Drug Development and Industrial Pharmacy, 25(3), 367–371 (1999)

COMMUNICATION

Evaluation of the Emulsifying Properties of Some Cationic Starches

An Vermeire, Filip Kiekens, Sam Corveleyn, and
Jean Paul Remon*

Laboratory of Pharmaceutical Technology, University of Gent,
Harelbekestraat 72, 9000 Gent, Belgium

ABSTRACT

Different cationic potato, maize, and waxy maize starches were evaluated for their emulsifying properties. Emulsions were prepared using 20% (w/w) arachidic oil and 80% (w/w) water. Emulsions with the cationic starches as emulsifier in a concentration ranging from 1% to 5% (w/w) were prepared and characterized by droplet size and viscosity measurements, and the stability was evaluated visually and by electrical conductance measurements. None of the cationic potato, waxy maize starches, and maize starches with a low degree of substitution (DS) showed adequate emulsifying properties. Emulsions prepared using non-pregelatinized (C☆bond 05914, 2% and 5% w/w; C☆bond 05907, 5% w/w) and pregelatinized (C☆bond 12504, 5% w/w) cationic maize starches with high-DS were visually stable. The initial mean droplet volume diameter of the emulsions prepared with these cationic starches in a 5% (w/w) concentration was similar and ranged from 2.40 to 2.84 μm; however, there was an important difference in droplet size distribution. The droplet size distribution of the emulsions prepared using the non-pregelatinized high-DS cationic starches was markedly narrower than in the case of the emulsions prepared using the pregelatinized high-DS cationic starches. The droplet size of the emulsions remained almost constant during 120 days of storage. Visual inspection and electrical conductance measurements showed that these emulsions were stable for at least 120 days.

INTRODUCTION

Cationic starches are predominantly used in the paper industry as wet-end additives, as size press starches, and as binders in paper coatings (1). Recently, there is an increasing interest in the use of cationic emulsions for transfection applications (2–4). Positively charged emulsions also exhibit more prolonged residence in the skin or

---

* To whom correspondence should be addressed.

www.dekker.com

cornea, thereby enhancing lipophilic drug biodisposition while sustaining the release of the drug (5,6). It was in view of these data that the emulsifying properties of some cationic starches were investigated.

MATERIALS AND METHODS

Preparation of the Emulsions

In all emulsions, water containing 0.02% (w/w) propylparahydroxy-benzoate and 0.08% (w/w) methylparahydroxybenzoate as preservative agents was used as the aqueous phase and arachidic oil (Federa, Brussels, Belgium) was used as the oil phase. The cationic starches used were obtained from Cerestar Eridania Béghin-Say (Vilvoorde, Belgium), and their characteristics are listed in Table 1.

All emulsions were prepared according to a standardized protocol. The emulsifier was added to the aqueous phase while mixing for 5 min with a Silverson mixer (Silverson Machines, Waterside, UK). Next, the arachidic oil was added, and the emulsion was mixed for an additional 5 min. The aqueous starch dispersions were always heated to 80°C, except for the dispersion of the pregelatinized maize starch (C☆Bond 12504), as it is a starch dispersible in cold water. Emulsions were prepared using the cationic starches at concentrations ranging from 1% to 5% (w/w). The emulsions that were visually stable for 7 days were characterized by droplet size and viscosity measurements, and the stability was evaluated by visual inspection and electrical conductance measurements during a 120-day storage period at 23°C ± 2°C. Therefore, additional 1 L emulsions were prepared according to the same standardized protocol. Immediately after preparation, 500 ml of the emulsion were poured in a specially designed glass cell for visual evaluation and electrical conductance measurements. The remaining 500 ml were divided in 250-ml glass bottles for initial viscosity and droplet size measurements and were stored at 23°C ± 2°C for droplet size measurements after 120 days.

Evaluation of the Emulsions

Droplet Size Measurements

The droplet size distribution of the emulsions was determined using a Coulter counter (Coulter Electronics, Hertz, UK) equipped with a 50-μm tube. Droplet size measurements were performed immediately after preparation of the emulsions and after storage for 120 days at 23° ± 2°C. For these measurements, the emulsions were subjected to a three-step dilution process (1 in 88,000 v/v): 400 μl of the emulsion were diluted in 20 ml of a 0.9% NaCl solution and gently shaken. Next, 350 μl of this dilution were diluted in 20 ml 0.9% NaCl; finally, 650 μl of the last dilution were diluted in 20 ml 0.9% NaCl. These dilutions were prepared in dust-free beakers, and the 0.9% NaCl solution was always filtered through a membrane filter (20 μm, Schleicher and Schuell, Dissel, Germany) before use. For this dilution, the coincidence index did not pass the ‘‘4% maximum’’ value; therefore, coincidence corrections were not necessary. With the applied instrument settings, a globule count for a sample volume of 0.5 ml diluted emulsion was performed. For

Table 1

Cationic Starch Characteristics

Origin	Modification	Product Code	DS
Potato	Low DS	C☆Size 35873	0.022
	Low DS	C☆Bond 35803	0.022
	High DS	C☆Bond 35904	0.034
	High DS	C☆Bond 35905	0.046
	High DS	C☆Bond 358H9	0.095
Maize	Low DS, thinned	C☆Film 05980	0.016
	Low DS, thinned	C☆Size 05962	0.017
	High DS	C☆Bond 05914	0.030
	High DS	C☆Bond 05907	0.060
	High DS, pregelatinized	C☆Bond 13504	0.030
Waxy maize	High DS, thinned	C☆Bond 069R1	0.037
	High DS, thinned	C☆Bond 069R3	0.040

DS = degree of substitution.

each emulsion, three dilutions were prepared and analyzed.

Viscosity Measurements

The emulsion viscosity was determined immediately after preparation of the emulsions using a Haake viscosimeter (Rotovisco RV12, Haake, Germany). The experimental parameters were kept constant during the measurements: rotating device MV I, attenuation 1, rotational speed 128 rpm, resolution factor 10, shear rate 30 sec^{-1}, and a constant temperature of 23°C ± 2°C.

Electrical Conductance Measurements

The stability of the emulsions was evaluated by electrical conductance measurements in specially designed cells as described by Kiekens et al. (7). These measurements were performed immediately after preparation and at regular time intervals during 120 days. The difference between the specific electrical conductance in the upper and lower parts of the cell in terms of percentage ($\Delta > L = (L_{under} - L_{upper})/L_{under} \times 100$) as a function of time was used for the evaluation of the stability of the emulsions.

Visual Evaluation

The stability of the emulsions was evaluated visually immediately after preparation and at regular time intervals during 4 months or until phase separation was seen.

RESULTS AND DISCUSSION

Visual evaluation of the emulsions revealed that none of the cationic potato, waxy maize starches, and maize starches with a low degree of substitution (DS) showed adequate emulsifying properties, whereas all high-DS cationic maize starches showed good emulsifying properties. Within the high-DS cationic maize starches, C☆Bond 05914 showed good emulsifying properties at a concentration of 2% and 5% (w/w), whereas C☆Bond 05907 and C☆Bond 12504 showed good emulsifying properties at a concentration of 5% (w/w). Emulsion characterization and long-term stability evaluation were performed for those emulsions showing a visual stability of at least 1 week.

The results of the droplet size and viscosity measurements are summarized in Table 2 and Fig. 1. The initial mean droplet volume diameter by number was similar for the emulsions prepared with the different types and concentrations of cationic starches and ranged from 2.40 to 2.84 μm. The droplet size distribution of the different emulsions, however, differed markedly. For the same type of cationic starch, the droplet size distribution was narrower for the emulsions prepared with 5% (w/w) cationic starch as emulsifier compared to that of the emulsions prepared with 3% (w/w) cationic starch as emulsifier. When the droplet size distributions of the emulsions prepared with the different cationic maize starches at a concentration of 5% (w/w) were compared, the C☆Bond 05907 emulsions showed the narrowest droplet size distribution, followed by the emulsion prepared with C☆Bond 05914. The emulsion prepared with the pregelatinized C☆Bond 12504 showed a markedly broader droplet size distribution. Although one would expect that the emulsions with a broader droplet size distribution would be less stable, during the period studied there was no relationship between the droplet size distribution and the emulsion stability as measured by visual inspection and electrical conductance measurements. After a 120-day storage period, the mean droplet volume diameter by number of the emulsions was almost unchanged and ranged from 2.35 to 3.28 μm. The viscosity of the emulsions with 5% emulsifier was higher for the non-pregelatinized cationic maize starches (C☆Bond 05907 and

Table 2

Mean Droplet Volume Diameter (Average ± SD, n = 3) by Number and Viscosity of Oil-in-Water Emulsions Prepared with C☆Bond 05907, C☆Bond 05914, and C☆Bond 12504 as Emulsifying Agents

Origin	Modification	Product Code	Concentration (% w/w)	Viscosity (mPa.s)	Mean Droplet Volume Diameter (μm) Initial	Mean Droplet Volume Diameter (μm) After 120 Days
Maize	High DS	C☆Bond 05914	2	83.73	2.75 ± 0.03	2.86 ± 0.07
			5	331.69	2.84 ± 0.02	2.68 ± 0.02
	High DS	C☆Bond 05907	5	288.54	2.63 ± 0.04	3.28 ± 0.45
	High DS, pregelatinized	C☆Bond 12504	5	106.91	2.40 ± 0.06	2.35 ± 0.03

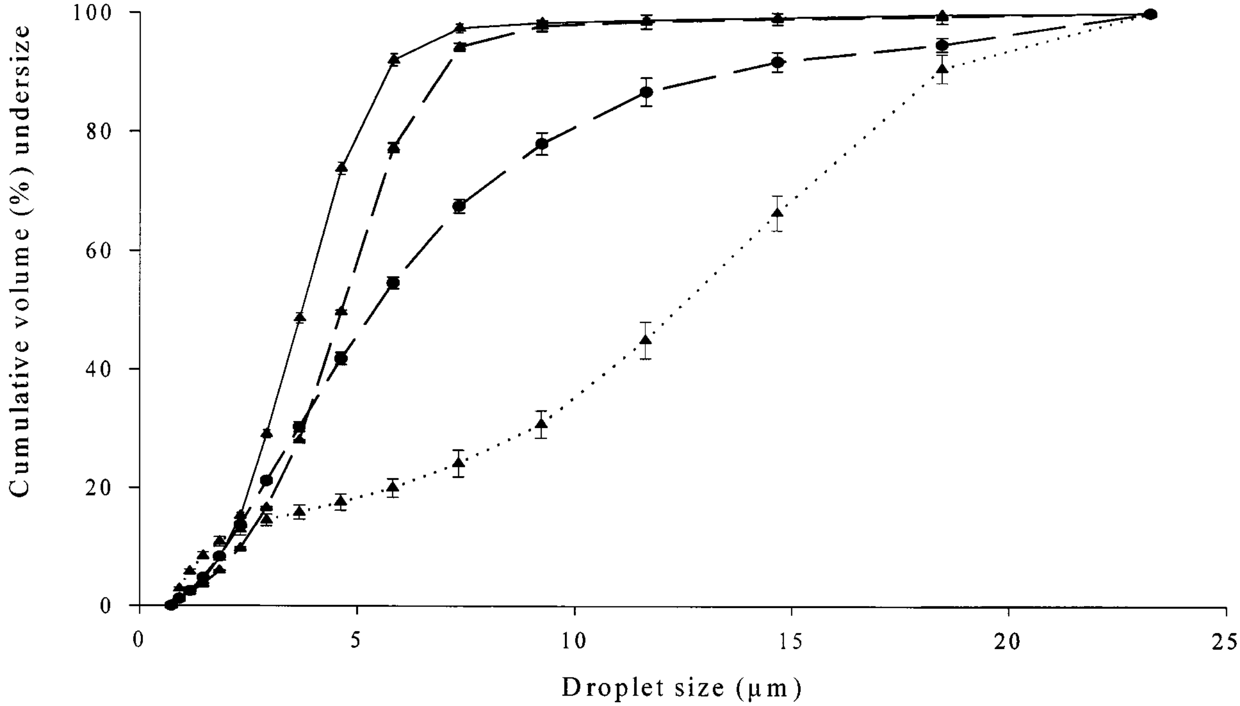

Figure 1. Cumulative distribution of the initial droplet volume diameter (average ± SD, $n = 3$) of oil-in-water emulsions prepared with C☆Bond 05907 (▲ with solid line, 5% w/w), C☆Bond 05914 (● with dashed line, 2% w/w; ▲ with dashed line, 5% w/w), and C☆Bond 12504 (▲ with dotted line, 5% w/w) as emulsifier.

C☆Bond 05914) than for the pregelatinized cationic starch (C☆Bond 12504). The emulsions with the highest viscosity showed the narrowest droplet size distribution.

The results of the stability evaluation of the emulsions by visual inspection and electrical conductance measurements are summarized in Table 3 and Fig. 2. Phase separation was not observed during the 120 days for any of the emulsions. The specific electrical conductance increased with increasing concentration of the cationic starches. The percentage difference in specific electrical conductance of the emulsions evaluated showed minor to important variations during the first days, but after 10

Table 3

Stability of Oil-in-Water Emulsions Prepared with C☆Bond 05907, C☆Bond 05914, and C☆Bond 12504 as Emulsifying Agents During Storage for 4 Months at 23°C ± 2°C Evaluated by Visual Inspection and Electrical Conductance Measurements

					Electrical Conductance (Days 1–20)		
Type	Modification	Product Code	Concentration (% w/w)	Visual Evaluation	L_{under} (μS/cm)	L_{under} (μS/cm)	ΔL (%)
Maize	High DS	C☆Bond 05914	2	[a]	284–549	368–506	4.0–0.4
			5	[a]	692–931	683–911	1.3–0.2
	High DS	C☆Bond 05907	5	[a]	2555–3000	2396–2691	6.2–3.1
	High DS, pregelatinized	C☆Bond 12504	5	[a]	3447–4216	3016–3604	12.5–6.1

[a] No phase separation seen during the period studied.

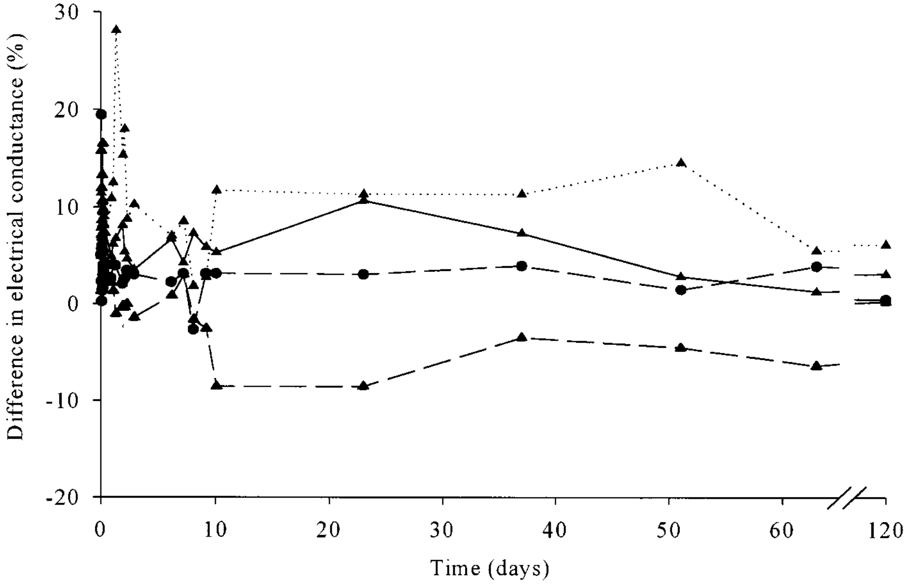

Figure 2. Percentage difference between the upper and lower part of oil-in-water emulsions prepared with C☆Bond 05907 (▲ with solid line, 5% w/w), C☆Bond 05914 (● with dashed line, 2% w/w; ▲ with dashed line, 5% w/w), and C☆Bond 12504 (▲ with dotted line, 5% w/w) as emulsifier during storage for 4 months at 23°C ± 2°C as a function of time.

days, this value remained almost constant. These results indicate that the emulsions studied are stable for at least 120 days.

As there is renewed interest in emulsions as a vehicle for drug delivery and, more specifically, in positively charged emulsion formulations for parenteral, ocular, and topical drug delivery, the use of cationic starches could offer a possible alternative to the currently used cationic emulsifiers. Further investigations are necessary to evaluate the toxicity, the biodegradability, and the ability of cationic starches to formulate submicron emulsions.

ACKNOWLEDGMENT

We are grateful to Cerestar Eridania Béghin-Say (Vilvoorde, Belgium) for providing the cationic starches and for the droplet size measurements.

REFERENCES

1. M. W. Rutenberg and D. Solarek, in *Starch Chemistry and Technology* (R. L. Whistler, J. N. BeMiller, and E. F. Paschall, eds.), Academic Press, New York, 1984, p. 312.
2. F. Liu, Y. Jingping, L. Huang, and D. Liu, Pharm. Res., 13, 1642 (1996).
3. C. Dubernet, H. Teixeira, S. Benita, and P. Couvreur, Proc. Int. Symp. Controlled Release Bioact. Mater., 24, 661 (1997).
4. S. W. Yi, T. Y. Yun, Y. H. Kim, E. H. Bae, I. C. Kwon, S. Y. Seong, Y. W. Choi, and S. Y. Yeong, Proc. Int. Symp. Controlled Release Bioact. Mater., 24, 653 (1997).
5. E. Elbaz, A. Zeevi, S. Klang, and S. Benita, Int. J. Pharm., 96, R1 (1993).
6. R. Ezra, S. Benita, I. Ginsburg, and R. Kohen1, Eur. J. Pharm. Biopharm., 42, 291 (1996).
7. F. Kiekens, A. Vermeire, N. Samyn, J. Demeester, and J. P. Remon, Int. J. Pharm., 146, 239 (1997).