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Short Communication

Actinomycetes: the Unparallel Potential Source of Antibiotics and Natural Products for Drug Discovery

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Actinomycetes are filamentous Gram-positive bacteria, having a complex life cycle belonging to the phylum Actinobacteria, representing one of the largest taxonomic units in the Domain Bacteria [1]. They are extensively distributed in both terrestrial and aquatic ecosystems. They produce several volatile substances like geosmin responsible of the characteristic "wet earth odor" [2]. They are also found as endophytes in plants. Actinomycetes include important genera such as *Micromonospora, Nocardia* and *Streptomyces* which produce several secondary metabolites, antibiotics, enzymes, antitumor agents, biocontrol agents [3,4]. There is an alarming scarcity of new antibiotics currently under development in the pharmaceutical industry. Still, microbial natural products remain the most promising source of novel antibiotics.

Actinomycetes have provided important bioactive compounds of high commercial values and they are being routinely screened for new bioactive substances. 45 % of the presently known bioactive microbial metabolites were isolated from various actinomycetale species, and *Streptomyces* species produces 74 % of all actinomycetales, while the rare actinomycetes represent 26% [5]. They produce the most diverse and most unique, unprecedented, sometimes very complicated compounds exhibiting excellent antimicrobial potency with low toxicity [5]. Their metabolic diversity is due to extremely large genome, which has hundreds of transcription factors that control gene expression, allowing them to respond to specific needs [6]. Many of these secondary metabolites are potent antibiotics. As a result of which streptomycetes have become the primary antibiotic-producing organisms exploited by the pharmaceutical industry [5]. Members of this group are producers of clinically useful antitumor drugs such as anthracyclines [7,8]. The streptomycetes have a particular capacity to produce a large variety of different bioactive compounds that have a wide spectrum of activity [9]. Rare actinomycetes are also considered as potential store house of novel antibiotics [10]. Novel microbial kind should contain new gene cluster synthesizing new secondary metabolites, so far as getting new kind is an important premise for obtaining new compounds [11]. Antimicrobial potentiality of *Streptomyces tanashiensis* A2D and *S. sannanensis* strain SU118 has been reported by Singh *et al*. from untapped habitats [12,13]. Despite extensive exploration of the actinomycetes for their antimicrobial products in the past, the search for novel molecules having unique therapeutic properties continues to be an active area of research. So far only a small fraction of actinomycetes have been discovered. Actinomycetes from unexplored habitats have gained considerable attention in recent years for the production of bioactive metabolites. The expanding list of novel microorganisms and the products derived from poorly explored areas of the world such as certain ecosystem of Manipur [12,13] suggest that a careful exploration of new habitats might continue to be useful. Antibiotic producing ability of the actinomycetes is highly influenced by culture conditions and media components [12]. Progress has been made recently on drug discovery from actinomycetes by using high-throughput fermentation and screening, combinatorial biosynthesis and mining genomes for cryptic pathways, to generate new secondary metabolites related to existing pharmacophores [14].

Endophytes live within plant tissues without causing any apparent harm to their host. They are ubiquitous in many plants

and within almost every tissue type studied [15]. Even so, they are still poorly investigated group of microorganisms [16] and their complex ecological functions remain to be extensively exploited. *Saccharopolyspora gloriosae* sp. nov., an endophytic actinomycete isolate has been obtained from the stem of *Gloriosa superba* L. [17]. Endophytic *Streptomyces* sp. SUK25 from the root of *Zingiber spectabile* has been reported to have a significant inhibitory effect against methicillin-resistant *Staphylococcus aureus* (MRSA) [18]. However, it has been estimated that only 6-7 % of the endophytes in existence have been described. Therefore, it is necessary to investigate the remaining 93 % of these microorganisms in other plant species. Endophytes have the capacity to produce antibiotics that act as antifungal and antibacterial which strongly inhibit the growth of other microorganisms. Streptomycetes are well known for its ability to produce secondary metabolites with diverse chemical structures and different activity against numerous pathogenic microorganisms. Baltz highlighted the proposition of "Renaissance in antibacterial discovery from actinomycetes" [14]. It is therefore pertinent to further put forward the necessity and the potential of exploring the hitherto untapped actinomycetes from plant as a resource for candidate for drug discovery program. In this context exploration and bioprospecting of endophytic actinomycetes especially the *Streptomyces* genera residing in plants including medicinal plants could be targeted systematically and extensively by researchers for the source of antimicrobial agents as well as host plant secondary metabolites towards the goal of obtaining novel, unique and more robust therapeutic agent towards drug discovery from microbial resources. Many companies and laboratories focused on new actinomycete resources from new habitats. So one such least explored habitat which could anticipate overwhelming finding towards the cause of search for novel actinomycetes for drug discovery is the hidden plant system where numerous endophytes reside. Thus in our view, making the uncultured from untapped habitat to pure cultured actinomycetes is one new hope for getting new drug leads which would offer great potential to mitigate ever increasing burden of drug resistance in health care sector.

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