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Development of microemulsion systems for Thai herbal extract

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Objectives: The objective of this work was to study the solubility of Thai herbal extract in different oils, surfactants, and co-surfactants, and then the suitable oil, surfactant, and co-surfactant were selected to prepare the pseudoternary phase diagram of microemulsion systems.
Methods: The different oils: castor oil, olive oil, Vitamin E, and caprylic acid, surfactants: Tween® 20, Tween® 60, Tween® 80, and co-surfactants: polyethylene glycol 400, and propylene glycol, and the mixture of Tween® 80:absolute ethanol (8:2) were selected to test the solubility of Thai herbal extract. The pseudoternary phase diagrams of microemulsion systems were prepared from suitable oil, surfactant, and co-surfactant. The selected region point from pseudoternary phase diagram of microemulsion systems was mixed with 1% w/w Thai herbal extract and then, evaluated for the particle size, size distribution, and zeta potential.
Results: The Thai herbal extract could be highly dissolved in caprylic acid and Tween® 20 that were 11.45 and 104.00 µg/mL, respectively. From solubility results, although the Thai herbal extract could be low dissolved in Tween® 80 (10.65 µg/mL), the Thai herbal extract could be increasingly dissolved in the mixture of Tween® 80 and absolute ethanol in a ratio of 8:2 (173.87 µg/mL). Thus, the caprylic acid was used as oil phase and Tween® 20 was used as surfactant phase as well as the mixture of Tween® 80 and absolute ethanol in ratio of 8:2 was used as surfactant/co-surfactant which was mixed with water phase to prepare the pseudoternary phase diagrams of microemulsion systems. The behavior formation of microemulsion systems was graded in 4 levels for the pseudoternary phase diagrams. The particle size of selected region points of microemulsion systems were found in range of 10 – 440 nm with low polydispersity index (less than 0.30). The zeta potentials were found in range of -6.02 to -41.35 mV.
Conclusion: We could prepare the new microemulsion systems for Thai herbal extract which will be developed to apply in herbal cosmetic products.

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Introduction

Emulsion is a conventional system which has particle size in range of 1 – 20 µm. Emulsion likes a milky heterogeneous system that can be defined as one of component dispersed throughout another component in the form of droplets. Microemulsion is an application system from emulsion that has a small particle size of one component dispersed in another component in the microemulsion form that has particle size in range of 10 – 200 nm. Microemulsion system has a transparency, low viscosity and more fundamentally thermodynamic stability when compared to normal emulsion. Water, oil, and surfactant components are homogeneously mixed as microemulsion which is a single optically isotropic and thermodynamically stable liquid solution. Microemulsion system evolves constantly between various structures ranging from droplet-like swollen micelles to bi-continuous structures. Microemulsion system can incorporate active drug or active compound into their system, leading to an increase in the extent of existence of the microemulsion region. The microemulsion can enhance bioavailability, give controlled rate of drug release, and afford protection to oxidation or hydrolysis.[1-4] Moreover, microemulsion can be easily applied and formulated to eliminate oiliness and staining, carrying water which is an excellent softener to skin.[1,5,6]

This work aimed to study the solubility of Thai herbal extract in different vehicles: oils (castor oil, olive oil, Vitamin E, and caprylic acid), surfactants (Tween® 20, Tween® 60, and Tween® 80), and co-surfactants (polyethylene glycol 400 (PEG400), propylene glycol (PG), and the mixture of Tween® 80:absolute ethanol (8:2)). Then, the suitable vehicles were used to prepare the pseudoternary phase diagram of microemulsion systems for Thai herbal extract. The size particle, size distribution, and zeta potential were analyzed.

Methods

Preparation of herbal extract formulation: The Thai herbal extract compound was composed of Curcuma *longa L., Areca catechu L., Oryza sativa L.,* and *Garcinia mangostana L.* in ratio of 1:1:1:1, respectively that was prepared by

Dr.Chonlatid Sontimuang, Faculty of Traditional Thai Medicine, Prince of Songkla University. A traditional Thai herbal recipe, namely “Ya-Sa-Marn-Phlae” has been used for the treatment of wounds and skin infections.[7,8]

***Solubility study of Thai herbal extract*:** The excess amount of Thai herbal extract was added in test tube containing 1 mL of different vehicles: castor oil, olive oil, Vitamin E, caprylic acid, Tween® 20, Tween® 60, Tween® 80, PEG400, PG, and the mixture of Tween® 80:absolute ethanol (8:2). Then, they were vortexed to facilitate mixing Thai herbal extract for 2 min.

***Preparation of pseudoternary phase diagrams of microemulsion systems for Thai herbal extract*:** The caprylic acid (P.C. Drug Center Co., Ltd, Thailand) was used as oil phase, and each Tween® 20 (P.C. Drug Center Co., Ltd, Thailand) or mixture of Tween® 80 (P.C. Drug Center Co., Ltd, Thailand) and absolute ethanol (8:2) was used as surfactant, with simple mixing using a vertex for 30 seconds at room temperature. The definition of the mixture compositions at different points in the pseudoternary phase diagrams was used the following equation.

$\%O + \%W + \%SU = 100\ \%$

Where O was oil phase, W was water phase, and %SU was surfactant/cosurfactant mixture.

The compositions are shown in Table 1. Then, the 1%w/w of herbal extract was mixed in suitable microemulsion point with a good clear microemulsion in appearance.

***The particle size, size distribution, and zeta potential evaluation*:** The Nanoplus 3 (Particulate system, USA) was used to determine the particle size, size distribution, and zeta potential at 25 ± 2ºC. The distilled water was used as dilutant at an appropriate concentration prior to microemulsion determination. The testing was recorded as a mean ± SD for ten sub-runs.

Results

***Solubility study of Thai herbal extract*:** Generally, the Thai herbal extract cannot be dissolved in water**.** Thus, the screening of appropriate solvents was very important to find out a suitable solvent to dissolve Thai herbal extract and then use to form microemulsion. The solubility of Thai herbal extract in various oils and surfactants were measured and the results are shown in Figure 1. The results showed that the solubility of Thai herbal extract in (1) oils: olive oil, castor oil, caprylic acid, and vitamin E were 9.3, 7.2, 11.45, and 10.90 µg/mL, respectively, (2) surfactant: Tween® 20, Tween® 60, and Tween® 80 were 104.00, 17.87, and 10.65 µg/mL, respectively, and (3) co-surfactant: PEG 400 and PG, and the mixture of Tween® 80:absolute ethanol (8:2) were 47.23, 114.89, and 173.87 µg/mL, respectively. Thus, caprylic acid and Tween® 20 showed the high solubility of Thai herbal extract, which was the best among the oil and surfactant type investigation. On the other hand, Tween® 80 gave the low solubility of Thai herbal extract, but the solubility of Thai herbal extract increased when it was mixed with absolute ethanol.

Table 1. Composition of microemulsion systems

Formulas	Caprylic acid (g)	Tween® 20 (g)	Tween® 80:Ehthanol (8:2) (g)	Water (g)
ME1-1	0.5139	4.0146	-	0.5132
ME2-1	1.5005	3.0082	-	0.5218
ME3-1	1.0052	3.5015	-	0.5016
ME4-1	0.5053	3.5080	-	1.0130
ME5-1	1.0124	3.0036	-	1.0087
ME6-1	0.5266	3.0168	-	1.5114
ME7-1	0.2577	4.5054	-	0.2522
ME8-1	2.0094	2.4991	-	0.5216
ME9-1	2.5554	2.0005	-	0.5101
ME10-1	1.5048	2.5121	-	1.0042
ME11-1	2.0103	2.0029	-	1.0348
ME12-1	0.5070	2.0105	-	2.5204
ME13-1	1.0087	2.5152	-	1.5429
ME1-2	0.5022	-	4.0211	0.4994
ME2-2	1.0000	-	3.5115	0.5098
ME3-2	1.5041	-	3.0015	0.5049
ME4-2	2.0051	-	2.5105	0.5121
ME5-2	0.5014	-	3.5078	1.0064
ME6-2	0.5014	-	3.0148	1.5125
ME7-2	0.5021	-	1.0000	3.5200
ME8-2	0.5015	-	2.0100	2.5021
ME9-2	3.0032	-	1.5181	0.5130
ME10-2	1.0042	-	3.0085	1.0135
ME11-2	1.5016	-	2.0038	1.5054

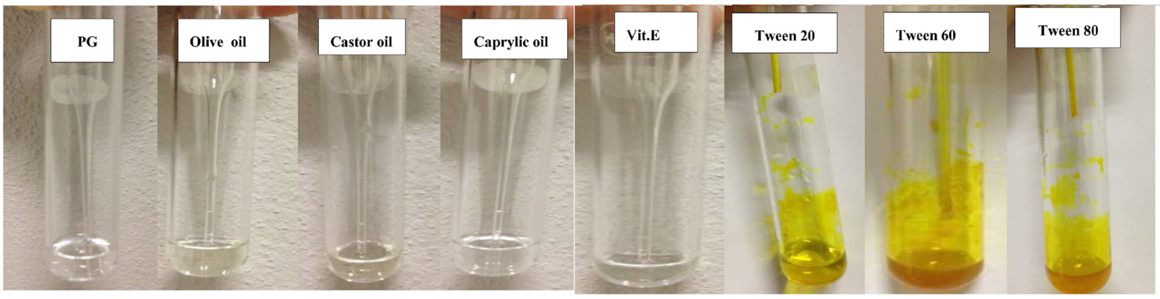

Figure 1. Solubility of Thai herbal extract in various vehicles at room temperature

Preparation of pseudoternary phase diagrams of microemulsion systems for Thai herbal extract: The phase behavior of microemulsion systems was indicated by the 4 levels in the pseudoternary phase diagrams (Figure 2). The mixture could rapidly form the microemulsion within 1 min that had a clear or slightly bluish in appearance defined as level A. The mixture could rapidly form the microemulsion that had a bluish white in appearance defined as level B. The mixture could form the bright white milk-like emulsion in appearance defined as level C. Finally, when the mixture could form the poor or minimal microemulsion that had an oil droplets on the surface, it was defined as level D.

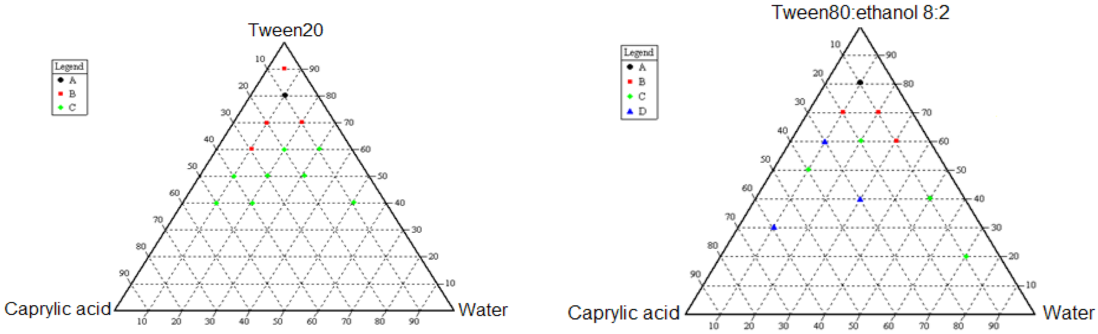

Figure 2. Pseudoternary phase diagrams of the caprylic acid/Tween® 20/water system (left) and the caprylic acid/mixture of Tween® 80 and absolute ethanol (8:2)/water system (right)

The particle size, size distribution, and zeta potential evaluation: The ME1-1, ME4-1, ME7-1, ME1-2, ME2-2, ME5-2, and ME6-2 formulas were selected to evaluate the particle size and size distribution that are shown in Table 2. The particle size of selected microemulsion formulas was found in range of 13.07 – 439.07 nm with low polydispersity index (PDI). After that, the 1%w/w Thai herbal extract was loaded in ME4-1 and ME2-2 formulas that showed the low particle size compared to those blank microemulsion systems. The zeta potential of ME4-1, ME4-1(E), ME2-2, and ME2-2(E) were -6.02±1.19, -41.35±15.02, -7.19±1.23, and -11.26±2.42 mV, respectively.

Table 2. The particle size and size distribution of selected microemulsion systems

Formulas	Size particle (nm)	PDI
ME1-1	111.67±0.65	0.27
ME4-1	138.03±0.81	0.24
ME7-1	13.07±0.12	0.08
ME1-2	17.80±0.35	0.24
ME2-2	192.30±1.97	0.22
ME5-2	25.27±0.40	0.28
ME6-2	439.07±24.95	0.28
ME4-1(E)	20.17±2.48	0.21
ME2-2(E)	177.00±0.26	0.21

Discussion

The compound might be solubilized in the oily core and/or on the interface membrane of surfactant and co-surfactant in the resulting microemulsion structures.[3,4] Thus, the solubility of Thai herbal extract could be affected from presence of various oils, surfactants, and co-surfactants in microemulsion systems. The Thai herbal extract showed high solubility in oil, caprylic acid. Although, Tween® 80 showed the Thai herbal extract solubilization less than Tween® 20, Tween® 80 had wide pharmaceutical applications more than Tween® 20 owing to its good biological acceptance.[9] In addition, Tween® 80 might give better emulsification capacity when compared to Tween® 20 and Tween® 40[9], and exhibited the maximum solubilizing capacity for Thai herbal extract when mixed with absolute ethanol in ratio of 8:2. Therefore, it was selected as the suitable surfactant used with absolute ethanol, co-surfactant. The result of various vehicles with high solubility for Thai herbal extract were used to construct the pseudoternary phase diagrams which was used to obtain an appropriate concentration ranges of components in the areas of forming microemulsion. The microemulsion systems of Tween® 20 and mixture of Tween® 80 and absolute ethanol (8:2) were compared by constructing pseudoternary phase diagrams with caprylic acid as oil phase and water phase. The mixture of caprylic acid, mixture of Tween® 80 and absolute ethanol (8:2), and water could form microemulsion area more than the mixture of caprylic acid, Tween® 20, and water. This was due to the ethanol might increase the solubility of the Thai herbal extract in microemulsion systems. The particle size of selected microemulsion had a small size when increased the content of surfactant or co-surfactant. The surfactant can reduce the surface and interfacial tensions in their formulation.[4,10,11] The Thai herbal extract affected to reduce the particle size when it was loaded in selected microemulsion point. The zeta potential is an electrostatic value measured by surface electrostatic double layer of droplets. The zeta potentials of selected microemulsion points were slightly changed between before and after loading Thai herbal extract.

Conclusion

In the present work, caprylic acid, Tween® 20, and the mixture of Tween® 80 and absolute ethanol in ratio of 8:2 showed a high solubility behavior of Thai herbal extract. The pseudoternary phase diagrams of microemulsion systems could be prepared from these vehicles for 1%w/w Thai herbal extract which was graded in 4 levels. Their particle sizes were found in range of 10 to 440 nm with low PDI and the zeta potential was in range of -6.02 to -41.35 mV. As a result, the new microemulsion systems for Thai herbal extract could be prepared by simple mixing in laboratory scale and will be developed for the herbal cosmetic products.

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