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Development of self-microemulsifying systems for Thai herbal extract

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Objectives: This work aimed to prepare the pseudoternary phase diagrams of self-microemulsifying systems for Thai herbal extract.
Methods: Thai herbal extract recipe, namely "Ya-Sa-Marn-Phlae", has been widely used for the treatment of wounds and skin infections. The Thai herbal extract was prepared by Dr.Chonlatid Sontimuang, Faculty of Traditional Thai Medicine, Prince of Songkla University. The pseudoternary phase diagrams of self-microemulsifying systems were prepared from caprylic acid, each Tween® 20 or mixture of Tween® 80 and absolute ethanol (8:2), and propylene glycol as oil phase, surfactant phase, and co-surfactant phase, respectively. The 1% w/w Thai herbal extract was mixed in self-microemulsifying systems. The appearance of self-microemulsifying systems was observed by visual observation and graded in 4 levels. Then, they were diluted with distilled water and analysed the particle size, size distribution, and zeta potential.
Results: The pseudoternary phase diagrams showed the 4 levels for self-microemulsifying systems which had the particle size in ranged of 36 – 182 nm with low polydispersity index. When the Thai herbal extract was loaded, the size of particle was less than their blank self-microemulsifying systems. In addition, the zeta potential of all self-microemulsifying systems showed between -8.22 to -2.22 mV.
Conclusion: This work could prepare the self-microemulsifying systems for Thai herbal extract recipe, namely "Ya-Sa-Marn-Phlae" that might be developed for the herbal cosmetic products.

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Introduction

Self-microemulsifying systems (SMEs) comprise of oil and surfactant, with or without co-surfactant and can form microemulsions upon mixing with aqueous phase.[1,2] SMEs have improved the solubility of poorly water compounds and drugs such as penciclovir[3], apigenin[4], and curcumin[5]. The SMEs is isotropic and thermodynamically stable solution consisting of oil, surfactant, co-surfactant and active compound which can homogeneously form into oil-in-water microemulsion. They has a small particle size that affect to a large interfacial surface area for active compound absorption. Thus, the active compound can be highly dissolved in their formulation. In addition, the Thai herbal extract is a poorly water soluble compound, thus the SMEs may increase of its solubility.
Objective of this work was to prepare and evaluate of a SMEs with the aim to improve the solubility and dissolution of Thai herbal extract recipe: *Curcuma longa L., Areca catechu L., Oryza sativa L.,* and *Garcinia mangostana L.* in ratio of 1:1:1:1, respectively. The pseudoternary phase diagrams were constructed to obtain the self-emulsification region in 4 levels, and the Thai herbal extract was mixed in suitable self-emulsification region. The particle size, size distribution, and zeta potential of SMEs after dilution with water were evaluated.3

Methods

***Preparation of herbal extract formulation*:** The herbal extract recipe: the *Curcuma longa L., Areca catechu L., Oryza sativa L.,* and *Garcinia mangostana L.* in ratio of 1:1:1:1, respectively was prepared by Dr.Chonlatid Sontimuang, Faculty of Traditional Thai Medicine, Prince of Songkla University. This herbal extract formulation is a traditional Thai herbal recipe, namely "Ya-Sa-Marn-Phlae" and has been used for the treatment of wounds and skin infections.[6,7]

***Preparation of pseudoternary phase diagrams of SMEs for Thai herbal extract*:** The caprylic acid (P.C. Drug Center Co.,Ltd, Thailand), 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), and propylene glycol (PG, P.C. Drug Center Co.,Ltd, Thailand) were used as oil phase, surfactant phase, and co-surfactant phase, respectively (Table 1). Then, the 1% w/w Thai herbal extract was mixed in the selected SMEs that had a good emulsion form.

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

Results

Preparation of pseudoternary phase diagrams of SMEs: The pseudoternary phase diagrams of SMEs are shown in Figure 1. The appearance of these SMEs was visually assessed using the following grading system: A, the system rapidly formed the SMEs within 1 min that was a clear or slightly bluish in appearance; B, the system rapidly formed the SMEs that was a bluish white in appearance; C, the system formed the bright white SMEs that was a milk-like emulsion in appearance; and D, the system that formed the poor or minimal SMEs that presented an oil droplets on the surface.

Table 1. Composition of SMEs

Formulas	Caprylic acid (g)	Tween® 20 (g)	Tween® 80:Ehtanol (8:2) (g)	PG (g)
SME1-1	0.5051	3.9989	-	0.4987
SME2-1	1.5009	2.9948	-	0.5017
SME3-1	1.0270	3.5033	-	0.5181
SME4-1	0.5247	0.5105	-	4.0032
SME5-1	0.5080	1.0128	-	3.5093
SME6-1	1.5122	0.5018	-	2.9911
SME7-1	0.5123	3.5074	-	1.0244
SME8-1	0.5022	2.9977	-	1.5205
SME9-1	0.5060	2.5073	-	2.0015
SME10-1	0.5069	2.0121	-	2.5116
SME11-1	0.5090	1.5044	-	3.0167
SME12-1	1.0026	3.0022	-	1.0123
SME13-1	1.0065	2.5079	-	1.5204
SME14-1	1.0018	2.0197	-	2.0125
SME15-1	1.5016	2.5015	-	1.0153
SME16-1	1.5194	2.0000	-	1.5026
SME17-1	1.9999	2.0060	-	1.0018
SME18-1	1.0014	1.5007	-	2.5102
SME1-2	0.5023	-	4.0000	0.5109
SME2-2	1.0030	-	3.5107	0.5095
SME3-2	1.5015	-	3.0080	0.5086
SME4-2	2.0026	-	2.5154	0.5059
SME5-2	2.5044	-	2.0139	0.5013
SME6-2	3.0020	-	1.5112	0.5046
SME7-2	3.5013	-	1.0046	0.5133
SME8-2	0.5030		3.5091	1.0060
SME9-2	0.5029		3.0200	1.5049
SME10-2	0.5026		2.5085	2.0068
SME11-2	0.5010		2.0170	2.5150
SME12-2	0.5027		1.5174	3.0060
SME13-2	1.0032		3.0194	1.0057
SME14-2	1.5002		2.5175	1.0051

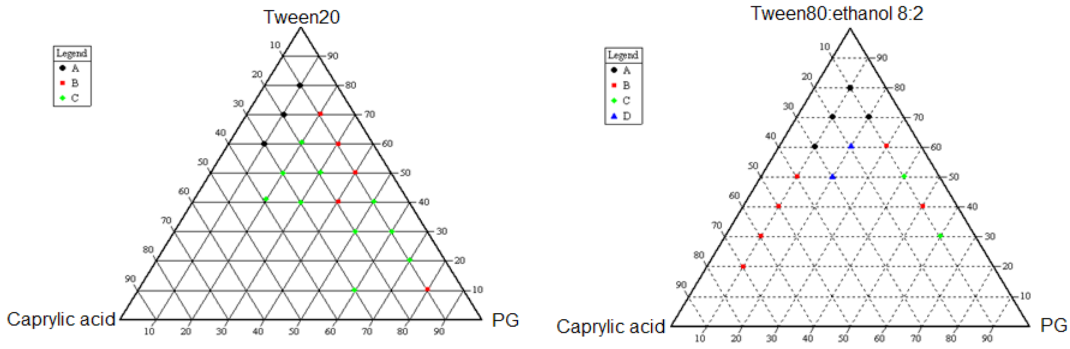

Figure 1. Pseudoternary ternary phase diagram of the caprylic acid/Tween® 20/PG system (left) and the caprylic acid/mixture of Tween® 80 and absolute ethanol (8:2)/PG system (right)

The particle size, size distribution, and zeta potential evaluation: The selected SMEs formulas were evaluated for the particle size and size distribution which are showed in Table 2. They were found that the particle size in range of 36 – 182 nm with low polydispersity index. The Thai herbal extract was loaded in SME7-1 or SME9-2 formulas. They had the size of particle less than their blank SMEs. In addition, they had low size distribution that were 0.26 and 0.23, respectively. The zeta potential of SME7-1, SME9-2, herbal extract–loaded SME7-1, and herbal extract–loaded SME9-2 were -6.98±0.51, -8.22±0.59, -2.22±0.19, and -7.89±0.65 mV, respectively.

Table 2. The particle size and size distribution of selected SMEs

Formulas	Size particle (nm)	Polydispersity index
SME1-1	156.27±0.70	0.25
SME7-1	181.23±1.00	0.27
SME1-2	36.83±0.55	0.28
SME2-2	174.17±1.92	0.18
SME8-2	113.93±0.74	0.32
SME9-2	148.47±0.93	0.30
Herbal extract–loaded SME7-1	85.33±0.29	0.26
Herbal extract–loaded SME9-2	133.03±1.70	0.23

Discussion

The Thai herbal extract was prepared in SMEs that composed of the caprylic acid/Tween® 20/PG system (SMEs I) and the caprylic acid/mixture of Tween® 80 and absolute ethanol (8:2)/PG system (SMEs II). The SMEs II could form self-microemulsion system more than SME I. They could form self-microemulsion system when decreased the content of mixture between Tween® 80 and absolute ethanol (8:2). The results showed an increasing of the microemulsion area in SMEs II. This was due to the SMEs II had the ethanol to increase the solubility of the Thai herbal extract. The selected SMEs had the small particle size when the composition of SMEs composed of the high content of surfactant or co-surfactant. The surfactant can reduce the surface and interfacial tensions in their formulation.[4,8,9] When the Thai herbal extract was loaded in selected SMEs, the particle size decreased from blank SMEs. The addition of Thai herbal extract in the SMEs decreased the particle size that obtained after diluting with distilled water. The zeta potentials of SMEs were not obviously changed before and after loading Thai herbal extract. The time required for microemulsion formation after dilution with distilled water was less than 30 s.[4] The resulting SMEs were rapidly formed the SMEs that was a bluish white in appearance and they did not show any effect of phase separation and precipitation of Thai herbal extract during experimental testing at room temperature.

Conclusion

In this study, a new SMEs were prepared in an attempt to incorporate the poorly water soluble Thai herbal extract. The SMEs containing 1% w/w Thai herbal extract were prepared from the pseudoternary phase diagrams, and evaluated for the particle size, size distribution, and zeta potential of selected SMEs formulas. They had the particles between 36.83 and 181.23 nm in size with low polydispersity index and had the zeta potential in ranged of -2.22 to -8.22 mV. Therefore, we successfully prepared the Thai herbal extract – based SMEs that will be used to develop for the herbal cosmetic products.

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