Review Article
Available online at www.ijpras.com

ISSN 2277-3657

Volume 4, Issue 4 (2015):28-32

International Journal of Pharmaceutical Research & Allied Sciences

Antibiotic Activity of Antimicrobial Metabolites Produced From Soil Microorganisms: An Overview

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Subject: Biotechnology

Abstract
The secondary metabolites isolated from microbes and exhibits either antimicrobial (antibacterial, antifungal and antiprotozoans), antitumor and/or antiviral activities, used to be called as antibiotics. Secondary metabolites are also known as bioactive metabolites which works against microbes.There are more than 70% of the antibiotics can be obtained from members of the *Actinomycetes*family and it has been suggested that a large number of *Actinomycetes* may still be unknown with a potential to produce antibiotics. The presence of Multidrug resistant bacteria (MDR) also responsible for the research of novel antibiotics and novel microbes.

Keywords: *Secondary metabolites, Bioactive metabolites, Multidrug resistant culture and Novel antibiotics*

Introduction
In Bacterial growth cycle the formation of secondary metabolites can be seen at the end of stationary phase. Some of the secondary metabolites act as antibiotic, which can be obtained from microorganisms like bacteria and fungi. **[1]**. The *Actinomycetes* come as a major family for the production of antibiotics. Antibiotics inhibit the growth of pathogens and their mode of action involved either by cell wall lysis or to block protein synthesis. According to Berdy, it was observed that most of the antibiotics can be obtained from *Actinomycetes* in which the *Streptomyces* family come at first position [2]. These are gram positive bacteria and the intermediate link between bacteria and fungi [3].According to WHO, the improper use of antibiotics has led to the generation of antibiotic resistance in many bacterial pathogens. Present time the drug resistant activity of microorganisms emerging, because of that many scientists and pharmaceutical industry have actively involved in isolation and screening of antibiotic producing bacteria [4,5]. *Staphylococcus aureus*, a virulent pathogen is responsible for infections, has developed resistance to most classes of antibiotics like methicillin so the name is given MRSA [6, 7]. So, there is need to rediscover new drugs against drug resistance pathogens. The maximum amount of *Actinomycetes* and other bacteria are unknown for their specific properties. Only 10% of the real population of *Actinomycetes* are isolated from nature[8, 9].The filamentous bacteria can be in the form of Actinobacteria which belong to *Actinomycetes.* Only *Streptomyces habitat* can be seen in the form of soil **[6]**.Soil is considered as a natural habitat for Actinobacteria, according to nutrient value, pH, moisture content and temperature level etc. As a result of this variation in soil the production of different metabolites along with different functional activity can be seen[10]. The MDR cultures (Multiple drug resistance) are the type of cultures which can show the resistance in the presence of multiple types of antibiotics. This also approaches to get novel secondary metabolites which should have capacity to work against MDR culture. The best example of MDR can be seen in the form of MRSA (Methicillin resistant *Staphylococcus aureus*). Initially the vancomycin was used for the treatment of MRSA but now a day the *S.aureus* has developed the resistance against vancomycin. Sometime the combination therapy is used for the treatment of enterococci, but some strains have developed the resistance against aminoglycosides for Beta lactam and so on[10]. *Actinomycetes* are industrially useful bacteria which produces secondary metabolites [11]. The comparative analysis of different types of *Actinomycetes*; like Streptomyces and Micromonospora are the producers of commercially important secondary metabolites [11,12,13,14,15,16]. The metabolites were isolated from Actinomycete are generally used for agriculture and medicine purposes [17,18]. The well-known of the secondary metabolites produced by *Actinomycetes* are the antibiotics.

Role of *Actinomycetes* as Potential Producer of Antibiotics
Actinomycetes are the milestone of the antibiotics industry [19]. The search for new antibiotics against multidrug resistant pathogenic bacteria is major

concern of antibiotic research. The Natural products having new structures have been observed along with useful biological significance [20]. Still progress is being made in the fields of chemically engineered biosynthesis of antibacterial compounds, nature itself contained a new metabolites which work like antibiotics [21,22,23,24]. Thousands of metabolites and antibiotics have been discovered but few of them are useful for society with respect to human and animals; the reason behind this is toxicity. To overcome this problem research of new antibiotic is in progress [25,26]. It was observed that almost 12,000 antibiotics have been discovered in last 5 decades. Out of which 70% of antibiotics are obtained from *Actinomycetes* and 30% from filamentous fungi [27].

Soil an inexhaustible source of microbial secondary metabolites

It is a thin layer in the form of earth crust which serves as a natural medium for the growth of microorganisms, plant vegetables etc. The different variety of soil can be seen in India like red soil, laterite soil, black soil and alluvial soil. The composition of soil plays a major role in the development of microbes like moisture content metal concentration, pH value and aeration for the growth of aerobic and anaerobic bacteria[28].The acidic or basic nature of soil is also responsible for the growth of microorganisms like in acidic condition the fungal growth can be seen and in basic condition the *Actinomycetes* growth can be seen[29].still research is going on to obtain novel microorganisms and also to obtain novel secondary metabolites. Soil can exist as a natural habitat for *Streptomyces*. The *Actinomycetes* which are obtained from soil are the major sources for more than 70% of known antibiotics [30].

Diversity of *Actinomycetes* population

Actinomycetes are well known microorganisms for the production of secondary metabolites in the form of antibiotics and immune-suppressor. In the case of sandy soil the pores can be seen through which proper aeration can be observed.The type of soil plays a major role for different variety of *Actinomycetes* in which it was observed that the high percentage of *Actinomycetes*can be obtained from vegetable soil (pH 5-8) [28].Rhizosphere refers the area which surrounds the plant roots. The area of rhizosphere can be more than 5mm in the case of plants which consist of a variety of microorganisms in which the chances are maximum to get *Actinomycetes.* The habitat of *Actinomycetes* can also be seen in root nodules where maximum bioactive metabolites producing bacteria are obtained [29].

***Streptomyces* - the largest producer of antibiotics**

Streptomyces belong to *Actinomycetales* which is subdivision of prokaryotes. It consists of 80 genera which can be from terrestrial soil. The bioactive compound in the form of antibiotics can be obtained from *Streptomyces* which comes under *Actinomycetes* family[30,31,32]. Some common antibiotics which were obtained from Streptomyces are listed below:

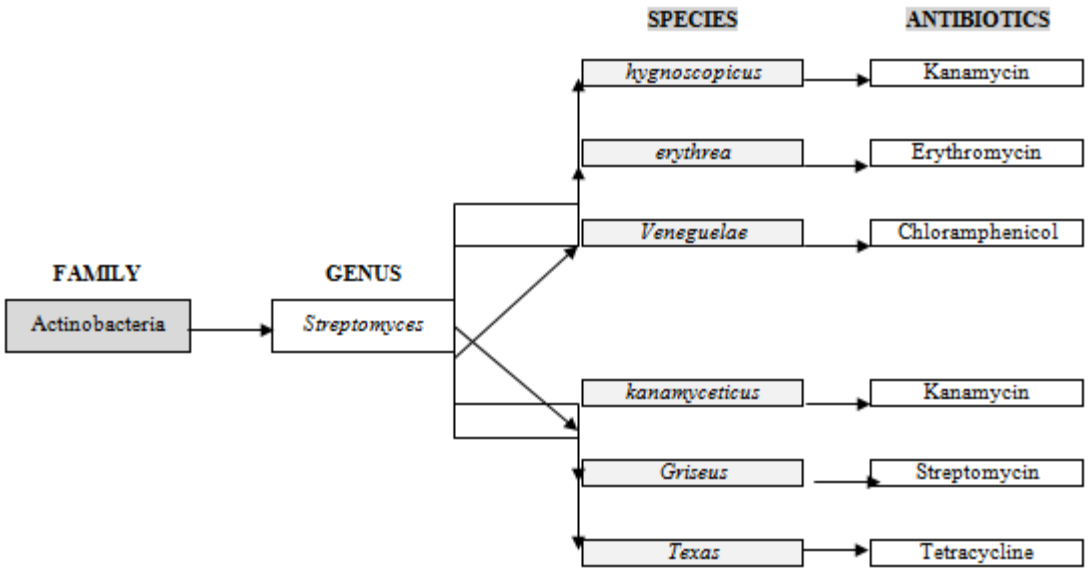

Figure 1: List of antibiotics obtained from *Streptomyces*

The major problem can be seen for the isolation of pure *Streptomyces* because the bacteria and moulds growth can be observed during the slow growth process of *Streptomyces.*

Different works for Antibiotic Research: There are so many antibiotics which can be obtained from microorganisms. some of them are listed below[36,37,38,39,40]:

Table1: Antibiotics obtained from Microbial sources

Antibiotic	Producer organism	Activity	Site or mode of action
Penicillin	*Penicillium chrysogenum*	Gram-positive bacteria	Wall synthesis
Cephalosporin	*Cephalosporium acremonium*	Broad spectrum	Wall synthesis
Griseofulvin	*Penicillium griseofulvum*	Dermatophytic fungi	Microtubules
Bacitracin	*Bacillus subtilis*	Gram-positive bacteria	Wall synthesis
Polymyxin B	*Bacillus polymyxa*	Gram-negative bacteria	Cell membrane
Amphotericin B	*Streptomyces nodosus*	Fungi	Cell membrane
Erythromycin	*Streptomyces erythreus*	Gram-positive bacteria	Protein synthesis
Neomycin	*Streptomyces fradiae*	Broad spectrum	Protein synthesis
Vancomycin	*Streptomyces orientalis*	Gram-positive bacteria	Protein synthesis
Gentamicin	*Micromonospora purpurea*	Broad spectrum	Protein synthesis
Rifamycin	*Streptomyces mediterranei*	Tuberculosis	Protein synthesis

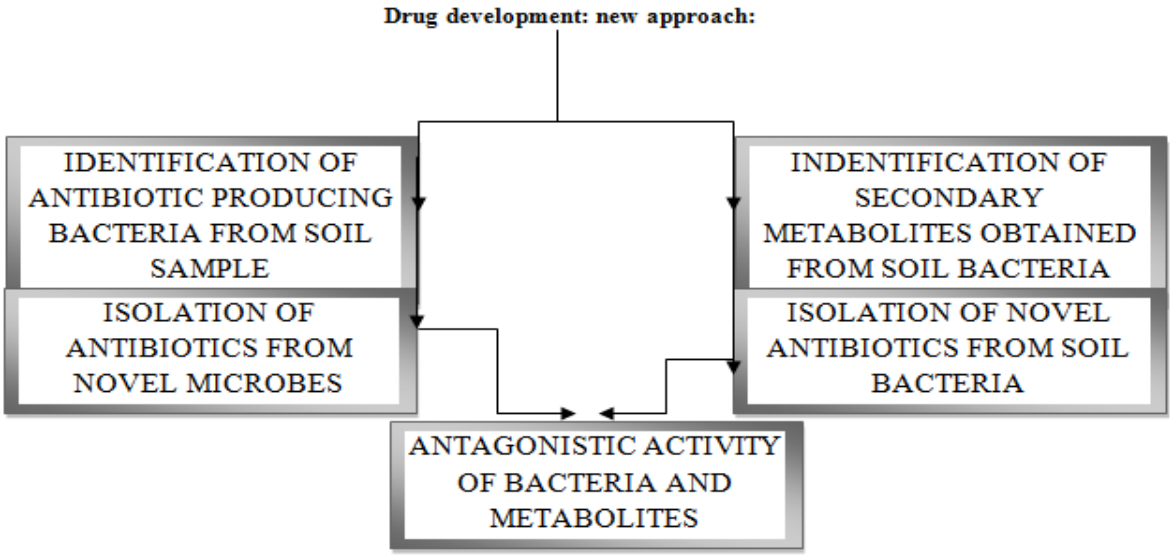

Figure 2: Process of drug discovery in the field of antibiotics

Present time where more than 100 years of research in pharmaceutical industries has been gone , there is still a great need for innovative drugs means the new drug which should have specific mode of action[33,34]. Only one third of all diseases can be treated efficiently. There is a need for new drug entities due to[35]:The presence of MDR (Multiple drug resistance) culture which can show the growth against the different type of antibiotics. *E. coli* and *Pseudomonas aeruginosa* are considered as MDR cultures, The presence of new type of disease are also the major concern and this require the discovery of new drug the diseases can be seen like Ebola and Lyme diseases etc. Drug dose is also important factor which represent the toxicity and side effects of the available drugs[41,42,43,44.45].

The biological activity like antibacterial and antifungal activity connect the bioactive microbial metabolites and differentiating them from the other "inactive" natural products, which evidently emerges an essential question.

This time the challenges can be seen in the form of 25000 to 30000 clinically described human diseases, which require the further increasing of this chemical diversity. Presently the symptomatic treatment can be seen in the case of smaller part, and can cure effectively only a minor portion of these diseases. The challenge of the future is that how we can discover more chemically new agents to fulfil needs of human therapy? In last 10 years some of the new metabolites have been discovered for the treatment of diseases. Currently the reason of the declining new chemical types or drugs or

secondary metabolites may be the result of the exhaustion of the biological sources [33]. All the type of chemotherapeutic agents used today belongs to a limited number of drugs which are discovered in the past by the classical methods [46,47,48,49,50].

"Cite this Article"

A Pandey, S Kumar "Antibiotic Activity of Antimicrobial Metabolites Produced From Soil Microorganisms: An Overview" Int. J. of Pharm. Res. & All. Sci. 2015;4(4):28-32

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