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Anne-Laure Fameau[1*], Yingzhen Ma[2], Miriam Siebenbuerger[3] and Bhuvnesh Bharti[2*]

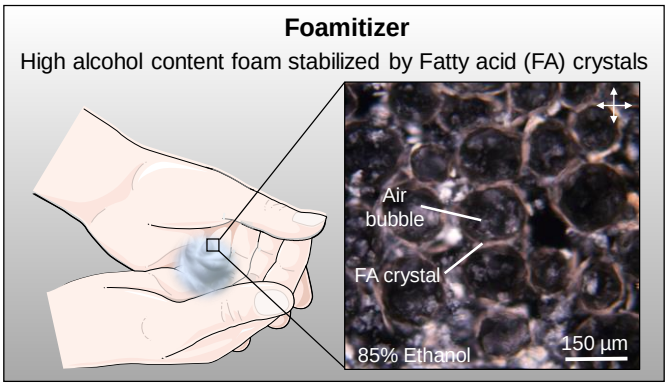
[1]*National Institute of French Agricultural and Environmental Research, INRAE, Nantes 44300, France*

[2]*Cain Department of Chemical Engineering, Louisiana State University, Baton Rouge, Louisiana 70803, USA*

[3]*Center for Advanced Microstructures and Devices, Louisiana State University, Baton Rouge 70806, USA*

*Corresponding authors emails: alfameauinra@gmail.com; bbharti@lsu.edu

Graphical abstract



Keywords : Crystals, fatty acids, foam, solvent effect, thermostimulable, soft-material

Abstract

Aqueous foams are encountered in many commercial products used in our everyday lives and are widely studied. However, the formation and stabilization of foams using high alcohol content (> 75%) solvents such as ethanol is still a scientific challenge. Herein, we report for the first-time foams based on high ethanol content showing long-term stability by using natural fatty acid crystals. The platelet-shape crystals are adsorbed at the air-water surface protecting the bubbles against coalescence. The melting of crystals triggers the foam destabilization leading to thermostimulable high ethanol content foams. These foams can be used as a new formulation strategy for alcohol-based hand sanitizers to better clean hands, protect the skin by the presence of fatty acids, and limit the transmission of virus and other pathogens.

Main Text

In early 2020, the World Health Organization (WHO) declared a global pandemic due to COVID-19. The rapid spread of this pandemic has highlighted the importance of disinfectants for personal and household hygiene. One of many ways to reduce the transmission of contagious bacteria and viruses is frequent and effective hand sanitization by the traditional handwashing or using alcohol-based hand sanitizers [1]. The WHO recommends formulating alcohol-based hand sanitizers using at least 80 % by volume (v/v) ethanol or 75 % isopropyl alcohol [2]. Alcohol-based hand sanitizers are known to damage lipids from the Stratum Corneum, the uppermost layer of the skin, leading to discomfort and cracking of skin, which opens routes for the entry of pathogens [1]. Moreover, these formulations alone are low-viscosity Newtonian liquids, thus pouring and rubbing these on hands is difficult [1,3]. Specially designed synthetic polymers lead to the gelling of such alcohol-water solution, but require a precise control over the pH, which is sometimes not feasible at an industrial scale [3]. Additionally, the short- and long-term impact of these synthetic polymers on skin (irritation) and on the virus inactivation are currently unknown [3]. Recently, foam-type disinfectant formulations have been introduced in the market to address the issues of solution dripping, runoff, and difficulty to cover the entire hand surface during the use [1]. Foams can be visually spread on the skin and are easier to handle and spread than the traditional gels. However, the formation and stabilization of foams using high ethanol content solvents such as the one recommended by WHO remains a challenge. Despite low surface tensions, the

absence of repulsive forces between the bubbles formed by alcohol-water mixtures is responsible for the film collapse when it thins due to the drainage [4]. The scientific challenge is to stabilize the bubbles against coalescence and to avoid thin film collapse thus providing a foam-based alternative to currently used hand sanitizers, which is easy to apply, and assists with limiting the spread of pathogens.

A recent study showed that foams from alcohol-water mixture containing 40 % ethanol can be stabilized using a mixture of sodium dodecyl sulphate (SDS) and long chain alcohol [5]. Another study showed that a short chain perfluorosurfactant enabled the formation and short-term stabilization of foams from ethanol-water mixture with maximum ethanol content of 50 % [6]. These initial studies on ethanol-water foams have three major limitations: (i) the alcohol content in the foam is significantly lower than the 80 % concentration as recommended by WHO for adequate hand sanitization, (ii) there is lack of long-term foam stability, and (iii) the precursors used in the foam production are synthetic and may adversely affect skin. In this article, we overcome these limitations by using crystalline particles of natural fatty acids as foam stabilizers. We demonstrate the formation and long-term stability of foams formed using high alcohol content solvents (up to 100 % ethanol and isopropanol) and these formulations could be used as *Foamitizer: Foaming Hand Sanitizer* [7]. In our case, the formation of foam is associated with the adsorption of fatty acid (FA) crystals at the air-water surface protecting the bubbles against coalescence rather than lowering the surface tension. These FA crystalline particles have never been applied to form and stabilize foams using high alcohol content solvents [8].

We demonstrate the principle of using FA crystalline particles as foam stabilizers on a series of linear saturated fatty acids with number of carbon atoms ranging from 14 to 22. We specifically focus on stearic acid ($C_{17}H_{35}COOH$ – C18) as foam stabilizer, as it is one of the major component of the Stratum Corneum and currently used in cosmetic formulations as a moisturizing agent [9].

Our strategy to produce high ethanol content foams is to use the concentration of FA in significant excess of its solubility limit in the respective ethanol-water mixture. The foams are obtained in two steps as shown in Figure 1.

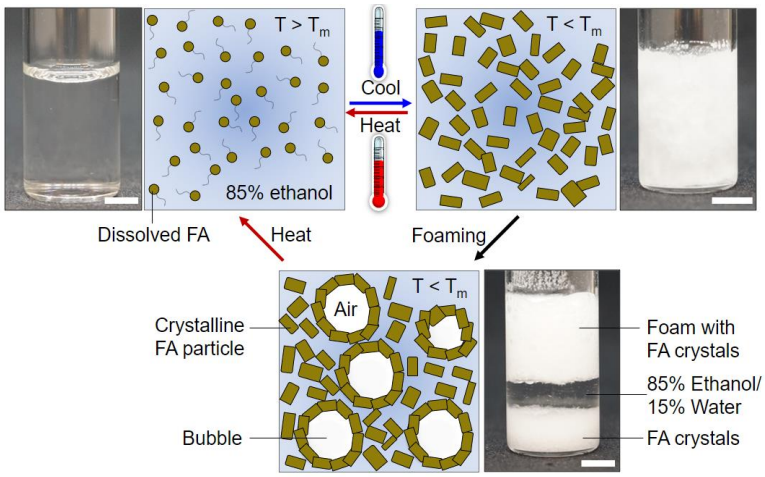


Figure 1: Schematic of the transparent sample containing molecularly dissolved fatty acids (FA) in the solvent at temperature above the melting temperature (T_m). Below T_m, crystals are formed by cooling, and a turbid dispersion is obtained. By introducing air into the dispersion, foams are formed due to the bubbles being stabilized by the FA crystals. By heating the foam above T_m, the crystals melt, and the foam disappears leading to the initial transparent solution of FA molecules. The scale bar is 5 mm.

In the first step, a large amount of C18 (concentration >> solubility limit) is added to aqueous solvent containing 85 % ethanol. The solvent was prepared by mixing water of pH 6.8 and ethanol with no additional acid/base or electrolyte. This dispersion is heated above the phase transition temperature to obtain molecularly dissolved fatty acid in the solvent. Then, by cooling down the mixture below the phase transition temperature, the solution becomes supersaturated leading to the formation of C18 crystalline particles. In the second step, foam is produced from the crystalline particles by introducing gas in the dispersion by well-established two-syringes method: where one syringe is filled with air and the other one filled with the liquid phase and connected to the first one by a constriction (see SI) [10-12].

The presence of crystalline particles in ethanol-water mixture is a pre-requisite to produce foam. The solubility of C18 in the ethanol-water mixture containing 85 % ethanol was determined by monitoring the change in transmittance (see SI). First, we determined the solubility limit by measuring the transmittance of C18 with increasing concentration from 0.2 to 2.0 wt.% at 25°C (Figure 2a). The solubility limit of C18 at 25 °C is ~1 wt.%. Below 1 wt.%, the transmittance was ~100% and the samples remained transparent. Above 1 wt.%, we observed the transition from a transparent liquid dispersion into a turbid dispersion leading to a decrease in transmittance. By optical and crossed polarized microscopy, we observed the presence of platelet-shape FA crystalline particles within size range ~40-70 µm (Figure 2a inset, S1). Then, we determined the melting temperature (T_m) of the crystals corresponding to the phase transition for C18 at 10 wt.% in the ethanol-water mixture using transmittance

measurements (Figure 2b). C18 shows a first order phase transition from a crystalline (turbid) to liquid phase (transparent) at 42 °C. The molecular ordering of C18 within the crystalline particles was determined by Wide-Angle X-ray Scattering (WAXS) as a function of the temperature in the range $0.1 < Q < 1.0$ Å^{-1}; where Q is the wave vector (Figure 2c). From 25 °C to 40°C, i.e. below the phase transition temperature, one intense peak at 0.155 Å^{-1} corresponding to a *d*-spacing of ~40.5 Å, followed by additional higher order Bragg peak were detected. Below the melting temperature, C18 crystals had a double layer structure and crystallized into the C-polymorphic form, which is known to be its most stable form [13]. From 42°C corresponding to T_m, no Bragg peaks were observed in WAXS, indicating the melting of the crystals and the presence of molecularly dissolved C18 in the solvent (Figure 2c).

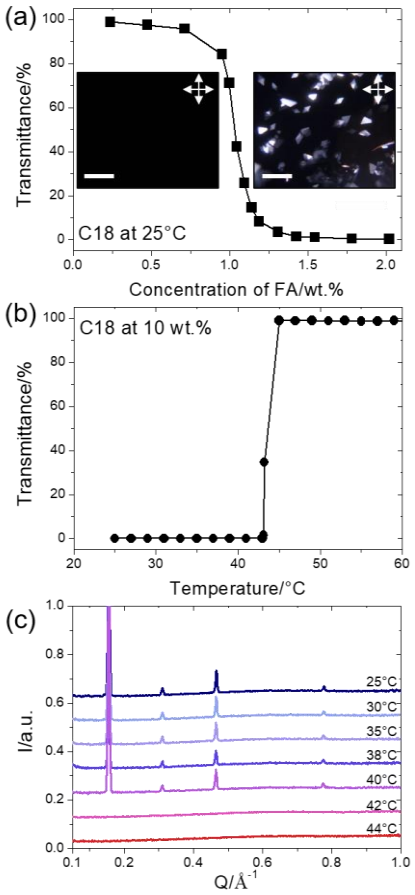


Figure 2: (a) Evolution of the transmittance as a function of fatty acid concentration in 85 % of ethanol with 15 % water (v/v) at 25 °C. The cross-polarized light microscopy pictures show the absence of crystals below 1 wt.% and the presence of crystals (bright spots) at 10 wt.%. The scale bars are 100 µm. (b) Evolution of the transmittance as a function of temperature for C18 at 10 wt.% in 85 % of ethanol. (c) WAXS spectra for C18 at 10 wt.% in 85 % of ethanol as a function of temperature. The spectra are shifted in intensity for clarity.

Foams were prepared at 25 °C as a function of C18 concentration and characterized for both foamability and foam stability. Below the solubility limit of 1 wt.% no foam was produced since no crystals were present. However, from 2 wt.% to 10 wt.%, the surface-active C18 crystals were present in the ethanol-water solvent and the foams were obtained (Figure 3a).

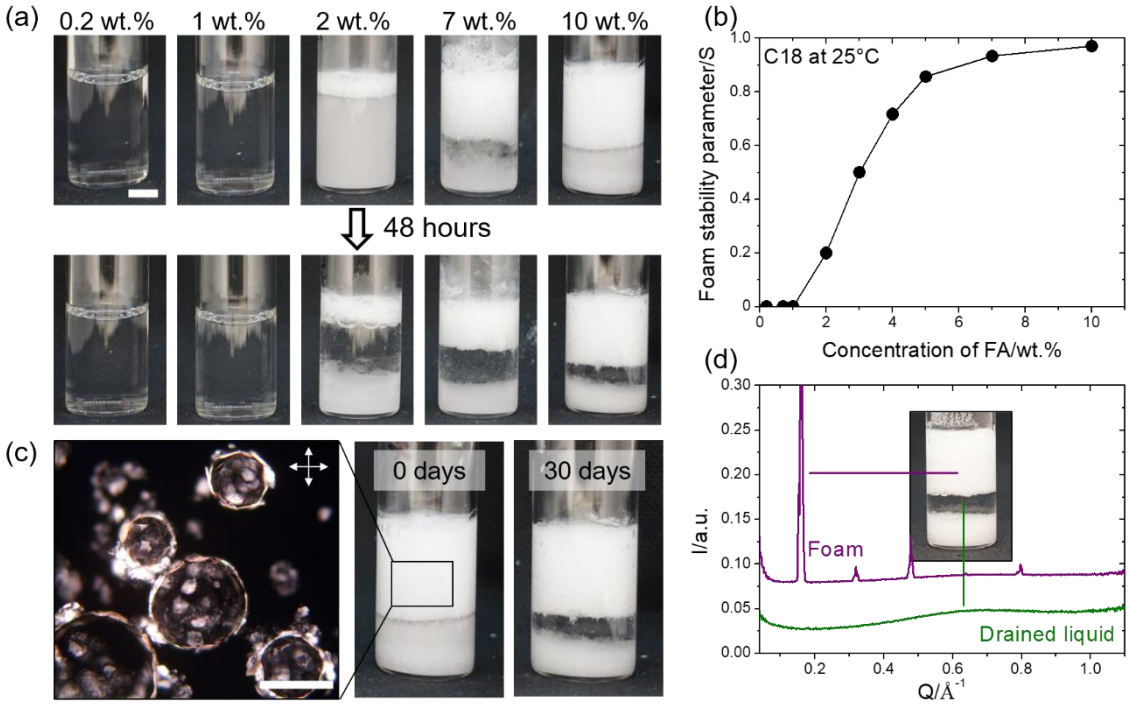


Figure 3: (a) Photographs of the change in foam volume as a function of C18 concentration just after the foam formation and after 48 hours at rest at 25°C. The scale bar is 5 mm. (b) Change in the foam stability quantified using the foam stability parameter (S) as a function of C18 concentration at 25°C. (c) Photographs of a foam made with C18 at 10 wt.% just after foam formation and after conservation of the foam for 30 days at 25°C, with the corresponding cross polarized light microscopy image showing the bubbles coverage by fatty acid crystalline particles and the non-spherical shape of the air bubbles. The scale bar is 50 µm. (d) WAXS spectra of the foam and the drained transparent liquid at 25°C.

The initial foam volume increased by increasing C18 concentration (Table S1). The stability of the foam was quantified using a foam stability parameter, S, defined as $S = v_{initial}/v_{final}$, where $v_{initial}$ and v_{final} are the volumes of foam immediately after foam production, and after 48 hours of equilibration at 25 °C, respectively. Here $S = 0$ represents an unstable foam and $S = 1$ represents an ultrastable foam. For C18 in ethanol-water mixture,

S increases from 0.2 to 0.94 upon increasing the fatty acid concentration from 2 wt.% to 10 wt.% (Figure 3b). The foam stability increases with C18 concentration due to the increasing amount of crystalline particles in the solution, as shown by microscopy both at the bubble surfaces and in bulk (Figure 3c, S2). We followed the foam stability for one month, and no change was observed in terms of foam volume and bubble size. This foam could be considered as ultrastable [14]. Note that the liquid fraction within the foam was high around 40-45 %, corresponding to very wet foams. The drainage was stopped quickly after the foam formation in few minutes. Similar observations were made for aqueous foams stabilized by SDS crystalline particles [9].

To understand the foam stabilization mechanisms, we performed multi-scale characterization using contact angle measurements, microscopy and WAXS experiments (see SI). The key parameter for crystals to adsorb at the air-solvent surface is to exhibit a suitable contact angle below 90° [15]. The contact angle of a drop of ethanol-water mixture in air on a C18 crystals was ~ 32°, consistent with adsorption of the crystalline particles to air bubble surface (Figure S3). The driving force for the adsorption of C18 crystals is to reduce the surface energy of the air-solvent surface [16]. The crystalline particles adsorbed onto bubble surfaces were clearly observed by bright-field and cross-polarized light microscopy as shown in Figure 3c. The bubble surface was rough and textured due to the adsorption of the crystalline particles at the surface. Some bubbles were also non-spherical which is characteristic of the particle-coated interfaces leading to solid-like interfaces [15,17]. By WAXS, we determined that the crystals structure of C18 was the same in bulk and inside the foam (Figure 3d). The drained liquid was composed of pure solvent for the transparent upper part as shown by WAXS and the lower part of sedimented FA crystals (Figure 3c-d). Coarsening and the coalescence of bubbles was arrested by the presence of C18 crystals. The crystals delayed the drainage by accumulating in the foam liquid channels between bubbles thus restricting film collapse, which was one of the main challenge to stabilize foams with high alcohol content. Therefore, foams were stable for months after production (Figure 3c).

The principle of using FA crystals to stabilize foams can be extended to solvents with 100 % alcohol content. We increased the ethanol content of the liquid phase from 75 % to 100 % and kept the concentration of C18 at 10 wt.% at 25 °C. For all tested ethanol amounts, foams were obtained due to the presence of C18 crystals (Figure 4a). The foam stability parameter, S, show a slight decrease from 0.94 to 0.86 upon increasing the ethanol content from 75% to 100%. We extended our approach to produce ethanol-based foams using

isopropanol, which is the other solvent recommended by the WHO for hand sanitization [2]. For C18 at 10 wt.% at 25 °C stable foams were obtained with aqueous mixtures containing 75 % to 100 % of isopropanol (Figure 4a). These results show that the main parameter to design stable foams from solvents such as ethanol and isopropanol was the presence of surface-active C18 crystals, since SDS cannot stabilize such type of foams (Figure 4a, S4). Foams were also obtained using crystals of other FA such as myristic acid (C14), palmitic acid (C16) and behenic acid (C22). They formed surface-active crystals in the solvents above their respective solubility limit, leading to the formation and stabilization of foams (Figure S5-8).

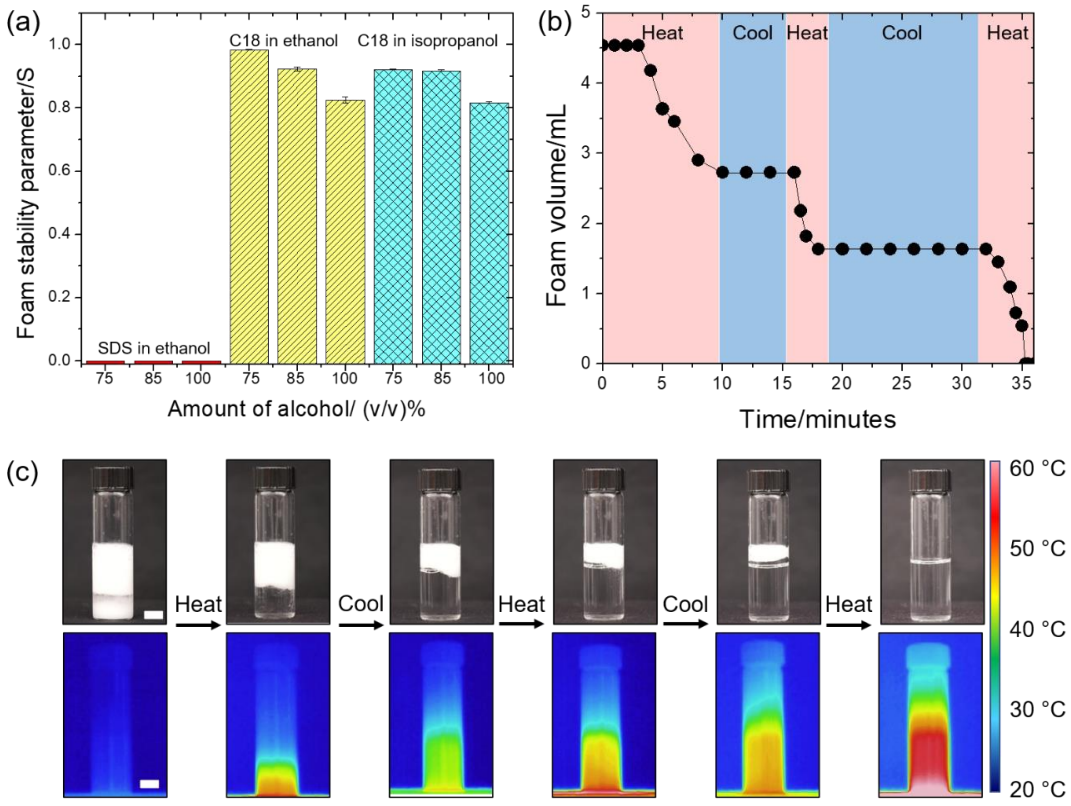


Figure 4: (a) Evolution of the foam stability parameter (S) for C18 at 10 wt.% and SDS at 10 wt.% with an amount of alcohol varying from 75 % to 100 % at 25°C. Stabilization/destabilization of a foam made with C18 at 10 wt.% in 85 % of ethanol during heating/cooling cycles: (b) Evolution of the foam volume as a function of time. (c) Photographs of foams with the corresponding Infrared images. The scale bar is 5 mm.

The destabilization of the foams can be triggered by heating the foams and melting the fatty acid crystals [18]. We studied the foam stability as a function of temperature using visible and infrared imaging (Figure 4b-c). The foams formed by C18 in the ethanol-water

mixture at 25 °C were quickly destabilized above T_m of the crystals (Figure 4c). We monitor the effect of the crystal melting by optical microscopy, where we observe that the C18 crystals stabilizing the bubbles and dispersed in bulk disappear at T_m leading to rapid destabilization of foam (SI movie 2). The foam destabilization process could be arrested by cooling down the foam below its melting temperatures before all the foam disappeared. This is demonstrated in Figure 4b, where the change in foam volume could be controlled by instantaneous cooling of the foam. The foam could be destabilized/stabilized at will, just by tuning the temperature below or above the corresponding T_m of the crystals. The foam destabilization temperature depends only on the T_m of the fatty acid, which is governed by the alkyl chain length of fatty acid, its concentration and the nature of the solvent (SI movie 3). We performed 10 multiple cycles of heating/cooling in order to follow the refoamability after foam destruction. We observed that the initial foam volume remained constant for the 10 cycles showing that even after the crystals melting and renucleation, the foamability remained nearly constant (Table S2).

Conclusion

The COVID-19 pandemic crisis has exposed significant scientific gaps in different fields such as in soft matter [3]. Here, we took the opportunity to fill one of this gap concerning the production and stabilization of foams using high alcohol content solvents. This is an important issue both from fundamental and applied standpoint, where new formulations are required for better hand sanitization and limit the transmission of pathogens. We show for the first time how foams with high content of alcohols such as ethanol or isopropanol can be formed using fatty acid crystalline particles, which are critical for skin nourishment. This new route to synthesize foams from high alcohol content solvents would help to tackle the disadvantages of commercial hand sanitizers.

Acknowledgments

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Associated Content

Supporting Information. Experimental section, Crystal-size determination by optical microscopy, Initial foam volume determination, Evolution of quantity of crystals in the foam as a function of fatty acid concentration evaluated by optical microscopy, Image of contact angle measurement, Fomability and foam stability for foams based on SDS in ethanol/water mixtures, Evolution of the transmittance and crystals shape and crystals structure by WAXS for C14, C16 and C22 in 85% (v/v) ethanol in water, Foamability and foam stability parameter for C14, C16 and C22 in 85% (v/v) ethanol in water, Evolution of spot temperature inside the foam as a function of time during heating/cooling cycles above and below the melting temperature of crystals, Initial Foam volume evolution during heating/cooling cycles.

Movies. Movie 1 showing foam formation, and Movie 2-3 showing melting of crystals and foam destabilization.

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