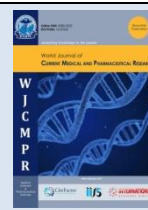




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THE ABILITY OF MICROORGANISMS TO PRODUCE ANTIBIOTICS- A REVIEW

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Article History	Abstract
Received on: 16-03-2023 Revised on: 24-04-2023 Accepted on: 09-05-2023	Antibiotics are chemicals that prevent or eliminate bacterial growth and are widely used in various applications. They were first discovered by Alexander Fleming in 1928 when he noticed that a mold called <i>Penicillium notatum</i> inhibited the growth of <i>Staphylococcus aureus</i> bacteria. Since then, antibiotics have been extensively studied and utilized to combat bacterial infections. There are several potential sources of antibiotic-producing microorganisms, including soil, water, plants, animals, and even fermented foods. Actinomycetes, a type of bacteria commonly found in soil, are known for their ability to produce a wide range of antibiotics. Marine environments are also considered a rich source of antibiotic-producing microorganisms. The production of antibiotics by bacteria is of great interest, as it offers the potential for the development of new natural product-based drugs. Actinomycetes, particularly <i>Streptomyces</i> species, have been a major focus of antibiotic research and have yielded thousands of distinct secondary metabolites, many of which are antibiotics. Antibiotics play various natural functions in microbial interactions in different environments. They can act as weapons or shields, protecting bacteria from predators or competing microbes. Antibiotics can also have concentration-dependent effects, acting as inhibitors at high concentrations and mediators of intracellular signaling at low concentrations. The production of antibiotics by bacteria in soil and plant-associated environments has been extensively studied. Bacterial genera such as <i>Bacillus</i> , <i>Pseudomonas</i> , and <i>Streptomyces</i> have been found to produce bioactive peptides with antimicrobial properties. These antibiotics can help bacteria survive in harsh environments by inhibiting the growth of predators or competitors.
Keywords: Antibiotics, Microorganisms, Soil associated bacteria, Medicine, Antibacterial.	



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Introduction

Antibiotic literally means "against life." However, in common parlance, we use the term to refer to a group of chemicals that prevent or eliminate bacterial growth. One of the most significant secondary metabolites produced by bacteria that is commercially harnessed and used in a variety of applications are antibiotics. In 1928, Alexander Fleming, a British scientist, is credited with being the first to recognise that another organism may suppress bacterial development. He discovered that a mould (fungus) on his plate was preventing the growth of the bacterium *Staphylococcus aureus*. *Penicillium notatum* was the name of the mould, and penicillin was the name given to the antibiotic that was found shortly after [1]. There are numbers of bacteria having potential to produce an antibiotic example of which is *Bacillus* species which produce antibiotic like bacitracin, pumulin and gramicidin which are active against Gram-positive bacteria such as *Staphylococci*,

Streptococci, *Corynebacter*, *Streptomyces* species which produce antibiotic like tetracycline, cloramphenicol, vancomycin, gentamycin which are active against Gram-negative bacteria and *Lactobacillus* species which antibiotic like nisin which is produce by *Lactobacillus lactis* [2].

Unquestionably, there is an urgent need for novel medicines to stop and reverse the persistent growth of antibiotic-resistant microorganisms that cause life-threatening illnesses and run the danger of jeopardising the sustainability of healthcare systems [3]. Over 10,000 of the 23,000 bioactive secondary metabolites described from microorganisms, or actinomycetes, make up 45% of all bioactive microbial metabolites. Therefore, the hunt for novel actinomycete has become increasingly important in recent years for the development of natural product-based drugs [4]. The majority of these soil-based microorganisms that could serve as drug sources continue to be unproductive, making them unavailable for the discovery of new antibiotics. This research is anticipated to play a significant role in the development of fresh natural bioactive items. The goal of the study was to separate and test actinomycetes from garden soil for antibiotic activity [5].

Marine conditions are generally undiscovered hotspot for the seclusion of new microorganisms with possibility to create dynamic auxiliary metabolites. Among such microorganisms, Actinomycetes are of extraordinary interest, since they are known to deliver synthetically different builds with a large number of organic exercises [6]. The interest for new antibiotics keeps on becoming because of the quick arising of numerous anti-toxin safe microbes causing perilous disease. Albeit, extensive headway is being made inside the fields of synthetic combination and designed biosynthesis of antibacterial mixtures, nature actually stays the most extravagant and the most flexible hotspot for new anti-microbial activity [7]. Actinomycetes address a universal gathering of organisms broadly dispersed in normal biological systems all over the planet and particularly huge for their job on the reusing of natural matter [8]. Microorganisms saw as in marine conditions have drawn in a lot of consideration, because of the development of different regular mixtures and their specific components for variation to outrageous climate [9]. Since marine residue address a climate which is notably not the same as that related with soil tests, it isn't clear how viable the pre-treatment of such silt would be for the recuperation of bioactive Actinomycetes. Marine residue is a limitless asset that has not been as expected took advantage of. Reports from the East Shoreline of India, proposes that dirt is a significant wellspring of Actinomycetes [10]. evaluating of microorganisms for the creation of anti-toxins has given the foundation of anti-microbial examination programs for the beyond thirty years. These projects were for the most part done involving growths and actinomycetes as they can deliver normal items with a large number of synthetic designs. To date, in excess of 400 peptides with antimicrobial exercises have been found from different sources like plants, bugs, microbes, and vertebrates. Two fundamental methodologies have been utilized during the screening interaction of anti-infection agents. The principal procedure screens out the auxiliary metabolites known to be futile anti-infection agents and the second system evaluates for obscure mixtures that have exhibited restraining qualities on certain chemicals and additionally natural exercises of certain objectives. The last option is generally finished utilizing new advancements. The best antitumor substances are mithramycin, bleomycin, daunomycin and Adriamycin [11].

Possible Sources Of Antibiotic-Producing Microorganisms

Antibiotic-producing microorganisms can be found in various environments, including soil, water, plants, and animals. Some possible sources of antibiotic-producing microorganisms are:

1. **Soil:** Soil is a rich source of antibiotic-producing microorganisms. Actinomycetes, a type of bacteria, are commonly found in soil and are known for their ability to produce a wide range of antibiotics.
2. **Water:** Many aquatic environments, including rivers, lakes, and oceans, contain microorganisms that produce antibiotics. Marine microorganisms, in particular, are known to produce unique and potent antibiotics.
3. **Plants:** Some plants, such as the bark of the Pacific yew tree, are a source of natural compounds with antibiotic properties. Other plants, such as garlic, have been used for centuries for their antibacterial properties.

4. **Animals:** Many animals, including insects, amphibians, and mammals, have been found to host antibiotic-producing microorganisms. For example, the skin of certain species of frogs has been found to contain antimicrobial peptides that can kill bacteria.

5. **Fermented foods:** Certain fermented foods, such as cheese, yogurt, and kefir, contain lactic acid bacteria that have been found to produce antibiotics.

Antibiotic Production by Soil-And Plant-Associated Bacteria

The majority of the knowledge of the structural diversity, activities, and natural functions of antibiotics produced by soil bacteria is derived from their cultured counterparts, despite the potential reservoir of novel antibiotic compounds from microbial genomes and uncultured soil microbes. From various soils and eukaryotic hosts, such as plants, nematodes, and insects, numerous genera and species of antibiotic-producing bacteria have been isolated. Scaffolds for clinical antibiotics and other treatments have primarily come from actinomycetes, particularly *Streptomyces* species. The majority of these prolific antibiotic producers are found in soil, but they can also be found in plant and insect microbial communities. *Streptomyces* isolates have yielded more than 7,000 distinct secondary metabolites to date, many of which are antibiotics [11,12,13,14]. the molecules involved in cell-cell interactions and predation, as well as their fascinating surface-gliding social behavior and ability to antagonize and kill competing microbes, have sparked significant interest in their highly structured biofilms [15]. . Although *Myxococcus xanthus* has received the most research, other genera are currently being investigated as a potential source of antibiotics with novel modes of action and distinctive structural characteristics [27]. In the accompanying areas, we give brief outlines of anti-infection agents delivered by a few bacterial genera tracked down in soil-and plant associated conditions. Antibiotics produced by bacteria that (a) control plant pathogens, (b) live inside plant tissues or in insects, or (c) cause plant diseases are described in greater detail within the context of plant pathology. Andersen and Sandaa [28] announced the perception of antibiotic medication determinants among Gram-negative microscopic organisms separated from marine residue. The procurement of antibiotic medication opposition qualities has additionally been accounted for *Mycobacterium* and *Streptomyces* species [29] [30] in announcing the similitude of the *ermG* of *B. sphaericus* to the conjugative transposon of *Bacteroides* give supporting proof to the exchange of opposition qualities between soil microbes and gastrointestinal microscopic organisms of man. [31] and [32] give proof that intimate, self transmissible, and mobilizable plasmids are far reaching in natural microorganisms and [34] demonstrated the way that PCR can be utilized to portray such plasmids. In their investigation of the *GyrA* protein, Waters what's more, Davies [33] found a high frequency of soil bacterial disengages with protection from fluoroquinolone anti-microbials. Erythromycin obstruction has been accounted for in many soil microbes including types of anti-microbial creating *Streptomyces* and *Bacillus* [52]. Protection from erythromycin, a macrolide anti-microbial, is accepted to be expected to a posttranscriptional change of the 23S rRNA by a N-methyltransferase encoded by *erm* qualities.

Macrolide obstruction additionally instigates protection from the related lincosamide and streptogramin B group of anti-toxins comprising what is alluded to as MLS opposition. That anti-toxin delivering species of *Streptomyces* harbor MLS opposition shows the creature's assurance from implosion by its own anti-toxin. In investigations of protection from anti-toxins furthermore, weighty metals in landfill microbes, Nwosu and Ladapo [35] tracked down a somewhat serious level of protection from various anti-toxins in confines of *Bacillus*, *Corynebacterium*, *Aeromonas*, and *Enterobacter*. They noticed that confines were by and large delicate to antibiotic medication and chloramphenicol furthermore, for the most part impervious to ampicillin, erythromycin and streptomycin with 3 of 14 segregates having various protection from ampicillin, erythromycin, and streptomycin. It is fascinating that the disengages were moderately delicate to antibiotic medication and chloramphenicol, two anti-microbials cwith current restricted clinical use, while moderately impervious to those anti-infection agents that are as yet utilized clinically in the review region. A relationship between protection from anti-infection agents and weighty metals was noted in an *Enterobacter* seclude that was impervious to 160 mg/L barium [36].

Natural Functions of Antibiotics

"Our anthropogenic vision of antibiotics in the clinical environment may not be transposable to the natural environment," stated on the basis of the limited examples of the weapon/shield function of antibiotics in natural environments [17]. The idea that antibiotics might be just a shield or weapon in the environment was further stoked by the apparent widespread occurrence of antibiotic resistance among soil microbes and their capacity to combat it [18]. The discoveries that anti-infection agents apply various consequences for microorganisms at subinhibitory focuses prompted a restoration in interest in the peculiarity called hormesis, i.e., the capacity of metabolites to actuate differential reactions subject to their focuses even alluded to anti-microbials and other optional metabolites as microbial pheromones, as they can evoke a explicit reaction from different individuals from the same species [19]. As a result, a number of reviews and commentaries have suggested that antibiotics work in a concentration-dependent manner, acting as inhibitors at high concentrations and mediators of intracellular signal at low concentrations [23]. In this section, we provide an overview of the potential roles that antibiotics might play for bacteria in environments that are associated with plants and soil. For a more in-depth look at antibiotics' roles and diversity in the symbiotic relationship between bacteria and non-plant eukaryotic hosts [21]. Soil-staying microbes are presented to a riches of ruthless specialists, including a variety of bacterivorous nematodes and protozoa. Special touching of microscopic organisms has been accounted for nematodes [36, 37] and protozoa [38] in soil frameworks, with bacterial genera, for example, *Pseudomonas* being leaned toward by specific protists over others like *Streptomyces* or *Bacillus* [39,40]. The creation and collection of optional metabolites might assume a huge part in restricting the defenselessness of microorganisms to the ruthless soil microfauna [41,42,43]. For sure, studies showed that 2,4-DAPG

created by specific *P. fluorescens* strains restrains development of protists, initiating encystment and cell lysis [45]. It was recommended that creation of 2, 4-DAPG improved the wellness of *P. fluorescens* strain CHA0 in the rice rhizosphere because of further developed protection from predation by the protozoan *Acanthamoeba castellanii* [46] and may add to obstruction of the bacterium to nematode brushing [47]. Alternately, 2, 4-DAPG-inadequate freaks of *P. fluorescens* strains Pf-5 and Q8r1-96 held protection from predation by *Naegleria* Yankee folklore and *Colpoda* sp., while the particular *gacA*-freaks were defenseless to brushing by these protists [48].

Numerous bacterial genera, including *Bacillus*, *Pseudomonas*, and *Streptomyces*, produce a variety of bioactive peptides by means of non-ribosomal peptide union [49,50,51]. Among these, LPs are known to upset film uprightness, prompting the lysis of different microbial life stages, including zoospores of oomycete microbes [52] and trophozoites of the bacterivorous one-celled critter whip *N. History of the U.S.* Creation of the LPs viscosin and massetolide by *P. fluorescens* strains SBW25 and SS101, individually, was displayed to essentially improve bacterial endurance when faced by *N. Yankee folklore*. The LP-delivering strains were especially more impervious to protozoan brushing in vitro than their relating LP-lacking freaks. Despite the fact that LP-creating and LP-lacking strains regularly endured in soil at comparative densities without a trace of *N. americana*, the perception that LP-delivering SS101 and SBW25 persevered at higher densities relative to their LP-lacking freaks in the presence of the protist showed that upgraded endurance was an immediate outcome of a prevalent capacity to stay away from predation. Moreover, the populace thickness of the single adaptable cell flog in the wheat rhizosphere was reduced within the sight of LP-delivering strains comparative with that achieved in the presence of the relating LP-insufficient freaks. The significance of this ruthless safeguard system is obviously reliant upon LP structure, as orfamide A creation in *P. fluorescens* Pf-5 didn't give opposition to brushing by *N. History of the U.S* [44].

Production of Antibiotics

Due to the indirect nature of the supporting evidence and the perceived constraints on antibiotic production in natural environments, the significance of antibiotics as weapons or shields in microbial interactions in soil environments is frequently questioned. In fact, most adverse effects of antibiotics on other microorganisms have been discovered through controlled in vitro assays [22]. stated, "In situ concentrations of compounds with antibiotic activities have never been measured, and there are few ecological examples of probable antibiotic functions in nature" in this context. This assertion is not entirely accurate, as various analytical chemical analyses and reporter gene systems have demonstrated (a) that genes involved in antibiotic biosynthesis are transcribed in situ and (b) that bacteria produce antibiotics in soil, spermosphere, and rhizosphere environments. Antibiotics do indeed play a role in microbial interactions in soil and on plant surfaces, according to comparative analyses of the behavior of bacterial strains and mutants disrupted in specific antibiotic biosynthesis or regulatory genes. Reporter gene systems are now widely used to track bacterial strain

populations introduced into complex ecosystems and provide data on the transcriptional activity of particular genes [24]. Keel and colleagues [23] recently cleverly combined various reporter genes with fluorescence-activated cell sorting to simultaneously monitor the biocontrol strain *P. fluorescens* CHA0's root colonization and in situ antibiotic gene expression. However, in most cases, reporter gene systems do not provide an accurate measurement of the concentration of antibiotics in situ. Thus, different insightful methods, including slender layer chromatography, elite execution fluid chromatography (HPLC), and fluid chromatography-mass spectrometry (LC-MS), have been utilized to evaluate in situ anti-microbial creation by biocontrol microscopic organisms. According to the findings of these studies, plant-associated environments encourage the production of antibiotics by introduced bacterial strains at concentrations ranging from about 5 ng to 180 g per gram of soil or plant tissue (Table 1). In these studies, specific bacterial strains introduced into soil or onto seeds, fruits, or plant surfaces at relatively high densities were found to produce antibiotics in situ. In two examinations, in situ creation of explicit anti-microbial mixtures not entirely set in stone for native soil microorganisms. The take-all pathogen *Gaeumannomyces graminis* var. is naturally suppressed in soils. On wheat roots, tritici, the antibiotic 2,4-DAPG, was found in concentrations ranging from 19 to 150 ng per gram of root fresh weight [25].

Even though analytical-chemical detection of antibiotics in situ adds to the indirect evidence provided by genetic methods, it only confirms that antibiotics have been produced; It does not provide an answer to the question of whether the amounts that were found are sufficient to stop the in-place growth of other microorganisms. When it comes to their roles as weapons and shields in microbial interactions, the time and location of antibiotic production are crucial. In some microsites, antibiotics may reach activity threshold levels while remaining far below these levels in others. O'Brien & Wright [26]. The dynamics of antibiotic production in live bacterial colonies in vitro are being resolved with significant progress [33]. It is hoped that these and other new approaches can be adapted for in-place monitoring of patterns of spatiotemporal antibiotic production.

Phylogenetically different microbes separated from various soils were displayed to remain alive on a few distinct anti-toxins as a sole carbon source [53]. Among the 18 different regular, semisynthetic, and manufactured anti-toxin compounds, all upheld bacterial development, and 6 out of the 18 anti-infection agents upheld development of bacterial disconnects from the 11 soils analyzed. The particular benefits and environmental wellness characteristics of anti-toxin use as a substrate for development are yet muddled. Anti-infection creation in the plant rhizosphere may likewise in a roundabout way upgrade the dietary status of the delivering life form or plant symbionts. *Azospirillum* is a class of plant-development advancing microorganisms regularly recuperated from the rhizosphere and as endophytes, particularly from grasses [54]. *Azospirillum* upgrades plant development through various implies, including cooperative nitrogen obsession [55]. 2,4-DAPG-delivering *P. fluorescens* F113, in any case, not its 2,4-DAPG-negative freak, was found to upgrade the development

advancing impact of *Azospirillum brasilense* as characterized by root volume and number of roots per plant [56].

Conclusion

There are numbers of bacteria having potential to produce antibiotic example of which is bacillus species which produce antibiotic like bacitracin, pumulin and gramicidin which are active against Gram positive bacteria such as Staphylococci, Streptococci, Corynebacter, Streptomyces species which produce antibiotic like tetracycline, cloramphenicol, vancomycin, gentamycin which are active against Gram negative bacteria and lactobacillus species which antibiotic like nisin which is produce by *Lactobacillus lactis*. "Our anthropogenic vision of antibiotics in the clinical environment may not be transposable to the natural environment," stated on the basis of the limited examples of the weapons shield function of antibiotics in natural environments. The idea that antibiotics might be just a shield or weapon in the environment was further stoked by the apparent widespread occurrence of antibiotic resistance among soil microbes and their capacity to combat it. The discoveries that anti-infection agents apply various consequences for microorganisms at subinhibitory focuses prompted a restoration in interest in the peculiarity called hormesis, i.e., the capacity of metabolites to actuate differential reactions subject to their focuses even alluded to anti-microbials and other optional metabolites as microbial pheromones, as they can evoke a explicit reaction from different individuals from the same species. As a result, a number of reviews and commentaries have suggested that antibiotics work in a concentration-dependent manner, acting as inhibitors at high concentrations and mediators of intracellular signal at low concentrations. In this section, we provide an overview of the potential roles that antibiotics might play for bacteria in environments that are associated with plants and soil.

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Conflict of Interest

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