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Various applications of microbial biosurfactant in the field of medical Sciences

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ABSTRACT

Amphipathic nature of biosurfactants enhances their applications in various field like health care, bioremediation, agriculture, mining. Biosurfactants can interact with hydrophilic surface as well as hydrophobic surface. As plasma membrane is made up of lipid bilayer, it is very easy for biosurfactant to diffuse into it and show its activity. So it is used as drug for many disorder and used as vehicle (liposome) to deliver dugs into body. In this study, different chemical nature and various medical applications of biosurfactants are reviewed. Antibacterial property of biosurfactant isolated from different species of *Lactobacillus* and *Bacillus* are reviewed. Effect of monoolein on cervical cancer (HeLA) and leukemia (U937) cells are studied. Antifouling, antifungal and antiviral nature of biosurfactant are also studied. This paper also focused on application of biosurfactant in nanotechnology, food industry and cosmetic industry.

Key words: Biosurfactants–antifungal–antiviral–antifouling–anticancer

1 INTRODUCTION

Biosurfactants are the hydrophobic or hydrophilic moieties that are excreted extracellular at the membranes of the cell or amphipathic compounds produced from microorganisms found in various areas. Biosurfactants reduce the surface tension between the individual molecules at surface and interface. These molecules have different chemical and molecular structures with various surface properties. These surfactants get activated with their functions at the surface. (Barkay T et al., 1999; Ron EZ, Rosenberg E, 2001; Adria AB et al., 2003 and Fakruddin M, 2012). According to Vijaykumar S et al. (2015), biosurfactant are the surface active molecules that alters the properties and lowers the surface tension at the contact between two phases and are produced by microorganisms on living surfaces especially microbial cell surfaces. They have a wide range of applications (Desai et al., 1997).

Biosurfactant are chemically amphillic and polyphillic polymers synthesized by microorganisms that interacts with the phase boundary between two phases present in a heterogenous system or interfaces of surfaces that have varying degrees of polarity and the ability of hydrogen bonding . They have the property of emulsification or breaking down activities. Biosurfactants are produced by certain microbes when they take up simple sugars, oils, hydrocarbons like substrates and break down hydrocarbons or oily things (Ligia RR et al., 2006 and Parthipan P et al., 2017).

Biosurfactants are useful in many commercial and agricultural sectors as in crop protection and agrochemical formulations, soil and water remediation, protection of environment, biodegradation, controls oil spills and oil production due to its biodegradability, low toxicity and better functionality nature. In case of oil production and recovery, it works by increasing the solubility of components present in petroleum (Hamme JD et al., 2006; Sachdev DP et al., 2013; Rita FSS et al., 2014 and Sudhanshu S et al., 2015). The production of biosurfactant is a characterized property of the microorganisms that degrades hydrocarbons. It has a wide application in working to prevent or stop the organic and metal contaminated sites. (Adria AB et al., 2003; Bento FM et al., 2005 and Juliana ML et al. 2012).

To produce large amount of biosurfactant there are two most important factors that affection the generation process of biosurfactants. These are very short period of time and

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reduce the cost of production of biosurfactants (Ahmed ME et al., 2015). The recovery process of biosurfactant is highly difficult in nature so its production is not an easy process. Biosurfactant can be easily obtained by the help of process development (Danyelle KFS et al., 2016). Biosurfactant is used in different industries but it is mainly used to generate petrol and also plays acrucial role in oil industry (Banat IM et al., 1999).

The sources of energy which can be used and replaced naturally are renewable sources of energy using which biosurfactants are produced from fungi (Garima B et al., 2013). Biosurfactants are generally less harmful, can be decomposed by bacteria and they do not lose their properties when exposed to different temperature (Tomasz J et al., 2010).The cost of production of biosurfactant is increasing day by day so waste products from different industries like agriculture are used as the substrate or raw materials (Christofl N et al., 2002). Some strains of microrganisms can resist high temperature like *Pichia anomala* PY which is obtained from foods that have been through a process of lactofermentation in which natural bacteria feed on the sugar and starch in the food creating lactic acid (Jiraporn T et al., 2008).

Not only environmental protection, biosurfactants also play remarkable role in medical field by acting as antimicrobial, antiviral, anticancer, antifouling agents. Biosurfactants are produced by the strain *Lactobacillus fermentum* RC-14 that prevents the attachment of different bacteria like *Enterococcus faecalis* (Das P et al., 2009). In this present study, different medical applications of microbial biosurfactants are discussed.

2 CHEMICAL NATURE OF BIOSURFACTANTS

Biosurfactant are amphiphatic molecules with hydrophobic or hydrophilic moieties (Rodrigues L et al., 2006 and Vijaykumar S et al., 2015). They are either anionic or neutral in nature and a carbohydrate or an amino acid or a phosphate group or some other compounds may be present at the hydrophilic moiety but the hydrophobic moiety contains mostly a carbon chain of fatty acid (Sarkar AK et al., 1989). Mostly biosurfactant are treated as secondary metabolites (Ligia RR et al., 2006). Biosurfactants have several classes like glycolipids, lipopeptides, phospholipids, neutral lipids or fatty acids and polymeric biosurfactant (Cooper DG and Zajic JE, 1980; Cooper DG, 1986 and Kosaric N, 1993). Biosurfactants can be categorized into 5 groups (Desai JD, Bannat IM, 1997).These are as follows: a) Glycolipids b) Lipopeptides c) Fatty acids d) Polymer type e) Particulate biosurfactant.

2.1 Glycolipids

Glycolipids mainly consists of carbohydrates attached to a long chain of hydroxyaliphatic acids or an aliphatic acids by an ester group. Glycolipids are of 3 categories: rhamnolipids, trehalolipids and sophorolipids (Vijaykumar S et al., 2015). Glycolipids are glycoconjugates of lipids that are generally found on the cell membrane. The glycolipids that are present outside the cell are called as extracellular glycolipids which are generally produced by different types of bacteria like *Arthrobacter sp.* (Masaaki M et al., 1993).

2.1.2 Rhamnolipid: These are the best known glycolipids in which one or two rhamnose molecules are attached to one or more molecules of hrdroxydecanoic acid (Vijaykumar S et al., 2015). On the basis of number of rhamnose molecules, it is of two types: mono-rhamnolipid and di-rhamnolipid. It helps in bioremediation, food and cosmetic industries and pharmaceutical companies dues to its physiochemical, antimicrobial and anticancer properties. It is also used in the treatment soil that is contaminated with iron or other heavy metals (Benincasa M et al., 2004 and Akintunde TA et al., 2015). An anionic mono-rhamnolipid is mostly obtained from *Pseudomonas aeruginosa* (Bai G et al., 1997 and Mulligan CN, 2005). Rhamnolipids have different properties like formation of emulsion, stabilize the emulsion, kills the microbes etc. So as a result of which it is used in food industry (Rikalovic GM et al., 2014).

2.1.2 Trehalolipids: Trehalose dimycolate containing lipid is called as trehalolipid. Wall of *Mycobacterium* sp. contains trehalolipid and plays important role in resistance to antibiotics (Pradhan AK, 2017). These are responsible to lower the tension at the surface from 25-40 and interface from 1-5mNm that are present in the culture media.

2.1.3 Sophorolipids: These contain a sophorose,that is a dimeric carbohydrate and is attached by a glycosidic linkage to a long chain of hrdroxyl fatty acid. These are produced by yeast and contains 6-9 sophorolipids and obtained from *Candida bombicola* (Mulligan CN, 2005 and Vijaykumar S et al., 2015).

2.2 Lipopeptides and lipoproteins

Lipopeptides possess emulsification property and are obtained from creosote contaminated soil (Bezza et al., 2015). Lipopeptides and lipoprotiens are formed by the linkage of lipid to a polypeptide chain. These show potent properties that are active at the surface (Ron EZ et al., 2001 and Vijaykumar S et al., 2015).

2.2.1 Surfactin: These are the strongest and most effective cyclic lipopeptide biosurfactant s produced from *Bacillus subtilis* that are capable to reduce the surface and interfacial tension and are made up of seven amino acids ring structure that are attached by a lactone linkage to a fatty acid (Masaaki M et al., 2000; Mulligan CN, 2005 and Vijaykumar S et al., 2015). It is generally used to kill the microbes and is obtained from *Bacillus subtilis* (Rajni D et al., 2016).

2.2.2 Lichenysin: They have excellent property to withstand at extreme temperature, pH and salt conditions and reduce the surface tension to 27 mN/m and infacial tension to 0.36 mN/m of water (Vijaykumar S et al., 2015).

2.3 Polymeric biosurfactant:

These include complexes like emulsan which has an effective emulsification or breaking down property or hydrocarbons present in water even when they are present at low concentrations (Vijaykumar S et al., 2015).

2.4 Phospholipids, fatty acids and neutral lipids:

Phospholipids were derived by the IVN51 strain from the soil that is polluted with hydrocarbons (Ijeoma VN et al., 2016). Neutral lipids are obtained from PAD-2 strain that uses the sole carbon source succinate (Nakano M etal 2012).These classes are mostly secreted by bacteria and yeasts. The genes that undergo isolation and cloning for the production of these surfactants can also work such during their fermentative process (Vijaykumar S et al., 2015).

3 APPLICATIONS OF BIOSURFACTANT IN MEDICAL FIELDS

3.1 Anticancer activity

The glycolipids which are attached to outside membrane of the cell, ie, extracellular help in distinguishing instead of increasing the number and amount of cells in human promyelocytic leukemia cell line. When PC 12 cells comes in contact to MEL it increases the activity of acetylcholine esterase and affects the G1phase of cell cycle which increases the number of neurites and it shows that MEL induces change in number of neurons in PC12 cells (Krishnaswamy M et al.2008).

Monoolein is the strongest surface active compound that shows the antiproliferative activity against cervical cancer (HeLA) and leukemia (U937) cell lines. The chemical structure of Monoolein was detected by the use of spectroscopy and NMR. (Chiewpattanakul 2010). Microorganisms that produces a Biosurfactant were isolated from oil contaminated soil, then collected from palm oil factory waste and then the culture were optimized under conditions to improve the yield. Then the potential anticancer activity was found after purification, examination of the structure and elucidation.

Nano formulations improves anticancer therapy by optimization of surfactin delivery. The cytotoxicity against many cancers are induced by surfactin , cyclic polypeptides Biosurfactant. (Yuan-Seng Wu etal 2017).

3.2 Antimicrobial effect

Biosurfactants can kill or stop the growth of microbes and it is one of their most important functions. As biosurfactants have different types of structures so they exhibit different functions. Due to different structures of biosurfactants they impose its harmfulness nature on the movement of substances across the membrane that leads to a detergent like effect (Zhao Z et al.2010).The biosurfactant producing lactobacilli also helps to maintain and protect the urogenital tract against the harmful microbes (Reid G et al. 2001). During an in vitro study of *Lactobacillus planatarum* 299v and *Lactobacillus rhamnosus* GG they had some strains which helped in the growth of beneficial substances ie, probiotic in nature and prevented the attachment of *Escherchia coli* to intestinal epithelial cells (Mack DR et al. 1999).

Fernandes et al.(2007) studied about the antimicrobial property of biosurfactant from *Bacillus subtilis* R14 against 29 bacterial strains. The marine *Bacillus circulans* also produces a biosurfactant which fights against the Gram positive,Gram negative, semi-pathogenic and MDR strain (Das P et al., 2009). Biosurfactant also allows gas and liquid to pass through the membrane ,ie it makes the membrane permeable(Desai JD etal.1997) .Microbial biosurfactants have a variety of compositions so they exibit a lot of characteristics (Ajesh K etal. 2009).

3.3 Antifungal effect

Many biosurfactants like Surfactin and iturin are showing antifungal property. Nearly seven different rhamnolipids were present in the media containing *Pseudomonas aeruginosa* AT10 which are obtained from wastes and they oppose the growth of fungi. Iturin also oppose the growth of fungi and affects the shape and membrane structure of yeast cells (Benicasa M et al., 2004 and Pooja S et al., 2004).

Biosurfactant like rhamnolipids attained from bacterial strain *Pseudomones aeruginosa* DS9 develops antifungal activity against *Colletotrichum falcatium* that causes red rot in sugarcane. Biosurfactant like sphorolipids have an limited antifungal activity. The development of effective and eco friendly antifungal agents that helps in agriculture and biomedical fields are highly affected by the antifungal activities against plant and human pathogens. Different carbon source mediums were used and after examination it was concluded that glucose has the maximum.

Various concentrations of RL-DS9 and standard RL-R95 were analyzed against *Colletotrichum falcatium* to study the antifungal activities using 96well plates by micridilution process. (Goswami D et al., 2015).

3.4 Antifouling effect

Bacterial attacment to the surface is the primary process in the formation of biofilm and it is affected by various components like the nature of the microorganism, charges which is present on the surface etc. Biosurfactants do not allow the attachment of harmful microorganisms to the infectious site (Das P et al.2009). Rodrigues L et al. (2006) also explained that the pre coating of vinyl urethral catheter by running the surfactin solution also reduced the biofilm formed by Salmonella enterica ,Salmonella typhimurium etc. Krishnaswamy M et al. (2008) also reported that before the treatment of silicone rubber with Salmonella thermophilus surfactant stopped 85% of attachment of *C. albicans* etc.

Biosurfactant posses anti adhesive properties by interacting with bacterial cells and helps in biofilm disruption. These biofilms have resistance power to antibiotics that have a negative impact on health. It stops the cells from growing on it when its surface is treated with rhamnolipids. (Diaz De Rienzo et al., 2015).

Biosurfactant gains the anti adhesive property by preventing adhesion and disruption of biofilm formation through the antimicrobial properties of biosurfactants. Ten lactobacilli species were isolated from Egyptian dairy products that developed this effect. The antimicrobial and anti adhesive properties of Biosurfactant acts against microorganisms that are responsible for diseases and infections like in urinary, vaginal and gastrointestinal tracts as well as skin and as effective probiotic strains (Zakaria Gomaa 2013).

The anti adhesive activities and properties of Biosurfactant were evaluated by several concentration of Biosurfactant (0.625-10 mg/ml) (Luna JM etal 2011). The potential

antimicrobial and anti adhesive property of rufisan helps in biomedical applications. (Rufino RD et al., 2011).

The Lactobacilli species has many uses like- site in the human body where disease causing bacteria gets attached and uses in treatment of some diseases due to its anti adhesive property (Pooja S et al., 2004).

3.5 Antiviral effect

The biosurfactant does not allow the growth of viruses like human immunodeficiency virus to develop in white blood cells (Okoliegbe IN et al., 2012).

3.6 Immunogenic property of biosurfactants

The lipopeptides of bacteria generally forms non-harmful immunological substances when mixed with a particular antigen. When molecular mass of antigens like Iturin AL and herbicolin A decreases it helps in the betterment of humoral humane response (Fathabad EG et al., 2011). Lipofection by the help of gene transfer method can be used to transfer an outside gene directly in to the desired cell (Zhang Y et al., 2010).

3.7 Cosmetics and biosurfactants

Biosurfactants is widely used in cosmetics for example it is used in hair to remove dandruff, to colour hair, perfume to kill insects, shampoos , facial products like- lip balm, eyeliner. Biosurfactants are used as cosmetics especially for glycolipids and lipopeptides due to its detergency, breaking down of fats, foam producing and hydrating of skin properties, stability at varying temperatures and pH and very low critical concentration of micelle. (Brown MJ 1991 and Varvaresou A et al,. 2015,)

Due to different properties of biosurfactants like- ability to form foam,water retaining capacity, formation of emulsion etc it is used in cosmetic industry (Kosaric N 1992).

3.8 Nanotechnology and biosurfactants

Biosurfactants plays a very important role in the field of nanotechnology. Some biosurfactants are used to control silver nano particles in liquid phase which was obtained from *P. aeruginosa* grown when it is grown in a media (Farias CBB et al., 2014). The biosurfactant used is known as BioS. BioS is a lipopeptides mixture especially sufactin and fengycin (Martinez DS et al., 2014). The first synthesized nanoparticle was sufactin Mediated gold nanoparticles that were anionic in nature (Reddy AS et al., 2009)

3.9 Food industry and biosurfactants

The process of breaking down of fat globules otherwise called as emulsification, helps in improving the quality of food. In the dairy industry emulsions has wide applications like butter, cream etc. Many scientists also reported the use of rhaminolipids to improve the quality of emulsifirers in frozen ice creams and other products. It is reported that a bioemulsifier was obtained from *Candida utilis* which is used in bioprocess engineering. (Campos JM et al., 2013)

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