Solid Lipid Microparticles as a Delivery Carrier for Turmeric Crude Extract Containing Curcuminoids

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Received 23 May 2007; accepted 19 November 2007

Abstract

Solid lipid microparticles comprising mixtures of stearic acid, glyceryl monostearate and medium chain triglyceride and containing turmeric crude extract were successfully developed in a one-step procedure, using a hot emulsion technique followed by high speed homogenization. A yellowish cream with a plastic flow behavior and thixotropic characteristics was obtained. Light microscopic investigations revealed that the turmeric extract loaded solid lipid microparticles possessed a narrow size distribution, ranging from 1-7 μm with high entrapment efficacy up to 100%. Dissolution studies using Franz diffusion cells demonstrated a fast release behavior suggesting that the curcuminoids were adsorbed on the particle surface. The stability of curcuminoids in the solid lipid microparticles could be maintained for at least 6 months in the lipidic preparation formulated together with Tween 80.

Keywords: Turmeric crude extract; Curcuminoids; Solid lipid microparticles; Hot emulsion technique

Introduction

The use of botanical products is expanding rapidly worldwide. Over $650 million is spent yearly on botanical products in the United States (Lantz et al., 2005). A number of traditional plants have been used in medicines and cosmetics for centuries. Botanical products can be prepared either from crude extract or purified compounds. Comparing the manufacturing procedure of pure compounds with those for crude extracts, the latter is cheaper and easier to be prepared and less time consuming. Moreover, a crude extract contains the original combination of the active ingredients which is difficult to imitate by purified compounds. However, the stability of many crude plant extracts is a major concern because they are notoriously light and water sensitive. They also may possess an unpleasant color and flavor. To overcome these disadvantages, we attempted to develop a crude extract formulation using solid lipid microparticles as a delivery carrier for curcuminoids in a cosmetic preparation. The extract of turmeric, the rhizome of *Curcuma longa* Lin, containing curcuminoids was used as a model compound. They are one of the most recognized Thai traditional plant compounds widely used in cosmetics for centuries.

Turmeric consists of 2 main ingredients: curcuminoids and volatile oil. Curcuminoids are one of the best investigated herbal antioxidants (Ahsan et al., 1999; Khopde et al., 1999; Sreejayan & Rao, 1994). They consist primarily of 3 phenolic compounds: curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Fascinatingly, they can prevent lipid peroxidation at a significantly higher degree than pine bark extract, grape seed extract and synthetic antioxidants like butylated hydroxytoluene (BHT) (Kim et al., 1997) and show therefore excellent properties in retarding skin aging. Unfortunately, they are degraded by acidic and alkaline hydrolysis, oxidation and photodegradation (Bernabe-Pineda et al., 2004; Pfeiffer et al., 2003; Price & Buescher, 1996; Tonnesen et al., 1986; Wang et al.,1997).

Many studies showed that curcuminoids decompose in a pH-dependent manner, with faster reactions at neutral to basic conditions. They are known to be stable at a pH below 6.5.

Many attempts have been made to overcome the curcuminoids' stability problem. Tonnesen found that micellar solubilization could stabilize curcumin against hydrolytic reactions, but the half life of curcumin in such system was only 2 months. Moreover, curcumin stabilized by micellar systems showed a higher photodecomposition rate compared to curcumin in aqueous solution (Tonnesen, 2002). We recently reported that curcuminoids in a cream base could be stabilized for 6 months when incorporated in solid lipid nanoparticles (SLNs), the particles size was in the nanometer range (Tiyaboonchai et al., 2007). However, the preparation process involved with filtration and freeze drying, both steps were considered as a time consuming processes.

Among modern drug delivery carriers, solid lipid microparticles (SLMs) seem to be a promising carrier system. SLMs made from biodegradable solid lipids exist in the micron size range and can be prepared by several methods. The advantages of SLMs are as follows: possibility of controlled drug release and drug targeting, protection of incorporated compound against chemical degradation, no biotoxicity of the carrier, avoidance of organic solvents and no problems with respect to large scale production (Marengo et al., 2000; Mehnert & Mäder, 2001; Müller et al., 2000)

In this study we further developed the incorporation of the components of turmeric crude extract in solid lipid microparticles by using a one-step, hot-melt, high-speed homogenization technique which is a less time-consuming process. The primary goal was to characterize the processing factors which affect the physical characteristics of the curcuminoids in SLMs, including the physical and chemical stabilities during storage. Additionally, the efficiency of drug incorporation as well as the drug release characteristics were also investigated.

Materials and Methods

Chemicals

Stearic acid, glyceryl monostearate (GMS) and medium chain triglycerides (Lexol) were obtained from Numsiang Trading (Bangkok, Thailand). Tween 80 was purchased from S. Tong Chemical (Bangkok, Thailand). Lipoid S100-3 was purchased from Lipoid (Ludwigshafen, Germany). Poloxamer 188 was a gift from BASF (Ludwigshafen, Germany). Standard curcuminoids were purchased from Sigma, (Lot No. 69-s3457, MO, USA). All other chemicals and solvents were of analytical grade. Polycarbonate membrane, diameter 25 mm, with a 0.22 μm pore size (Isopore^{TM}) and polyethersulfone membrane, diameter 76 mm, with a molecular weight cut off of 100,000 Da (Millipore® YM100) were purchased from Millipore Corporation (MA, USA).

Preparation of turmeric crude extract

Turmeric was collected from Bangkratum, Phitsanulok, Thailand in April 2004. The voucher specimen was deposited at the Faculty of Pharmaceutical Science, Naresuan University, Phitsanulok, Thailand.

The rhizome of turmeric was washed and dried at 60 ^{o}C. The dried material was ground and macerated with 95% ethanol for 3 days and filtered. The residue was macerated again using the same procedure twice. The filtrates were combined and evaporated under reduced pressure until dryness.

Preparation of curcuminoid loaded SLMs

Curcuminoid loaded SLMs were prepared by a hot emulsion technique followed by a high-speed homogenization using a Silverson-SL2 high shear homogenizer (Chesham Bucks, England). The water phase, consisting of water and 4% w/w emulsifier was heated to ~ 75 ^{o}C. The oil phase, consisting of 3-13% (w/w) stearic acid, 7-27% (w/w) glyceyl monostearate and 3-13% (w/w) Lexol were melted together at ~75 ^{o}C. Turmeric extract was dissolved in ethanol before added to the melted lipid. An O/W emulsion was obtained by a phase inversion process when the warm aqueous phase was added to the warm oil phase. The warm emulsion was then homogenized using a high-speed homogenizer at 8,000 rpm for 3 minutes. Finally, SLMs were obtained by rapidly cooling the fine emulsion in an ice bath while continuously stirring.

The SLMs were prepared under different processing parameters to study the effect of a number of variables on their physicochemical properties. Processing parameters were varied as follows: The ratio of stearic acid and GMS was varied from 1:1.5 to 1:3; the types of emulsifiers were chosen from Tween80, Lipoid S100-3 and Poloxamer188; and the total lipid concentration was varied from 10-40% (w/w). The selection of these variables was based on preliminary experiments. Empty microparticles were prepared using the same procedure variables. All samples were prepared in triplicate.

Physicochemical characterization of the curcuminoids loaded SLMs

The morphology of the curcuminoids loaded SLMs was determined using an optical microscope (BX51, Olympus, Tokyo, Japan) at 400-fold magnification. Samples were diluted with water prior to microscopic examination. The mean particle size and particle size distribution were also analyzed by the same procedure. The particle size was determined by measuring the Feret's diameter, which is the distance between two parallel tangents on opposite sides of the particle. At least 300 microparticles were measured for the size distribution analysis. The cumulative percentage, frequency, undersize and normalized Z-value were calculated. The normalized Z-value was calculated from the cumulative percentage frequency undersize. In order to calculate the geometric mean diameter (D50), the particle diameter was transformed into a logarithm value (Martin, 1993).

The rheological measurements were performed with a rheometer (Model DV-III, Brookfield, MA, USA) equipped with a cone-and-plate test geometry (model spindle CP51, plate diameter 12 mm, cone angle 1.5 ^{o}C). All measurements were carried out at a temperature of 25 ^{o}C. Continuous flow measurements were performed by increasing the shear rate from 5 to 150 s^{-1} followed by decreasing the shear rate from 150 to 5 s^{-1}. The resulting shear stress was measured. Yield stresses were determined by extrapolation of the steady state shear stress to zero shear rate.

Determination of curcuminoids incorporation efficiency into SLMs

One hundred milligrams of curcuminoids loaded SLMs were accurately weighed and dissolved in 10 ml methanol. The dispersion was centrifuged at 13,000 x g for 3 minutes. Then the amount of curcuminoids in the supernatant was determined from its absorption at 420 nm using UV-Vis spectrophotometer (Model Cary-1E, Varian, MA, USA). The percentage of curcuminoids incorporation was then calculated using a calibration curve from the range of 0.5-8.0 μg/ml of standard curcuminoids.

In vitro dissolution studies

In vitro release of curcuminoids loaded SLMs was studied using vertical Franz diffusion cells (Model No. 57-951-061, Meditron, V lklingen, Germany) at 37 ± 0.5 ^{o}C. The area

for diffusion was 1.77 cm^2 and the receptor chamber volume was 7.8 ml. Polycarbonate hydrophilic membrane (Isopore® Membrane 0.22 μm, 25-mm diameter) was fitted between donor and receptor compartment. The receptor medium consisting of 50% v/v ethanol was continuously stirred. The vertical Franz diffusion cell was allowed to equilibrate for 15 minutes before applying the sample. An amount of curcuminoids loaded SLMs containing 250 μg curcuminoids was evenly spread on the membrane surface. Half a milliliter of the receptor medium was taken at predetermined time intervals of 10, 30, 60 and 180 minutes. The amount of curcuminoids released was determined using their absorbance at 420 nm.

Stability studies of curcuminoids loaded solid lipid microparticles

Curcuminoids loaded SLMs were stored in well-closed amber glass containers and were kept at room temperature for 6 months. The rheological properties and the content of curcuminoids were evaluated at various time intervals. The content of curcumin, demethoxycurcumin and bisdemethoxycurcumin was determined by a HPLC method which was modified from Jayaprakasha et al. (2002). An HPLC apparatus (Model LD10A, Shimadzu, Kyoto, Japan) equipped with a 250 x 4.6 mm (i.d.) reversed-phase C18 column with 5-μm particle size (Luna, Phenomenex, CA, USA) and a UV-VIS detector was used. The mobile phase consisted of acetonitrile and acetate buffer in a ratio of 1:1 (v/v), the pH of mobile phase was adjusted to 3.1 with glacial acid. A flow rate of 1.2 ml/min and detection wavelength of 425 were employed. Twenty milligrams of curcuminoids loaded SLMs were accurately weighed and dissolved in 1 milliliter of methanol. The dispersion was centrifuged at 13,000 x g for 10 minutes. The supernatant was decanted and then further filtered through 0.2-μm membrane before injecting into the column. The amounts of curcumin, demethoxycurcumin and bisdemethoxycurcumin were calculated by the peak areas using a calibration curve constructed from 1-100 μg/ml of standard curcuminoids. All experiments were done in triplicate.

Results and Discussion

Preparation of turmeric crude extract

Turmeric crude extract was prepared by the maceration method using ethanol as an extraction solvent. From 32 Kg of dried material, 1.2 kg of a brown syrupuos crude extract was obtained. The yield of the extract was 3.91 % (w/w). The HPLC analysis revealed that the extract contained 25.15% of curcuminoids: 6.41% of bisdemethoxycurcumin, 6.83% of demethoxycurcumin and 11.91% of curcumin.

Physicochemical characterization of the curcuminoids loaded SLMs

Morphology

Curcuminoid loaded SLMs were successfully prepared in a one-step employing a hot-melt, high-speed homogenization technique at a temperature range of 70-75 ^{o}C. Yellowish semisolid SLMs were obtained after the fine emulsion was rapidly cooled down. Light microscopical investigations revealed that loaded SLMs were uniformly distributed. They were spherical in shape with a light-yellowish color (Figure1A-C). The morphology of particles was found to be independent of the processing conditions.

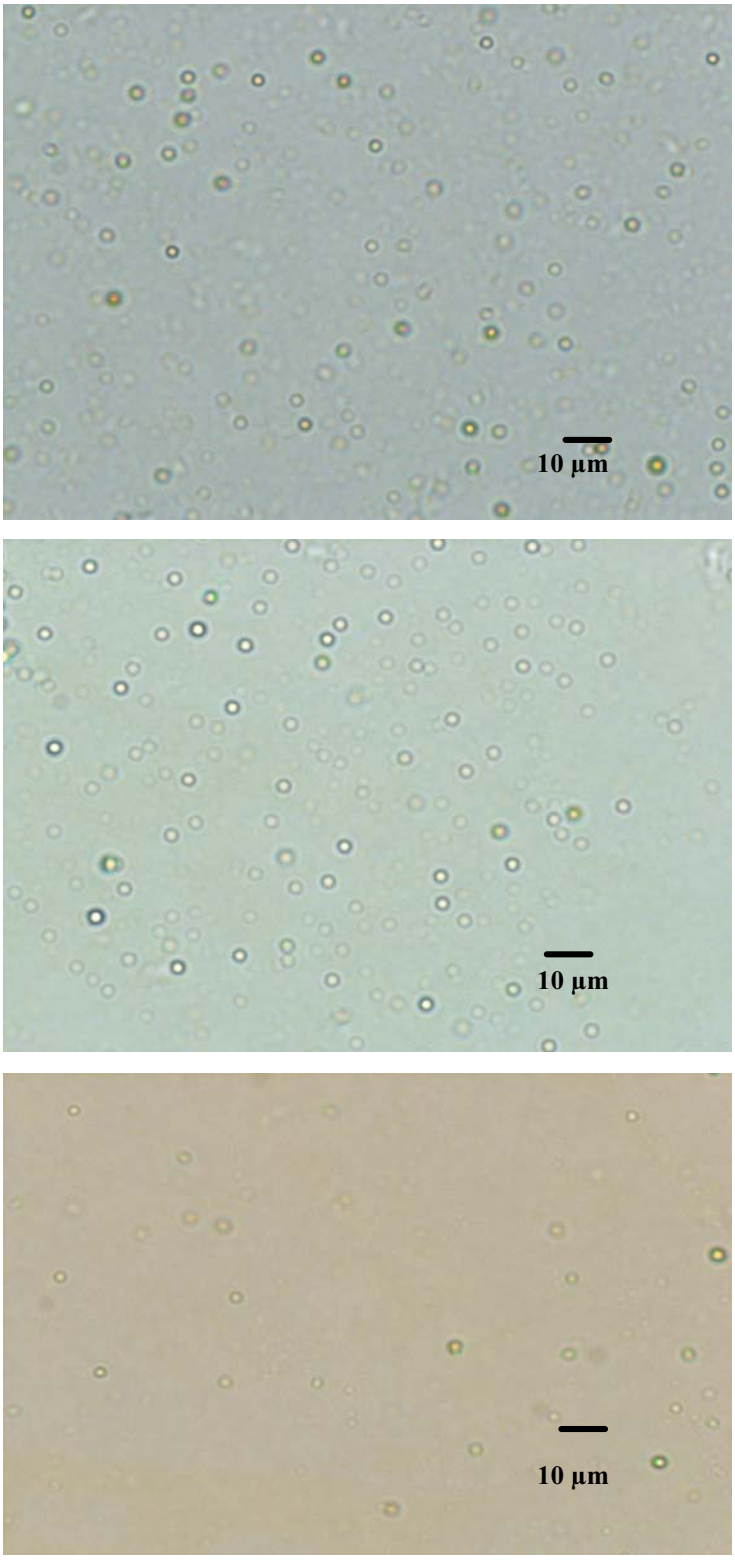

Figure 1. Micrographs of curcuminoids loaded SLMs consisting of 6.67% (w/w) stearic acid and 13.33% (w/w) GMS with different types of emulsifiers (4% w/w): (A) Tween80, (B) Poloxamer188, and (C) Lipoid S100-3.

Mean particle size and size distribution of curcumionids loaded SLMs were determined by light microscope. The results showed that the mean particle size was independent of the processing conditions. Almost all formulations studied showed a mean particles size of ~ 3 μm with a size distribution ranging from 1-7 μm. However, the mean particle size was affected by the concentration of the lipids. By varying the amount of lipids ranging from 10-40% (w/w) while maintaining the ratio of stearic acid and GMS at 1:2 and Tween 80 at 4% (w/w), the results showed that as the amount of lipid increased, the mean particle size increased as well (Table 1). This finding was in agreement with Mehnert et al. who reported that increasing the lipid content over 5-10% w/w in most cases resulted in larger mean particle sizes (Mehnert & Mäder, 2001).

Table 1. Effect of the ratio of stearic acid and GMS on the mean particle size and the yield value of curcuminoids loaded microparticles

The ratio of stearic acid : GMS	D_{50} (μm)*	Yield value (dynes/cm^2)*
1 : 1.5	3.6 ± 1.2	674 ± 170
1 : 2.0	2.8 ± 1.3	631 ± 89
1 : 2.5	3.9 ± 1.2	1533 ± 168
1 : 3.0	3.8 ± 1.3	1506 ± 263

*Data represent mean ± SD.
Composition of the SLMs (w/w): 20% stearic acid and GMS and 4% Tween 80.

The application and acceptance of cosmetic products is also based on the flow properties of the final product. Thus, the rheological properties of turmeric loaded SLMs were studied to reveal their flow and deformation behavior. The rheograms of curcuminoids loaded SLMs are shown in Figure 2-4. All formulation displayed a plastic flow characteristic with thixotropic properties as indicated by the hysteresis loops as ascending and descending flow curves did not overlap. These hystereses indicated that the solid lipid microparticles were loosely interacting with each other to form a three-dimentional gel network. Thus, a distinct stress was needed to break down the gel structure (shear thinning). Thereafter, only small stresses were needed to keep the systems flowing.

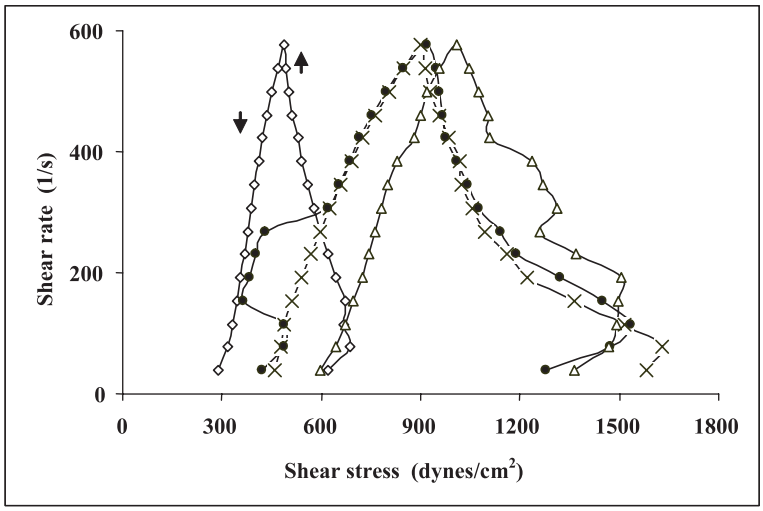

Figure 2. Flow curve of curcuminoids loaded SLMs consisting of stearic acid and GMS (20% w/w), Tween 80 (4% w/w). The ratio of stearic acid and GMS were: (◊) 1.0:1.5; (x) 1.0:2.0; (•) 1.0:2.5; and (Δ) 1.0:3.0.

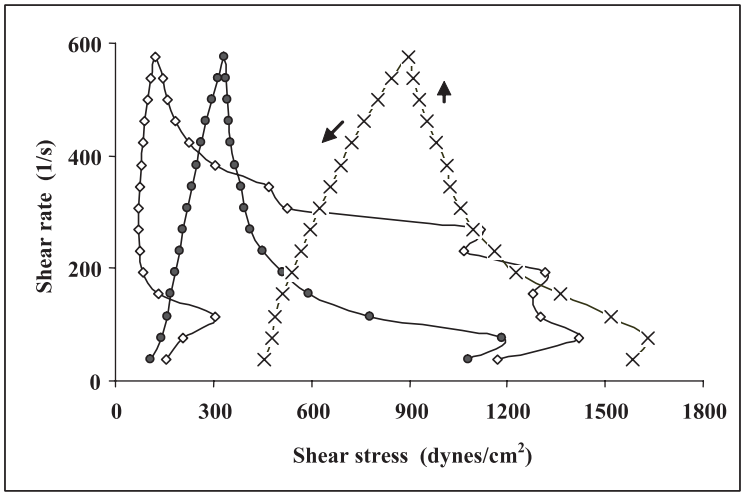

Figure 3. Flow curve of curcuminoids loaded SLM consisting of stearic acid (6.67% w/w), GMS (13.33% w/w) and different emulsifiers (4% w/w): (x) Tween 80, (•) Poloxamer 188 and (◊) Lipoid S100-3.

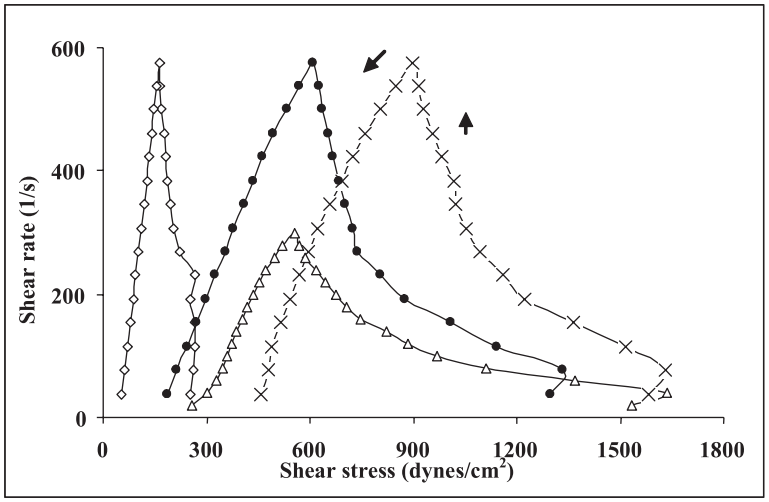

Figure 4. Flow curve of curcuminoids loaded SLM consisting of stearic acid and GMS in a ratio of 1:2, Tween 80 (4% w/w), and the different amounts of lipid (w/w): (◊) 10%, (x) 20%, (•) 30% and (Δ) 40%.

The effect of the amount of lipids, stearic acid and GMS, on the rheological properties of the systems was evaluated by varying the amount of lipids ranging from 10-40% (w/w) while maintaining the ratio of stearic acid and GMS at 1:2 and Tween80 at 4% (w/w). The results in Table 3 show that the formulation with 10% (w/w) of lipids resulted in the lowest viscosity with a yield value of 265 dyne/cm^2. This may be a result from the low content of SLMs in the preparation. Increasing the amount of lipids of the formulation resulted in dramatic changes of the viscosities. Changing the lipid content from 10 to 20% (w/w) resulted in higher viscosity and a yield value of ~ 1600 dyne/cm^2. Thus, the increased amount of particles and increased interaction with each other to create a three-dimensional gel structure resulted in a higher viscosity. The ratio of stearic acid and GMS also showed profound effects on the rheological properties of the systems (Table 1). The yield value increased as the amount of GMS was increased. The formulation with the ratio of stearic acid to GMS at 1:1.5 showed the lowest yield value of ~ 670 dyne/cm^2

as GMS also acts as a co-emulsifier. Formulation with different types of emulsifiers showed minor effect on the rheograms (Table 2). The broadest hysteresis loops were observed with Lipoid S100-3 indicating a slow recovery of 3-dimentioal gel like structure (Figure 3).

Table 2. Effect of the types of emulsifiers on the mean particle size and the yield value of curcuminoids loaded microparticles

Types of emulsifiers	D_{50} (μm)*	Yield value (dynes /cm^2)*
Tween 80	2.8 ± 1.3	1631 ± 89
Poloxamer 188	3.3 ± 1.2	1182 ± 94
Lipoid s100-3	3.0 ± 1.3	1422 ± 317

*Data represent mean ± SD.
Composition of the SLMs (w/w): 6.67% stearic acid, 13.33% GMS, and 4% emulsifier.

Table 3. Effect of the concentration of lipids on the mean particle size and the yield value of curcuminoids loaded microparticles

The amount of lipid (%w/w)	D_{50} (μm)*	Yield value (dynes /cm^2)*
10	2.8 ± 1.2	265 ± 73
20	2.8 ± 1.3	1631 ± 89
30	4.0 ± 1.1	1334 ± 50
40	5.1 ± 1.2	1638 ± 19

*Data represent mean ± SD.
Composition of the SLMs: stearic acid and GMS in a ratio of 1:2 and 4% (w/w) Tween 80.

Determination of curcuminoids incorporation efficacy

All formulations studied demonstrated high curcuminoids incorporation efficacy in the range of 90-100% (w/w). The experimental results indicated that the processing conditions had no effect on the incorporation efficiency (data not shown).

In vitro dissolution studies

Curcuminoids possess very poor aqueous solubility. Thus, to provide sink conditions, 50% (v/v) ethanol was chosen as an acceptor medium. The *in vitro* release studies from curcuminoids loaded SLMs applied in a cream formulation demonstrated a fast release characteristics (Figure 5). Eighty percent of the curcuminoids were released within 1 hr. Therefore, the results indicated that most of curcuminoids must have been adsorbed on the solid lipid particle surface and diffused from the surface into the dissolution medium. However, a 25% burst release of the curcuminoids within 10 minutes was observed, suggesting a partition of the curcuminoids from the SLMs into the continuous phase. The types of emulsifiers and the amount of lipid showed minor effects on the drug release profiles. The formulation with 40% of lipids possessed a lower release rate profile. This may be due to its highest viscosity compared to those formulated with lower amounts of lipids (Table 3). The same phenomena were observed with the formulation prepared with Poloxamer 188 which also demonstrated the lowest yield value compared to other formulations formulated with Tween 80 and Lipoid S100-3 (Table 2). This findings are in agreement with those of Thakker and Chern who reported that the higher viscosity of the semisolid formulation, the slower was the release rate of the active ingredient (Thakker & Chern, 2003).

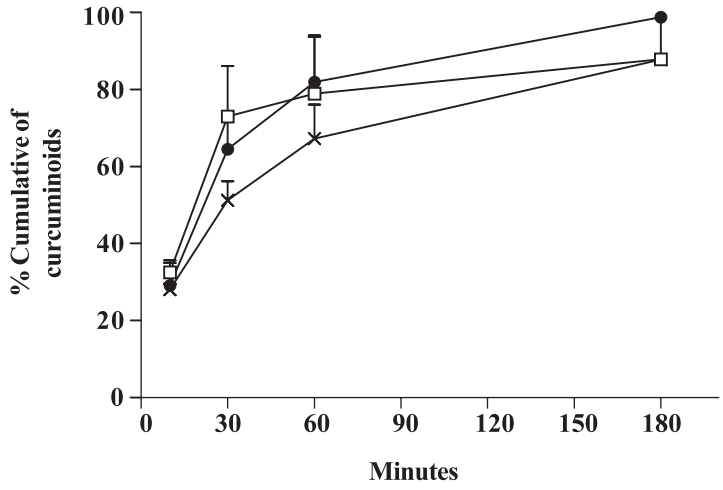

Figure 5. Release profiles of curcuminoids from turmeric loaded SLMs consisting of 6.67% (w/w) stearic acid, 13.33% (w/w) GMS and 4% (w/w) emulsifier: (□) Tween 80, (●) Poloxamer 188, and (x) Lipoid S100-3.

Stability studies

The physical and chemical stabilities of the final product during storage are crucial factors for the performance of a cosmetic product. Curcuminoids are also very light and oxygen sensitive substances. Thus the rheological properties and the amount of curcuminoids after 6-month storage at room temperature in the absence of light were investigated. The results revealed that the processing conditions had a critical effect on the physical and chemical stabilities of the tested products. However, the flow curves of all formulation tested after 6-month storage showed to have maintained their thixotropic characteristics similar to those of the freshly prepared formulations (data not shown). The yield stress value after 6-month storage was slightly lower than those of freshly prepared formulations (Table 4-5).

Table 4. Effect of the types of emulsifiers on the yield stress value of curcuminoids loaded microparticles after 1-and 6-month storage at room temperature

Types of emulsifiers	Yield value (dynes/cm^2)*	
	1 month	6 months
Tween 80	1631 ± 89	1573 ± 379
Poloxamer188	1182 ± 94	682 ± 200
Lipoid S100-3	1422 ± 317	1045 ± 250

*Data represent mean ± SD.

Table 5. Effect of the amount of lipids on the yield stress value of curcuminoids loaded microparticles after 1-and 6-month storage at room temperature

The amount of lipids (%w/w)	Yield value (dynes/cm^2)*	
	1 month	6 months
20	1631 ± 89	1573 ± 379
30	1334 ± 50	934 ± 163
40	1638 ± 19	1688 ± 243

*Data represent mean ± SD.

Among the different types of emulsifiers used in the formulations, those with Tween 80 showed the highest stability of the curcuminoids. After 6-month storage, the percentage of the remaining curcumin in formulations prepared with Tween 80,

Poloxamer and Lipoids were 90, 78 and 82, respectively (Figure 6). The percentage of the remaining bisdemethoxycurcumins and demethoxycurcumins showed the same trend of decomposition as curcumin. The physical appearance of the tested products was in agreement with their chemical degradation. The results showed that the appearance of the formulation with Tween 80 after 6-month storage was similar to the freshly prepared yellowish cream. In accordance with the remaining amount of intact curcuminoids, a color change from yellow to orange was evident in the formulation with Poloxamer 188 and Lipoid S100-3 after 6-month storage (data not shown).

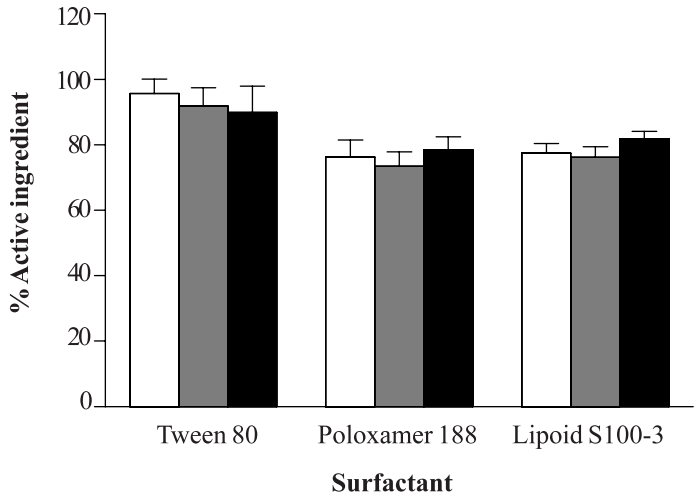

Figure 6. Percentage of (□) bisdemethoxycurcumin (▒) demethoxycurcumin and (■) curcumin remaining in curcuminoids loaded SLMs after six-month storage at room temperature in the absence of sunlight. The tested preparation consisted of 6.67% (w/w) stearic acid and 13.33% (w/w) GMS with different types of 4% (w/w) emulsifiers: Tween 80, Poloxamer 188 and Lipoid S100-3.

In addition, the stability of the curcuminoids incorporated into SLMs was further investigated after varying the amount of lipids. After 6-month storage, the percentage of the remaining curcumin in formulations prepared with a lipid content of 20, 30 and 40% (w/w) were 90, 79 and 74, respectively (Figure 7). The percentage of the remaining bisdemethoxycurcumin and demethoxycurcumin showed the same tendency as curcumin. The stability of curcuminoids decreased as the concentration of lipid increased. This may be a result from the layer of curcuminoids around the particles which is thinner at high lipid contents than those of systems with low lipid content and hence the curcuminoids may dissolve faster into the surrounding aqueous medium. Thus, the curcuminoids in the continuous medium tend to degrade faster than those incorporated into the SLMs.

The efficacy of the SLMs system to improve the curcuminoids stability is similar to a previous study which showed that more than 90% of curcuminoids could be detected intactly after the cream base was kept in the absence of sunlight for 6 months. On the other hand, after storage of the non-encapsulated curcuminoids in the cream base in the absence of sunlight for 3 months, a 50% degradation of curcuminoids was observed (Tiyaboonchai et al., 2007). Thus, these findings strongly confirm that SLMs significantly improve the curcuminoids stability against oxidation reaction during storage.

It is worth noting that most of the systems studied showed no phase separation. Nevertheless, almost all systems showed a separation of oleoresin after 6-month storage in various degrees. This may be a result of a high drug loading (5% (w/w)) with turmeric crude extract. The turmeric crude extract contained curcuminoids, volatile oil and oleoresin.

Thus, the concentration of the emulsifiers used in the cream system may not be sufficient, thus leading to the separation of oleoresin from the cream during the long term storage. This may be solved by decreasing the amount of turmeric crude extract loading.

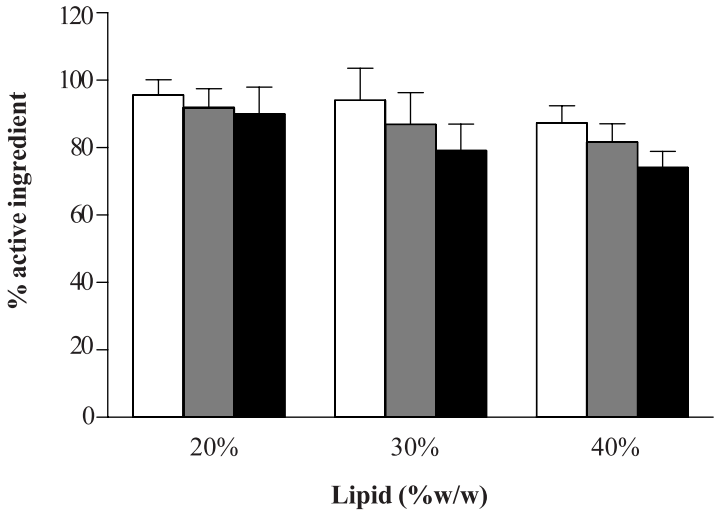

Figure 7. Percentage of (□) bisdemethoxycurcumin (▒) demethoxycurcumin and (■) curcumin remaining in curcuminoids loaded SLMs after six-month storage at room temperature in the absence of sunlight. The tested preparation consisted of 4% (w/w) Tween 80, stearic acid and GMS in the ratio of 1:2 and varying amount of lipids: 20, 30 and 40% (w/w).

Conclusions

SLMs loaded with curcuminoids isolated from the turmeric rhizome were successfully prepared in a one-step hot emulsion technique followed by high-speed homogenization. This SLMs preparation technique did not involve with filtration and freeze drying. Therefore, it showed to be a less time and energy consuming process compared to SLNs that previously reported using microemulsion technique. Moreover, the curcuminoids chemical stability could be maintained both in SLMs and SLNs delivery system. The process parameters, such as the ratio of stearic acid and GMS, type of emulsifiers and the amount of lipids, showed minor effect on the particle size and entrapment efficiency. All formulation possessed a mean particles size of 3 micrometer with narrow size distribution, ranging from 1-7 micrometer, which is suitable for a cosmetic cream formulation. A high percentage of entrapment efficacy up to 100 was observed. Curcuminoids loaded SLMs showed thixotropic flow characteristics which is a desirable feature for semisolid drug carriers for topical application. All formulation studied showed fast release characteristics suggesting that the curcuminoids were only adsorbed onto the particles' surface and not incorporated into the SLMs. The physical and chemical stabilities of curcuminoids loaded SLMs were affected by the types of emulsifiers and the content of lipids. The optimal formulation with good stability for 6-month storage was as follows: the ratio of stearic acid to GMS of 1:2, the lipid content 20% (w/w) and 4% (w/w) Tween 80. After 6-month storage at optimal conditions, 90% remaining curcumin was observed. No phase separation and color change were detected. Moreover, the flow curves and yield stress values were similar to those of the freshly prepared formulations. Thus, It can be concluded that, given their numerous advantages and their ability to maintain the physical and chemical stabilities of the incorporated active substances, SLMs can reasonably be considered as a promising drug carrier system for curcuminoids

isolated from the crude extract of turmeric rhizome.

Acknowledgements

The authors would like to thank Prof. Hans E. Junginger for his help in preparing the manuscript and for discussion of the results. This study was supported by a grant from Naresuan University, Thailand.

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