TS_TS11735 – 27.3.02/druckhaus köthen

M. J. L. Castro, J. Kovensky and A. Fernández Cirelli, Buenos Aires, Argentina

Synergistic Effects of Alkyl Glucosides and Nonionic Sugar-Based Gemini Surfactants

The interfacial properties of a new family of nonionic surfactants derived from alkyl glucosides were studied. The physico-chemical parameters of these dimeric compounds were compared with those of their monomeric counterparts. Synergistic effects were found for *C*-12/*C*-14 alkyl glucosides and for *C*-12/*C*-14 gemini derived compounds.

Synergistische Effekte von Alkylglucosiden und nichtionischen Geminitensiden auf Zuckerbasis. In dieser Arbeit werden Grenzflächeneigenschaften einer neuen Klasse von nichtionischen Tensiden aus Alkylglucosiden untersucht. Die physikalisch-chemischen Eigenschaften dieser dimeren Verbindungen wurden mit denen der entsprechenden monomeren Verbindungen verglichen. Für *C*-12/*C*-14-Alkylglucoside und *C*-12/*C*14 Geminitenside konnten synergistische Effekte gefunden werden.

1 Introduction

Alkyl glycosides are biosynthesized as glycolipids by microorganisms from rhamnose, sophorose and trehalose. They are currently prepared in industry from long-chain alcohols and carbohydrates. As these compounds display surfactant properties, they are gradually replacing other known nonionic surfactants in industry, owing to their excellent biodegradability and the absence of toxic effects. Food elaboration, polymer manufacture, and solubilization of biological membranes are some of the wide spectrum of applications of alkyl glycosides.

The carbohydrate polar head has multiple hydroxyl groups with defined orientation, allowing the formation of strong cooperative hydrogen bonds between the surfactant molecules. This fact, together with the hydrophobic interaction between the long hydrocarbon chains, lead to spontaneous association in water [1].

In recent years, a new class of surfactants called gemini, carrying two hydrophobic chains and two hydrophilic groups connected by a spacer, has been prepared. These dimeric compounds showed improved surfactant properties when compared to monomeric surfactants [2].

The interesting properties of gemini surfactants prompted us to design and synthesize a new type of amphiphilic molecule comprising two alkyl glucosides linked through a spacer [3]. The use of ecologically safe surfactants such as alkyl glycosides as monomers is mainly because of their biodegradability, and the fact that they can be easily prepared from renewable raw materials such as carbohydrates and long-hydrocarbon-chain alcohols.

Two molecules of alkyl α-D-glucopyranoside were connected through ester linkages. Selective protection/deprotection sequences led to the synthesis of gemini surfactants linked through *O*-6 of the sugar moieties by succinic acid as the spacer. The synthesized dimers constitute a new family of gemini surfactants. We have previously prepared and analyzed the butyl glucoside family, and the results showed that the surfactant properties of the *C*-4 dimers are better than those of the monomers, specially in the values for critical micellar concentration (c.m.c.) [3].

Long-chain alcohols are readily available from coconut and palm kernel oils , and the commercial mixture of dodecyl and tetradecyl alcohols is one of the most widely distributed in the market. Taking into account the fact that the alkyl a-glucoside prepared from this mixture displays better surfactant properties than the butyl glucoside [4], we decided to prepare the corresponding dimers [5].

We now report on the interfacial properties of the *C*-12 and *C*-14 dimers in comparison with their monomers. The following properties were analyzed: c.m.c.; $\gamma_{c.m.c.}$, the surface tension at c.m.c.; Γ_m, the surface excess concentration at surface saturation, a useful measure of the effectiveness of adsorption; a_m^s, the area per molecule at the interface at surface saturation; ΔG°_{mic}, the standard free energy of micellization; ΔG°_{ads}, the standard free energy of adsorption; pC_{20}, the negative logarithm of the bulk liquid phase concentration of surfactant required to depress the surface tension of the solvent by 20 mN/m, a good measure of the efficiency of the adsorption of the surfactant; and the c.m.c./C_{20} ratio, a convenient way of measuring the relative effects of structural factors on the micellization and adsorption processes.

The aim of the present paper is to compare the relative efficiency of alkyl glycosides and gemini surfactants prepared from pure long-chain alcohols with those synthesized using commercial mixtures.

2 Experimental

2.1 Materials

Dodecyl-α-D-glucopyranoside (**1**), and tetradecyl-α-D-glucopyranoside (**2**), and dodecyl/tetradecyl-α-D-glucopyranoside (**5**), were synthesized from glucose and purified as previously described for *n*-butyl glucosides [3a, 5]. 1,4-bis-[6-*O*-(*n*-dodecyl-α-D-glucopyranoside)] succinate (**3**), 1,4-bis-[6-*O*-(*n*-tetradecyl-α-D-glucopyranoside)] succinate (**4**), and compound **6** were prepared as described.

2.2 Methods

Determination of interfacial properties

Air-water surface tensions were measured at 25 °C in a specially adapted tensiometer based on the bubble presure method [6]. Calibration was performed against a range of standard liquids; excellent agreement with the literature values was found [7]. Critical micellar concentrations (c.m.c.) were determined by extrapolation of surface tension vs. concentration curves. All compounds showed the typical graphs,

TS_TS11735 – 27.3.02/druckhaus köthen

with an abrupt change in slope at the zone corresponding to c.m.c.

Other interfacial properties were calculated according to known methods [8]. For example, ΔG°_{ads} and ΔG°_{mic} were calculated using equations 1 and 2 respectively

$$\Delta G^0_{ad} = -\frac{RT \ln C_\pi}{55,5} - \pi a^s_m \; (1) \qquad \Delta G^0_{mic} = RT \ln\left(\frac{c.m.c.}{55,5}\right) \; (2)$$

where π (= $\gamma_o - \gamma$) is the surface pressure in the region of surface saturation (that is, where $\Gamma = \Gamma_o$ and the molar area of the surfactant $a^s = a^s_m$), and C_π is the molar concentration of surfactant in the aqueous phase at a surface pressure π.

3 Results and discussion

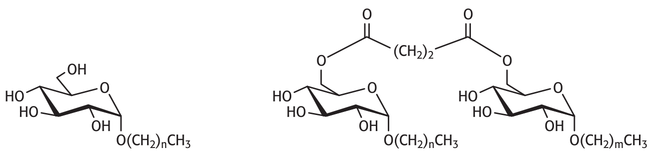
3.1 Interfacial properties of the alkyl glucosides and of the gemini compounds derived from them

The interfacial properties of dodecyl-α-D-glucopyranoside (**1**), tetradecyl-α-D-glucopyranoside (**2**), and those of the new dimers 1,4-bis-[6-*O*-(*n*-dodecyl-α-D-glucopyranoside)] succinate (**3**), and 1,4-bis-[6-*O*-(*n*-tetradecyl-α-D-glucopyranoside)] succinate (**4**, Figure 1) are shown in Table 1. The dimers of *C*-12 (**3**) and *C*-14 (**4**) displayed higher c.m.c. values than the starting monomer, and are therefore less efficient at forming micelles. This behaviour would be related to self-coiling [9, 10] of the alkyl chains and to the formation of sub-micellar aggregates [11].

The area per molecule at the interface at surface saturation a^s_m was calculated and is also shown in Table 1. In general, for both the known ionic and nonionic surfactants present, the value of the surface area per molecule, a^s_m, appears to be determined by the area occupied by the hydrated hydrophilic group rather than by the hydrophilic group, because the chains in the usual ionic or nonionic surfactants with the hydrophilic groups at one end of the molecule do not lie flat at the interface either but are somewhat tilted with respect to the interface. If a second hydrophilic head is present in the molecule, the a^s_m value increases [12]. The a^s_m values of the dimers were up to two times higher than those of the monomers, which is in accordance with previous studies of ionic gemini surfactants where a^s_m is larger for gemini surfactants.

The c.m.c. values of the monomers decrease with the alkyl chain length, because the c.m.c. for the tetradecyl-α-D-glucopyranoside **2** is three times lower than that of dodecyl-α-D-glucopyranoside **1**. On the other hand, this behaviour is not observed for the dimeric compounds which show closer c.m.c. values, and therefore for this family it is difficult to correlate the c.m.c. or log c.m.c. of the gemini compounds with the alkyl chain length.

A higher c.m.c./C_{20} ratio indicates that the hydrophobic groups are less suitably oriented to accommodate themselves in the internal part of the micelles. In general, for gemini surfactants, adsorption onto the surface of aqueous solutions is preferred over the formation of micelles, leading to c.m.c./C_{20} ratios higher than those of the monomers. In the *C*-12 and *C*-14 gemini compounds prepared, the opposite results were obtained. As can be seen from Table 1, the c.m.c./C_{20} ratios of both dimers (compounds **3** and **4**) are *lower* than those of the corresponding monomers **1** and **2**, respectively. In spite of their higher c.m.c. values, the reduction in c.m.c./C_{20} ratios observed for the dimers indicates that the gemini compounds prepared are about one order of magnitude more efficient at reducing the surface tension than the monomers.



1 n = 11
2 n = 13
5 n = 11 and n = 13

3 n = m = 11
4 n = m = 13
6 n = m = 11 and n = 11, m = 13

Figure 1 Structures of monomers and dimers of alkyl glucosides **1**–**6**

3.2 Synergistic effects of alkyl glucosides

The commercial material readily accessible (medium-chain alcohols) is in fact a mixture of dodecyl and tetradecyl linear alcohols in a 3 : 1 ratio. From this starting material we prepared the corresponding alkyl glucoside (compound **5**, Figure 1). The ^{1}H and ^{13}C NMR spectra and the mass spectra showed that the same 3 : 1 ratio of *C*-12 and *C*-14 alcohols is present in the glucoside. The interfacial properties of this compound are shown in Table 1. It is clear that the dodecyl/tetradecyl-α-D-glucopyranoside **5** obtained from the commercial mixture exhibits improved properties with regard to almost any of the different parameters displayed.

The c.m.c. value of **5** is not intermediate, but lower than that of both pure *C*-12 and *C*-14 glucosides (compounds **1** and **2**). Solubilization, that is the dissolving of normally water-insoluble organic compounds into aqueous solutions of surfactants, occurs only above their c.m.c., where micelles are present. In consequence, the synergistic effect will operate for solubilization, because the lower c.m.c. value of the mixture indicates that it is a more efficient solubilizer than any of its pure components.

It is interesting to note that although both dodecyl and tetradecyl glucosides **1** and **2** have identical a^s_m values, the 3 : 1 mixture (compound **5**) shows different values.

Compound	Spacer	Linked through	c.m.c. (mM)	γ_{CMC} (mN/m)	Γ_m (mol/cm$^2 \times 10^{10}$)	$a_m{}^s$ (Å^2)	ΔG^0_{mic} (kJ/mol)	ΔG^0_{ads} (kJ/mol)	pC_{20}	c.m.c./C_{20}	HLB
1 (n: 12)	–	–	2.3 ± 0.3	36.9	3.9	43 ± 4	–25.0	–32.0	3.9	1.8	11.0
2 (n: 14)	–	–	0.8 ± 0.2	48.8	3.9	43 ± 4	–27.7	–33.1	3.2	1.1	10.2
3 (n: 12)	Succinyl	*O*-6	3.4 ± 0.3	46.7	2.1	79 ± 15	–24.0	–34.9	2.6	1.3	11.6
4 (n: 14)	Succinyl	*O*-6	2.6 ± 0.3	54.4	1.8	92 ± 14	–24.7	–33.3	2.5	0.8	10.8
5 (n: 12/14)	–	–	0.4 ± 0.2	30.6	4.4	38 ± 4	–29.2	–38.1	3.9	3.5	10.7
6 (n: 12/14)	Succinyl	*O*-6	1.3 ± 0.3	41.7	2.2	76 ± 15	–26.4	–39.9	3.3	2.5	11.4

Table 1 Interfacial properties of compounds **1**–**6**

TS_TS11735 – 27.3.02/druckhaus köthen

Both micellization and adsorption processes are favoured by the synergistic effect, as can be seen from the ΔG°_{mic} and ΔG°_{ads} values (Table 1).

The largest difference is found in the c.m.c./C_{20} ratio. The higher value for this parameter suggests that in the mixture the micellization process is less favoured than the adsorption process.

3.3 Synergistic effects of gemini compounds derived from alkyl glucosides

As before, a gemini compound linked through *O*-6 of the sugar moieties by succinic acid as the spacer was prepared from the mixed dodecyl/tetradecyl-α-D-glucopyranoside **5**. The product (compound **6**, Figure 1) was characterized by NMR spectroscopy and mass spectrometry. In the chemical ionization mass spectrum two molecular ions were detected, the major one corresponding to the linkage through the succinic spacer of two molecules of dodecyl-α-D-glucopyranoside, and the minor one to a dodecyl-α-D-glucopyranoside linked to a tetradecyl-α-D-glucopyranoside molecule. A 7 : 3 ratio between these two dimers could be estimated from the relative abundances of their respective molecular ions. No peak corresponding to a dimer composed of two molecules of the minor tetradecyl-α-D-glucopyranoside was detected. Taking into account these findings, compound **6** is not exactly a mixture of compounds **3** and **4**, but a mixture of **3** and a mixed dodecyl/tetradecyl-α-D-glucopyranoside dimer. Nevertheless, the supposition of synergistic effects still applies, because compound **6** is in fact composed of two different gemini compounds.

The interfacial properties of compound **6**, displayed in Table 1, show that its c.m.c. is lower than those of both pure C-12 and C-14 dimeric sufarctants (compounds **3** and **4**), indicating an improvement in micelle formation. The behaviour of compound **6** suggests that the mixed product would be less affected by the self-coiling effect than compounds **3** and **4**. In fact, the c.m.c. value for compound **6** (1.3) is very close to that of the structurally related gemini compound prepared from octyl-α-D-glucopyranoside (1.8) [5].

Both micellization and adsorption processes are favoured by the synergistic effect, as can be seen from the ΔG°_{mic} and ΔG°_{ads} values (Table 1), but a larger effect is observed for the adsorption process.

Again, the c.m.c./C_{20} ratio shows the most striking synergistic effect, suggesting some influence of the presence of two different alkyl chains on the micelle formation process.

On the other hand, the pC_{20} values are distinctly affected in the monomeric surfactants and the dimers. While for dodecyl/tetradecyl-α-D-glucopyranoside **5**, the pC_{20} value is identical to that for dodecyl-α-D-glucopyranoside **1**, the pC_{20} value for compound **6** is higher than those calculated for gemini compounds **3** and **4**. The mixed compound **6** has a greater efficiency to adsorb at the surface than **3** or **4** separately.

Synergistic effects have been previously reported for anionic surfactants in surface tension reduction, especially when mixed with nonionic surfactants [13]. To our knowledge, our results are the first report of synergistic effects between nonionic, sugar-based gemini surfactants. On the other hand, the results indicate that the use of the commercial mixture of these long-chain alcohols rather than pure alcohols as the starting material is more convenient for the preparation of sugar-based surfactants, not only as regards cost but also in terms of the surfactant efficiency of the products.

4 Acknowledgements

This work was carried out with the financial contribution of UBA (Universidad de Buenos Aires) and CONICET (Consejo Nacional de Investigaciones Científicas y Técnicas). M. J. L. Castro would like to thank UBA for a fellowship. J. Kovensky and A. Fernández Cirelli are research members of CONICET.

References

1. *von Rybinski, W.; Hill, K.*: Angew. Chem. Int. Ed. *37* (1998)1328.
2. (a) *Zana, R.*: Novel Surfactants Preparation, Applications, and Biodegradability, Surfactant Science Serie; Vol. 74, p 241; Holmberg, K., Eds.; Marcel Dekker, Inc., New York, 1998. (b) *Eastoe, J.; Rogueda, P.*: Langmuir *10* (1994) 4429. (c) *Eastoe, J.; Rogueda, P.*: Langmuir *12* (1996) 2701. (d) *Pestman, J. M.; Terpstra, K. R.; Stuart, M. C. A.; van Doren, H. A.; Brisson, A.; Kellogg, R. M.; Engberts, J. B. F. N.*: Langmuir *13* (1997) 6857. (e) *Duivenvoorde, F. L., Martinus, C. F.; van der Gaast, S. J.; Engberts, J. B. F. N.*: Langmuir *13* (1996) 3737. (f) *Menger, F. M.; Keiper, J. S.; Azov, V.*: Langmuir *16* (2000) 2062. (g) Menger, F. M.; Mbadugha, M. N. A.: J. Am.Chem. Soc. *123* (2001) 875. (h) *McGregor, C.; Perrin, C.; Monck, M.; Camilleri, P.; Kirby, A. J.*: J. Am. Chem. Soc. *123* (2001) 6215.
3. (a) *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: Tetrahedron Lett. *38* (1997) 3995. (b) *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: Tetrahedron *55* (1999) 12711. (c) *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: J. Carbohydr. Chem. *19* (2000) 1174. (d) *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: National Patent (Arg.) AR990196476 in progress.
4. (a) *Focher, B.; Savelli, G.; Torri, G.* Chem. Phys. Lipids *53* (1990) 141. (b) Adasch, S.; Hoffmann, B.; Milius, W.; Platz, G.; Voss, G.: Carbohydr. Res. *314* (1998) 177.
5. *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: National Patent (Arg.) AR010101084 in progress.
6. (a) *Becher, P.*: Emulsions, Theory and Practice. Litton Educational Publishing, 1965. (b) *Fainerman, V. B.; Miller, R.*: The Maximum Bubble Pressure Tensiometry. Drops and Bubbles in Interfacial Research; p 279; Möbius, D.; Miller, R., Eds.; Elsevier Science, 1998. (c) *Castro, M. J. L.; Kovensky, J.; Fernández Cirelli, A.*: J. Chem. Ed. *78* (2001) 347.
7. *Lide, D. R.*: CRC Handbook of Chemistry and Physics; pp. 6–135; CRC Press: Boca Raton, FL, 1997–1998.
8. *Rosen, M. J.*: Surfactants and Interfacial Phenomena, John Wiley, New York, 1989.
9. *Mukerjee, P.*: Adv. Colloid Interface Sci. (1967) 241.
10. (a) *Menger, F. M.; Littau, C. A.*: J. Am. Chem. Soc. *113* (1991) 1451. (b) *Menger, F. M.; Littau, C. A.*: J. Am. Chem. Soc. *115* (1993) 10083.
11. *Vold, M. J.*: J. Colloid Interface Sci. *135* (1990) 520.
12. *Schick, M. J.*: J. Colloid Sci. *17* (1962) 801.
13. *Rosen, M. J.*: Gemini Surfactants, in New Horizons, R. T. Coffey, Princeton, New Jersey, 1996.

Received: November 06, 2001

Correspondence to

Prof. Dr. Alicia Fernandéz Cirelli
Centro de Estudios Transdisciplinarios del Agua (CETA)
Facultad de Ciencias Veterinarias
Avda. Chorroarín 280
1427 Buenos Aires
Argentina
E-mail: AFCirelli@fvet.uba.ar

The authors of this paper

Professor *Alicia Fernández Cirelli* obtained her PhD in chemistry in 1972 with work on the structural characterization of fungal polysaccharides at the University of Buenos Aires. She then worked as visiting researcher at the Institut für Organische Chemie, Universität Düsseldorf, Germany in 1973. She has been a Professor at the University of Buenos Aires in the Organic Chemistry Department (FCEyN) since 1975 as well as a research member of the Argentine Research Council, CONICET, since 1983.

Her fields of work: include carbohydrates analysis and synthesis, synthesis and interfacial properties of gemini surfactants, characterization and distribution of humic substances and analysis of organic contaminants in water.

Professor *José Kovensky* obtained his PhD in Chemistry in 1992 with work on glycosaminoglycan chemistry in the Organic Chemistry Department (FCEyN) of the University of Buenos Aires. He joined the Ecole Normale Supérieure, Paris, France in 1993 on a CONICET post-doctoral fellowship for two years, working on the synthesis of heparan sulfate oligosaccharides. He returned to the University of Buenos Aires, where he is Assistant Professor as well as a research member of the Argentine Research Council, CONICET. Since 2000, he has also been an Invited Professor at the Ecole Normale Supérieure. His field of work includes carbohydrate chemistry, *C*-glycosides and enzyme inhibitors.

Dr. *Mariano J. L. Castro* studied chemistry at the University of Buenos Aires, where he finished his doctoral thesis on gemini surfactants in 2000 in the Organic Chemistry Department (FCEyN) and became a teaching assistant. He joined the University Chemical Laboratory at Cambridge, UK in 2001 on a CONICET post-doctoral fellowship.