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Ecofriendly Approach for Steroids, Terpenes, and Alkaloids-based Biosurfactant

Mahipal Singh Sankhla [1], Kapil Parihar [2], Rajeev Kumar [3], Devidas S. Bhagat [4], Swaroop S Sonone [5], Gaurav Kumar Singh [6], Varad Nagar [1], Garima Awasthi [7], Chandra Shekhar Yadav [8]

[1] Department of Forensic Science, Vivekananda Global University, Jaipur, Rajasthan; mahi4n6@gmail.com (M.S.S.); varad.leo10@gmail.com (V.N.);
[2] Regional Forensic Science Laboratory, Jodhpur, Rajasthan; kparihar94@gmail.com (K.P.)
[3] Department of Forensic Science, School of Basic and Applied Sciences, Galgotias University, Greater Noida, U.P. India; rajeev4n6@gmail.com (R.K.);
[4] Government Institute of Forensic Science, Aurangabad, M.S India; dsbhagat999@gmail.com (D.S.B.);
[5] Department of Forensic Science, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, M.S India; sononeswap4@gmail.com (S.S.S);
[6] Department of Forensic Science, University Institute of applied health science, Chandigarh University, Gharuan, Mohali, Punjab, India; grvsngh01@gmail.com (G.K.S.);
[7] Department of Life Sciences, Vivekananda Global University, Jaipur, Rajasthan; gariimaa21@gmail.com (G.A.);
[8] School of Forensic Science, National Forensic Science University, Gandhinagar, Gujrat; yadavcs82@hotmail.com (C.S.Y.);
* Correspondence: mahi4n6@gmail.com (M.S.S.);

Scopus Author ID 57219964786

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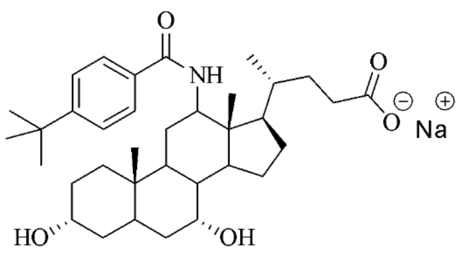
Abstract: In the last decade, the investigation of biosurfactants (BS) has been extensively studied due to the application of BS to remove or minimize the use of toxic synthetic surfactants into the ecosystem. Contaminated soil, air, and water cause a serious hazard to human health and the environment. Usually, biosurfactants exhibited remarkable emulsification with minimum surface tension values less than 16.5 dynes/cm. The BS exhibited significant bioactivities against bacterial and fungal pathogens. The plant-based surfactants have a more than 80% free radical scavenging nature and show potential antioxidant activity. BS are amphiphilic motifs obtained from plants and microorganisms' extract. BS has distinct hydrophilic and hydrophobic properties, leading to micellization formation. BS has a special molecular structure with hydrophilic glycoside linkage and lipophilic (Hydrophobic) triterpene derivative. BS has a broad spectrum of numerous sectors, including food, agriculture, personal care, petroleum, cosmetic, pharmaceutical, textile. The features of BS are low toxicity, environmental capability, biodegradability, multi-functionality, and availability of resources. The biosurfactant is today's need of society because synthetic surfactants have high toxicity and high ecological impact due to carcinogenic and mutagenic effects on human health. The proteins and polysaccharides act as emulsifiers. The chemical composition of this kind of surfactant is protein, glycolipid, carbohydrates, steroids, terpenoids. We focused on the steroids, terpenes, and alkaloids based surfactants. Currently employed plant and microbes-based surfactants, study their production, chemical composition, and effect of synthetic biosurfactant on human health and ecosystem.

Keywords: biosurfactants; environment protection; micellization; applications; production; microorganisms; natural products.

1. Introduction

There has been an increased recognition that more attention needs to be paid to this area of renewable raw materials, which are the sum of all matters obtained from the living biosphere, including the plant and animal kingdom. Natural products like steroids, terpenes, and alkaloids are used to manufacture surfactant industries [1]. The addition of natural products to surfactants helps environmental protection by phasing out toxicological effects on natural resources [2]. Besides, biodegradability has become an important factor in the environmental acceptance of a surfactant [3]. Nowadays, the research community focuses on minimizing the use of organic solvents in production due to environmental restrictions and tries to facilitate the adoption of a few green chemistry guidelines. To overcome this burning issue, volumetric production of aqueous bioconversion addition of sparing water-soluble hydrophobic candidate in the surfactant like steroids, terpenes, and alkaloids [4]. Several studies have explored the significance of the biomolecules like steroids obtained from the natural resource possesses a common skeleton of condensed four rings commonly found in plants and animals with vital biological functions. The steroid-based detergent also reported literature such as C-12 and C-3 (**1**-**2**) substituted bile salts steroid surfactant isomers having excellent amphiphilic properties [5]. The terpenoids-based biosurfactant is also obtained from natural resources having excellent micellization properties. The terpenoids are commonly found the plant resources. The functionalized terpenoids have a wide range of properties like hydrophobicity and this basic requirement of biosurfactant. The phytol (**3**) shows excellent biosurfactant stuff obtained from the aquatic weed *Hydrilla verticillata*. The phytol is a natural linear diterpene-based fatty alcohol found in an integral part of the chlorophyll of the weed *Hydrilla verticillata*. The phytol is used as the precursor for synthesizing vitamins E and K worldwide. It has very high hydrophobicity, so have intends to use it in excellent application as a surfactant in various fields [6]. The thymol (**4**) is oil-in-water nanoemulsions as a possible natural alternative to harmful synthetic antioxidant agents in chemical surfactants. Thymol is diterpene with distinct antioxidant properties, proven and improved through emulsification [7]. The alkaloid also has the miscellaneous property of these rare alkaloids, also called the miscellaneous alkaloids such as Fenazine (**5**), a rare class of glycosidic-alkaloids obtained by a filamentous bacterium *Streptomyces sp.* possess glycosidic linkages [8].



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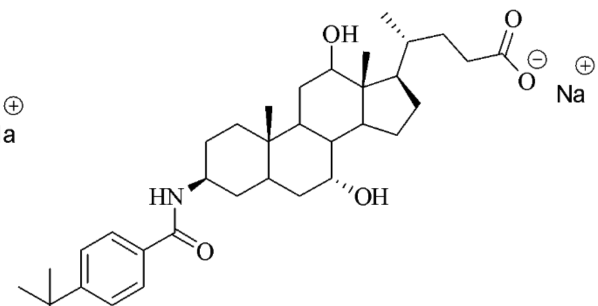

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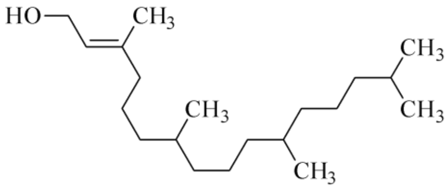
1: C-12, **2**: C-3 substituted bile salts steroid surfactant



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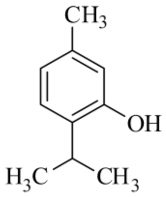

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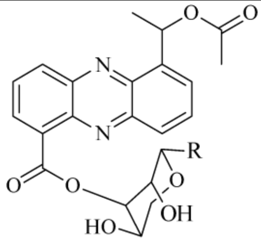

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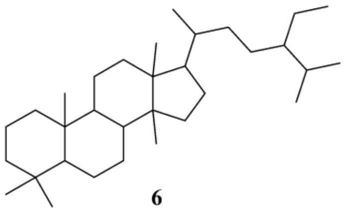
3: Phytol, **4**: Thymol, **5**: Fenazine

1.1. Classification of biosurfactants.

Studies have demonstrated a strong and consistent link between natural resources and surfactants. The synthetic surfactant is artificially manufactured in industries that have the composition of antioxidants, emulsifiers, foaming agents, and wetting agents. The biosurfactant does not have an analog composition to synthetic surfactant. Generally, the classification is based on the type of natural products and chemical skeleton present in the surfactants. Those surfactants are obtained from lipophilic and hydrophobic microorganisms, decreasing surface tension at the surface of the liquid [9]. The hydrophilic part of surfactant is made up of carboxylic acids, alcohol, phosphates, carbohydrates, amino acids, proteins, and motifs [10]. The lipophilic part is made up of carbon chains and fatty acids. Both lipophilic and hydrophilic parts are joined by ester, ether, and amide linkage [11]. The general lipid-based surfactant coined based on chemical composition glycolipid (glucose and lipid), phospholipid (phosphate group and lipid), lipopeptides (lipid and protein), and lipopolysaccharides (lipid and carbohydrates). These biosurfactants have various micellization, emulsification, and physicochemical possessions**.**



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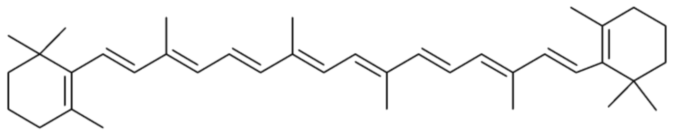

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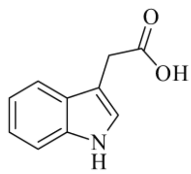

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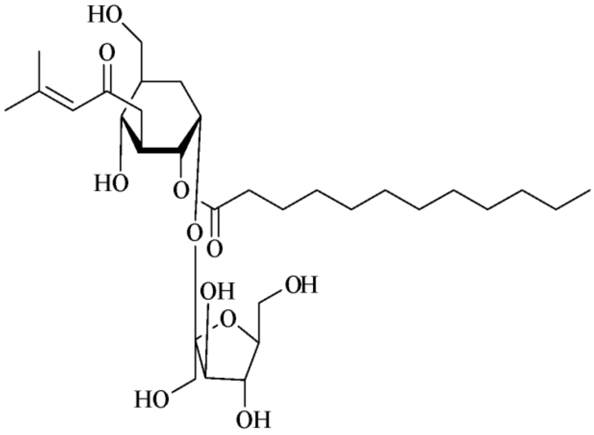
6:Steroids, **7**: Carotenoids, **8**: Gibberellic acid.

Terpenoids are a wide family of natural products bearing functional and structural common features such as steroids (**6**), carotenoids (**7**), and gibberellic acid (**8**). The Terpenoids are the most important class of active natural products in plants with more than 20,000 reported structures and which derivatives isoprene unite [12]. Actinobacteria of the genus Rhodococcus give trehalolipid (**9**) biosurfactants that possess dynamic physicochemical properties with low toxicity. The trehalolipid has biomedical agents with significant immunological activities that have been reported [13]. Rhamnolipid (**10**) is superlative and well-studied among all biosurfactants having emulsification, foaming, cleansing, surface activeness, wetting, and phase separation properties, and due to all these distinct possessions, it preferred to the convention in the petroleum industries [14].



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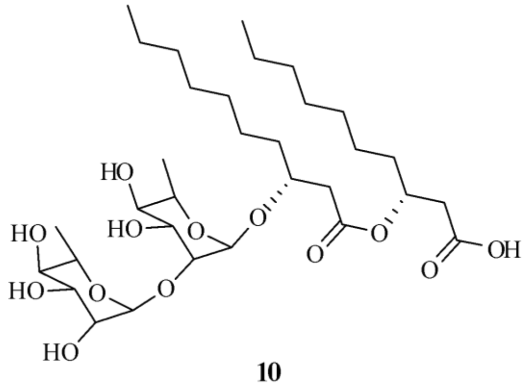

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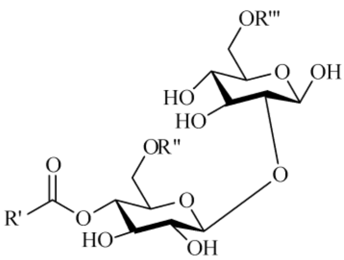
9: Trehalolipid, **10**: Rhamnolipid.

Sophorolipid (**11**) is one of the simplest biosurfactants with a well-defined structure and it is obtained from *Starmerella bombicola*. It shows surface tension reduction and accomplished low critical micelle concentrations [15]. The mannosylerythritol lipids (**12**) were obtained from glucose and sucrose without the use of any vegetable oils, and it was also produced from *Pseudozyma antarctica* JCM 10317 and *Ustilago maydis* NBRC 5346. It possesses distinct interfacial properties like low critical micelle concentration [16]. Surfactin (**13**) is the most powerful lipopeptide-type biosurfactant, and it isolates from the gram-positive Bacillus subtilis. It shows remarkable applications in the therapeutic applications and environmental applications [17].



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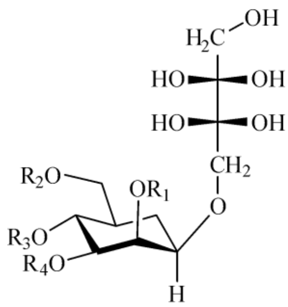

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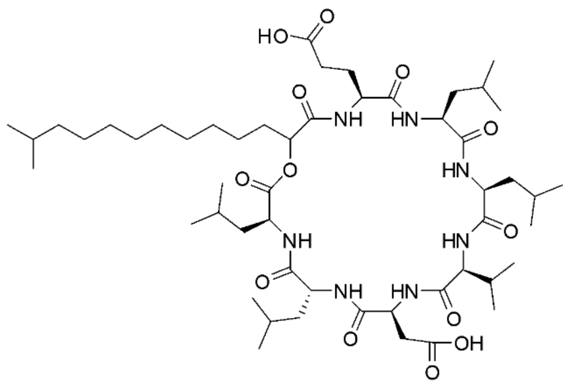

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11: Sophorolipid, **12**: mannosylerythritol lipids, **13**: Surfactin

1.2. Comparison of biosurfactants to synthetic surfactants.

Surfactants synthesized in laboratories or industries is known as synthetic surfactant, and those surfactant obtained from microbe is coined as biosurfactant. The origin of synthetic surfactants is petrochemical, whereas biosurfactants are isolated from bacteria, yeast, and fungi [18]. The classification of biosurfactants is based upon structure, physicochemical properties, and microbial species producing them. Biosurfactants are attracting much interest from every community due to their potential advantages over their synthetic surfactant counterparts in many fields such as environmental, food, biomedical, and petroleum industries [19]. Globally chemical-based/ synthetic surfactants have been steadily increasing since their discovery, and now a day, these synthetic chemicals are used in routine life by humankind for numerous propose. However, the toxicity of chemical-based surfactants to the ecosystem is well documented. It encourages us to use eco-friendly biosurfactants [20] to compare the natural surfactant and synthetic surfactants based on the wide range of applicability and properties. Natural products-based surfactants are superior to chemical surfactants due to their milder unique properties [21].

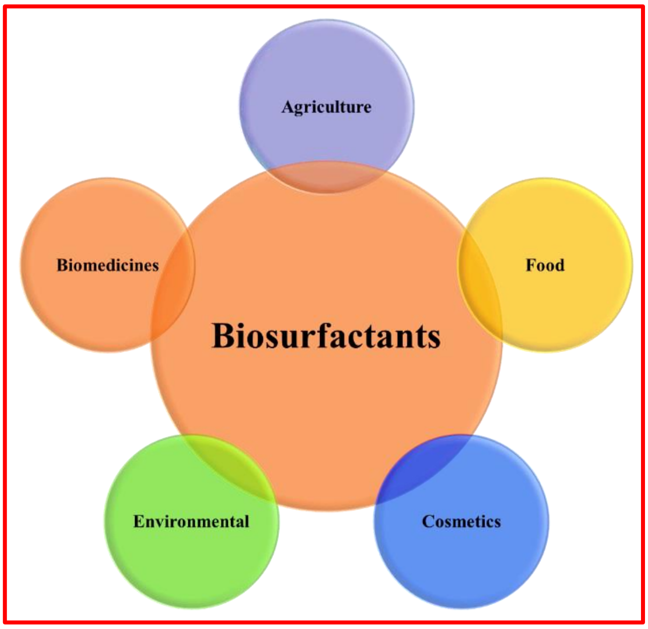

Figure 1. The application spectrum of natural products-based surfactants.

The researcher community is increasing their interest in natural products based surfactants because of their unique properties like low toxicity, excellent functionality, based on renewable substances, and biodegradability. Natural surfactants are amphiphilic biological scaffolds produced by the extracellular secretion of numerous microorganisms. The diversity of these natural product-based surfactants shows their potential application in petroleum, medicine, agriculture, food, and cosmetics Figure 1 [22]. Biosurfactant shows excellent degradation properties due to its origin from living sources. It may get degraded within 24 hours or a few days. The synthetic surfactant does not degrade in minimum time; it requires a few years for complete degradation [23].

Synthetic surfactants have very high toxicity and are less environmentally benign. Hence, natural surfactants are preferred to use in the food industries due to their low toxicity. Biosurfactant acts as an antimicrobial agent, and it does not affect the taste and flavor quality of the food products [24]. Natural surfactant is preferred in the cosmetic industries due to its less toxic nature and may be used in high-grade bathing soap, detergent, and lotions [25]. The agriculture sector is a fast, spontaneously growing sector and plays a vital role in sustainable development. So, the researcher community focused on applying natural pesticides in farming in pesticides, agrochemicals, and biocontrol agents. The biosurfactant has distinct antimicrobial activity, and this kind of pesticide possesses remarkable bioavailability [26].

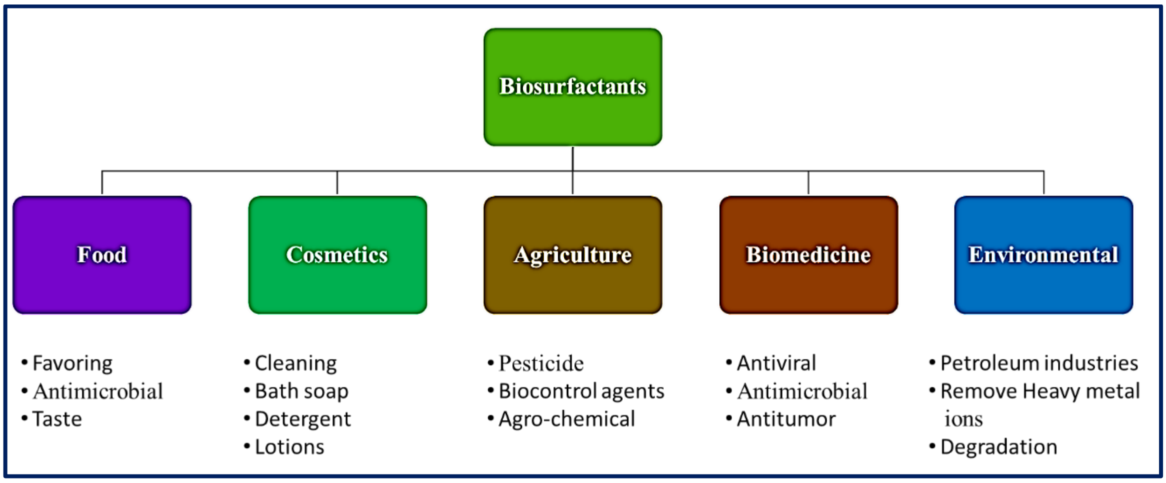

Figure 2. Broad-spectrum application summary of natural products-based surfactants.

Drug discovery is emerging field addition novel protocols and technology are introduced in this field, such as a natural products-based surfactant. This biosurfactant shows outstanding pharmacological properties like antiviral, antimicrobial, antitumor [27]. Biosurfactants are also used in the petroleum industries due to their less toxic, bioremediation, and biodegradable nature [28].

1.3. Environmental impact synthetic surfactant.

Environmentally friendly surface-active compounds are known as green surfactants or biosurfactants. Synthetic surfactants show adverse effects on the ecosystem due to their high toxicity levels. This surfactant has been persistent in the environment for a long time due to low biodegradability, which causes environmental pollution. Worldwide annual consumption of synthetic surfactants is about 15 million tons, and an estimated 60% of surfactant waste is discharged into the aquatic environment [29]. The surfactants are made up of salt of fatty acid, alcohol, alcohol sulfate, and long-chain alcohol and their use in numerous cleaning products [30]. Presently, nonionic, anionic, cationic, and amphoteric surfactants are used worldwide for daily routine purposes. The absorption of the ionic surfactant into the soil is the major cause of environmental pollution due to the increase in the ionic strength, pH of the soil, and other soil physicochemical properties [31]. Synthetic surfactants pollute every sphere of the environment, including water pollution, air pollution, soil pollution. It also shows the harmful effect on human health that causes numerous diseases) [32].

2. Properties of Steroids, Terpenes and Alkaloids based Surfactants

2.1. Saponins.

Saponin is a natural surfactant with an unbending structure of a minimum of 4 hydrocarbon rings to which sugar in a group of 1 or 2 are joined, commonly not more than 10 units. The existence of saponin has been described in greater than 100's families of plants. Its active component shows the exclusive characteristics of foaming & emulsifying. [33,34]. Because of its amphiphilic natures of saponin, it got greater surface activities, having a different molecular structure concerning the types of its hydrophobic fragments like triterpenoids or steroids aglycone and a number of sugar-chains [35,36]. Chief features of saponins adsorption layer in the means of area/molecule, adsorption energy, the energy of interaction between the adsorbed molecules, surface dilatational and shear elasticities, and viscosities.) [37]. Extract of saponin also displaying the greatest elastic moduli were Escin, Tea saponin, and Berry saponin, consisting mainly of mono-desmosidic triterpenoid saponin. Both steroidal and triterpene saponin might consist of other functional groups like –COOH, –CH3, –OH, which give them added variety [33].

2.2. Betaine.

Betaines are zwitterionic surfactants having quaternate nitrogen and the –COOH group in the chemical structure. Betaines are non-charged at neutral pH but would show a + charge in extremely lower pH conditions. This feature makes betaine behave like a nonionic surfactant rather than the ionic surfactant and enables them to be well-matched in formulation with anionic surfactant in the pH variety of various home care and personal formulation. The alkyl-amido betaine is the utmost main type of amphoteric surfactant with greater hydrolytic stability in today's use in the markets, especially CAPB or Cocamidopropyl betaine, Alkyl betaines like lauryl betaine [38, 39]. Betaine is striking as a foaming agent as their foam is comparatively resilient to the effect of hard waters, unlike anionic surfactants. Betaine also foams even at extreme pH, in contrast to anionics which try to foam poorly at higher pH [40].

2.3. Steroid-based surfactants.

In some research's steroid-based surfactants designed for solubilization of poorly soluble drugs surfactants based on naturally occurring by linking hydrophilic and hydrophobic moieties, these surfactants are Cholesteryl-glutamic acid, Cholesteryl-poly[N-2-hydroxyethyl-L-glutamine] (PHEG), Ursodeoxycholic-PHEG (UDCAPHEG), Ursodeoxycholic-poly-L-glutamic acid (UDCA-PGA).

All surfactants are water-soluble except for cholesteryl-glutamic acid, which was poorly soluble in water. Polar heads of these three surfactants are polymeric, leading to larger polar head volumes than a single glutamic acid [41]. Ethoxylated cholesterol is a steroidal nonionic surfactant mainly used to solubilize three structurally related androgenic steroids like testosterone, methyltestosterone, and testosterone propionate [37].

2.4. Terpene-based surfactants.

Phosphine oxide-based surfactants are chemically fairly resilient are temperature and pH stable. These are used in two classes of nonionic surfactants, i.e., alkyl polyglycol ethers CiEj and alkyl polyglycosidesCnGm, [42]. These phosphine oxides and CiEj surfactants are sturdily depending on the temperature. While CiEj surfactant degrades at a higher temperature, the particular phosphine oxides are steady. Phosphine oxide surfactants can be premeditated like that they can be utilized to create highly effective micro - emulsion [43].

3. Production of Steroids, Terpenes, and Alkaloids based Surfactants

3.1. Saponins.

For obtaining saponin from plant materials, various extraction techniques are utilized by utilizing a solvent like methanol, ethanol, water, or hydro-alcoholic mixture in the Soxhlet extractor or orbital shaker. Another solvent like glycerol and alcoholic or aqueous surfactant solution was also stated. New techniques use lesser quantities of solvents but include additional chemical/physical methods like pressure, multi-stage extraction, ultrasounds, microwaves, or supercritical fluid extraction. Such procedures can be central to an upsurge in an effective process. Though it shall be taken into account that in certain more difficult situations like high temperatures and pressures, saponin can be dissected and tainted, milder procedures should be utilized [44-47].

3.2. Betaine.

The alkyl betaine and alkyl amido betaine are synthesized by multiple steps dependent on the coconut/palm-kernel oils [38,39]. Alkyl betaine depends on the usage of fatty alcohols, while alkyl amido betaine utilizes fatty acids or fatty acid esters. Surfactant precursor is trialkyl amine or amide-trialkyl amine, which is later transformed into the final betaine surfactants by mixture with SCA or sodium chloroacetate. An amphiprotic surfactant such as betaine provides greater detergent capacity when attached with higher foam capability and mild to the skin. Most alkyl betaine & alkyl amido betaine have greater solubility in liquid water for formulating. It is noted that the last steps in its production are performed in water, and they are particularly traded as 30% to 40% solution in waters. Betaine may act as a cationic surfactant at a lower pH and may precipitate with anionic surfactant but not affect the hard water [40].

3.3. Steroid-based surfactants.

CHAPS 3-[(3-Cholamidopropyl) dimethylamino]-1-propanesulfonate are zwitter ion forming surfactants, resultant from bile salt, and it may be synthesized from cholic acid. It contains an end with a dipolar sulpho-betaine head group with one + and one – charges. Its steroid ring-like structure confer to two surfactants, the features noticed in planar molecules with a hydrophobic and hydrophilic face. The existence of 3 -OH groups in the sterol ring enables establishing parallelism with the behavior of a few bile salts like glycocholic acid, cholic acid, and, especially, taurocholate (TC), [48]. Ethoxylated cholesterol is a Steroidal nonionic surfactant. Ethoxylated cholesterols are synthesized by the ethoxylates, a portion of lanolin alcohol-containing chiefly of cholesterols. The structures of surfactants may be regarded as R-0 R', where R denotes 24 poly-oxyethylene units and R' the cholesterol and related lanolin alcohol. Steroid has been earlier proposed that solubilization by ethoxylated surfactant possibly takes place by the linkage of the polar group of the steroid with the hydrated polyoxymethylene chain of the surfactant [49].

3.4. Terpene-based surfactants.

Tertiary phosphine oxides: 3^0 phosphine oxide become surfactants if 2 of the 3 components are shorter alkyl chains like ethyl or methyl, while the 3^{rd} component is a longer alkyl chain or greater polar ring system. For example, dimethyl alkyl phosphine oxides with linear alkyl chains ranging from 9 carbon atoms to 14 carbon atoms are classic surfactants [50-52].

4. Metabolism of Steroids, Terpenes, and Alkaloids based Surfactants

4.1. Metabolism of steroids.

Steroids are a diverse group of chemicals found in abundance in nature, and many of their derivatives have essential physiological effects. In mammals, all steroid hormones and bile acids, and vitamin D are generated from cholesterol, which is their common precursor. Cholesterol is found in the human body in amounts ranging from 200 to 300 grams per adult. Because of the links between food, blood cholesterol levels, atherosclerosis, and heart disease, cholesterol has gotten a lot of attention since it was first isolated from gallstones in 1784 [53]. Manufactured (e.g., synthetic ethinyl estradiol) and natural (e.g., human urine and cattle dung) sources of steroid hormones are continually discharged into the environment [19]. Steroids are a kind of lipid with 17 carbon atoms organized in four rings, and a unique ring structure termed the cyclopentanoperhydro-phenanthrene ring system. Not only because their chemical structures are identical but also because their quantities in biological fluids are exceedingly low, determining steroids in the body remains a difficult analytical task.

4.2. Corticosteroids.

For more than 50 years, oral corticosteroids have been routinely used in medical practice to treat asthma, inflammatory joint problems, and other illnesses of the gastrointestinal tract and central nervous system. Osteoporosis is one of the most dangerous side effects of oral corticosteroid therapy, despite being typically beneficial in certain circumstances. Several investigations have found that oral corticosteroid therapy causes a reduction in bone mineral density, regardless of the condition being treated. This significant and fast bone loss is linked to the dosage of oral corticosteroid medication and occurs more quickly in trabecular than cortical bone [48,54]. Inhaled corticosteroids have transformed asthma treatment and become the standard of care for chronic illness patients [55]. The latest evidence on the effectiveness and safety of inhaled corticosteroids was reviewed in a supplement to this journal published 5 years ago [56]. Our understanding of the molecular processes by which glucocorticoids decrease inflammation in asthma has lately increased dramatically. This has thrown fresh insight into the molecular causes of asthma and may pave the way for the future development of more targeted treatments [57,58]. Corticosteroids released by the adrenal cortex easily penetrate the brain, where they coordinate the organism's capacity to cope with stress with other components of the stress system. They govern the excitability of neural networks that underpin learning and memory processes by diverting energy supply to challenged regions. Corticosteroids aid in the processing and storage of new information while also eliminating no longer relevant behavior. Despite the evident role of stress hormones for mental health and homeostasis [59], corticosteroids' potentially disruptive effects on brain function and behavior have recently garnered much attention [43,45,60-62]. Why is the action of corticosteroid hormones necessary and positive while regarded as disruptive for memorizing specific tasks at other times? When addressing this contradiction, this essay suggests that two points are critical. First, the influence of corticosteroid hormones on memory function can only be properly recognized when the two receptor types for these hormones in the brain are considered separately. Corticosterone (in rodents) and cortisol (in humans) bind to mineralocorticoid receptors (MRs) and glucocorticoid receptors (GRs), with a tenfold difference in affinity [63].

4.3. Anabolic-androgenic steroids

Androgens are the main regulator of this ratio by stimulating proliferation and inhibiting apoptosis. So, prostate cancer depends on a crucial level of androgenic stimulation for growth and survival. Androgen ablation causes cancer regression because without androgen, the rate of cell proliferation is lower, and the rate of cell death is increased, leading to the extinction of these cells [40]. Anabolic-androgenic steroids (AAS) are misused to a great extent in sports by athletes to improve their physical performance. Sports federations consider the use of these drugs in sports as doping. The misuse of AAS is controlled by detecting the parent AAS (when excreted into the urine) and (or) their metabolites in athletes' urine. I present a review of the metabolism of AAS [5]. The diverse effects of AR are mediated by complex cell type-specific signaling pathways. During the past several years, there have been a number of new insights into the mechanism of AR action in normal cells. Detailed molecular genetic analyses elucidate the functional domains of the AR molecule and the deciphering of the three-dimensional crystal structure [46].

4.4. Progesterone.

The reproduction-related targets of progesterone include the uterus, the ovary, the mammary gland, and the hypothalamic-pituitary axis. The physiological effects of progesterone include differentiation of the endometrium, control of implantation, maturation of the mammary epithelium, and modulation of GnRH pulsatility. Progesterone also plays an important role in oocyte release from the ovary. These actions have led to major pharmacological applications of progesterone and progestins in contraception, control of uterine bleeding, and HRT. Soon after discovering the progesterone receptor (PR) [64-67], it was appreciated that the development of a PR antagonist would have major therapeutic potential. The first report was on mifepristone (RU 486), a progesterone and glucocorticoid receptor antagonist. Since then, a wide range of similar molecules has been produced, ranging from pure progesterone receptor antagonists (PA) to mixed agonists/antagonists. Antagonists are all names for these substances: selective progesterone receptor modulators (SPRM), progesterone receptor modulators (PRM), mesoprogestins, and partial agonist–antagonists.

4.5. Metabolism of Terpenes.

Terpenes (terpenoids) are the second-largest group of secondary metabolites (nearly 23,000 are known). They are incredibly diverse in structure and activity, although they all originally derive from a simple isoprene molecule. Many terpenes are hydrocarbons, but oxygen-containing compounds such as alcohols, aldehydes, or ketones (terpenoids) are also isolated from natural sources. Their building block is the hydrocarbon isoprene CH2=C(CH3)–CH=CH2. The German chemist Otto Wallach was the first to propose that monoterpenoids were constructed of a linkage of isoprene units (in head-to-tail form) [8,68]. Wallach (born March 27, 1847, in Königsberg, died February 26, 1931, in Göttingen) was awarded a Nobel Prize in Chemistry in 1910. His interest began with analyzing fragrant essential oils—oils removed from plants by steam distillation, with industrial uses; He next began looking into their molecular structure. In 1895, Wallach discovered the structure of numerous terpenes, including limonene [69,70]. He demonstrated that isoprene was the source of terpenes, C5H8—his "isoprene rule"—and therefore had the general formula $(C5H8)_n$. Such compounds were classified by molecular size in a way that was systematic but not consistent with the idea of isoprene as the structural unit. Later, Leopold (Lavoslav) Ruzicka (pronounced closely following the French transcription, "Rougitchka"; born on September 3, 1887, in Vukovar, Croatia; died on September 26, 1976, in Zürich, Switzerland) [71,72] formulated a classification system in which he defined monoterpenes as having carbon skeletons with two 5-carbon isoprene units, sesquiterpenes with three isoprenes, and so on. In 1953 his "biogenetic isoprene rule," which was pioneered by Wallach, became the crowning achievement of his lifetime. Ruzicka's main work started in 1921 involved macrocyclic compounds, higher terpenes, and steroids. He shared the Nobel Prize with Adolf Friedrich Johann Butenandt (1903–1995) in 1939. The hemiterpene isoprene, which contains five carbons (one isoprene unit, C5), is a gas emitted into the atmosphere by many plant species. A monoterpene (monoterpenoid) contains 10 carbons (two isoprene units, C10); a sesquiterpene, 15 carbons (three isoprene units, C15); and a diterpene, 20 carbons (four isoprene units, C20). Sesterpenes (five isoprene units, C25) were isolated from insect protective waxes and from fungal sources. Triterpenes (six isoprene units, C30) are important structural components of plant cell membranes. Many plant pigments, including the yellow and red carotenoids, are tetraterpenes (eight isoprene units, C40). Natural rubber is a polyterpene containing more than 40 isoprene units. Terpenes are largely found in essential oils, and they were known and used in ancient Egypt for various religious aims. The terpene camphor, obtained from the camphor tree (*Cinnamomumcamphora*syn. *Lauruscamphora*, Lauraceae), was used to reduce fevers, soothe gums, and treat epilepsy. Camphor trees are native to China and Japan, and they're grown for their wood, which is used to make camphor oil. According to Marco Polo, the Chinese employed camphor oil as a medicinal, fragrance, and embalming fluid. Camphor crystals are used as a counterirritant and analgesic liniment to relieve arthritic and rheumatic pains, neuralgia, and back pain. They have strong antiseptic, stimulant, and antispasmodic properties and are applied externally as unguents or balms to relieve arthritic and rheumatic pains, neuralgia, and back pain. It may also be applied for skin problems such as cold sores and chilblains and used as a chest rub for bronchitis and other chest infections. Camphor was introduced in Europe from the East by the Arabs around the 11th century. The early Middle Ages knew the process of obtaining plant essential oils by fat extraction. These compounds have important uses as flavorings, perfumes, and intermediates in producing other commercial products such as solvents and adhesives. Many terpenes play roles as plant hormones and in the chemical defenses of plants against microbial diseases and insect herbivores; many others have important medicinal properties. Many terpenoids and isoprenoids are toxic to insects, and a few are also repellents and toxicants to subterranean termites, although the mechanism of toxicity is not well known [73,74].

Terpenes can be acyclic, mono-, bi-, tri-, tetra-, and pentacyclic with 3-membered to 14- membered rings [75-80]. Deviations from the rule occur through rearrangement reactions or degradation of molecule parts during biosynthesis. The broader term terpenoids also cover natural degradation products, such as ionones, and natural and synthetic derivatives, e.g., terpene alcohols, aldehydes, ketones, acids, esters, epoxides, and hydrogenation products. An overview of the most important basic structures demonstrates the structural variety of terpenes [81]. The compounds are normally known by their trivial names, as the systematic nomenclature is frequently less practicable for complicated structures.

4.6. Metabolism of alkaloids based surfactants.

Alkaloids often contain one or more rings of carbon atoms, usually with a nitrogen atom in the ring. The nitrogen atom's position in the carbon ring varies with different alkaloids and with different plant families, microorganisms, and/or invertebrates. In reality, the characteristics of these alkaloids are influenced by the exact location of the nitrogen atom [82-89]. Biosurfactants perform a physiological function in nature by enhancing the bioavailability of hydrophobic compounds, boosting microorganism swarming motility, and partaking in cellular signaling and differentiation processes. [90]. They are also involved in the production of biofilms. Surfactants interact with microbial proteins and can be used to influence enzyme shape, affecting enzyme activity, stability, and specificity [91]. Chemical surfactants have been used as antimicrobial agents in disease prevention and to promote the breakdown of chemical pollutants because they may replicate the latter effects of biosurfactants. Chemical and biosurfactants are potentially hazardous to certain microorganisms and might be used as antimicrobial agents against microbial infections in plants, animals, and humans. [60,63,92]. The physiological effects of biosurfactants and chemical surfactants in nature were reviewed in Part 1 of this study [93]. Surfactants' specific applications in biotechnological processes, including upstream and downstream processes, are also discussed, as well as their novel applications in biocatalysis. Finally, we examine the processes for the production of microbial biosurfactants by fermentation and chemoenzymatic methods to synthesize specific chemical surfactants. Compared to chemically derived surfactants, biosurfactants are independent of mineral oil as a feedstock; they are readily biodegradable and can be produced at low temperatures. They're also said to be less hazardous, effective at low doses, and have bioremediation benefits. Industry interest in biosurfactants stems from their bioactivity and the larger ecological awareness associated with their use, which is fueled by sustainability programs and green agendas [19]. Surfactants are amphiphiles containing hydrophobic (water-hating) and hydrophilic (water-loving) moieties, enhancing the reduction of surface and interfacial tensions. The amphiphilicity of surfactants makes them suitable for applications like detergency, wetting, froth floatation, emulsification, oil recovery, etc. A large amount of synthetic surfactants used for domestic and industrial work are dispersed in diverse environmental sections like soil, water, sediment, etc. Studies show that about 60% of the total surfactant production enters the aquatic environment. The worldwide production of surfactants was about 12.5 million tonnes in 2006, and Western Europe produced over 3 million tonnes in 2007 [94]. Surfactants are amphiphilic compounds that can reduce surface and interfacial tensions by accumulating at the interface of immiscible fluids and increasing solubility, mobility, bioavailability, and subsequent biodegradation of hydrophobic or insoluble organic compounds. Chemically produced surfactants are extensively utilized as emulsifiers and wetting agents in the petroleum, food, and pharmaceutical sectors. Because of their unique modes of action, low toxicity, the relative simplicity of manufacture, and extensive applicability, biosurfactants generated by several microbes are becoming essential biotechnology products for industrial and medicinal uses.[95].

5. Applications of Steroids, Terpenes, and Alkaloids based Surfactants

5.1. Applications of steroids.

During the previous 20 years, estimating metabolites of steroid hormones in fecal samples has become a broadly understood strategy. It has ended up being an incredible, noninvasive means that gives significant data about a creature's endocrine status (reproductive status and adreno-cortical action). Even though examining is generally simple to perform and liberated from input, a cautious thought of different components is important to accomplish legitimate outcomes that lead to sound ends. This article means to give guidelines to a sufficient utilization of these methods. It is implied as an agenda that tends to the primary subjects of concern, for example, collection of samples and capacity, time defer extraction strategies, assay determination and approval, biological significance, and some perplexing components [96]. The segregation, synthesis, and depiction of testosterone in 1935 by several independent researchers in Europe [61,71,97,98] led to further study of this hormone and a better understanding of its biological effects.

5.1.1. Application of corticosteroids.

This is supported by the perception that systemic steroids are regularly useful in patients without nasal impediment due to polyps or clear inflammatory changes. Additionally, the site of activity of corticosteroids is not completely clear. In particular, it has been estimated that the site of irritation pertinent to olfactory failure may not generally be in the mucosa; however, it might be in the zone of the cribriform plate or the olfactory bulb [99,100]. Corticosteroids have a broad range of effects. In a clinical context, their anti-inflammatory and immunosuppressive properties are utilized. Local effects comprise membrane stabilization, modification of mediator release, or inhibition of cell migration [101,102]. These mechanisms assume to play a role in restoring olfactory function at the level of the olfactory mucosa. Despite the fact that it is unclear whether corticosteroids can reestablish tissue design and receptor function, there is information recommending a directing role of steroids in mucosal function [103]. Aside from such peripheral impacts, corticosteroids show particular effects on the central nervous system [104,105]. In particular, central nervous system sensitivity increases, edges for various stimulus characteristics are brought down, and disposition adjustment may happen, prompting steroid-initiated psychosis. It very well might be speculated that these central nervous impacts of corticosteroids additionally may prompt improved olfactory capacity. however, tests in dogs demonstrated that dexamethasone prompts expanded limits for scent identification, i.e., a reduction in olfactory function) [106]. Furthermore, after the organization of corticosteroids, female mice display decreased inclination for male scents [107]. Thus, in spite of the fact that these models propose a negative impact of corticosteroids in an unblemished olfactory framework, the activity site of corticosteroids in olfactory failure stays to be explained. Overall, in numerous patients, local use of corticosteroids seems to have next to zero constructive outcomes on olfactory brokenness, particularly while considering long-term changes. Duration of infectivity, the patient's age/sex, or parosmia presence doesn't anticipate the reaction to treatment with oral corticosteroids.

5.1.2. Application of anabolic-androgenic steroids

Depending upon the biological relevance, the steroid hormones can be further categorized [108]. The first class is the family of vertebrate steroid hormones: androgens, estrogens, progestogens, corticosteroids, and cholecalciferol. The second class is Brassinolids which comprises the development of advancing hormones of plants. Ecdysteroids have a place in the third class of steroid hormones found in insects; however, they are likewise present in different arthropods, other invertebrate phyla, and plants. In insects, they go about as shedding hormones, directing transformation, and a few other significant life-cycle measures [109].

Likewise, they may function in the reproduction, embryogenesis, and diapause of certain arthropods (insects, crustaceans, arachnids, and myriapods). The utilization of phytoecdysteroids is a hopeful option in contrast to anabolic-androgenic steroids due to the obvious absence of unfriendly impacts. The forthcoming utilization of phytoecdysteroids may reach out to medicines of obsessive conditions where anabolic steroids are regularly applied. Perhaps the most referred to part of phytoecdysteroid use (on the Internet) is the expansion of muscle size. Anyway, too rigid exploration is required in this field as a satisfactory cytological clarification isn't yet accessible for the anabolic steroids [58]. After numerous long periods of serious examination, it has become certain that steroids may apply their activity on living cells in two different ways. One notable genomic pathway includes hormone binding to intracellular cytosolic (classic) receptors and subsequent modulation of gene transcription followed by protein translation. Different options are the working sign transduction pathways that don't demonstrate straightforwardly on the genome, showing non-genomic activity. The non-genomic idea of an especially noticed wonder is moderately simple to affirm by utilizing transcription or translation inhibitors, yet recognizing and depicting these pathways, and the ligand restricting proteins are troublesome. So far, a significant disagreement exists about the identity of receptors that mediate these responses. Several approaches have been applied to this question, including pharmacology; the radioligand was [3 H]Dihydrotestosterone. Phytoecdysteroids and anabolic-androgenic Steroids Current Medicinal Chemistry, 2008 Vol. 15, No. 1 83 numerous biochemical and molecular biological studies and knockout animals. There is evidence for and against the involvement of traditional receptors or similar proteins and the involvement of new membrane steroid receptors that are poorly known. The number of clinical consequences for a wide spectrum of non-genomic steroid effects is increasing today [110].

5.1.3. Application of progesterone.

Current medication disclosure procedures (e.g., progresses in high throughput screening techniques, the presentation of combinatorial science) have increased the number of medication competitors being chosen that low display solvency in water. By certain appraisals, over 40% of new medication competitors are lipophilic and have poor fluid dissolvability [111-113,120, 124]. The points of this exploration were to create numerical mass transport models to clarify the effect of atomic complexation with cyclodextrins on intestinal membrane saturation and to mechanistically explain the interchange between the restricting impacts of cyclodextrins on obvious solvency and penetrability. To assess the numerical hypothesis, the models were applied to the profoundly lipophilic, low solubility, BCS class II medication progesterone, [114, 122, 123] utilizing a few *in vitro* and *in situ* intestinal layer transport models, that is, PAMPA, Caco-2 cell monolayers, and single-pass rodent jejunal perfusion. Generally speaking, this work gives an expanded comprehension of the fundamental systems that administer the impacts of sub-atomic complexation on intestinal layer transport and empowers the more productive and clever utilization of sub-atomic complexation methodologies to encourage oral absorption.

5.1.4. Application of Terpenes.

The principle application of terpenes as aromas and flavors relies upon the total setup of the mixes in light of the fact that enantiomers present distinctive organoleptic properties. Biotransformations permit the creation of regio-and stereos elective mixes under gentle conditions. These items might be marked as bnaturalQ. Monetarily valuable substance building blocks and drug stereo isomers can likewise be created by bioconversion of terpenes. Enzymes and concentrates from microscopic organisms, cyanobacteria, yeasts, microalgae, plants, and animal cells have been utilized for the creation as well as bioconversion of terpenes. Likewise, entire cell catalysis has additionally been utilized [115,125,129,130]. Monoterpenes in plants are known to have fundamentally natural jobs in going about as impediments against taking care of by herbivores, as antifungal safeguards and attractants for pollinators [116,126-128]. They are additionally utilized as seasoning specialists (for example, lemon oil), in perfumery (for example, rose oil), or as beginning materials for the combination of other significant items (for example, turpentine oil). Other than these applications, terpenes (constituents of volatile oils) display permeation improving impacts to encourage transdermal medication conveyance. Terpenes can improve the penetration of both lipophilic medications (for example, testosterone) and hydrophilic medications (for example, propranolol) [117,131,132]. Terpenes have been utilized for remedial purposes since old times. In any case, as of late, they have discovered applications as adjuvant as penetration enhancers for enhanced transdermal and trans mucosal medication conveyance. They are protected, non-irritant and non-harmful to skin and are the best class of sorption supporters for a broad assortment of medicaments. Terpenes like menthol, cineole, and limonene have been utilized for pervasion upgrade of both hydrophilic and lipophilic medications.

5.1.5. Application of alkaloids-based surfactants.

Alkaloid-based surfactants are utilized as emulsifiers, de-emulsifiers, wetting and frothing agents, practical food ingredients, and as cleansers in oil, petrochemicals, natural administration, agrochemicals, nourishments and drinks, makeup and drugs, and in the mining and metallurgical businesses. Expansion of a surfactant of synthetic or organic source quickens or now and then restrains the bioremediation of poisons. Surfactants additionally assume a significant part in upgraded oil recovery by expanding the obvious solvency of oil segments and adequately decreasing oil and water interfacial pressures *in situ*. Be that as it may, the impacts of surfactants on bioremediation can't be anticipated without experimental proof since surfactants here and there invigorate bioremediation and now and again hinder it. For clinical applications, biosurfactants are valuable as antimicrobial specialists and immunomodulatory molecules [95,132,136, 137. The toxicological profile of ergot alkaloids was the subject of examination. The capability of ergot alkaloids to move across the blood-brain boundary (BBB) was studied *in vitro* by Mulac *et al*. utilizing essential porcine brain endothelial cells [118,121,138]. The authors have distinguished the active transport of ergometrine as a substrate for the breast cancer resistance protein (BCRP)/ATP-binding cassette subfamily G part 2 (ABCG2) carrier, showing that ergot alkaloids can move across the BBB in high amounts in a couple of hours. The 8-(S) isomers of ergot alkaloids were found to meddle with the BBB integrity, requesting the danger appraisal of ergot alkaloids in food and feed. The authors found that ergocristinine can possibly accumulate in brain endothelial cells. Prior, an examination directed likewise by Mulac *et al*. depicted the *in vivo* poisonous impacts of the six most dominating ergot alkaloids, to be specific, ergotamine, ergocornine, ergocryptine, ergocristine, ergosine, and ergometrine, along with their - inine isomeric structures [119,139].

6. Conclusions

Natural products-based surfactants have low toxicity and high biodegradability. Due to this, they cause minimum environmental pollution. Synthetic surfactants have persisted in the ecosystem for a long time and have low biodegradability. Biosurfactants are isolated from natural microorganisms and natural resources. The natural products-based surfactant may be an alternative to synthetic surfactant. The natural products include steroids, terpenoids, and alkaloids. These natural product-based surfactants have low toxicity and high biodegradability; hence, they are analogous to biosurfactants. It can also use in cosmetic industries, food industries, biomedicine, and the agriculture sector. The natural product-based surfactant is eco-friendly, which helps to avoid environmental pollution.

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Conflicts of Interest

None.

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