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RESEARCH PAPER

Stability Study of W/O/W Viscosified Multiple Emulsions

Ö. Özer,[1,]* V. Muguet,[2] E. Roy,[2] J. L. Grossiord,[2]
and M. Seiller[2]

[1] *Ege University, Faculty of Pharmacy, Bornova-Izmir-Turkiye*
[2] *Laboratoire Pharmacie Galenique, URA CNRS 1218 University of Paris-Sud, 92296, Chatenay-Malabry, France*

ABSTRACT

Stable multiple emulsions with a small proportion of primary emulsion containing different viscosifying agents in the outer aqueous phase were formulated. The multiple systems were assessed by evaluating several parameters, such as the macroscopic aspect, droplet size, release rate, and accelerated stability under elevated temperatures. The effect of different viscosifying agents at different concentrations on the stability and the multiplicity of the multiple emulsions was examined. The viscosity increased by increasing the concentration of the viscosifying agents. It also appeared that the viscosifying agents increased the temperature stability of the multiple emulsions. As a result, the formulation viscosified with Klucel was more stable, while the one prepared with carbomer viscosified the outer phase at much lower concentrations with much better skin feel.

Key Words: *Carbomer; Klucel; Viscosifying agents; W/O/W multiple emulsions.*

INTRODUCTION

Water/oil/water (W/O/W) multiple emulsion systems permit the protection of the entrapped substances and the prolongation of their release from the inner aqueous phase (1). The release could be due to a diffusion (passive diffusion or facilitated transport through the oily phase) of the emulsion or to the bursting of the multiple globules after dilution in water (swelling-breakdown phenomenon) or by application of a shear stress (2–5).

There have been various factors that affect the stability of W/O/W emulsions. These include the method of preparation; the nature of entrapped materials; the phase volumes; the concentration and the type of emulsifiers, oil, electrolytes, and all ingredients introduced in the outer aqueous phase (2,6).

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* To whom correspondence should be addressed. Fax: 90.232.3885258. E-mail: ozero@eczacilik.ege.edu.tr

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In a previous study, a very stable multiple emulsion was formulated with 80% of primary emulsion dispersed in the outer phase (7). The aim of this study was to obtain a multiple emulsion as stable as the previous one, but with a much smaller proportion of primary emulsion. This study examined the influence of the nature and the concentrations of the viscosifying agents introduced in the outer phase on the stability. It is also possible to adapt the formulations to obtain significant release under the effect of shear during application on the skin (5,8,9).

EXPERIMENTAL

Materials and Composition

The oil used was Arlamol HD®, an isohexadecane (ICI, Clamart, France). The lipophilic surfactant was Abil EM90®, a cetyl dimethicone copolyol (Goldschmid, France), and the hydrophilic surfactant was Synperonic PE/F127®, an ethoxylated propylene oxide copolymer (ICI). The hydrated magnesium sulfate ($MgSO_4 \cdot 7H_2O$) used in the inner aqueous phase was purchased from Prolabo.

The viscosifying agents introduced in the outer phase were chosen in different derivatives (mineral, vegetable, semisynthetic, and synthetic): Laponite XLS®, a magnesium silicate and tetrasodium phosphate (Laporte, France); Veegum®, a colloidal magnesium–aluminum silicate (Vanderbilt, France); Aerosil COK 84®, an amorphous silice (Degussa AG, France); Klucel®, a hydroxypropylcellulose (HPC; Aqualon, France); Benecel®, a hydroxypropylmethylcellulose (HPMC; Aqualon); Blanose®, a hydroxyethylcellulose (HEC; Aqualon); a gum xanthan (Lambert Rivire, France); Jaguar®, a gum guar (Rhone-Poulenc, France); a carrageenan (SATIA, France); Carbopol 974P®, a synthetic polymer obtained from acrylic acid (BF Goodrich, Polyplastics, France); Acrysol 44®, a synthetic polymer obtained from acrylic acid (Rohm and Haas, France).

To investigate the influence of the viscosifying agents on the stability, they were introduced in the outer aqueous phase at different concentrations, and the proportion of primary emulsion was changed. The formulations, which were described in the previous study, are given in Table 1 (5).

Table 1

Composition of Multiple Emulsions

	% (w/w)
W/O primary emulsion	
Arlamol HD	24
Abil EM 90	3
$MgSO_4$	0.7
Distilled water q.s.	100
W/O/W multiple emulsion	
Primary emulsion	40
Synperonic PE/F127	0.7
Viscosifying agent	Klucel or Carbomer[a]
Distilled water q.s.	100

[a] The concentrations, which were given according to the outer aqueous phase, were 10%, 20%, and 5% for Klucel and carbomer, respectively.

Method of Preparation

The multiple emulsions were obtained at room temperature by a two-step process with a Rayneri mixer. In the first step, the primary W/O emulsion was prepared by adding water containing the electrolyte to the oily phase at high speed (3000 rpm) for 40 min. In the second step, the primary emulsion was added slowly to the aqueous phase containing the hydrophilic surfactant and the viscosifying agent while the system was stirred at 400 rpm for 15 min (2). It is worthwhile to note that, when the multiple emulsion viscosified with the carbomer, the W/O primary emulsion was introduced into an aqueous phase composed of nonneutralized carbomer. The neutralization of the polymer was carried out with a 10% sodium hydroxide solution just after this incorporation phase. During this step, the stirring rate was reduced to avoid bursting of the multiple globules (10).

Evaluation Techniques

Macroscopic Analysis

The skin feel, consistency, and homogeneity of the viscosified aqueous phase and the multiple emulsions were assessed visually.

Microscopic Analysis

The W/O/W multiple emulsions were observed with an optical immersion microscope (Olympus BX60) connected to a video camera (Sony) at ×100 magnifying power. This analysis was carried out to determine the size of the globules and to verify the multiplicity of the multiple emulsions.

Conductometric Analysis

The conductivity was measured with a CDM 230 conductometer (Tacussel, Radiometer Copenhagen, France) on multiple emulsions diluted (1/20) in an isoosmotic

Table 2

Macroscopic Analysis of the Viscosified Aqueous Phase

	Skin Feel	Consistency	Homogeneity
Mineral			
Veegum	+	Compact	+++
Aerosil COK 84	+	Compact	+++
Laponite	+	Compact	+++
Vegetable			
Xanthan gum	++	Compact	++
Guar gum	++	Compact	++
Carrageenan	++	Compact	+
Semisynthetic			
Blanose	++(+)	Compact	+++
Benecel	++(+)	Compact	+++
Klucel	++(+)	Very compact	+++
Synthetic			
Carbopol 974P	+++	Very compact	+++
Acrysol 44	+++	Fluid	+++

+++ = very good; ++ = good, + = medium.

glucose solution to the inner aqueous phase. The conductometric test allowed the measurement of the weight fraction $\beta(t)$ of the electrolyte released into the outer aqueous phase at a given time t,

$$\beta(t) = M(t)/M_0$$

where M_0 is the initial amount of electrolyte incorporated, and $M(t)$ is the amount of electrolyte present in the outer phase at a given time (t). They were performed after the establishment of a calibration curve.

The β value can give us the entrapment yield Y of the multiple emulsions:

$$Y = 1 - \beta$$

Stability Studies

Stability was followed by the analysis mentioned above. It was realized at 25°C and 40°C at equal time intervals.

Rheological Analysis

This analysis was performed with a Haake RS100 controlled stress rheometer (Rheo, Champlan, France) at 20°C ± 1°C using a cone plate geometry.

RESULTS AND DISCUSSION

Viscosified Aqueous Phase

The macroscopic aspects of the outer aqueous phase prepared using different viscosifying agents are given in Table 2. The homogeneities of the preparations with xanthan gum, guar gum, and carrageenan were insufficient, and the preparations were opaque. The preparation with acrysol was not compact, but fluid. The mineral viscosifying agents were eliminated because of their unsuitable feel to the skin.

Due to their good properties, only the cellulose derivatives and carbomer were chosen for preparing multiple emulsions.

Viscosified Multiple Emulsions

First, the multiple emulsions prepared with 40% primary emulsion showed better stability. Whatever the na-

Table 3

Properties of Multiple Emulsions Viscosified with Cellulose Derivatives and Carbomer

	Klucel	Blanose	Benecel	Carbomer
Skin feel	++(+)	++(+)	++(+)	+++
Consistency	Very compact	Compact	Compact	Very compact
Homogeneity	+++	+++	+++	+++
Internal droplet size (μm)	1–5	1–5	1–5	1–5
Multiple droplet size (μm)	7–10	5–7	5–8	5–7
Conductivity (μS)	136	135	140	180
Entrapped yield (%)	94	94	95	66
Stability				
25°C	>3 m	>3 m	>3 m	2 m
40°C	>1 m	>1 m	>1 m	1 m

m = month.

ture of the viscosifying agents, the main properties of all formulations evaluated just after processing and at the end of the test period were constant. The emulsions checked every day did not show any sign of phase separation or microbial contamination. Microscopic analysis did not reveal any property changes in the nature or size of the aqueous and oil droplets.

Second, the formulations viscosified with cellulose derivatives showed a very high $MgSO_4$ entrapment yields (94–95%), while the multiple emulsion viscosified with carbomer showed much lower entrapment yield (66%). The ones viscosified with cellulose derivatives had a lower breakdown rate and better stability than the ones viscosified with carbomer (Table 3).

The conductometric measurements were performed after the establishment of a calibration curve. The validity of the model was tested by plotting conductivity versus concentration. The obtained curve confirms the linearity, and thus the validity, of the model ($r = 0.99$).

The measurements were made at 20°C ± 1°C on the multiple emulsion diluted with a 1/20 solution of glucose characterized by the same osmolarity as the inner aqueous phase (54 mosmol/L) under magnetic stirring. This determination was made with the help of tables found in Ref. 11.

Conductometric measurements did not show any change in the fraction of $MgSO_4$ released (Fig. 1). This means that there was no passive diffusion or facilitated $MgSO_4$ transport. This was confirmed by many formulations made previously (12–15).

Rheological Analysis

Rheology of the Primary Emulsion

As can be seen in Fig. 2, the primary emulsion showed shear-thinning behavior.

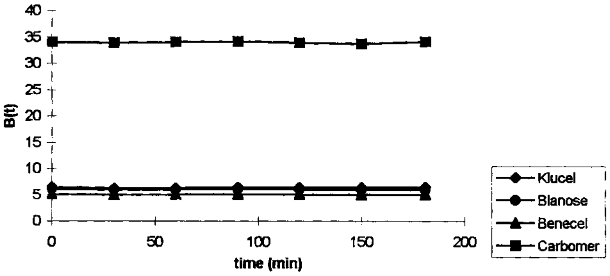

Figure 1. Comparison of the electrolyte release versus time under isoosmotic conditions for the multiple emulsions prepared by cellulose derivatives and carbomer.

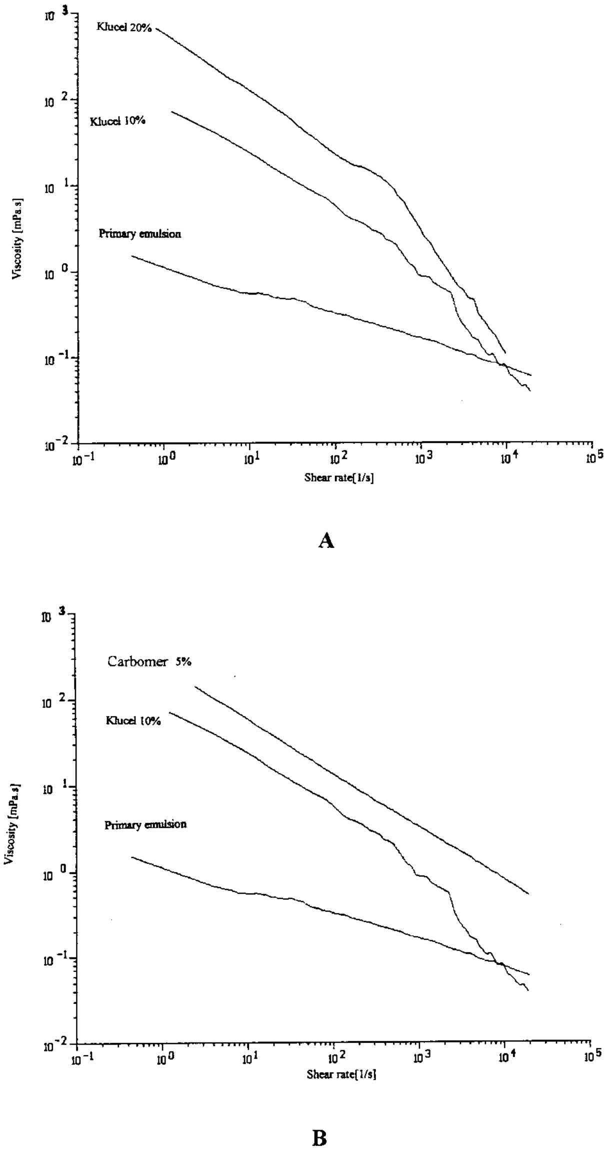

Figure 2. Plots of the viscosity versus shear rate of primary emulsion and aqueous phase viscosified with (A) Klucel 10% and 20% and (B) carbomer 5%.

Rheology of the Viscosified Multiple Emulsion

The formulations viscosified with Klucel and carbomer showed a shear-thinning character. Figures 2A and 2B demonstrate the plots of the outer aqueous phase viscosified with Klucel and carbomer, respectively. As seen in Fig. 2A, the viscosity was much higher when the concentration of the viscosifying agent was higher, but when the shear increased, this difference was reduced.

Carbomer was found less shear thining according to the cellulose derivatives. In fact, the carbomer is characterized by plastic behavior, whereas the cellulose derivatives display a shear thinning behavior. Carbomer is a gelifying agent able to adopt a tridimensional network in solution (gel), while the cellulose derivatives act only as thickening agents and do not form a gel. These differences in the intermolecular organization in solution are reflected by specific rheological properties for the polymers as a function of the shear rate. This phenomenon is related to the high viscosifying power of carbomers, the viscosity of which decreases less rapidly under shear than that of celluloses.

CONCLUSION

This study was of W/O/W multiple emulsions containing different viscosifying agents introduced at different concentrations in the outer aqueous phase. The main purpose was to manufacture stable multiple emulsions with much smaller proportions of primary emulsion (40%) and to assess the improvement of the stability versus the nature and the concentration of the viscosifying agents. The nature and the concentration of the viscosifying agents were chosen according to the skin feel, consistency, and homogeneity of the multiple emulsions. It appeared clearly that viscosifying agents increased the compactability, thickness, and stability of the multiple emulsions not only at room temperature, but also at 40°C.

Consequently, a stable multiple emulsion with a quite low proportion of primary emulsion could be obtained using different viscosifying and gelling agents, such as cellulose derivatives and carbomer.

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