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RESEARCH ARTICLE

The influence of glicerides oil phase on O/W nanoemulsion formation by pic method

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Abstract

The aim of this work was preparation and characterization of nanoemulsions containing Caprylic/Capric Triglyceride, Caprylic/Capric/Linoleic Triglyceride and Caprylic/Capric/Succinic Triglyceride as the oil phase. Stable emulsion system was obtained by using Polisorbate 40 as emulsifier and n-buthanol as cosurfactant.

The formulations were prepared by phase inversion composition method (PIC), one of the low energy emulsification method, by stepwise water addition to the mixture of oil and surfactant, at room temperature(25°C).The mixture was stirred by using a magnetic stirrer. The type of the emulsions was confirmed by conductivity measurement. The particles size distribution was analyzed by Dynamic Light Scattering measurement technique using Zetasizer Nano ZS (Malvern Instruments, UK). Rheological studies of the systems were carried out using Brookfield Rheometer Model -R/SPlus.

The obtained results showed that properties of the emulsions depend on kind of the oil phase. It was observed that the increase of oil phase polarity causes the increase of the particle size of internal phase.

Keywords
triglycerides · nanoemulsion · PIC method

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1 Introduction

Nanoemulsions are the novel class of emulsions with high degree of inert phase dispersion.Particles of nanoemulsions are too small to scatter visible light (droplet size are in the range between 20 - 200 nm), that makes them optically transparent or translucent. In contrast to microemulsions, nanoemulsions are characterized by kinetic stability [1-6]. As a form of cosmetics products they can relatively easily penetrate into the skin, exhibit a high degree of hydration and soften the skin and have a very good user properties (ease of spreading on the skin, no greasy feeling). An additional advantage of these emulsions type, as a form of cosmetic, is no inherent creaming, sedimentation, flocculation or coalescence usually have observed in case of macroemulsions.

Triglycerides, are the popular cosmetic and pharmaceutical ingredients. From chemical point of view they are esters of glycerin and fatty acids. They usually applied in skin care products as emollients, lipophilic vehicles, skin permeation enhancers and solubilisers. Their properties strongly depend on chemical composition [7,8,9]. The natural sources of triglycerides used as the cosmetic ingredients are vegetable oil. Also the synthetic esters including caprylic/ capric triglycerides (Fig. 1) are popular.

Caprylic/capric triglycerides are fully saturated triglycerides, with excellent emolliency and good user properties, e.g. easy spreading orno occlusive feeling. It is entirely derived from vegetable resources and offers a stable alternative to mineral or vegetable oil. They are non-toxic and non-irritating

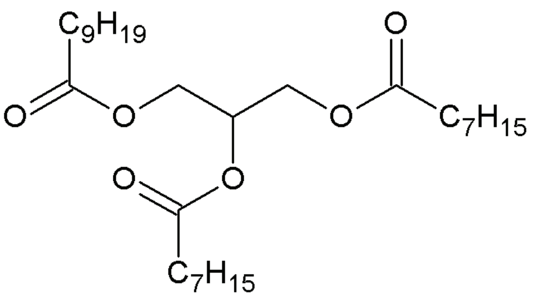

Fig. 1. Chemical structure – caprylic/capric triglyceride.

to skin, often used as solvent and vehicle for vitamins and nutritional active [8]. They have very low reactivity with chemically sensitive pharmaceutical actives. They were selected as the oil phase in microemulsion O/W, used as the drug delivery system, to transport ketoprofen [10] and in nanoemusion O/W containing lidocaine, [2] also as based emulsions for danazol [11].

The aim of this work was preparation and characterization of nanoemulsions containing as the oil phase Caprylic/Capric Triglycerides, Caprylic/Capric/Linoleic Triglycerides and Caprylic/Capric/Succinic Triglycerides. The emulsions were stabilized by different type of Polisorbates. Stable emulsion system was obtained by using Polisorbate 40 (PEG-20 Sorbitan Palmitate) as emulsifier and n-buthanol as cosurfactant.

2 Experimental

2.1 Materials

In the studies, on the basis of elaborated formulation, stable emulsion were obtained. As an oil phase in the formulations, different kind of triglycerides have been applied (Table 1).

Polisorbates 40, 60 and 80 were used as the emulsifiers. Additionally, the short-chain alcohols (ethanol, 1-propanol, buthanol) were tested as cosurfactants. The aqueous phase was distilled water. All ingredients used in the formulation are characterized in Table 2.

2.2 Formation of O/W nanoemulsions

The emulsions systems were prepared by phase inversion method (PIC) by stepwise water (W) addition to the mixture of oil (O) and surfactant (S) and co-surfactant (CoS), at room temperature (25°C). The mixture was stirred by using a magnetic stirrer, IKAC-MAG H 7 equipped with speed control. The emulsification process parameters are shown in Table 3.

2.3 Assessment of rheological properties

Rheological properties of the emulsifiers and the obtained emulsions were studied using Brookfield Rheometer Model R/S-plus, equipped with a cone-plate type measuring system (cone C75-1), at room temperature 25°C (298 K). The rheological studies were carried out with variable viscosity shear rate in the range of values from 1 to1000 s^{-1}.

2.4. Measurement of droplet size

The average internal phase droplet size of the emulsions were measured by Dynamic Light Scattering (DLS) method, using Malvern Zetasizer Nano ZS apparatus , which measures particle size (range from 0.3nm to 10µm) by scattering photons from a sample and determine the change in diffracted light intensity. Scattering angle was 173^0.

3 Result and discussion

3.1 Composition of obtained formulation

The results of the first stage of the study are presented in Table 4. After many tests it turned out that the stable emulsion system with Miglyol 812 could be obtain only when as the stabilizers mixture of Polisorbate 40 and n- buthanol was used, and only in specific concentration area (S:CoS=1:1, S/CoS:O=90:10).

Tab. 1. Composition of fatty acids [9].

Ingredient	Chemical structure	Caprylic/Capric Triglyceride (M812)	Caprylic/Capric/Linoleic Triglyceride (M818)	Caprylic/Capric/Succinic Triglyceride (M829)
Caprylic Acid	$C_7H_{15}COOH$ ($C_{8:0}$)	50.0 – 65.0	45 – 65	45 – 55
Capric Acid	$C_9H_{19}COOH$ ($C_{10:0}$)	30.0 – 45.0	30 – 45	30 – 40
Linoleicacid	$C_{17}H_{39}COOH$ ($C_{18:2}$)	-	2 – 5	-
Succinic Acid	$(CH_2COOH)_2$	-	-	15 – 20

Tab. 2. Components used in the studies.

Trade name	INCI name	Characterization	Name of suppliers
Tween 80®	Polysorbate 80 PEG 20 Sorbitan Oleate	emulsifier; HLB=15.0	Croda Poland
Tween 60®	Polysorbate 60 PEG 20 Sorbitan Stearate	emulsifier; HLB = 14.9	Croda Poland
Tween 40®	Polysorbate 40 PEG 20 Sorbitan Palmitate	emulsifier; HLB=15.6	Croda Poland
Miglyol 812®	Caprylic/Capric/Triglyceride	emollient	Sasol
Miglyol 818®	Caprylic/Capric/SuccinicTriglyceride	emollient	Sasol
Miglyol 829®	Caprylic/Capric/LinoleicTriglyceride	emollient	Sasol
ethanol	-	cosurfactant	POCh
1-propanol	-	cosurfactant	POCh
buthanol	-	cosurfactant	POCh

In the next step of studies different type of triglycerides were used as an oil phase (Table 5).

From the results shown in table 5 it could be concluded that only emulsions containing Miglyol 829 weren't stable. It means that stability of formulation depend on kind of the used triglycerides. It probably caused by differences in polarity of the oils. When more polar oil had been used in formulation the less stable emulsions were obtained.

3.2 Characterization of the stable emulsions

The data presented in table 6 and on the figure 2 show that the stable, transparent, o/w nanoemulsion, containing as an oil phase Miglyol 812 and Miglyol 818, could be obtained using Polisorbate 40 as the emulsifier and n-buthanol as cosurfactant.

Tab. 3. Emulsification process parameters.

Parameter	Value
Emulsification time	20 min.
Emulsification temperature	25°C
Stirrer speed	300 rpm
Method of phase connection	drop by drop
Phase inversion composition (PIC)	W→O/S/CoS

Fig. 2. Macroscopic picture of composition NE5M812.

Tab. 4. Formulations with Miglyol 812 as the oil phase.

Ingredient	Composition [% mas]								
	NET80E	NET80P	NET80B	NET60E	NET60P	NET60B	NET40E	NET40P	NET40B
Miglyol 812	5	5	5	5	5	5	5	5	5
Aqua	45	45	45	45	45	45	45	45	45
Polisorbate 80	25	25	25	-	-	-	-	-	-
Polisorbate 60	-	-	-	25	25	25	-	-	-
Polisorbate 40	-	-	-	-	-	-	25	25	25
Ethanol	25	-	-	25	-	-	25	-	-
1-propanol	-	25	-	-	25	-	-	25	-
buthanol	-	-	25	-	-	25	-	-	25
Stability	no	no	no	no	no	no	no	no	yes

Legend: NET80E – emulsion stabilized by Polisorbate 80 and ethanol, NET80P – emulsion stabilized by Polisorbate 80 and 1-propanol, NET80B – emulsion stabilized by Polisorbate 80 and buthanol, NET60E – emulsion stabilized by Polisorbate 60 and ethanol, NET60P – emulsion stabilized by Polisorbate 60 and 1-propanol, NET60B – emulsion stabilized by Polisorbate 60 and buthanol, NET40E – emulsion stabilized by Polisorbate 40 and ethanol, NET40P – emulsion stabilized by Polisorbate 40 and 1-propanol, NET40B – emulsion stabilized by Polisorbate 40 and buthanol.

Tab. 5. Formulations stabilized by Polisorbat 40 and n-buthanol.

Ingredient	Composition [% mas]								
	NE3M812	NE5M812	NE8M812	NE3M818	NE5M818	NE8M818	NE3M829	NE5M829	NE8M829
Aqua	45	45	45	45	45	45	45	45	45
Polisorbate 40	26	25	23.5	26	25	23.5	26	25	23.5
n-buthanol	26	25	23.5	26	25	23.5	26	25	23.5
M812	3	5	8	-	-	-	-	-	-
M818	-	-	-	3	5	8	-	-	-
M829	-	-	-	-	-	-	3	5	8
S/CoS:O	95:5	90:10	85:15	95:5	90:10	85:15	95:5	90:10	85:15
Stability	yes	yes	yes	yes	yes	yes	no	no	no

Legend: NE3M812 – emulsion w 3% content of Miglyol 812, NE5M812 – emulsion w 5% content of Miglyol 812, NE8M812– emulsion w 8% content of Miglyol812, NE3M818 – emulsion w 3% content of Miglyol 818, NE5M818 – emulsion w 5% content of Miglyol 818, NE8M818– emulsion w 8% content of Miglyol 818, NE3M829 – emulsion w 3% content of Miglyol 829, NE5M829 – emulsion w 5% content of Miglyol 829, NE8M829– emulsion w 8% content of Miglyol 829.

Tab. 6. Properties of the stable emulsion systems.

Formulations	Type of emulsion	pH	Appearance	Surface tension [mN/m]	Average droplet size [nm]	PDI
NE3M812	O/W	6.00	transparent	25.16	242.5	0.039
NE5M812	O/W	6.02	transparent	25.33	170.5	0.054
NE8M812	O/W	5.85	transparent	25.25	115.9	0.156
NE3M818	O/W	6.03	transparent	26.18	264.1	0.117
NE5M818	O/W	6.07	transparent	26.43	123.5	0.087
NE8M818	O/W	5.97	transparent	26.35	124.9	0.106

It should be noticed that the concentration of oil phase influences on internal phase droplets size. The emulsion NE8M812, which contains highest concentration (8%) of Miglyol 818 is characterized bythe smallest droplets size of the dispersed phase. Moreover, the obtained results showed that the ratio of oil phase to the surfactant mixture affects th properties of prepared emulsions.

On the other hand, it was observed that there is no significant difference between particle size of emulsions based on Miglyol 812 and Miglyol 818 with the same concentration of internal phase. Figures 3 – 5 show the comparison of particle size distribution between nanoemulsions based on Miglyol 812 and Miglyol 818 with different oil phase concentration.

3.3 Stability of nanoemulsions

The samples were stored, at ambient temperature, for 24 hours, 47 hours, one week and one month. During the time

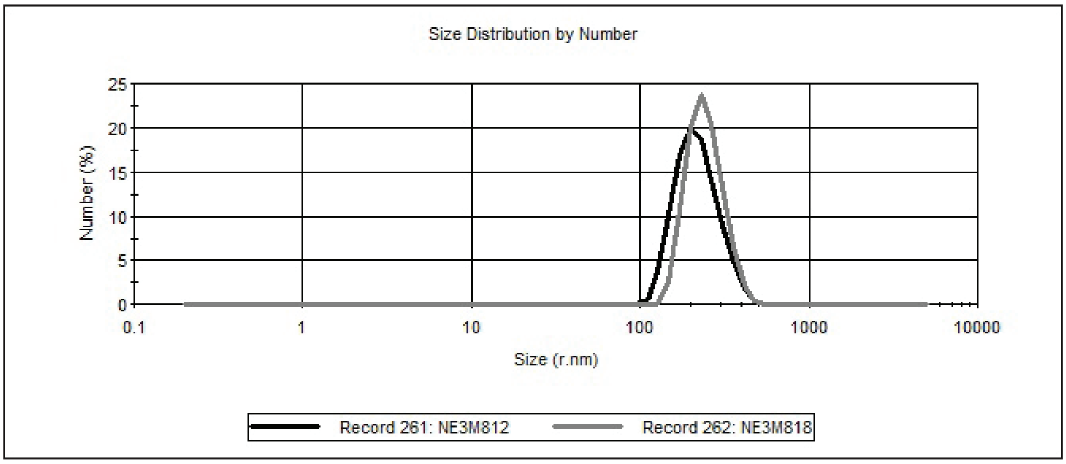

Fig. 3. Comparison of particle size distribution of nanoemulsion NE3M812 and NE3M818 with 3% of oil phase.

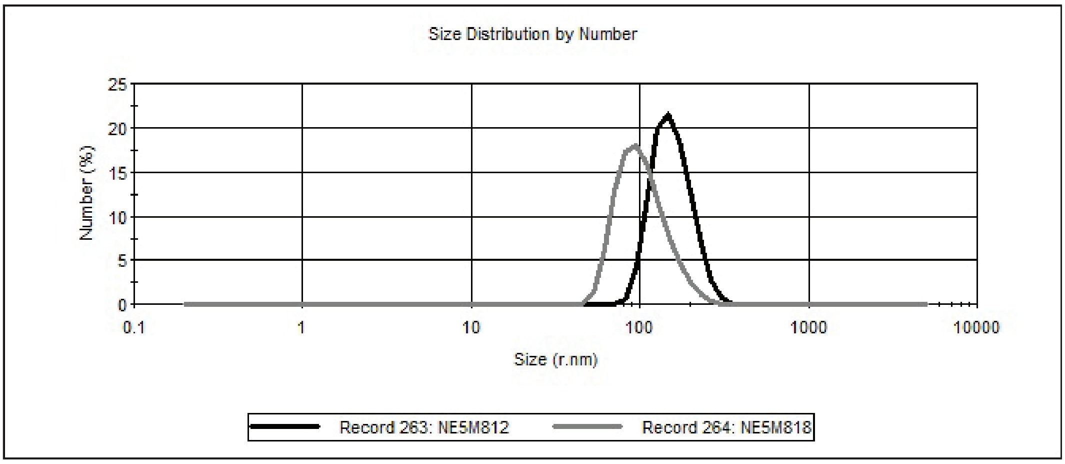

Fig. 4. Comparison of particle size distribution of nanoemulsion NE5M812 and NE5M818 with 5% of oil phase.

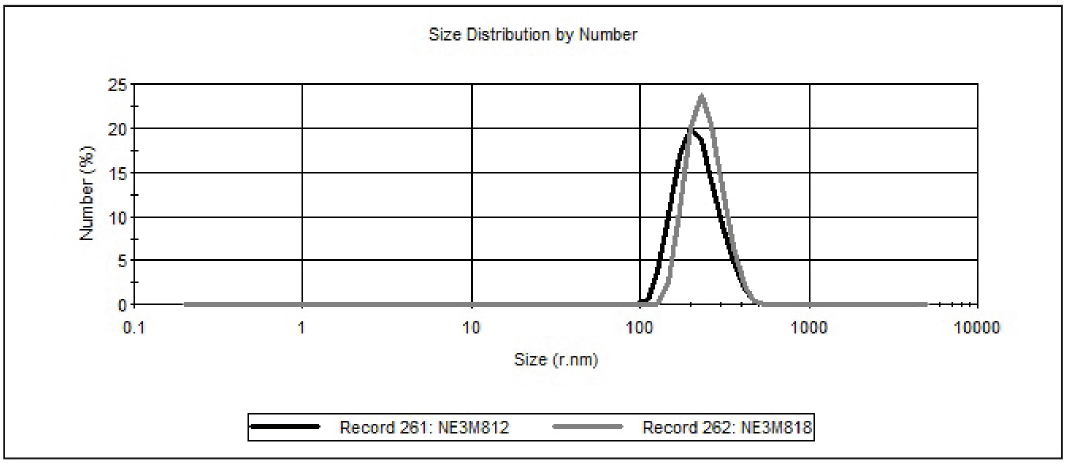

Fig. 5. Comparison of particle size distribution of nanoemulsion NE8M812 and NE8M818 with 8% of oil phase.

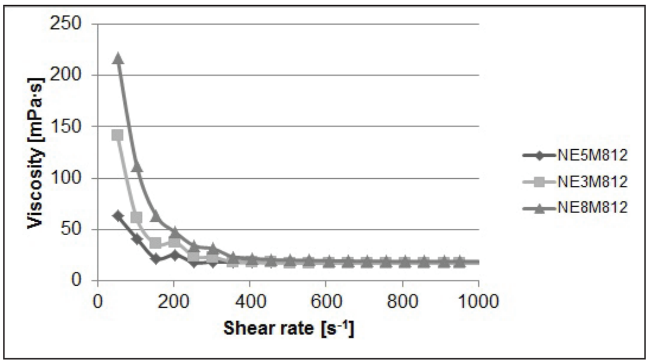

Fig. 6. Comparison of the viscosity of nanoemulsions based on Miglyol 812, at 250°C.

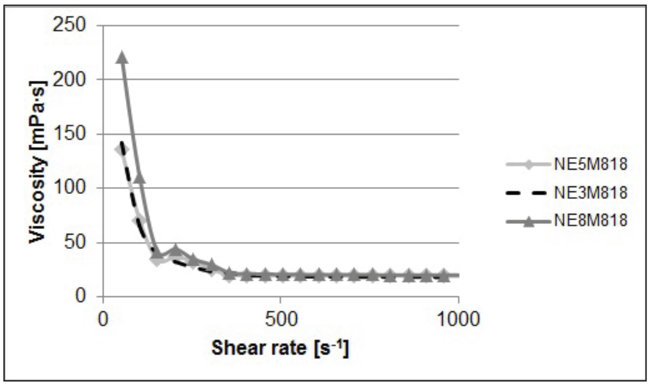

Fig. 7. Comparison of the viscosity of nanoemulsions based on Miglyol 818, at 250°C.

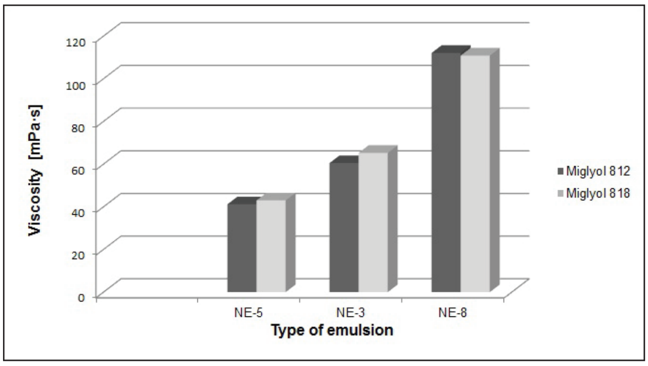

Fig. 8. Comparison of the viscosity of nanoemulsions based on Miglyol 812 and Miglyol 818, at shear rate $\gamma = 100\ s^{-1}$.

the stability of the formulations were assessed visually. The emulsions were transparent and stable. The phase separation and degradation were not observed during these 2 months. All nanoemulsions showed no change in clarity and phase behavior.

3.4 Rheological characterization

Figure 6 and 7 show that all nanoemulsions based on Miglyol 812 and Miglyol 818 are characterized by pseudoplastic behaviour. It is worth noting that the emulsions NE8M812 and NE8M818 with highest amount of oil phase are characterized by the highest viscosity. Moreover as figure 8 shown there was no significant effect of the oil phase type on the rheological properties of obtained formulations.

4 Conclusions

The obtained results showed that properties of the emulsions depend on kind of the oil phase. Stable emulsion systems were prepared based on Miglyol 812 and 818 and stabilized by Polisorbat 40 as emulsifier and n-buthanol as cosurfactant. It may indicate that if the more polar oil base have been used (Miglyol 829) the less stable emulsion were obtained. Moreover, there was no significant effect of the oil base on the rheological properties of the obtained formulations. All nanoemulsions are non-Newtonian liquids with pseudoplastic rheological behavior. Although, there are no significant differences in the physicochemical properties of nanoemulsions based on Miglyol 812 and Miglyol 818, however Miglyol 818 may be more efficient in the transport of active substances to the skin, due to the content of linolenic acid in its structure.

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