DOI: 10.21276/sajp

Scholars Academic Journal of Pharmacy (SAJP)
Sch. Acad. J. Pharm., 2017; 6(7): 320-329
©Scholars Academic and Scientific Publisher
(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

ISSN 2320-4206 (Online)
ISSN 2347-9531 (Print)

Review Article

Application of Bio-Surfactants in Cosmetics and Pharmaceutical Industry

Bireswar Bhattacharya, Tarun Kanti Ghosh, Nilimanka Das*
Regional Institute of Pharmaceutical Science & Technology, Abhoynagar, Agartala- 799 005, Tripura, India.

***Corresponding author**
Nilimanka Das
Email: aandeehere@yahoo.co.in

Abstract: Bio-surfactants are a class of surface-active molecules derived from microorganisms (yeast, fungi, bacteria). This diverse group of surface active molecules possesses both hydrophilic and hydrophobic moieties in their structure which allows their partitioningin the liquid/liquid, gas/liquid or solid/liquid interfacesresulting into lower interfacial tension. This facilitates their emulsification, foaming, solubilization, detergent and dispersing functioning. These non-toxic, biodegradable and eco-friendlybio-molecules are competent to replace their chemically synthesized counterparts and divulge themselves as a green alternative to be applied in the application field of food, cosmetic, pharmaceutical, petrochemical, bioremediation and others. The chemical composition of bio-surfactants depends on the substrate and the microorganism present. They are also divided into two large sections based on their molecular weight namely low molecular weight and high molecular weight bio-surfactants. The high molecular weight bio-surfactants are also known as bio-emulsifiers. Apart from their well acknowledged surface properties, they are also widely active against a large number of microorganism and functioning as antimicrobials.Glycolipids are most studied low molecular weight bio-surfactants, composed of different carbohydrates linked with fatty acids. They are able to form pores and destabilize biological membrane thus functioning as antibacterial, antifungal and hemolytic agents. Lipo-peptides are another type of low molecular weight bio-surfactant that shows antibacterial and antifungal activities. They are made of cycloheptapeptides with amino acids linked to fatty acids. From the scientific investigations of recent times, it is observed that the bio-surfactants and bio-emulsifiers are widely used in the field of applied science. Hence the authors have made an attempt to discuss the microbial derived bio-surfactants along with their advantages over the chemically synthesizedcounterparts, their properties and their application in cosmetic & pharmaceutical industry in this review article.
Keywords: Bio-surfactants, advantages, classification, application in cosmetic & pharmaceutical industry.

INTRODUCTION:

Bio-surfactants are a class of surface-active molecules derived from microorganisms like yeast, fungi and bacteria [1]. They have gained considerable attention due to their advantages over synthetic surfactants in terms of their derivation from renewable resources, low or non-toxicity, biodegradability, excellent surface activity, high specificity and effectiveness under extreme temperature and pH conditions [2]. They promote solubilization, emulsification, dispersion, wetting, foaming and detergent functions. The broad range of properties and functions of bio-surfactants warrants their possible application in cosmetics, pharmaceuticals, food, petrochemicals, mining, metallurgy, agrochemicals, fertilizers, beverages and other industries [3]. Bio-surfactants are amphiphilic molecules containing both hydrophilic and lipophilic moieties. They are fatty acid esters of sugars and fatty acid esters or amides of amino acids. Due to this polarized nature, the molecules tend to partition into the oil-water interface to reduce the interfacial tension and stabilize the newly created interfaces. The interfacial/surface tension reducing ability and biodegradability of bio-surfactants have made them an attractive alternative in the development of cosmetic and pharmaceutical products [4].

Cosmetic products play a vital role in human life. People use a large number of products like soap, shampoo, toothpaste, deodorant, skin care, and perfume and make-up items in their daily life. Moreover, these products that containnatural ingredients and exhibit equal or better benefits in comparison to the chemical-based products are in greater demand [5].

Bio-surfactants can serve as a green alternative in pharmaceutical industry. They can improve the solubility of drugs, particularly of those that are poorly water soluble. This includes an increasing number of newer bioactive molecules like small molecular therapeutics, peptides, proteins, vitamins, vaccines and oligonucleotides. Solubility is a prerequisite for *in-vivo* absorption of drugs. Bio-surfactants also improve the stability of encapsulated drugs and possibly the thermodynamic activity and rate of diffusion. They are particularly important to enable the penetration of drugs across cell walls and membranes, skin and other biological interfaces. Bio-surfactants as plasticizers, improve the fluidity and *in-vivo* dissolution of semisolid dosage forms like suppositories. They can serve as wetting agents and dispersants for powders, granules and nanoparticles [6].

ADVANTAGES OF BIO-SURFACTANTS [7]:

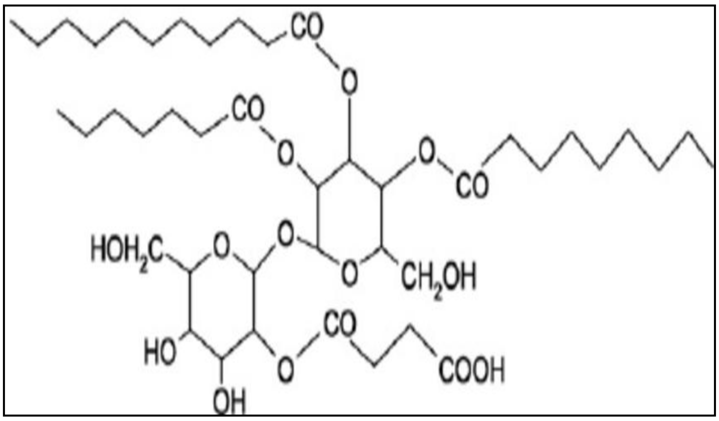
There are many advantages of bio-surfactants as compared to their chemically synthesized counterparts.Some of those are:

- **i)** **Surface and interface activity:** An effective surfactant can lower surface tension of water from 75 to 35 dyne/cm and the interfacial tension water/ hexadecane from 40 to 1 dyne/cm. Surfactinhas come up as a powerful bio-surfactant by reducing the surface tension of water to 25 dyne/cmand the interfacial tension of water/hexadecane to less than 1 dyne/cm [8].
- **ii)** **Biodegradability:** Bio-surfactants are easily degraded by microorganism compared to the synthetic surfactantsand are suitable for environmental applications such as bioremediation/biosorption. Synthetic chemical surfactants impose environmental hazard and hence, biodegradable bio-surfactants are thought as green alternative.
- **iii)** **Low toxicity:** Bio-surfactants demonstrate lower or no toxicity in comparison to the chemically derived surfactants. Moreover, they are highly effective to decrease the test population by 50% than the synthetic counterparts [9].
- **iv)** **Bio-compatibility and digestibility:** This property warrants their utility in cosmetics, pharmaceuticals and as functional food additives.
- **v)** **Specificity:** Bio-surfactants are complex bio-molecules with specific functional groups which are responsible for their reaction specificity. This is of particular interest in detoxification of specific pollutants; de-emulsification of industrial emulsions; specific in cosmetic, pharmaceutical &food applications [10].
- **vi)** **Efficient in different environmental setting:**Many bio-surfactants can comfortably function at different environmental setting like high temperature, wide pH range and ionic strength. Lichenysin produced by Bacillus licheniformis,can function at a temperature upto 50°C, a pH range of 4.5- 9.0, and NaCl concentration of 50gm/l and Ca concentration of 25gl/l [11].
- **vii)** **Cheap raw materials:** Bio-surfactants can be produced from cheap and easily available raw materials. Carbon based substrate is the vital material for bio-surfactant production. This substrate may come from hydrocarbons, carbohydrates and/or lipids, which may be used separately or in combination with each other [12].
- **viii)** **Acceptable production economics:** Depending on the application, bio-surfactants can be produced in larger quantity from industrial wastes and byproducts. This is of particular interest when they are used in petroleum related technologies [13].
- **ix)** **Use in environmental control:** Bio-surfactants can be efficiently used in handling industrial emulsions, control of oil spills, biodegradation and detoxification of industrial effluents and in bioremediation of contaminated soil [14].

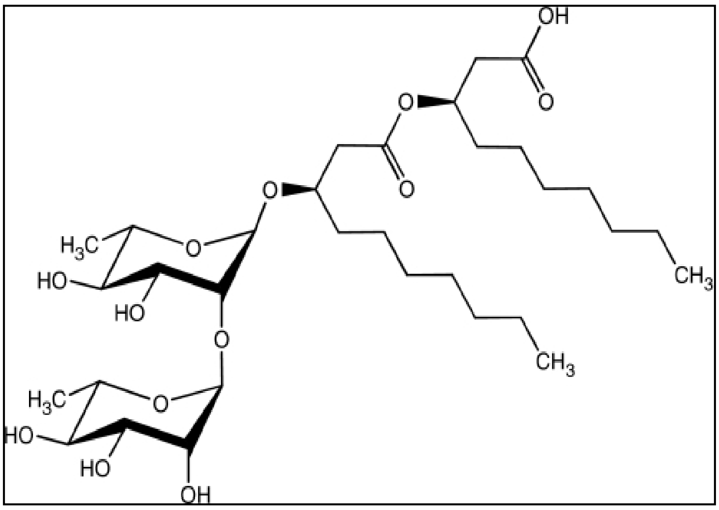
CLASSIFICATION OF BIO-SURFACTANTS [15]:

The synthetic surfactants are generally classified according to the nature of their polar group but bio-surfactants are classified based on their chemical composition and microbial origin. Bio-surfactants are classified into two broad sections based on their molecular weight. Low molecular weight bio-surfactants are efficient in lowering surface and interfacial tension. This section includes glycolipids; lipopeptides& lipoproteins; and fatty acids, phospholipids& neutral acids. High molecular weight polymers are more effective as emulsionstabilizing agents and known as bio-emulsifier. This section includes polymeric and particulate bio-surfactants. Most bio-surfactants are either anionic or neutral with a long-chain fatty acids or fatty acid derivatives as hydrophobic moiety, whereas the hydrophilic moiety can be carbohydrate, amino acid, phosphate or cyclic peptide. The major five types of bio-surfactants include glycolipids; lipopeptides &lipoproteins;fatty acids, phospholipids & neutral lipids; polymeric bio-surfactants; and particulate bio-surfactants **(Table 1)**.

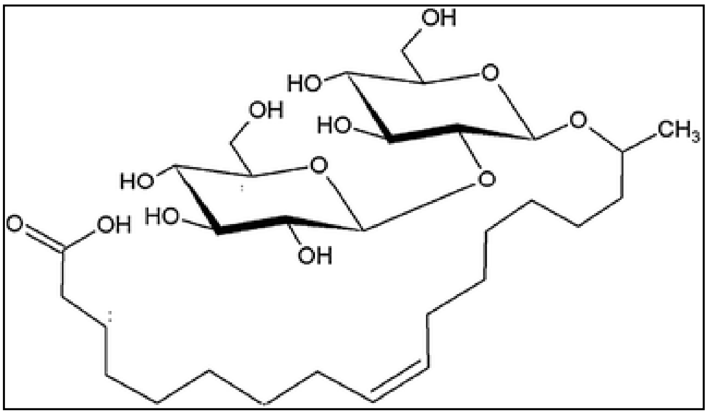
1) **Glycolipids:** Glycolipids are the most acknowledged bio-surfactants.Chemically they are carbohydrates in combination with long chain aliphatic acids or hydroxyaliphatic acids. Here the carbohydrate molecules are attached with lipids by a glycosidic bond.Rhamnolipids, trehalolipids and sophorolipids are the well known examples of glycolipids.



Fig–1 Rhamnolipid



Fig–2 Trehalose lipid



Fig–3 Acidic form of Sophorolipid

2) **Lipopeptides and lipoproteins:** Lipopeptides and lipoproteins are a class of biomolecules known for their bio-surfactant activities. They are cyclic lipopeptide containing a lipid linked to a polypeptide or amino acid chain. Cyclic lipopeptides like gramicidins (decapeptide antibiotic) and polymyxins (lipopeptide antibiotic) show remarkable surface active properties. Surfactin is another well studied cyclic lipopeptide of this type and a powerful bio-surfactant, made of seven amino acid ring attached with fatty acid, hydroxy-methyl tetradecanoic acid. Lichenysinis another of this type which act synergistically and exhibit excellent temperature, pH and salt stability.

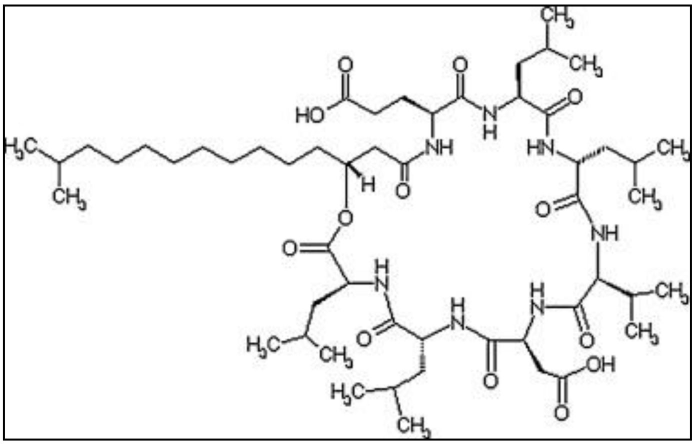


Fig-4 Surfactin

3) **Fatty acids, Phospholipids and Neutral acids:** Several fungi, yeasts and bacteria that grow on hydrophobic substrate like alkane, produces a large quantum of phospholipids, fatty acids or neutral lipids. The hydrophilic and lipophilic balance is directly proportional to the length of the hydrocarbon chain in their structures. These types of bio-surfactants are essential for different biomedical applications.

4) **Polymeric Bio-Surfactants [10]:** Emulsan, liposan, alasan, lipomanan and other polysaccharide-protein complexes are classics examples of high molecular weight polymeric bio-surfactants popularly known as bio-emulsifiers. Emulsan is an extracellular polyanionic lipopolysaccharide bio-emulsifier produced by *Acinetobacter calcoaceticus.* Liposan is a water soluble bio-emulsifier obtained from the yeast *Candida lipolytica*. It is made of 83% carbohydrate and 17% protein. Alasan is an anionic bio-emulsifier produced by *Acinetobacter radioresistens*. It is a complex of alanine, polysaccharide and proteins with a high molecular weight of 1 MDa. Alasan can effectively emulsify different hydrocarbons like long chain alkanes, polyaromatic hydrocarbons, paraffins, crude oils etc. It also facilitates solubilization of polyaromatic hydrocarbons.

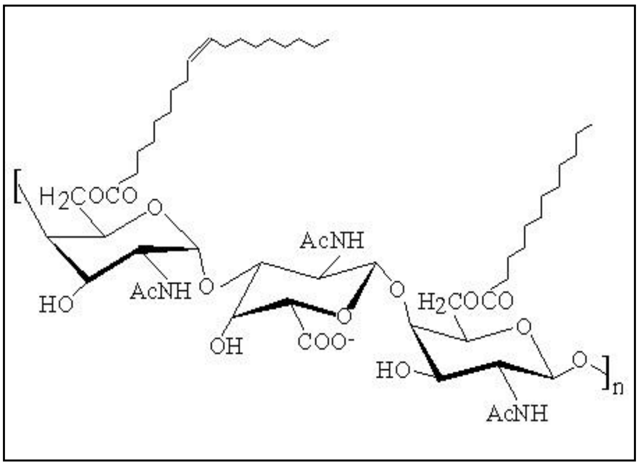


Fig-5 Emulsan

5) **Particulate Bio-Surfactants [10]:** Particulate bio-surfactants are extracellular membrane vesicles that partition hydrocarbons that form microemulsion and play an important role in alkane uptake by microbial cells. Vesicles of *Acinetobacter* sp. strain HO1-N with a diameter of 20-50 nm and a buoyant density of 1.158 g/cm^3 are composed of protein, phospholipid and lipo-polysaccharide

Table: 1 Classification of Bio-surfactants Based on Chemical Composition and Microbial Origin [16]

Bio-Surfactant Type	Bio-Surfactant Name	Name of Microorganism	Type of Microorganism
Glycolipids	Rhamnolipid	*Pseudomonas aeruginosa*	Bacteria
	Treahalolipid	*Micrococcus luteus Rhodococcuserythropolis*	Bacteria
	Sophorolipids	*Torulopsisbombicola, Wickerhamielladomercqiae*	Yeast
	Mannosylerythritollipid	*Candida Antarctica*	Yeast
	Xylolipid	*Lactococcuslactis*	Bacteria
	Cellobiolipids	*Ustilago maydis*	Fungi
	Flocculosin	*Pseudozymaflocculosa*	Fungi
	Glucolipid	*Burkholderiacenocepacia*	Bacteria
	Glucose, Fructose Sucrose-lipids	*Arthrobacterparaffineus, Corynebacterium, Nocardia* and *Brevibacterium*	Bacteria
	Monoacylglycerol	*Candida ishiwadae*	Yeast
	Diglycosyl diglycerides	*Lactobacillus fermenti*	Bacteria
	Polyol lipids	*Rhodotorulaglutinis, Rhodotorulagraminis*	Yeast
	Lipopolysaccharide	*Klebsiellaoxytoca*	Bacteria
Lipopeptides and lipoproteins	Surfactin	*Bacillus subtilis*	Bacteria
	Arthrofactin	*Arthrobacter sp.*	Bacteria
	Iturin	*Bacillus subtilis*	Bacteria
	Fengycin	*Bacillus subtilis*	Bacteria
	Lichenysin	*Bacillus licheniformis*	Bacteria
	Pumilacidin	*Bacillus pumilus*	Bacteria
	Peptide-lipid	*Bacillus licheniformis*	Bacteria
	Serrawattin	*Serratia marcescens*	Bacteria
	Viscosin	*Pseudomonas fluorescens*	Bacteria
	Gramicidin	*Brevibacillus brevis*	Bacteria
	Polymixin	*Bacillus polymyxa*	Bacteria
	Ornithine, lysine lipid	*Pseudomonas sp.*	Bacteria
Fatty acids, Phospholipids and Neutral lipids	Fatty acids	*Corynebacterium lupus*	Bacteria
	Corynomycolic acid	*Penicillium*	Fungi
	Spiculicporic acid	*Penicillium spiculisporum*	Fungi
	Oleic acid	*Issatchenkiaorientalis*	Yeast
	Neutral lipids	*Nocardia erythropolis*	Bacteria
	Phospholipids	*Acidithiobacillusthiooxidans*	Bacteria
Polymeric Bio-surfactants	Emulsan	*Acinetobacter calcoaceticus*	Bacteria
	Liposan	*Candida lipolytica*	Yeast
	Alasan	*Acinetobacter radioresistens*	Bacteria
	Mannan-lipid-protien	*Candida tropicali*	Yeast
	Biodispersan	*Acinetobacter calcoaceticus*	Bacteria
	Mannoprotein	*Saccharomyces cerevisiae*	Yeast
	Carbohydrate-protein-lipid	*Pseudomonas fluorescens*	Bacteria
	Protein PA	*Psedomonas aeruginosa*	Bacteria
	Bioemulsan	*Gordinia sp.*	Bacteria
Particulate Bio-surfactant	Vesicles andfimbriae	*Acinetobacter calcoaceticus*	Bacteria
	Whole cell	Variety of bacteria	-

CRITICAL MICELLE CONCENTRATION OFBIO-SURFACTANTS:

The critical micelle concentration (CMC) is a good parameter to evaluate the surface active efficiency ofbio-surfactants. **Table 2** offers certain CMC values that may demonstrate the effectiveness of bio-surfactant as surface active molecules in comparison to their chemical counterparts. Lower the CMC, greater the efficacy of the surfactant at lower concentrations. So, a small amounts of bio-surfactant is needed to reduce surface tension coupled with their known biodegradability makes them excellent candidates for “green” detergents and surfactants.

Table−2: Critical micelle concentrations of surfactants and bio-surfactants [16]

Name of Surfactants	CMC (mg/L)
Phosphatidylethanolamine	30
Phosphatic acid	70
Rhamnolipid	20
Surfactin	11
Alkylbenzene sulfonate	590
Sodium lauryl sulfate	2000 to 2900

COSMETOCEUTICAL APPLICATIONS OF BIO-SURFACTANT:

Anti-aging skin care products [17]:

Generally there are two types of aging that the human body undergoes. One is the intrinsic aging and the other is the extrinsic aging. In case of intrinsic aging the collagen and elastin fibers become thicker, more clumped and looser, resulting in inelastic and brittle skin and eventually in wrinkling and sagging whereas extrinsic aging occurs due to the effect of environmental factors like smoke, pollution and ultraviolet rays which give rise to free radicals that binds with the skin layer and causes chemical changes that result in aging. To reduce or slower the effect of skin aging certain antioxidants containing products like anti-aging facial gel, anti-aging creams are used.Takahashi *et al.* evaluated the antioxidant capacity of mannosylerythritol lipid (MEL) derivatives A, B and C by using a 1,1-diphenyl-2-picryl hydrazine (DPPH) free-radical method and superoxide anion scavenging assay with fibroblasts NB1RGB cells. MEL-C showed the highest antioxidant activity (50.3% at 10 gm/l) and also presented good protective effects in cells against oxidative stress (30.3% at 10lgm/ml of MEL-C). Based on their results, it is suggested that MELs have potential as anti-aging skin care property.

Conditioning hair mask [18, 19]:

Hair is the outer protective layer of the head (or skull) against heat and UV rays. It also keeps the skull cool and provides the face with a beautiful look. So, hair and its care becomes an important task from cosmetoceutical point of view. Among all other hair care products, conditioning hair mask generally moisturize the hair.Owen and Fan, evaluated the use of oligomer bio-surfactants in the conditioning hair mask formulation with promising result.

Skin nourishing cosmetic [20]:

Skin is a vital part of the body. Harsh weather conditions and climatic changes affect the skin tone and make it dry due to which peeling of skin takes place. UV rays also responsible for skin aging and skin becomes dry. Kitagawa *et al*. included a bio-surfactant obtained from *Pseudomonas antarctica*in the formulation to develop skin nourishing cosmetic.

Shampoo [21]:

In a recent study conducted by Desanto*et al*. proposed the use of rhamnolipid bio-surfactant obtained from *Pseudomonas aeruginosa* to formulate a shampoo comprising 2% of rhamnolipid dissolved in water. The antimicrobial effect of the said bio-surfactant kept the scalp free from odor for three days and maintained a luster.

Shower gel [22]:

Showergel is a liquid product used to cleanthe body. It is an emulsion of water and detergent base (derived from petroleum), usually with added fragrance. It has advantages over soap because it is less irritating to the skin.Trevor *et al*. prepared a mild formulation suitable for shower gel formulations using a sophorolipid bio-surfactant in combination with an anionic surfactant. This patented formulation was composed of 1-20% (w/w) sophorolipid; 1-20% of a chemical anionic surfactant; 0-10% of foam boosting surfactant; 0-2% of additional electrolyte; 0-10% of additional detergent additives and 40-98% of water.

Moisturizing skin cleanser [23]:

A skin cleanser is a facial care product that is used to remove make-up, dead cells, oil, dirt and other types of pollutants from the skin. This helps to unclog pores and prevent skin conditions such as acne. A cleanser can be used as part of a skin care regimen combined with a moisturizer. Allef *et al*. studied many cosmetic formulations containing at least one bio-surfactant and one fatty acid. Rhamnolipids and sophorolipids were used in combination with 10% of oleic oil, to develop different cosmetic formulations like conditioning anti-dandruff shampoo, moisturizing skin cleanser, body cleanser, shower gel etc.

Toothpaste [24]:

In a recent study, a bio-surfactant obtained from Nocardiopsis bacterial genus was used as an alternative to Sodium dodecyl sulfate (SDS) in toothpaste preparation. Based on theresults, the authors suggested that bio-surfactants could replace synthetic surfactants, like SDS because they are more effective and less toxic.

PHARMACEUTICAL APPLICATIONS OF BIO-SURFACTANT:

Gene Delivery [10]:

Gene delivery is an efficient and safe method for introducing exogenous nucleotides into mammalian cells for clinical application. It has been reported that lipofection using cationic liposome, a method of gene transfection is considered to be a potential way to deliver foreign gene into the target cells without any side effects.A study of cationic liposome and liposome based on bio-surfactants shown increased efficiency of gene transfection.

AntibioticActivity [25]:

Antibiotics are a group of drugs that either inhibits the growth of microorganism or kill them. But the uncontrolled consumption of these drugs has prompted the microbes to develop resistance. Under these circumstances, it is very much important to search for newer antibiotics. Sophorolipid (SL) bio-surfactants exhibit substantial antimicrobial property and are being tried to address this issue. The complete inhibition of *Staphylococcus aureus* was not possible by tetracycline in more than 6 hrs, but the combinatorial therapy using SL-Tetracycline was found to be quite satisfactory eliminating the microbe in 4 hrs only which suggest the strong synergistic effect of SL. In a separate study, SL-Cefaclor mixture was shown to be more effective against *Escherichia coli,* inhibiting more than 48% of the organism within 2 hrs of exposure when compared to Cefaclor alone. Scanning electron microscopy of the *Escherichia coli*treated with SL-Cefaclormixture revealed bacterial cell membrane damage and pore formation. This led to the speculation that SLs being amphiphilic in nature can span through the structurally alike cell membrane and facilitate the entry of drug molecules.

Antimicrobial Activity [26]:

Structural compositions of bio-surfactants confer them to exert their toxicity on the plasma membrane permeability similar to the detergent. The antimicrobial activity of two bio-surfactants obtained from *Lactococcuslactis* and *Streptococcus thermophilus A*, bacteria have been investigated against a wide variety of bacterial and yeast strains isolated from explanted voice prostheses. It was found that both the bio-surfactants have a high antimicrobial activity even at low concentration. Bio-surfactants are known for their anti-adhesive property. They interfere in the microbial adhesion and formation of bio-film on catheter materials and voice prostheses thus functioning as antimicrobials. In a recent study,this anti-adhesive property was demonstrated where the bio-surfactants obtained from three *Lactobacillus acidophilus* strains inhibited the formation of a bio-film produced by *Staphylococcus epidermidis* and *S. aureus*. Adhesion of *Streptococcus sobrinus*and *Streptococcus mutans* to bare enamel was also prevented by a bio-surfactant obtained from*Streptococcus mitis.* It was suggested that these reductions may be attributed to the increased electrostatic repulsion between the biofilm producing bacteria and the bio-surfactant.Glycolipid bio-surfactants obtained from *Candida antartica*&*Pseudomonas aeruginosa* and lipopeptides produced by *Bacillus subtilis*&*Bacillus licheniformis* have been shown to have potent antimicrobial activities. A lipopeptide type of bio-surfactant obtained from *Bacillus subtilis* R14 shown antibacterial activity against 29 bacterial strains. Similarly, another bio-surfactant produced by a marine *Bacillus circulans* had strong antibacterial activity against gm (+) and gm (-) pathogens.

Antifungal Activity [27]:

In a recent study, a glycolipid bio-surfactant named flocculosin was shown to display *in-vitro* antifungal activity against several pathogenic yeasts, associated with human mycoses.

Antiviral activity [28]:

Surfactin and its analogues have been reported to have antiviral activity. The potential inactivation of enveloped viruses, such as retroviruses and herpes viruses, compared to non-enveloped viruses, suggests that this inhibitory action may be mainly due to physico-chemical interactions between the virus envelope and the surfactant.An antimicrobial lipopeptides produced by B. subtilis, inactivated cell-free virus of porcine parvovirus, pseudorabies virus, newcastle disease virus and bursal disease virus, while it effectively inhibited replication and infectivity of the newcastle disease virus and bursaldisease virus but had no effect on pseudorabies virus and porcine parvovirus. The biosurfactantsophorolipids have activity against human immunodeficiency virus. Similarly, a rhamnolipid and its complex with alginate both produced by a Pseudomonas sp. strain, showed significant antiviral activity against herpes simplex virus types 1 and 2. The suppressive effect of the compounds on herpes simplex virus replication was dose-dependent and occurred at concentrations lower than the critical micelle concentration.

Anti-human Immunodeficiency Virus and Sperm-immobilizing Activity [29]:

The incidence of human immunodeficiency virus (HIV)/AIDS in women between 15-49 years has called for female-controlled, effective and safe vaginal microbicide.Sophorolipidbio-surfactant produced by *Candida bombicola* and its structural analogues are reported to have anti-HIV, spermicidal and cytotoxic activities. Sophorolipid diacetate ethyl ester derivative is the most potent spermicidal and virucidal agent of the series of sophorolipids studied.Its virucidal activity against HIV and sperm-immobilizing activity against human semen are similar to those of nonoxynol-9. However, it also induced enough vaginal cell toxicity to raise concerns about its applicability for long-term microbicidal contraception.

Anticancer Activity [30]:

Glycolipids produced by some bacteria and yeasts have potent anticancer activity. Microbial extracellular glycolipids like mannosylerythritol lipids (MEL)-A, MEL-B, polyol lipid, rhamnolipid, sophorose lipid, succinoyltrehalose lipid (STL)-1 and STL-3 have been investigated and found that except rhamnolipidall other glycolipids are involved in induced cell differentiation instead of cell proliferation in humanpromyelocytic leukemia cell line. STL and MEL markedly increased common differentiation characteristics in monocytes and granulocytes respectively. Exposure of B16 cells to MEL resulted in the condensation of chromatin, DNA fragmentation and sub-G1 arrest (the sequence of events of apoptosis). In addition, exposure of PC12 cells to MEL enhanced the activity of acetylcholine esterase and interrupted the cell cycle at the G1 phase, with resulting outgrowth of neurites and partial cellular differentiation. This suggests that MEL induces neuronal differentiation in PC12 cells and provides the groundwork for the use of microbial extracellular glycolipids as novel reagents for the treatment of cancer cells.It have been suggested that the sophorolipid produced by*Wickerhamielladomercqiae* have anticancer activity. The cytotoxic effects of sophorolipid on cancer cells of H7402, A549, HL60 and K562 were investigated by MTT assay. The results showed a dose-dependent inhibition ratio on cell viability according to the drug concentration <62.5 gm/ml.

Immunological Adjuvants [26]:

Immunological adjuvants are the agents that may be added to a vaccine to modify the immune response by boosting it so that a higher amount of antibodies are produced for a longer lasting protection, thus minimizing the amount of injected foreign material. These adjuvantsstimulate the immune system's response to the target antigen, but do not provide immunity themselves. Some potent non-toxic, non-pyrogenic bacterial lipopeptides are investigated as immunological adjuvants. When they are mixed with a conventional antigen, a marked improvement in the humoral immune response was observed with low molecular mass antigens iturin AL, herbicolin A and microcystin (MLR) coupled to poly-l-lysine (MLR-PLL) in rabbit and chickens.

Immunomodulatory Agent [31]:

Immunomodulators are the active agents of immunotherapy. They are a group of orally bioavailable agents, used for the treatment of multiple myeloma. It has been reported that sophorolipids are promising modulators of the immune response. It has been also demonstrated that sophorolipids, decreased sepsis related mortality at 36 hrs in vivo in a rat model of septic peritonitis by modulation of nitric oxide, adhesion molecules and cytokine production. In addition to that it also decreased IgE production in vitro in U266 cells possibly by affecting plasma cell activity. The results show that sophorolipids decrease IgE production in U266 cells by suppressing the genes involved in IgE pathobiology in a synergistic manner. This data can support the utility of sophorolipids as an anti-inflammatory agent and a novel potential therapy in diseases of altered IgE regulation.

Anti-adhesive Agents [2]:

The bio-surfactants inhibit the adhesion of pathogenic organisms or the formation of bio-film on the surgical instruments. Pre-coating vinyl urethral catheters treated with surfactin before the inoculation inhibited bio-film formation by gram-negative bacteria like *Salmonella typhimurium*, *Salmonella enteric*, *Escherichia coli* and *Proteus mirabilis*. Microbial surfactants significantly reduced microbial population on prostheses and also induced a decrease in the air flow resistance that occurs on voice prostheses after bio-film formation.

Pharmaceutical emulsions [6, 32]:

Emulsions are biphasic liquid dosage forms which are generally intended for both external and internal use and are dispersions of oil-in-water (O/W) or vice versa (W/O). Emulsions are thermodynamically unstable and to make this heterogenous system stable for the purpose, an emulsifying agent is essential. Rhamnolipid bio-surfactant produced by *Pseudomonas aeruginosa* and Mannosylerythritol lipids produced by *Candida Antarctica* acts as emulsifying agents to stabilize emulsion.

Essential oil based emulsion [33]:

Essential oil also known as volatile oil is a concentrated, aromatic, hydrophobic liquid obtained from plant. Rhamnolipid bio-surfactants are being investigated to produce essential oilbased emulsions using titration method. The essential oilsare extracted from Melaleuca alternifolia, Cinnamomumverum, Origanum compactum and Lavandulaangustifolia plants species. Ternary phase diagrams were designed to evaluate emulsion stability, which differed depending on the essential oil. The *in vitro* antimicrobial activity of the essential oil alone and the emulsions was evaluated. The antimicrobial activity presented by the essential oils alone increased with emulsification. The surface properties of rhamnolipids might have contributed to the dispersion of essential oil and thus increased their availability and antimicrobial activity against *Candidaalbicans* and *Staphylococusaureus*. The refore, rhamnolipid based emulsions represent a promising approach to the development of essential oil delivery systems.

Microemulsions [34]:

Microemulsions are clear, thermodynamically stable, isotropic liquid mixtures of oil, water, surfactant and frequently a co-surfactant with aglobule size in the order of 10^{-9} m.The sophorolipidbio-surfactants being more hydrophobic than sodium bis(2-ethyl) dihexyl sulfosuccinate, which is more hydrophobic than sodium dihexylsulfosuccinate and rhamnolipid bio-surfactant,sophorolipid played an important role as the hydrophobic component in lecithin/rhamnolipid/ sophorolipidbio-surfactant formulation. This bio-surfactant formulation was able to produce Winsor Type I, III and II microemulsions. The phase behavior of this formulation with isopropyl myristate did not change significantly with changing temperature (10, 25, 40°C) and electrolyte concentration (0.9% and 4.0% w/v), making it desirable for drug delivery applications.

CONCLUSION:

Microbe derived bio-surfactants are diverse group of bio-molecules possessing huge potential to be applied in cosmetic and pharmaceutical industry as a green alternative.These non-toxic, biodegradable and eco-friendly bio-molecules are competent to replace their chemically synthesized counterparts. Their surface active property is being explored in different industrial aspect where the newly formed surface is needed to be stabilized. Their anti-biofilm activity is widely explored for pharmaceutical application in clinical setting. Their hydrophilic lipophilic balance is used to improve the solubility of poorly water soluble drugs. They are investigated for their wetting, foaming, dispersing, emulsifying and lot of other properties. Though the low production and high cost are the limitations, but their enormous potential has endowed them with huge opportunities in different industrial settings in near future.

ACKNOWLEDGEMENT:

The authors gratefully acknowledge the support extended by Regional Institute of Pharmaceutical Science & Technology, Agartala, Tripura, India.

CONFLICT OF INTERESTS: Declared none.

REFERENCES:

1. Desai JD, Banat IM. Microbial production of surfactants and their commercial potential. Microbiology and Molecular biology reviews. 1997 Mar 1; 61(1):47-64.
2. Rodrigues L, Banat IM, Teixeira J, Oliveira R. Biosurfactants: potential applications in medicine. Journal of Antimicrobial Chemotherapy. 2006 Feb 9; 57(4):609-18.Vijayakumar S, Saravanan V. Biosurfactants-types, sources and applications. Research Journal of Microbiology. 2015 May 1; 10(5):181.
3. Pacwa-Plociniczak M, Plaza GA, Piotrowska-Seget Z, Cameotra SS. Environmental applications of biosurfactants: recent advances. International journal of molecular sciences. 2011 Jan 18; 12(1):633-54.
4. Youssef NH, Duncan KE, Nagle DP, Savage KN, Knapp RM, McInerney MJ. Comparison of methods to detect biosurfactant production by diverse microorganisms. Journal of microbiological methods. 2004 Mar 31; 56(3):339-47.
5. Corazza M, Borghi A, Lauriola MM, Virgili A. Use of topical herbal remedies and cosmetics: a questionnaire-based investigation in dermatology out-patients. Journal of the European Academy of Dermatology and Venereology. 2009 Nov 1; 23(11):1298-303.
6. Bhadoriya SS, Madoriya N, Shukla K, Parihar MS. Biosurfactants: a new pharmaceutical additive for solubility enhancement and pharmaceutical development. Biochem Pharmacol. 2013;2(2):113.
7. Kosaric N. Biosurfactants in industry. Pure and Applied Chemistry. 1992 Jan 1; 64(11):1731-7.
8. Rosenberg E, Ron EZ. High-and low-molecular-mass microbial surfactants. Applied microbiology and biotechnology. 1999 Aug 16;52(2):154-62.
9. Fakruddin Md. Biosurfactant: Production and Application. J Pet Environ Biotechnol. 2012. 3:124. doi:10.4172/2157-7463.1000124
10. Gharaei-Fathabad E. Biosurfactants in pharmaceutical industry: a mini-review. American Journal of Drug Discovery and Development. 2011; 1(1):58-69.
11. McInerney MJ, Javaheri M, Nagle DP. Properties of the biosurfactant produced byBacilluslicheniformis strain JF-2. Journal of industrial microbiology. 1990 Apr 1; 5(2-3):95-101.
12. Muthusamy K, Gopalakrishnan S, Ravi TK, Sivachidambaram P. Biosurfactants: properties, commercial production and application. Current science. 2008 Mar 25:736-47.
13. Perfumo A, Rancich I, Banat IM. Possibilities and challenges for biosurfactants use in petroleum industry. Biosurfactants. 2010:135-45.
14. Silva RD, Almeida DG, Rufino RD, Luna JM, Santos VA, Sarubbo LA. Applications of biosurfactants in the petroleum industry and the remediation of oil spills. International journal of molecular sciences. 2014 Jul 15; 15(7):12523-42.
15. Vijayakumar S, Saravanan V. Biosurfactants-types, sources and applications. Research Journal of Microbiology. 2015 May 1; 10(5):181.
16. Sobrinho HB, Luna JM, Rufino RD, Porto AL, Sarubbo LA. Biosurfactants: Classification, properties and environmental applications. Recent Developments in Biotechnology. 2013; 11:1-29.
17. Takahashi M, Morita T, Fukuoka T, et al. Glycolipid biosurfactants, mannosylerythritol lipids, show antioxidant and protective effects against H(2)O(2)- induced oxidative stress in cultured human skin fibroblasts. J Oleo Sci. 2012;61:457–464
18. Owen D, Fan L. Oligomeric biosurfactants in dermatocosmetic compositions. Patent US 8431523 B2; 2013.

19. Owen D, Fan L. Polymeric biosurfactants. Patent US 8586541 B2; 2013.
20. Masaru K, Michiko S, Shuhei Y. Skin care cosmetic and skin and agent for preventing skin roughness containing biosurfactants (World Patent 2007/060956). Toyo Boseki Kabu Shiki Kaisha and National Industrial Science and Technology, Osaka, Japan. 2007.
21. Desanto K. Rhamnolipid-based formulations. Patent WO 2008013899 A2; 2008
22. Cox TF, Crawford RJ, Gregory LG, Hosking SL, Kotsakis P, inventors; Conopco, Inc., assignee. Mild to the skin, foaming detergent composition. United States patent US 8,563,490. 2013 Oct 22.
23. Allef P, Hartung C, Schilling M. Aqueous hair and skin cleaning compositions comprising biosurfactants. Patent US 20140349902 A1; 2014
24. Das I, Roy S, Chandni S,. Biosurfactant from marine actinobacteria and its application in cosmetic formulation of toothpaste. Pharm Lett. 2013; 5:1–6.
25. Gualerzi CO, Brandi L, Fabbretti A, Pon CL, editors. Antibiotics: Targets, mechanisms and resistance. John Wiley & Sons; 2013 Sep 5.
26. Prasad B, Kaur HP, Kaur S. Potential biomedical and pharmaceutical applications of microbial surfactants. WJPPS. 2015 Mar 19; 4(4):1557-75.
27. Mimee B, Labbe C, Pelletier R, Belanger RR. Antifungal activity of flocculosin, a novel glycolipid isolated from Pseudozymaflocculosa. Antimicrobial agents and chemotherapy. 2005 Apr 1;49(4):1597-9.
28. Kracht MA, Rokos H, ozel M, Kowal M, Pauli G, Vater J. Antiviral and hemolytic activities of surfactin isoforms and their methyl ester derivatives. The Journal of antibiotics. 1999 Jul 25; 52(7):613-9.
29. Shah V, Doncel GF, Seyoum T, Eaton KM, Zalenskaya I, Hagver R, Azim A, Gross R. Sophorolipids, microbial glycolipids with anti-human immunodeficiency virus and sperm-immobilizing activities. Antimicrobial agents and chemotherapy. 2005 Oct 1; 49(10):4093-100.
30. Chen J, Song X, Zhang H, Qu Y. Production, structure elucidation and anticancer properties of sophorolipid from Wickerhamielladomercqiae. Enzyme and microbial technology. 2006 Jul 3;39(3):501-6.
31. Cameotra SS, Makkar RS. Recent applications of biosurfactants as biological and immunological molecules. Current opinion in microbiology. 2004 Jun 30; 7(3):262-6.
32. Williams K.Biosurfactants for cosmetic application: Overcoming production challenges. 2009. MMG 445 Basic Biotechnology
33. Haba E, Bouhdid S, Torrego-Solana N, Marques AM, Espuny MJ, Garcia-Celma MJ, Manresa A. Rhamnolipids as emulsifying agents for essential oil formulations: Antimicrobial effect against Candida albicans and methicillin-resistant Staphylococcus aureus. International journal of pharmaceutics. 2014 Dec 10;476(1):134-41.
34. Nguyen TT, Edelen A, Neighbors B, Sabatini DA. Biocompatible lecithin-based microemulsions with rhamnolipid and sophorolipidbiosurfactants: formulation and potential applications. Journal of colloid and interface science. 2010 Aug 15; 348(2):498-504.