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# Novel approaches to developing new antibiotics

## Abstract

Antibiotics are an essential part of modern medicine. The emergence of antibiotic-resistant mutants among bacteria is seemingly inevitable, and results, within a few decades, in decreased efficacy and withdrawal of the antibiotic from widespread usage. The traditional answer to this problem has been to introduce new antibiotics that kill the resistant mutants. For the treatment of infectious diseases some antibiotics like penicillin, erythromycin, and methicillin are used but now these antibiotics become less effective because bacteria have become more resistant to such antibiotics. Natural products are metabolites from micro-organisms, plants and animals. These natural products have served as sources of lead molecules, which yielded many synthetic drugs. Actinomycetes have ability to produce a variety of bioactive substances, which have found application in combating a variety of human infections. Teixobactin was discovered using a new method of culturing bacteria in soil from "a grassy field in Maine." It is active against gram-positive bacteria this review article focuses on different sources of new antibiotics.

**Keywords:** antibiotics, actinomycetes, endophytic bacteria, teixobactin, bacteriophages

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## Introduction

World human population is increasing with an alarming rate, and a variety of new types of health issues are raising up.[1] Antibiotics are an essential part of modern medicine. The emergence of antibiotic-resistant mutants among bacteria is increasing within a few decades and results in decreased efficacy and withdrawal of the antibiotic from widespread usage.[2] The increase in number of drug-resistant bacteria is a cause of concern. To tackle the growing problem of antibiotic resistance, the research on new antibiotics and other microbial natural products is important.[1] For the treatment of infectious diseases some antibiotics like penicillin, erythromycin, and methicillin are used but now these antibiotics become less effective because bacteria have become more resistant to such antibiotics.[3] Actinomycetes are prokaryotes of Gram-positive bacteria provide many important bioactive substances which have found application in combating a variety of human infections.[4] More than 70% of naturally occurring antibiotics have been isolated from different genus of actinomycetes.[5] Endophytes are micro-organisms that are found in many important medicinal plants, weeds, and ornamental and fruit trees from wild and domesticated settings[6] and natural products obtained from endophytic microbes are found to be antimicrobial, antiviral, anticancer, antioxidants, anti diabetic and immunosuppressant.[7]

## Different sources of new antibiotics

### Endophytic bacteria

Endophytes are micro-organisms that are found in many important medicinal plants, weeds, and ornamental and fruit trees from wild and domesticated settings.[6] Both endophytic bacteria and endophytic fungi can co-exist in a single host plant. The natural products obtained from endophytic microbes are found to be antimicrobial, antiviral, anticancer, antioxidants, anti diabetic and immunosuppressant.[7] Natural products are metabolites from micro-organisms, plants and animals. These natural products have served as sources of lead molecules, which yielded many synthetic drugs. An outstanding example of a natural product is the world's first billion-dollar anticancer-drug, paclitaxel (Taxol) is from Yew tree, Taxus wallachiana.[8] Some examples of the novel antibiotics produced by endophytic bacteria are Ecomycins, Pseudomycins, Munumbicins, Kakadumycins.

### Bacteria from soils

**Actinomycetes:** Actinomycetes are widely distributed in natural and man-made environments and they are found in large numbers in soils, fresh waters, lake, river bottoms, manures, composts and dust as well as on plant residues and food products.[9] Actinomycetes have ability to produce a variety of bioactive substances which has been utilized in a comprehensive series of researches in numerous institutional and industrial laboratories. Thus there are certain agents isolated from them, which have found application in combating a variety of human infections.[4] More than 70% of naturally occurring antibiotics have been isolated from different genus of actinomycetes.[5] Streptomyces is the largest genus known for the production of many secondary metabolites which have different biological activities, such as antibacterial, antifungal, antiparasitic, antitumor, anticancer and immunosuppressive actions.[10]

**Bacillus species:** Bacillus sps isolated from soil exhibited antibacterial activity against bacteria. The study was conducted by ahmed et al in which soil sample from the Post Graduate Hostel of the Permanent Site campus, University of Ilorin, Nigeria was screened for antibiotic-producing microorganisms by agar sensitivity assay. Seven bacterial species were isolated. The bacterial species were identified by their cellular characteristics, colonial morphology and biochemical tests. The bacterial isolates include; Staphylococcus aureus, Proteus vulgaris, Bacillus spp., Pseudomonas aeruginosa, Micrococcus luteus, Escherichia coli and Micrococcus varians. Of all the screened isolates Bacillus spp. was the only bacterial isolate that demonstrated antibiotic producing ability against the tested organisms, showing zones of inhibition around the colonies of two other tested bacteria. Bacillus sps shows antibacterial activity against Escherichia coli and Staphylococcus aureus.[11]

**Teixobactin:** Teixobactin was discovered using a new method of culturing bacteria in soil from "a grassy field in Maine." It is active against gram-positive bacteria.[12] Teixobactin is an inhibitor of cell wall synthesis that acts primarily by binding to lipid II, a fatty molecule which is a precursor to peptidoglycan. Lipid II is also targeted by the antibiotic vancomycin. Binding of teixobactin to lipid precursors inhibits production of the peptidoglycan layer, leading to lysis of vulnerable bacteria.[13] Teixobactin was reported to be potent in vitro against all gram-positive bacteria tested, including Staphylococcus aureus and difficult-to-treat enterococci, with Clostridium difficile and Bacillus anthracis being exceptionally vulnerable. It also killed Mycobacterium tuberculosis.[13]

**Bacteriophages:** Bacteriophages and their fragments are also used to kill the bacteria. By an estimate in every 2days, half of the world's bacterial population is destroyed by bacteriophages.[14] Now in the former Soviet Union bacteriophages are used to treat patients with infectious diseases.[15] In 2006, the FDA approved the use of bacteriophages in the treatment of Listeria monocytogenes contamination of meat and poultry.[16]The development of phage gene products is another potential route for new anti bacterials. Phage lysins, which are cell wall hydrolases and are produced late in the viral infection cycle, bind to peptidoglycan and disrupt the cell wall of Gram-positive bacteria that results in hypotonic lysis.[16] lysins may be active against non-multiplying bacteria and biofilms and this could help in the treatment of catheter-associated infections.[17]

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## Conflict of interest

The author declares no conflict of interest.

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