Book chapter

**Biosurfactants: Needs and Future of new pharmaceutical additive to improve solubility in Global pharmaceutical and cosmetic industries**

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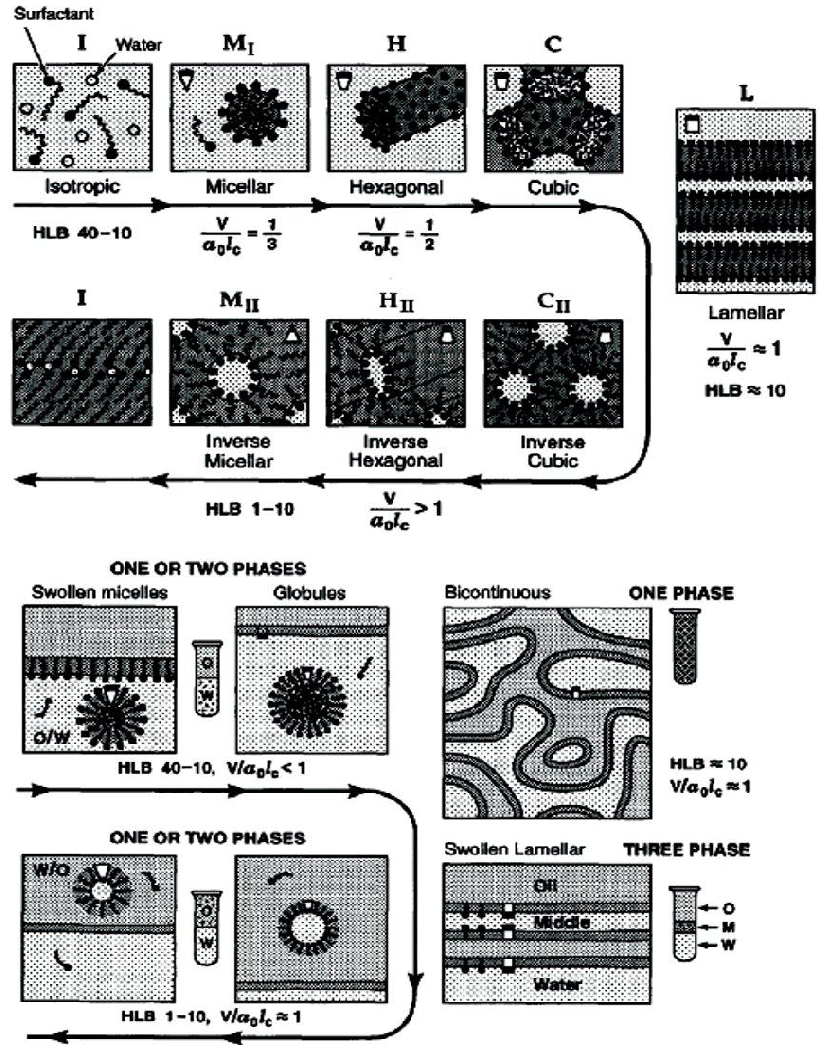
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**Introduction**

Surface active agents are amphiphilic molecules that aggregate at interfaces, reducing cross-linking and forming cluster structures such as micelles [1]. Many synthetic and mainly petroleum-based surfactants are now available to meet the current surfactant needs of the market. Only 32% of the world production of surfactants is used in industry and about 54% of this is used in household/laundry detergents [2]. Surfactants come in many forms and are generally divided into four groups based on their charge: anionic, nonionic, cationic, and amphoteric. Most chemically derived antibiotics are cationic surfactants that are also effective against Gram-positive bacteria. Anionic and nonionic surfactants are non-toxic and effective against gram-negative bacteria. There are many important surfactants such as fatty alcohol ethoxylates (FAEO), linear alkylbenzene sulfonates (LAS) and lauryl ether sulfates (LES) [3]. Growing information of the application of renewable resources and "green products" has encouraged the development of alternatives to conventional surface active agents. Biosurfactant (BS) is an example of environmentally friendly alternatives [4]. Biosurfactants can be prepared from biologically continuous materials by microbial fermentation or enzymatic synthesis [5]. The main characteristic of biosurfactants is their low micelle concentration (Critical micellar concentration). This indicates that biosurfactants are more effective at lower concentrations than many chemically prepared surfactants. Biosurfactants are good choices for "green" detergents and surfactants because they can be biodegradable and only require a minimal amount to solve the problem. Important Components in Pharmaceutical Products: Surfactants, substances that reduce the surface energy of liquid, solid and/or gas phase interactions, have many roles in medicine [6,7]. Surfactants, in addition to their chemical structure, are amphiphilic, containing both hydrophilic and lipophilic domains. Their main role in medicine is to make drugs more soluble, especially those that are poorly soluble in water, including new and improved bioactive drugs (such as small molecular drugs, bio-peptides, bio- proteins, vitamins, vaccines and essential oligonucleotides) that can be delivered in-vivo. In addition, they increase the thermodynamic efficiency and diffusion rate as well as stability of the encapsulated drug. They are particularly crucial in the application of drugs to cell surface, cell membranes, skin surfaces and other biological surfaces. Bioactive Surfactants are also essential plasticizers needed to improve the flowability and in vivo solubility of semi-solid delivery vehicles and viscous fillers such as those used in suppositories. For example, fatty acid esters of sucrose are essential lubricants for tablets [8]. They can also be used as a wetting agent when mixing chemicals with powder, granule and nanoparticle-like carriers and dispersions. The most common application of surface-active agent is self-assembly in drug delivery devices. Self-mixing structures based on surfactant monolayers are emulsions, oil-in-water dispersions or vice versa. Emulsions are relatively large, typically microns to millimeters, and are thermodynamically unstable and often require mixing to achieve long-term stability. Both aerosol and microencapsulated media are prepared using emulsions. High-pressure homogenization can be used to prepared nanoemulsions or "microemulsions" with an average size of 0.05-1.0 ¬µm, which can be sterilized by application of microfiltration due to their small size and, again, easily prevent physiological clearance. enter interfaces in life. Nano-emulsions are commonly used for parenteral administration (as depicted in Figure 1). Water-oil-surface active agent mixtures often form thermodynamically stable microemulsions with a nanoscale structure [9,10]. Hydrophilic and lipophilic surfactant systems form O/W and W/O microemulsions, mainly consisting of spherical nanoparticles. Layered or bi-continuous microemulsions are dynamically mixed networks of oil and water separated by surface active agent monolayers and formed by a system of surfactants with balanced hydrophilicity and lipophilicity. Mixing water with ingredients that themselves microemulsify (emulsify itself) on contact with water is one way to create microemulsions (and emulsions) in vivo. Surfactants are also used as therapeutic agents. Examples of antimicrobial agents include glycolipid biosurfactants, amino acid surfactants and sugar fatty acid esters [11,12]. Glyco-lipid biosurfactant and polyunsaturated fatty acid monoacylglycerol (MAG) have anti-inflammatory properties [12,13]. Sophoro-lipid biosurfactants are anti-inflammatory agents [8]. Many cosmetics, emulsions and personal care products often contain surfactants (Figure 2 Represent commonly used conventional surfactants in Pharmaceutical and cosmetic Industry) [10, 11]. Conventional surfactants are nonionic and highly biocompatible. Separation of oligonucleotides requires the use of cationic surfactants. Recent studies have shown that bio-based cationic arginine derivatives can act as biocompatible carriers [12]. Phospholipids are a different class of bio-surfactants. Besides synthetic pulmonary surfactants used in the treatment of acute and neonatal depression [14,15], they are an important part of carriers called liposomes, that can consist of one or more phospholipid bilayers (single layer or multilayer) [16-18].



**Figure 1:** Surfactant self-assembly structures formed in: a) water surfactant and b) water-surfactant-oil systems as a function of the surfactant’s hydrophilic-lipophilic balance.

**Merits of Biosurfactants**

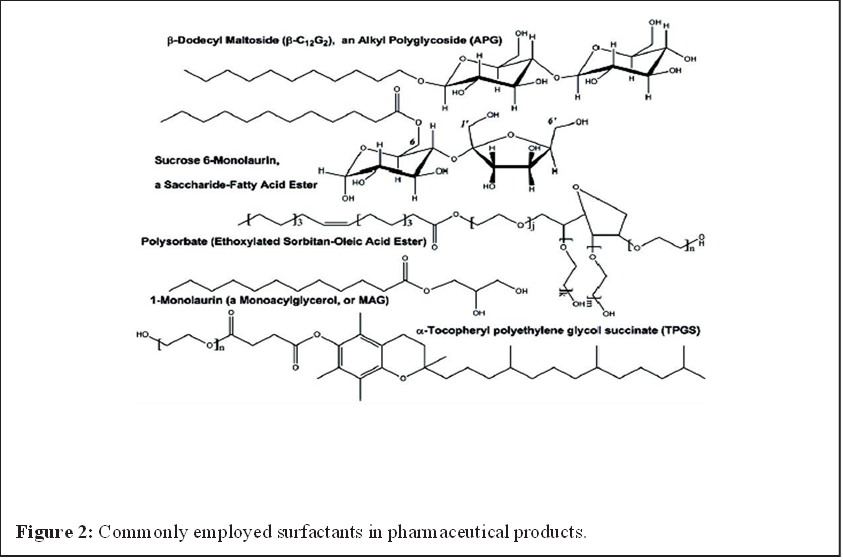
Biosurfactants have many merits over conventional chemically synthesized surfactants, some of which are: **Biodegradability** – Bio-active surfactants can be easily degraded by microorganisms [6]. **Low toxicity** - Biosurfactants are less toxic than conventional surfactants made from chemicals. In addition, it was shown that the EC50 values ​​of biosurfactants were higher than those of synthetic dispersants [7] (effective concentration reduces 50% of the test population). **Availability of starting materials** - Biosurfactants can be made from readily available and very cheap raw materials. The three main carbon sources are - hydrocarbons, lipids, and or, carbohydrates - can be used individually or in combination [8]. **Physical Factors** - Many bio-active surfactants are unaffected by physical factors such as raised temperature, pH variation, and ionic strength tolerances. Lichen produced by Bacillus licheniformis strain was unaffected by temperatures up to 50 °C, pH range 4.5-9.0, and NaCl content of 50 g/l and Ca content of 25 g/l [9]. **Surface Tension reduction Activity** – A group of researcher stated that an ideal surfactant can reduce the surface tension of water from 75 to 35 mN/m and the surface tension of water/hexadecane from 40 to 1 m N/m [10]. Surfactin has the ability to lower the surface tension of water to 25 m N/m and the surface tension of water/hexadecane to <1m N/m [9].

**Applications of Biosurfactants**

**1. Bio-compatibility and digestibility** – This is an important application of biosurfactants as pharmaceutical additives, cosmetics adjuncts and functional food additives [8].

**2. Surfactants used in Pharmaceutical industry are Primarily Natural resources based (Bio-based)**

The development of "bio-based" surfactants is expanding, primarily because the cost of crude oil as a raw material has risen relative to petrochemical raw materials (due to increased global demand and decreased production and availability) and because the use of renewable raw materials is becoming more sustainable [19]. Additionally, dependence on depleting crude oil supplies—exacerbated by rising global demand—has been linked to environmental harm, notably the largest environmental catastrophe of the year in 2010, the Deepwater Horizon oil leak in the Gulf of Mexico. The creation of greenhouse gases like CO2 and its consequences on climate change, as well as American history. Customer desire for more ecologically friendly items has increased as a result of these factors. Typically, the production costs of bio-based surfactants and their processing costs are equivalent. Usually, the processing costs of bio-based surfactants are comparable to the production costs of petroleum-based surfactants. As a result, the market share of bio-based surfactants has recently raised and this trend is expected to continue. Most of the surface active agents are produced from renewable natural resources [19,20]. Sugar esters, polysorbates, MAG and fatty acid ethoxylates all derive fatty acid acyl components from oleo-chemicals, with fatty acid methyl or ethyl esters as the main feedstock, which make up the majority of biodiesel. Since fuels, chemical intermediates and bio-based products are produced in oil refineries, the development and expansion of petrochemical biorefineries effectively complement each other [19,20]. Raw materials enriched with saturated C10-C16 fatty acyl groups include palm, palm kernel (especially palm stearin, an acyl-rich by-product of palmitic acid fractionation of palm kernel oil), coconut oil and calyx oil. Cheap sources of 16:0, 18:0, 18:1, and 18:2 fatty acid groups are bacon, used cooking oils, waste oils, jatropha oil, sapineberry oil, sea-wood oil and soap. Castor oil, which is produced in Brazil, India and several other countries around the world, is a source of ricinoleic acid. Using heterogeneous catalytic reactions, medium chain fatty alcohols - the lipophilic group of APGs (Alkyl Polyglycosides) - can be prepared from either petroleum or fatty acid methyl esters. Rubber, soap, gums and other by-products of petrochemical production can be used directly for the production of phospholipids [21].

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**Applications of Biosurfactant in Pharmaceuticals and Cosmetic Industries**

Biosurfactants have been suggested as a replacement for chemically produced surfactants in the cosmetics industry due to their effects on viscosity and product consistency through emulsification, foaming, water binding capacity, spreading, and wetting qualities (Table 1). These surfactants are used in insect repellents, antacids, bath products, acne pads, anti-dandruff products, contact lens solutions, baby products, mascara, lipsticks, toothpaste, dentine cleansers, and other items as emulsifiers, foaming agents, solubilizers, wetting agents, cleaners, antimicrobial agents, and mediators of enzyme action [22,23].

**Table 1:** Glycolipid biosurfactants' applicability to the pharmaceutical and cosmetics industries [23].

|  |  |  |  |
| --- | --- | --- | --- |
| **Glycolipid Type** | **Producing Organism** | **Activity** | **Pharmaceutical/Cosmetic Applications** |
| Sophorolipids | *Candida bombicola*, *Candida apicola* | Antibacterial, Antioxidant, Moisturizing, Wetting, Foaming agent, Emulsifying agent, Stimulates dermal fibroblasts | Lotions, hair growth supplements, lip color products, eye shadow, Anti-acne treatment, Body- -washes, deodorants, skin smoothing, anti-wrinkle, and anti aging products |
| Rhamnolipids | *Pseudomonas aeruginosa* | Antimicrobial, Emulsifying agent | Anti-wrinkle, and anti-aging products |
| Mannosylerythritol lipids | *Candida antarctica* | Antimicrobial, Emulsifying agent, Dispersant | Skin smoothing products and anti-wrinkle products |

**Bioprocessing Technology to Prepare biosurfactants for Pharmaceuticals**

Enzymes can potentially produce many biobased surfactants [19]. Bioprocessing provides various advantages over chemical processing, including increased durability, lower energy consumption (due to low temperature), decreased waste and byproduct production, absence of hazardous metal catalysts or acids/alkalis, and safer working conditions. When compared to chemical catalysts, the main drawbacks of utilising enzymes are their expensive cost (although this issue is alleviated if the enzymes are immobilised to allow re-use) and the frequently observed slower reaction speeds of enzymatic reactions. The starting materials must also have undergone prior purification due to the requirement to decrease inhibitory chemicals; for instance, material containing fatty acyls cannot contain phospholipids, aldehydes/ketones, peroxides, or other contaminants. Enzymatic bioprocessing is anticipated to become cost-competitive, despite rising energy costs (as anticipated) and greater safety advantages (due to improved biotechnologies). Enzymatic bioprocessing is expected to become more competitive and attractive.

**Discussion**

High molecular weight hydrophobic substances or medications can be made more bioavailable by biosurfactants by expanding their surface area, desorbing them from surfaces, and enhancing their apparent solubility. Using this crucial biosurfactant feature, medication formulations can be created to increase bioavailability. Bioprocessing techniques have been demonstrated to offer significant application potential in the creation of bio-based surfactants for pharmaceutical purposes, despite the fact that the technology is still in its infancy. Better durability, improved product selectivity, and reduced waste output make biocatalytic manufacturing particularly appealing. This strategy needs biotechnology to generate more durable enzymes at more affordable prices. As interest grows, scientists and engineers will eventually create new biobased surface active agents.

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