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Correlation of rheological properties of an oil in water emulsion with manufacturing procedures and stability

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Summary

Some process variables of a liquid paraffin-in-water emulsion prepared with two nonionic surfactants and cetostearyl alcohol were examined initially and following a forced aging process using particle size analysis and rheological techniques (continuous shear, creep and oscillation). The highest viscosities were obtained for emulsions made by adding the aqueous phase to the oil phase through an in-line homogeniser, homogenising at the highest speed or agitating at the lowest speed during cooling. The lowest viscosities were obtained for emulsions agitated to room temperature, cooled fastest or emulsified at the lowest possible emulsification temperature. On aging the consistency, of emulsions made by adding the oily phase to the aqueous phase or adding the surfactant with the lowest HLB value to the aqueous phase before emulsification, had deteriorated most, suggesting comparatively lower long term stability for emulsions made this way. The consistency of emulsions cooled at the slowest rate or agitated to room temperature deteriorated least suggesting comparatively better long term stability. The rheological properties of the emulsions were not related to variations in particle size distribution except when the homogenisation speed was increased but rather to the stabilities of viscoelastic networks formed in the continuous phase and around the oil droplets. The composition and extent to which these structures are formed during manufacture is likely to be largely responsible for the rheological properties and the stability of an emulsion, and this will be investigated further in a later paper.

Introduction

Emulsions are frequently used as topical delivery systems for drugs. They consist of complex mixtures of a wide variety of excipients (Fox, 1984). In their simplest form emulsions consist of water, oil and surfactant. The colloidal structures, which are formed from these components not only determine the viscoelastic properties but may also be responsible for the stability of the product (Eccleston, 1977). The potential effect of the manufacturing procedure on the formation and final composition of these structures is often overlooked (Bornfriend, 1978).

This paper is the first of a series investigating the effect of manufacturing procedures on the structure and stability of an emulsion and will

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concentrate on process variables effects on the rheological properties of an emulsion. Since the majority of cosmetic and pharmaceutical emulsions belong to the oil-in-water type and contain liquid paraffin, cetostearyl alcohol and a blend of at least two nonionic surfactants (Idson, 1980; Fox, 1984), this investigation is concerned with such an emulsion. The composition of the selected o/w emulsion is: Steareth 21, 1.36% w/w; sorbitan oleate, 0.64% w/w; cetostearyl alcohol, 8.00% w/w; liquid paraffin, 12.00% w/w; dowicil 200, 0.20% w/w; water, 77.80% w/w.

In an investigation into the optimum processing conditions for an emulsion many factors need to be considered. An o/w emulsion can be made by either adding the oil to water or water to oil. The latter process involves phase inversion and is generally regarded as a better way of producing emulsions with fine droplet sizes (Becker, 1966). To establish if this also affected the structure and stability of the emulsion the method of addition was investigated. Lin (1978) found, on a small scale that by initially placing of the surfactants in the oil phase and then saturating this phase with water before emulsification ensured a smaller droplet size in the final emulsions. The effect of the composition of the phases for emulsification was therefore investigated. Lin (1978) also showed that lowering the rate of aqueous phase addition during emulsification produced an emulsion with smaller droplet size. This investigation also looked at the effect of speed of addition. The melting point for cetostearyl alcohol is around 60°C, the minimum emulsification temperature for emulsions containing cetostearyl alcohol is therefore 60°C. It has been suggested that emulsifying at higher temperatures may reduce the droplet size (Bornfriend, 1978). The effect of emulsification temperatures above 60°C was therefore investigated. Homogenisation while the emulsion is hot will reduce the droplet size and distribution (Becker, 1966) and improve uniformity in the continuous phase. A great variety of equipment has been used to homogenise emulsions, the rotating turbine and paddle impeller are the most commonly used followed by ultrasonic vibrators (Fox, 1980). Emulsification equipment subjects the emulsion to a shearing action. Oldshue (1959) found that the optimum for different impellers were similar in terms of flow to shear ratio. For this reason the effect of the homogenisation speed was investigated using only a rotating turbine. The effect of varying the homogenisation time was also investigated. Bornfriend (1978) showed that the colloidal structures will vary according to the cooling rate of the product. The resultant effect on the viscoelastic properties and stability of an emulsion differs from formulation to formulation, but could be an important tool in controlling the viscosity of an emulsion without sacrificing the stability of the product and for this reason the effect of the cooling rate was also included in the study. Emulsions containing cetostearyl alcohol are shear-thinning beyond a certain level of shear (Fox, 1974). Not only may agitation speed affect the viscosity of an emulsion but also the agitation end temperature could affect the viscosity (Jass, 1967), these two parameters were, therefore, also investigated.

Materials and Methods

Materials

The components cetostearyl alcohol (Lanette O, Henkel), Steareth 21 (Brij 721, ICI), sorbitan oleate (Span 80, ICI), liquid paraffin BP (BP Oil), 1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride (Dowicil 200, Dow Chemicals), were used without further purification. Demineralised water was used.

Manufacture of emulsions

10 kg of cream was prepared by each procedure using a 15 l Becomix Homogenising Mixer type RW15 (Berents GmbH). This mixer consists of a double jacketed vessel of conical construction, a bottom entry turbine homogeniser with a variable speed (800–6400 rpm), a stepless speed control (25–200 rpm) anchor agitator with baffle and wall scrapers and temperature probes in jacket and vessel.

The standard cream (sample a) was made by weighing the liquid paraffin, Brij 721, Span 80 and Lanette O into one container and the water into another and heating to 70°C. The lipid mixture was transferred to the Becomix. Once both phases had reached 70°C the water was pumped into the Becomix via the lid at a speed fo 200 ml/min. At the same time the agitator (speed 30 rpm) and the homogeniser (speed 1500 rpm) were started. Homogenisation was continued for 40 min and the temperature remained at 70°C throughout. The batch was cooled at a rate of 1°C every 5 min. Between 51 and 50°C the Dowicil 200 solution was added. At 45°C the agitation was discontinued. The cream was left for 10–20 h in the Becomix and scooped into air-tight glass containers and stored at 30°C. The variations made from the standard procedure are given in Table 1. The samples under investigation were 2–8 months old. To observe possible time-dependent effects, samples of the same batches were studied following 1 year at a 24 h cycling temperature from 5 to 37 to 5°C.

Particle size analysis

A photomicrograph was taken of all the samples using a Nikon Optiphot2 following 2 months storage at 30°C and 1 year storage on the cycling schedule 8 inch × 10 inch enlargements were made and droplet size analysis were performed using an image analyser (Joyce-Loebi Magiscan). The data from each count were used to determine the mean length of the droplets.

Freeze-etch scanning electron microscopy

Freeze-etch scanning electronc microscopy was taken of samples following 2 months storage at 30°C and following 1 year storage on the cycling

TABLE 1

Variations from standard manufacturing procedure

Order of addition		Method of addition		Speed of addition		
Sample	Water to oil (1) Oil to water (2)	Sample	Phase composition	Sample	Addition rate (ml/min)	Homogenisation time (min)
a	1	a	Span 80, Brij 721 in water	h	50	138
b	2	e	Span 80, Brij 721 in water	i	200	138
c	1 [a]	f	Brij 721 in water	a	200	40
d	2 [a]	g	Span 80 in oil	j	800	40

Emulsification temperature		Homogenisation speed		Homogenisation time	
Sample	Emulsification temperature (°C)	Sample	rpm	Sample	min
k	60	a	1500	a	40
a	70	n	3500	o	80
l	80			i	138
m	90				

Cooling rate		Agitation speed		Agitation end temperature	
Sample	Rate	Sample	Agitation speed (rpm)	Sample	°C
p	1°C/min	r	6	t	30
a	1°C/5 min	a	30	u	40
q	1°C/10 min	s	60	a	45
				v	50

All samples were manufactured as sample a except for one process parameter, this parameter being listed above. In all, nine different process parameters were investigated. a is the standard procedure.

[a] Phase addition through the homogeniser.

schedule. The preparation of the samples was carried out using a Hexland CT 1000A (Cryotrans Cryogenic Preparation Systems) attached to a Phillips 500 SEM. A small sample of cream was placed on a rivet and inserted onto a specimen stub. The assembly was frozen in liquid nitrogen at −210°C. The specimen was fractured with a blade and lightly etched in the microscope at −80°C. After coating with gold, the specimen was examined on a temperature-controlled stage at −150°C in the scanning electron microscope.

Measurements of rheological properties

Oscillatory experiments The behaviour of the o/w emulsions stored at 30°C for 7–8 months and on the cycling schedule for 1 year in forced oscillation was investigated using a Carri-Med Controlled Stress Rheometer CSL50 (Carri-Med Ltd, Dorking, U.K.) fitted with a 4 cm acrylic parallel plate and using a gap of 1 mm. The system was fitted with a solvent trap. Initial tests for linearity were performed, and the emulsions were all examined in their linear viscoelastic region by applying sinusoidally varying strain with a displacement amplitude of 2.0×10^{-4} rad of frequencies from 10 to 0.01 Hz. The storage modulus (G^{1}) and the loss modulus (G^{11}) were obtained from the frequency sweep. Every single experiment was completed within 40 min, since the water evaporation from the sample was found to be significant for runs longer than 1 h, and was repeated at least twice with a deviation of 5% or less. All experiments were performed at a temperature of 30 ± 0.2°C.

Creep experiments Creep experiments were performed on emulsions stored at 30°C for 2 months and on the cycling schedule for 1 year using the CSL 50 fitted with a 4 cm diameter 4° acrylic cone and a solvent trap. For each determination four creep experiments were carried out on the same sample followed by a continuous shear measurement. The shear stress was increased in a stepwise manner from 10 to 100 dyne cm^{-2} for each sample. It was assumed that the emulsion was behaving in a linear viscoelastic manner in the region where the Newtonian viscosity (η_0) was constant for gradually increasing shear rate values, and only creep determinations

TABLE 2

The mean droplet length of the emulsions stored for 2 months at 30°C and for 1 year on a cycling schedule (5°C–37°C–5°C every 24 h)

Manufacturing Method	Mean droplet length (μm)	
	Stored 2 months at 30°C	Stored 1 year on cycling
Order of addition		
a	6.4	3.9
b	7.7	3.4
c	7.2	3.2
d	5.8	3.6
Method of addition		
a	6.4	3.9
e	7.2	3.3
f	5.7	3.4
g	6.2	3.6
Speed of addition		
h	3.2	3.5
i	3.2	3.6
a	6.4	3.9
j	7.0	3.4
Emulsification temperature		
k	7.4	4.0
a	6.4	3.9
l	5.7	3.2
m	7.1	3.4
Homogenisation speed		
a	6.4	3.9
n	1.5	2.3
Homogenisation time		
a	6.4	3.9
o	6.1	4.0
i	3.2	3.5
Cooling rate		
r	6.5	3.8
a	6.4	3.9
g	6.5	3.6
Agitation speed		
r	6.4	3.5
a	6.4	3.9
s	6.3	3.4
Agitation end temperature		
t	7.9	3.4
h	6.5	3.5
a	6.4	3.9
v	7.0	3.9

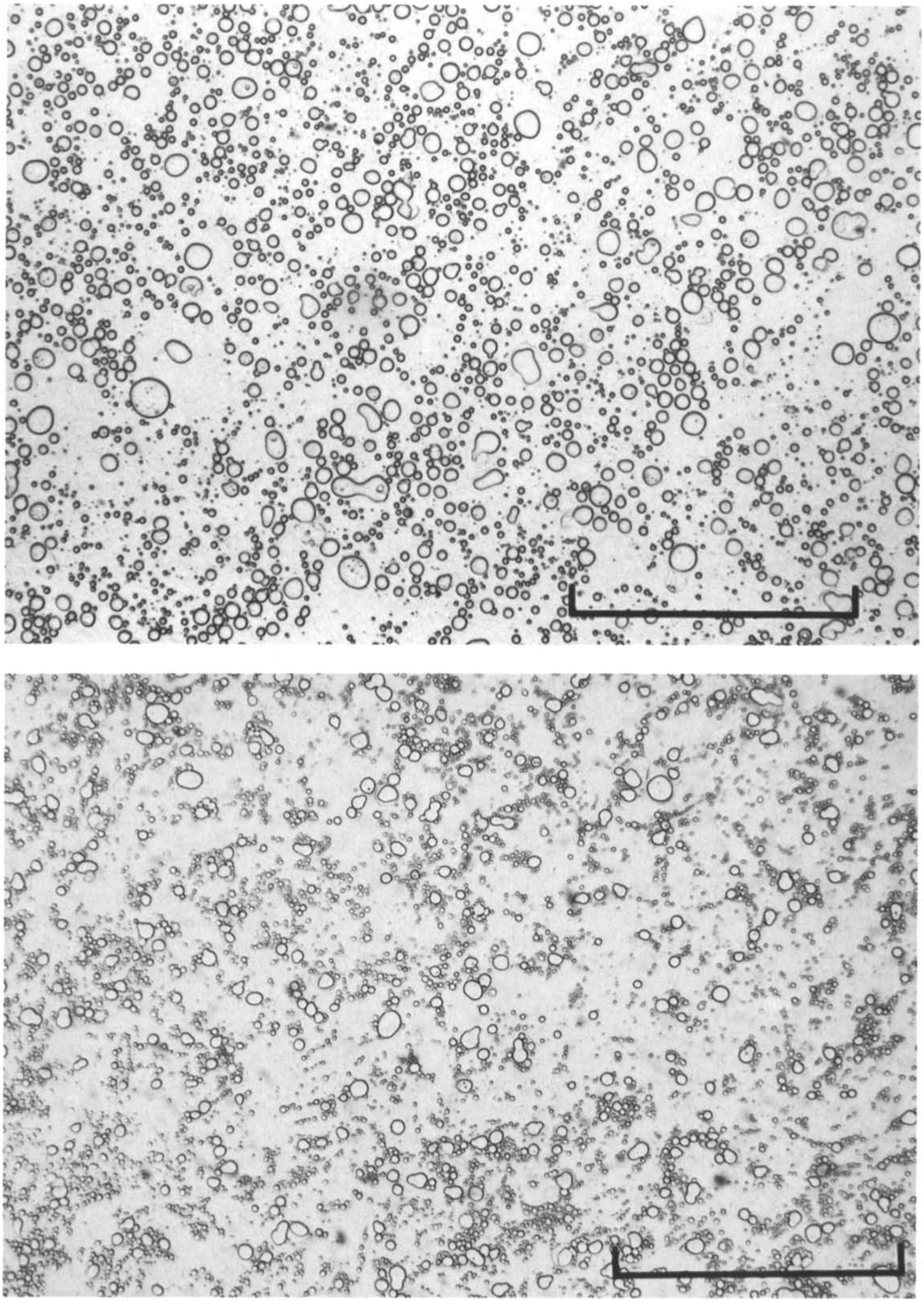

Fig. 1. Photomicrograph of the emulsion manufactured according to the standard procedure taken following 2 months storage at 30°C (a) and 1 year storage on cycling schedule (5°C–37°C–5°C every 24 h) (b). Scale bar = 200 μm. Electron micrographs of the sample following the same storage conditions (c, d). Scale bar = 2 μm (c); 5 μm (d).

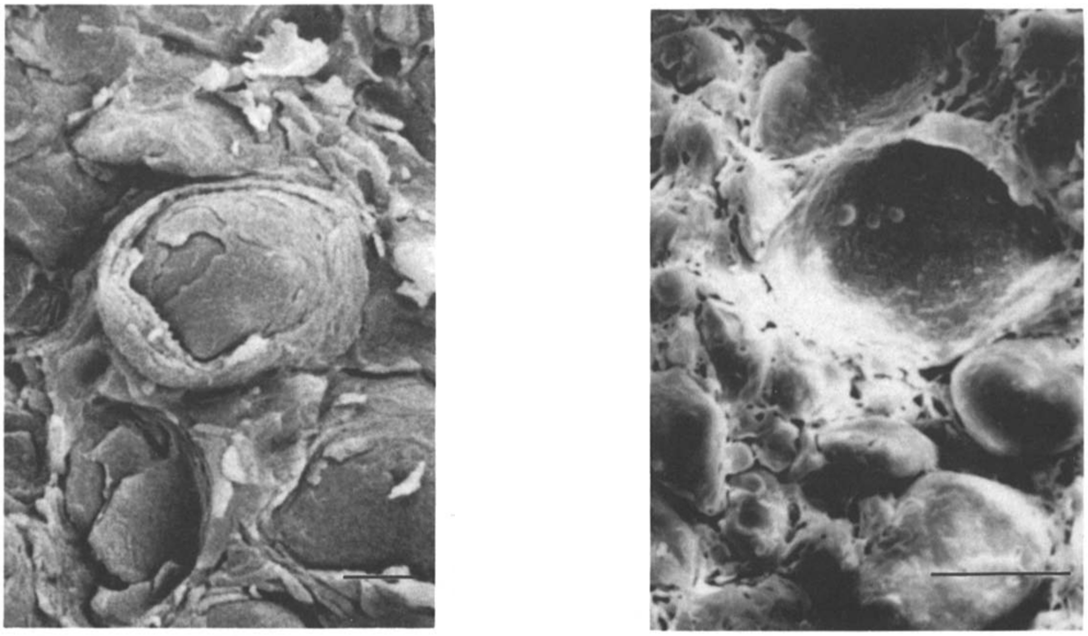

Fig. 1. (continued).

in this region was used. Each determination was completed within 65 min at 30 ± 0.2°C. The results are the average of at least three creep determinations from each run and two or more runs.

Continuous shear A continuous shear measurement was carried out as the last step following the series of creep measurements using a maximum shear stress value of 2000 dyne cm^{-2}.

Results and Discussion

Particle size analysis

The results form the particle size analysis are listed in Table 2; the data show that the mean droplet size generally decreased slightly with time. Photomicrographs of the standard sample at the two time points shown in Fig. 1 indicate that this was due to the appearance of clusters of small droplets around larger droplets. A number of the different manufacturing procedures resulted in smaller than average droplet size. These were the method using the highest homogenisation followed by the method using the longest homogenisation run and the method where homogenisation took place at 80°C for these samples one would expect a higher than average viscosity for the emulsions.

The droplet size analyses were performed on undiluted emulsions, since dilution would destroy the lamellar structure and encourage coacevation of the oil droplets. However, this made the size analyses difficult to perform since the concentration of droplets on each slide was so high that they often had to be manually separated, also the colloidal network was difficult to remove completely from the image, and this may have added to the inaccuracy of the determination. The unexpected reduction in droplet size with time can be explained by the disappearance of some of the colloidal structures around the droplets which is shown in freeze-fracture electron micrographs taken following the same storage conditions and shown in Fig. 1.

Creep

The Berger model was used to describe the viscoelastic response for samples stored at 30°C for 2 months and 1 year on a cycling schedule.

The purely elastic response J_0, the purely viscous response η_0^* and up to 2 Voight units was found.

η_0^* from the creep determinations and the infinite viscosity η_∞ from the continuous shear experiments were used to calculate the zero shear viscosity (η_0).

$$\frac{\eta_0 - \eta_\epsilon}{\eta_\infty^* - \eta_\infty} = (K\gamma)^m \text{ cross equation}$$

where γ is the shear rate and K and m are constants.

The results are given in Fig. 2. The data obtained following 2 months storage at 30°C showed that differences in consistency could be obtained by means f the manufacturing procedure. Following the cycling schedule the consistency of the emulsions had generally halved. Comparing the results for samples a–d in order to evaluate the order of addition, it was found that adding the oil phase to the aqueous phase produced a less viscous product and adding the second phase through the homogeniser produced a more viscous product. Evaluation of the method of addition by comparing samples a and e–g indicated that differences in droplet size as suggested by Becker (1966) could no alone explain the differences in viscosity. Adding both surfactants to the aqueous phase, sample e, initially produced the most viscous product even though the Span 80 was only dispersed in this phase. However, with age the consistency of samples e and g where Span 80 also had been added to the aqueous phase had more than halved, suggesting that the surfactants only may be equally effectively incorporated into the bilamellar structures from both the aqueous and lipid phase when they have been dissolved before emulsification and that the final

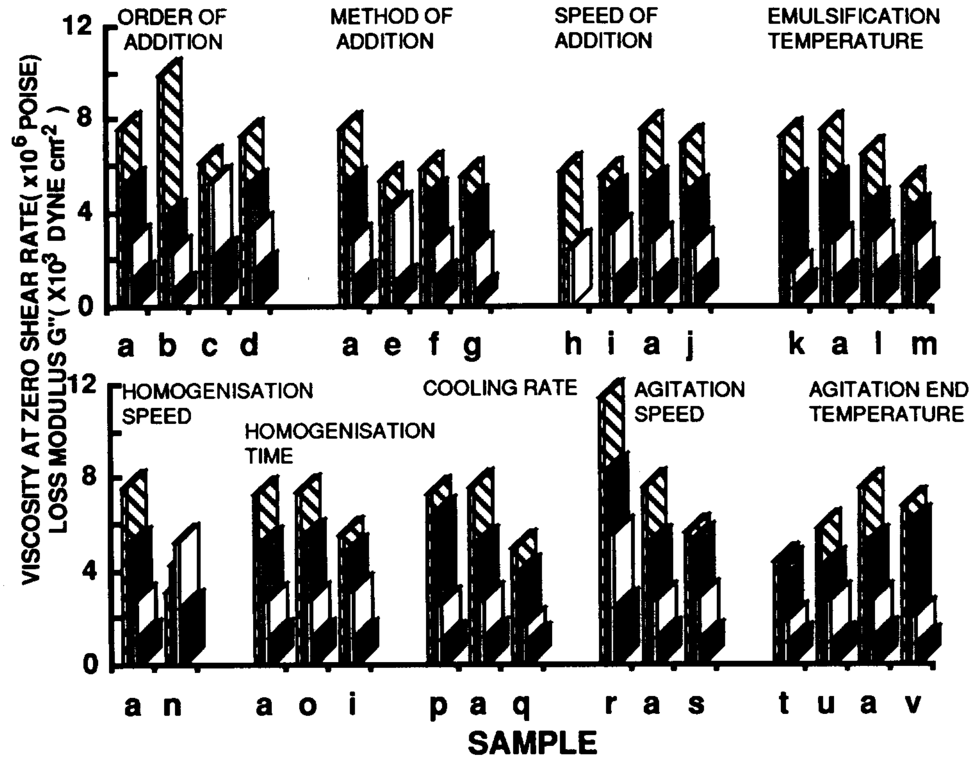

Fig. 2. The extrapolated viscosity at zero shear rate (P) following 2 months storage at 30°C (□) and following 1 year on a cycling schedule from 5 to 37 to 5°C every 24 h (■), and the loss modulus G^{II} (dyne cm^{-2}), at 10 Hz following storage of the emulsions for 7–8 months at 30°C (▨) and for 1 year on the cycling schedule (▦).

droplet size was not affected by the different methods of addition which is in contrast to Lin's (1978) findings. The speed with which the aqueous phase was added was evaluated by comparing samples h, i, a and j, and this apparently had little effect on the viscosity of the sample. Comparison of samples k, a, l and m suggested that the optimum emulsification temperature for high viscosity for the sample was 80°C. Increasing the emulsification temperature did reduce the droplet size as Becker (1966) and Bornfriend (1978) suggested, but this correlation was found to have an optimum and the droplet size reduction was only slight, increasing temperatures seemed to have more effect on the viscosity. Comparison of samples a and n suggested that increasing the homogenisation speed markedly increased the viscosity and this could be correlate to the reduction in droplet size which may be supported by the reduction in consistency on storage which corresponded with an increase in droplet size. Comparison of samples a, o and i surprisingly suggested that the homogenisation time seemed to have little effect on the consistency. Evaluation of the cooling rate by comparing samples p, a and q suggested that fast cooling rate had little effect on the viscosity of the sample, whereas slow cooling produced a product with much lower viscosity, the latter may however be explained by the extended agitation the sample was subjected to. Comparison of samples r, a and s–v suggested that high agitation rate and low agitation end temperature produced a lower viscosity. The reduction in viscosity following the cycling schedule was greater than average for samples e, g and b, suggesting that the shelf life for samples made by this method will be shorter than average. Surprisingly, the deterioration for samples g and t and slow cooling agitation to 30°C was less than average which may suggest that these samples may have a longer shelf life. The highest viscosities were found for samples c, n and r. This suggests that these samples would have a long shelf life.

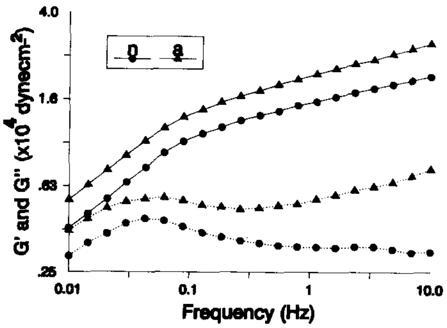

Fig. 3. Variation of storage modulus, G^{I} (———) and loss modulus G^{II} (······) form 10 to 0.01 Hz for samples a and n stored at 30°C for 7–8 months.

Oscillation

The variations of storage modulus, G^{I} and loss modulus G^{II} with frequency for the emulsions after 7–8 months storage at 30°C were similar for all the samples except for sample n; therefore, the variations with frequency are only shown for samples a and n in Fig. 3.

The oscillatory data show that the storage modulus decrease linearity with decreasing frequency and that this decrease is accelerated below a frequency of 0.1 Hz. This pattern was similar for all the samples. The loss modulus displayed differences at high frequencies. In Fig. 2, the variations of loss modulus only at 10 Hz are therefore shown listed. The G^{II} values are affected in a similar way to the zero rate viscosity by the method of manufacture and storage time with a few exceptions, notably sample n for high homogenisation speed.

In conclusion, it is possible to vary the consistency of an emulsion by altering the manufacturing procedure for the emulsion. A high viscosity cream was obtained for this emulsion by adding the aqueous phase to the oil phase through the in-line homogeniser, homogenising at the highest speed or agitating at the lowest speed during cooling. The lowest consistencies for the emulsion were obtained by agitating the cream to room temperature, cooling the emulsion fast or emulsifying at the lowest possible temperature. On aging part of the colloidal structure around the oil droplets disappeared resulting in the droplets becoming smaller and clustering together. The rheological data suggested that this aging process could be slowed down by cooling the emulsion very slowly or agitating the sample to room temperature.

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