HAL open science

Physicochemical, foaming and biological properties of lowly irritant anionic sugar-based surfactants

Rémy Bois, Bemba Abdellahi, Benjamin Mika, Séma Golonu, Pascale Vigneron, Vincent Chagnault, Audrey Drelich, Gwladys Pourceau, Anne Wadouachi, Muriel Vayssade, et al.

To cite this version:

Rémy Bois, Bemba Abdellahi, Benjamin Mika, Séma Golonu, Pascale Vigneron, et al.. Physicochemical, foaming and biological properties of lowly irritant anionic sugar-based surfactants. Colloids and Surfaces A: Physicochemical and Engineering Aspects, 2020, 607, pp.125525. 10.1016/j.colsurfa.2020.125525 . hal-02946872

HAL Id: hal-02946872

https://hal.science/hal-02946872v1

Submitted on 9 Sep 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Version of Record: https://www.sciencedirect.com/science/article/pii/S0927775720311183
Manuscript_a8827956059d5626d55ad69daa3a2c2f

Physicochemical, foaming and biological properties of lowly irritant anionic sugar-based surfactants

Rémy Bois[a], Bemba Abdellahi[b], Benjamin Mika[c], Séma Golonu[b], Pascale Vigneron[c], Vincent Chagnault[b], Audrey Drelich[a], Gwladys Pourceau[b], Anne Wadouachi[b], Muriel Vayssade[c], Isabelle Pezron[a], Alla Nesterenko[a*]

[a]*Université de technologie de Compiègne, ESCOM, TIMR (Integrated Transformations of Renewable Matter), Centre de recherche Royallieu - CS60319 - 60203 Compiègne Cedex*
[b]*Laboratoire de Glycochimie des Antimicrobiens et des Agroressources (LG2A), UMR CNRS 7378, Institut de Chimie de Picardie FR 3085, Université de Picardie Jules Verne, FR-80039 Amiens Cedex, France*
[c]*Université de technologie de Compiègne, CNRS, Biomechanics and Bioengineering, Centre de recherche Royallieu-CS 60319 -60203 Compiègne Cedex*
* corresponding author: alla.nesterenko@utc.fr

Abstract

Surface-active compounds derived from biomass, especially sugar-based amphiphiles, have received wide attention regarding their biodegradability, low toxicity and ecological acceptability. Compared to nonionic sugar-based surfactants, the anionic ones show significantly better solubility, higher surface activity and foaming performance. Thus they are largely used in personal care formulations and many technological applications. However, anionic surfactants are well known to induce skin and eye irritation.

In this study, three sugar-based anionic surfactants, bearing a lipidic chain grafted to the anomeric position of a monosaccharide (glucose or xylose) and a sulfate group on the primary hydroxyl, were synthesized: 6-*O*-sulfo-*N*-(β-D-glucopyranosyl) dodecanamide (GlcNC12S), *N*-dodecyl-6-*O*-sulfo-D-gluconamide (GlcCC12S) and *N*-dodecyl-6-*O*-sulfo-D-xylonamide (XylCC12S). These molecules were investigated in details for their self-assembling behavior, foaming properties and biological effects. All their properties were compared to those of two commercially available anionic surfactants, sodium laureth sulfate (SLES) and sodium dodecylsulfate (SDS).

Results revealed that the three anionic glycolipids show surface properties and foaming behavior comparable to those of SDS. Furthermore, their cytotoxic and irritation potentials

© 2020 published by Elsevier. This manuscript is made available under the CC BY NC user license
https://creativecommons.org/licenses/by-nc/4.0/

are significantly lower compared to commercial molecules, which make these renewable molecules potential candidates for replacement of petroleum-based compounds.

Keywords: anionic surfactant, sugar-based surfactant, glycolipid, foaming properties, cytotoxic activity, irritation potential

Introduction

Surface-active compounds performing detergency, wetting, emulsifying, solubilizing, dispersing and foaming effects are among the most representative chemical products consumed on a world scale [1, 2]. Depending on the charge of the hydrophilic group, surfactants can be nonionic, anionic, cationic or amphoteric. Anionic surfactants are used in greater volume compared to other surfactants (about 60% of worldwide surfactant production) because of their excellent performance in cleaning processes and low cost manufacture [3]. During the transition period from 1940 to 1970 due to the shift from the use of powder detergents to liquid ones, anionic amphiphiles became widely used in formulation of laundry detergents, domestic and industrial cleaning products, agricultural and pharmaceutical formulations, cosmetic and personal care products. Anionic surfactants are mainly constituted of a hydrophobic part (linear aliphatic hydrocarbon chain with length between C_8 and C_{18}, alkylphenyl ethers, alkylbenzenes, etc) linked to a hydrophilic part containing a sulphate, sulfonate, carboxyl or phosphate group, associated to a counter ion (for example, Na^+, K^+, NH_4^+ or an alkanolamine cation) [4-6].

However, the use of these surfactants is somewhat limited by their irritation profiles. Anionic surfactants show an important skin and eye irritation potential [6]. Moreover, cytotoxicity studies showed that anionic surfactants were more toxic than nonionic ones [4]. The development of new anionic amphiphiles with tailored functionalities and showing at the same time skin tolerance, has become a priority in the field of surface and colloid science.

Over the past few decades, the pressure from legislation and growing consumer trend toward environmentally benign chemicals had a strong impact on surfactants development. There is a growing need for the substitution of anionic surfactants of particular concern in different applications. The biodegradability and biocompatibility of surfactants have become very important not only to the consumer but also to its functional performance. To increase the environmental sustainability of amphiphilic molecules, new surface-active compounds, commonly referred as “green surfactants”, have been intensively developed [7]. Different

biomass substrates such as peptides and amino acids [8, 9][8, 10], sugars [10], fatty acids and alcohols [11] [12, 13]have been extensively studied for the production of these surfactants.

Sugar-based surfactants have increasingly become a viable bio-based alternative to petrochemical-based amphiphiles. Particularly, nonionic ones showed high performance, environmental compatibility, low toxicity and low irritancy towards living organisms [10, 12-15][11, 14-16, 18]. The raw material sources used are mainly sucrose from sugar beet or sugarcane, carbohydrate-based residues from hemicellulose and starch derivatives (glucose, galactose, mannose, xylose, sorbitol, lactose). Nowadays, most important sugar-based surfactants used for different applications are nonionic alkylpolyglucosides, sorbitan esters and sucrose esters. Numerous syntheses of such amphiphilics molecules have been described [10, 16-18]. Nevertheless, to the best of our knowledge, only few studies on anionic sugar-based surfactants have been reported. Among them, several articles dealt with the synthesis and properties characterization of anionic D-glucopyranoside derivatives; these molecules showed good adsorption properties similar to other ionic surfactants [19-21] and can also been applied for enantiomeric separation of racemic compounds [22, 23]. Otherwise, the analysis of literature data demonstrates a significant decrease in Krafft temperature (T_K) for anionic sugar derived surfactants [20] compared to their nonionic homologous with the same chain length [24]. The micelle formation is also impacted by addition of anionic group, higher value of critical micelle concentration (CMC) is observed for sulfated alkyl glucoside [25] compared to nonionic one [26]. Besides, anionic sulfosucrose derivatives showed very promising surface-active properties with CMC values from two to three orders of magnitude lower than those of commercial anionic molecules [27]. Other studies demonstrated that anionic galactoside [28] and glucoside [17] derivatives had interesting wetting properties for, respectively, textile treatment applications and enhanced oil recovery.

Nevertheless, there is no data in the literature dealing with neither foaming behavior, which is an important property for various surfactants applications, nor dermal irritation potential of anionic sugar-based amphiphiles. Based on the facts mentioned above, studying the potential of eco-friendly anionic glycolipids for the substitution of petroleum-derived anionic surfactants is worthy of experimental study.

The present contribution reports the complete characterization of three anionic surfactants based on sugar-derived hydrophilic units. These molecules were chosen from among a number of glycolipids synthesized in our laboratory after pre-sreening of physicochemical properties. The main objective of this work is to identify new surfactants which can potentially replace analogues petroleum-derived amphiphiles for specific applications. Thus,

all the properties analyzed were compared to commercial standard anionic surfactants with the same alkyl chain length. Surface tension was measured to study micellar and interfacial phenomena. Foaming behavior was studied using gas-sparging method. To evaluate the biological effects of surfactants, cellular and tissue models (mouse dermal fibroblasts and reconstituted human epidermis (RHE)) were treated with the molecules and the cell metabolic activity and IL-1α release (skin irritation) were measured.

2. Materials and methods

2.1. Synthesis of anionic glycolipids

Three sugar-based surfactants with anionic sulfated polar head and alkyl chain, constituted of 12 carbon atoms, were synthetized in this study. 6-*O*-Sulfo-*N*-(β-D-glucopyranosyl) dodecanamide (GlcNC12S, M_w=463.5 g.mol^{-1}) was prepared from commercial glucose following the procedure described in literature [29]. *N*-dodecyl-6-*O*-sulfo-D-gluconamide (GlcCC12S, M_w=465.5 g.mol^{-1}) and *N*-dodecyl-6-*O*-sulfo-D-xylonamide (XylCC12S, M_w=435.5 g.mol^{-1}) were produced in three steps, by 1) oxidation of commercial glucose and xylose [30], 2) ring-opening aminolysis of the as-obtained glyconolactone and 3) sulfation using Pyr-SO_3 complex [25]. The monosulfated sugars were separated from disulfated compounds using reverse phase chromatography. Produced anionic surfactants were stored at -20°C.

In addition, two commercially available anionic surfactants were used: Sodium Laureth Sulfate (SLES, M_w=370 g.mol^{-1}) provided from THOR Personal Care SAS (La Croix Saint-Ouen, France) as 27 wt% aqueous solution (Texapon® NSO UP) and Sodium Dodecylsulfate (SDS, M_w=288 g.mol^{-1}, purity>99%) was purchased from Sigma-Aldrich (Saint-Quentin Fallavier, France). The chemical structures of studied anionic surfactants are presented in Fig. 1.

2.2. Preparation of surfactant solutions

Water from Milli-Q Millipore system with a resistivity of 18.2 MΩcm produced by a PureLab Classic purification chain (Elga/Veolia, Wissous, France) was used to prepare aqueous solutions of surfactants for surface tension and foaming properties evaluation. Cell-culture medium was prepared as described previously [31] and used for preparation of solutions for biological responses evaluation. Surfactant solutions with different concentrations were

prepared by dissolving a known quantity of pure surfactant in water or cell-culture aqueous medium. All surfactants were soluble in water at 25°C.

2.3. Surface tension measurement

2.3.1. Equilibrium surface tension

Equilibrium surface tensions (γ_{eq}) of aqueous surfactant solutions prepared in pure water and cell-culture medium were measured using K100 KRÜSS tensiometer (Hamburg, Germany) by the Wilhelmy plate method. The Wilhelmy plate has a length, width and thickness of 19.9 mm, 10 mm and 0.2 mm, respectively and is made of platinum. The tensiometer operates by holding a plate in a fixed vertical position attached to a microbalance (resolution 10 µg) measuring the force acting on the plate. The surface tension is directly determined from the force-balance measurement. The surfactant solution was put in a glass vessel surrounded by a circular thermostated system maintained at 25±1°C throughout the duration of the test. Prior to each determination, the plate was thoroughly cleaned and burnt to red hot conditions in a blue flame to ensure perfect wetting (zero contact angle). The measurement of surface tension at the air/liquid interface was conducted over 12 000s. The surface tension values are reported as the mean of three repeat measurements. The Critical Micelle Concentration (CMC) of each surfactant was determined from the minimum point of the plot of the surface tension with respect to the logarithm of the concentration. The efficiency of surfactant adsorption (pC_{20}) was associated to the surfactant concentration required to reduce the surface tension of pure water by 20 mN/m. The surface tension of pure water measured at 25°C was equal to 72.8 $mN.m^{-1}$.

The maximum surface excess of surfactant at the air/water interface, Γ_{max}, was calculated using the Gibbs adsorption isotherm equation [32]:

$$\Gamma_{max} = \frac{-1}{nRT}\frac{d\gamma}{d\ln(C)} \quad (1)$$

where n=2 for a conventional ionic surfactant, assuming electrical neutrality of the interface [33], R is the universal gas constant (8.314 $J.mol^{-1}.K^{-1}$), T is the absolute Kelvin temperature and $(\frac{d\gamma}{d\ln(C)})$ is the slope of γ versus ln(C) determined at the CMC. The minimum area occupied by a surfactant molecule, A_{min}, at the interface:

$$A_{min} = \frac{1}{\mathcal{N}\Gamma_{max}} \quad (2)$$

where $\mathcal{N}$ is Avogadro's number.

2.3.2. Dynamic surface tension

Measurement of dynamic surface activity of the surfactant solutions were performed using the maximal bubble pressure method (BP2 Krüss tensiometer, Hamburg, Germany). This method is the most appropriate one for the determination the kinetics of surface tension decrease at very short times. Briefly, an inert gas (nitrogen) is slowly bubbled through a fine capillary, which is immersed in the test aqueous solution. Hydrophobically modified glass capillary with an inner diameter of 0.24 mm was used for the measurements. When the bubble area growths at the tip of the capillary, the pressure within the bubble increases and passes through a maximum. The surface tension can be calculated from the measured maximum capillary pressure using the Laplace equation [34]. The time associated with the interface formation (surface age) was varied from 30 ms to 50 s in every single experiment. The constant temperature of 25±1°C during measurements was assured by the external thermostat. Analyses were performed in triplicate.

2.4. Foaming properties

The determination of foaming properties of surfactant solutions was performed using an automated foaming device (FoamScan, Teclis, France). This instrument produces foam by blowing gas through a porous frit at a controlled gas flow rate. The conductivity measurement and image analysis are used to monitor different foam properties such as foam ability, foam stability, liquid fractions, drainage rate, and bubble size distribution. The experimental setup consisted of a glass column (diameter 3.5 cm, height 30 cm) equipped with a porous glass frit at its bottom. The foam generated was observed with two CDD cameras: one camera allowing the measurement of total foam and liquid amounts and a second camera equipped with a macro objective used to record the variation of the air bubbles size. The experimental conditions for determination of foam-related properties using gas-sparging method were established in our previous work [35]. Low frit porosity, low concentration and high gas flow rate turned out to the best choice for the screening of foaming performances of surfactants. In the present study, 40 mL of surfactant solution at a concentration of C=0.1CMC was introduced into the column equipped with frit porosity of grade P3 (ϕ=16-40 μm), at ambient temperature (24 ± 2°C). Foam was generated by injection of pressurized air (0.5 bar) at a flow rate of 200 $mL.min^{-1}$ during 60 s. The total duration of one experiment was set to 30 minutes for measurement of foam stability. All experiments were carried out in triplicate. Several foaming properties were examined, namely foaming capacity, foam stability, half-life time of foam and maximum foam density.

189 The foamability at the end of bubbling is defined by the foam capacity, FC:

190 $$FC = \frac{V_{foam,0}}{V_{gas}} \quad (3)$$

191 where $V_{foam,0}$ is the volume of foam at the end of gas injection and V_{gas} is the volume of the
192 sparged gas.

193 Foam stability is a parameter taking into account the whole behaviour of the foam collapse
194 process as a function of time. For evaluation of foam stability (S) the Experimental area under
195 the plot V_{foam}=f(time) starting at the end of gas-injection was calculated and compared to the
196 Maximal area (ideal behaviour in which the foam would remain stable all along the
197 experiment).

198 $$S = \frac{\text{Experimental area}}{\text{Maximal area}} \quad (4)$$

199 Foam half-life time ($t_{1/2}$) corresponds to the time (seconds) needed for the reduction of the
200 foam volume to half of the initial volume value ($V_{foam,0}$).

201 Maximum foam density (MD), related to the amount of liquid in the foam, was measured at
202 the end of gas bubbling. The density was determined by conductivity measurements within
203 the bottom solution.

204 $$MD\ (\%) = \frac{V_{solution,0} - V_{solution,f}}{V_{foam,0}} \times 100 \quad (5)$$

205 $V_{solution,0}$ is the initial volume of liquid, $V_{solution,f}$ is the volume of liquid at the end of gas-
206 injection.

207

208 *2.5. Biological responses on cellular and tissue models*

209 *2.5.1. Cell and tissue models*

210 The mouse fibroblast L929 cell line was obtained from ATCC (ATCC-CCL-1, LGC
211 Standards, France). Cells (passage 15-40) were cultured in 75 cm^2 Falcon® cell culture flasks
212 with DMEM (Gibco, Thermofisher scientific, France) supplemented with fetal bovine serum
213 (FBS, Gibco), 2 mM L-glutamine (Gibco), 100 U/mL penicillin (Gibco) and 100 µg/mL
214 streptomycin (Gibco). Cells were maintained in a humid atmosphere at 37°C with 5% CO_2.

215 Reconstituted Human Epidermis (RHE) model (EpiDerm™ EPI-200-SIT kit) was purchased
216 from MATTEK (Bratislava, Slovakia). This model consists of normal human epithelial
217 keratinocytes, which have been cultured at air/liquid interface to form a multilayered, highly
218 skin-like structure on specially prepared permeable cell culture inserts. Upon reception, RHE
219 were pre-conditioned by standard protocol following manufacturer's instructions.

220

221 *2.5.2. Cell metabolic activity assay*

222 The cytotoxic potential of surfactants was evaluated by measuring the cell metabolic activity
223 of both fibroblasts L929 and RHE. Cells and RHE were cultured and treated by surfactants at
224 different concentrations following the procedure described previously [31, 36].

225 Shortly, L929 cells (2600 cells/cm^2) were seeded in Costar® culture plate with culture
226 medium (2 mL). After 24h cell adhesion, surfactant dissolved in culture medium was added to
227 the cells at different concentrations for 48h. The tetrazolium salt (200 µL), commonly referred
228 as MTS (Cell titer 96® Aqueous One solution cell proliferation assay, Promega, France), was
229 added to each well. After 4 h, 3 aliquots (100 µL) from each well were transferred into a 96
230 well cell culture plate.

231 The effects of surfactants on RHE were evaluated according to the OECD N° 439 guideline
232 for *in vitro* skin irritation (OECD 439, 2019). Surfactants dissolved in phosphate buffer saline
233 (PBS) (30 µL, 1 mg/mL) or negative control (30 µL PBS) were applied for 1h (25 min at
234 room temperature and 35 min at 37°C) on the top of each tissue with nylon meshes used to
235 cover the tissue surface and to guarantee the spreading of liquids. Tissues in inserts were
236 extensively washed to discard surfactants and RHE were incubated for 24h. Then the culture
237 media were harvested and stored for a second end point, release of the cytokine IL1-α. Fresh
238 culture medium was added on tissues, RHE were cultured for 18h and then were transferred
239 into wells of Costar 24-well plate containing 270 µL of Hank's buffered salt solution (HBSS,
240 Life Technologies) and 30 µL of MTS. After incubation period (3h at 37°C), 3 aliquots (100
241 µL) from each well were transferred into a 96 well cell culture plate.

242 The amount of viable cells was evaluated by the measuring their dehydrogenase activity. The
243 MTS was reduced by living cells into a formazan compound with characteristic adsorption
244 band at 490 nm. The absorbance (A) of all samples was read at 490 nm using microplate
245 reader (Bio-Rad Model 680, Bio-Rad, USA). Cell-less controls were used in each test to avoid
246 any background absorbance due to possible interactions between MTS and tested molecules.
247 Metabolic activity of L929 cells and RHE model related to the amount of living cells in
248 culture was determined as: Cell metabolic activity = (A of sample treated with surfactant – A
249 of culture medium with surfactants without sample)/(A untreated sample – A of culture
250 medium). All experiments were performed six times.

251

252 *2.5.2. Irritation test on RHE*

253 The irritant effect of commercial and synthetized anionic surfactants on the RHE model was
254 evaluated by measuring the secretion rate of human interleukin-1α (IL-1α) in culture
255 medium. IL-1α cytokine concentrations were quantified after 1h surfactant exposure
256 (followed by 24h post-incubation according to the RHE manufacturer's instructions) by
257 ELISA test according to the kit manufacturer's instructions (Human IL-1α Platinum ELISA
258 kit, ThermoFisher Scientific, France). Six repetitions were performed for each surfactant
259 solution.
260
261 *2.6. Statistical analysis*
262 Statistical analyses of foaming properties and biological responses were performed using
263 GraphPad InStat software. Different variables are expressed as means ± standard deviation.
264 For foaming properties, experimental data was studied using one-way analysis of variance
265 (ANOVA). Tukey's test was used for the multiple comparison procedure and the significance
266 was accepted at the $P<0.05$ level.
267 For biological responses, non-parametric Dunn and Kruskal-Wallis tests were used for
268 comparisons as most of the continuous values measured had a non-Gaussian distribution. A
269 value of $P<0.05$ was taken as significant.
270
271 **3. Results**
272
273 *3.1. Surface tension reduction and CMC*
274 For comparison purposes, different surface properties of the three selected glycolipids were
275 studied and the two classical anionic surfactants (SDS and SLES). The CMC values of
276 anionic glycolipids were determined using equilibrium surface tension measurement at
277 different concentrations and are taken in consideration at the minimum point of the decreasing
278 surface tension curve. Plots of surface tension versus glycolipids and model anionic
279 surfactants concentration are shown in Fig. 2A. Physicochemical properties of surfactants in
280 water determined from these experimental curves are reported in Table 1.
281 When compared to commercial surfactants, sugar-based molecules have the same order of
282 magnitude of CMC values as that of SDS. However, the CMC of SLES is significantly lower.
283 For instance, the CMC of GlcNC12S is 20 times higher than that of SLES. The minimum
284 observed for all curves indicated the presence of small amount of residual molecules with
285 amphiphilic properties participating in the surface tension reduction. This particularity is

generally observed for SDS solutions due to the presence of dodecanol impurity [37, 38]. The surface tension values at CMC (γ_{CMC}) indicate the effectiveness in surface tension reducing. By comparing the γ_{CMC} of five anionic surfactants, results indicate that highest value of 34.9 $mN.m^{-1}$ was obtained for SDS and the lowest of 27.3 $mN.m^{-1}$ for SLES. The γ_{CMC} of sugar-based molecules were comprised between those of commercial surfactants. Similar tendencies can be observed for the results of calculated adsorption efficiency (pC_{20}), maximum surface excess (Γ_{max}) and corresponding minimal area per molecule (A_{min}). For these physicochemical parameters, the values obtained for sugar-based molecules were comprised between those of SLES and SDS. Results reveal that GlcCC12S was characterized by highest pC_{20} value of 3.92, followed by XylCC12S with pC_{20} of 3.43 and GlcNC12S with pC_{20} of 2.89. In regards to Γ_{max} and A_{min} parameters, estimated by applying Gibbs adsorption isotherm to the surface tension curves, the values obtained for anionic glycolipids were in the range of 1.68×10^{-10}–2.33×10^{-10} $mol.cm^{-2}$ and 71.3–99.1 $Å^2$/molecule respectively.

The dynamic surface adsorption of surfactant was characterized using maximum bubble pressure method. This technique allows an accurate regulation of air/solution surface adsorption with time, ranges from 0.03 to 50 s. Fig. 2B presents the plots of dynamic surface tension of studied anionic surfactant as a function of bubble age at concentration equal to 0.1CMC. For a new liquid/gas interface formation, the initial surface tension (γ_0) corresponds to 72.8 $mN.m^{-1}$, which is a surface tension for pure water/nitrogen interface at room temperature and at atmospheric pressure. It can be observed that at short times, before surface age of 1 s, the dynamic surface tension of SLES and sugar-based surfactants changes very little and remains close to that of pure water, whereas SDS is characterized by lower surface tension of about 68–70 $mN.m^{-1}$, suggesting faster adsorption at the air/water interface. For higher surface ages, a little decrease in dynamic surface tension can be noticed for SLES after 1 s and for XylCC12S after 20 s. In addition, results show that dynamic surface tension is not significantly affected by the increase in air bubble age for GlcCC12S and GlcNC12S.

From the results presented in Figure 2 and Table 1, it can be concluded that for the same alkyl chain length, the structure of the hydrophilic head group significantly affects adsorption at the air/water interface of anionic surfactants.

3.2. Foaming properties

Foaming behavior of the three synthesized anionic sugar-based surfactants and the two anionic reference surfactants was studied using gas-sparging method. Fig. 3 displays the foam

volume and liquid volume as a function of time for surfactant solutions and Table 2 presents the summary of experimental data on foaming properties. In order to compare foaming properties of different surfactant systems, it is more appropriate to consider these systems in the same thermodynamic state. Below CMC, surfactants are under a monomer form. Thus the flux of surfactant molecules to the interface and the foaming behavior of solution are not influenced by kinetic of micellization and break-time of micelles [39]. Moreover, the results of our previous study showed that low concentration conditions are favorable for the discrimination of foaming behavior of different surfactants [35]. Thus, solution concentration applied for all surfactants was 0.1CMC.

The results obtained demonstrated that the whole foam process consists of two stages: the generation of the foam (from 0s to 60s) and the destabilization of the foam (from 60s to 1800s). In the first stage, i.e. gas sparging into the liquid, the liquid volume decreases and the foam volume increases gradually. In the decay stage, the foam volume decreases because of different destabilization processes, and the liquid volume increases due to the liquid drainage through foam.

As can be seen on Fig.3A, the volume of formed foam is close to 200 mL (maximal volume of produced foam at gas flow rate of 200 $mL.min^{-1}$ during 60 s) for all surfactants except GlcCC12S and GlcNC12S. Another information which can be observed from this figure is the collapsing rate or foam stability expressed by area under the curve (S, Table 2). This property is closely related to the half-life time of foam ($t_{1/2}$). SLES solution showed significantly higher foam stability S of 0.79 compared to other surfactants. The stability of the foams produced by XylCC12S (0.36) and SDS (0.27) was intermediate, whilst in the case of GlcCC12S and GlcNC12S a significant reduction in the foam stability was observed.

The variation of liquid volume with time (Fig. 3B) showed that the liquid volume of GlcCC12S slightly decreased during bubbling and remained higher than that of other surfactants throughout the experience. The liquid drainage rate for foams produced with SDS, XylCC12S and GlcNC12S was similar. These observations are in agreement with maximum foam density values (MD, Table 2) representing the amount of liquid in the foam and measured at the end of bubbling. It can be seen that GlcCC12S formed very dry foam (MD=2.0%) whereas liquid content in foams produced by other anionic surfactants varied from 16.9 to 20.6%.

3.3. Cell metabolic activity and irritation response of RHE after surfactant treatment

352 The interaction of surfactants with L929 model cells was assessed to study surfactant-
353 membrane interaction at low surfactant concentration (below CMC). The results reported on
354 Fig.4 illustrates the metabolic activity of cells treated with anionic glycolipids at different
355 concentrations. As can be seen, in the studied concentration range, the results show that cell
356 viability decreased with increase in surfactant concentration, but for the concentrations below
357 0.006 mM, the three molecules did not modify significantly the cell metabolic activity
358 compared to untreated cells. A significant cytotoxic effect is observed for 0.06 mM of
359 surfactants, with no difference observed between the three anionic glycolipids. The biological
360 effects of anionic sugar-based surfactants were compared to responses of commercial anionic
361 surfactants at the same molar concentration, 0.2 mM. This maximal concentration was fixed
362 based on our previous studies, as at this concentration a significant cytotoxic effect of
363 commercial surfactants on the cell metabolic activity was observed [36, 40]. The anionic
364 glycolipids show the same cytotoxicity than SDS and SLES. However, at this concentration,
365 the metabolic activity of cell treated with SLES seems to be lower compared to those of other
366 molecules.
367 Table 3 summarizes the results obtained after treatment of RHE tissues with surfactant
368 solutions, according to the OECD 439 guideline for the surfactant concentration and exposure
369 conditions. These results show that the treatment with the anionic sugar-based surfactants did
370 not modify significantly the cell metabolic activity of keratinocytes in RHE tissue compared
371 to untreated RHE. Cells exposed to anionic glycolipids still maintain high metabolic activity
372 (75.3-89%) even at high surfactant concentrations (1 $mg.mL^{-1}$). Metabolic activity of cells
373 seems to be affected by SLES, but considerable variability of obtained results (51.1±34.6%)
374 leads to no significant statistical difference between SLES and glycolipids. In contrast, the
375 commercial anionic surfactant SDS shows clear cytotoxic effect on cells.
376 Simultaneously, the irritation effect of surfactants on RHE tissue was evaluated by measuring
377 the release of IL-1α in culture medium after 24h of surfactant treatment. A significant
378 increase of IL-1α concentration in RHE models treated by SDS and SLES was observed,
379 compared to non-treated control (PBS), indicating a strong irritant effect of both commercial
380 surfactants on the *in vitro* skin models. Synthetized anionic glycolipids showed a lower
381 release of IL-1α, and were not considered different from negative control PBS.
382
383 **4. Discussion**
384

385 *4.1. Surface active properties in water*

386 To act as an efficient surfactant, an amphiphilic molecule is usually characterized by
387 adsorption properties leading to decrease in surface tension and by formation of aggregates
388 from a certain concentration. Since these properties are mainly affected by the structure, it is
389 fundamental to characterize the potential on new surfactants from an amphiphilic point of
390 view.

391 The particular low CMC value of SLES compared to anionic glycolipids can be attributed to
392 intermolecular and intramolecular attractive ion-dipole interactions between the sulfate group
393 (SO_4^-) and the O→CH_2 dipole of oxyethylene group [41]. Such attractive interaction is very
394 specific and arising only with oxyethylene group adjacent to sulfate ion. It is not occurring for
395 SDS and anionic sugar-based surfactants micelles, where strong self-repulsion between
396 sulfate groups is dominant. Consequently, the self-assembling for these molecules was
397 observed at higher concentrations. A higher value of pC_{20} usually indicates a higher ability for
398 the reduction of surface tension, assuming that lower energy is needed to bring the surfactant
399 molecule from the bulk to the air/water interface [42]. pC_{20} values of anionic glycolipids
400 presented in Table 1 suggest a high surfactant efficiency in lowering the surface tension of
401 water comparable to commercial anionic surfactants.

402 The size of hydrophilic head group is dominant factor to determine the adsorption quantity of
403 surfactant molecules at the air/water interface, Γ_{max}, and corresponding area occupied by a
404 single surfactant molecule, A_{min} [32]. Γ_{max} and A_{min} values calculated for anionic surfactants
405 can be correlated with their molecular structure. SDS with lowest size of polar moiety has
406 high packing density at the interface air/water. The cross-sectional area of the hydrophilic
407 group increases for SLES and glycolipids resulting in lower Γ_{max} value and thereby, larger
408 A_{min} value. The same tendency, where an adsorption quantity of surfactant molecules at the
409 air/water interface decreases with the increasing of the polar part size, was reported for
410 anionic polyethylene oxide derivatives [43, 44]. Moreover, for sugar-based surfactants the
411 intermolecular interactions of the -OH groups and their steric hindrance can be responsible for
412 higher distance between the molecules in the adsorption layer and increased A_{min} value. For
413 the same length of hydrophobic chain, the surface adsorption properties of sugar-based
414 surfactants depend not only on headgroup size, but also on the linker type and structure [45].
415 Consequently, the differences in physiochemical properties of studied anionic glycolipids can
416 be related to the nature of linker group. Similar results on surface adsorption properties for
417 other families anionic surfactants have been reported in the recent literature [17, 42, 43, 46].

Dynamic surface tension measurements have been performed in order to get information on the instantaneous decrease of surface tension at very short times. After creation of the fresh surface, the dynamic tension decreases with time as amphiphilic molecules diffuse and adsorb at the interface. The results demonstrate that SLES exhibits faster adsorption kinetics compared to other surfactants. Surprisingly, the dynamic surface tension of three sugar-based surfactants was not changing significantly over time period considered, indicating the absence of surfactant adsorption at short times. In this case, it can be suggested that the time required to attain the equilibrium surface tension is higher for glycolipids compared to commercial molecules, and the adsorption of sugar-based surfactants is controlled not only by the diffusion of molecules. The repulsive electrostatic interactions of anionic groups might explain the higher potential barrier of glycolipids adsorption and slower adsorption rate at the gas/liquid interface for these surfactants [33, 47]. Additionally, this low surfactant diffusivity and slow reduction in dynamic surface tension can be linked to the low concentration of analyzed solutions (C = 0.1CMC).

4.2. Evaluation of foaming behavior

Aqueous foams are thermodynamically unstable disperse systems. They consisted of gas bubbles separated by liquid films where gas/liquid interface is generally stabilized by surfactants. Different self-destructive processes take place simultaneously in foam during ageing. The main processes limiting the foam stability are drainage of the liquid under the action of gravity, and foam ageing phenomena like coalescence (film rupture) and ripening (exchange of gas between bubbles due to differences in Laplace pressure) [48, 49]. These factors cause the transformation of foams to their thermodynamically most stable state – complete destabilization to initial liquid.

Foaming capacity describes the ability of a surfactant solution to produce foam. It depends on both the rate of transport of the surfactant to the gas/liquid interface and the total adsorbed amount of surfactant [50]. High foam capacity of SLES and SDS could be related to the decrease of dynamic surface tension for these solutions. This result indicates that the diffusion of the surfactant to the surface is fast enough for the formation of interfacial layer in the foam generation process. However, despite low adsorption rate and dynamic surface tension reduction, anionic glycolipids XylCC12S and GlcNC12S showed high foaming capacity close to those of commercial molecules. Significant differences in foam properties, such as foam stability (S), maximum foam density (MD) and foam half-life time ($t_{1/2}$) can be attributed to the variation of head group structure, since all surfactants studied have the same length of

452 hydrophobic chain. The organization of the hydration water around an ethylene oxide and
453 sugar group under similar conditions, were found to be completely different [51, 52].
454 Moreover, flexible hydrophilic part of negatively charged surfactants can cause the adoption
455 of various molecular configurations on the air/water interface. The compactness of adsorbed
456 molecules on the two air/water interfaces of the foam lamellae affects both foamability and
457 foam stability [42]. While SDS and SLES have short and flexible hydrophilic units,
458 XylCC12S and GlcCC12S have more voluminous open chain sugar part, and the cyclic sugar
459 GlcNC12S head group behaves like a hard disk with reduced conformational flexibility.
460 These mentioned differences influence the behavior of surfactants in solution as well as their
461 adsorption and foaming properties. It is important to indicate that the viscosity of aqueous
462 surfactant solution could significantly affect its foaming properties. Typically, the foam
463 stability increased for bulk solutions with higher viscosity [53]. In this study, very diluted
464 solutions were analyzed in foaming experiments (C = 0.1 CMC), the viscosity remained
465 constant and very close to that of pure water.
466 To sum up, foaming properties of two of the three synthetized anionic glycolipids (XylCC12S
467 and GlcNC12S) are close to those of commercial anionic surfactants. They form the similar
468 amount of foam that SDS and SLES, and exhibit foaming stability comparable to that of SDS.
469 Since foaming performances of anionic surfactants are of great importance in formulation of
470 personal care products, an interesting approach is to study the biological activity of new
471 glycolipids and to evaluate their potential use in such applications.
472
473 *4.3. Biological responses*
474 The potential use of surfactants in several cosmetic and pharmaceutical applications depends
475 on their cytotoxicity, biocompatibility and toxic effects. Our previous studies revealed a
476 significant difference in biological responses, such as metabolic activity, cytotoxicity and
477 irritancy, between commercial model surfactant and bio-based nonionic glycolipids [31, 36].
478 Biological effects of anionic glycolipids have not been investigated before. In the present
479 study, the metabolic activity related to the amount of viable cells was studied on L929 model
480 cells and on RHE tissue. As expected, cell metabolic activity decreases with the rise of
481 surfactant concentration. While at fixed concentration, cells treated with sugar-based
482 surfactants showed similar metabolic activity. We used an *in vitro* RHE EpiDerm system and
483 the OECD guidelines for the testing of chemicals and cosmetic formulations (irritant effect)
484 were strictly applied to characterize the surfactant's effect on a human skin model [54]. The
485 significant differences in keratinocyte metabolic activity observed in RHE models treated

with commercial or synthesized anionic glycolipids revealed that glycolipids are mild and tolerant towards epidermal cells. Notably no significant difference between the three glycolipids was found, suggesting that the structure of polar part (cyclic or acyclic) of surfactant cannot be directly correlated to biological responses. In contrast, significant loss in metabolic activity was found after the exposure of human keratinocytes to SDS and SLES solutions suggesting an important amount of damaged cells. The irritancy potential measurements showed clear difference in IL-1α release between the three anionic glycolipids and model anionic surfactants, highlighting that SDS and SLES had significantly higher irritation potential. Previous study reported that skin irritation profile of SDS was significantly higher compared with 15 other nonionic, amphoteric and anionic surfactants [55].

Overall, all obtained results confirmed that in the concentration range studied, GlcCC12S, GlcNC12S and XylCC12S are significantly less toxic than SLES or SDS. *In vitro* test systems used here were particularly interesting for pre-screening of new surfactants for novel formulation development in cosmetics, avoiding the use of animals for testing. Obviously, surfactant combinations are used in formulation, and it is necessary to evaluate biological responses of fully formulated products.

5. Conclusion

A multidisciplinary approach taking into account surface properties, foaming behavior and biological responses of three anionic surfactants (GlcNC12S, GlcCC12S, XylCC12S), obtained from renewable raw materials (carbohydrates) comparatively to model commercial anionic surfactants (SDS and SLES) has been chosen. Sugar-based surfactants were found to exhibit good surface activities including low surface tension and CMC values close to those of commercial surfactant (SDS). Foam capacity and foam stability of XylCC12S and GlcNC12S were found to be similar to those of SDS at the same C/CMC concentration. The analysis of biological responses on model cells and RHE tissues indicated significantly lower toxic effects of the three anionic glycolipids compared to those of commercial anionic surfactants. The lowest irritant effect, evaluated on a human skin model, was also observed for the new synthesized surfactants, GlcNC12S and XylCC12S. The analysis of obtained data demonstrates that the three sugar-derived anionic surfactants can be categorized as bio-based compounds and considered as excellent potential candidates for the substitution of petroleum-based surfactants for cosmetic and detergence applications. These promising results contribute to the knowledge about sugar-based surfactants and encourage us to explore other anionic sugar-based structures for future work.

Acknowledgements

This work has been performed, in partnership with the SAS PIVERT, within the frame of the French Institute for the Energy Transition P.I.V.E.R.T. (www.institut-pivert.com) selected as an Investments for the Future. This work was supported, as part of the Investments for the Future, by the French Government under the reference ANR-001-01.

References

1. C. Negin, S. Ali, and Q. Xie, *Most common surfactants employed in chemical enhanced oil recovery.* Petroleum, **2017**. 3(2). 197-211. https://doi.org/10.1016/j.petlm.2016.11.007
2. L.L. Schramm, E.N. Stasiuk, and D.G. Marangoni, *Surfactants and their applications.* Annual Reports Section "C" (Physical Chemistry), **2003**. 99(0). 3-48. http://dx.doi.org/10.1039/B208499F
3. A. Barra Caracciolo, M. Cardoni, T. Pescatore, and L. Patrolecco, *Characteristics and environmental fate of the anionic surfactant sodium lauryl ether sulphate (SLES) used as the main component in foaming agents for mechanized tunnelling.* Environmental Pollution, **2017**. 226. 94-103. https://doi.org/10.1016/j.envpol.2017.04.008
4. T. Cserháti, E. Forgács, and G. Oros, *Biological activity and environmental impact of anionic surfactants.* Environment International, **2002**. 28(5). 337-348. https://doi.org/10.1016/S0160-4120(02)00032-6
5. M.J. Scott and M.N. Jones, *The biodegradation of surfactants in the environment.* Biochimica et Biophysica Acta (BBA) - Biomembranes, **2000**. 1508(1). 235-251. https://doi.org/10.1016/S0304-4157(00)00013-7
6. A. Wibbertmann, I. Mangelsdorf, K. Gamon, and R. Sedlak, *Toxicological properties and risk assessment of the anionic surfactants category: Alkyl sulfates, primary alkane sulfonates, and α-olefin sulfonates.* Ecotoxicology and Environmental Safety, **2011**. 74(5). 1089-1106. https://doi.org/10.1016/j.ecoenv.2011.02.007
7. K. Holmberg, *Natural surfactants.* Current Opinion in Colloid & Interface Science, **2001**. 6(2). 148-159. https://doi.org/10.1016/S1359-0294(01)00074-7
8. R. Bordes and K. Holmberg, *Amino acid-based surfactants – do they deserve more attention?* Advances in Colloid and Interface Science, **2015**. 222. 79-91. http://doi.org/10.1016/j.cis.2014.10.013
9. D.B. Tripathy, A. Mishra, J. Clark, and T. Farmer, *Synthesis, chemistry, physicochemical properties and industrial applications of amino acid surfactants: A review.* Comptes Rendus Chimie, **2018**. 21(2). 112-130. https://doi.org/10.1016/j.crci.2017.11.005
10. C.C. Ruiz, *Sugar-Based Surfactants. Fundamentals and Applications*. 2008: CRC Press.
11. V.M. Dembitsky, *Astonishing diversity of natural surfactants: 1. Glycosides of fatty acids and alcohols.* Lipids, **2004**. 39(10). 933-953. http://doi.org/10.1007/s11745-004-1316-1
12. T. Gaudin, P. Rotureau, I. Pezron, and G. Fayet, *Investigating the impact of sugar-based surfactants structure on surface tension at critical micelle concentration with structure-property relationships.* Journal of Colloid and Interface Science, **2018**. 516. 162-171. http://doi.org/10.1016/j.jcis.2018.01.051

13. O.J. Rojas, L.A. Lucia, Y. Habibi, and C. Stubenrauch, *Interfacial Properties of Sugar-based Surfactants*, in *BioBased Surfactants and Detergents: Synthesis, Properties, and Applications*. 2009.

14. T. Yoshimura, S. Umezawa, A. Fujino, K. Torigoe, K. Sakai, H. Sakai, M. Abe, and K. Esumi, *Equilibrium Surface Tension, Dynamic Surface Tension, and Micellization Properties of Lactobionamide-Type Sugar-Based. Gemini Surfactants.* **2013**. 62. 353-362. http://doi.org/10.5650/jos.62.353

15. X.M. Liu, X. Liao, S.H. Zhang, S. Chang, L. Cheng, M. Ge, and X. Ge, *Physicochemical Properties of Noncovalently Constructed Sugar-Based Pseudogemini Surfactants: Evaluation of Linker Length Influence.* Journal of Chemical & Engineering Data, **2019**. 64(1). 60-68. https://doi.org/10.1021/acs.jced.8b00459

16. S. Ji, W. Shen, L. Chen, Y. Zhang, X. Wu, Y. Fan, F. Fu, and G. Chen, *Synthesis and properties of sugar-based surfactants alkoxyethyl β-D-glucopyranoside.* Colloids and Surfaces A: Physicochemical and Engineering Aspects, **2019**. 564. 59-68. https://doi.org/10.1016/j.colsurfa.2018.12.034

17. T.-H. Zhao, J.-Y. Gu, W.-F. Pu, Z.-M. Dong, and R. Liu, *Study on the synthesis and properties of an eco-friendly sugar-based anionic-nonionic surfactant.* RSC Advances, **2016**. 6(74). 70165-70173. http://dx.doi.org/10.1039/C6RA11596A

18. G. Chen, Z. Li, L. Chen, S. Ji, and W. Shen, *Synthesis and properties of Alkyl α-D-Galactopyranoside.* Journal of Dispersion Science and Technology, **2017**. 38(4). 506-514. https://doi.org/10.1080/01932691.2016.1180628

19. R.C. Bazito and O.A. El Seoud, *Sugar-based cationic surfactants: Synthesis and aggregation of methyl 2-acylamido-6-trimethylammonio-2,6-dideoxy-d-glucopyranoside chlorides.* Journal of Surfactants and Detergents, **2001**. 4(4). 395-400. https://doi.org/10.1007/s11743-001-0193-1

20. R.C. Bazito and O.A. El Seoud, *Sugar-Based Surfactants: Adsorption and Micelle Formation of Sodium Methyl 2-Acylamido-2-deoxy-6-O-sulfo-d-glucopyranosides.* Langmuir, **2002**. 18(11). 4362-4366. https://doi.org/10.1021/la0117552

21. T. Kida, K. Yurugi, A. Masuyama, Y. Nakatsuji, D. Ono, and T. Takeda, *Preparation and properties of new surfactants containingd-glucosamine as the building block.* Journal of the American Oil Chemists' Society, **1995**. 72(7). 773-780. https://doi.org/10.1007/BF02541024

22. R.F.D. Jones, P. Camilleri, A.J. Kirby, and G.N. Okafo, *The synthesis and micellar properties of a novel anionic surfactant.* Journal of the Chemical Society, Chemical Communications, **1994**. 11. 1311-1312. http://dx.doi.org/10.1039/C39940001311

23. C. Tano, S.-H. Son, J.-i. Furukawa, T. Furuike, and N. Sakairi, *Dodecyl thioglycopyranoside sulfates: Novel sugar-based surfactants for enantiomeric separations by micellar electrokinetic capillary chromatography.* Electrophoresis, **2008**. 29(13). 2869-2875. https://onlinelibrary.wiley.com/doi/abs/10.1002/elps.200800045

24. S. Matsumura, Y. Kawamura, S. Yoshikawa, K. Kawada, and T. Uchibori, *Surface activities, biodegradability and antimicrobial properties of glucosamine derivatives containing alkyl chains.* Journal of the American Oil Chemists' Society, **1993**. 70(1). 17-22. https://doi.org/10.1007/BF02545361

25. T. Böcker, T.K. Lindhorst, J. Thiem, and V. Vill, *Synthesis and properties of sulfated alkyl glycosides.* Carbohydrate Research, **1992**. 230(2). 245-256. https://doi.org/10.1016/0008-6215(92)84036-R

26. H. Lu, I. Pezron, T. Gaudin, and A. Drelich, *Non-equilibrium micelles formed by sugar-based surfactants under their Krafft temperature.* Colloids and Surfaces A: Physicochemical and Engineering Aspects, **2018**. 540. 167-176. https://doi.org/10.1016/j.colsurfa.2017.12.053

611 27. H.G. Bazin, T. Polat, and R.J. Linhardt, *Synthesis of sucrose-based surfactants through*
612 *regioselective sulfonation of acylsucrose and the nucleophilic opening of a sucrose cyclic*
613 *sulfate.* Carbohydrate Research, **1998**. 309(2). 189-205. https://doi.org/10.1016/S0008-
614 6215(98)00121-9

615 28. I. Pezron, G. Bourgain, and D. Clausse, *Influence of 1-decanol on the surface tension and*
616 *wetting power of a new anionic surfactant derived from sugar.* Colloid and Polymer Science,
617 **1996**. 274(2). 166-171. https://doi.org/10.1007/BF00663449

618 29. J. Tang, E. Ozhegov, Y. Liu, D. Wang, X. Yao, and X.-L. Sun, *Straightforward Synthesis of*
619 *N-Glycan Polymers from Free Glycans via Cyanoxyl Free Radical-Mediated Polymerization.*
620 ACS Macro Letters, **2017**. 6(2). 107-111. https://doi.org/10.1021/acsmacrolett.6b00928

621 30. M. Omri, G. Pourceau, M. Becuwe, and A. Wadouachi, *Improvement of Gold-Catalyzed*
622 *Oxidation of Free Carbohydrates to Corresponding Aldonates Using Microwaves.* ACS
623 Sustainable Chemistry & Engineering, **2016**. 4(4). 2432-2438.
624 https://doi.org/10.1021/acssuschemeng.6b00263

625 31. B. Lu, M. Vayssade, Y. Miao, V. Chagnault, E. Grand, A. Wadouachi, D. Postel, A. Drelich,
626 C. Egles, and I. Pezron, *Physico-chemical properties and cytotoxic effects of sugar-based*
627 *surfactants: Impact of structural variations.* Colloids and Surfaces B: Biointerfaces, **2016**.
628 145. 79-86. https://doi.org/10.1016/j.colsurfb.2016.04.044

629 32. M.J. Rosen and J.T. Kunjappu, *Surfactants and Interfacial Phenomena, 4th Edition*. 2012:
630 Jonh Wiley & Sons. http://dx.doi.org/10.1002/9781118228920

631 33. J. Eastoe and J.S. Dalton, *Dynamic surface tension and adsorption mechanisms of surfactants*
632 *at the air–water interface.* Advances in Colloid and Interface Science, **2000**. 85(2). 103-144.
633 http://doi.org/10.1016/S0001-8686(99)00017-2

634 34. V.B. Fainerman and R. Miller, *Maximum bubble pressure tensiometry—an analysis of*
635 *experimental constraints.* Advances in Colloid and Interface Science, **2004**. 108-109. 287-301.
636 https://doi.org/10.1016/j.cis.2003.10.010

637 35. R. Bois, E. van Hecke, I. Pezron, and A. Nesterenko, *Screening of Surfactant Foaming*
638 *Properties Using the Gas-Sparging Method: Design of an Optimal Protocol.* Journal of
639 Surfactants and Detergents, **2020**. 23(2). 359-369.
640 https://aocs.onlinelibrary.wiley.com/doi/abs/10.1002/jsde.12376

641 36. B. Lu, Y. Miao, P. Vigneron, V. Chagnault, E. Grand, A. Wadouachi, D. Postel, I. Pezron, C.
642 Egles, and M. Vayssade, *Measurement of cytotoxicity and irritancy potential of sugar-based*
643 *surfactants on skin-related 3D models.* Toxicology in Vitro, **2017**. 40. 305-312.
644 https://doi.org/10.1016/j.tiv.2017.02.002

645 37. A. Javadi, N. Mucic, D. Vollhardt, V.B. Fainerman, and R. Miller, *Effects of dodecanol on the*
646 *adsorption kinetics of SDS at the water–hexane interface.* Journal of Colloid and Interface
647 Science, **2010**. 351(2). 537-541. https://doi.org/10.1016/j.jcis.2010.07.033

648 38. K.J. Mysels, *Surface tension of solutions of pure sodium dodecyl sulfate.* Langmuir, **1986**.
649 2(4). 423-428. https://doi.org/10.1021/la00070a008

650 39. A. Patist, S.G. Oh, R. Leung, and D.O. Shah, *Kinetics of micellization: its significance to*
651 *technological processes.* Colloids and Surfaces A: Physicochemical and Engineering Aspects,
652 **2001**. 176(1). 3-16. https://doi.org/10.1016/S0927-7757(00)00610-5

653 40. B. Lu, *Evaluation of physico-chemical properties of biorefinery-derived amphiphilic*
654 *molecules and their effects on multi-scale biological models*. 2015, Université de Technologie
655 de Compiègne.

656 41. M. Aoudia, T. Al-Maamari, and F. Al-Salmi, *Intramolecular and intermolecular ion–dipole*
657 *interactions in sodium lauryl ether sulfates (SLES) self-aggregation and mixed micellization*

with Triton X-100. Colloids and Surfaces A: Physicochemical and Engineering Aspects, **2009**. 335(1). 55-61. https://doi.org/10.1016/j.colsurfa.2008.10.026

42. P. Kanokkarn, T. Shiina, M. Santikunaporn, and S. Chavadej, *Equilibrium and dynamic surface tension in relation to diffusivity and foaming properties: Effects of surfactant type and structure.* Colloids and Surfaces A: Physicochemical and Engineering Aspects, **2017**. 524. 135-142. http://doi.org/10.1016/j.colsurfa.2017.04.043

43. X. Liu, Y. Zhao, Q. Li, T. Jiao, and J. Niu, *Surface and interfacial tension of nonylphenol polyethylene oxides sulfonate.* Journal of Molecular Liquids, **2016**. 216. 185-191. https://doi.org/10.1016/j.molliq.2016.01.009

44. J. Tan, Z. He, Y. Bai, and P. Yan, *Synthesis, characterization and surface properties of novel polyether based siloxane surfactants.* Journal of Dispersion Science and Technology, **2020**. 41(2). 188-194. https://doi.org/10.1080/01932691.2018.1561303

45. T. Gaudin, H. Lu, G. Fayet, A. Berthauld-Drelich, P. Rotureau, G. Pourceau, A. Wadouachi, E. Van Hecke, A. Nesterenko, and I. Pezron, *Impact of the chemical structure on amphiphilic properties of sugar-based surfactants: A literature overview.* Advances in Colloid and Interface Science, **2019**. 270. 87-100. http://doi.org/10.1016/j.cis.2019.06.003

46. A.M. Tolpa, A.I. Meaad, M.A.M. AbdElReheim, and E.A. ElSharkawy, *SYNTHESIS AND SURFACE PROPERTIES OF A NOVEL ANIONIC SURFACTANT.* Sinai Journal of Applied Sciences, **2015**. 4(1). 1-12. http://dx.doi.org/10.21608/sinjas.2015.78477

47. V.B. Fainerman, A.V. Makievski, and R. Miller, *The analysis of dynamic surface tension of sodium alkyl sulphate solutions, based on asymptotic equations of adsorption kinetic theory.* Colloids and Surfaces A: Physicochemical and Engineering Aspects, **1994**. 87(1). 61-75. http://doi.org/10.1016/0927-7757(94)02747-1

48. W. Drenckhan and S. Hutzler, *Structure and energy of liquid foams.* Advances in Colloid and Interface Science, **2015**. 224. 1-16. https://doi.org/10.1016/j.cis.2015.05.004

49. R.J. Pugh, *Bubble and Foam Chemistry*. 2016: Cambridge University Press. http://dx.doi.org/10.1017/CBO9781316106938

50. C. Stubenrauch, L.K. Shrestha, D. Varade, I. Johansson, G. Olanya, K. Aramaki, and P. Claesson, *Aqueous foams stabilized by n-dodecyl-[b]-d-maltoside, hexaethyleneglycol monododecyl ether, and their 1 : 1 mixture.* Soft Matter, **2009**. 5(16). 3070-3080. http://dx.doi.org/10.1039/B903125A

51. P.M. Claesson, M. Kjellin, O.J. Rojas, and C. Stubenrauch, *Short-range interactions between non-ionic surfactant layers.* Physical Chemistry Chemical Physics, **2006**. 8(47). 5501-5514. http://dx.doi.org/10.1039/B610295F

52. E. Tyrode, C.M. Johnson, A. Kumpulainen, M.W. Rutland, and P.M. Claesson, *Hydration State of Nonionic Surfactant Monolayers at the Liquid/Vapor Interface: Structure Determination by Vibrational Sum Frequency Spectroscopy.* Journal of the American Chemical Society, **2005**. 127(48). 16848-16859. https://doi.org/10.1021/ja053289z

53. N. Denkov, S. Tcholakova, and N. Politova-Brinkova, *Physicochemical control of foam properties.* Current Opinion in Colloid & Interface Science, **2020**. https://doi.org/10.1016/j.cocis.2020.08.001

54. OECD, *test N° 439 : In vitro skin irritation: reconstructed human epidermis test method.* OECD Publishing, **2019**. section 4.

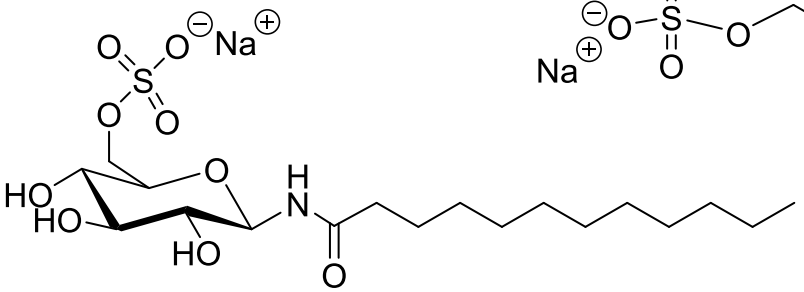
55. R. Walters, L. Gandolfi, M. Catherine Mack, M. Fevola, K. Martin, M. T Hamilton, A. Hilberer, N. Barnes, N. Wilt, J. R Nash, H. A Raabe, and G.-E. Costin, *In Vitro Assessment of Skin Irritation Potential of Surfactant-based Formulations by Using a 3-D Skin Reconstructed Tissue Model and Cytokine Response.* Alternatives to laboratory animals, **2016**. 44(6). 523-532. http://doi.org/10.1177/026119291604400611

Fig. 1. Anionic surfactants studied for their surface-active properties, foaming behavior and biological effects.

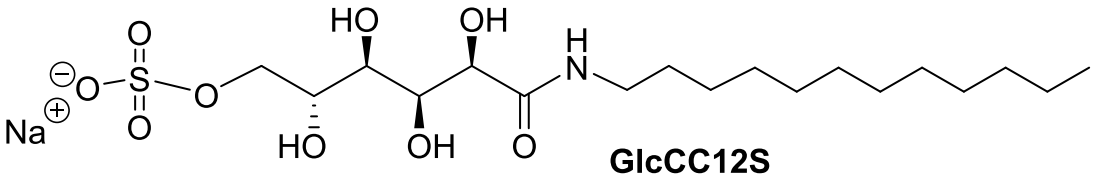
Fig. 2. (A) Plots of surface tension versus concentration of anionic surfactants. Dotted lines are displayed as a visual guide. (B) Dynamic surface tension behavior of anionic surfactants at C=0.1CMC; standard deviation bars are smaller than used symbols (n=3).

Fig. 3. Variation of the foam volume (A) and liquid volume (B) with time for different surfactants at C=0.1CMC. The bubbling rate is 200 mL.min-1.

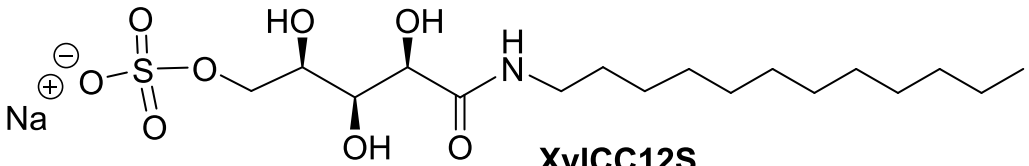
Fig. 4. Metabolic activity of L929 cells after surfactant treatment. n=6 per group, data are presented as mean value with standard deviation. * $P<0.05$ and *** $P<0.001$ indicate significant difference *versus* untreated cells.



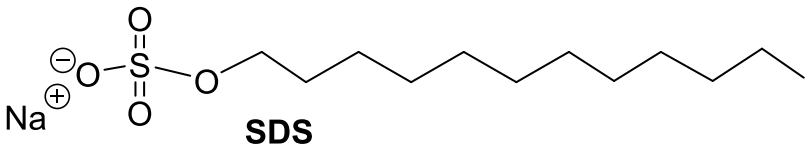
GlcNC12S



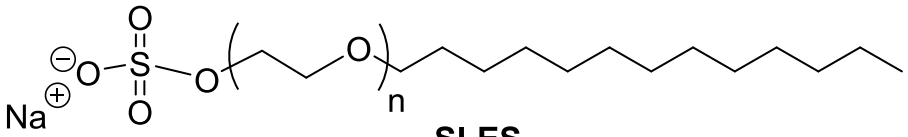
GlcCC12S



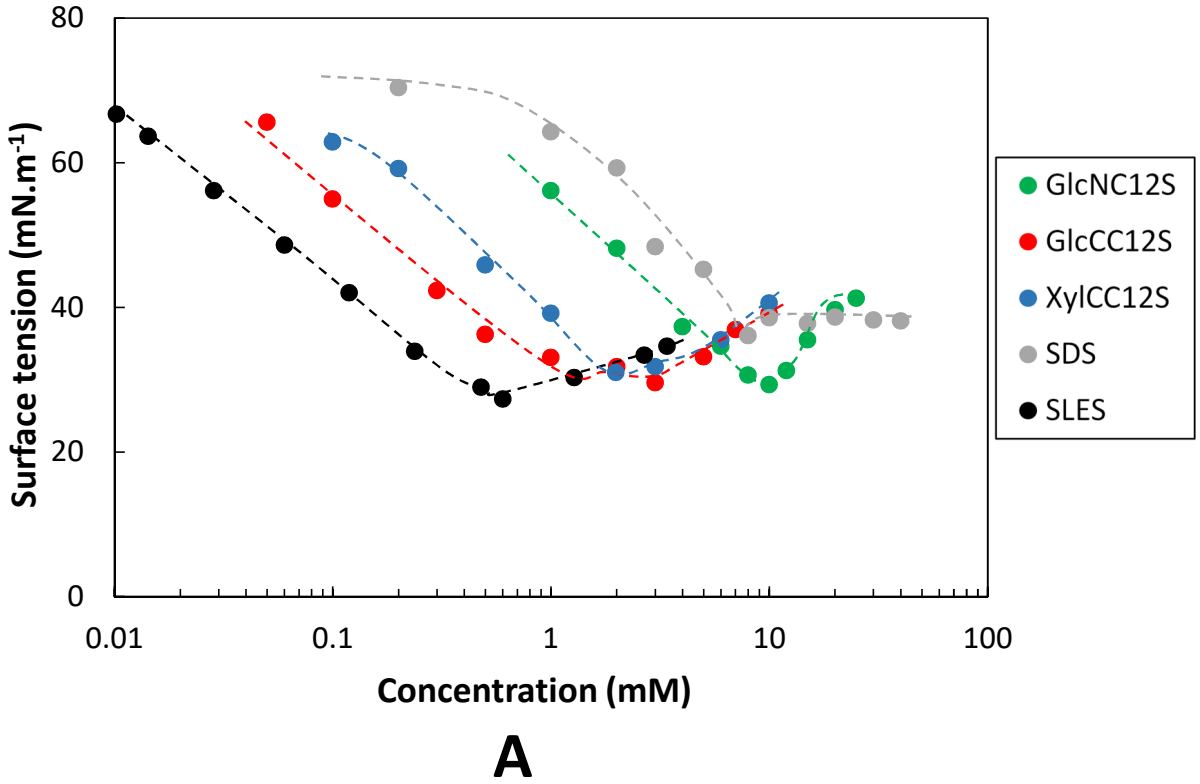
XylCC12S



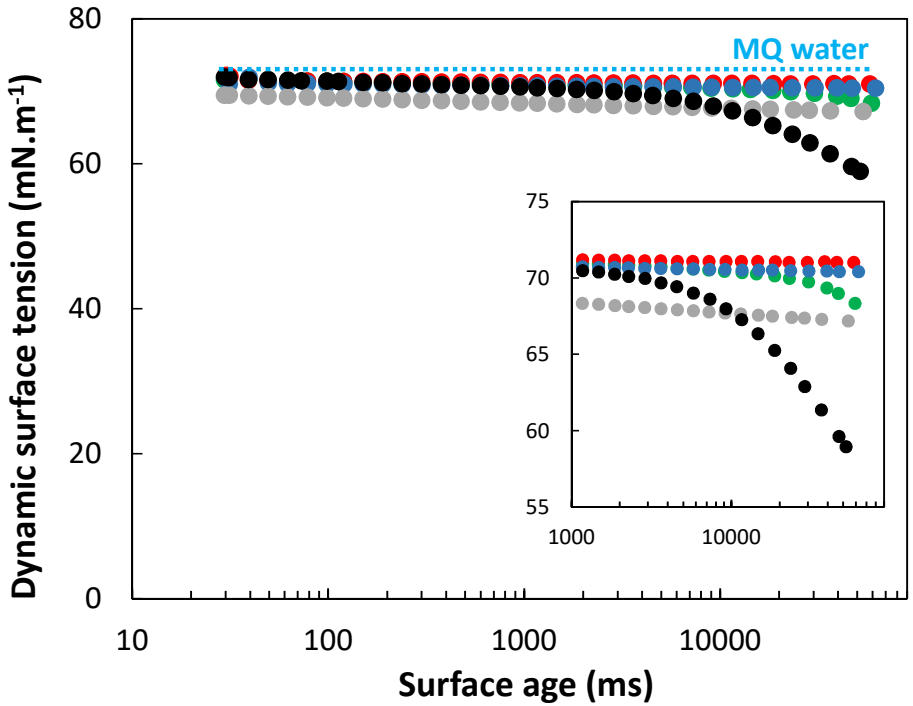
SDS



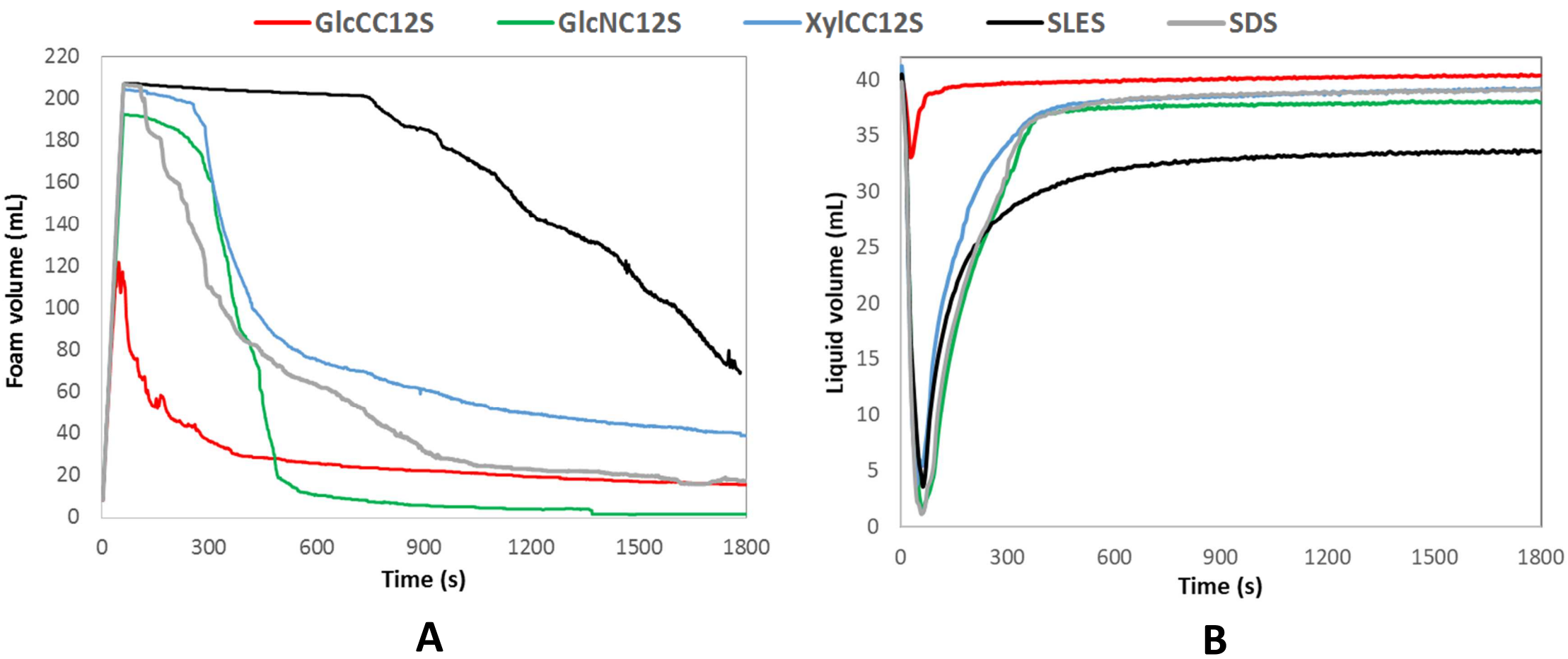
SLES


80
60
40
20
0
Surface tension (mN.m-1)
0.01
0.1
1
10
100
Concentration (mM)
GlcNC12S
GlcCC12S
XylCC12S
SDS
SLES

A


80
60
40
20
0
Dynamic surface tension (mN.m-1)
10
100
1000
10000
Surface age (ms)
MQ water
75
70
65
60
55
1000
10000

B


GlcCC12S
GlcNC12S
XylCC12S
SLES
SDS
Foam volume (mL)
Time (s)
Liquid volume (mL)
Time (s)
A
B

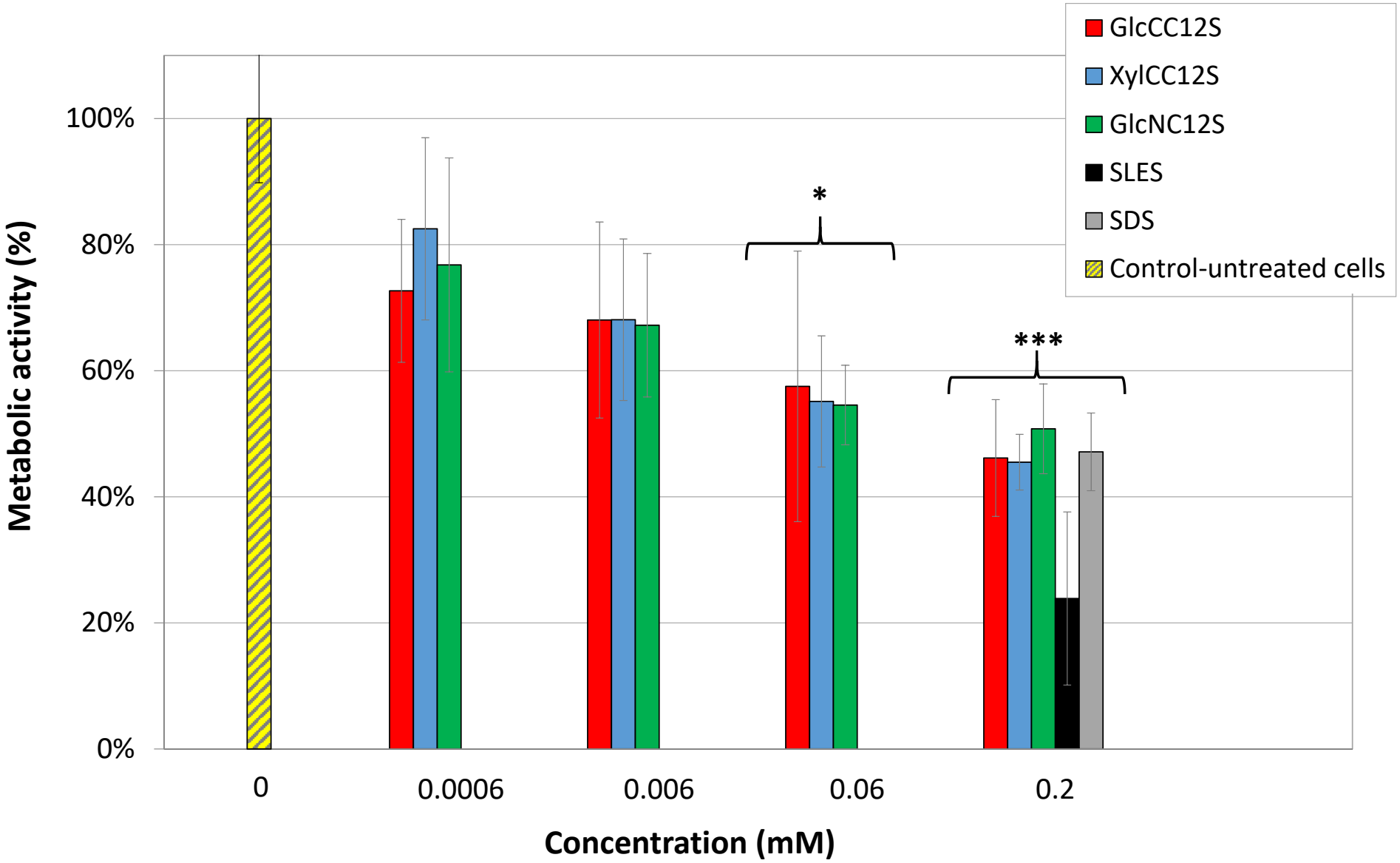

GlcCC12S
XylCC12S
GlcNC12S
SLES
SDS
Control-untreated cells
Metabolic activity (%)
100%
80%
60%
40%
20%
0%
*
***
0
0.0006
0.006
0.06
0.2
Concentration (mM)

Table 1. Summary of surface properties and foaming properties of surfactants: the critical micelle concentration (CMC), the equilibrium surface tensions at CMC (γ_{CMC}), the adsorption efficiency (pC_{20}), the maximum surface excess (Γ_{max}) and corresponding minimal area per molecule (A_{min})	CMC (mM)	γ_{CMC} (mN.m^{-1})	pC_{20}	$10^{10}.\Gamma_{max}$ (mol.cm^{-2})	A_{min} (Å^2)

determined from plots in Fig.2A.Surfactant					
SDS	8.0	34.9	2.52	3.86	42.9
SLES	0.5	27.3	4.40	1.31	127.0
GlcCC12S	3.0	31.5	3.92	1.68	99.1
XylCC12S	2.0	31.0	3.43	2.33	71.3
GlcNC12S	10.0	28.7	2.89	1.76	94.2

Table 2. Summary of foaming properties of surfactants: the foaming capacity (FC), the foaming stability (S), the maximum foam density (MD) and the half-life time of foam ($t_{1/2}$) determined from curves in Fig.3.

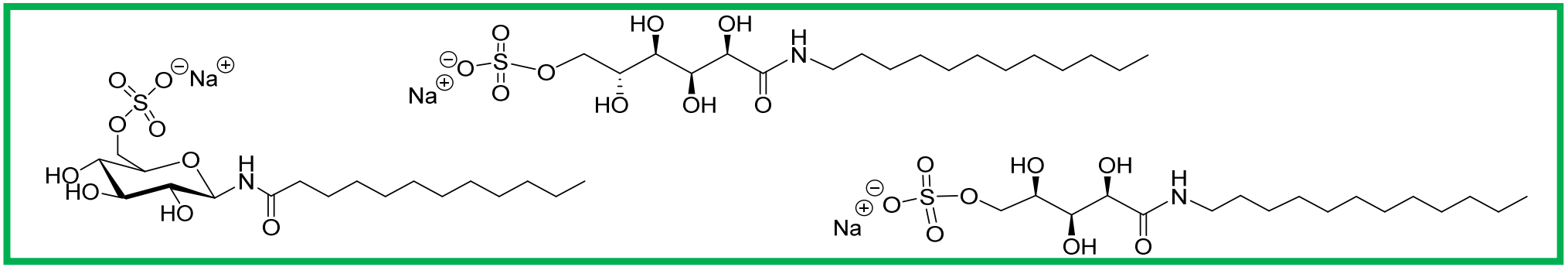
Surfactant	Foaming properties*			
	FC	S	MD (%)	$t_{1/2}$ (s)
SDS	1.05±0.01[a]	0.28±0.01[c]	18.8±0.2[b]	271±46[bc]
SLES	1.05±0.01[a]	0.79±0.01[a]	17.8±0.2[c]	1502±85[a]
GlcCC12S	0.57±0.05[c]	0.23±0.01[cd]	2.0±0.4[d]	133±2[c]
XylCC12S	1.04±0.01[a]	0.36±0.06[b]	16.9±0.5[c]	356±58[b]
GlcNC12S	0.98±0.02[b]	0.20±0.02[d]	20.6±0.5[a]	324±50[b]

[a-e] Mean values in the same column followed by different letters indicate a statistical difference ($P<0.05$, n=3)
*Measurement of foaming properties was realized at C=0.1CMC

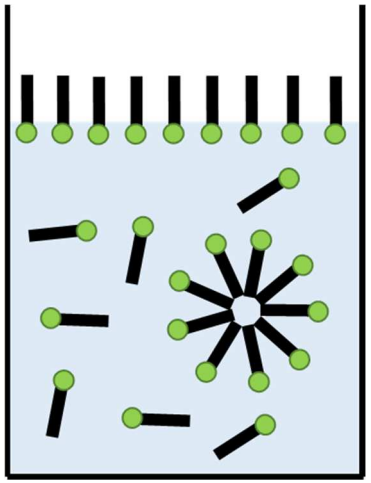
Table 3. Metabolic activity of cells and IL-1α concentrations detected in culture medium of RHE after surfactant treatment.

Surfactant	PBS (negative control)	GlcCC12S	GlcNC12S	XylCC12S	SDS	SLES
Metabolic activity (%)[a]	100±4.9	89.0±12.3	85.4±10.0	75.3±19.6	2.9±2.7***	51.1±34.6
IL-1α concentration ($pg.mL^{-1}$)[b]	5.3±2.7	68.7±9.0	35.1±9.0	54.8±8.4	157.4±23.0***	155.5±26.7***

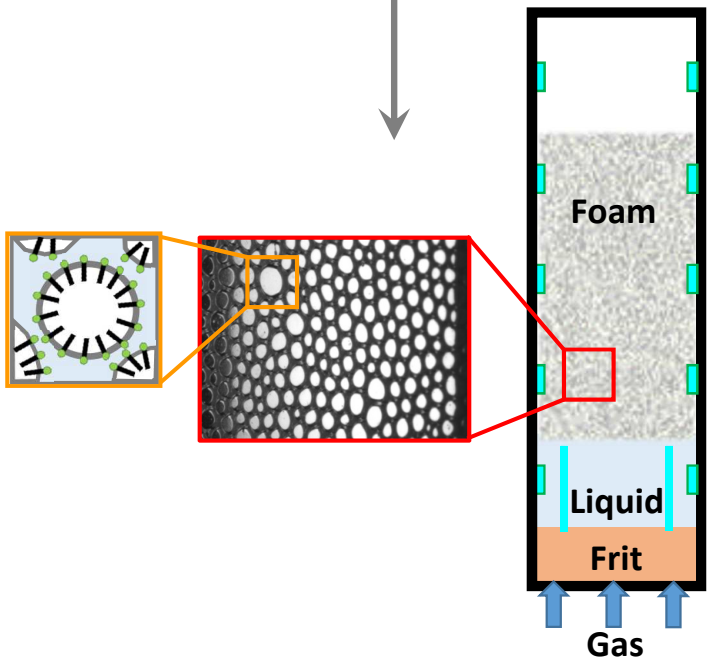
[a] Metabolic activity was measured by absorbance of cells in RHE models at 490 nm
[b] IL-1α concentration of RHE model was assessed by ELISA test after 1h surfactant exposure
*** $P< 0.001$ indicate significant difference versus untreated cells



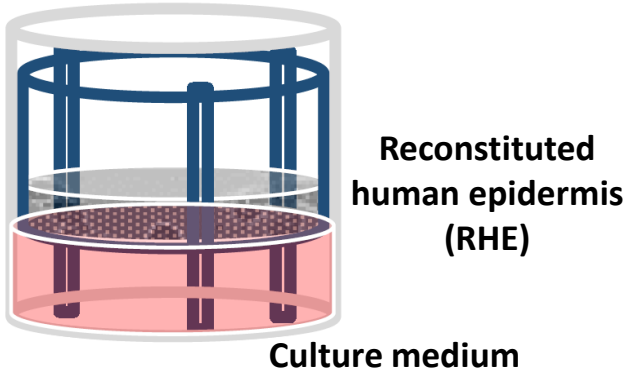
anionic sugar-based surfactants



surface properties



foaming behavior



biological responses