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Original Article

FORMULATION AND STABILITY EVALUATION OF KETOPROFEN LOADED VIRGIN COCONUT OIL BASED CREAMY EMULSION

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ABSTRACT

Objective: To formulate and optimize a topical formulation; a virgin coconut oil (VCO) based Ketoprofen loaded creamy emulsion containing Tween 80® as the surfactant and to evaluate the stability of samples.

Methods: In preformulatory studies optimization of the formulae was done using ternary phase diagrams with water titration method and emulsions were formulated using two methods; spontaneous emulsification and homogenization. Their stability was analyzed under visual observation to optimize the best formulae for Ketoprofen incorporated creamy emulsion. 2.5% w/w Ketoprofen topical formulations are available in the market.

Results: Centrifugation provided more comparable data than visual observation. Phase separation was the main instability condition observed in unstable emulsions. Composition 23.60% VCO: 29.53% Tween 80®: 45.87% water was identified as the best optimized formulae in both with and without Ketoprofen formulations and all the samples with different Ketoprofen concentrations were stable for 14 days under centrifugation and visual observation stability studies.

Conclusion: Homogenization was more effective in stable emulsion formation than spontaneous emulsification in VCO, Tween 80®, water emulsion. The best optimized formula was 23.60% VCO: 29.53% Tween 80®: 45.87% water.

Keywords: Ketoprofen, Cream, Virgin coconut oil, Analgesic.

INTRODUCTION

Emulsions are widely used in many industries such as food, agrochemical, paint and oil [1] and preferably in medicinal, pharmaceutical industry due to their advantages over other dosage forms and can be used either as end products or in-progress products. Emulsions can be used as natural or synthetic materials or fluids in industries [2]. An emulsion is essentially a liquid/ semisolid preparation containing a mixture of oil and water that is rendered homogeneity by the addition of an emulsifying agent [3] and is also thermodynamically unstable.

Emulsion with nano-size droplets, which is exploded recently as a promising drug delivery system [4], is widely applied in cosmetic and pharmaceutical applications as novel systems generating nanoparticles [5]. It is a transparent or translucent heterogeneous system with the droplets size between 20 to 500 nm [4, 6]. Emulsions with small droplets size compromise many favorable characteristics over other dosage forms. Creaming or sedimentation occurs on storage is prevented via controlled small droplet size [5], coalescence is prevented by non-deformable small droplets which prevent surface fluctuations allowing uniform deposition on substrates [4] and flocculation of the droplets is minimized resulting relatively long-term stability [6]. It is a powerful solubilizer [6] and the large surface area allows rapid penetration of drug efficiently even through rough skin minimizing the need of extra penetration enhancers [4]. Uniform spreading may be achieved via small droplet size [7]. Due to its long term kinetic stability; shelf life of product particle size can be enhanced [5].

Ketoprofen or 2-(3-benzoylphenyl)-propionic acid, an anionic, potent non-steroidal anti-inflammatory agent (NSAID); is an aryl propionic acid derivative which is widely engaged in the treatment of rheumatoid arthritis, osteoarthritis and mild to moderate pain [6,8,9] due to its analgesic and antipyretic activities [6]. It has lipophilic properties [10] and consists of appropriate partition coefficient [9]. Ketoprofen topical delivery systems as gels, creams, ointments, patches, gelled self emulsifying delivery system and microemulsions [5, 8, 11] are studied in past years.

VCO is defined as a vegetable oil that is obtained from fresh, mature kernel of the coconut (*Cocosnucifera L.*) by mechanical or natural means, with or without the use of heat and without undergoing chemical refining, bleaching or deodorizing and therefore does not lead to the alteration of the nature of the oil [12]. As it comprises of various health and nutraceutical benefits and acts as a high-value functional food [13]; it has become popular in the scientific field. Asian Pacific Coconut Community (APCC) and member countries are strongly promoting VCO for health concerns [13]. VCO is non-skin irritating and widely available in Sri Lanka. It is available in the market as functional oil [14] in two different forms specifically for food products and cosmetic/ pharmaceutical/ medicinal products. The main fatty acid in VCO is lauric acid (~45.1% [13]), which has been reported to have antiviral, antibacterial, antiscaries, antiplaque and antiprotozoal activities [12]. VCO is documented to have more beneficial effects in clinical trials such as having more antioxidant potential compared to refined coconut oil [14].

Emulsions separate into two separate phases and become unstable on standing although they are thoroughly mixed because the phases are not miscible in one another. Surfactants are emulsifying agents, which lower the interfacial tension and decline the destabilizing effects of emulsion by reducing the increase in surface area of the dispersed phase [15]. The study was aim to formulate, and optimize a VCO based Ketoprofen loaded creamy emulsion containing Tween 80® as the surfactant and to analyze the stability of optimized formulae with and without incorporation of Ketoprofen (with and without high sheer homogenization).

MATERIALS AND METHODS

Chemicals and reagents

Tween 80® (HiMedia, India) was obtained from Analytical Instruments (Pvt) Ltd. and Virgin Coconut Oil (VCO) (Sri Lanka) was

obtained from Serendipol (Pvt) Ltd. Ketoprofen (Sigma-Aldrich, USA) was purchased from Astron Pharmaceutical Pvt. Ltd. Distilled water was used as the external phase.

Preformulatory studies

In preformulatory studies optimization of the emulsion was done with appropriate ratio of oil: water: surfactant via pre-formulation studies by developing ternary phase diagrams. Water titration method was used for the optimization. First, a mixture of VCO and Tween 80® was prepared with the total mass of 9g depending on the series in *table 1* (ex: VCO: Tween 80® 8:1 in series 1)**.** Then mixture was diluted by adding water with magnetic stirring at 600rpm for 20 minutes at 25^{0}c to make the total volume of emulsion to be 10g. 1g of prepared emulsion was removed and checked for the texture and type. To the remaining 9g of emulsion 1g of water was added with stirring. Procedure was repeated until the emulsion diluted up to 90% of water. Texture of emulsion as gel/ cream/ ointment/ liquid was analyzed organoleptically and the emulsion type whether water-in-oil or oil-in-water, of each sample was determined by diluting the emulsion with water and recorded. Two separate ternary phase diagrams resembling emulsion texture and type were developed using Chemix analytical software. The five ratios which represent oil-in-water creamy emulsions were selected via ternary phase diagrams.

Table 1: Composition of initial components of series for water titration method to develop required ternary phase diagrams

Series	Initial amounts of components (g)		
	VCO	Tween 80®	Distilled water
1	8	1	1
2	7	2	1
3	6	3	1
4	5	4	1
5	4	5	1
6	3	6	1
7	2	7	1
8	1	8	1

Preparation of emulsion

Method for preparing emulsions was adopted from a published report of Sakeena *et al*., 2010. 10g of emulsions were formulated by 2 methods using selected ratios of VCO: water: Tween 80® which resembles O/W creamy emulsion.

Method 1- Magnetic stirrer (Spontaneous emulsification)

VCO and Tween 80® were mixed thoroughly under a magnetic stirrer (1 "MLH" magnetic

stirrer, Rajendra Electrical Industries Limited, Mumbai, India) at 600 rpm and 25 ^{0}C for 15 minutes until a clear mixture was formed and to the resulting mixture, distilled water was added drop by drop with the constant stirring at 600 rpm at 25 ^{0}C. The theory behind magnetic stirrer is stirring of the sample due to rotating magnetic field causing a stir bar immersed in a liquid to spin in a predefined speed.

Method 2- High shear homogenization

Another set of samples were prepared for each ratio first performing magnetic stirring of VCO and Tween 80® at 600 rpm and 25 ^{0} C for 15 minutes and distilled water was added drop by drop with the constant stirring at 600 rpm and 25 ^{0}C. The resulting mixture was mixed further under high shear homogenizer (homogenizer OV5, VELP scientifica, Italy) at 1200 rpm and 25 ^{0}C for 5 minutes. Mixing by homogenizer is obtained through axial automatically sucking of components into dispersing head due to high rotor speed and then expelling radially through slots. Speed of the homogenizer can be adjusted from 10,000 to 29,000 rpm due to built-in electronic motor and top speed of high 29,000 rpm rate, reduces processing time significantly.

Stability Evaluation

After the optimization of appropriate formulae based on proper oil, water and surfactant ratio, their stabilities were checked for centrifugation and visual observation.

Visual Observation

The texture and appearance of each formulation of Method 1 and Method 2 were evaluated through naked eye for phase separation, sedimentation, coalescence, creaming and flocculation for the period of 2 months on 1st, 3rd, 5th, 10th, 15th, 29th, 45th and 60th days.

Centrifugation

Centrifugation tests were performed for each sample immediately after the preparation of emulsions tests were repeated for 15 days on 1st, 3rd, 5th, 10th and 15th days. 5 g of each formulation of Method 1 and Method 2 were placed in a centrifugal tube and centrifuged in a centrifuge (C-854/6, Medico / Doctor Centrifuge /Mini Centrifuge, Rajendra Electrical Industries Limited, Mumbai, India) for 3 minutes at a "g" centrifugal force of 1200 and 25 ^{0}C and appearance was observed under naked eye. C-854/6 is a powerful clinical centrifuge machine which provides precise and controlled way of centrifuge testing and its speed can be maintained up to 1600 'g" of acceleration or 3500 rpm of angular velocity.

Drug Incorporation and Stability Evaluation

Ketoprofen was incorporated into stable samples obtained via Method 1 and Method 2.

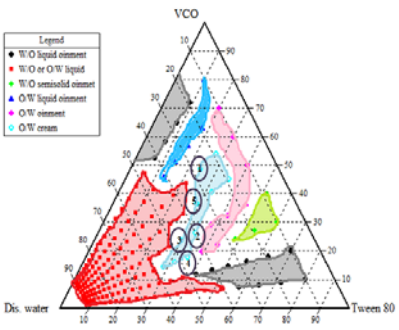
Method 1- Magnetic stirrer (Spontaneous emulsification)

VCO and Tween 80® were mixed thoroughly under magnetic stirrer at 600 rpm and 25 ^{0}C for 15 minutes until a clear mixture was formed and to the resulting mixture Ketoprofen was added and mixed well for 5 minutes. Then, distilled water was added drop by drop with the constant stirring at 600 rpm and 25 ^{0}C to formulate 2.5 g of 2.5 (w/w)% Ketoprofen emulsion.

Method 2- High shear homogenizer

Another set of emulsion samples were prepared for each ratio. First, magnetic stirring of VCO and Tween 80® at 600 rpm and 25 ^{0}C was performed for 15 minutes. Then, while performing constant stirring at 600 rpm and 25 ^{o}C, Ketoprofen and distilled water were added drop by drop. The resulting mixture was mixed further under high shear homogenizer at 1200 rpm and 25 ^{0}C for 5 minutes to formulate 5 g of 2.5 (w/w) % Ketoprofen emulsion. Stability of drug loaded formulations were checked for 2 weeks on 1st, 2nd, 3rd, 5th, 8th, 11th, 14th days through visual observation and centrifugation as given in 2.3.1 and 2.3.2. Then the most stable drug loaded emulsion was selected and re-formulated via Method 2 (high shear homogenization) with changing drug concentrations as 0.625%, 1.25% and 2.5%. Finally, their stabilities were evaluated for 2 weeks on 1st, 2nd, 3rd, 5th, 8th, 11th, 14th days through visual observation and centrifugation as given in 2.4.1 and 2.4.2.

RESULTS



Preformulatory studies

Fig. 1: Ternary phase diagram of VCO, water and Tween 80® representing type and texture of emulsion

The ternary phase diagram given above (*figure 1*) gives an idea that high number of different compositions of VCO, water, Tween 80® emulsions is available as oil-in-water emulsions. They represent 4 different textures as semisolid ointments, liquid ointments, liquids and creams at different compositions. Emulsions which represented creamy texture had average composition of two components as ~25%-40% of water, ~15%-52% of Tween 80® and higher percentage of VCO as ~45%- 85%. At these compositions VCO and Tween 80® mixture was less thick and transparent but became whitish and creamy when adding water.

Stability evaluation of emulsions without Ketoprofen

Optimized compositions of the different samples of emulsions tested are given in table 2.

Table 2: Emulsions of different compositions after optimization (samples of 10 g)

Sample	VCO	Tween 80®	Water
1	4.860	2.429	2.710
2	2.620	3.392	4.095
3	2.360	3.053	4.587
4	1.772	3.543	4.686
5	4.116	2.232	3.652

Stability data of visual observation of emulsions formulated via Method 1 and Method 2 are given in table 3.

Table 3: Stability data of visual observation of emulsions formulated via Method 1 and Method 2

Sample	Day 1(fresh)	Day 3	Day 5	Day 10	Day 15	Day 29	Day 45	Day 60
Method 1								
1.1	P	P	P	P	P,F	P,F	P,F	P, F
1.2	S	S	S	S	S	S	S	S
1.3	S	S	S	S	S	S	S	S
1.4	S	S	S	S	S	S	S	S
1.5	S	S	P	P	P	P	P	P
Method 2								
2.1	S	S	S	P	P	P,F	P,F	P,F
2.2	S	S	S	S	S	S	S	S
2.3	S	S	S	S	S	S	S	S
2.4	S	S	S	S	S	S	S	S
2.5	S	S	S	S	P	P	P	P

S - stable**F** - flocculation**C** -coalescence**X** - creaming**E** –sedimentation**P** -phase separation

According to the results given in table 3, Method 1 samples 1.1 and 1.5 were unstable at room temperature but, sample 1.5 was more stable than 1.1. Phase separation was the instability occurred in samples 1.5 and in 1.1 both phase separation and flocculation occurs but instabilities were absent or insignificant. Samples 1.2, 1.3 and 1.4 were stable for even 60 days after preparation. In Method 2, samples 2.1 and 2.5 were unstable at room temperature but, sample 2.5 was more stable than 2.1. Phase separation was the instability occurred in samples 2.5. In sample 2.1 both phase separation and flocculation were observed but, instabilities were absent or insignificant. Samples 2.2, 2.3 and 2.4 were stable for even 60 days after preparation. And it was revealed that both unstable samples 1 obtained from Method 2 (2.1 and 2.5) were stable for longer time than unstable samples obtained in Method 1 (1.1 and 1.5). Stability data of centrifugation of emulsions formulated via Method 1 and Method 2 is given in table 4.

Table 4: Stability data of centrifugation of emulsions formulated via Method 1 and Method 2

Sample	Day 1	Day 3	Day 5	Day 10	Day 15
Method 1					
1.1	U	U	U	U	U
1.2	S	S	S	S	S
1.3	S	S	S	S	S
1.4	S	S	S	S	S
1.5	S	U	U	U	U
Method 2					
2.1	U	U	U	U	U
2.2	S	S	S	S	S
2.3	S	S	S	S	S
2.4	S	S	S	S	S
2.5	S	S	U	U	U

S- Stable**U**- Unstable

Upon centrifugation, samples 1.1 and 2.1 was unstable even on the formulation day and 1.5 on the 3rd day whereas 2.5 on 5th day. It was an acceleration stability study. Other six samples remained stable for even 15 days. With centrifugation results also it is proved that both unstable samples obtained from Method 2 (2.1 and 2.5) were stable for longer time than unstable samples obtained in Method 1 (1.1 and 1.5).

Stability Evaluation of 2.5% Ketoprofen loaded Emulsions

Visual Observation

Visual observation stability data of Ketoprofen loaded emulsions formulated via Method 1 and Method 2 is given in table.

Centrifugation

Centrifugation stability data of 2.5% Ketoprofen emulsions formulated via Method 1 and Method 2 is given in table 6. Although all the samples were stable under visual observation, sample number 2 (1.2' and 2.2') and 4 (1.4' and 2.4') obtained from both methods became unstable in the latter stages of centrifugation studies. But 1.4' was longer stable than 1.2'. When compare sample 2 obtained from both methods (1.2' and 2.2'), sample was longer time stable in Method 2 than in Method 1 whereas sample 4 (1.4' and 2.4') was equally stable in both methods. Sample 3 was stable in both methods.

Table 5: Visual observation stability data of Ketoprofen loaded emulsions formulated via Method 1 and Method 2

Sample	Day 1(fresh)	Day 2	Day 3	Day 5	Day 8	Day 11	Day 14
Method 1							
1.2’	S	S	S	S	S	S	S
1.3’	S	S	S	S	S	S	S
1.4’	S	S	S	S	S	S	S
Method 2							
2.2’	S	S	S	S	S	S	S
2.3’	S	S	S	S	S	S	S
2.4’	S	S	S	S	S	S	S

S - stable**F** - flocculation**C** -coalescence**X** - creaming**S** -sedimentation**P** -phase separation

All the Ketoprofen loaded emulsion samples prepared via Method 1 and Method 2 were stable for 14 days upon visual observation.

Table 6: Centrifugation stability data of 2.5% Ketoprofen emulsions formulated via Method 1 and Method 2

Sample	Day 1	Day 2	Day 3	Day 5	Day 8	Day 11	Day 14
Method 1							
1.2’	S	S	S	S	S	U	U
1.3’	S	S	S	S	S	S	S
1.4’	S	S	S	S	S	S	U
Method 2							
2.2’	S	S	S	S	S	S	U
2.3’	S	S	S	S	S	S	S
2.4’	S	S	S	S	S	S	U

S- Stable**U**- Unstable

In this study, centrifugation studies are conducted as accelerated stability studies. Results revealed that Ketoprofen loaded samples are more stable in Method 2 than in Method 1. Therefore, to compare stability of with and without Ketoprofen emulsion samples (2 and 4), centrifuged stability data of samples prepared via Method 2 were compared and given in graph 1 and 2.

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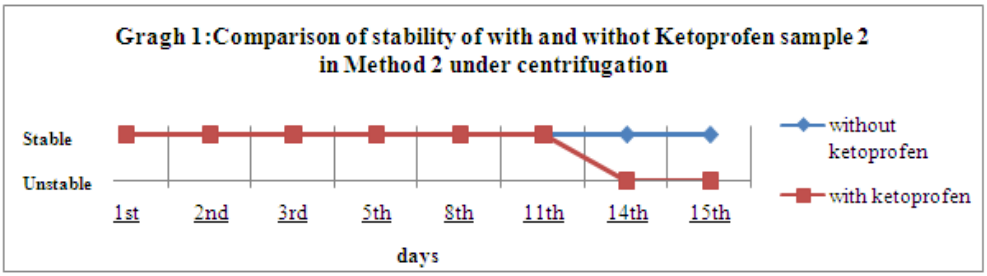

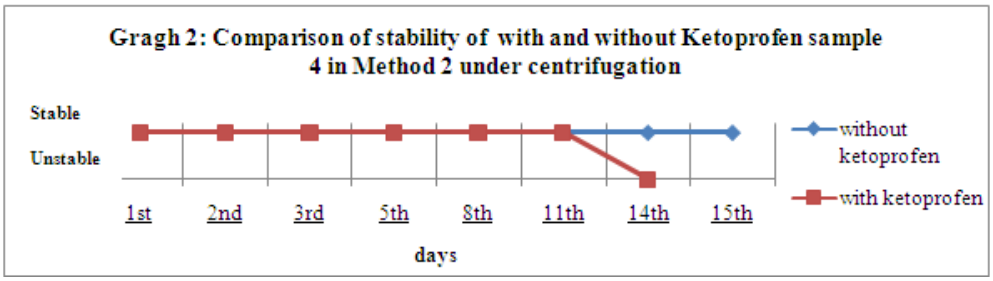

In both samples 2.2 and 2.4 Ketoprofen incorporated samples were less stable than without Ketoprofen emulsion samples.

Table 7: Stability data of visual observation (V) and centrifugation (C) of Ketoprofen emulsions with different concentrations formulated via Method 2

Ketoprofen Concentration	Day 1		Day 2		Day 3		Day 5		Day 8		Day 11		Day 14	
	V	C	V	C	V	C	V	C	V	C	V	C	V	C
0.625%	S	S	S	S	S	S	S	S	S	S	S	S	S	S
1.25%	S	S	S	S	S	S	S	S	S	S	S	S	S	S
2.5%	S	S	S	S	S	S	S	S	S	S	S	S	S	S

S – stable, **F** – flocculation, **C** –coalescence, **X** – creaming, **E** –sedimentation, **P** -phase separation

Study on the effect of drug concentration

Stability data of visual observation and centrifugation of Ketoprofen emulsions with different concentrations formulated via Method 2 is given in table 7.

In both visual observation studies and centrifugation stability studies; comparative stability data on samples with 0.625%, 1.25% and 2.5% Ketoprofen were unable to obtain, as all the three samples were stable for 14 days

DISCUSSION

Emulsions with nano-size droplets are advantageous over other formulations because of relatively high kinetic stability, minimizing of creaming, sedimentation and flocculation, and high solubility due to small droplet size. Due to its large surface area, it allows rapid penetration of active ingredients. These properties facilitate efficient transdermal delivery systems for active ingredients incorporated in many personal care and health products [5]; especially previous research has shown that emulsions with small droplet size improve the bioavailability of lipophilic drugs [4]. So that it was chosen as the dosage form for Ketoprofen (lipophilic drug) transdermal formulation in this study.

Selection of emulsion components was the most crucial step in the emulsion preparation as emulsion stability and formulation's effectiveness mainly depend on its components. Considering following factors VCO, Tween 80®, distilled water and Ketoprofen were chosen as emulsion components. VCO is widely available in Sri Lanka and had gained a great attention all over the world due its high availability, cost effectiveness and numerous health benefits. As it is natural pure oil, the health benefits preserve than in refined coconut oil. VCO shows anti-inflammatory, analgesic, and antipyretic properties [16], fastening of wound healing, collagen cross-linking, increase in fibroblast proliferation, neovascularization [17], strengthen skin tissues and repair skin damages [18], moisturizing properties [19], antiwrinkle and antisagging properties [20]. Saturated and unsaturated fatty acids act as effective penetration enhancers for a variety of drugs [11] and VCO is rich in medium chain saturated fatty acids [14] and consists of considerable amount of unsaturated fatty acids [20]. Compared to other NSAIDs; Ketoprofen is considered to be an effective drug in transdermal drug delivery due to its appropriate partition coefficient [9]. Poorly water soluble compounds as Ketoprofen can be effectively incorporated in O/W emulsion to obtain high bioavailability via increased transdermal absorption [8] and usually surfactants exhibiting an HLB (Hydrophile-Lypophile Balance) between 9 and 16 are most preferable to produce O/W emulsions (termed O/W emulsifying agents) and Tween 80® has a HLB value of 15.0 [15].

In preformulatory studies, standards and procedure of "water titration method" was adopted from a previous research [21]. Phase separation boundaries were not completed as delineating phase boundaries is difficult and time consuming. Also, for this study as only 5 creamy emulsion ratios were needed, delineating was not essential. In this study initially five appropriate formulas which resemble O/W creamy emulsion (*table 2*) were selected from the pre-formulation studies by overlapping constructed ternary phase diagrams.

According to *figure 1* creamy texture of the emulsions occurred with the higher percentages of VCO as ~45%- 85% and average compositions of water as ~25%-40% and Tween 80® as ~15%-52%. Similar results had been achieved in literature where viscous creamy emulsions were obtained at average percentages of aqueous phase and surfactant having HLB value of 15 (Tween 80®); and higher percentages of oil phase [22]. It was proved that these creaminess results of emulsions were due to high viscosity and higher oil volume fraction of the formulation [23].

Figure 1 shows that all the samples which contain lower than about 45% of Tween 80® and higher than about 55% of water composition; represent water-in-oil emulsions. Emulsion type depends on the type and amount of emulsifier [1] which was also similarly studied and obtained in literature [22]. The reason was clarified in literature as; because Tween 80® is a hydrophilic emulsifier (HLB value of 15) which is strongly dissolved in aqueous phase rather than oily phase and form O/W emulsions [24]. When the amount of hydrophilic emulsifier is reduced weakening of O/W interfacial film will occurred and in most cases W/O emulsions will be formed as hydrophilic effect of emulsifier towards final emulsion is reduced [1, 24]. And *figure 1* also shows that high number of different compositions of VCO, water, Tween 80® emulsions is available as oil-in-water emulsions. Similar results were obtained in literature [22] and it is due to the fact that there is a more tendency for the surfactant to produce the type of emulsion in which the surfactant can readily dissolved in the external phase of the emulsion [22]. Therefore, it is justified that Tween 80® will mostly produce O/W emulsions as it is hydrophilic.

Emulsion formulation methods were adopted by studying previously performed researches; study on the "Influence of an optimized non-ionic emulsifier blend on properties of oil-in-water emulsion" [24] and study of "Formulation and in vitro Evaluation of Ketoprofen in Palm Oil Esters Nano-emulsion for Topical Delivery" [6] and emulsion stability evaluation and characterization methods were adopted from a research study performed on cosmetic multiple emulsion system with macadamia nut oil [25].

Although spontaneous emulsification (Method 1) is preferred over high shear homogenization (Method 2), gentle mixing may be sufficient to form small droplets [26] due to low interfacial tension of O/W emulsions [7]. In this study, Method 2 was mostly preferable. It is because creamy emulsion was the interested formulation in the study and they have somewhat high viscosity. So that magnetic stirring was not sufficient to mix the emulsion components well depending on the oil: water: surfactant ratios. VCO and Tween 80 ® were completely mixed via Method 1 and Ketoprofen also could completely dissolve via that. However, when water was added to the mixture, it got thicker and was hard to mix via Method 1. To study the effect of Ketoprofen concentration on the stability of the emulsion, Method 2 was used as all the samples were longer stable under Method 2 than Method 1 despite whether without Ketoprofen (*table 3 and table 4*) or with Ketoprofen (*table 6*). As well-mixed fine emulsions were more stable than coarse emulsions, utilization of high stirring intensity could stabilize the emulsion system. According to stability data in *table 3* and *table 4,* sample 5 was more stable than sample 1. And *table 6* shows that sample 4 was stable than sample 2. Both results were obtained because, the more stable sample had higher Tween 80® amount than the less stable sample. As a surfactant Tween 80® reduces the interfacial tension and declines destabilizing effects of emulsions [15] therefore, emulsion stability depends on the surfactant concentration.

Table 3, table 4, table 5 and *table 6* shows that in both Method 1 and Method 2, centrifugation studies provided more comparable data in shorter time than visual observation data. Although visual observation is the easiest "real-time" normal storage condition stability test [27], due to time limit in this study centrifugation studies proved to be effective. Other than normal storage conditions stability testing, accelerated stability testing has been used in similar studies as temperature cycle and multisample analytical centrifugation [27].

In this study, high shear centrifugation studies were performed as acceleration stability test to predict the long term kinetic stability of emulsions. Under the external centrifugal force, emulsions tend to breakdown faster than in normal conditions [27]. And as the final formulation is an O/W emulsion, creaming/ flocculation can occur by moving low density VCO dispersed droplets upward the emulsion because water has higher density than VCO as mentioned above [28]. Sample 2.1 was stable for 5 days in visual observation studies and it was unstable even in the 1st day of centrifugation studies (*table 3* and *table 4*). Other samples also showed similar results.

In literature it was proved that rather than normal visual observation stability tests, creaming/sedimentation (phase separation) can be accelerated directly by using a centrifugal field [27, 29]. All the stability evaluation tests were performed in similar conditions for all the samples to minimize the temperature effect as solubility of the surfactant normally changes when temperature changes, resulting the change in stability of emulsion [30].

CONCLUSION

It can be concluded that the best optimized formulae for 2.5% Ketoprofen loaded creamy emulsion is 23.60% VCO: 29.53% Tween 80®: 45.87% water and homogenization is more effective in stable emulsion formation than spontaneous emulsification in VCO, Tween 80®, water emulsion.

AKNOWLEDGEMENT

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CONFLICT OF INTEREST

This research has no conflict of interest.

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