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Mini review

Marine fungi: An untapped bioresource for future cosmeceuticals

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ABSTRACT

A number of useful metabolites with cosmeceutical potential have been reported from marine sources over the last several years. Marine life, particularly sponge, algae, tunicates, bacteria and fungi, produces a wide variety of bioactive metabolites whose diversity is enhanced by the varied environmental conditions present in the oceans. The marine environment has a large biological and chemical diversity and serves as a source of novel chemical entities with potential industrial application, including pharmaceuticals, cosmetics, nutraceuticals, and agrochemicals. Marine fungi represent a relatively untapped bioresource for novel natural product discovery, although over the past decade marine fungi have providing a number of new secondary metabolites. These secondary metabolites isolated from marine fungi have been used in a range of applications, including cosmeceutical application such as anti-ageing, skin-whitening and anti-acne. In addition, a number of lead compounds have been identified from marine fungi for further development as cosmeceuticals. This review article aims to summarize studies on marine fungal secondary metabolites for application in skin health and cosmeceuticals.

1. Introduction

Nature provides a high diversity of pharmacologically active biomolecules. These natural products are important as leads for the development of novel pharmaceuticals, nutraceuticals and cosmeceuticals. The marine ecosystem covers about 70% of the earth's surface and is extraordinarily rich in biological diversity, particularly in tropical environments. According to the Global Biodiversity Assessment by the United Nations Environment Program, the oceans consist of 178,000 marine species across 34 phyla (Mitra and Zaman, 2016). Marine organisms comprise approximately half of the total biodiversity on earth and produce a wide range of novel biomolecules (Jimeno et al., 2004; Vignesh et al., 2011). Between 1989–2002 around 60% of FDA approved drugs and pre-NDA (New Drug Application) candidates were obtained from the natural environment (Chin et al., 2006; Grabley and Thiericke, 1998). In the past 50 years, exploration of marine bioresources for their unique natural products has been an important area of research. Of the estimated 270,000 known natural products, 30,000 compounds have been obtained from marine organisms (Blunt et al., 2015). Out of these, 9 are approved as medical drugs and 13 are undergoing clinical trials (Gerwick and Moore, 2012; Rangel and Falkenberg, 2015). As examples from fungi, the diketopiperazine halimide (or phenylahistin) obtained from the marine fungi *Aspergillus ustus,* and its synthetic analog Plinabulin (NPI 2358), are in Phase 3 clinical trial for the treatment of non-small cell lung cancer (Raphael et al., 2017) and Phase 2 clinical trial for Neutropenia prevention (Nalley, 2017).

2. Cosmetics-cosmeceuticals from marine sources

The word cosmeceutical was derived from a blending of the terms ‘cosmetic’ and ‘pharmaceutical’ by Abbert Kligman in 1984 (Draelos, 2005). Cosmeceuticals are topical or oral cosmetic, pharmaceutical hybrids, intended to enhance beauty through the application of a bioactive ingredient having drug like benefits (Dureja et al., 2005; Kim, 2011). Therefore, cosmetics have been placed between non-prescribed and prescribed products in a regulatory sense (Amer and Maged, 2009). Cosmetics are defined as substances intended to be applied to the human body for cleaning, beautifying and promoting attractiveness, without affecting the bodies structure and function. Skin is the largest organ in our body and it plays an important role in protecting our body from external environmental stress and pathogens (Slominski et al., 2008). However a range of lifestyle and environmental factors cause cosmetics and dermatology problems (Kim, 2011). Skin cosmeceuticals were developed after research on common skin problems like hyperpigmentation, skin cancer, skin microbial infections, wound healing, and wrinkles associated with sun damage and ageing (Fig. 1). It has been reported that the global cosmeceuticals market will reach US$ 430 Billion by 2020 (https://www.alliedmarketresearch.com).

Natural cosmeceutical products that are safe and efficacious are

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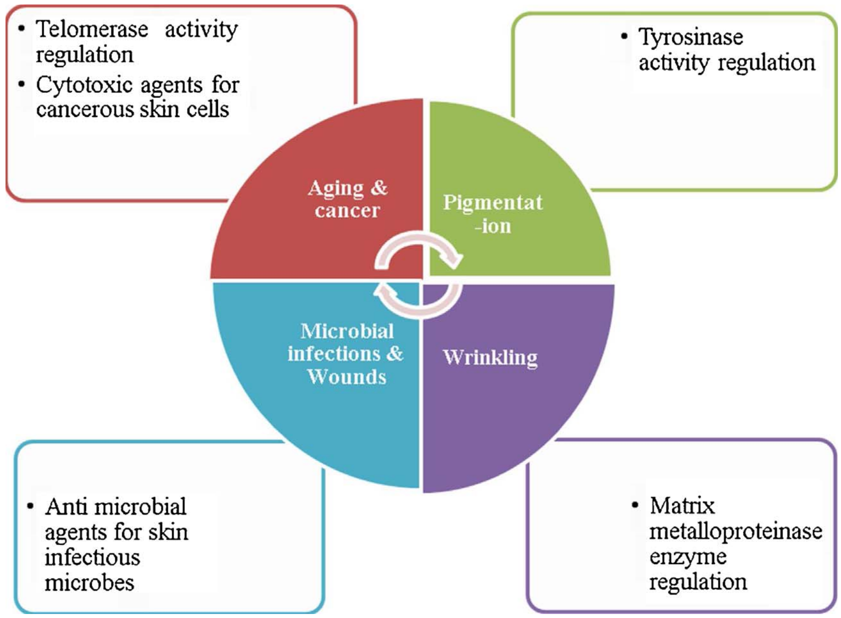

Fig. 1. Major worldwide skin problems and their probable solutions.

important for overcoming skin health problems. Plant derived ingredients have some limitations because plants generally grow too slowly and their chemical composition varies from season to season (Chermahini et al., 2011). However, marine flora and fauna produce chemically different biomolecules in comparison to terrestrial sources and so are of interest, particularly where organisms can be grown rapidly and cost effectively in large quantities, such as for macroalgae and microalgae. Examples include the Greek company Apivita that is using sea fennel in sun care products, whilst Italy-based Lacote has a comprehensive range of anti-cellulite skin care products formulated with Guam seaweed. Sea algae, rich in vitamins and minerals, is becoming a prolific source of anti-ageing bioactives.

The popularity of marine ingredients is leading to concerns that large-scale sourcing, or non-sustainable production methods, could disrupt marine ecosystems already under strain. Cultivable marine microorganisms can be grown outside the ocean in fermenters and so are sustainable. Many classes of bioactive molecules have been isolated from marine microbes for cosmeceutical applications, including phlorotannins, polysaccharides, carotenoid pigments, collagen, chitooligosaccharide (COS) derivatives, enzymes, peptides and other natural materials (Corinaldesi et al., 2017; Kim, 2011).

The potential of secondary metabolites from marine fungi as cosmeceutical ingredients has only being partially evaluated. Relative to the available biological and chemical diversity, only a few compounds have been isolated and utilized as cosmetic ingredient from marine fungi (Corinaldesi et al., 2017). Therefore, there is considerable potential in screening marine fungal isolates and their secondary metabolites for cosmeceutical activity. In the following sections we summarize research performed over the last 10 years on marine fungal natural products with cosmeceuticals activities.

3. Marine fungi and secondary metabolites

Marine fungi are an ecologically rather than physiologically or taxonomically defined group of microorganisms. Marine fungi are divided into two groups on the basis of their ability to grow in marine conditions, these being obligate and facultative marine fungi (Borse et al., 2012). Obligate marine fungi grow fast and sporulate exclusively in a marine or estuarine habitat, while facultative marine fungi have generally developed in terrestrial environments and adapted to the marine environment. Marine fungi are found to be associated with algae, corals, and detritus of marine macrophytes. Over 1500 species of marine fungi, including about 530 species of obligate marine fungi are known. Sometimes it is difficult to differentiate the obligate or facultative nature of fungi and therefore, a more general expression "marine-derived fungi" is used (Bugni and Ireland, 2004).

Marine fungi are major decomposers of woody and herbaceous substrates in marine ecosystems, and they also degrade dead animal or their parts (Hyde et al., 1998). Moreover, marine fungi are important pathogens of marine plants and animals and also form symbiotic relationships with other organisms (Hyde et al., 1998). A broad variety of substrates are available in marine and estuarine environments for fungal growth. These include seaweeds, decaying leaves, mangroves, dead animals, algae, shells of various mollusks (Rateb and Ebel, 2011). Most of these fungi grow on lignocellulosic material in the coastal as well as deep sea environments (Jones et al., 2009). To date 3047 species of fungi have been reported from aquatic habitats around the world. Worldwide, nearly 100000 fungal species are known and about 27500 species have been reported in India. The higher filamentous marine fungi include 530 species in 321 genera, which includes Ascomycota (424 sp. 251 genera), Mitosporic fungi (94 sp. 61 genera) and Basidiomycota (12 sp. 9 genera) (Jones, 2011a, 2011b).

Extreme physical and chemical conditions in the marine environment contribute to the production of a diverse chemical scaffolds by marine organisms (Kijjoa and Sawangwong, 2004). Some marine fungi have developed specific metabolic pathways which are not seen in terrestrial fungi (Abdel-Lateff, 2008; Liberra and Lindequist, 1995). Marine mangroves and algicolous fungi are significant sources of new bioactive compounds (Bugni and Ireland, 2004). Coral reefs are also a rich source of marine fungi that produce novel secondary metabolites due to the presence of other biotic components present in the reefs (Thomas et al., 2010). It is impossible to estimate how many marine derived fungi have been screened so far for bioactive compounds. However, it is clear that the number of new bioactive compounds reported from marine fungi has increased steadily over the years (Duarte et al., 2012; Rateb and Ebel, 2011; Saleem et al., 2007).

Some marine fungi have provided promising new lead structures for drug discovery (Murphy et al., 2012; Waters et al., 2010). An important example is the discovery of cephalosporin C (a non-ribosomal peptide secondary metabolite) from a marine fungi *Cephalosporium* sp. (Rateb and Ebel, 2011). Over the past decade, more than 10,000 marine natural products have been isolated from marine organisms, including marine fungi (Blunt et al., 2015; Kijjoa and Sawangwong, 2004). During this period, approximately 1000 new natural products have