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Review

Emerging biopharmaceuticals from marine actinobacteria

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ABSTRACT

Actinobacteria are quotidian microorganisms in the marine world, playing a crucial ecological role in the recycling of refractory biomaterials and producing novel secondary metabolites with pharmaceutical applications. Actinobacteria have been isolated from the huge area of marine organisms including sponges, tunicates, corals, mollusks, crabs, mangroves and seaweeds. Natural products investigation of the marine actinobacteria revealed that they can synthesize numerous natural products including alkaloids, polyketides, peptides, isoprenoids, phenazines, sterols, and others. These natural products have a potential to provide future drugs against crucial diseases like cancer, HIV, microbial and protozoal infections and severe inflammations. Therefore, marine actinobacteria portray as a pivotal resource for marine drugs. It is an upcoming field of research to probe a novel and pharmaceutically important secondary metabolites from marine actinobacteria. In this review, we attempt to summarize the present knowledge on the diversity, chemistry and mechanism of action of marine actinobacteria-derived secondary metabolites from 2007 to 2016.

Contents

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1. Introduction

Newly drugs, particularly antibiotics, are desperately required to counter and reverse the distribution of antibiotic resistant pathogens (Anjum et al., 2016; Liang et al., 2016) and to fight life-threatening diseases such as cancer (Olano et al., 2009). Nature still stay on the richest and the most resourceful cause for new antibiotics (Blunt et al., 2016), however, considerable advancement is being generated within the domains of engineered biosynthesis and chemical synthesis of antimicrobial compounds.

Actinobacteria, which are the fertile producers of antibiotics, as well as significant providers to the pharmaceutical industry, can give rise several kinds of secondary metabolites (Manivasagan et al., 2013). The actinobacteria contribute with two-thirds of the total the lion's share of the antibiotics producers. Actinobacteria are well known for their power to produce secondary metabolites belonging to the family Actinomycetaceae including the genera of Streptomyces, Actinobaculum, Acanobacterium and several others, most of them are more active to fight against pathogenic organisms. Moreover, these bacteria have been isolated from terrestrial origins as compared to marine origins, although the first report of actinobacterium like mycelium from the marine sediments seemed several decades ago (Weyland, 1969). More than latterly that marine actinobacteria have got an edge as a source of novel antibiotics and anticancer agents with unique construction and properties (Manivasagan et al., 2013, 2014).

Recent information powerfully proposes that actinobacteria are widely distributed in marine environments such as fishes, molluscs, sponges, seaweeds, mangroves, besides seawater and sediments. These organisms are obtaining importance not only for their taxonomic and ecological perceptions, but also for their invention of unique bioactive compounds like antibiotics, antioxidants, Cytotoxic, antitumor agents, immunosuppressive agents, Cardiovascular, enzymes, enzyme inhibitors, pigments (Dharmaraj, 2010).

2. Marine actinobacteria

The phylum Actinobacteria represents as one of the largest taxonomic units among the 18 major lineages recently approved within the domain bacteria (Ventura et al., 2007). The best known of these is the subclass Actinobacteridae, which involves the family Actinomycetales whose members are commonly referred to as actinomycetes (Garrity et al., 2004).

Marine actinobacteria are economically priceless prokaryotes and a good source of unique secondary metabolites for the discovery of new antibiotics. Marine actinobacteria produce secondary metabolites retain a varied kind of biological activities (Manivasagan et al., 2014; Blunt et al., 2016). The family Streptomyces alone served as a big natural hotspot of bioactive molecules. It has a massive biosynthetic perspective that remains open without a possible participant among other microbial groups. Streptomyces sp. have been isolated and screened with an enormous quantity from soil in the past several decades (Watve et al., 2001). Subsequently, possibilities of isolating a novel Streptomyces strain from terrestrial habitats have reduced. More or less 500 species of Streptomyces account are reported for 70–80% of related secondary metabolites, with various biological activities such as anticancer activity; antitumor activity; anti-inflammatory activity; antioxidant activity, etc. Although, some of other genera like Saccharopolyspora, Amycolatopsis, Micromonospora and Actinoplanes show minor part of the attention. An imperative cause for determining novel secondary metabolites is to outfox the problem of resistant pathogens, which are shorter susceptible to the presently used drugs (Lam, 2006). The integer of deaths is on the rise due to these knowing pathogenic organisms. The procedure for the synthesis of novel therapeutic drugs is to get from the secondary metabolites of marine actinobacteria, which may be effectual to combat a variety of resistant microbes (Fenical and Jensen, 2006). The presence of terrestrial actinobacteria has been described in the relatively available marine ecosystem. The enormous diversity of this habitat along with it's below manipulation is the fundamental reason for fascinating researchers toward it for discovering novel metabolite producers. The taxonomic description of the first marine actinobacteria *Rhodococcus marinonascens* is an indication of the occurrence of distinct rare genera in the marine ecosystem (Helmke and Weyland, 1984). Actinobacteria can be isolated from marine sediments which comprise about 10% of the bacteria colonizing marine collections (Ward and Bora, 2006). The deep sea actinobacteria contain non-ribosomal polyketide synthetase (NRPS) and polyketide synthetase (PKS) pathways, which are the hallmarks of secondary metabolite production (Salomon et al., 2004). Researchers are verdict new genera from marine environments on a regular basis and determining new metabolite producers not ever reported before. Despite of the enhancements being improved in the isolation methods of rare marine actinobacteria, however, many of these microorganisms still persist uncultivable and have to be identified by using molecular techniques (Mincer et al., 2005). To characterizing microbes will be useful with metagenomic methods, which cannot be cultivated and can also be used to isolate their genes (Tringe et al., 2005).

3. Marine actinobacteria as a source of new bioactivities

Marine actinobacteria are well-known to have the potential to produce a prodigious amount of biomolecules with interesting novel bioactivities. Certainly, each strain of actinobacteria is assumed to have the genetic potential for the production of 15–25 secondary metabolites (Lam, 2006). About 23,000 antibiotics have been exposed from microorganisms. It has been evaluated that around 10,000 of them have been isolated from actinobacteria (Thomas et al., 2010) (Table 1). Actinobacteria, primarily the genus *Streptomyces*, have the capability to produce a varied range of secondary metabolites as bioactive compounds, including antibiotics. The group has a vast biosynthetic potential that remains unopposed among other microbial groups. The massive diversity, along with its underutilization is the important purpose of attracting the researchers toward determining novel metabolites. A schematic representation of actinobacteria from collection till marketed drug (collection, isolation, culture, purification, structure elucidation, bioassay, clinical trials, target identification, and publication) has been followed step by step (Fig. 1).

3.1. Anti-bacterial activity

The bacterial infection is the major cause of morbidity and mortality throughout the world (Anjum et al., 2016). At the beginning of the twenty century, the first antibiotics detection left the scientific and social society untrained, when the antibiotic-resistant bacteria emerged. This antibiotic-resistance bacterium has multiplied very swiftly and creates a considerable problem while both *Staphylococcus aureus* and some pathogenic bacteria are involved in causing the infections. The importance of drug-resistant bacterial infection has produced an imperative requirement for the quick and sustained development of new antibiotics classes, which may keep pace with the varying face of bacterial antibiotic vulnerability. Therefore, the first precedence of a biochemical research community is the innovation and improvement of new antibiotics (Anjum et al., 2016).