The use of Sophorolipids as anti-angiogeneic therapy for cancer treatment

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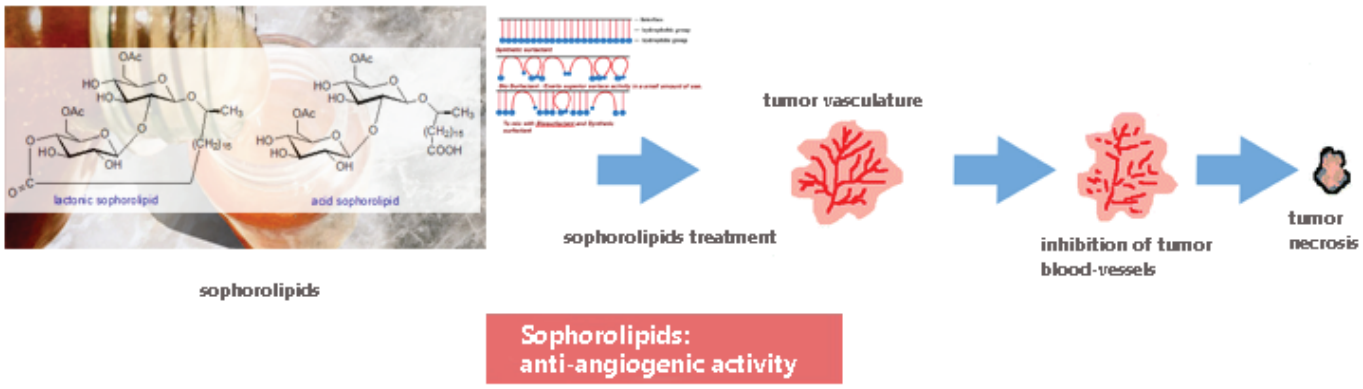
Graphical Abstract



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The use of Sophorolipids as anti-angiogeneic therapy for cancer treatment

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Abstract

Sophorolipids are of growing commercial interest because they can be easily produced in extreme1y high yields from cheap raw materials, such as vegetable oils, n-alkanes and industrial waste products. Sophorolipids have been reported to possess bacteriostatic properties, hence they are used in cosmetics and deodorants. They are also used in the manufacturing of detergents (Furstner A et.al., 2000). Studies have shown that Sophorolipids that have a single double bond in their fatty acid chain have anticancer activity (Dey G et. al., 2014). Recently, Chen et al. have demonstrated that sophorolipids had an effect against hepatocellular carcinoma. In those studies, sophorolipids were found to induce apoptosis when cultured with human liver cancer cells (H7402). Sophorolipids exist in a natural mixture, and, although there have been reports of their effects against malignancy, this is the first study to examine sophorolipids against any cancer cell line. These anticancer responses were dose- and derivative-dependent and likely kill cancer cells by necrosis.

Keywords: Sophorolipids, Cancer, Angiogenesis

Abbreviations: VEGF, vascular endothelial growth factor

Sophorolipids

Sophorolipids have been known for more than 40 years, yet they have garnered much public interest as of late as renewable biosurfactants due to their biodegradability and low ecotoxicity (Van Bogaert et.al., 2007). Sophorolipids are produced as complex mixtures containing both the free acid and lactone forms. These mixtures are typically brown oils, which are viscous and denser than water. Acidic sophorolipids naturally have better solubility and foaming power as compared to their lactonic form (Shin JD et. al, 2010). Also, sophorolipids benefit the organisms that produce them as they aid in the solubility and thus accessibility of lipophilic substrates (Vedaraman N et. al., 2010).

The acidic and lactone forms of sophorolipids determine its properties as well as specific applications. Acetylated lactonic sophorolipids had shown commercial and scientific importance as they show biocide activity, anticancer activity and have been used in cosmetics as antidandruff, bacteriostatic agents, deodorant, shampoo and moisturizing agent. They also act as agents for stimulating skin fibroblast metabolism. Acidic sophorolipids have been used in various therpeutic applications for skin diseases, such as in fibrinology, healing, desquamation, depigmenting, and also for macrophage activation (Shah S et. al., 2006).

Chemistry of Sophorolipids

Sophorolipids can only be synthesized by a select number of yeast species as they are known to be surface-active compounds . The non-pathogenic yeast, Candida bombicola is used in this fermentation process in order to produce sophorolipids. Candida bombicola uses glucose as the primary carbon source, converting the fermentation medium and oil into sophorolipids. Thus, the sophorolipids formed has two glucose molecules. The study of the anti-cancer property of sophorolipids has so far attracted little interest from the scientific community but recent studies on their

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effect on the growth and apoptosis of H7402 human liver cancer cells was investigated and the agent was found to cause dose-and time-dependent inhibition of cell proliferation (Chen et al., 2006).

Sophorolipids form clusters of biosurfactant that are delivered extracellularly by the yeast, Candida bombicola when it is in a non-developing or stationary/resting stage. Yeasts create an expansive scope of biomolecules, a great extent of which are vital to the yeasts for development and digestion systems, coined as "essential metabolites". Notwithstanding, auxiliary metabolites, not known to be fundamental for development are also delivered extracellularly which are exacerbates that Yeast metabolites can categorized in two groups, either broad metabolites, which are synthesized by a substantial number of living beings, or particular metabolites, which are delivered and produced by a confined number of species. The most broadly accessible microbial surfactants are glycolipids, whilst the best examined ones are the rhamnolipids of Pseudomonas aeruginosa and trehalose lipids of Rhodococus erythropolis (Cooper and Zajic, 1980; Zajic and Seffens, 1984; Georgiou et al., 1992).

Most yeast surfactants have been typically identified as glycolipids. Glycolipid biosurfactants are carbohydrates attached to a long-chain of aliphatic acids or hydroxyaliphatic acids. The most interesting glycolipids are the Sophorolipids. They are produced in the form of extracellular oily secretions that are heavier than water (Van Bogaert and Soetaert, 2011). Sophorolipid yields can be increased if vegetable oils are supplied along with glucose as carbon sources (Wadekar et al., 2012b).

Surfactants incorporate a variety of amphiphilic mixes with unmistakable hydrophobic and hydrophilic spaces created through engineered pathways. These spaces prompt division especially at the interface between liquids of diverse extremity and hydrogen holding (Georgiou et al ., 1992). The advancement of a micellar layer at the interface diminishes the free vitality of the framework by supplanting the mass particles having higher vitality . Artificially created surfactants are often dangerous to the environment as they are non-biodegradable. They might bio-collect and their generation forms by-products that can be environmentally unsafe. Surfactants spill over and oil slicks are diminishing the capacity of the sea to assimilate climatic gas and to create cloud structure cores. In this manner CO2 levels are expanding and the world's albedo, the degree to which it diffusely reflects light from the sun, is diminishing. Fixing ecological regulations and expanding public concern over the need to secure biological systems have brought about an expanding enthusiasm for biosurfactants as could be allowed distinct options for compound inferred surfactants. As far as the reduction in interfacial pressure potential, numerous biosurfactants have been coordinating quality to the manufactured surfactants, which are essentially delivered from petrochemicals. Moreover, the synthetic assortment of biosynthetic amphiphilic mixes offers a wide choice of surface-dynamic operators, which may be helpful for particular applications.

On the other hand, because of specialized or monetary limitations, biosurfactants are, as of yet, not generally used in industry (Fiechter, 1992a and 1992b). This issue however is changing as the raising costs of fossil fuels and evident absence of predictable successful option essential assets . Also, new oil wells are being added to the pipeline at a slower rate in recent years. Unexpectedly, biosurfactants, which are completely and quickly biodegradable, have promising applications particularly in zones of ecological dangers concerning bioremediation and the scattering of oil slicks (West and Harwell, 1992; Harvey et., al 1990). Along these lines, the era and usage of biosurfactants might change in the coming years.

Potential use of sophorolipids in angiogenesis-based diseases

Angiogenesis implies the development of novel blood vessels from the original vessels. It is a critical procedure that occurs in the body while both healthy and ill. Angiogenesis occurs in the body during wound healing, development and for restoring blood stream to tissues after damage or affront. The healthy body controls angiogenesis through a series of "on" and "off" switches. At the point when pro-angiogenic cues are in greater abundance over angiogenesis inhibitors, the balance is tipped toward vessel formation. Conversely, when inhibitors are in abundance over pro-angiogenic signals, angiogenesis is ceased. The normal, healthy body maintains a perfect balance of angiogenesis modulators. When all is said and done, angiogenesis is then sharper turned "off" by the generation of a larger number of inhibitors, thus tipping the scale towards anti-angiogenesis. In numerous genuine illnesses, the body loses control over angiogenesis (Harris, 1997). Angiogenesis-subverting illnesses arise when novel vessels either become unreasonable or deficientl. Uncontrolled angiogenesis occurs in maladies, for example, disease, diabetic visual impairment, age-related macular degeneration, rheumatoid joint inflammation, psoriasis, and more than 70 different conditions. In these conditions, fresh recruits vessels bolster diseased tissues, decimate typical tissues, and due to their presence, the new vessels permit tumor cells to escape into the blood flow and metastasize to different organs (Harris, 1997). Exorbitant angiogenesis happens when unhealthy cells over-produce pro-angiogenic compounds, thus overpowering the effects of normal angiogenesis inhibitors. Anti-angiogenic treatments that will halt this fresh blood vessel development are being produced to treat these conditions. Inadequate angiogenesis can also happen in various maladies, for example, coronary conduit infection, stroke, and deferred injury mending. In these conditions, improper veins develop, and blood dissemination is not appropriately

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restored, prompting the danger of tissue death. Inadequate angiogenesis happens when the tissue cannot deliver a satisfactory amount of pro-angiogenesis signals to the blood vessels.

Anti-angiogenic treatment hinders the development of fresh blood vessels. Angiogenesis hindrance is a way to treat issues that cause visual deficiency, joint inflammation and tumor metastasis in light of the fact that fresh blood vessel assume a vital part in numerous infection conditions as specified prior. Anti-angiogenic medications either debilitate the operators that enact and advance cell development or simply obstruct the development of fresh recruits vessels. Angiogenesis inhibitory properties have been found in more than 300 substances, incorporating particles created normally in creatures and plants, to recent chemicals developed in the laboratories.

Conclusion

In conclusion, sophorolipids are an interesting avenue of research in the field of anti-angiogenesis based medicine to treat a plethora of ailments. Compared with regular chemotherapeutic agents that affect all rapidly dividing cells in the body, being able to treat patients with an environmentally safe compound that inhibits angiogenesis, thus not greatly affecting healthy tissue since blood vessels are already formed, could be a radically different way to treat cancers and other maladies. Sophorolipids have been shown to halt cancer cell line growth and induce cell death. It will be interesting to explore if sophorolipids have this same effect on normal healthy tissue and how they could be used to treat patients in the future in order to stray away from the use of synthetic chemicals in the treatment of human illnesses.

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Author Contribution

Shazmin K. M. made substantial contributions to the conception of the review.

Competing financial interests

The author(s) declare no competing financial interests.

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