Journal of Advances in Science and Technology
Vol. 17, Issue No. 1, March-2020, ISSN 2230-9659

Antimicrobial Anticancer and Molecular Docking of Soil Bacterial Metabolites

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Abstract - Bacteria produce several secondary metabolites that they use as biocontrol agents. Inducing systemic resistance (ISR) in host plants to a wide range of diseases and/or abiotic stressors, competing for an ecological niche or a substrate, and producing inhibitory allelochemicals are all well-established mechanisms by which PGPB mediate biocontrol. Both the aggressive colonisation of PGPBs and the defensive maintenance of rhizosphere niches are promoted by the bacterial synthesis of allelochemicals such iron-chelating siderophores, antibiotics, biocidal volatiles, lytic enzymes, and detoxifying enzymes.

Keywords - Antimicrobial, Anticancer, Molecular Docking, Soil Bacterial Metabolites

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INTRODUCTION

Soil microorgan isms tend to congregate in clusters around certain soil particles, including clay-organic matter complexes (Foster, 1988). Single cells and microcolonies of microorganisms are both possible, and both forms are often found inside a polysaccharide matrix. Microorganisms in soil are essential to the biogeochemical cycles that keep all life on Earth going (Paul and Clark 1996). By fixing atmospheric nitrogen via nitrogen fixation, oxidising it through nitrification, and recycling it back into the atmosphere through denitrification, microbes play a crucial part in the nitrogen cycle. Important microorganisms are required for the oxidative and reductive reduction of metals like iron and mercury. Animal and plant health may also be affected by the bacteria in the soil. The 20th century saw significant advances in science, medicine, and agriculture, giving us many more reasons to continue to respect the earth than just its role in feeding us. Antibiotics, anticancer agents, and immunosuppressants are only few of the lifesaving medications that have resulted from this century's discoveries regarding soil microorganisms. Similarly, modern research in soil microbiology often takes scientists by surprise by illuminating answers to a wide range of problems in human health and agriculture.

Soil Microorganism

Microbiology of soils examines the organisms that live in soils, the roles they play, and the effects they have on the soil itself. It is believed that the earliest bacteria and microbes originated in the early waters of Earth between two and four billion years ago. As they developed over time, these bacteria released oxygen into the atmosphere and had the capacity to fix nitrogen. Bacteria evolve as a result of the release of oxygen. The microorganisms in the soil are important because they have an influence on the structure and fertility of different soils. Bacteria, actinomycetes, fungi, cyanobacteria, algae, and protozoa are among the many kinds of soil microorganisms. Each of these groups has unique characteristics that describe the creatures inside it and different functions in the soil it occupies.

Actinomycetes

Actinomycetes were formerly thought to represent a third category of organisms, somewhere between bacteria and fungus, due to the high G+C (>55%) concentration in their DNA (Remya and Vijayakumar, 2008). Actinomycete comes from the Greek words aktis (a ray beam) and mykes (a kind of bacterium) (fungus). Both in natural and artificial environments, actinomycetes are common and essential to the decomposition of organic waste. Actinomycetes are widespread soil organisms that share traits with both fungus and bacterium. Both prokaryotic and eukaryotic fungi-like morphological structures, such as filaments and chains of conidia, are present in their cell walls. They vary from fungi in terms of their cellular structure, and they are far more vulnerable to antibacterial than antifungal agents (Das et al., 2006). They are well known for being an excellent source of antibiotics and bioactive chemicals, and they are important to industry. Actinomycetes are a possible source of a number of bioactive compounds with various clinical effects and important applications in human health (Chater, 1998; Chater and Losick, 1997; Flardh and Buttner, 2009). Actinomycetes multiply rapidly in a lab environment. Standard isolation techniques were

used to collect the majority of the isolates, which were then categorised as belong to the species Streptomyces, the most common actinomycete in soil (Lechevalier and Lechevalier, 1967; Nolan and Cross, 1988; Iwai and Takahashi, 1992). Choosing the screening source, making the appropriate preparations, utilising a selective medium, maintaining the culture conditions, and spotting viable colonies on a primary isolation plate are just a few of the factors to consider while screening novel bioactive chemicals (Nolan and Cross, 1988). Streptomyces, a member of the order Actinomycetales and family Streptomycetaceae and a prolific producer of secondary metabolites, is one of the bacteria in this group (Anderson and Wellington, 2001; Magarvey et al., 2004). Most of the actinomycetes that produce the chemical known as geosmin, which has an earthy odour, are found in Streptomyces sp (Schrader and Blevins, 2001).

The practically unlimited potential of actinomycetes to create secondary metabolites with a range of chemical structures and biological functions has proven extremely useful to the pharmaceutical sector. Several of these chemicals have been developed into medications for the treatment of a broad variety of ailments in the human, animal, and agricultural sectors after being isolated and characterised. The development of pharmaceuticals based on natural products depends on the discovery of novel actinomycetes. Antibacterial compounds are mostly produced by actinomycetes and other microorganisms. Actinomycetes have a long history of being successful sources of novel bioactive compounds for drug screening programmes. Actinomycetes have the ability to synthesise novel metabolites with the potential to be transformed into useful commercial items, as shown by the frequent reporting of new compounds despite the frequent presence of recognised compounds (Berdy, 2005).

Streptomycetes

Streptomycetes, a kind of Gram-positive filamentous bacteria, are abundant in both natural and artificial environments and represent a significant proportion of the microorganisms present in the soils in which most people live (Hwang et al., 1994). Streptomycetes, a kind of common bacteria, have a convoluted life cycle. The germinating Streptomyces spore divides into substrate mycelium with a diameter of 0.5–1.0 m. When under stress, such as when there is a lack of nutrients, these branching filaments cease developing, this results in the formation of hyphae tips that differentiate into aerial mycelium. Conidia, asexual spores generated by the aerial mycelium, are much smaller than those produced by fungi (Fig. 1.1). These desiccation-resistant spores form in Streptomyces colonies, giving them a leathery or powdery texture (Weber, 2003). Differentiation is triggered by environmental cues such a lack of nutrients or water, resulting in the production of new spores that are resistant to desiccation and starvation. The production of pigments, antibiotics, and other secondary metabolites starts about the same time.

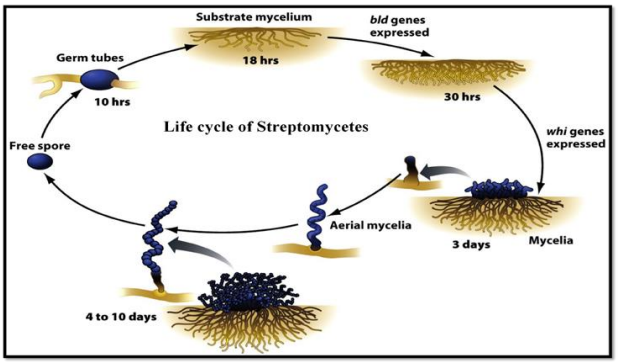

Figure 1: Streptomycetes Life cycle

In the majority of soils, streptomycetes make up 64-97% of the culturable actinomycetes and 1-20% of the total viable count (Kutzner et al., 1986). With more dry soil and colder temperatures, the percentage of Streptomycetes in the total number of actinomycetes rises (Witt et al., 1990). Streptomycetes plate counts were from 103 to 106 cfu/g dry weight soil in peat, mining waste, and acidic soils. Streptomycetes have been excluded from both freshwater and marine settings, while it is debatable whether they are native or have washed off from neighbouring soils. According to studies by Moran et al., (1995) streptomycetes were a native population in sediment and constituted up 2-5% of the microbial community. Streptomycetes may sometimes grow in drinking water reservoirs, where they produce volatile secondary metabolites including geosmin and methyl iso-borneol that have an effect on the water quality and give off earthy odours. The number of Streptomyces species continues to rise. From 464 officially defined species and 45 subspecies reported in 1997, the German Collection of Microorganisms and Cell Cultures now have around 2000 species as of September 2008. As a result, the genus is the biggest in the class Actinobacteria and the order Actinomycetales (Stackebrandt et al., 1997). Streptoverticillium and Kitasatospora have both been placed in the genus Streptomyces, despite the fact that the precise taxonomic placement of Kitasatospora is unclear (Witt and Stackebrandt 1990; Wellington et al., 1992).

Antibiotics used in medicine are mostly derived from Streptomycetes since their secondary metabolites are so effective (Raja and Prabakaran, 2011). More than half (45%) of all bioactive microbial metabolites are produced by actinomycetes, and these microbes are responsible for the almost 10,000 reported bioactive secondary metabolites. Streptomyces species, which are actinomycetes, are responsible for the production of more than 7,600 chemicals (Raja and Prabakaran, 2011). Some of the secondary metabolites produced by streptomycetes have been linked to antimicrobial, antifungal, antiparasitic, anticancer, and immunosuppressive activities (Demain, 1999).

Although certain species have been shown to be powerful in vitro and in vivo inducers of inflammatory responses, they are not very pathogenic (Mishra et al., 1980), despite the fact that they may cause infections (Hirvonen et al., 1997; Jussila et al., 2002).

Secondary metabolites

The term "natural product," when used generally, refers to products derived from both primary and secondary metabolism. Every living organism has a common fundamental metabolism that results in the byproducts of nucleic acids, proteins, lipids, and polysaccharides. Bioactive chemicals are a class of secondary metabolites that are present in very few plant and animal species. To name just a few examples, there are amino sugars, quinones, coumarins, epoxides, ergot alkaloids, glutarimides, glycosides, indole derivatives, lactones, macrolides, naphthaleines, nucleosides, peptides, phenazines, polyacetylenes, polyenes, pyrroles, quinolines, terpenoids, and (Martin and Demain, 1980).

Secondary metabolites with antimicrobial (antibacterial, antifungal, antiprotozoal), anticancer, anti-inflammatory, and/or antiviral characteristics have been found as antibiotics from microbes and other living things. It is understood that secondary metabolites, such as antibiotics, help the organisms that make them survive. secondary metabolites have been shown to function as metal transporters, facilitators of symbiotic interactions between microbes and higher animals, sexual hormones and differentiation effectors, and competitive weapons against other bacteria, fungi, amoebas, plants, insects, and giant animals (Demain, 1998; Berdy, 2005).

Antimicrobials from microorganism

Microorganisms have shown to be an excellent source of novel natural chemicals. In the microbial community, it has been shown that *Bacillus* sp., Pseudomonas sp., Myxobacteria, Cyanobacteria, and Actinomyces often create significant natural products. *Bacillus* species and Pseudomonas species often create peptides or modified peptides, phenazines, and aliphatic compounds (Berdy, 2005). It has been shown that polyketides and peptides produced by cyanobacteria may be harmful or non-toxic (Carmichael, 1992; Grond and Meurer, 2007). Actinomycetes are the main group of microorganisms whose products are utilised in everyday life.

Particularly the Streptomyces genus of microbes is widely recognised for being a prolific producer of antibiotics, herbicides, insecticides, and anti-parasitic compounds, as well as economically relevant bioactive chemicals like cellulase and xylanase. Among the many metabolites that actinomycetes are credited with producing are polyketides like rapamycin and FK-506, peptide antibiotics like virginiamycin and pristinamycin, antibiotics with the -lactum prefix like doxorubicin and daunorubicin, anthracyclines like daunorubicin, and aminoglycosides like gentamicin and kanamycin (Demain, 1999).

In addition to having genes for multidrug resistance, microbes produce an astounding variety of medicines, which combined suggest ongoing "intermicrobial warfares." Since then, a lot of researchers have been inspired by the idea that antibiotics are used to compete with other microorganisms (Stein, 2005). Microbial fermentation is a cheaper alternative to synthetic chemistry for producing natural commodities. In the struggle for survival and to interact with other microbes, the makers of these products have developed in response to the demands and obstacles of their specialised environment. As a consequence, nature provides diversely structured chemicals generated from microbes that have potential as antibiotics (Verdine, 1996). There are a huge variety and abundance of antibacterial substances in nature. According to Roessner and Scott (1996), microbes and plants have produced between 100,000 and 200,000 secondary metabolites.

Molecular Docking

Molecular docking is carried out to foretell the structure of the intermolecular complex produced by two or more molecules. The "ideal" ligand orientation for binding a target protein is described by this optimization issue. Given its potential for pharmaceutical use, the protein ligand interaction is the most exciting possible situation. Ligands are small compounds that bind to specific locations on proteins. Several potential mutual conformations result in binding. These are also called binding modes in other contexts (Sharma et al., 2010). To better understand the interaction between a medication and its receptor, modern drug design often makes use of molecular docking. Molecular docking provides valuable insight into drug receptor interactions by predicting the binding mode of small molecule therapeutic candidates to their protein targets**.**

Bioremediation

There has been a recent uptick in research on microbial biodegradation of pollutants as people look for long-term answers to the problem of cleaning up polluted environments. Bioremediation and biotransformation techniques seek to degrade, transform, or accumulate a wide variety of substances, including hydrocarbons (like oil), polychlorinated biphenyls (PCBs), polyaromatic hydrocarbons (PAHs), heterocyclic compounds (like pyridine or quinoline), pharmaceuticals, radionuclides, and metals. Due to recent advances in methodology, extensive high-throughput studies of environmental microorganisms may now be conducted on a genomic, metagenomic, proteomic, bioinformatic, and other level. These analyses have allowed us to better understand the most crucial biodegradative systems and the capacity of living things to adapt to shifting environmental conditions.

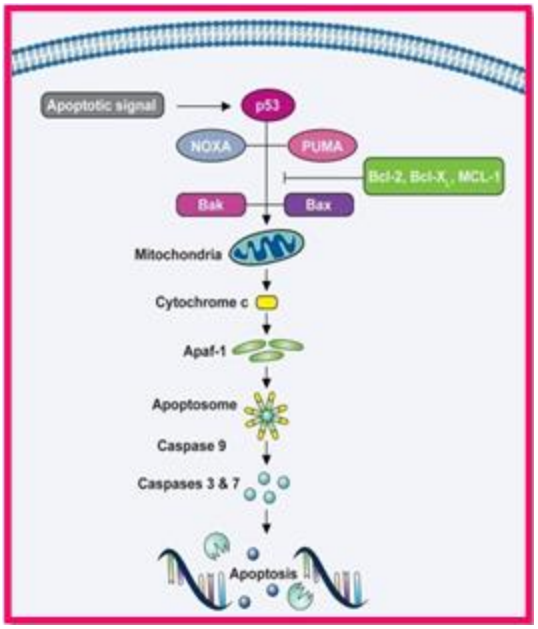

Figure 2: Pathway is evident by the large number of tumours that bear amutation in this gene.

Table 1: Secondary metabolites produced by *Streptomyces* with antimicrobialand anticancer activities

Compound Name	Activity	Organism
Kanamycin	Antibacterial	*Streptomyces kanamyceticus*
Streptomycin	Antibacterial	*Streptomyces griseus*
Kalafungin	Antimicrobial	*Streptomyces tanashiensis*
Enduracidin	Antibacterial	*Streptomyces fungicidicus*
Lomofungin	Antimicrobial	*Streptomyces lomodensis*
Fosfomysin	Antibacterial	*Streptomyces fradiae*
Chlorocarcins A, B, C	Antitumor, antibacterial	*Streptomyces lavendulae*
Mimosamycins	Antibacterial	*Streptomyces lavendulae*
Ileumycin	Antifungal	*Streptomyces lavendulae*
Cephamycin C	Antibacterial	*Streptomyces lactamdurans*
Fredericamycin A	Antitumor	*Streptomyces griseus*
Granaticin	Antibacterial	*Streptomyces thermoviolaceus*
Scopafungin	Antimicrobial	*Streptomyces hygroscopicus* var.
Spiramycin	Antibacterial	*Streptomyces ambofaciens*
Lavendamycin	Antitumor	*Streptomyces lavendulae*
Kazusamycin	Antitumor	*Streptomyces* sp.
Biphenomycin A and B	Antibacterial	*Streptomyces griseorubiginosus*
Lavendomycin	Antibacterial	*Streptomyces lavendulae*
Sohbumycin	Antitumor	*Streptomyces* sp.
Capuramycin	Antibacterial	*Streptomyces griseus*
Elloramycin	Antitumor	*Streptomyces olivaceus*
Maggiemycin and anhydromaggiemycin	Antitumor	*Streptomyces* sp.
Himastatin	Antitumor	*Streptomyces hygroscopicus*
Novobiocin	Antibacterial	*Streptomyces niveus*
Dunaimycins	Antimicrobial	*Streptomyces diastatochromogenes*
Furaquinocins C to H	Antitumor	*Streptomyces* sp.
Okicenone	Antitumor	*Streptomyces* sp.
Hydramycin	Antitumor	*Streptomyces violaceus*
Cinerubin R	Antibacterial	*Streptomyces*

Tylosin	Antibacterial	*Streptomyces fradiae*
Midecamycin	Antibacterial	*Streptomyces mycarofaciens*
Virginiamycin M	Antibacterial	*Streptomyces virginae*
Saptomycins	Antitumor, antimicrobial	*Streptomyces* sp.
Oxaprapalines B, D, G	Antitumor	*Streptomyces* sp.
Vicenistatin	Antitumor	*Streptomyces* sp.
Shurimycins A and B	Antimicrobial	*Streptomyces hygroscopicus*
Lankacidin	Antibacterial	*Streptomyces rochei*
Lankamycin	Antibacterial	*Streptomyces rochei*
Actinomycin C	Antitumor	*Streptomyces chrysomallus*
Duanomycin	Antitumor	*Streptomyces* sp.

Medecamycin	Antibacterial	*Streptomyces mycarofaciens*
Urdamycin A	Antitumor	*Streptomyces fradiae*
RS-22 A, B and C	Antimicrobial	*Streptomyces violaceusniger*
Nogalamycin	Antibacterial	*Streptomyces nogalater*
Kanchanamycins	Antimicrobial	*Streptomyces olivaceus*
Rapamycin	Antifungal	*Streptomyces hygroscopicus*
Pristinamycin I	Antibacterial	*Streptomyces pristinaespiralis*
Nikkomycins	Antifungal	*Streptomyces ansochromogenus*
Blasticidin S	Antifungal	*Streptomyces griseochromogenes*
Mitomycin C	Antitumor	*Streptomyces lavendulae*

Medecamycin	Antibacterial	*Streptomyces mycarofaciens*
Urdamycin A	Antitumor	*Streptomyces fradiae*
RS-22 A, B and C	Antimicrobial	*Streptomyces violaceusniger*
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Pristinamycin I	Antibacterial	*Streptomyces pristinaespiralis*
Nikkomycins	Antifungal	*Streptomyces ansochromogenus*
Blasticidin S	Antifungal	*Streptomyces griseochromogenes*
Mitomycin C	Antitumor	*Streptomyces lavendulae*

Gilvusmycin	Antitumor	*Streptomyces* sp.
Zelkovamycin	Antibacterial	*Streptomyces* sp.
Vinylamycin	Antibacterial	*Streptomyces* sp.
Avilamycin A	Antibacterial	*Streptomyces viridochromogenes*
Streptocidins A–D	Antibacterial	*Streptomyces* sp.
Aclacinomycin A	Antitumor	*Streptomyces galilaeus*
Pipalamycin	Apoptosis	*Sreptomyces* sp.

Mithramycin	Antitumor	*Streptomyces argillaceus*
Ripromycin	Antibacterial, antitumor	*Streptomyces* sp.
Rimocidin	Antifungal	*Streptomyces diastaticus* var.
Pimaricin	Antifungal	*Streptomyces natalensis*
Chloramphenicol	Antibacterial	*Streptomyces venezuelae*
Retamycin	Antitumor	*Streptomyces olindensis*
Frigocyclinone	Antibacterial	*Streptomyces griseus*
Tetracycline	Antibacterial	*Streptomyces aureofaciens*
Leptomycin	Antifungal, antitumor	*Streptomyces lividans*
Landomycin E	Antitumor	*Streptomyces globisporus*

YM-216391	Anticancer	*Streptomyces nobilis*
Ipomicin	Antibacterial	*Streptomyces ipomoeae*
Daptomycin	Antibacterial	*Streptomyces roseosporus*
Apramycin	Antibacterial	*Streptomyces tenebrabrius*
Phenalinolactones A–D	Antibacterial	*Streptomyces* sp.
Zorbamycin	Antitumor	*Streptomyces flavovirdis*

CONCLUSION

Previously, various anti-infection agents have been separated from different microorganisms. Nonetheless, studies are still underway to find novel and potential anti-microbial mixtures that are viable against different dangerous sicknesses. In the ongoing situation, microbial diseases and different kinds of tumors make significant nervousness people. Thus, the advancement of new anticancer and antimicrobial specialists, ideally from normally happening organisms with novel instruments of activity is required. Consequently, soil microorganisms with tremendous potential to deliver bioactive mixtures with an extensive variety of primary variety could be utilized for the different applications in drugs.

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