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ORIGINAL CONTRIBUTION

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Colloidal microstructure of binary systems and model creams stabilized with an alkylpolyglucoside non-ionic emulsifier

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Abstract The aim of this study was to examine the lyotropic potential of an alkylpolyglucoside mixed emulsifier (Cetearyl glucoside&Cetearyl alcohol), which belongs to the new generation of natural (sugar) surfactants, and to elaborate the potential stabilization mechanism and relation between the colloid microstructure and water distribution within the systems. Polarization and ordinary light as well as transmission electron microscopy, wide and small-angle X-ray diffraction, thermal analysis and rheological measurement were employed for the systems characterization.

It was suggested that Cetearyl glucoside&Cetearyl alcohol stabilizes the o/w creams by synergistic effects of viscoelastic hydrophilic gel of lamellar type and lipophilic gel network built up from cetostearyl alcohol semi-hydrates as well as by lamellar liquid crystalline bilayers surrounding the oil droplets. The hydrophilic gel consists of mixed cetearyl glucoside/cetearyl alcohol crystalline bilayers entrapping the water interlamellarly by hydrogen bonding. It is also showed that oil addition into the chosen binary system influences the creams microstructure significantly, which particularly reflects onto the mode of water distribution within the creams and consequently their potential of skin hydration.

Keywords Sugar-based emulsifier · Lamellar gel phase · Lamellar liquid crystals · Interlamellar water · Skin hydration potential

Introduction

Dermatological emulsion lotions and particularly creams are common multiphase systems with stability and physico-chemical properties connected with mesomorphic phase behaviour of emulsifier, rather than with droplets interaction, what has been explained by classical theories of emulsion systems [1, 2, 3].

According to Eccleston [1, 4], a lamellar, crystalline gel phase is formed within ternary or emulsion system, due to swelling properties of distinct entities of mixed emulsifier, thus preventing the oil droplets coalescence and controlling the system consistency. In addition, this type of system is considered as four-phase system, with two different colloidal gel phases, the hydrophilic and lipophilic one [5]. Due to different swelling capacities of hydrophilic gel phases, the different ratios of two types of water, the bulk (free) and interlamellar (fixed), could appear within the system [6, 7, 8]. The interlamellarly fixed, so called ''depot'' water, could contribute to the moisturizing potential of dermatological and cosmetic formulations, and affect the diffusion rate and penetration ability of actives [5, 9]. Furthermore, the stratum corneum (SC) hydration, which is affected by application of dermopharmaceutical and/or dermocosmetic preparations onto healthy or diseased skin, could result in significant changes of

the skin barrier, i.e. of skin permeability. Thus, in recent years there were a lot of words on preparations for so called controlled skin hydration [10, 11, 12], which is very important in therapy of some dermatoses (eczema, psoriasis, etc.).

Recently, sugars based emulsifiers, so called glucolipids, were proposed as an alternative to traditionally used polyoxyethylene (PEG) derivatives in the stabilization of oil in water (o/w) emulsions [13, 14, 15]. The head moiety of sugar-based emulsifiers contains a number of free hydroxyl groups, which bind water and could provide additional skin moisturization, having an impact on the SC pliability and penetration potential of drugs and cosmetic actives [14]. Previous findings pointed to the significantly better skin hydration, barrier improving and non-erythematic potential of creams based on an alkylpolyglucoside emulsifier (Montanov 68 PHA, Cetearyl Glucoside&Cetearyl Alcohol) compared with commonly used polyethoxy non-ionic emulsifiers [16], but without any insight to colloidal structure of the samples.

As amphiphilic molecules, glucolipids form both, the thermotropic liquid crystalline phases, in their pure state upon heating, and the lyotropic liquid crystalline phases upon addition of a solvent [17]. There is more literature data on thermotropic and lyotropic properties of long alkyl chain-disaccharides than on monosaccharides, the lack of data for the latter being the consequence, at least partly, of their insolubility in water, due to the high Kraft temperature [17, 18]. Furthermore, there is no comprehensive information on mesomorphic behaviour of long alkyl chain-glucosides combined with fatty alcohols, in the form of well known mixed emulsifiers.

Therefore, we were induced to elucidate the structure-properties relationship of binary systems and creams stabilized with Cetearyl Glucoside&Cetearyl Alcohol, a non-ionic glucolipid/fatty alcohol mixed emulsifier and to develop an optimal formulation with the acceptable rheological performance and balanced bulk/fixed water ratio. Polarization and ordinary light as well as transmission electron microscopy (PLM, OLM, TEM), small and wide-angle X-ray diffraction (SAXD and WAXD), continual and oscillatory rheology and thermal analysis were used for the systems characterisation.

Materials and methods

Materials The glucolipid non-ionic emulsifier Cetearyl Glucoside&Cetearyl Alcohol (Montanov 68 PHA, kindly provided by Seppic, France) was used for all binary systems and model creams preparation. Due to their moderate polarity, medium chain triglycerides (Miglyol 812, Huls, Germany) were considered as suitable oil phase for model creams. All samples were prepared with double distilled water and properly preserved (0.5 wt% Euxyl K 300, Schülke & Mayr, Germany).

Preparation of systems Binary systems (emulsifier/water ratios: 8.75:91.25; 10:90; 20:80; 30:70; 37:63; 40:60) were prepared by heating the preserved water and emulsifier in sealed glass vial to 70 °C and then stirring at constant temperature for 3 min (700 rpm), then 3 min at 500 rpm. Upon emulsification/solubilization cooling was started whilst mixing at 500 rpm (1 min), then at 300 rpm to the room temperature. Regarding to increasing percentage of emulsifier, binary systems were labelled: BS1, BS2, BS3, BS4, BS5 and BS6.

Additionally, a series of cream samples with fixed ratio emulsifier/water (8.75:91.25, i.e. 1:10.43) and increasing percentage of oil phase (5, 10, 15, 20, and 25 wt% of Miglyol 812) was prepared. For this purpose emulsifier and oil were heated together at 70 °C, and then added to the water phase at the same temperature using the same mixing procedure like in binary systems preparation. The samples were designated as Mg5%–Mg25%, indicating the oil percentage.

After preparation all samples were equilibrated for a week prior to the measurements.

Microscopy Samples were examined microscopically in bright field (OLM) and between crossed polarizers (PLM) using the photomicroscope with λ plate (Zeiss, Type III, Oberkochen, Germany). In addition, TEM micrographs (Leo, Germany) of sample replicas (freeze fracture technique) were taken.

SAXD SAXD measurements were performed using a position-sensitive detector (Braun, Munich, Germany) in all investigated samples. The semisolids were pressed between Capton foils (Krempel, Voihingen, Germany) to thickness of 1 mm avoiding air bubbles. X-rays were produced by a PW-1730 generator (Philips, Kassel, Germany) with a copper anode (current 25 mA, λ 0.154 nm, accelerating voltage 40 kV). The exposure time was 300 s at ambient temperature. From diffraction angle theta (Θ) the interlayer spacings were calculated in reference to Bragg's law.

WAXD To obtain structural information on the samples, short-range ordering was examined using WAXD measurements. Diffraction patterns were collected using an X-ray goniometer PW-1050/25 (Philips), coupled with a Xe-filled linear counter (Fuji, Japan). X-rays were produced by an X-ray generator PW-1730 (Philips) using a copper anode (anode current 25 mA; λ 0,154 nm, accelerating voltage 40 kV). From diffraction angle theta (Θ) the intermolecular distances were calculated according to Bragg's law.

Differential scanning calorimetry (DSC) To investigate the phase transition behaviour, DSC measurements were carried out with pure emulsifier, binary systems and cream samples. Measurements were performed using a Differential Scanning Calorimeter DSC 220 (Seiko, Germany), with closed aluminium pan, employing the heating/cooling program with temperature change rate of 2 °C/min between 20 and 105 °C. An empty aluminium pan served as reference.

Thermogravimetric analysis (TGA) In a trial to differentiate bulk and potentially fixed (interlamellar water), measurements were conducted using a TG 220 with disk station 5200 H (Seiko, Japan). The measurements were performed with open aluminium pans in temperature range 20–100°C with a heating rate of 2°C/min (in triplicate).

Rheological measurements Continual and oscillatory measurements, as well as yield value determination were performed with binary system BS1 and cream samples (CSR/CSS Rheometer Bohlin Instruments, Germany).

All measurements were carried out under the following conditions (in triplicate): cone and plate measuring system (diameter 40 mm, angle 1°), with thickness of sample of 0.030 mm, at 20 ± 0.1 °C.

During continual testing, controlled shear rate procedure was applied (shear rate 0.29–200 1/s and back again to start point, each stage lasting 120 s).

Yield value determination was carried out by continual applying of controlled shear stress to the sample within the measuring range 0–30 Pa.

Oscillatory measurements were conducted in order to determine linear viscoelastic region of the sample (amplitude sweep), at constant frequency of 1 Hz and amplitude sweep ramp from 0.5–30 Pa. A frequency sweep ramp from 0.1–10 Hz was performed at constant shear stress (6 Pa), which was within the previously marked linear viscoelastic region for all the samples. Yield stress value and apparent viscosity, storage (G′) and loss (G″) modulus, as well as phase angle (δ) were used for rheological characterisation of investigated samples.

Results and discussion

Microscopic analysis (PLM, OLM, TEM)

Polarized light microscopy (PLM) revealed an anisotropic texture within binary systems as well as in cream samples (Figs. 1a,c, 2a,b). Liquid lamellar phase is attributed by mosaic texture, oily streaks and Maltese crosses [3, 19, 20]. In the case of model surfactant/fatty alcohol/water mixture, Eccleston calls these anisotropic structures as distorted Maltese crosses, implicating the lamellar phase, too [4].

In binary systems with lower amount of emulsifier (BS1–BS3) the distorted Maltese crosses were seen (Fig. 1a,c), being more numerous when mixed emulsifier percentage increased. Gradual increase of emulsifier concentration influenced the anisotropy of the mosaic texture type and the partial presence of the crystallized fatty alcohol, resulting in dry waxy solid consistency of the mixtures. Only the systems with 91.25% and 90% of water (BS1 and BS2) had the appearance of a viscoelastic cream.

Creams were shiny, white semisolids of different consistency corresponding to different density of oil droplets packaging within the system. Figure 2a,b as well as micrograph from OLM (Fig. 2c) showed the anisotropic droplets (‘‘onion rings’’) uniformly dispersed into the continuous phase with the remnants of the gel network surrounding larger droplets and floccules of smaller oil droplets. This type of structure is similar to those seen in creams stabilized with the cetrimide/cetostearyl alcohol or polyoxyethylene alkyl ether surfactants/cetostearyl alcohol mixed emulsifiers [21, 22]. Accordingly, it seems that in creams based on cetearyl glucoside/cetearyl alcohol mixed emulsifier oil droplets act as a focus for multilayers of gel phase, which become more randomly oriented as they progress into the continuous phase [21].

This observation could be substantiated by TEM micrographs of binary systems and cream sample with 20% of the oil phase (Figs. 1b,d, 2d–f). In figures which represent the binary mixtures the widespread lamellar sheets could be seen, the typical feature of an ordered gel phase [23]. In cream sample (Mg20%, Fig. 2d–f) multilayers of planar arrangement within the continuous phase are observed. In some peculiarities micrograph of Mg20% (Fig. 2f) is comparable with freeze fractured micrograph of Water Containing Hydrophilic Ointment DAB 10 given by Junginger [6]. This system contains 9% of an anionic mixed emulsifier, 21% of oil/fatty phase and 70% of water. Accordingly, it could be suggested that in Mg20% cream sample, with 7% of glucolipid mixed emulsifier, 20% of oil and the 72.5% of water, the lamellar sheets are consisted of mixed crystals bilayers, the greatest part of cetearyl glucoside molecules randomly distributed between the part of cetearyl alcohol molecules. In addition, by the insertion between the polar surfactant monosaccharide units, the part of the water could be entrapped like interlamellarly fixed water, producing the hydrophilic gel phase. Within formed gel network the bulk water may be kept, presumably mechanically, by capillary attraction forces [5]. However, within the hydrophilic ointment (DAB 10) the oil phase is dispersed within an additional, lipophilic gel phase, which is built up from cetostearyl alcohol semi-hydrates [5], rather than in form of oil droplets comprised by entire gel matrix.

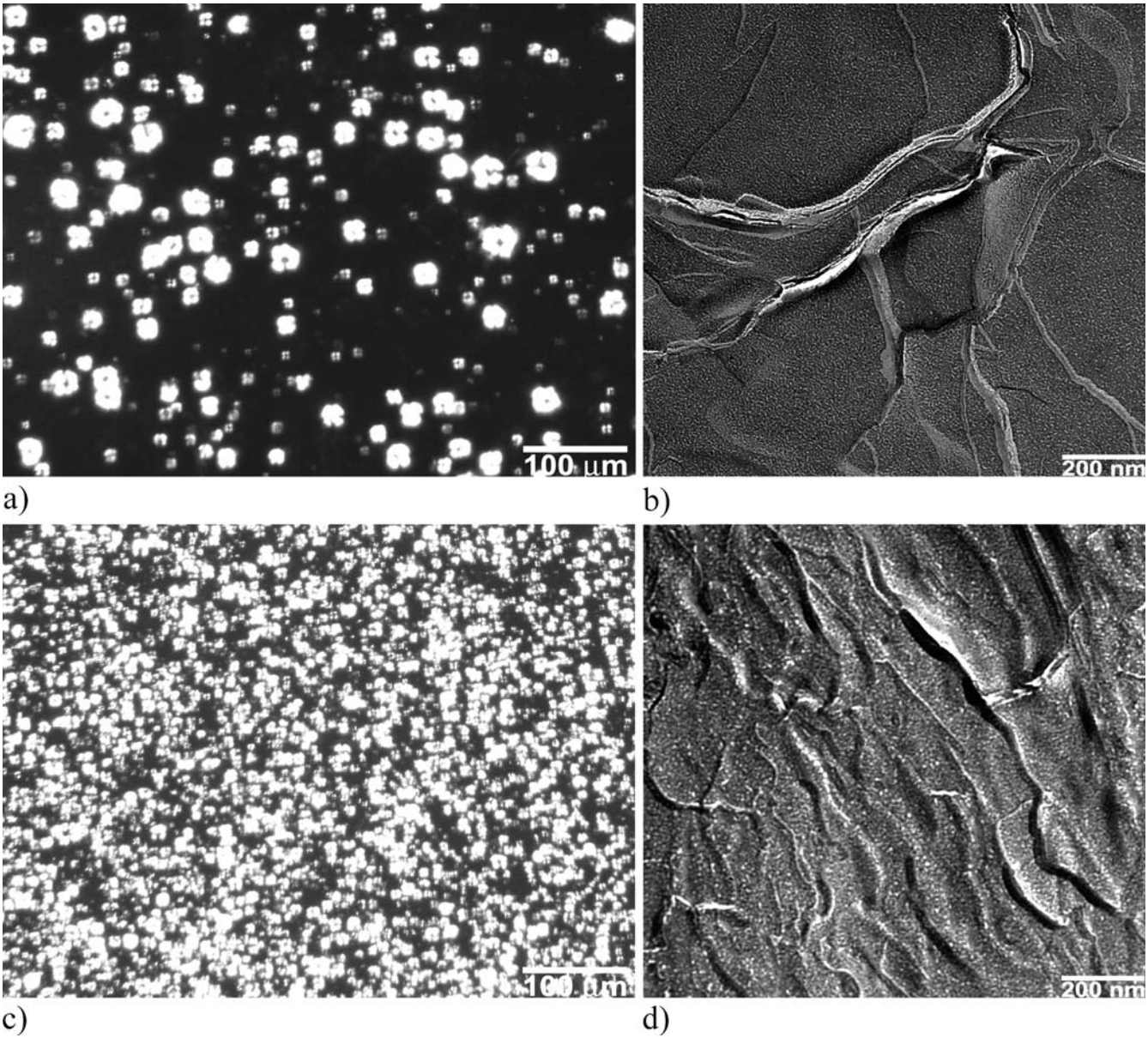


Fig. 1a–d PLM and TEM micrographs of binary systems BS1 (8.25% of emulsifier) and BS3 (20% of emulsifier): **a** PLM/BS1/bar 100 µm; **b** TEM/BS1/bar 200 nm; **c** PLM/BS3/bar 100 µm; **d** TEM/BS3/bar 200 nm

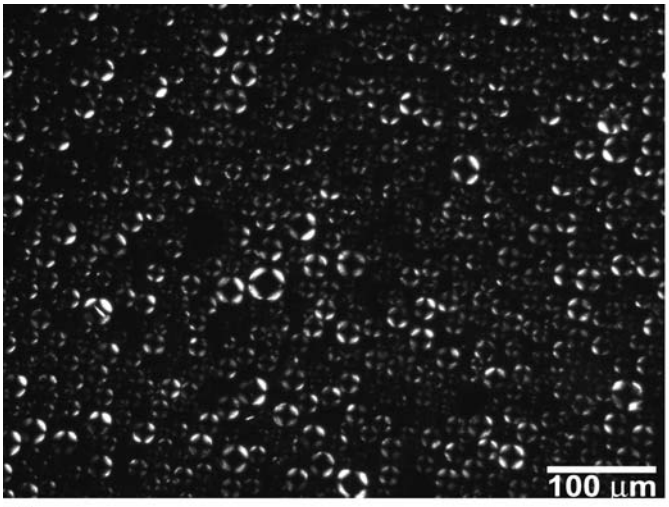
In similar fashion, Eccleston [1] emphasizes the dominancy of complex crystalline gel phase in stabilization of multiphase oil-in-water (o/w) emulsions based on either ionic or non-ionic mixed emulsifiers over the presence or absence of multilayers of lamellar liquid crystals around the oil droplets, like it was described by the Friberg model [1, 4]. Nevertheless, the birefringence seen at the oil droplets border (Fig. 2a,b) could indicate the presence of the lamellar liquid crystalline phase in addition to the complex viscoelastic gel phase, leading to the assumption that creams based on alkylpolyglucoside mixed emulsifier could be stabilized by synergistic effects of both structures.

WAXD and SAXD measurements

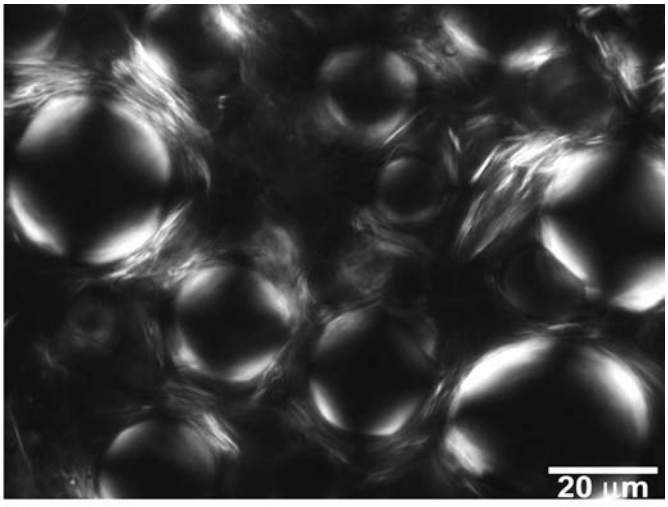
X-ray diffraction in the wide-angle region ($2\Theta = 2–50°$) provides the information about the short-range order-

►

Fig. 2a–f PLM, OLM and TEM images of sample with 20% of oil phase (Mg20%) and the emulsifier/water ratio 1:10.43: **a** PLM/ bar 100 µm; **b** PLM/bar 20 µm; **c** OLM/bar 20 µm; **d** TEM/bar 500 nm; **e** TEM/bar 200 nm; **f** TEM/bar 100 nm



a)



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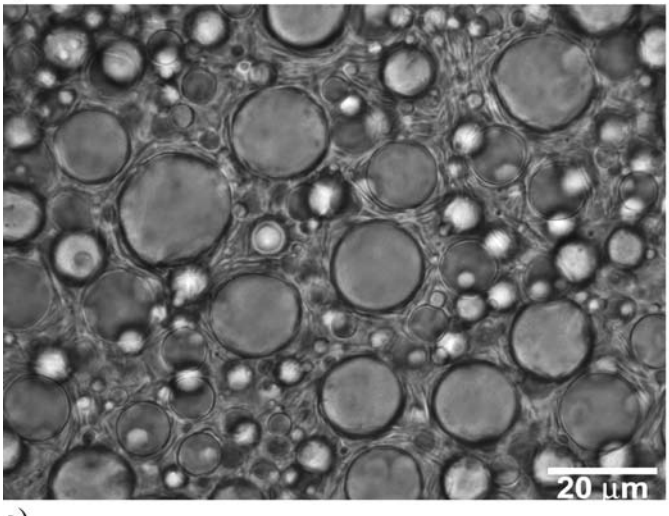

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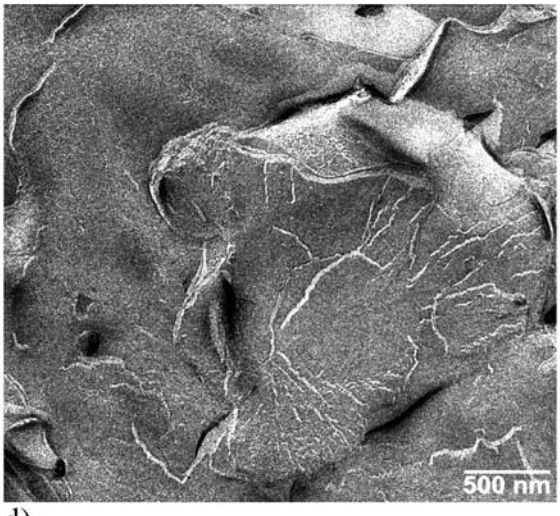

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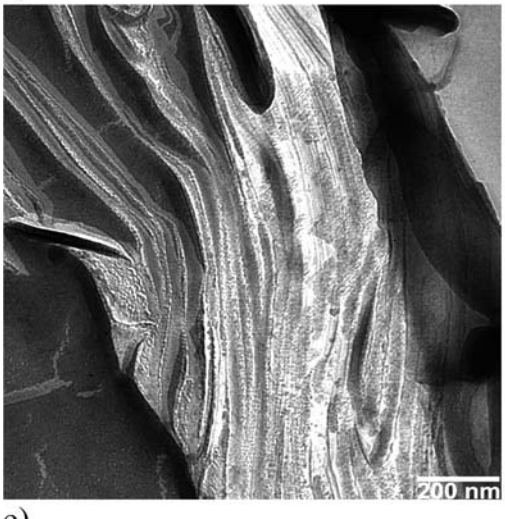

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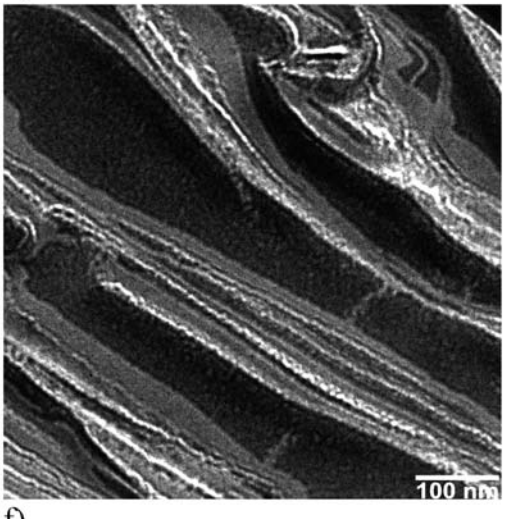
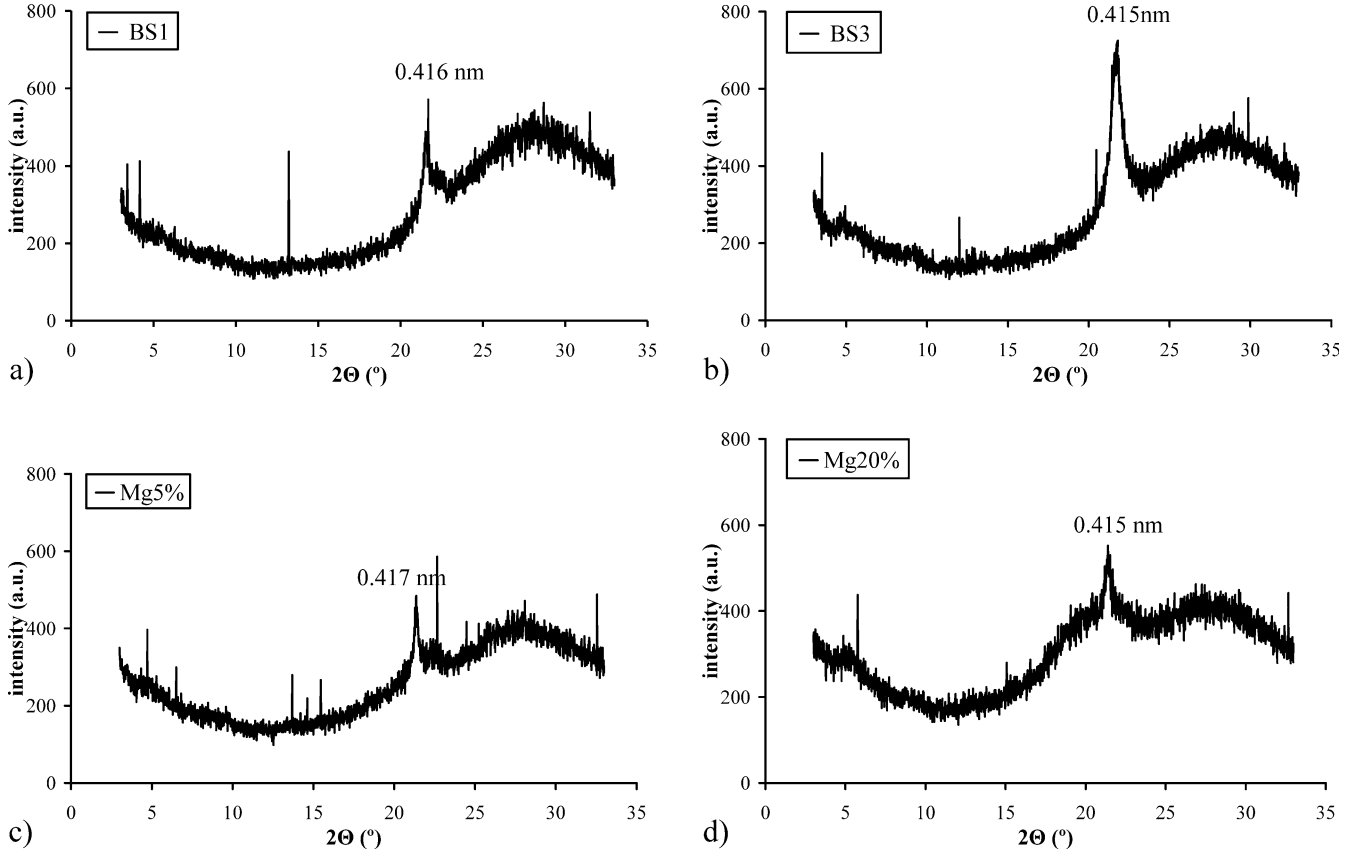


f)

ing, i.e. on hydrocarbons chain conformation [19]. It is known that the diffraction characteristics of hydrocarbon chains in liquid state are the occurrence of a diffuse halo in the wide-angle region with its centre at 0.45 nm and additional patterns within the small-angle region [19, 24]. In contrast to the liquid crystalline phase, the α-crystalline gel phase (L_β) is characterized by a single sharp reflection at 0.415–0.42 nm [19, 25].

Figure 3a–d depicts the WAXD patterns of binary systems BS1 and BS3, with 8.75% and 20% of emulsifier, respectively, as well as of the creams with 5% (Mg5%) and 20% (Mg20%) of the oil and the same emulsifier/water ratio as BS1 (8.75:91.25, i.e. 1:10.43). Single sharp reflections between 0.415 and 0.42 were detected in all investigated samples, confirming the predominant presence of α-crystalline gel phase within the system. Within the gel phase, the bilayers have rigid, mostly all-trans ordered alkyl chains (just with rotational freedom), with the hexagonal mode of chains packaging and normal or tilted orientation to the layer planes [19, 22, 25]. In contrast, the water fixed between the gel lamellae is in a "liquid like" state, with pronounced rotational and translational mobility [19]. It seems reasonable to assume that glucopyranoside part of the surfactant is directed to the interlamellarly fixed water with monosaccharide hydroxyl groups capable of hydration and swelling. Alkyl chains of surfactants are placed between the alkyl chains of fatty alcohols, in their extended forms, producing the lipophilic bilayer. In comparison to the binary systems, creams are also with sharp WAXD reflections (Fig. 3c,d), although in sample Mg20% the pattern reveals the possible overlapping of the diffuse band at 0.45 nm by sharp interference at 0.415 nm. This could mean that alongside with ordered lamellar gel the Mg20% cream sample is stabilized also by phase of liquid crystals organized in form of layers surrounding the oil droplets. Namely, it is possible that during emulsification a certain insertion of alkyl chains of medium chain triglycerides (C_8–C_{12}), from the oil phase, between the alkyl chains of mixed surfactant/fatty alcohols crystals occurs, creating the new-disordered liquid crystalline structure of lamellar type, placed either at the border of oil droplets or randomly widespread toward the continuous phase, together with previously described gel phase. This, presumably, occurs in all creams but it is more detectable in samples with higher oil content.

Fig. 3a–d WAXD profiles of binary systems: **a** BS1 with water content 91.25%; **b** BS3 with water content 78.27%; **c** cream with 5% oil phase; **d** cream with 20% oil phase



To elaborate the colloidal structure of the investigated systems in more detail SAXD measurements were performed in the following course of investigation.

Considering the analysis of SAXD patterns, the dependence of the interlayer distance on the water concentration in binary systems (Fig. 4a,b) as well as on oil percentage in cream samples (Fig. 4c) could be derived from the first-order interference. In binary systems the repeated distance slightly increases with the emulsifier concentration from 5.77 nm in the sample with 8.75% of emulsifier (BS1) up to 6.14 nm for the sample with 40% of emulsifier (BS6). This is in apparent disagreement with results of SAXD measurements performed with some traditional non-ionic surfactants [9, 22, 31], although in the case of long chain alkyl glucopyranosides no distinguished correlation between interlayer spacing and water content is observed [18]. Discrepancy obtained could result from varying ratios of the hydrophilic alkyl glucopyranosides to the more lipophilic cetearyl alcohol within the fully hydrated α-crystalline gel phase consisting of both surfactant types. Due to their higher hydrophilicity alkyl glucopyranosides may dissolve from the combined gel phase with increasing water contents. It is interesting to note that in binary systems with 37% and 40% of emulsifier a clear interference at 9.84 nm and 9.14 nm, respectively, appears (Fig. 4a,b) differing these samples in that way from the other binary systems. This interference may be due to a fully hydrated lamellar liquid crystals consisting of mainly alkyl glucopyranosides which gradually dissolve at increasing water concentrations.

Otherwise, within the first order peak a shoulder was recorded at 5.02–5.14 nm (Fig. 4a,b) in all examined samples that corresponds to the cetearyl semi-hydrates within the lipophilic gel phase of o/w creams described by Junginger [5, 6, 22]. Having in mind this result and the producers' designated composition of the mixed emulsifier, which was at least 12% of Cetearyl glucoside and 42% of cetostearyl alcohol [13], we propose that, in addition to hydrophilic gel, the lipophilic gel phase comprised of surplus of cetostearyl alcohol in form of semi-hydrates, also exists within the systems, forming together the complex gel matrix. That means that, along with the bulk and interlamellar water from hydrophilic gel phase, some water could be entrapped within this cetostearyl alcohol gel network [5, 6].

In contrast to the Eccleston findings obtained with ionic mixed emulsifier [22], in our study the addition of the oil phase produced the expanding of the long spacing in all cream samples (Fig. 4c). The greatest enlargement is observed upon the addition of 5% of the oil phase (Mg5%, 7.85 nm), whereas in the rest of the creams the increase was smaller and almost the constant. This increase could be connected with the limited solubilization of the oil phase within the mixed crystals bilayers from gel network, causing certain structural alterations within the hydrocarbon core and possible bilayer extension. Namely, we assume that the bulk of the oil phase is dispersed in form of oil droplets, whereas some oil, together with mixed crystals of surfactant and fatty alcohols, provokes formation of lamellar liquid crystalline layers around the droplets and the third part is incorporated in the manner which could provide an additional extending of the hydrophilic gel lipid bilayers as well as the additional hydration and swelling through the hydrogen bonding of water molecules by ester functional group originated from triglycerides. The latter processes could elicit the repeated distance increase. The moderate decrease of repeated distances recorded in rest of the creams compared to Mg5% could be explained by supersaturation phenomena. Anyway, the repeated distances measured by SAXD were in good agreement to those found by TEM.

In the formation of the gel phase different swelling mechanisms are involved, depending on type of the surfactant, the ionic or the non-ionic one. Therefore, the gel phase could be stabilized predominantly either by electrostatic or steric repulsions. In commonly used PEG non-ionic mixed emulsifiers, the swelling is due to hydration of the polyoxyethylene (POE) chains which are proposed to be oriented into the interlamellarly fixed water in their "zig-zag form" [4, 5, 6]. We suggest that stabilisation of the glucolipid non-ionic gel phase is, essentially, due to hydrogen bonding of water to the monosaccharide hydroxyl moieties, causing the specific conformation, and could be assigned like steric hindrance. This gel phase gives the structured continuous phase with increased viscosity, thus contributing to the oil droplets immobilisation and both, the flocculation and the coalescence are inhibited [22].

DSC and TGA analysis

The DSC thermal behaviour of the pure emulsifier, binary systems with 8.75% (BS1) and 20% of emulsifier (BS3) and cream with the 20% of oil (Mg20%) is shown in Fig. 5a–d.

The pure emulsifier had two marked peaks (the second is split) with total enthalpies of 48.2 mJ/mg and 128.1 mJ/mg, respectively (Fig. 5a). The first peak may correspond to the free cetostearyl alcohol transition (from crystalline to α-crystalline), whereas the second, the complex one, could be from the melting of the surfactant/cetearyl alcohol mixture. This is in agreement with the literature data indicating that cetostearyl alcohol possesses two melting peaks at 36.5 °C (crystalline to α-crystalline transformation) and 49.5 °C (α-form to melt transition) [7]. Within the binary system with 20% of emulsifier (BS3) the successive shift of second peak maxima to the higher temperature has appeared (Fig. 5b), alongside with decrease in total enthalpy.

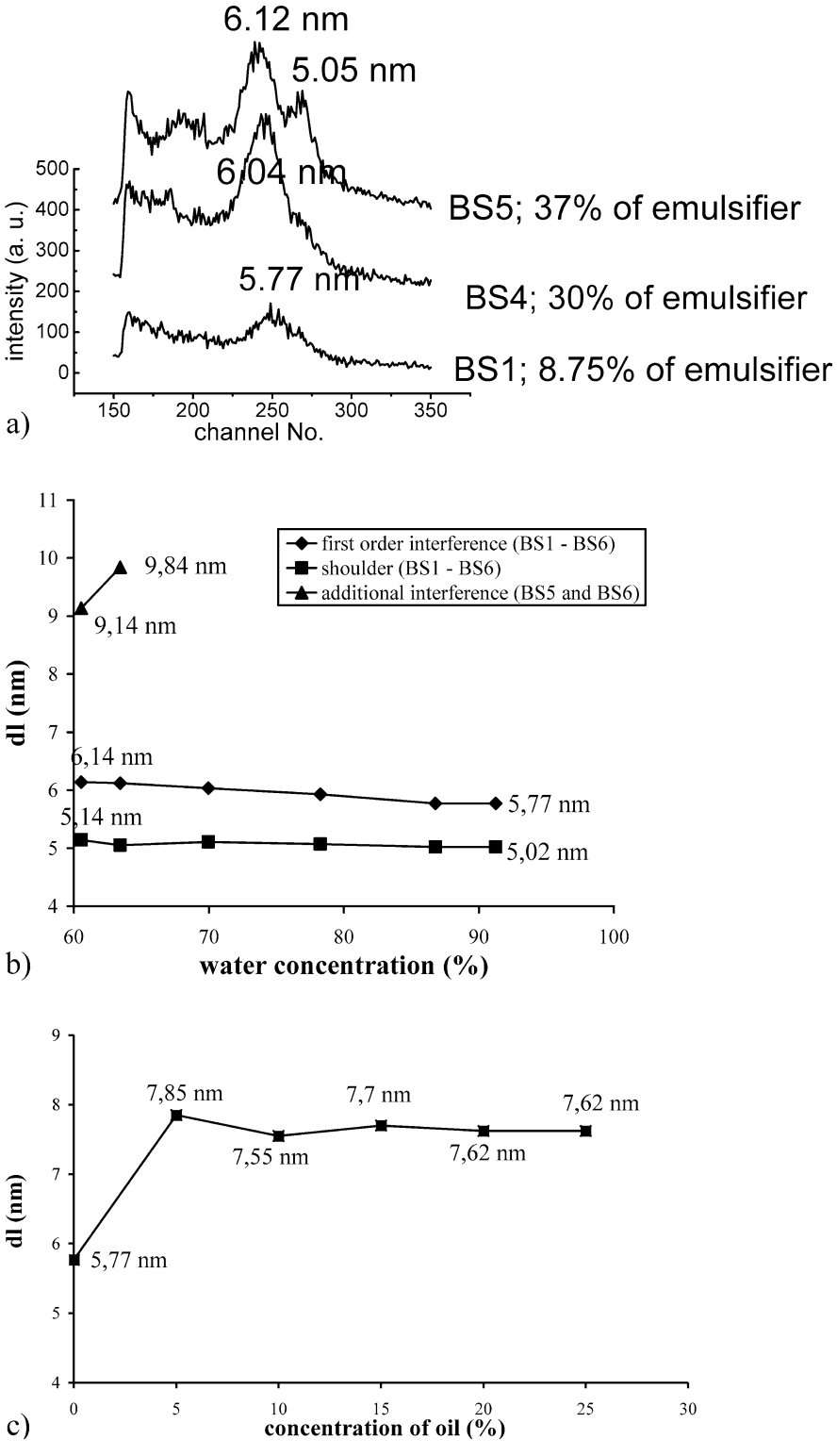


Fig. 4 **a** SAXD patterns of binary systems BS1 (8.75% of emulsifier), BS4 (30% of emulsifier) and BS5 (37% of emulsifier). **b** Long spacings vs water concentration in binary systems (BS1–BS6). **c** Long spacings vs oil concentration in cream samples (Mg5%–Mg25%) with the same emulsifier/water ratio (1:10.43)

The similar trend in enthalpies change was recorded in sample of BS1 and cream with 20% of oil (Mg20%) (Fig. 5c,d), though the peak temperatures did not alter significantly. The incorporation of the water between the lipid bilayers could modify the phase transition behaviour; thus the new structures are characterized with higher peak temperatures than pure emulsifier. This is in accordance with literature describing higher

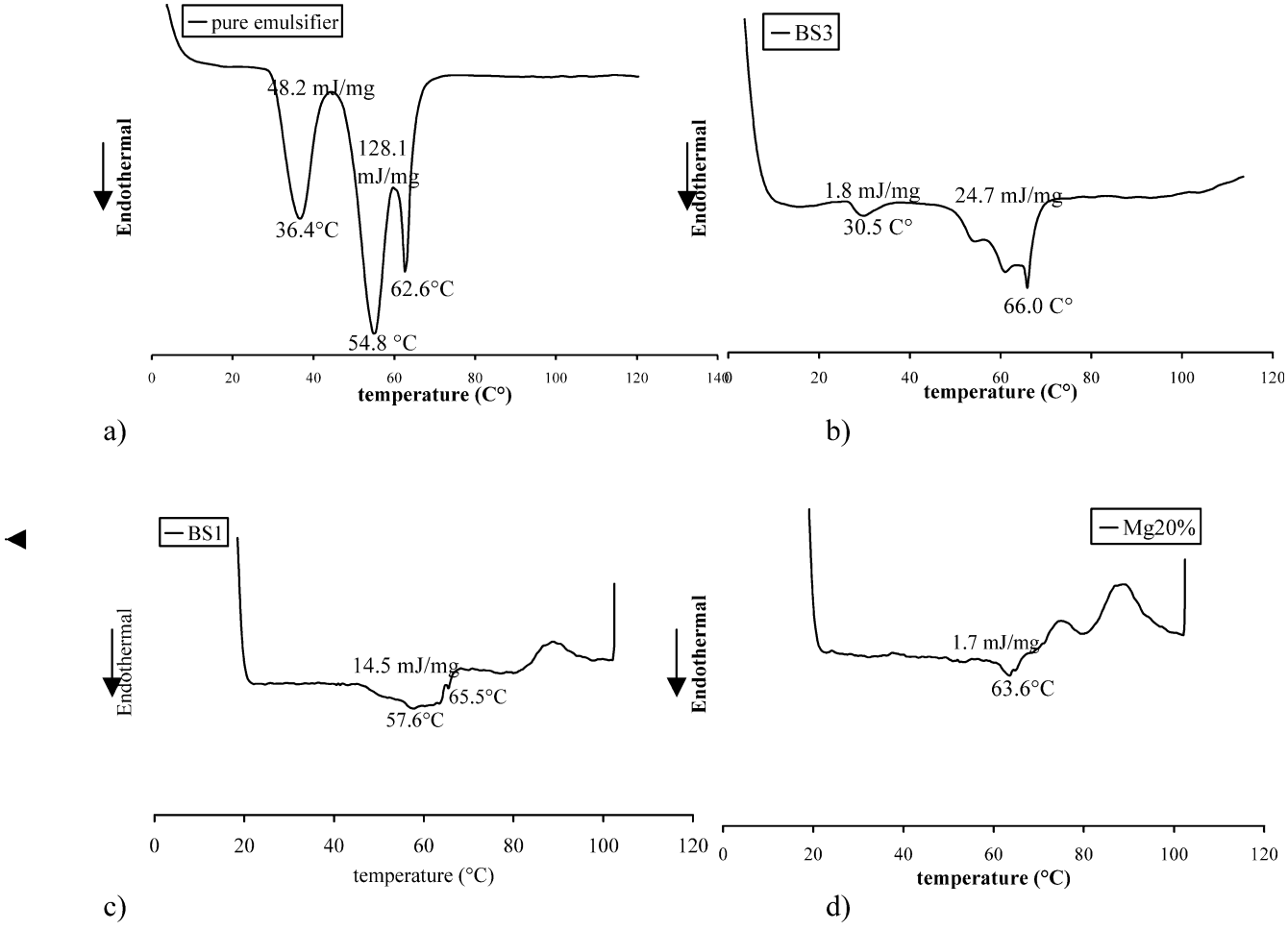


Fig. 5a–d DSC profiles: **a** pure emulsifier; **b** binary systems with 78.27% (BS3) of water; **c** binary systems with 91.25% (BS1) of water; **d** cream (Mg20%) with the emulsifier/water ratio 1:10.43 and 20% of oil phase

melting point of hydrated α-phase vs dehydrated one [1, 4].

For the gel phase a large transition heat on melting has been attributed, typically 25%–75% of the crystalline surfactant melting transition [19]. Consequently, it seems that, in addition to the complex crystalline gel phase (PLM, OLM, TEM, WAXD), cream samples are also stabilized by the bilayers of lamellar liquid crystals surrounding the dispersed oil droplets. From the comparison of the enthalpies of binary system BS1 and cream sample Mg20% it is obvious that phase transition of the BS1 takes about eight times more energy than cream. As was said before, it seems that insertion of medium alkyl chains from oil within the mixed lipid bilayers influences not only their swelling behaviour but also alters the mobility of other molecules causing the shift from ordered crystalline toward the liquid crystalline structures. It sounds reasonable that layered liquid crystalline structures are formed at oil droplets border, whereas the complex crystalline gel dominates within the continual phase.

From thermogravimetric analysis the total weight loss of the samples (BS1, Mg5%–Mg25%) is obtained (Table 1), as well as the derivative curves (DTGA-curves of BS1 and Mg20%, Fig. 6a,b). It is known that the TGA characterisation could be useful in investigation of water distribution within the creams [6, 7, 8, 26].

Table 1 shows that total weight loss is in accordance with the total amount of water within the systems (Karl-Fisher titration). The specified temperature ranges are chosen following the DTGA-curves in order to differentiate types of the water incorporated (Table 1, results are given as mean ± standard deviation). In binary system BS1 the evaporation rate of the bulk water increases up to 43.3 °C; thus, about 20% of total water is lost until 50 °C is reached. Percentages of bulk water ranging from 20 to 26% are found within all cream samples, but the lowest is in samples with 20% of oil phase (Mg20%, Table 1, 19.62%). At a temperature of 53–54 °C the DTGA-curve (sample BS1, Fig. 6a) showed a point of inflection. After that temperature the evaporation rate increases again, but in a different manner, dependent on

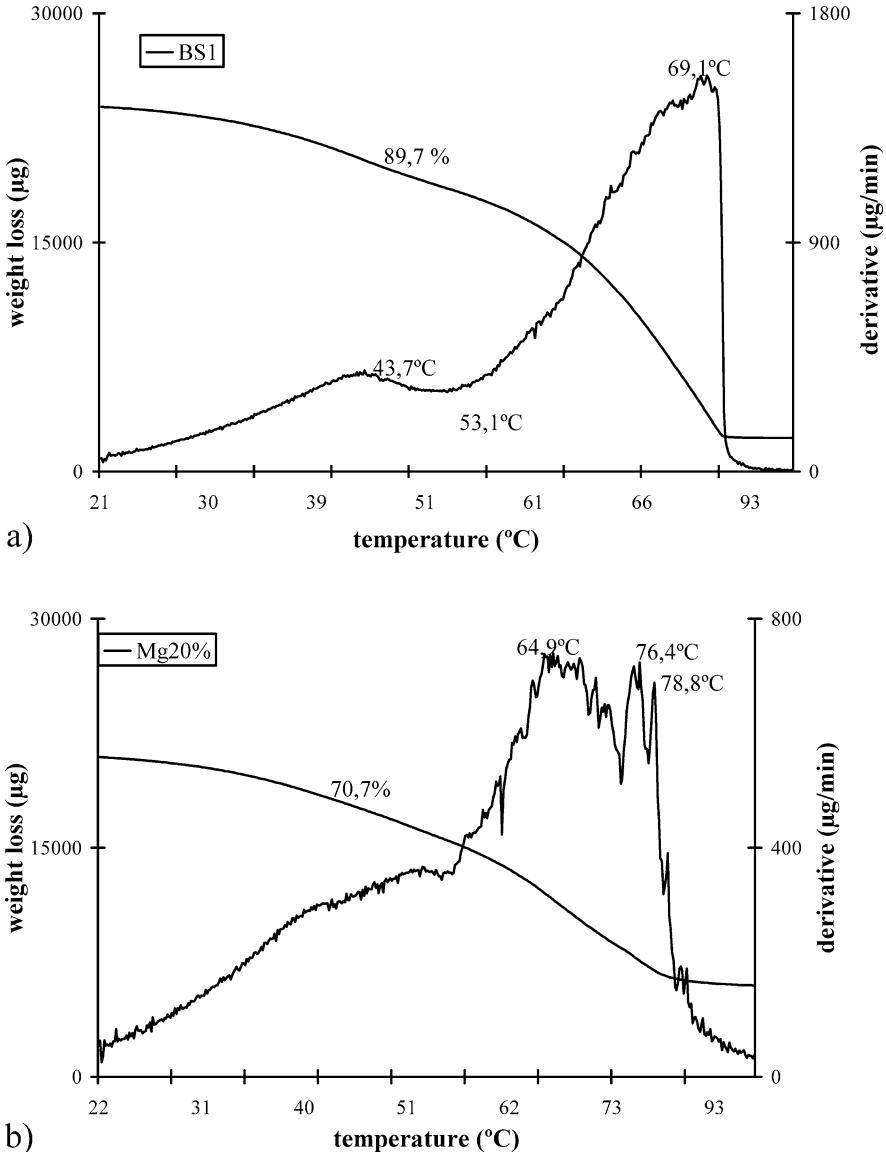


Fig. 6a,b DTGA-curve profiles: **a** binary system with 1:10.43 emulsifier/water ratio (BS1); **b** corresponding cream with 20% of oil (Mg20%)

samples composition. Generally, the strong increase of the evaporation rate between 50 °C and 70 °C could be, at least partially, due to the melting of cetostearyl alcohol semi-hydrates (lipophilic gel phase) and loss of the water entrapped mechanically within. Although the melting of hydrophilic gel phase begins also within this temperature range (but in a minority), it ends at temperatures near to 92 °C. For that reason, the percentage of water evaporated during the second stage gradually decreased from 64.64% in binary system BS1 to the 33.76% in cream with 20% of oil (Table 1), whilst during the third stage (70–100 °C) the same cream

Table 1 Percentage weight loss values over the specified temperature ranges for binary system (BS1) and cream samples with different amount of oil (5–25%); results are presented as mean ± standard deviation

[a]Determined by Karl-Fisher titration

Sample	Amount of water[a] (%)	Total weight loss (%)	20–50 °C (%)	50–70 °C (%)	70–100 °C (%)
BS1	91.25 ± 3.77	89.70 ± 3.45	20.08 ± 1.12	64.64 ± 3.89	4.98 ± 1.05
Mg5%	85.00 ± 2.97	83.4 ± 2.89	24.10 ± 1.34	58.43 ± 3.87	0.87 ± 0.16
Mg10%	80.35 ± 2.65	80.2 ± 2.46	26.30 ± 2.23	51.69 ± 2.58	2.21 ± 0.25
Mg15%	75.76 ± 3.02	74.50 ± 2.37	24.34 ± 2.10	46.25 ± 3.21	3.91 ± 0.89
Mg20%	71.26 ± 2.32	70.70 ± 2.21	19.62 ± 1.29	33.06 ± 2.17	18.02 ± 0.83
Mg25%	67.44 ± 3.21	66.70 ± 2.01	22.92 ± 2.85	35.76 ± 2.13	8.02 ± 1.34

Mg20% had the largest water loss (18.02%). This finding indicates that about two third of total water within the cream sample Mg20% is entrapped, either within the lipophilic gel phase or as water fixed between the lamellae (hydrophilic gel; ''depot'' water). Accordingly, a significant skin hydration potential could be expected from that sample.

Table 2 Flow parameters of binary system (1:10.43, BS1) and cream samples with increasing content of the oil phase (5–25%)

Sample	Yield value (Pa)	ηmin (Pas) at 1.3 s^{-1}	ηmax (Pas) at 200 s^{-1}
BS1	8.35 ± 1.27	0.29 ± 0.11	14.44 ± 1.76
Mg5%	7.69 ± 1.15	0.52 ± 0.21	10.40 ± 1.72
Mg10%	15.00 ± 1.47	0.45 ± 0.10	18.00 ± 1.72
Mg15%	16.13 ± 1.29	0.48 ± 0.09	23.00 ± 1.87
Mg20%	24.38 ± 1.36	0.59 ± 0.12	28.20 ± 2.05
Mg25%	14.63 ± 1.72	0.53 ± 0.17	19.80 ± 1.30

Rheological measurements

All samples exhibited ''shear-thinning'' pseudoplastic flow behaviour (Table 2, Fig. 7a), with slightly (sample BS1) to moderately pronounced thixotropy (Mg20%), increasing linearly with oil percentage. Since the samples were produced using the standard procedure and investigated a week after preparation, different aging and shear stress during sample preparation could be

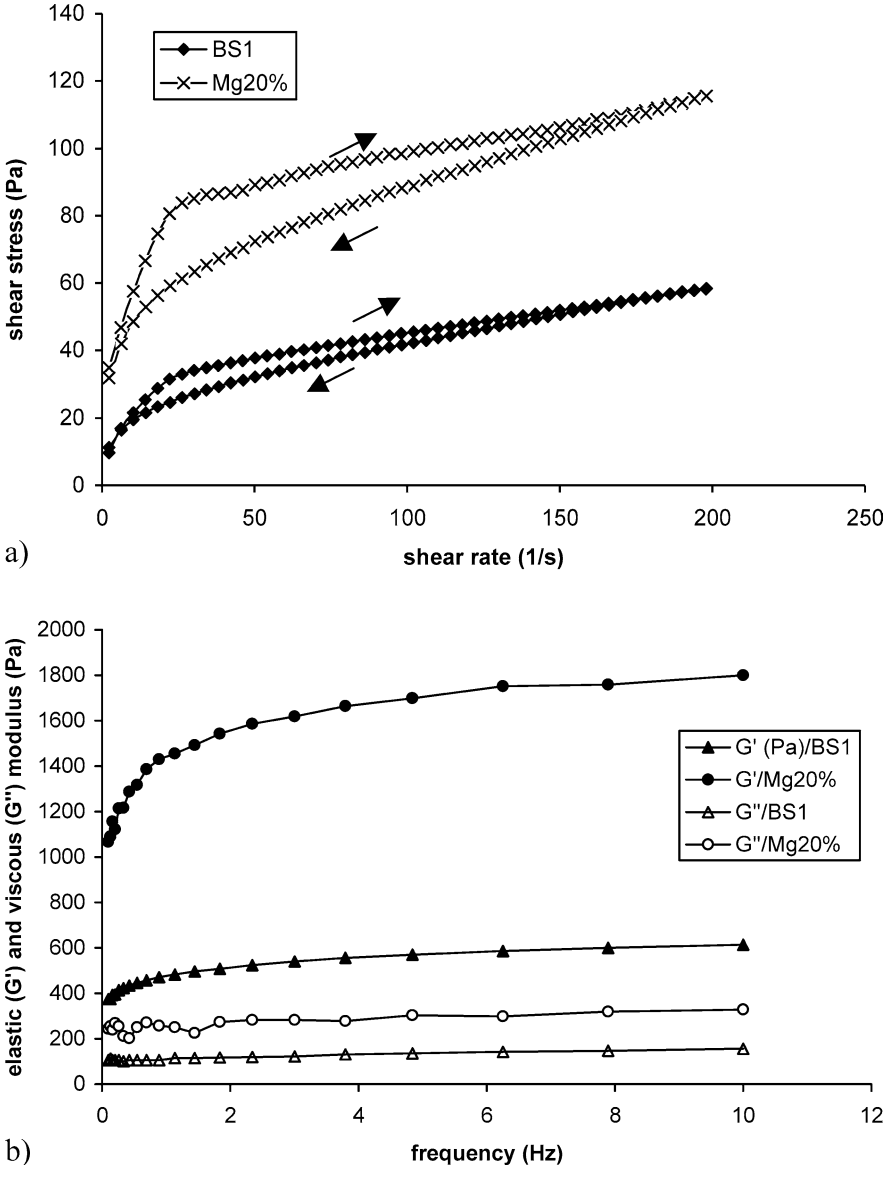


Fig. 7a Flow behaviour of binary system with emulsifier/water ratio 1:10.43 (BS1) and corresponding cream with 20% of oil (Mg20%). **b** Elastic and viscous modulus of the same samples dependent on frequency (0.1–10 Hz)

Table 3 Oscillatory parameters at the frequency of 1 Hz of the binary system (BS1) and cream samples with increasing oil concentration (5–25%)

Sample	δ (°)	G′ (Pa)	G″ (Pa)
BS1	13.3 ± 0.5	484.2 ± 19.2	114.3 ± 9.1
Mg5%	14.6 ± 1.2	1140.7 ± 55.3	296.7 ± 16.3
Mg10%	11.7 ± 0.9	1053.7 ± 45.5	218.3 ± 13.7
Mg15%	10.4 ± 0.8	1021.7 ± 47.2	188.7 ± 11.3
Mg20%	9.8 ± 0.7	1460.0 ± 71.5	250.3 ± 15.4
Mg25%	10.1 ± 1.1	1340.7 ± 75.7	239.2 ± 15.1

excluded as potential reason of different flow behaviour profiles. Obtained shear-thinning behaviour is desirable property in creams, since they should be ''thin'' during the application and ''thick'' otherwise [27]. Yield value, minimal and maximal apparent viscosity were evaluated (Table 2). The highest yield value and maximal apparent viscosity, 24.38 ± 1.36 Pa and 28.20 ± 2.05 Pas (D 200 1/s), respectively, are recorded in cream with 20% of oil (Mg20%). The yield stress is a measure of viscoelastic properties of the system and good indicator of the physical stability of semisolids [28].

Semisolids, such as creams, combine the viscous (liquid) and the elastic (solid) properties at the same time. Analysis of viscoelastic materials is designed not to destroy the structure, so the measurements could provide information on the intermolecular and inter-particle forces within the system [29].

In our study the linear viscoelastic region was determined first. For most of the samples it was between 3 Pa and 8 Pa; thus the stress value of 6 Pa was chosen for the subsequent oscillatory experiments.

In Table 3 the phase angle (δ), elastic-storage (G′) and viscous-loss (G″) modulus are shown. All samples had phase angle lower than 15°, pointing to the pronounced elastic over viscous component. This finding correlates well with the measured yield values. In all samples elastic modulus was significantly higher than viscous component, from around fourfold in a binary system (BS1) to about sixfold in a cream sample (Mg20%), throughout the whole frequency range (0.1–10 Hz, Table 3). Dependence of storage and loss modulus on the frequency is given in Fig. 7b. While the storage modulus has a weak dependence on applied frequency in sample Mg20%, the loss modulus shows certain fluctuations at lower frequencies. According to some authors this behaviour is attributed to the lamellar mesophase [9, 30, 31].

The highest yield value and elastic modulus in the sample with 20% of oil could be a sign of the strongest gel network within the continual phase of cream as well as of uniform packaging of the oil droplets. This is in line with the finding of TG analysis. Moreover, this sample exhibited the best applicative and aesthetic properties compared to the others.

Conclusion

Alkylpolyglucoside non-ionic emulsifier (Cetearyl glucoside&Cetearyl Alcohol) enables the stabilization of o/w creams by synergistic effects of viscoelastic hydrophilic and lipophilic gel networks as well as by lamellar liquid crystalline bilayers surrounding the oil droplets. The hydrophilic gel phase is of lamellar type and consists of mixed cetearyl glucoside/cetearyl alcohol crystalline bilayers entrapping the water by hydrogen bonding. Therefore, it could be assumed that gel phase is stabilized by steric hindrance. Addition of the oil into the binary system influences both the bilayer thickness and the amount of water interlamellarly fixed. This could point at certain solubilization potential of the alkylpolyglucoside mixed emulsifier and possibility of managing the hydration potential of creams by the oil incorporation up to level allowing the sample physical stability. Thus, the specific partition of water and its evaporation rate could be a reason for the significant barrier improvement and moisturisation properties of cream based on glucolipid mixed emulsifier. Moreover, the uniform packaging of the oil droplets affects the cream rheological performance and aesthetics.In this study, the cream with emulsifier/water ratio 1:10.43 and 20% of medium chain triglycerides, as oil phase, is chosen as an optimal model formulation. The coming question is how the water incorporation mode governs the drug bioavailability, particularly in treatment of diseased skin.

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