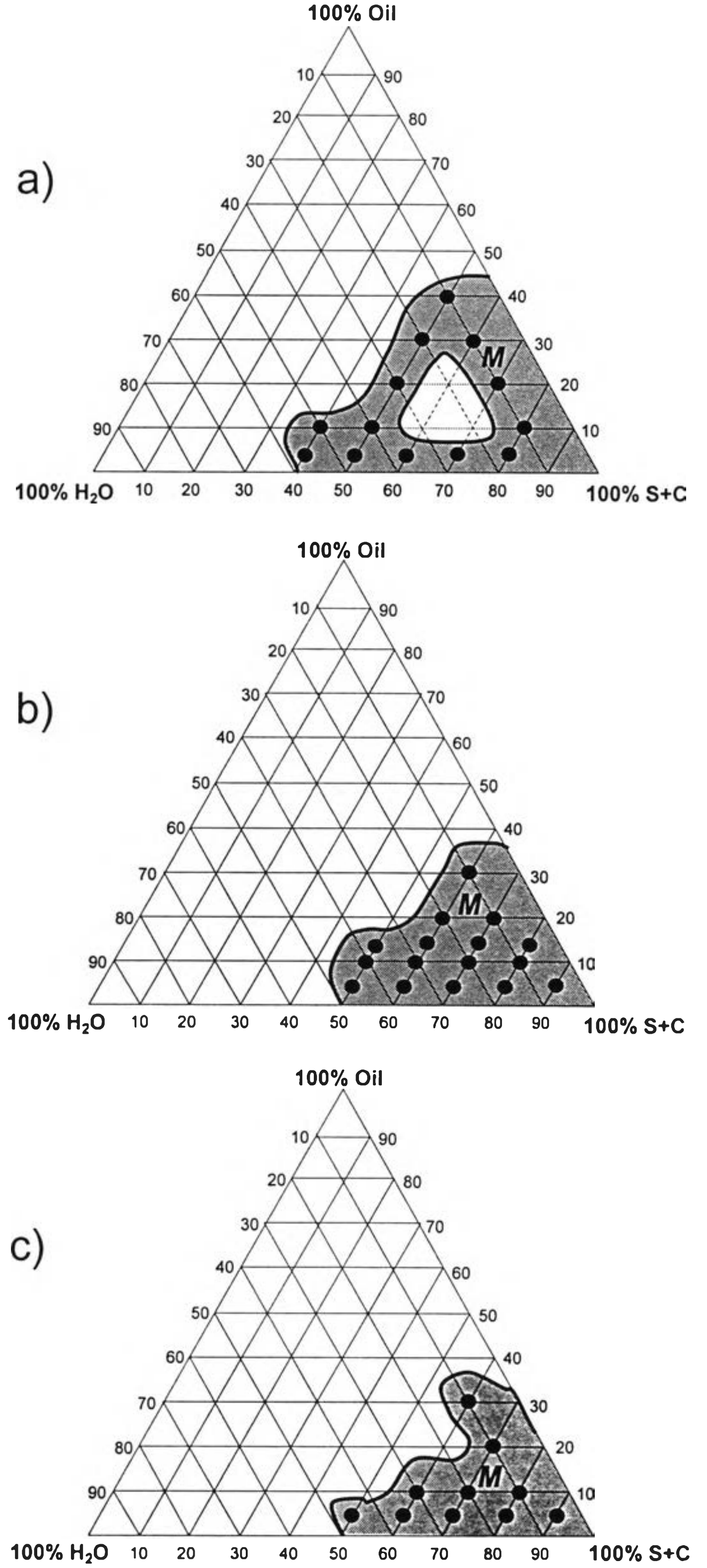


Figure b10. Pseudo-ternary phase diagram of IPM / Sol / PG / water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

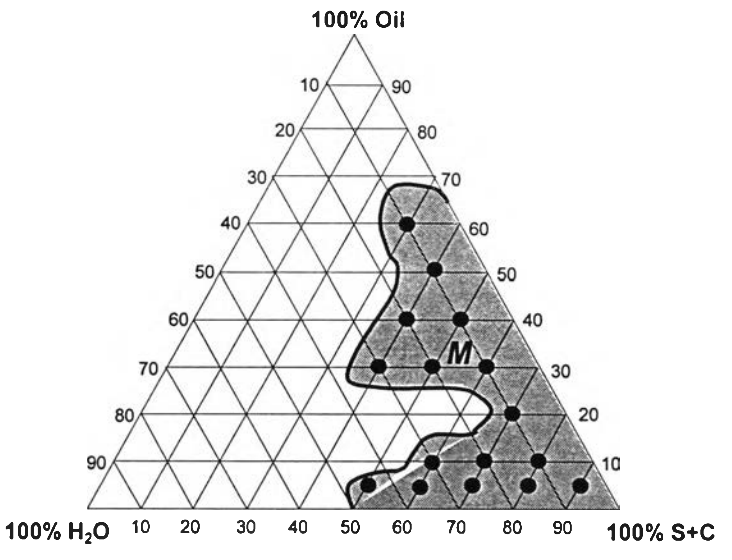


Figure b11. Pseudo-ternary phase diagram of IPM /Sol/Im/water (24 hrs) system at 4:1 weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

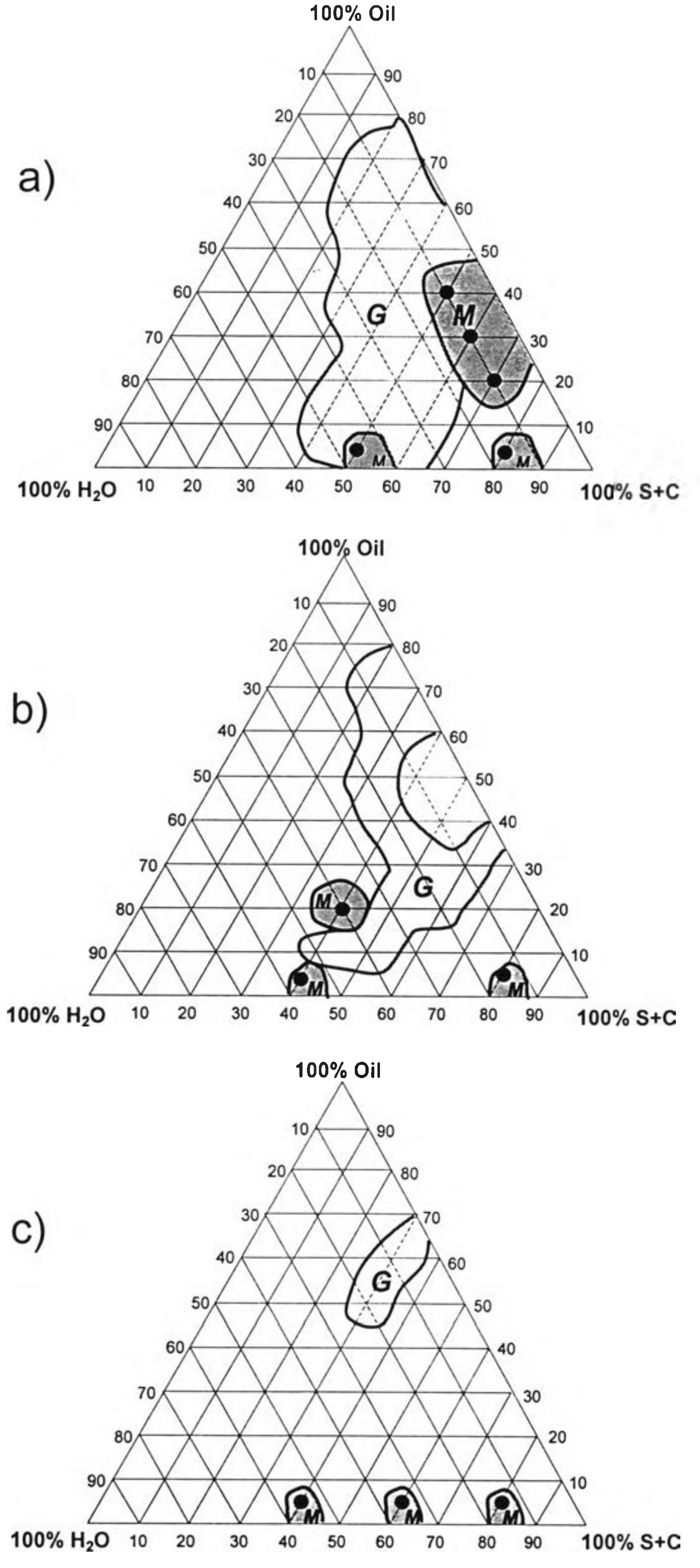


Figure b12. Pseudo-ternary phase diagram of IPM / Cre / Gly / water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

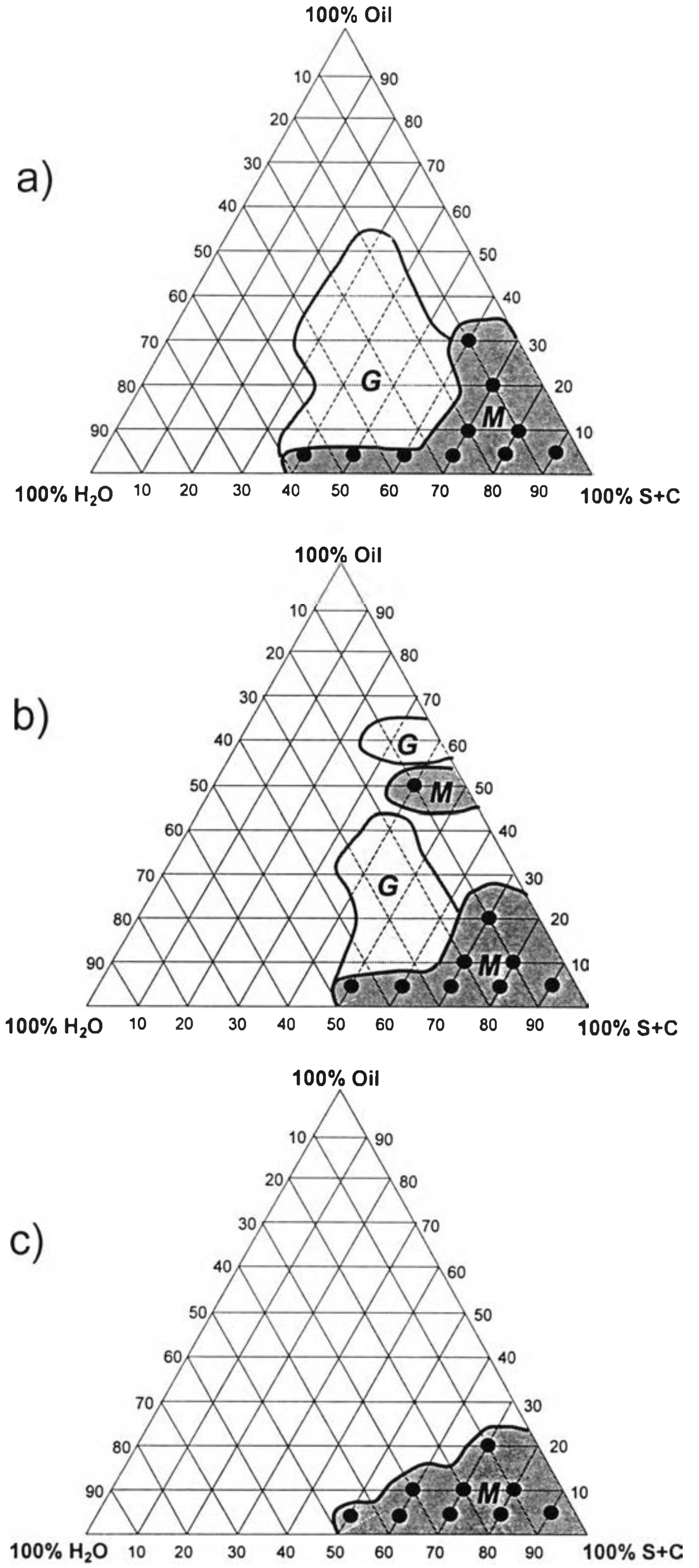


Figure b13. Pseudo-ternary phase diagram of IPM/Cre/PG/water (24 hrs) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

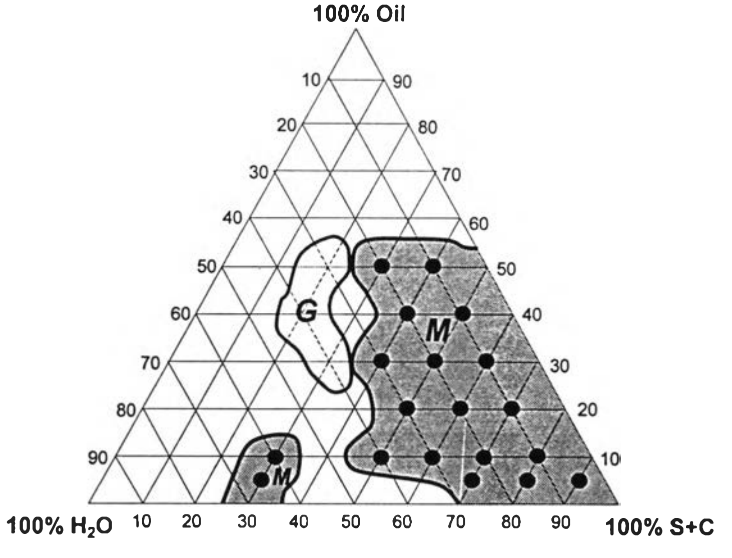
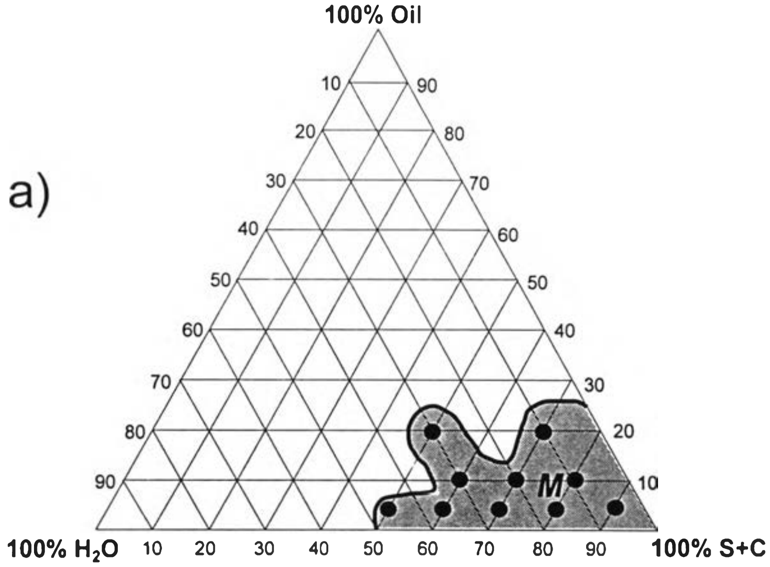


Figure b14. Pseudo-ternary phase diagram of IPM/ Cre/Im/water (24 hrs) system at 4:1 weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

a)



b)

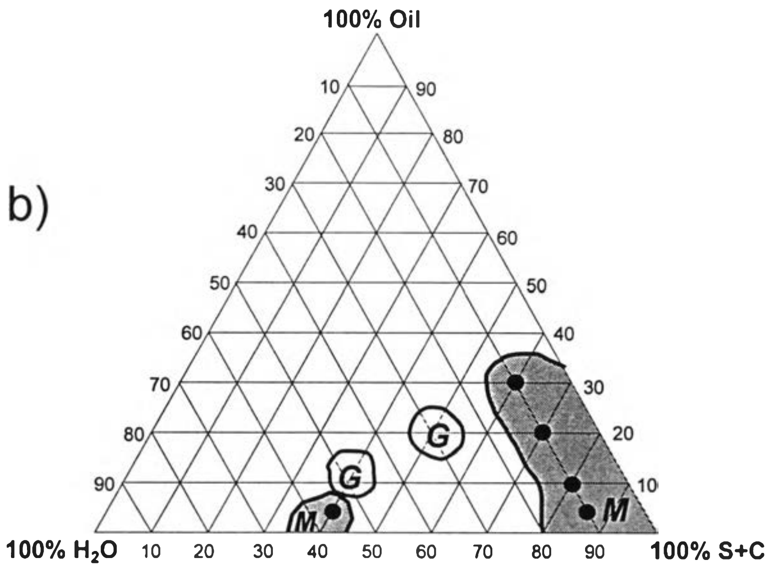


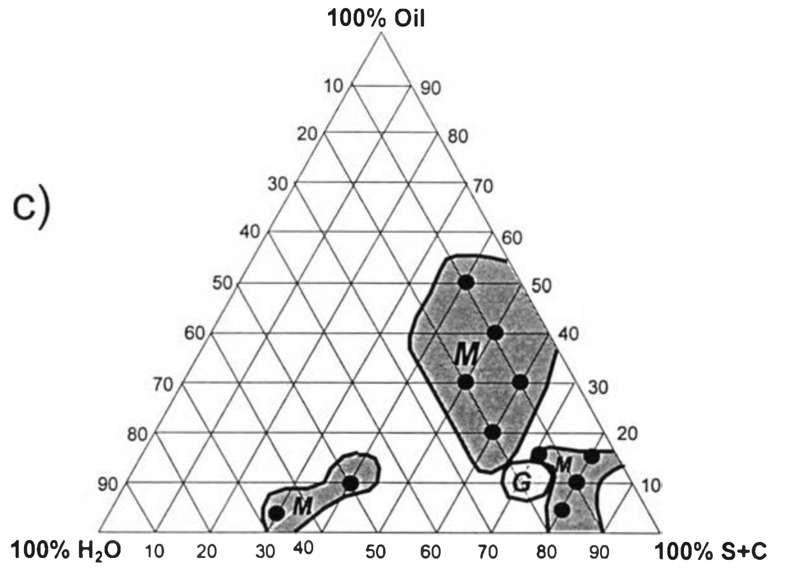
Figure b15. Pseudo-ternary phase diagram of surfactant / IPM / water microemulsion (1 week)

a) IPM / T20 / water **b) IPM / T80 / water**

G = Gel, M = Microemulsion

● **Represented the clear solution**

c)



d)

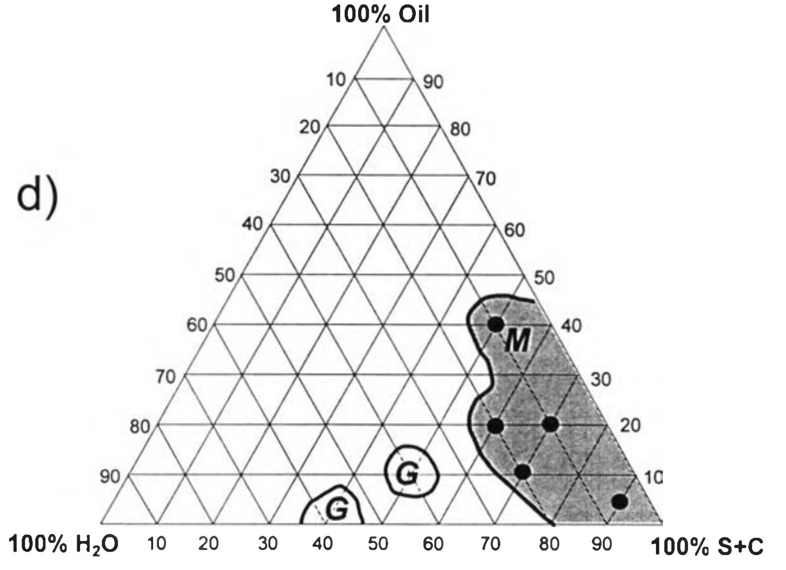


Figure b15. Pseudo-ternary phase diagram of surfactant / IPM / water microemulsion (1 week)(continued)

a) IPM / Sol / water **b) IPM / Cre / water**

G = Gel, M = Microemulsion

● **Represented the clear solution**

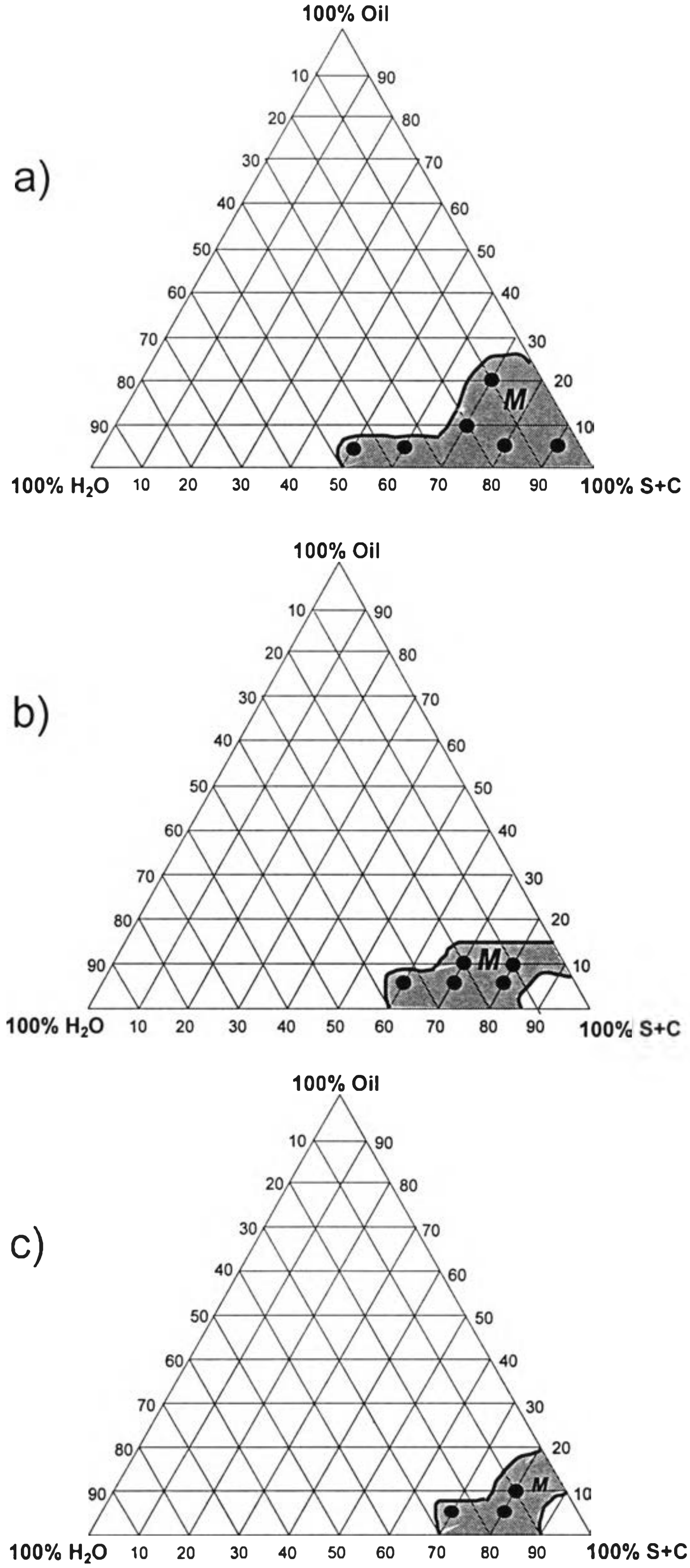


Figure b16. Pseudo-ternary phase diagram of IPM / T20 / Gly/ water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **<u>Represented the clear solution</u>**

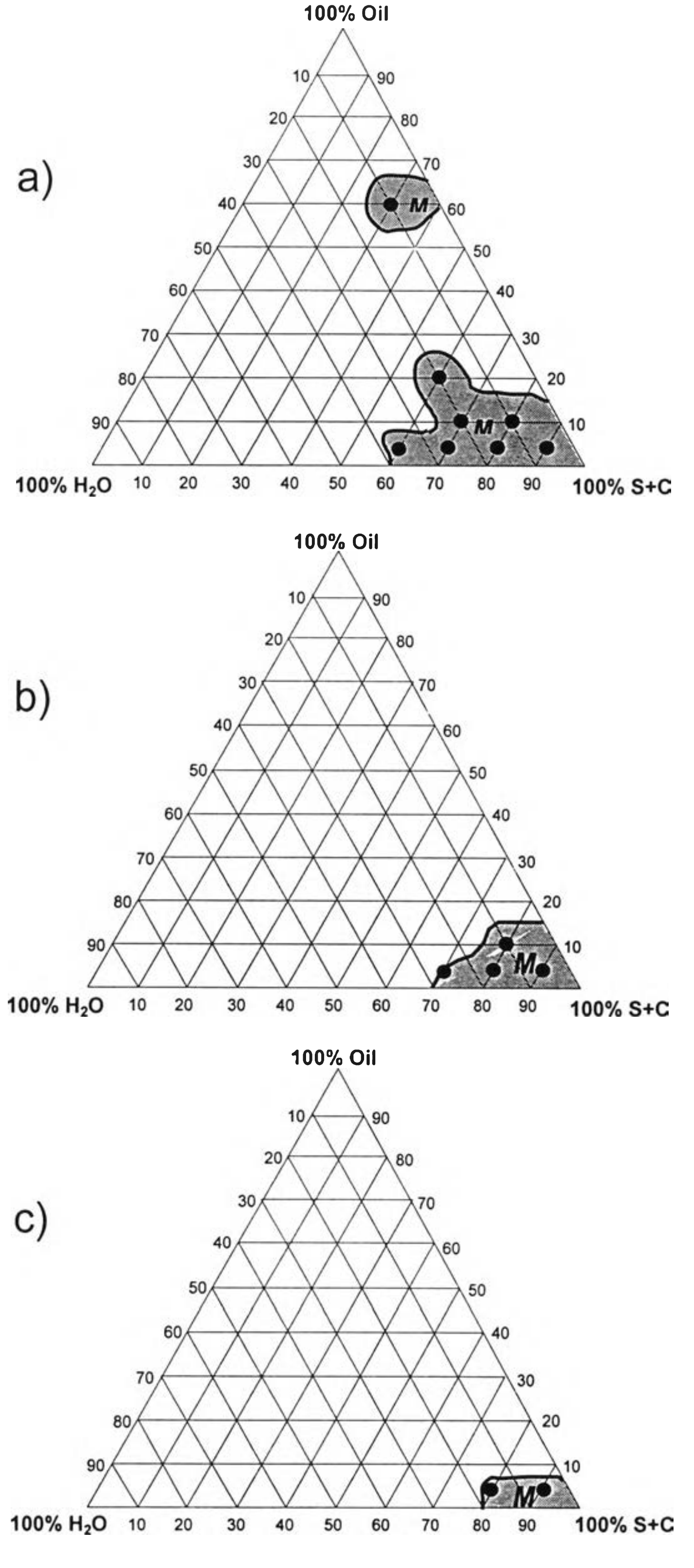
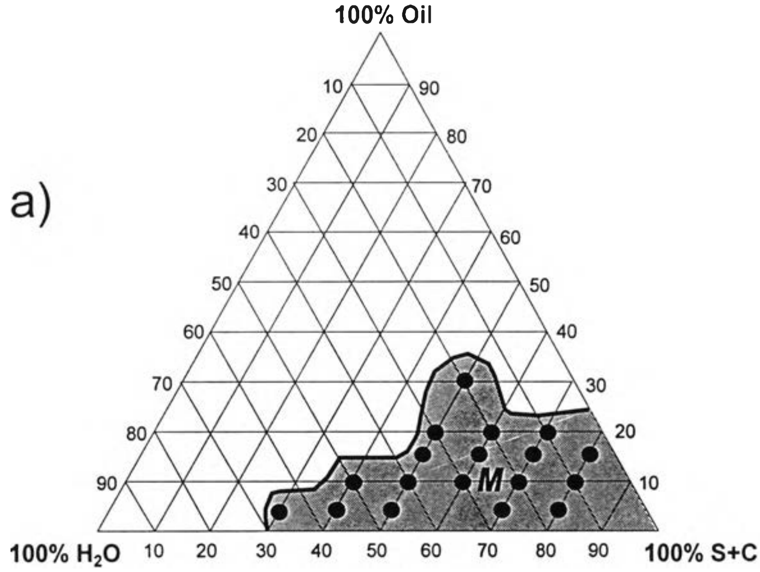


Figure b17. Pseudo-ternary phase diagram of IPM / T20 / PG / water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

a)



b)

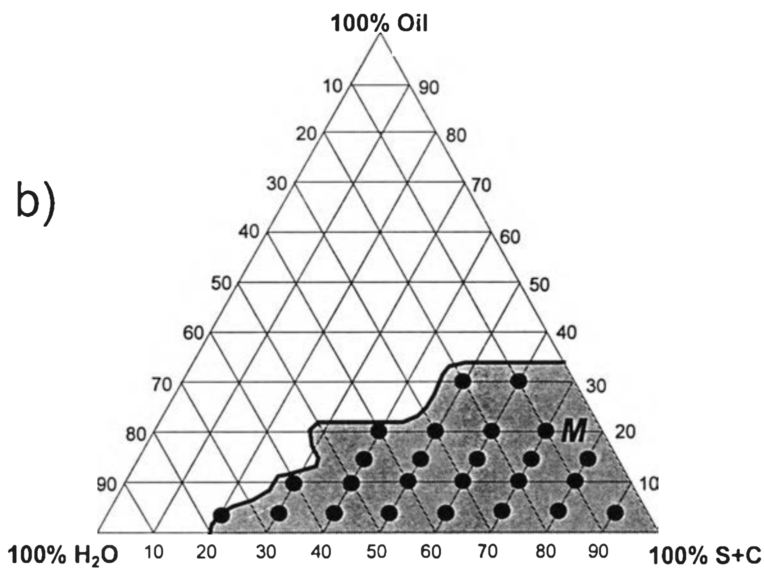


Figure b18. Pseudo-ternary phase diagram of IPM / T20 / Im/ water (1 week) system at 4:1(a) and 2:1(b) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **<u>Represented the clear solution</u>**

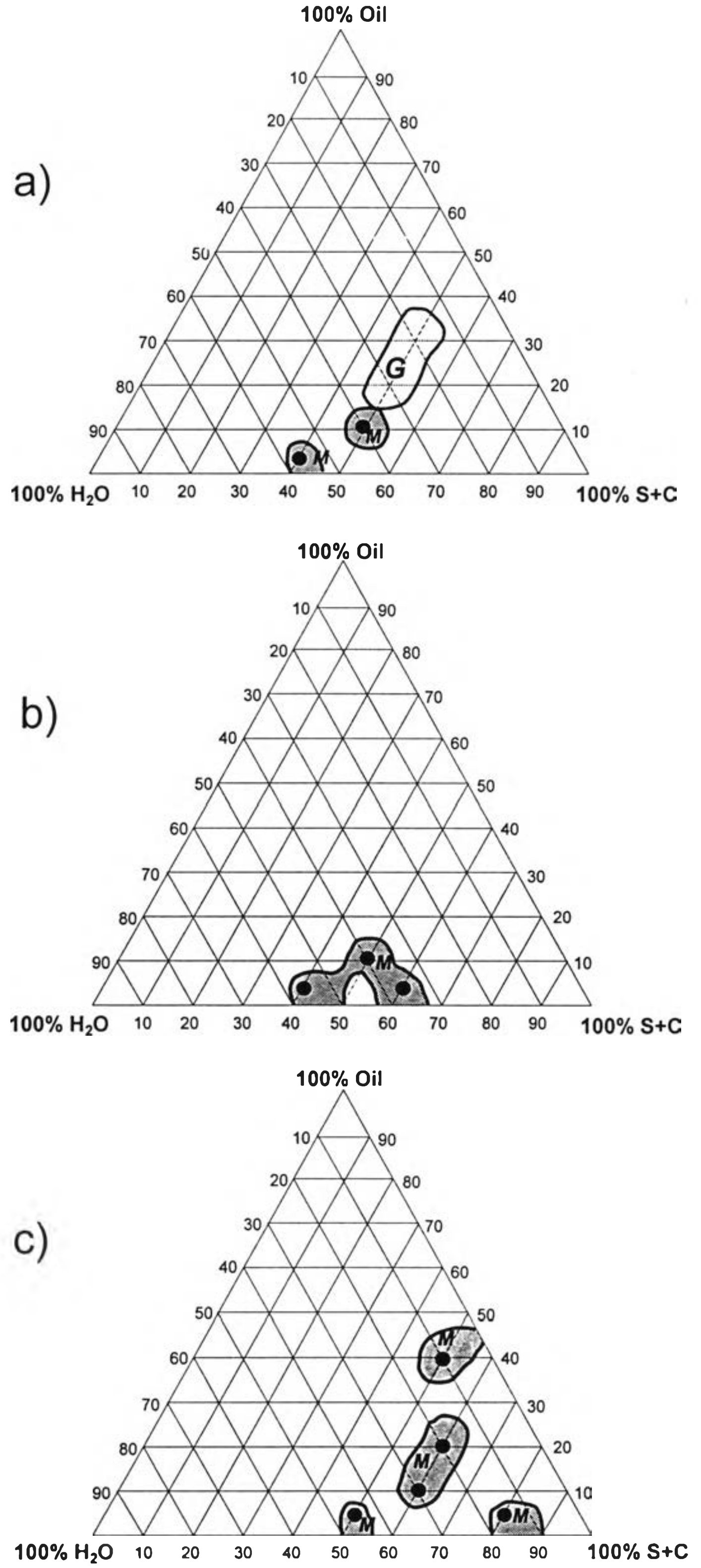


Figure b19. Pseudo-ternary phase diagram of IPM / T80 / Gly/ water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

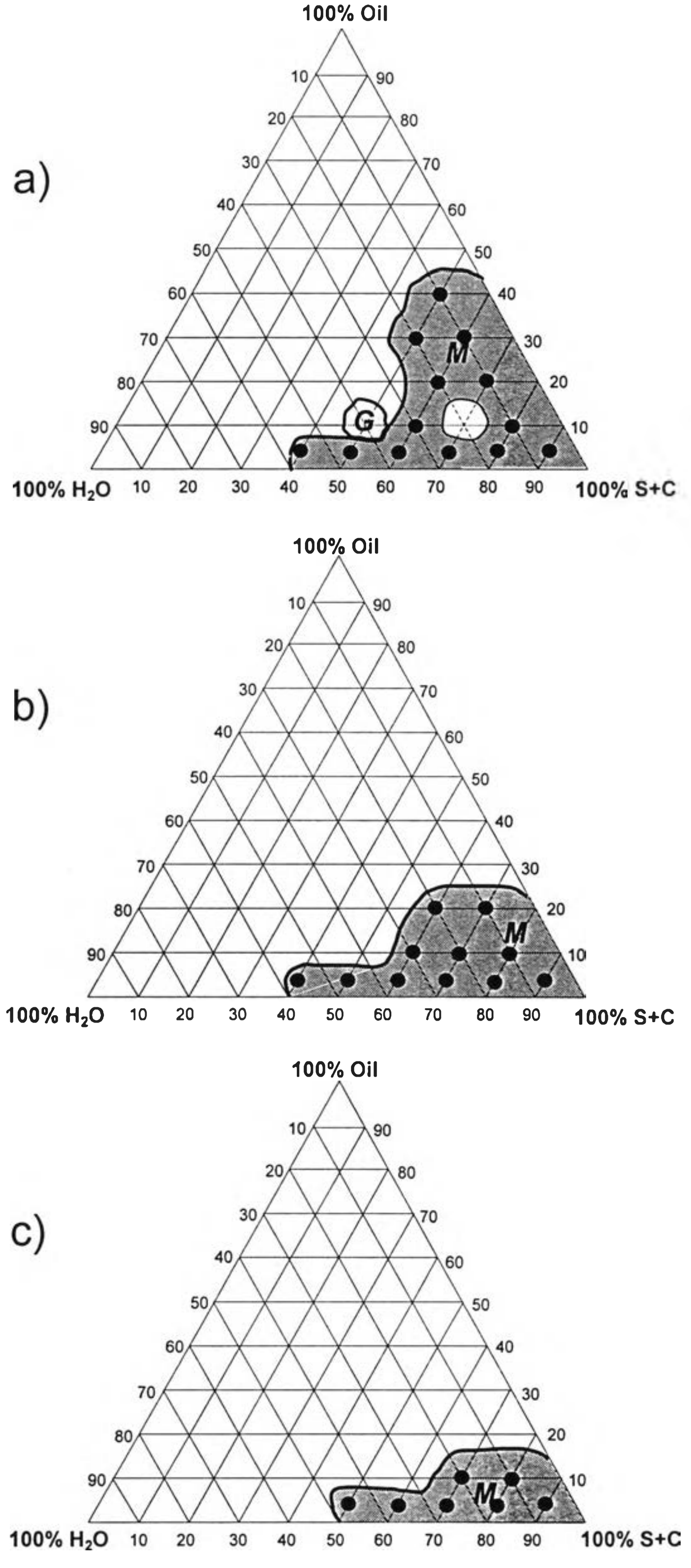


Figure b20. Pseudo-ternary phase diagram of IPM / T80 / PG / water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● Represented the clear solution

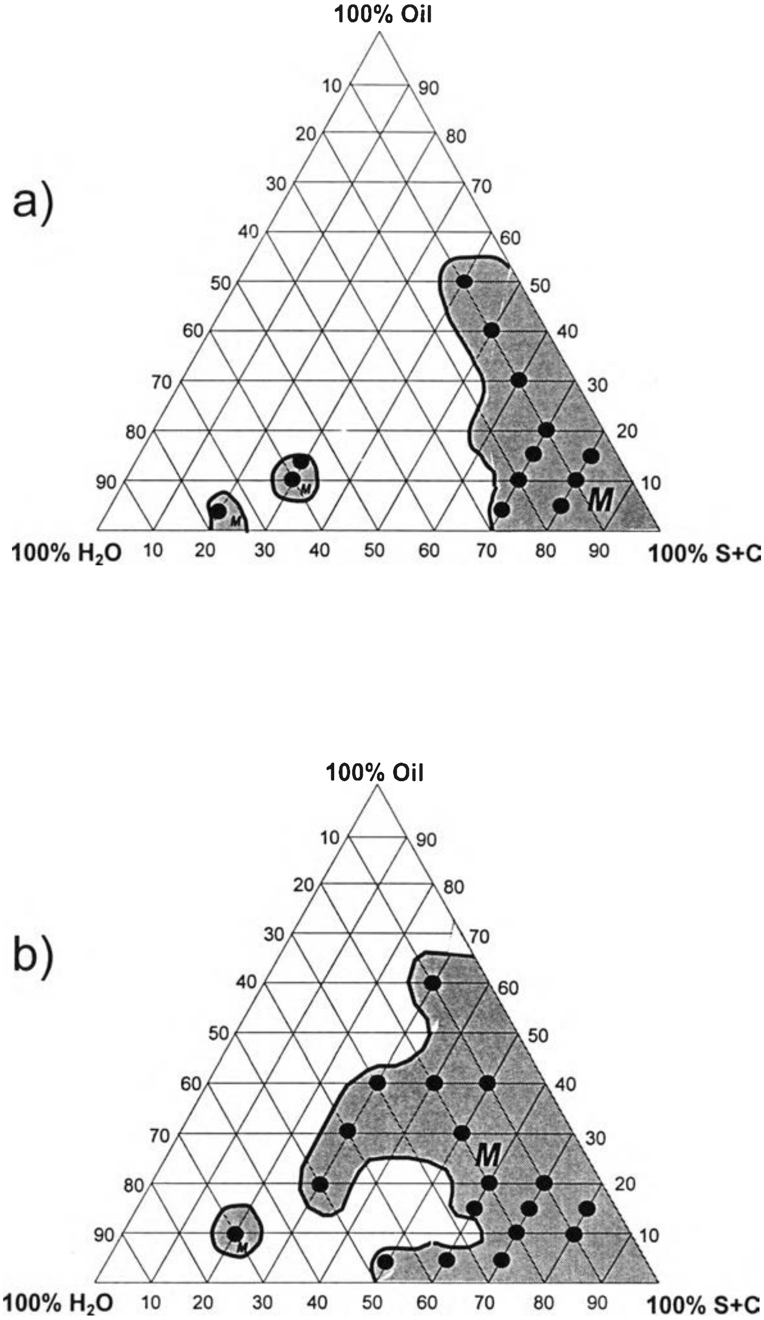


Figure b21. Pseudo-ternary phase diagram of IPM / T80 / Im/ water (1 week) system at 4:1(a) and 2:1(b) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

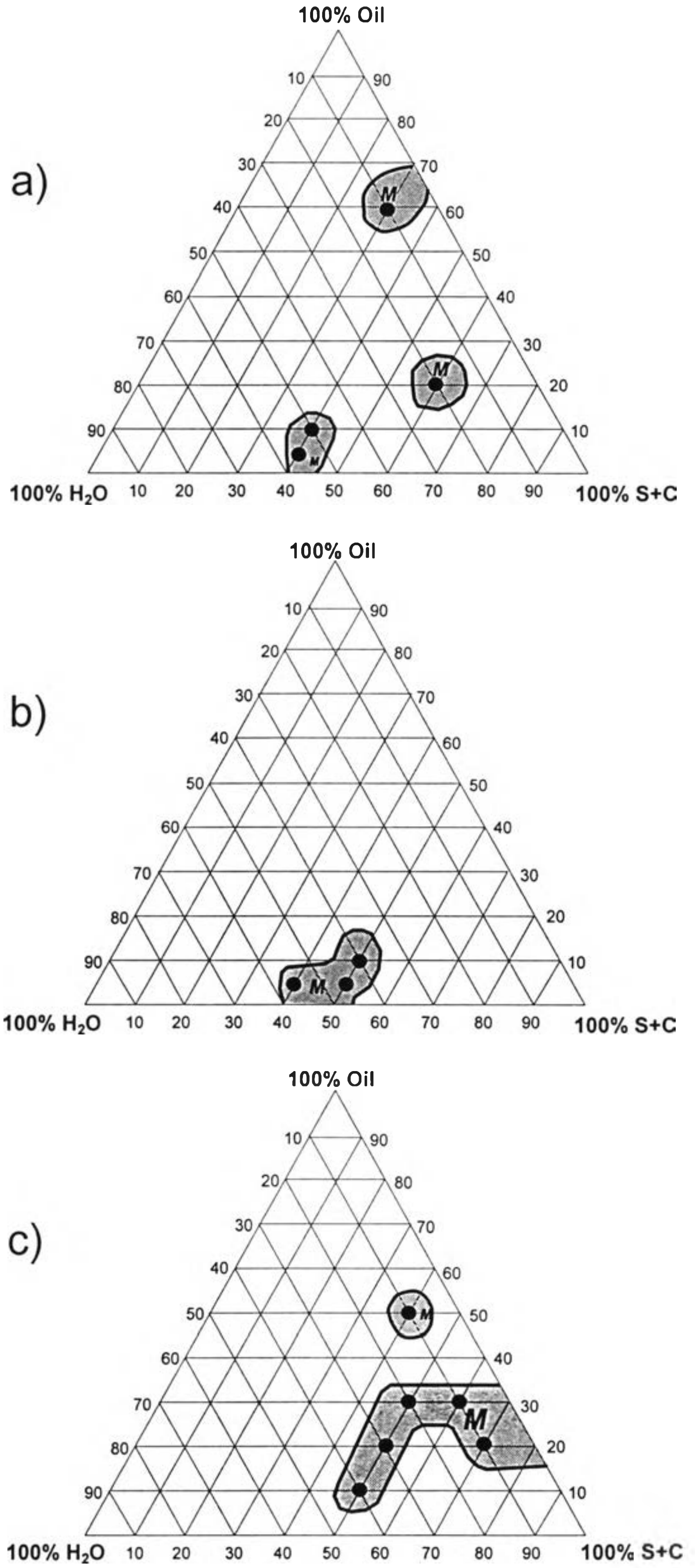


Figure b22. Pseudo-ternary phase diagram of IPM / Sol / Gly / water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **<u>Represented the clear solution</u>**

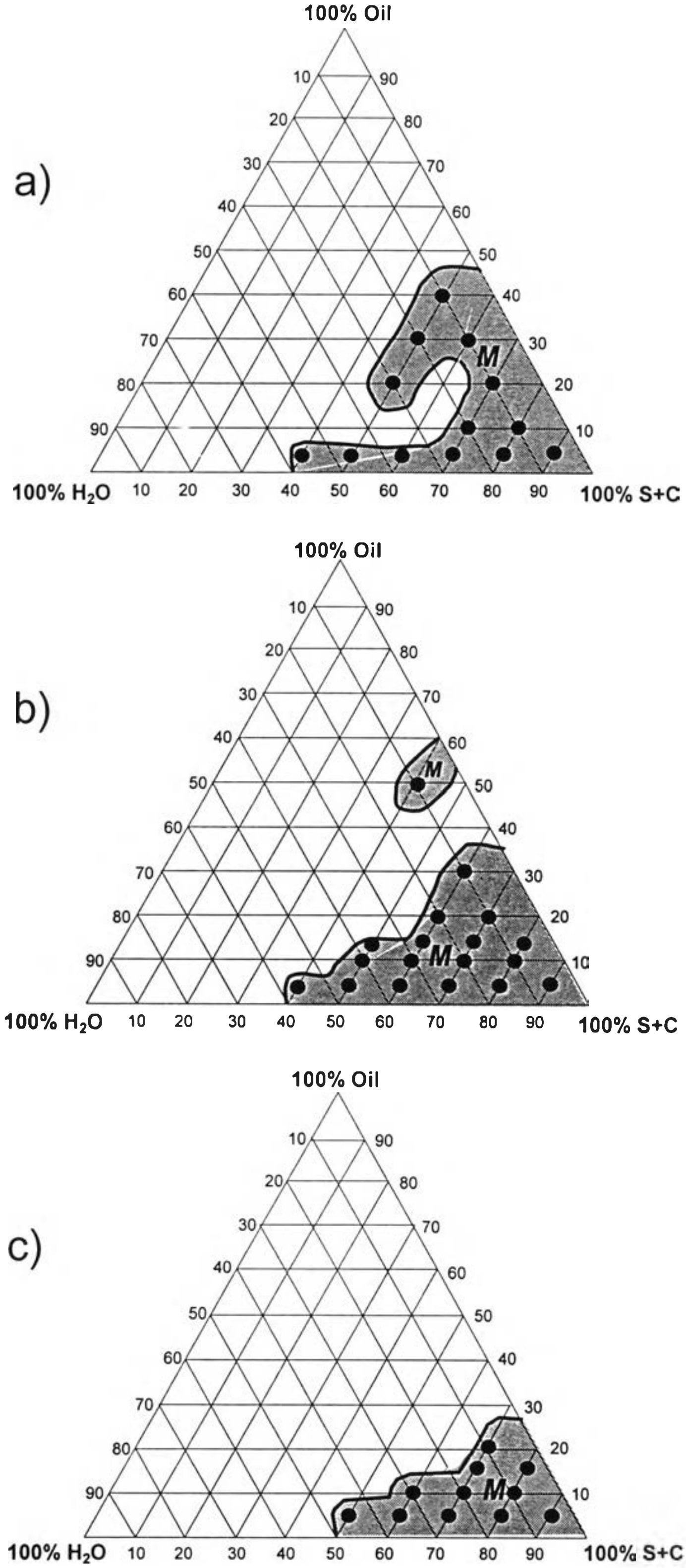


Figure b23. Pseudo-ternary phase diagram of IPM / Sol/ PG/ water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **<u>Represented the clear solution</u>**

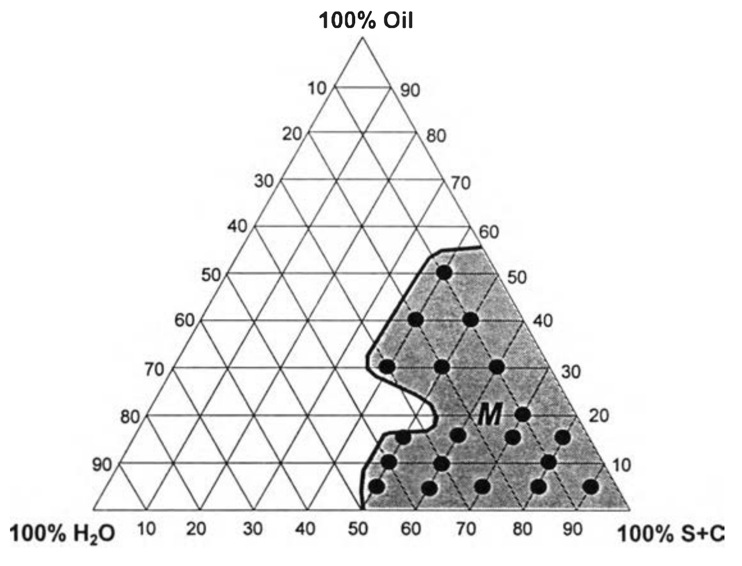


Figure b24. Pseudo-ternary phase diagram of IPM/ Sol/ Im /water (1 week) system at 4:1 weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● Represented the clear solution

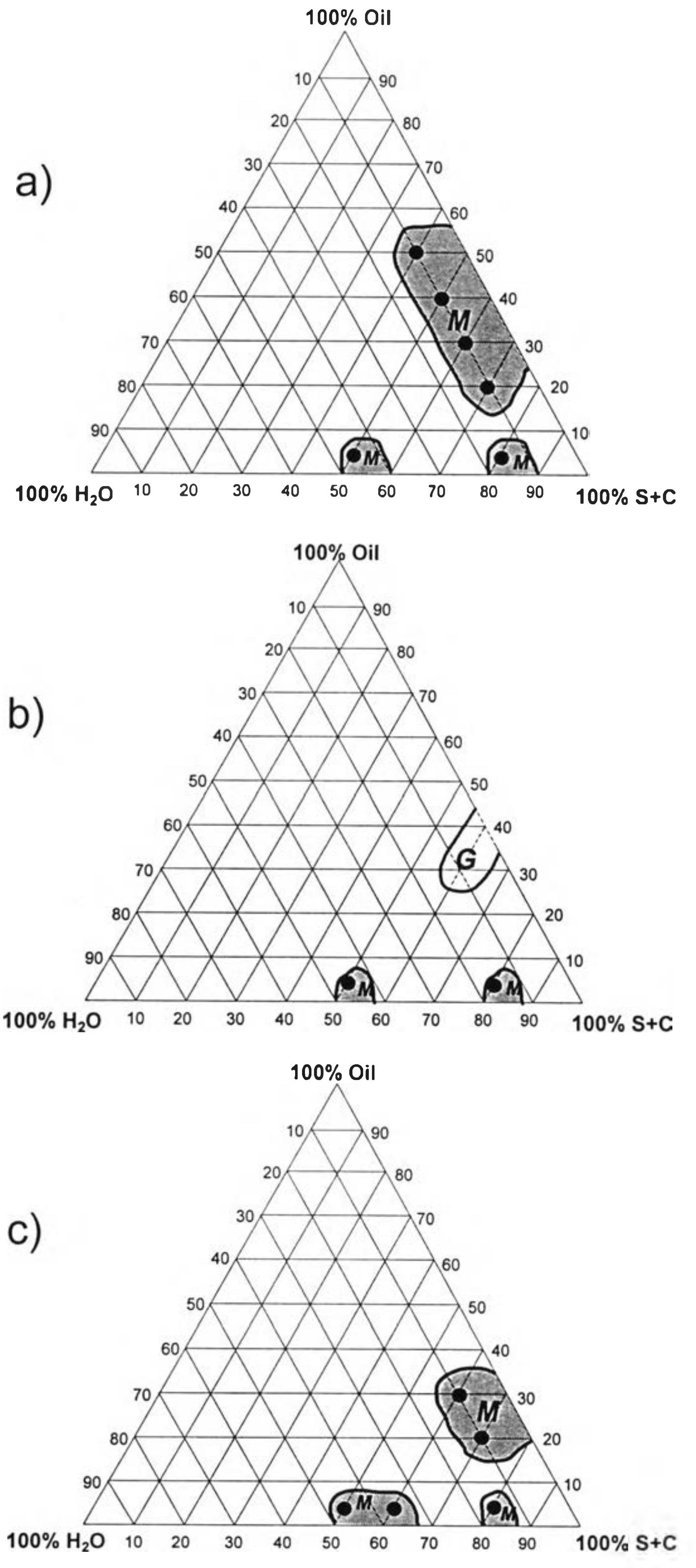


Figure b25. Pseudo-ternary phase diagram of IPM / Cre / Gly/ water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

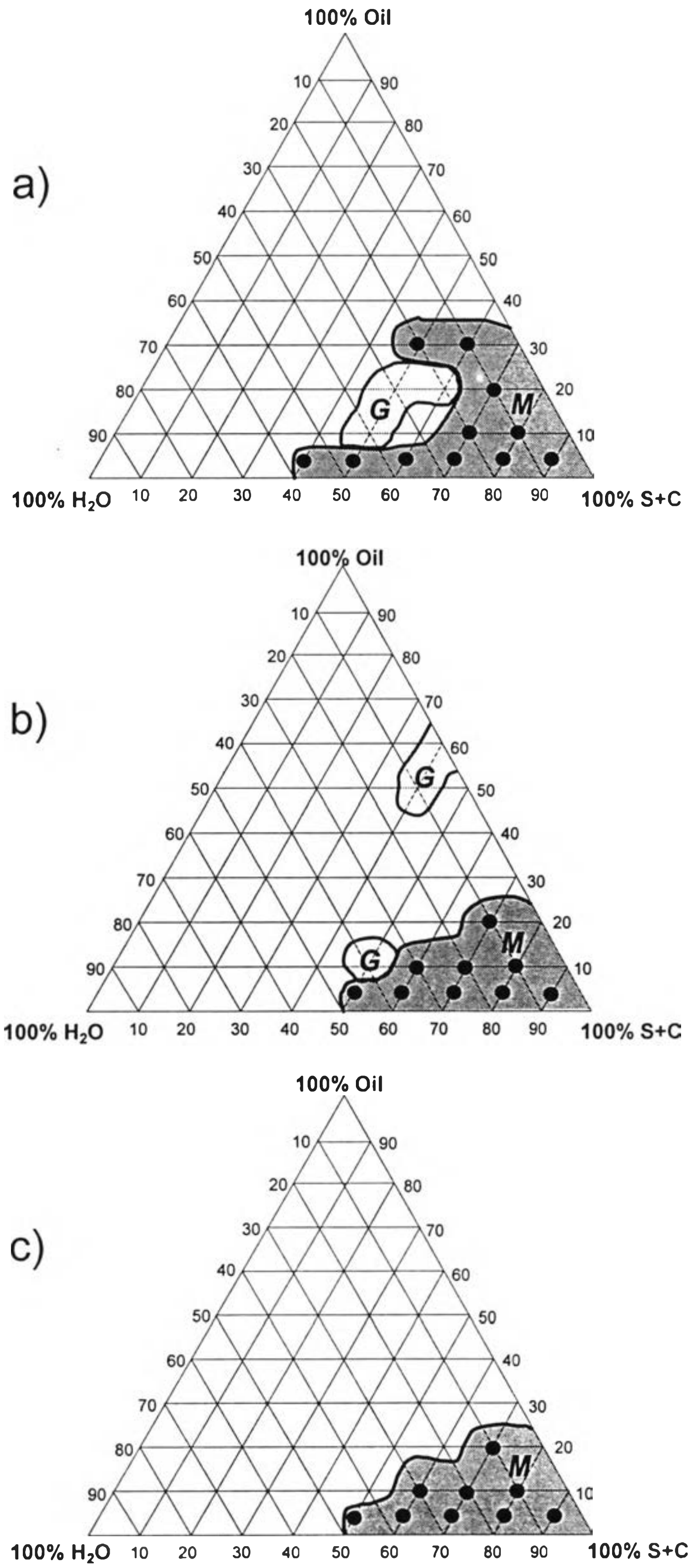


Figure b26. Pseudo-ternary phase diagram of IPM/Cre/PG/water (1 week) system at 4:1(a), 2:1(b) and 1:1(c) weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

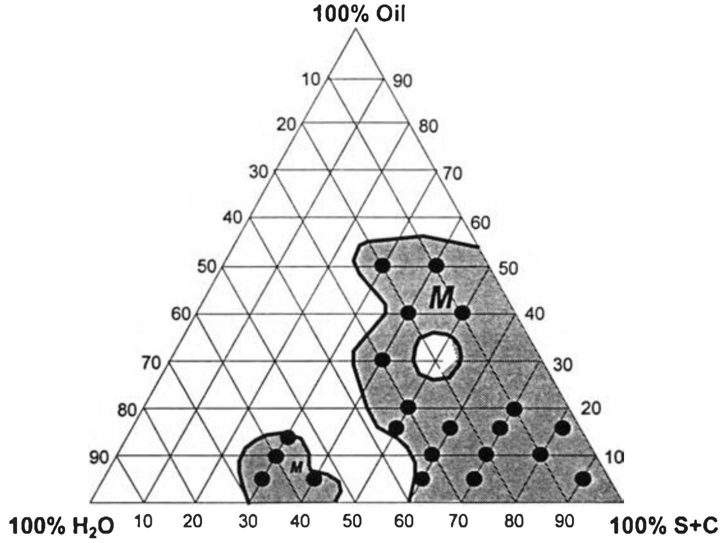


Figure b27. Pseudo-ternary phase diagram of IPM/Cre/Im/water (1 week) system at 4:1 weight ratio of surfactant to cosurfactant

G = Gel, M = Microemulsion

● **Represented the clear solution**

APPENDIX C

Particle size and size distribution.

The particle size and size distribution of microemulsion was determined by Malvern ® 4700, the photon correlation spectroscopy(PCS).

Photon correlation is a powerful technique for measuring the size of very small particles, from as little as 10 nm up to a few micrometres. It operatess by measuring the diffusion coeffcient of the particles and calculating their equivalent spherical diameter. It does this by measuring the fluctuations in scattered light intensity at a fixed angle; these fluctuations are due to diffusion of the particles in and out of the measuring volume by Brownian movement. Since large particles diffuse more slowly than small ones, the fluctuations in scattered light intensity from large particles occur over a longer timescale than the fluctuations induced by small particles. By measuring the statistical properties of the fluctuations in the scattered light (the so-called *correlation function or noise spectrum*), the size of the particles can be determined (Washington, 1992).

The movement of particles in suspension can be characterised by a diffusion coefficient that is effectively the rate of change of x^2 as defined aboved. This quantifies how far from some arbitrary initial position the particle might be expected to be after a certain time. This is a statistical quantity. It will not be expected to make predictions about any one particles' movement, which is an essentially random process, but for a large number of particles it makes accurate predictions about the average displacement. The translational diffusion coefficient (D) for the Brownian process is then 'normalised' by the wave vector (K) to give the relaxation time for the diffusion.

$$T = 1 / DK^2$$

This tells us that the actual relaxion time(T) observed in the correlation fuction will depend on both the angle of observation and the wavelength of illumination. The correlation function that is measured in a normal light scattering measurement arises from the multiplication of the intensity of scattered light by itself, the so-called *homodyne processing.*

The diffusion process is actually quantified by the first-order auto-correlation function which predicts the degree of correlation in the signal as a function (G) of ,τ, the correlation time.

$$G_1(\tau) = e^{-\tau/T}$$

The correlator in a homodyne scattering experiment actually measures the second order auto-correlation function where the constant **a** measures the 'baseline' and **b** the degree of coherence achieved in a particular optical arrangement.

$$(\tau)^2 = G_2(\tau) = a + b\,[G_1(\tau)]^2$$

We see that as τ - > ∞ the average intensity squared = **a** since G_1 - > 0 as τ - > ∞. The baseline can thus be measured by the correlation, and **b** obtained by extrapolating measured G to zero time. For a monosized particle the translational diffusion coefficient (D) can be related to particle diameter using Strokes' diffusion law and the Einstein equation for Brownian motion. Putting these together.

$$D = kt / 6\pi\eta R_h$$

t being the absolute temperature, k (not K !) Boltzmann's constant, η the solvent viscosity, and R_h the *hydrodynamic radius which* is generally very close to, but slightly larger than the geometrical radius of a sphere due to solvent and some interaction effects. In principal these can be interpreted as giving information about the shape of the distribution of 'decay time' and hence particle size. Generally it truncates the series to only 2 or 3 terms and use the 1st moment to derive a 'z Average' mean size and the 2nd ('polydispersity') a measure of width of distribution.

$$\mathrm{LOG}[\{G_2(t) / B\}-1] = a + bt + ct^2 + \ldots$$

Where **G(t)** are the measured correlation points, **B** is baseline (from the far-point or monitor channels); **a, b, c** are the coefficients of the cumulants fit determined by a simple linear-least-squares fitting procedure. **a** is refered to as the 'intercept', **b** the 'slope' measures the 'relaxation time' for the signal, **c** the 'departure from linearity' i.e.. curvature of the fit. Futhur interpretation shows that the Diffusion coefficient, **D**, can be extracted if we write :

$$T_c = 1 / b = 2DK^2$$

Where **K** the scattering vector as defined above. It can be shown that the 'polydispersity' defined as **c/2b** measures the 'variance' (standard deviation squared) of the distribution of decay times and hence particle size. Hence we can generate a Log Normal intensity distribution with the correct moments that corresponds with the measured data.

Table c1. Particle size of microemulsion and micelle with various surfactant and cosurfactant at 4:1 and 2:1 weight ratios of surfactant to cosurfactant

Surfactant/ Cosurfactant	Weight ratio of Surfactant: Cosurfactant	Conc* (%w/w)	Oil (%w/w)	Particle size (nm)			polydispesity		
				Sample1	Sample2	Sample3	Sample1	Sample2	Sample3
Tween® 20/ Imwitor® 308	2:1	50	0	10.6	10.4	10.6	0.11	0.17	0.16
Tween® 20/ Imwitor® 308	2:1	50	1	10.4	10.2	10.3	0.19	0.24	0.19
Tween® 20/ Imwitor® 308	2:1	50	3	10.6	10.4	10.7	0.14	0.17	0.11
Tween® 20/ Imwitor® 308	2:1	50	5	11.2	11.1	11.1	0.12	0.13	0.17
Tween® 20/ Imwitor® 308	2:1	50	7	12.5	12.3	12.4	0.14	0.09	0.07
Tween® 20/ Imwitor® 308	2:1	50	10	12.7	12.6	12.7	0.10	0.07	0.07
Tween® 20/ Imwitor® 308	4:1	60	5	10.3	10.3	10.1	0.13	0.04	0.09
Tween® 80/ Imwitor® 308	4:1	60	0	22.7	23.4	25.3	0.22	0.26	0.32
Solutol® HS15/ Imwitor® 308	4:1	60	0	14.0	14.0	13.9	0.05	0.04	0.04
Solutol® HS15/ Imwitor® 308	4:1	60	5	14.0	14.0	14.0	0.05	0.04	0.04
Cremophor® EL/ Imwitor® 308	4:1	60	0	12.3	12.3	12.5	0.04	0.04	0.00
Cremophor® EL/ Imwitor® 308	4:1	60	5	14.5	14.5	14.4	0.02	0.02	0.04

APPENDIX D

Conductivity and dye test

The investigation and the conductivity of dye test are in Method 5.1 and 5.2.

The result of the determination of type of microemulsion using method 5.1 and 5.2 are shown in Table d1.

The abbreviation of Table d1. are listed below.

ϕ_s = Weight fraction of surfactant and cosurfactant to total amount of system.

ϕ_o = Weight fraction of oil to total amount of system.

ϕ_w = Weight fraction of water to total amount of system.

ND = not determined

Table d1. The conductivity and dye test of microemulsion using Tween® 20 as surfactant

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
none	0	0.90	0.05	0.05	10	/	
none	0	0.80	0.10	0.10	10	/	
none	0	0.70	0.20	0.10	10		/
none	0	0.70	0.10	0.20	20	/	
none	0	0.70	0.05	0.25	30	/	
none	0	0.60	0.10	0.30	40	/	
none	0	0.60	0.05	0.35	50	/	
none	0	0.50	0.05	0.45	80	/	
none	0	0.40	0.05	0.55	10	/	
Gly	4:1	0.90	0.05	0.05	10	/	
Gly	4:1	0.80	0.05	0.15	10	/	
Gly	4:1	0.70	0.20	0.10	10	/	
Gly	4:1	0.70	0.10	0.20	10		/
Gly	4:1	0.60	0.05	0.35	50	/	
Gly	2:1	0.80	0.10	0.10	10	/	
Gly	2:1	0.80	0.05	0.15	10	/	
Gly	2:1	0.70	0.10	0.20	20	/	
Gly	2:1	0.70	0.05	0.25	20	/	

Table d1. The conductivity and dye test of microemulsion using Tween® 20 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
Gly	1:1	0.80	0.10	0.10	10	/	
Gly	1:1	0.80	0.05	0.15	10	/	
Gly	1:1	0.70	0.05	0.25	20	/	
PG	4:1	0.90	0.05	0.05	10	/	
PG	4:1	0.80	0.10	0.10	10	/	
PG	4:1	0.80	0.05	0.15	20	/	
PG	4:1	0.70	0.10	0.20	20	/	
PG	4:1	0.70	0.05	0.25	30	/	
PG	4:1	0.60	0.05	0.35	50	/	
PG	2:1	0.90	0.05	0.05	10	/	
PG	2:1	0.80	0.10	0.10	10	/	
PG	2:1	0.80	0.05	0.15	20	/	
PG	2:1	0.70	0.05	0.25	30	/	
PG	1:1	0.90	0.05	0.05	10	/	
PG	1:1	0.80	0.05	0.15	20	/	
Im	4:1	0.90	0.05	0.05	10	/	
Im	4:1	0.80	0.10	0.10	10	/	
Im	4:1	0.80	0.05	0.15	20	/	

Table d1. The conductivity and dye test of microemulsion using Tween® 20 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
Im	4:1	0.70	0.20	0.10	10	/	
Im	4:1	0.70	0.10	0.20	20	/	
Im	4:1	0.70	0.05	0.25	30	/	
Im	4:1	0.60	0.20	0.20	50	/	
Im	4:1	0.60	0.15	0.25	30	/	
Im	4:1	0.50	0.20	0.30	30	/	
Im	4:1	0.50	0.15	0.35	50	/	
Im	4:1	0.50	0.10	0.40	60	/	
Im	4:1	0.50	0.05	0.45	70	/	
Im	4:1	0.40	0.10	0.50	90	/	
Im	4:1	0.40	0.05	0.55	90	/	
Im	4:1	0.30	0.05	0.65	10	/	
Im	2:1	0.90	0.05	0.05	30	/	
Im	2:1	0.80	0.15	0.05	10	/	
Im	2:1	0.80	0.10	0.10	10	/	
Im	2:1	0.80	0.05	0.15	20	/	
Im	2:1	0.70	0.20	0.10	10	/	
Im	2:1	0.70	0.15	0.15	10	/	

Table d1. The conductivity and dye test of microemulsion using Tween® 20 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
Im	2:1	0.70	0.10	0.20	20	/	
Im	2:1	0.70	0.05	0.25	20	/	
Im	2:1	0.60	0.30	0.10	10	/	
Im	2:1	0.60	0.15	0.25	20	/	
Im	2:1	0.60	0.10	0.30	30	/	
Im	2:1	0.60	0.05	0.35	40	/	
Im	2:1	0.50	0.30	0.20	20	/	
Im	2:1	0.50	0.20	0.30	30	/	
Im	2:1	0.50	0.15	0.35	40	/	
Im	2:1	0.50	0.10	0.40	50	/	
Im	2:1	0.50	0.05	0.45	60	/	
Im	2:1	0.40	0.20	0.40	50	/	
Im	2:1	0.40	0.10	0.50	50	/	
Im	2:1	0.40	0.05	0.55	70	/	
Im	2:1	0.30	0.10	0.60	80	/	
Im	2:1	0.30	0.05	0.65	80	/	
Im	1:1	ND	ND	ND	ND	ND	ND

ND = not determined

Table d2. The conductivity and dye test of microemulsion using Tween® 80 as surfactant

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
none	0	0	0	ND	ND	ND	ND
Gly	4:1	ND	ND	ND	ND	ND	ND
Gly	2:1	0.70	0.20	0.10	10		/
Gly	2:1	0.60	0.30	0.10	10		/
Gly	2:1	0.50	0.10	0.40	10	/	
Gly	2:1	0.40	0.05	0.55	10	/	
Gly	1:1	0.60	0.20	0.20	30	/	
Gly	1:1	0.60	0.10	0.30	50	/	
Gly	1:1	0.50	0.05	0.45	60	/	
PG	4:1	0.80	0.10	0.10	10	/	/
PG	4:1	0.70	0.20	0.10	10		/
PG	4:1	0.70	0.05	0.25	20	/	
PG	4:1	0.50	0.40	0.10	10		/
PG	4:1	0.40	0.05	0.55	140	/	
PG	2:1	0.80	0.10	0.10	10	/	
PG	2:1	0.80	0.05	0.15	10		/
PG	2:1	0.70	0.20	0.10	10		/
PG	2:1	0.70	0.10	0.20	20	/	

Table d2. The conductivity and dye test of microemulsion using Tween® 80 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
PG	2:1	0.70	0.05	0.25	20	/	
PG	2:1	0.60	0.1	0.30	40	/	
PG	2:1	0.60	0.05	0.35	40	/	
PG	2:1	0.40	0.05	0.55	110	/	
PG	1:1	0.90	0.05	0.05	10	/	
PG	1:1	0.80	0.1	0.10	10		/
PG	1:1	0.80	0.05	0.15	10	/	
PG	1:1	0.70	0.1	0.20	20	/	
PG	1:1	0.50	0.05	0.45	60	/	
Im	4:1	0.80	0.05	0.15	10	/	/
Im	4:1	0.60	0.3	0.10	10		/
Im	4:1	0.50	0.4	0.10	10		/
Im	4:1	0.40	0.5	0.10	20	/	
Im	4:1	0.30	0.1	0.60	110	/	
Im	2:1	0.80	0.05	0.15	10	/	
Im	2:1	0.60	0.2	0.20	20		/
Im	2:1	0.50	0.4	0.10	10		/
Im	2:1	0.50	0.3	0.20	20		/

Table d2. The conductivity and dye test of microemulsion using Tween® 80 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSA	ϕ_S	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
Im	2:1	0.40	0.50	0.10	10	/	
Im	2:1	0.30	0.60	0.10	10		/
Im	2:1	0.30	0.40	0.30	80	/	
Im	2:1	0.20	0.70	0.10	10		/
Im	2:1	0.20	0.10	0.70	90	/	
Im	1:1	ND	ND	ND	ND	ND	ND

ND = not determined

Table d3. The conductivity and dye test of microemulsion using Solutol® HS15 as surfactant

Cosurfactant	Ratio of SAA:CoSA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
none	0	0.70	0.15	0.15	20		/
none	0	0.60	0.20	0.20	10		/
none	0	0.50	0.40	0.10	10		/
none	0	0.50	0.30	0.20	10	/	
none	0	0.40	0.50	0.10	10		/
none	0	0.40	0.10	0.50	190	/	
none	0	0.30	0.05	0.65	220	/	
Gly	4:1	0.70	0.10	0.20	10		/
Gly	4:1	0.40	0.10	0.50	20	/	
Gly	4:1	0.30	0.60	0.10	10		/
Gly	2:1	0.40	0.05	0.55	10	/	
Gly	1:1	ND	ND	ND	ND	ND	ND
PG	4:1	0.80	0.10	0.10	20		/
PG	4:1	0.70	0.20	0.10	10	/	
PG	4:1	0.60	0.30	0.10	10		/
PG	4:1	0.60	0.05	0.35	90	/	
PG	4:1	0.50	0.40	0.10	10		/
PG	4:1	0.50	0.30	0.20	40	/	

Table d3. The conductivity and dye test of microemulsion using Solutol® HS15 as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
PG	4:1	0.50	0.20	0.30	70	/	
PG	4:1	0.40	0.05	0.55	180	/	
PG	2:1	0.80	0.10	0.10	20	/	
PG	2:1	0.60	0.30	0.10	20		/
PG	2:1	0.60	0.20	0.20	40	/	
PG	2:1	0.60	0.10	0.30	70	/	
PG	2:1	0.50	0.10	0.40	110	/	
PG	1:1	0.70	0.20	0.10	20	/	
PG	1:1	0.70	0.10	0.20	30	/	
PG	1:1	0.50	0.05	0.45	10	/	
Im	4:1	0.70	0.10	0.20	30	/	
Im	4:1	0.60	0.30	0.10	10	/	
Im	4:1	0.50	0.10	0.40	40	/	
Im	4:1	0.40	0.50	0.10	10		/
Im	4:1	0.40	0.40	0.20	20	/	
Im	4:1	0.40	0.30	0.30	50	/	
Im	2:1	ND	ND	ND	ND	ND	ND
Im	1:1	ND	ND	ND	ND	ND	ND

ND = not determined

Table d4. The conductivity and dye test of microemulsion using Cremophor® EL as surfactant

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
none	0	0.80	0.10	0.10	10		/
none	0	0.70	0.20	0.10	10		/
none	0	0.60	0.20	0.20	10	/	
Gly	4:1	0.80	0.20	0.00	10		/
Gly	4:1	0.80	0.05	0.15	10		/
Gly	4:1	0.50	0.40	0.10	10		/
Gly	4:1	0.50	0.05	0.45	10	/	
Gly	2:1	0.80	0.05	0.15	10	/	
Gly	2:1	0.50	0.05	0.45	90	/	
Gly	1:1	0.80	0.05	0.15	10	/	
Gly	1:1	0.60	0.30	0.10	10		/
Gly	1:1	0.50	0.05	0.45	80	/	
PG	4:1	0.90	0.05	0.05	10		/
PG	4:1	0.80	0.10	0.10	10		/
PG	4:1	0.70	0.20	0.10	10		/
PG	4:1	0.70	0.05	0.25	30	/	
PG	4:1	0.60	0.30	0.10	10		/
PG	4:1	0.40	0.05	0.55	130	/	

Table 4. The conductivity and dye test of microemulsion using Cremophor® EL as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
PG	2:1	0.90	0.05	0.05	10		/
PG	2:1	0.80	0.10	0.10	10	/	
PG	2:1	0.70	0.20	0.10	10		/
PG	2:1	0.70	0.05	0.25	40	/	
PG	2:1	0.60	0.10	0.30	40	/	
PG	2:1	0.60	0.05	0.35	10		/
PG	2:1	0.50	0.05	0.45	70	/	
PG	1:1	0.90	0.05	0.05	10	/	/
PG	1:1	0.80	0.10	0.10	10	/	
PG	1:1	0.80	0.05	0.15	20	/	
PG	1:1	0.70	0.20	0.10	10	/	
PG	1:1	0.70	0.10	0.20	20	/	
PG	1:1	0.50	0.05	0.45	60	/	
Im	4:1	0.80	0.10	0.10	10		/
Im	4:1	0.60	0.30	0.10	10		/
Im	4:1	0.60	0.20	0.20	20	/	/
Im	4:1	0.60	0.10	0.30	20		/
Im	4:1	0.50	0.40	0.10	10	/	

Table d4. The conductivity and dye test of microemulsion using Cremophor® EL as surfactant (continued)

Cosurfactant	Ratio of SAA:CoSAA	ϕ_s	ϕ_o	ϕ_w	Conductivity (uS/cm)	Methyl Orange	Sudan III
Im	4:1	0.40	0.50	0.10	10		/
Im	4:1	0.40	0.40	0.20	10		/
Im	4:1	0.40	0.30	0.30	20	/	
Im	4:1	0.30	0.50	0.20	10		
Im	4:1	0.30	0.10	0.60	130	/	
Im	2:1	ND	ND	ND	ND	ND	ND
Im	1:1	ND	ND	ND	ND	ND	ND

APPANDIX E

The viscosity of microemulsion and micelle

Table e1. The viscosity of microemulsion

Surfactant : Cosurfactan	Weight ratio of surfactant : cosurfactant	Conc (%w/w)	Oil (%w/w)	Viscosity* (mPaS)										
				1	2	3	4	5	6	7	8	9	10	Everage(n=10)
T 20	0	50	5	527.80	525.40	525.30	528.10	531.10	529.10	526.90	529.80	526.70	532.90	528.30
T20 and Im	2 : 1	50	0	66.53	68.27	66.35	68.27	65.98	67.91	66.52	68.33	66.43	67.91	67.25
T20 and Im	2 : 1	50	1	58.21	58.38	58.41	58.50	58.65	58.76	58.79	58.96	58.96	59.14	58.68
T20 and Im	2 : 1	50	3	58.29	60.85	59.07	58.32	61.65	58.13	61.41	58.61	62.06	58.49	59.69
T20 and Im	2 : 1	50	5	56.23	59.67	56.04	58.03	58.48	58.44	58.90	57.77	59.10	57.96	58.06
T20 and Im	2 : 1	50	7	56.48	59.43	56.96	58.60	57.43	58.41	57.86	58.07	58.04	58.38	57.96
T20 and Im	2 : 1	50	10	62.23	59.30	61.97	61.45	59.67	61.75	60.01	61.83	59.69	62.12	61.00
T20 and Im	2 : 1	50	12	58.42	60.91	58.52	60.45	58.48	60.67	58.58	60.91	58.68	58.15	59.38
T20 and Im	2 : 1	50	15	59.52	62.61	59.86	59.89	62.62	59.93	62.77	59.89	62.70	60.00	60.98
T20 and Im	4 : 1	60	5	137.30	135.20	139.00	135.30	138.50	134.90	139.10	135.20	138.50	134.70	136.80
T20 and Im	4 : 1	60	10	140.80	137.40	139.10	139.20	137.60	140.70	140.20	139.40	138.20	140.80	139.30
T20 and Im	4 : 1	60	15	125.60	123.10	126.60	123.10	126.90	124.10	126.80	123.10	127.30	124.00	125.10
T80	0	50	0	120.30	121.40	122.30	119.50	122.70	119.50	122.60	119.70	123.00	119.70	121.10
Sol and Im	4 : 1	60	0	196.30	198.30	194.10	197.70	194.50	197.60	197.60	197.30	195.10	198.80	196.70
Sol and Im	4 : 1	60	5	204.50	200.60	203.80	202.70	202.10	204.00	203.70	203.20	201.80	204.40	203.10
Cre	0	60	0	398.50	395.80	401.50	398.50	400.20	397.10	403.10	400.20	401.70	399.50	399.60
Cre and Im	4 : 1	60	5	326.90	328.00	324.80	330.00	327.80	331.30	327.70	331.00	328.80	332.30	328.90

* viscositv at 10 observations

APPENDIX F

Hemolysis study

1. Dose-response relationship with a quantal response (Bowman and Rand, 1980)

The result of an experiment are plotted with proposion responding on the y axis and the log dose on x axis. The S-shape curve is produced and it can be converted into a straight line by re-scaling the y axis. The proportion or percentage responders to each dose is transformed into another unit known as a probit(Figure f1). The regression line is then calculated from the probits corresponding to the percentage responding and log concentration. The rationale of probit transformation depends on the considerations already discussed in connection with the Gaussian distributions (Normal distribution). The deviations from the mean in standard deviation unit corresponding to various probabilities (i.e. proportions of responders) can be read from Z table. These figures are termed normal equivalent deviation. They are converted to probit by adding 5 (Table f1).

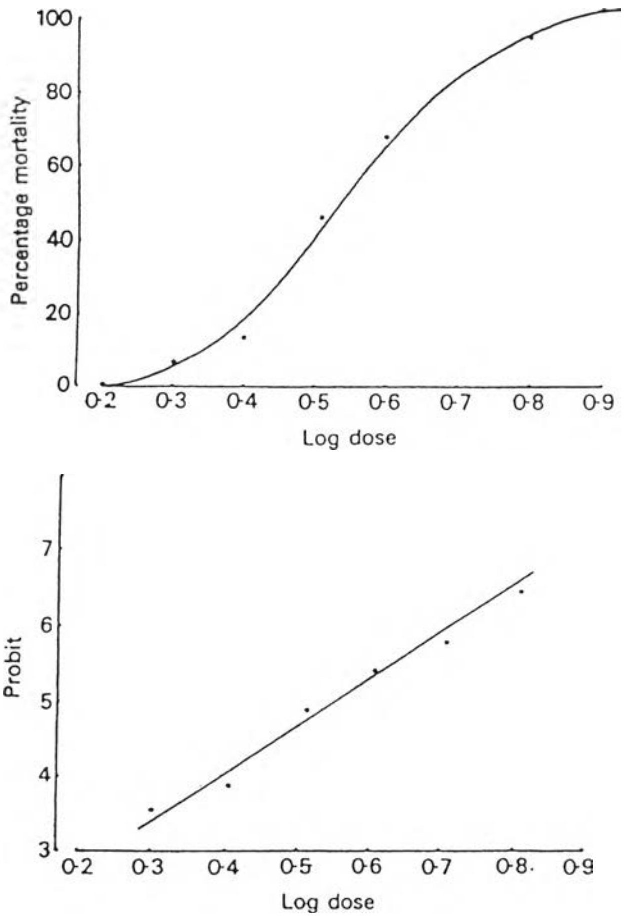


Figure f1. Effect of probit transformation in converting sigmoid curve of percentage mortality versus log dose (upper graph) to straight line (lower graph) (From (Bowman and Rand, 1980)

Table f1. Toxicity test showing relation between concentration and hemolysis (The probit value corresponding to hemolysis of 50%w/w at 2:1 Tween® 20/Imwitor® 308 microemulsion with 5%oil)

conc	log conc	% Hemolysis	Proportion hemolysis	z	Probit
0.075	1.12	7.58	0.08	-1.57	3.43
0.100	1.00	18.00	0.18	-1.09	3.91
0.250	0.60	20.80	0.21	-0.99	4.01
0.500	0.30	76.90	0.77	0.74	5.74
1.000	0.00	90.10	0.90	1.29	6.29

2. The calculation of the concentration producing 50% of maximal respond (IC_{50})

The estimate of the concentration producing 50 % of maximal response (X_E) is:

$$X_E = \overline{X} + \frac{Y - \overline{Y}}{b_{YX}}$$

Where X $= \Sigma X_T / N_T$

Y = response

Y = 5 (for probit relationship)

The b_{yx} equation:

$$b_{YX} = \frac{\Sigma(X - \overline{X})(Y - \overline{Y})}{\Sigma(X - \overline{X})(X - \overline{X})} = \frac{SXY}{SX}$$

Where SXY $= \Sigma XY - (\Sigma X \Sigma Y)/N_T$

N_T $= \Sigma N$

SX $= \Sigma X^2 - (\Sigma X)^2/N_T$

And the confidence limits are given by:

$$X_E = \overline{X} + \frac{Y - \overline{Y}}{b_{YX}} \pm \frac{t_{(P,n)}\sqrt{(s_b^2)}}{b_{YX}} \sqrt{\left\{\frac{SX}{N} + \frac{(Y - \overline{Y})^2}{b_{YX} \cdot c}\right\}}$$

The c can be taken as unity for an approximate value, or, more precisely

$$c = 1 - t^2_{(P,n)}(1 - SY/s_b^2)/(N - 2)$$

where value of t is for n = N-2

$$s_b^2 = \frac{SY(X)}{(N-2)SX}$$

$$SY = \Sigma Y^2 - (\Sigma Y)^2/N_T$$

3. The percent hemolysis of micelle and microemulsion

Table f2. Hemolysis of Tween® 20 micelle with/without Imwitor® 308 micelle in PBS

-log conc (%w/v)	%hemolysis of T20/Im Micelle	SD	%hemolysis T20Micelle	SD
2.30	0.50	0.22	0.10	0.13
2.00	0.40	0.39	0.00	0.11
1.30	8.00	4.72	1.30	0.7
1.12	43.70	13.62	6.30	2.53
1.00	74.10	8.84	9.00	2.34
0.60	91.10	7.37	32.90	12.46
0.30	90.70	1.39	50.20	10.89
0.00	96.00	1.77	94.00	30.49

Table f3. Hemolysis of Tween® 20/Imwitor® 308/IPM/PBS of 50% w/w concentration and 2:1 weight ratio of Tween20 to Imwitor 308 with 5, 10 and 15 %w/w oil

-log conc (%w/v)	%hemolysis ME with 5% oil (w/w)	SD	%hemolysis ME with 10 % oil (w/w)	SD	%hemolysis ME with 15% oil (w/w)	SD
2.30	0.30	0.16	0.30	0.19	0.70	0.31
2.00	0.30	0.29	0.00	0.22	0.20	0.11
1.30	1.80	1.03	1.10	0.89	0.60	0.10
1.12	7.58	2.68	1.00	0.28	1.00	0.19
1.00	18.00	6.83	2.20	1.08	2.30	1.20
0.60	20.80	1.58	22.60	3.74	73.60	7.74
0.30	76.90	6.31	92.10	3.58	83.00	2.18
0.00	90.10	8.64	94.20	2.77	86.60	1.42

Table f4. Hemolysis of Tween® 80 and Imwitor® 308 micelle in PBS

-log conc (%w/v)	%hemolysis of T80/Im Micelle	SD	%hemolysis T80Micelle	SD
2.30	0.20	0.18	0.10	0.13
2.00	0.10	0.08	0.10	0.18
1.30	0.30	0.07	0.00	0.00
1.12	0.40	0.19	0.00	0.03
1.00	0.20	0.12	0.00	0.00
0.60	2.40	0.26	0.00	0.00
0.30	41.10	6.58	0.10	0.09
0.00	89.90	6.91	0.90	0.16

Table f5. Hemolysis of micelle with/without Imwitor® 308 and microemulsion of Solutol® HS15/Imwitor® 308/IPM/PBS of 60% w/w concentration and 4:1 weight ratio of to Solutol® HS15/ Imwitor ® 308 with 5 %w/w oil

-log conc (%w/v)	%hemolysis Sol/Im micelle	SD	%hemolysis Sol/Im micelle	SD	%hemolysis ME with 5% oil (w/w)	SD
2.30	0.30	0.19	0.00	0.13	0.70	0.31
2.00	0.00	0.22	0.10	0.08	0.20	0.11
1.30	1.10	0.89	0.20	0.24	0.60	0.10
1.12	1.00	0.28	0.00	0.1	1.00	0.19
1.00	2.20	1.08	0.00	0.05	2.30	1.20
0.60	22.60	3.74	0.10	0.12	73.60	7.74
0.30	92.10	3.58	0.00	0.05	83.00	2.18
0.00	94.20	2.77	0.10	0.05	86.60	1.42

Table f6. Hemolysis of micelle with/without Imwitor® 308 and microemulsion of Cremophor® EL/Imwitor® 308/IPM/PBS of 60% w/w concentration and 4:1 weight ratio of Cremophor® EL to Imwitor® 308 with 5 %w/w oil

-log conc (%w/v)	%hemolysis Cre/Im Micelle	SD	%hemolysis Cre micelle	SD	%hemolysis ME with 5% oil (w/w)	SD
2.30	0.10	0.11	0.20	0.11	0.00	0.00
2.00	0.10	0.07	0.30	0.07	0.00	0.00
1.30	0.00	0.05	0.30	0.05	0.00	0.07
1.12	0.00	0.00	0.20	0.00	0.00	0.00
1.00	0.00	0.00	0.50	0.00	0.00	0.03
0.60	0.20	0.21	0.30	0.21	0.10	0.11
0.30	0.00	0.09	0.10	0.09	2.10	0.34
0.00	1.00	0.56	0.20	0.56	12.40	4.29

APPENDIX G

Osmolality

The osmolality is the concentration expressed as moles of solute particle per kilogram of water. Thus, the osmolality (mOsm/kg) linearly increase with an increase in solute concentration and the number of particles in solution. The osmolality, O is described as

$$O = \phi \, n \, c/M$$

Where ϕ is the osmotic coefficient that accounts for the degree of molecular dissociation, n is the number of particle or ions into which a molecule would dissociate, c is concentration of solution (g/kg or g/l) and M is the molecular weight. For nonionic solutes such as dextrose and urea, n and ϕ are equal to 1. Although, in the case of nonionic interacting molecules n can be a value less than 1 because of the take out of play effect (Viegas and Henry, 1998).

BIOGRAPHY

Miss Niyaporn Aroonrat was born on October 26, 1975 in Bangkok province, Thailand. She received her Bachelor of Pharmacy Degree from Faculty of Pharmacy, Chaing-Mai University, Chaing-Mai, Thailand in 1999. After graduation, she works at Pranangklao Hospital, Nonthaburi province.