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A REVIEW OF THE APPLICATION OF ACTINOMYCETES IN THE CONTROL OF *SALMONELLA* SPECIES

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ABSTRACT

This review is purposed to highlight the potential of finding novel antibiotics by screening various metabolites of actinomycetes among science educators. Very much of concern is inadequate actinomycetes to handle spread of salmonella species in view of emerging growth of pathogenic microorganisms. A significant global issue is drug-resistant bacteria and fungi that cause infectious illnesses. The emergence of multi-drug resistant Salmonella species has caused immense public health concern due to the resulting negative impacts. Salmonella causes food borne illnesses, which result in significant monetary loss and a high death rate. The majority of Salmonella species are zoonotic infections, meaning they can spread from animals to people when they consume tainted meat, animal products, or other food items that have been contaminated with excrement from other animals. The overuse of antibiotics in treating Salmonella infections have increased the urgency to search for new potential sources of effective antibiotics. Actinomycetes are a group of bacteria species found in soil that create vital biological products, primarily powerful antibiotics. actinomycetes make up about two-thirds of all antibiotics, with Streptomyces species producing the majority of them. Several studies have shown that there is abundant of potent antibiotics produced by actinomycetes. These bioactive compounds have been extensively demonstrated to cause bactericidal and bacteriostatic activities. Thus, more intensity should be put into unraveling more potential antibiotics from actinomycetes to help reduce the burden of drug resistance.

INTRODUCTION

The earth's soil is home to a wide variety of microbial organisms. Actinomycetes are a group of bacteria species found in soil that create vital biological products, primarily powerful antibiotics. Actinomycetes are actually the primary source from which the majority of antibiotics are created (Ceylan*et al.,* 2008). Antibiotics are typically low-molecular-weight compounds that are able to prevent or limit the growth of harmful bacteria. They are frequently actinomycetes' secondary metabolites and don't appear to be specifically involved in the development of the cell source (Bentley *et al.,*2002). During the late log phase of growth and up to their stationary phase, actinomycetes naturally create antibiotics. One of their main advantages for the source organism is reportedly their capacity to suppress the growth of other microorganisms thriving in the same habitat in nature, giving the source an advantage over those organisms in a given setting. Actinomycetes, a creature that produces antibiotics, can then coexist with other species and endure for a very long time in the natural world (Barris-Gonzalez *et al.,*2003). A class of organisms known as actinomycetes was once thought to be an intermediary between fungi and bacteria. Actinomycetes have a cell wall structure that is similar to that of gram-positive bacteria. Additionally, they are branching unicellular microbes. They create mycelium, which can grow on the substrate where the microorganism is developing or aerial (Singh *et al.,*2006). In some species, the mycelia can split into rod- or coccoid-shaped forms. Many genera also produce spores, which can be detected as sporangia or spore cases on aerial hyphae, on the surface of the colony, or floating freely in the environment. They have DNA that has a high Guanine + Cytosine content (>55%). Streptomyces are the most prevalent microbe in these categories.The others are referred to as rare actinomycetes, or non-actinomycetes. Most actinomycetes are free-living organisms (Ceylan*et al.,* 2008).

Due to their intricate metabolic processes, actinomycetes are known to create a variety of metabolites. Beta-lactam antibiotics like penicillin and cephalosporins as well as various forms of shikimic acid, such chloramphenicol, are among the over 23,000 known secondary metabolites produced by microorganisms (Barrios-Gonzalez *et al.,* 2003). Actinomycetes are known to create 42% of these compounds, followed by fungi and other bacteria with 16% each. Streptomyces, Saccharopolyspora, Amycolatopsis, Micromonospora, and Actinoplanes are the principal producers of commercially significant biomolecules among numerous species. The environment receives these metabolites. Their pharmacological effects are wide-ranging and include immunosuppressive, antiparasitic, insecticidal, anticancer, antiviral, enzme inhibitory, and antooxidant properties etc.(Scallan*et al.,*2015). The primary impact of those who produce antifungal and antibacterial metabolites on their immediate environment is to prevent other microbes from proliferating or developing. The biological antagonistic types relate to these classes of actinomycetes. Since these are utilized and their metabolites are used to make antibiotics, they are of particular importance (Singh *et al.,* 2006). Microbial metabolites provide bacterial and fungi infections with habitats that can save their lives. This is so that some of the most potent antibiotics, such penicillin, erythromycin, streptomycin, tetracyclines, vancomycin, and amphotericin, may be produced. These microbial natural compounds stand out for their frequent presentation of beneficial pharmacokinetic features necessary for clinical development in addition to their powerful therapeutic activity (Levy and Marshall, 2004). As they present a novel remedy for the threat, actinomycetes' production of bioactive substances is essential in the fight against newly emerging drug-resistant pathogenic bacteria (Pui*et al.,*2011).

A significant global issue is drug-resistant bacteria and fungi that cause infectious illnesses (Jiasin*et al.,*2006). To tackle them, new antimicrobial agents must be developed. Actinomycetes are a significant source of bioactive compounds with significant medical and commercial value, especially in the field of biotechnology (Mitchell *et al.,* 2004). According to Takizawa *et al.,* (2000), actinomycetes make up about two-thirds of all antibiotics, with Streptomyces species producing the majority of them. This bacterial group is intriguing since it has a complicated life cycle and a variety of species that produce antibiotics (Chater, 2001; Bentley *et al.,* 2002).
Streptomyces species produce a large number of commercially available antibiotics, including the antibacterial drugs chloramphenicol, clindamycin, erythromycin, imipenem, streptomycin, and tetracycline, as well as the antifungal drugs amphotericin B and nystatin (Shibhghatula*et al.,*2015). When treating salmonella infections, the usage of antibiotics made for commercial purposes has proven to be lifesaving (Singh *et al.,*2006).

Among the most common harmful bacteria that infect both humans and animals are the Salmonella species. Worldwide, Salmonella spp. is responsible for human infections and financial losses (Andino and Hanning, 2015). Salmonella spp. can flourish in a variety of meals, including poultry, pork, vegetables, and other foods. Salmonella spp. are commonly found in chicken products, which are also a significant source of this infection in both humans and animals (Jiansen*et al.,* 2016; Pui*et al.,* 2011). Salmonella causes foodborne illnesses, which result in significant monetary loss and a high death rate. The majority of Salmonella outbreaks in the past ten years were linked to reservoirs in poultry (Andino*et al.,* 2015). Finding new, powerful alternatives for the prevention and treatment of Salmonella infections is therefore crucial.This review is aimed at assessing the potential of actinomycetes as a source of antibiotics for the control of *Salmonella* species.

Salmonella spp

Salmonella are gram-negative, motile, non-spore forming, rod-shaped facultative anaerobic bacteria that belong to the Enterobacteriaceae family (Scallan*et al.,* 2015). Salmonella species enterica and bongori are further classified into six subspecies based on taxonomy created by Le Minor and Popoff in 1987 (McNamee and Smyth, 2000; (Scallan*et al.,* 2015). Because it was formerly believed that

each each serotype had its own species, the genus Salmonella was previously divided into a number of other species (Chiraporn*et al.,* 2014). With the development of more sophisticated genetic methods like DNA sequencing and hybridization, it was shown that many of the serotypes shared a significant degree of genetic similarity (Allesia*et al.,* 2015).

Sources of *Salmonella*

The majority of Salmonella species are zoonotic infections, meaning they can spread from animals to people when they consume tainted meat, animal products, or other food items that have been contaminated with excrement from other animals (Douglas *et al.,* 2015). Contamination of food and water initiates pathogenesis (Piu*et al.,* 2011). Salmonella spreads by direct or indirect contact with animals that have the infection, as well as intake of tainted water or food. Animals such as mammals, birds, reptiles, amphibians, fish, shellfish, and even insects could harbor salmonella in their intestines (Douglas *et al*., 2015; George *et al.,* 2012). Salmonella does not typically come from natural water. Therefore, if they are discovered in water, it means that the water has been contaminated by feces (George *et al.,*2012).

The primary cause of food and water contamination, which significantly contributes to Salmonella's spread across the environment and into the food supply, is fecal contamination (Douglas et al., 2015). Salmonellae are stored in meat animals (Douglas *et al.,* 2015). Salmonella is transmitted to chickens both vertically (through their parents) and horizontally (via feed, insects, rodents, people, transportation, and environmental facilities). However, horizontal transmission is a significant issue for Salmonella infection in hens (Andino*et al.,* 2015).

Pathogenesis of *Salmonella* in human

Salmonellosis can cause four different types of illness in humans, including enteric fever, gastroenteritis, bacteremia, and various nontyphoidal salmonellosis-related consequences, in addition to the chronic carrier condition (Adamu*et al.,* 2015; Pui*et al.,* 2011).

Enteric fever

Typhoid fever is brought on by Salmonella Typhi, whereas paratyphoid fever is brought on by Salmonella paratyphi A, B, and C. (Adamu*et al.,* 2015; Pui*et al.,* 2011). Salmonella enterica serovars Paratyphi and Typhi are the particular pathogens that cause enteric fevers in humans (Andino*et al.,* 2015).

Gastroenteritis

At least 150 Salmonella serotypes, including S. Typhimurium and S. Enteritidis, are responsible for nontyphoidal salmonellosis or enterocolitis. Instead of human waste, infection always happens when someone consumes contaminated food or water (Adamu*et al.,* 2015; Pui*et al.,* 2011). Farm animals are the reservoirs for nontyphoidal salmonellae, and they are not human-restricted (Andino*et al.,* 2015).

Bacteremia and other complications of nontyphoidal salmonellosis

Bacteremia develops in about 8% of untreated salmonellosis cases. Bacteria entering the circulation after crossing the intestinal barrier causes the dangerous illness known as bacteremia. In cases with fever of unknown etiology, Salmonella-caused bacteremia should be considered (Adamu*et al.,* 2015; Pui*et al.,* 2011).

Chronic carrier state

Salmonellosis can spread through chronic carriers, who may infect a large number of people, especially those who work in the food industry. Depending on the serotype, nontyphoidal serotypes typically survive in the digestive system for 6 weeks to 3 months (Pui*et al.,* 2011).

Drug resistance of *Salmonella*

Early in the 1960s, it was discovered that Salmonella was resistant to just one antibiotic. Salmonella enterica's multi-drug resistance (MDR) is defined as a resistance to the conventional first-line antibiotics chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole (Pui*et al.,* 2011). Antibiotic resistance manifested by a species of bacteria to at least three different antibiotic classes is known as multi-drug resistance (MDR) (Das *et al.,*2008). The majority of multidrug resistant Salmonella infections are contracted by ingestion of tainted items derived from animals, such as swine and chicken eggs. This raises serious concerns about multidrug resistance (Pui*et al.,* 2011). Over 47 million new cases of domestically acquired foodborne disease occur each year in the United States, and at least 70% of the pathogenic organisms implicated are resistant to a minimum of one antimicrobial medication, according to the Centers for Disease Control (CDC) (Allesia*et al.,*2015). Every year, chronic disorders claim the lives of about 3,000 patients in the US. The CDC website states that drug-resistant infections result in a lengthier stay in the hospital and more expensive treatments, some of which may even be harmful to the patient. The issue seems to be getting worse rather than better as more germs developed multidrug resistance (Douglas *et al.,* 2015). Chicken is the primary source for non-typhoidal Salmonella and is associated with antibiotic resistance. Salmonella spreads via the food chain, such as poultry production, and has multiple medication resistance profiles (Chaudhary*et al.,* 2016).

Actinomycetes

The gram-positive, aerobic Actinomycetes are members of the Actinomycetales order and exhibit both substrate and aerial mycelium growth during their entire life cycle. Out of the 18 primary lineages that have so far been identified as existing inside the bacterial domain, it constitutes one of the major taxonomic groups (Chatter*et al.,* 2001). The word "Actinomycetes" originally came from the Greek words "attacks," which means "a ray," and "mykes," which means "fungus." As a result, it shares traits with both bacteria and fungi (Das *et al.,* 2008). Actinomycetes are potential manufacturers of medicinal chemicals, antibiotics, and bioactive substances found in secondary metabolites. These consist of enzymes, immunosuppressive substances, anticancer substances, and antibiotics. Actinomycetes exhibit a variety of life cycles that are unique to prokaryotes and become important players in the cycling of organic materials in soil environments (Challis and Hopwood, 2003). The production of numerous bioactive secondary metabolites by actinomycetes has been demonstrated, and on this premise, the identification of novel antibiotic and non-antibiotic guide molecules using microbial secondary metabolite screening is becoming increasingly significant (Chaudhary *et al.,* 2013). Actinomycetes (Actinobacteria) are also crucial for agriculture, human medicine, and food production. Their ability to collaborate with other creatures is the main driver behind this activity.

Ecology and Habitat of Actinomycetes

The most prevalent microorganisms, actinomycetes, have a hyphae-like appearance under cultivation and are the cause of the characteristically "earthy" odor of recently dug well dirt. In nature, actinomycetes emerge as thread-like filament structures (Babalola *et al.,*2009). The actinomycetes are a widespread collection of microorganisms that are widely disseminated in typical ecosystems roughly all over the world. They have a diversity of environmental habitation patterns (George *et al.,* 2012). They mostly live on the soil (soli), but they have also been widely dispersed in a variety of aquatic biological units, including sediments from marine settings (Berdy, 2005).

Additionally, it has been confirmed that they may survive under harsh environmental circumstances, particularly in cryophilic locations (Raja et al., 2010). Actinomycetes are the most numerous occupants in soil sources according to a proportionate survey, and they produce a surface layer that gradually disappears as depth increases. In all soil levels, actinomycete strain characteristics can be identified (Baltz, 2008).

The most common class of microorganisms in nature are called actinomycetes (Elghary*et al.,*2015). When rain follows a spellbindingly dry spell of weather, a potent odor fills the air, thanks to the soil actinomycetes' synthesis of geosmin. Streptomyces species have widespread populations and typically make up the majority of the actinomycete occupants in their ecological settings (Bentley *et al.,*2002). Other actinomycete genera including Actinoplanes, Catenuloplanes, Amycolatopsis, MicromonosporaKineospora, Dactylosporangium, Microbispora, and Nonomuraea are referred to as "rare actinomycetes" since they can be difficult to isolate and culture because of their slow growth (Jiansen*et al.,* 2016).

Actinomycetes are frequently heterotrophic in their surroundings as well. While some of them come via parasitic or mutualistic relationships with other plants and animals, the majority of these are strict saprophytes. Actinomycetes, some of which are anaerobic like actinomycetes, are usually thought to play a part in the recycling of nutrients (Berdy, 2005). Many actinomycetes are growing on the common bacteriological media used in the laboratory, such as nutrition agar, blood agar, trypticase agar, starch casein agar, and brain heart infusion agar. However, other species, such as Frankia, require extremely specific growth media and incubation conditions. For the enhancement of spore characteristics and pigment formation in sporoactinomycetes, however, particularly special media are required (Levy and Marsha, 2004)

Antibiotic Production by Actinomycetes in Soil

Although antibiotics have never been found in natural soil, research have been done to look at the development of secondary metabolites in unamended and modified sterile soil microcosms that have been inoculated with the microbes that produce them. One of the clearest examples demonstrated how Streptomyces venezuelae created chloramphenicol when the bacterium grew in sterilized soil (Das *et al.,* 2008). The amount of nutrients incorporated into sterile soil microcosms and the amount of antibiotic synthesis by a bacterial inoculant were shown to be directly correlated (Berdy, 2005).

CONCLUSION

With the ever-increasing number of antimicrobial resistant microorganisms, the application of actinomycetes in controlling the growth of pathogens is key to winning the arms race against super bugs. *Salmonella* species are well known for contaminating food sources especially in developing countries where safety practices and regulations are not strictly adhered. Frequent and indiscriminate use of antibiotics too treats Salmonella infections have resulted to their resistance to commonly used antibiotics. Actinomycetes offer us hope and high potential of solving this pressing world health challenge, and science educators' should actively inform
the public about salmonella hazards to human to decrease its cases.

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