

Utilization Feasibility of Emulsifying Polymers in Cream Base

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ABSTRACT

Objective: Emulsifying polymer has been employed for low energy emulsification. This study investigated effect of some crucial factors on the physical properties of cream prepared from these polymers. **Method:** Systems containing various emulsifying polymers, distilled water and isopropyl isostearate were prepared. Formula and process variables including type and amount of emulsifying polymer, type and amount of solvents, and order of mixing on physical properties of cream base, were evaluated. **Results:** Viscosity of emulsions was increased as amount of emulsifying polymer was increased. Additionally, viscosity of systems depended on the type of emulsifying polymer and the type of solvent. Viscosity of formulation was different as order of mixing was changed. **Conclusion:** Type and amount of emulsifying polymers or solvent and order of mixing notably affected viscosity of cream base. However, these polymeric emulsifiers have potential use for emulsion both in pharmaceutical and cosmetic products.

Keywords: cream base, emulsifying polymers, utilization

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Introduction

Emulsion prepared using low energy concept has been presented for the great saving in time and energy since it was not necessary to heat the entire water phase to emulsification temperature and also permitted no use of the remaining water to cool the emulsion.^{1,2} Emulsifying polymer is a polymer generated by hydro-swelling droplets polymer technology. It is classified as a gelling and thickening agent. Its original polymer structure gives a set of specific properties such as light feeling, ready-to-use liquid form, and time saving at the industrial level by eliminating the dispersion, neutralization and maturing stages. Emulsifying polymer could be used to create gel-emulsions without heating and without a high energy supply by using principle of low energy emulsification. Emulsifying polymer composed of acrylate polymer (such as polyacrylamide copolymer), oil (such as isoparaffin, squalene, and isohexadecane) and

surfactant (such as laureth-7, polysorbate 20, polysorbate 60, and polysorbate 80). This polymer is a pre-neutralized polymer having the non-ionic surfactant catching around it and being dispersed in oil phase. After adding water, it is inverted and the polymer network expands instantly. Therefore it can be used in cold processing and ideal for use in the presence of heat-sensitive ingredients. Cold processing has been claimed as the method to achieve a great saving in time and energy (expenditure) and to obtain a better emulsion (smaller particle size and narrow distribution of particle size) than that produced from the conventional methods. Emulsifying polymer has been used in many cosmetic products. Polyacrylamide + C13-14 Isoparaffin + Laureth-7 (Sepigel 305[®]) has been reported to be used for creams containing various substances such as vegetable extracts from *Salvia officinalis*, *Centella asiatica* and *Calendula spp.*³ or vitamins E and A.⁴ Emulsifying polymer is designed for all skin and hair care preparations,

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formulated as gels⁵, cream gels³, shampoo and after-sun product.⁶ Therefore these emulsifying polymers have been used in pharmaceutical and cosmetic applications.

Isopropyl isostearate is a non-ionic liquid fatty acid ester, an ester of isopropyl alcohol and isostearic acid. It is used as a skin conditioning agent or emollient in cosmetic products. The synonyms of isopropyl isostearate include isooctadecanoic acid, 1-methylethyl ester, isopropyl 16-methylheptadecanoate and isopropyl isodecanoate.⁷ Advantages of isopropyl isostearate include non-greasy feeling and good spreadability. It is a good solvent for many hydrophobic compounds. It is classified as a slight ocular irritant. Repeated applications of a 10% aqueous suspension of isopropyl isostearate to the skin of albino rabbits is well-tolerated and therefore safe to use as cosmetic ingredient.⁸

Physical stability testing is the necessary and vital means to help assure that a formulation will maintain its integrity. Various physical parameters including phase separation, viscosity and pH are used to monitor the stability of emulsions during the stability test. Stability of the emulsion can be affected by various factors such as type and amount of emulsifier, amount of oil, solvents, agitation, temperature and order of mixing. However the investigation of the above factors of this emulsifying polymer has not yet been reported. Therefore, it is of great interest to study factors affecting physical properties of cream base prepared from emulsifying polymer. Isopropyl isostearate was used as oil phase for this research work.

This study was undertaken to investigate the effect of various factors on physical properties of cream prepared from emulsifying polymers. These factors included type and amount of emulsifying polymers, type and amount of solvent, and order of mixing.

Materials and Methods

Materials

The following chemicals were purchased from Seppic, Paris, France: Sepiplus 265[®] (Se 265) (ammonium acrylate/acrylamide copolymer & Polyisobutene & Polysorbate 20) (batch no. T44031), Sepigel 305[®] (Sg 305) (Polyacrylamide + C13-14 Isoparaffin + Laureth-7) (batch no.

T52135), Sepiplus 400[®] (Se 400) (Polyacrylate & Polyisobutene & Polysorbate 20) (batch no. T43131), Simulgel EG[®] (Si EG) (Sodium acrylate / Sodium acryloyldimethyl taurate + Isododecane + Polysorbate 80) (batch no. T51411), Simulgel NS[®] (Si NS) (Hydroxyethylacrylate / Sodium acryloyldimethyl taurate copolymer & squalane & Polysorbate 60) (batch no. 32631). Absolute alcohol (batch no. 0501252, VWR International, EC), glycerin (batch no. 20784G, Carlo Erba, Rodano, U.K) and isopropyl isostearate (Prisorine 2021[®]) (batch no. 1129023, Uniqema, U.K.) were used as received. Methyl hydroxyl benzoate (batch no. A16/18), propylhydroxyl benzoate (batch no. 000130), polyethylene glycol 400 (PEG 400) (batch no. P077241) and propylene glycol (batch no. 3164824094) were supplied by P.C. Drug Center Co., Ltd., Thailand.

Preparation of Cream Base

The oil phase or phase A (isopropyl isostearate, or Prisorine[®] 2021) and aqueous phase or phase B (water and emulsifying polymer) were weighed into separate container. Phase A was gradually added to phase B (A to B) at room temperature with appropriate manual agitation to form the emulsion. Finally, the remaining ingredient of phase C (paraben concentrate) was added to the bulk. The emulsion was mixed until it was homogenous.

Study of Physical Properties

The viscosity of prepared systems was measured using Brookfield helipath viscometer (Brookfield Engineering Laboratories Inc., Stoughton, USA). The sample of 200 g was prepared and filled into a glass bottle before test. The pH of formula was measured using a pH meter (Professional Meter PP-15 Sartorius, Goettingen, Germany). All measurements were performed at room temperature in triplicate for each sample. The physical stability of prepared creams was also tested after 6 cycles of temperature cycling. For any given cycle, all formulations were kept at 10 °C for 24 h in the refrigerator and then at 40 °C for 24 h in the hot-air oven (FED 720, Scientific Promotion, Bangkok, Thailand). Viscosity alteration and phase separation were used to indicate the physical stability. The stable formulation

should not have the phase separation and apparent viscosity change.

Study of Factor Effects on Physical Properties of Cream Base

Effect of Order of Mixing

To determine the effect of order of mixing, two methods of component mixing were employed for preparing the cream. The percent compositions of the formulations are shown in Table 1. Se 265 was employed as an emulsifying polymer. For the first method, oil phase (Prisorine[®] 2021) was slowly added to aqueous phase (water and emulsifying polymer) (A to B) and vice versa (B to A) for the second method. Phase C (paraben concentrate) was then added to the mixture in the final step. The methods to study physical properties of prepared cream were performed as mentioned previously.

Table 1 Composition of the cream base.

Compositions	Formulation (% w/w)
Emulsifying polymer (Se 265)	3
Prisorine [®] 2021	10
Paraben concentrate	1
Water	q.s.

Effect of Emulsifying Polymer Type

Five emulsifying polymers (Se 265, Se 400, Si NS, Si EG and Sg 305) were used in this study. The cream base was prepared by adding A to B. The method for studying the physical properties of the prepared cream was performed as mentioned previously. The percent compositions of the systems are shown in Table 1.

Effect of Amount of Emulsifying Polymer

The amount of emulsifying polymer (Se 265) in each formulation was 1, 3, 5 and 7% w/w. The methods for preparing the cream base and the methods for studying the physical properties were mentioned previously. The percent compositions of the systems are shown in Table 2.

Table 2 Composition of the cream base using different amount of emulsifying polymer (Se 265).

Compositions	Formulation (% w/w)
Se 265	1, 3, 5, 7
Prisorine [®] 2021	15
Paraben concentrate	1
Water	q.s.

Effect of Type and Amount of Solvent

Solvents used in this study were ethanol, PEG 400, propylene glycol and glycerin. The amount of each solvent in selected formulation was varied as 50% and 80% v/w. The selected cream base contained 15% Prisorine[®] 2021, 3% Se 265, 1% paraben concentrate and water. Solvent was added at the end of the preparation process. The methods for preparing the cream base and the study of the physical properties were performed as mentioned previously.

Statistical Analysis

The significance of the differences between mean values (where $P < 0.05$) was tested using ANOVA and paired *t*-test from SPSS for Windows version 11.0. Each data point represents the average of three determinations with SD.

Results and Discussion

Preparation of Cream Bases and Their Physical Properties

Emulsifying polymers are useful component for producing creamy emulsion products. In this study, viscosity of cream bases was evaluated under several factors such as mixing order, type and amount of emulsifying polymer or solvent.

Effect of Order of Mixing

The viscosity of the prepared cream bases was in the range of $187,111 \pm 16,883$ to $239,556 \pm 4,682$ cps as shown in Figure 1. The viscosity of cream base prepared by using different order of mixing could be ranked in the following descending order: oil phase to aqueous phase (A to B) > control (control comprising of 3 % emulsifying in water) > aqueous phase to oil phase (B to A). The pH values of the prepared cream bases were in the range of 7.39 ± 0.01 to

7.44 ± 0.04 (data not shown). The viscosity of all cream bases after 6 cycles of temperature cycling showed no significant difference from freshly prepared cream base. All cream bases before and after 6 temperature cycles offered good appearance with a homogeneous texture, smoothness and absence of phase separation and color change. It was noted that the control formula was more translucent than the others. The effect of order of mixing of A to B on cream viscosity was significantly different ($P < 0.05$) from control and the mixing of B to A.

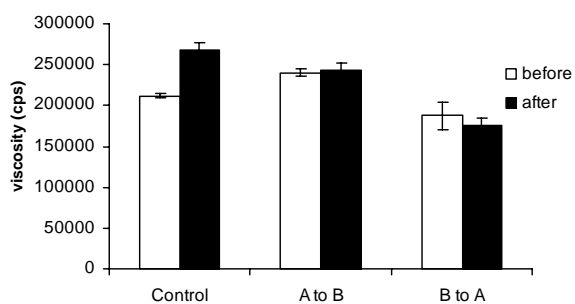


Figure 1 Viscosity of cream base prepared using different order of mixing, before and after 6 temperature cycles. Presented as mean ± SD.

Order of mixing apparently affected the viscosity of cream base using emulsifying polymer. Addition of the oil phase to the aqueous phase gave higher viscosity of the cream base than adding aqueous phase to oil phase. Water was one of the main factors influencing the gel-forming properties of emulsifying polymer. The absorption of water into the polymer resulted in the formation of the gel. The viscosity of the cream base prepared using emulsifying polymer by adding the oil phase to the aqueous phase was higher than the control comprising of emulsifying polymer mixed with water. This finding might be due to the presence of oil droplets in a system which led to an increase of viscosity. This result suggested that adding the oil phase to the aqueous phase was the best method because the cream base prepared from this emulsifying polymer exhibited good appearance with a homogeneous texture and smoothness, and viscosity higher than the others.

Effect of Emulsifying Polymer Type

The viscosity of the prepared cream bases was in the

range of 175,556 ± 6,012 to 268,000 ± 5,812 cps as shown in Figure 2. The viscosity of cream base prepared using different emulsifying polymers was ranked as followed: Se 265 > Se 400 > Si EG > Sg 305 > Si NS. The pH of cream bases prepared from different types of emulsifying polymer was in a range of 5.88 ± 0.07 to 7.49 ± 0.07 (data not shown). The viscosity of all cream bases after 6 cycles of temperature cycling showed no significant difference from freshly prepared cream base. All cream bases before and after 6 cycles of temperature cycling presented the good appearance with a homogeneous texture and smoothness. There was no phase separation or color change. The effect of emulsifying polymer type on cream viscosity was significantly different ($P < 0.05$) between 3 following pairs: 1) Si NS and Se 265, Si NS and Si EG, 2) Si NS and Se 400, and 3) Si NS and Sg 305.

Type of emulsifying polymers affected viscosity of cream base. Viscosity of cream base prepared by using Se 265 was significantly higher than that prepared by using the other emulsifying polymers. The viscosity of each formulation was different depending on types of emulsifying polymer. The variations in amount and type of acrylate polymer, oil, and surfactant in different emulsifying polymers could probably affect viscosity of the prepared dosage forms. This study selected Se 265 as an emulsifying polymer to prepare the cream base in the following step because a cream base prepared from this emulsifying polymer exhibited the physical appearance and viscosity more appropriate than the others.

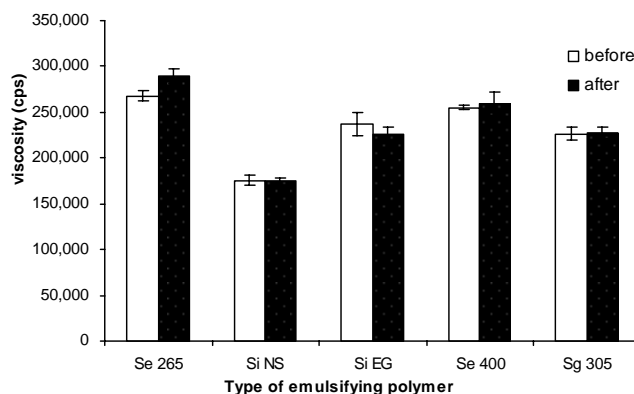


Figure 2 Viscosity of cream base prepared using different emulsifying polymers, before and after 6 temperature cycles. Presented as mean ± SD.

Effect of Emulsifying Polymer Amount

The viscosity of the prepared cream bases was in the range of $48,444 \pm 8,037$ to $579,111 \pm 42,002$ cps as shown in Figure 3. The viscosity of cream base comprising Se 265 increased with the increasing amount of this emulsifying polymer. The similar result was also reported for the direct correlation between the emulsion viscosity and the viscosity of the external phase induced by gelation of the continuous phase.⁹ Based on such correlation, a paste-like consistency developed from a liquid-like emulsion could be achieved. This process also provided a more stable emulsion by reducing the flocculation rate of the emulsion.¹⁰⁻¹² The phase volume ratio could also play a role in the variation of the apparent viscosity. The use of a thickener increased the viscosity of the continuous phase, reducing the frequency of collision and coalescence of drops, thereby increasing the stability of the preparation. Thus, the thickening agent with suitable concentrations should incorporate into the external phase of the emulsion to improve its viscosity. The pH values of the prepared cream bases were in a range of 7.19 ± 0.01 to 7.32 ± 0.01 (data not shown). The viscosity of all cream bases after 6 temperature cycling showed no significant difference from freshly prepared cream base. All cream bases before and after 6 cycles of temperature cycling were found to have homogeneous texture and smoothness, and no separation or color change. There was no effect of the amount of emulsifying polymer on pH of the cream. The nonionic emulsifiers in the emulsifying polymer minimized the incompatibility phenomenon and thus resulting in a greater degree of compatibility with other ingredients than anionic or cationic surfactants.¹³ 3% w/w Se 265 was selected to incorporate in the cream base in the following step because a cream base prepared from this emulsifying polymer exhibited the physical appearance and viscosity better than the others.

Effect of Type and Amount of Solvent

Viscosity of the prepared cream bases containing solvent at amount of 50% and 80% was in ranges of $119,556 \pm 6,577$ to $334,667 \pm 8,000$ cps and $177,333 \pm 5,333$ to $399,556 \pm 16,074$ cps respectively, as shown in Figures 4A and 4B. It was found that viscosity of cream base prepared

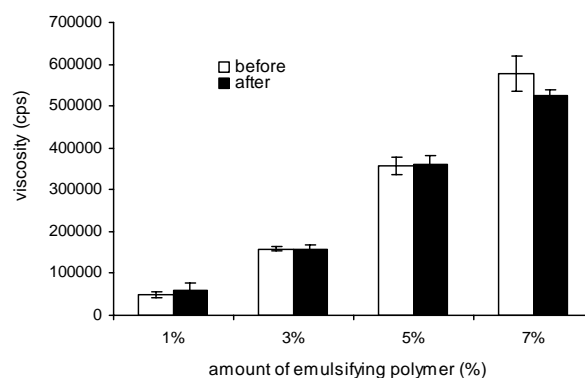


Figure 3 Viscosity of cream base containing different amount of emulsifying polymer, before and after 6 temperature cycles. Presented as mean \pm SD.

by using different types of solvent at amount of 50% and 80% could be ranked in the following descending order: glycerin > water > PEG 400 > propylene glycol > EtOH and glycerin > water > propylene glycol, respectively. There was a precipitation of formulation containing solvent at 80% of PEG 400 and EtOH. The pH of the prepared cream base containing solvent at amount of 50% and 80% was in ranges of 7.43 ± 0.04 to 7.66 ± 0.03 and 7.57 ± 0.02 to 7.66 ± 0.02 , respectively (data not shown). Cream bases before and after 6 cycles of temperature cycling presented the good appearance with a homogeneous texture and smoothness. The translucence of cream base using different amount of solvent at 50% and 80% could be ranked as the following: glycerin > PEG 400 > propylene glycol > EtOH 95% > water and glycerin > propylene glycol > water, respectively. The viscosity of all cream bases after 6 temperature cycles was not significantly different from the one of freshly prepared cream base. Cream bases containing glycerin after passing temperature cycling showed a rather yellow color and phase separation. The effect of solvent type on emulsion viscosity was considered to be significantly different ($P < 0.05$ for either at 50% or 80% of solvent used).

Practically, solvent optimization was a very important step applicable to emulsion preparation by spontaneous emulsification in field of pharmaceuticals and cosmetics uses. This study selected solvent at rather high concentration such as 50% and 80% v/w because it was claimed that emulsifying polymers could tolerate solvent at such high concentration. The viscosity of cream base was stable after

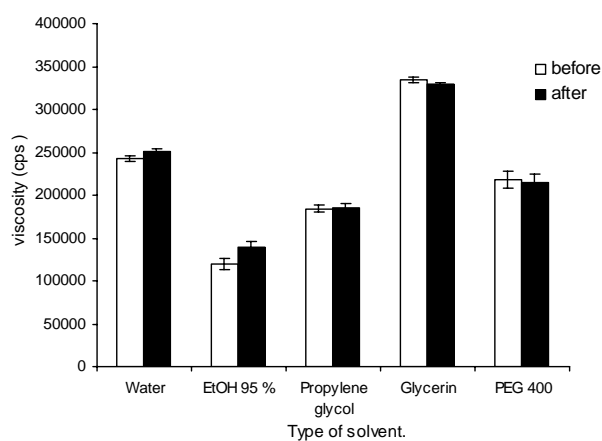
addition of solvents up to 50% v/w. However an increased amount of absolute ethanol and PEG 400 content decreased the stability of the cream. The 3% w/w emulsifying polymer could not accommodate 80% v/w PEG 400 and EtOH because the emulsion crack was evident. Poptoshev et al. (2004)¹⁴ mentioned that increase of the ethanol amount increased the interfacial layer thickness which was attributed to a reduction in the interchain electrostatic repulsion. Thus, increasing concentration of the organic solvent diminished the viscosity of systems as observed in this study. Polyethylene glycol is a hydrophilic nonionic polymer which could form directional bonds with water and exhibits complex phase behavior.¹⁵ Therefore the emulsion was cracked after addition the high amount of this solvent. In the similar study, Hua and Liu (2007)¹⁶ mentioned that higher amount of PEG 400 led to the decrease in the rigidity and stability of the noisome membrane until the structure with organized assemble was disrupted. Our study signified that type and amount of solvent was also an important parameter in stability of cream prepared from emulsifying polymer. By comparison with the solvent used in this study, EtOH had a greater effect on stability of cream base than did PEG 400.

Conclusion

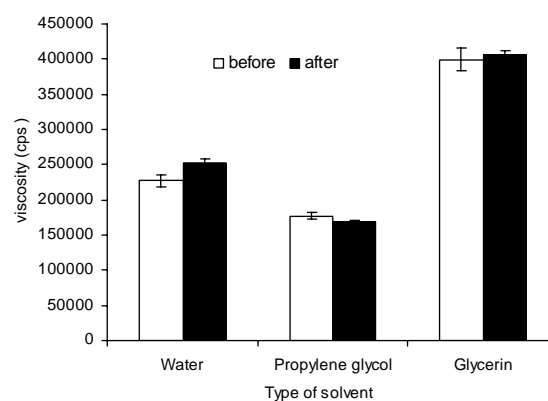
The type and amount of emulsifying polymers, type of solvent and order of mixing affected viscosity of cream base. The utilization of these polymeric emulsifiers in cream preparations should be considered for the type and amount of them. The order of mixing, type and amount of oil used in emulsion preparations using these emulsifiers should be also considered. However, these polymeric emulsifiers have potential use as emulsifier for emulsion both in pharmaceutical and cosmetic products. Our further study will apply the emulsifying polymers for preparation of clotrimazole cream with low energy emulsification.

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(A)



(B)

Figure 4 Viscosity of cream bases containing 50% w/w (A) and 80 % w/w (B) of different solvents, before and after 6 temperature cycles. Presented as mean \pm SD.

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