JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

APPLICATION OF ACTINOMYCETES IN SECONDARY METABOLITES PRODUCTION: AN OVERVIEW

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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 work 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) is also responsible for the research of novel antibiotics and novel microbes. Exhibiting various bioactivities, they provide valuable approved drugs in clinical use. Actinobacteria, which share the characteristics of both bacteria and fungi, are widely distributed in both terrestrial and aquatic ecosystems, mainly in soil. They are considered as the biotechnologically valuable bacteria that are exploited for its secondary metabolite production. Approximately, 10,000 bioactive metabolites are produced by Actinobacteria, which is 45% of all bioactive microbial metabolites discovered. Especially *Streptomyces* species produce industrially important microorganisms as they are a rich source of several useful bioactive natural products like biosurfactant, enzyme, bioherbicides, vitamins, pigments, bioremediation, phytohormone production, odor and flavor compounds production etc. with potential applications. Though it has various applications, some Actinobacteria have its own negative effect against plants, animals, and humans. In this survey, a large number of the actinomycetes inhabit natural substrates which have the capacity to inhibit the growth of bacteria and other microorganisms. The ability of these actinomycetes to exert an inhibiting effect upon microorganisms is highly specific. Antagonistic actinornycetes produce a variety of antibiotics that vary in chemical nature, in antimicrobial action, in toxicity to animals, and in their chemotherapeutic potentialities. The antibiotics that have, so far, been isolated from actinomycetes vary in the degree of purification include: actinomycctin, actinomyces lysozyme, actinomycin, micromonosporin, streptothricin, streptomycin, and mycetin. Some actinomycetes produce more than one antibiotic substance. Some antibiotics are produced by several different organisms.

Keywords: Secondary metabolites; Multidrug resistant bacteria (MDR); Actinobacteria; natural products; antibiotics.

INTRODUCTION

Actinomycetes are high GC, gram-positive microorganism with plant life morphology. they're made supply of secondary metabolites with numerous biological activity. The gram-positive microorganism with high guanine+cytosine in their DNA [3] is 2 major phylogenetic divisions, "low-GC" and "high-GC". GC content is an abbreviation for the proportion of GC base pairs in an organism's DNA. People who have a low GC content, have additional AT base pairs in their DNA. GC content may be crude measure of the connection of microorganisms, however continues to be helpful for differentiating massive phylogenetic divisions. They exhibit a large vary of life cycles, that are distinctive amongst the prokaryotes. Gram-positive bacteria that are placed among the phylum Actinobacteria, class Actinobacteria, subclass Actinobacteridae, order Actinomycetales that presently consists of 10 suborders, quite 30 families and over 160 genera. Being an outsized cluster of microbial resources of wide sensible use and high industrial worth, actinomycetes contribute to around 70% of the supply of antibiotics and conjointly manufacture various non-antibiotic bioactive metabolites, like enzymes, enzyme inhibitors, immunological regulators, anti-oxidation reagents, and so on. Actinomycetes are cosmopolitan in natural habitats, particularly soil and ocean. [1] The marine environment harbors countless species of microorganisms that play necessary role in mineralization of complex organic matter, degradation of dead plankton, plants, animals, degradation of pollutants and toxicants and primary and secondary productivity. Marine microorganisms have a diverse range of enzyme activity and capable of catalyzing various biochemical reaction with novel enzymes like amylase, lipase, deoxyribonuclease and protease. Among the marine microorganisms actinomycetes includes a very important cluster. The foremost cluster studied very well was the marine Streptomyces [2]. They're filamentous bacteria that manufacture 2 kinds of branching mycelium, particularly aerial and substrate mycelium. Factors influencing the number and kinds of actinomycetes present in explicit soil are a geographical location, like soil type, temperature, organic matter content, moisture content, cultivation and aeration. Actinomycetes act as a serious part of the microbial population in most of the soil. About 90% of the whole actinomycetes population consists of Streptomyces species [4]. Virtually 80% of the world's antibiotics are known to come back from actinomycetes, largely from the genera Streptomyces and Micromonospora [5]. The most multiple drug-resistant bacteria inflicting necessary community-acquired infections embody methicillin/oxacillin-resistant staphylococcus aureus (MRSA), vancomycin-resistant staphylococcus aureus (VRSA), vancomycin-resistant Enterococcus (VRE), extended-spectrum beta-lactamase (ESBL) manufacturing bacteria like E. coli and Klebsiella spp and penicillinresistant Streptococcus pneumoniae (PRSP). Marine actinomycetes are established as an upscale supply of many secondary metabolites like novel bioactive molecules like antibiotics, antifungal, and anticancer compounds, plant growth hormones, industrially necessary enzymes, enzyme inhibitors, and pigments [6, 7]. α-Amylases (1, 4-α-D-glucan glucanohydrolases, E.C. 3.2.1.1) are one of the most necessary industrial enzymes. Alkaline α-Amylases have high catalytic efficiency and stability at the alkaline pH starting from 9.0 to 11.0 [8] and hydrolyze starch under high pH conditions within the starch and textile industries and conjointly as ingredients in detergents for automatic dishwashers and laundries [9, 10]. Most amylases according from Streptomyces sp. are active in the pH ranges of 5.0–7.5, with limitations for industrial applications [11–15].

CHARACTERISTICS AND NUTRITION OF ACTINOMYCETES

Actinomycetes are heterotropic in nature. Most of them are strict saprophytes, whereas some from parasitic or mutualistic associations with plants and animals. Actinomycetes are normally believed to own a job within the recycling of nutrients. They're aerobic and a few like actinomycetes are anaerobic [16]. Several actinomycetes are growing on the common bacteriological media employed in the laboratory like nutrient agar, trypticase agar, blood agar, brain heart infusion agar and starch casein agar. Sporoactinomycetes need special media to permit differentiation and also the development of characteristic spores and pigments. Some of these media don't seem to be on the market commercially and should be ready within the laboratory using colloidal chitin, soil extract and decoctions of plant materials [17]. Actinobacteria includes a bunch of branching unicellular microorganisms, most of that are aerobic-forming mycelium called substrate and aerial. They reproduce by binary fission or by manufacturing spores or conidia, and sporulation of Actinobacteria is through fragmentation and segmentation or conidia formation.

Aerial mycelium

The aerial mycelium is usually thicker than the substrate mycelium. This is often selected joined of the foremost necessary criteria for the classification of the genus Streptomyces into species, comprising structure (cottony, velvety, or powdery), formation of rings or concentric zones, and pigmentation.

Substrate mycelium

The substrate mycelium of Actinobacteria varies in size, shape, and thickness. Its color ranges from white or just about colorless to yellow, brown, red, pink, orange, green, or black. **Morphological appearance**

Morphology has been a very important characteristic to spot Actinobacteria isolates that was employed in the primary descriptions of actinomycete species. This is often created various standard culture media, together with International Streptomyces Project (ISP). For nonstreptomycetes or rare Actinobacteria, strains maintained on ATCC Medium No.172 (NZ-amine glucose starch agar) (American Type Culture Collection, 1982) were used. Varied morphological observations, together with germination of spores, elongation and branching of vegetative mycelium, formation of aerial mycelium, color of aerial and substrate mycelium, and pigment production, are accustomed determine Actinobacteria [18]. Light microscopy was accustomed study the formation of aerial mycelium and substrate mycelium, and scanning electron microscopy was accustomed study the spores, the spore surface, and spore structure.

OCCURRENCE & HABITATS OF ACTINOMYCETES

Terrestrial environment

Soil remains the foremost vital surround for Actinobacteria with streptomycetes existing as a significant part of its population. Streptomyces was encountered to be the foremost abundant genus isolated in every of the study. In anoxic mangrove rhizosphere, Actinobacterial species like Streptomyces, Micromonospora, and Nocardioform were found to be abundant in soil [19]. Similarly, Nocardia isolated from flowering tree soil made new cytotoxic metabolites that powerfully inhibited human cell lines, like gastric adenocarcinoma [20]. In dessert soil particularly Microcoleus used as a source of food. There are many reports showing the distribution of Actinobacteria in numerous locations, like sandy soil (Cario, Egypt; Falmouth, MA), black alkaline soil (Karnataka, India), sandy loam soil (Keffi Metropolis, Nigeria; Presque island, PA), alkaline dessert soil (Wadi El Natrun, Egypt; gully Araba, Egypt), and subtropical dessert soil (Thar, Rajasthan), wherever Streptomyces sp. were dominant followed by the other organisms, like Nocardia, Nocardiopsis, and Actinomycetes [21]. Priyadharsini et al [22] in her study isolated 45 morphologically distinct colonies from 12 completely different paddy field soils and ascertained their ability to inhibit the expansion of Cyperus rotundus. The isolates include Streptomyces sp., Streptoverticillium sp., Actinomadura sp., Kitasatosporia sp., Nocardiopsis sp., Pseudonocardia sp., and Kibdelosporangium sp. Most actinomycetes isolates behave as neutrophiles in culture, with a growth vary from pH 5.0 to 9.0 and an optimum pH around 7.0. The pH may be a major environmental factor determinant the distribution and activity of soil actinomycetes. Neutrophiles occur in less range in acidic soils below pH 5.0, whereas acidophilic and acidoduric streptomycetes are unit various in acidic soils. However, there are few reports of to 9.5 was isolated from soil close to a salt lake. Most actinomycetes behave as mesophiles in the laboratory, with optimum growth temperature at 25^{o}C to 30^{o}C [16].

Compost and connected materials:

Several mesophilic actinomycetes are active in compost within the initial stages of decomposition. However, the capability for self-heating throughout decomposition provides ideal conditions for obligate or facultative thermophilic actinomycetes. Some genera like Thermo-actinomycetes and Saccharomonospora are strictly thermophilic. Thermophilic actinomycetes grow well on animal manure. They have been active in fermentation of pig faeces, straw and deodorization of pig faeces. Thermomonospora species notably grow throughout the second indoor phase of preparation of manure for mushroom cultivation, whereas streptomycetes diastaticus and Thermo actinomycetes vulgaris predominate within the spent, steamed compost and its dirt. Thermomonospora curvata was shown to be active in decomposition of municipal waste compost and to supply thermostable C1 and Cx cellulose. Actinoplanes and connected organisms are common in soils, rivers and lakes and may grow on plant litter in rivers. The Micromonospora were thought of to be native to fresh water ecosystem and they had a task within the turnover of cellulose, chitin and lignin [17].

Aquatic environment

Actinobacteria arecosmopolitan in aquatic habitats, which can generally be washed in from close terrestrial habitats, like Thermoactinomyces and Rhodococcus coprophilus that are identified to be good indicators of the terrestrial part of Actinobacterial propagules in water and sediments.

Freshwater

Cross [23] in his study proven that Actinobacteria will readily be isolated from fresh water sites. Some of the kinds of Actinobacteria habitation in freshwater include Actinoplanes, Micromonospora, Rhodococcus, streptomycetes, and also the endospore-forming Thermoactinomyces. Actinoplanes are normally found in soils, rivers, and lakes, and also the spore vesicles of those organisms have the power to resist prolonged desiccation, however they unleash their motile spores for dispersal when rehydrated [24]. Micromonospora also are thought of to be a common freshwater Actinobacteria and located to be indigenous to such habitats wherever they turnover cellulose, chitin, and lignin. Various reports confirmed the presence of Micromonospora in streams, rivers, and river sediments.

Marine

Marine Actinobacteria had to adapt from extraordinarily high pressure and anaerobic conditions at temperatures just under 0- 8°C on the deep sea floor to high acidic conditions at temperatures of over 8- 100°C close to hydrothermal vents at the mid-ocean ridges. Rhodococcus marinonascene, the primary marine actinomycete species to be characterized, supports the existence of marine Actinobacteria. Members of the genera Dietzia, Rhodococcus, streptomycetes, Salinispora, Marinophilus, Solwaraspora, Salinibacterium, Aeromicrobium marinum, Williamsia maris, and Verrucosispora are selected as native marine Actinobacteria [25– 29]. Innagi et al [30] isolated numerous marine Actinobacteria, like Dietzia maris, Rhodococcus erythropolis, and Kocuria erythromyxa, from a subseafloor sediment core collected at a depth of 1225 meters off island. Uncommon Actinobacteria, belonging to Micrococceae, Dermatophilaceae, and Gordoniaceae are isolated from sponges. Dhanasekaran et al [31] isolated 17 Actinobacteria from soil samples belonging to the saltpan regions of Cuddalore, Parangipettai, and screened for primary antibacterial activity among that streptomyces spp. and Saccharomonospora sp [32].

TYPES OF ACTINOBACTERIA

Thermophilic Actinobacteria

Number of studies has been applied by the researchers to substantiate the existence of extremophilic and extreme tolerant soil Actinobacteria (acid tolerant and alkali tolerant, psychrotolerant and thermotolerant, and halotolerant and haloalkalitolerant or xerophilic). Mesophilic Actinobacteria will grow at associate in Nursing best temperature from 20^0C to 42^0C, among that thermotolerant species exist, which might survive at 50°C. Moderately thermophilic Actinobacteria have associate in nursing optimum growth at 45°C–55°C [36], whereas strictly thermophilic Actinobacteria grow at 37°C–65°C with the optimum temperature at 55°C–60°C [33].

Incubation temperatures of 28°C, 37°C, and 45°C are thought of best for isolation of soil mesophilic, thermotolerant, and moderately thermophilic Actinobacteria.

Acidophilic Actinobacteria

Acidophilic Actinobacteria, that are common in terrestrial habitats like acidic forest and mine drain soil, grow within the pH vary from regarding three.5 to 6.5, with optimum rates at pH 4.5 to 5.5 [34, 35]. it's been shown that acidophilous Actinobacteria systematically type 2 distinct mixture taxa (namely, the neutrotolerant acidophilous and strictly acidophilous cluster groups) supported numerical phenetic data; members of the 2 groups share common morphological and chemotaxonomic properties [34]. Conjointly some members of the strictly acidophilous cluster type a definite biological group, like the genus Streptacidiphilus, that has been assigned to the revised family Streptomycetaceae, beside the genera Kitasatospora and Streptomyces.

Halophilic Actinobacteria

Halophilic Actinobacteria are categorized into differing types supported their growth in media containing completely different concentrations of salt. Extreme halophiles grow best in media containing 0.5–5.2 M salt, whereas borderline extreme halophiles grow best in media containing 1.5–4.0 M salt, moderate halophiles grow best in media containing 0.5–2.5 M salt, and finally halotolerants that don't show an absolute demand to salt for growth however grow originate to usually terribly high salt concentrations and tolerate 100 g/l salt (equivalent to 1.7 M NaCl) a minimum of. Seawater, saline soils, salt lakes, brines, and alkaline saline habitats are thought of because the best habitats for isolating halophilic Actinobacteria. Generally, most of the halophilic Actinobacteria are isolated from saline soils. Halophilic Actinobacteria isolated from marine environments are assigned to a few of genera, together with Micromonospora, Rhodococcus, and Streptomyces [37].

Endophytic Actinobacteria

Endophytic Actinobacteria are defined as those who inhabit the interior part of plants, inflicting apparently no visible changes to their hosts. These Actinobacteria play specific roles, for instance, protective the host plants against insects and diseases. Endophytic Actinobacteria represent a large part of the rhizosphere that are also found within plants in which the extensively studied species are from the genus Frankia, nitrogen-fixing bacterium of nonleguminous plants [38] and a few species of the genus streptomyces that are phytopathogens. Generally, the endophytic Actinobacteria include Streptomyces, however the genera Streptoverticillium, Nocardia, Micromonospora, Kitasatospora, Pseudonocardia, Microbispora, Kibdelosporangium, Actinopolyspora, Nocardioides, Brevibacterium, Actinomadura, Glycomyces Plantactinospora, Polymorphospora, Promicromonospora, and Streptosporangium are found within the plants, like Palicourea longifolia, Calycophyllum acreanum, Monstera spruceana, Croton lechleri, Cantua buxifolia, Siparuna crassifolia, and Eucharis cyaneosperma.

Symbiotic Actinobacteria

About 15% 1945 of the world's nitrogen is fixed naturally by the symbiotic relationships between numerous species of the Frankia belonging to the family of Actinobacteria. The plants that form symbiotic relationships with Frankia are referred to as actinorhizal plants. Researchers have found over 160 plants that have Actinobacteria as their host, together with alders, Russian olive, bayberry, sweet fern, bitterbrush, and cliff rose. The Frankia have the ability to supply most or all of the host plant's nitrogen desires. [39]

Endosymbiontic Actinobacteria

An endosymbiont is any organism that lives inside the body or cells of another organism. Endosymbiosis method is typically obligate, that is, either the endosymbiont or the host cannot survive without the other. Members of the phylum Actinobacteria are known as abundant members of sponge-associated microbial communities. Mycobacterium along with Micrococcus, Micromonospora, Microbacterium, Brevibacterium, Kocuria, Corynebacterium, Rhodococcus, Brachybacterium, Rubrobacter, Streptomyces, Dietzia, Salinispora, Actinokineospora, Gordonia, Arthrobacter, Nocardiopsis, and Rothia species were found to measure as endosymbionts in marine sponges Callyspongia aff. Implexa, Aplysina aerophoba, Spheciospongia vagabunda, Hemimycale culumella, Hyrtios erecta, Dysidea tupha, Callyspongia sp., Dysidea avara, Amphimedon sp., and Negombata magnifica. However, the Actinobacterial endosymbionts have conjointly been reportable in alternative cluster of animals, like mammal genus Hylobates hoolock, Rhinopithecus roxellanae, Rhinopithecus bieti, Panthera tigris altaica, Panthera tigris tigris, Panthera tigris amoyensis, Ailurus fulgens, Cavnlvara zlrsidae, Ursus thibetanus, Cervus elaphus, Elaphurus davidianus, and Vicugna pacos.

Gut Actinobacteria

Tan et al [40] isolated Streptomyces, Nocardiopsis, and Oerskovia from healthy goat feces. The ability of the probiont Streptomyces sp. JD9 from gut of chicken possesses all the characteristics required to satisfy the indigenous Actinobacterial probiont for increased broiler production [41].

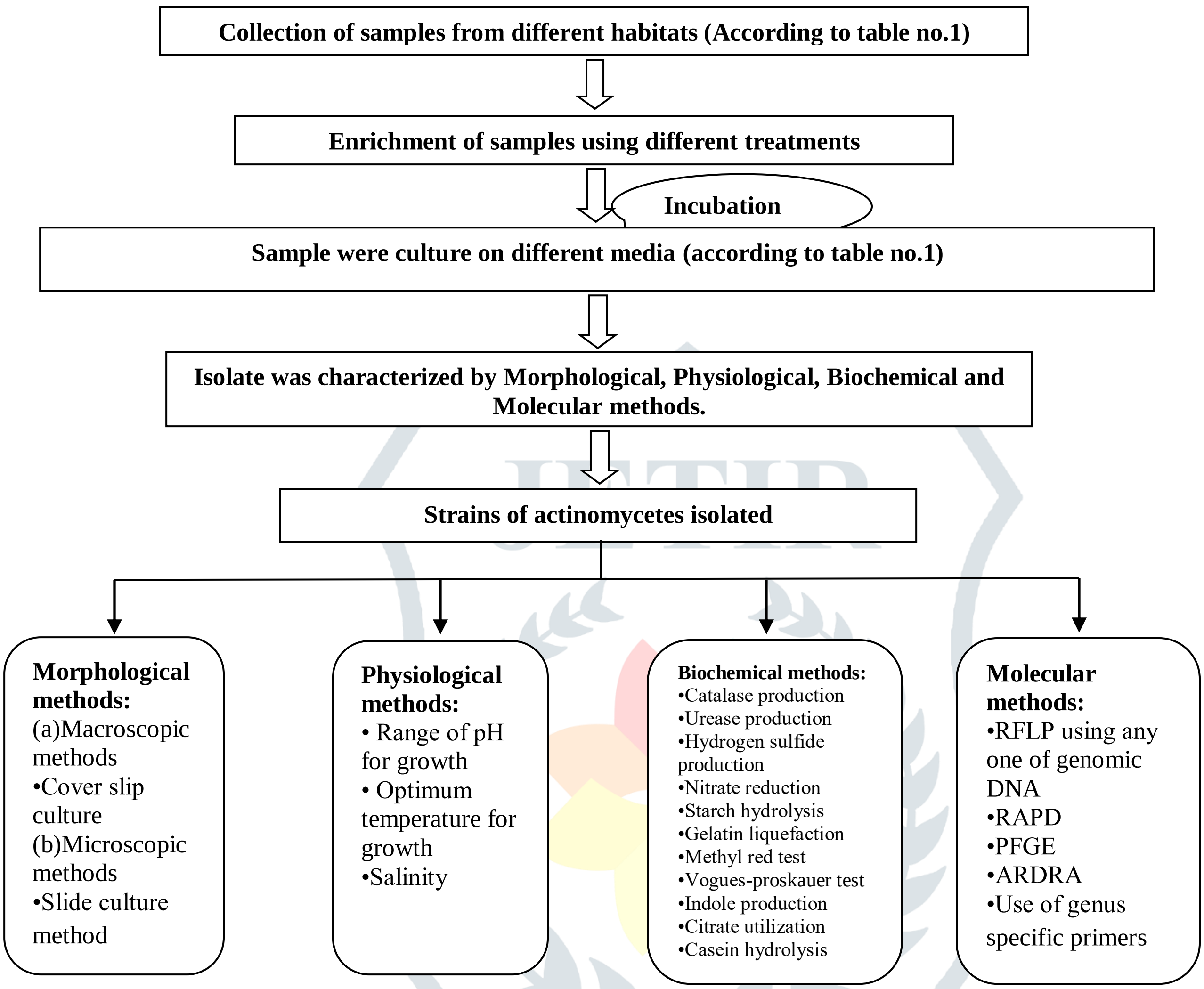
MATERIALS AND METHODS

Sources and Media

Table.1: Different sources and media for isolation of actinomycetes. [42]

SOURCE	MEDIA	REFERENCES
FROM SOIL		
Forest Soil	Starch-casein medium	Kuster & Williams(1964)
Humus Layer of Forest Soil	(a)Humic acid-vitamin agar	Cho et al, 1994
	(b)Starch casein nitrate agar(SCS)	Hayakawa et al, 1987a
	(c)Hair hydrolysate vitamin agar(HHVA)	Hayakawa et al, 1987b
	(d)Bennet‟s agar(BA)	Seong C.N., 1992
Corn Field, Cow Barn yard, Forest	(a)Arginine-glycerol salt(AGS) medium	Porter et al, 1960
	(b)Chitin medium	Lingappa & Lockwood, 1961
	(c)Modified Benedict‟s medium	Porter,Wilhelm & Tresner, 1960
	(d)Soybean meal-glucose medium	Tsao,Leben & Keitt, 1960
	(e)Gauze‟s agar medium	Rehacek, 1959
	(f)Czapek‟s agar medium	Waksman, 1961
	(g)Egg albumen medium	Waksman, 1961
	(h)Glucose-asparagine medium	Waksman, 1961
	(i)Glycerol-asparaginate agar 2	Waksman, 1961
Lake Soil	Chitin agar	S.C. HSU & J.L. Lockwood, 1975
Soil	Coal-vitamin agar	Wakisaka et al, 1982
Antartic Soil	Mineral salt(MS) medium	Kosmachev (1954)
Mitidja plain (Algeria)	Yeast extract-malt extract agar	Shirling & Gottlieb, 1966
Marine Soil	Starch casein nitrate(SCN) agar medium	Ravel J, Amorso (1998)
FROM WATER		
Stream Sediments & Lake muds	(a)Chitin agar media	Lingappa & Lockwood (1961,1962)
	(b)M3 agar medium	Jones, 1949
	(c)Benett‟s medium	Jones, 1949
Marine Sediments	(a)Starch-casein agar	A.Grein & S.P. Meyers, 1958
	(b)Asparagine agar	A.Grein & S.P. Meyers, 1958
	(c)Glycerol-glycine agar	Lindenbein, 1952
Marine Sediments(South China)	(a)AIM medium	J.L. You et al
FROM OTHER SOURCES		
FROM ROOT & STEM SAMPLES OF FOUR PLANTS		
Cinnamomum zeylanicum Zingiber spectabile Elettariopsis curtisii Labisia pumila	Starch yeast casein agar(SYCA) Actinomycetes Isolation agar (AIA) Humic Acid vitamin gellan gum (HVG) Tap water yeast extract agar (TWYE) Coal –vitamin agar (CVA)	Zin et al, 2007
Mangroove Sediments	Asparagine-glucose agar medium	Shirling & Gottlieb, 1966

Procedure: Various steps for the Isolation and characterization of actinomycetes were performed which are mentioned below: [42]



APPLICATIONS AND IMPORTANCE OF ACTINOMYCETES

The attention given to the actinomycetes in biotechnological applications may be a natural result of the great metabolic diversity of those organisms and their long association with the surroundings. Actinomycetes are a novel cluster of organisms within the prokaryotes having completely different morphological, cultural, biochemical and physiological characters [43]. They have the ability to degrade a good range of hydrocarbons, pesticides, and aliphatic and aromatic compounds. They perform microbial transformations of organic compounds, a field of great commercial value.

Antibiotics

Actinomycetes are referred to as the best supply of antibiotics. 2/3 of today‟s antibiotics are obtained from actinomycetes. The necessary antibiotics from actinomycetes include anthracyclines, aminoglycosides, beta-lactams, chloramphenicol, macrolides, tetracyclines, nucleosides, peptides and polyethers. Untill 1974 antibiotics of actinomycetes origin were virtually completely confined to Streptomyces. Recently efforts are created to explore rare actinomycetes like Actinomadura, Actinoplanes, Ampullariella, Actinosynnema and Dactylosporangium for the search of latest antibiotics [44].

Enzyme Inhibitors

Actinomycetes synthesize enzyme inhibitors of low mass. Umezawa reported the first low molecular weight enzyme inhibitors, by a streptomycetes strain. Since then over 60 inhibitors are reported as well as leupreptins which inhibit papain, plasmin and trypsin. Antipain inhibits papain, chymotrypsin, trypsin and cathepsnin B. Enzyme inhibitors are unit finding possible uses in cancer treatment. e. g. revistin, an enzyme inhibitor from streptomycetes species inhibit reverse transcriptase. Streptonigrin and retrostatin synthesized by streptomycetes inhibit reverse transcriptase. Alistragin found in culture filtrates of streptomycetes roseoviridis which inhibits carboxypeptidase B. Phosphoramiden, that inhibits metallo-proteases is made by S. tanashiensi [45].

Enzymes present in Actinomycetes

Amylase enzyme

α-Amylases are starch-degrading enzymes that catalyze the hydrolysis of internal a-1, 4-O-glycosidic bonds in polysaccharides with the retention of a α-anomeric configuration within the product. Most of the α-amylases are metalloenzymes that need Ca ions (Ca^{2+}) for his or her activity, structural integrity and stability. They belong to family 13 (GH-13) of the glycoside hydrolase group of enzymes. α-Amylases are one of the most vital industrial enzymes that have a large style of applications starting from conversion of starch to sugar syrups, to the production of cyclodextrins for the pharmaceutical business. The α-amylase family will roughly be divided into 2 groups: the starch hydrolyzing enzymes and the starch modifying, or transglycosylating enzymes [46].

Lipase enzyme

Lipases are part of the family of hydrolases that act on carboxylic ester bonds. The natural perform of lipases is to hydrolyse triglycerides into diglycerides, monoglycerides, fatty acids, and glycerol. Lipases are widely distributed throughout the plant and animal kingdoms, yet as in molds and bacteria. Additionally to lipases, carboxylic ester bonds are often hydrolyzed by esterases [47].

Thermos table/alkalophilic enzymes

The importance of thermostable lipases for various applications has been growing quickly. Most of the studies accomplished to this point are applied with mesophilic producers. Several lipases from mesophiles are stable at elevated temperatures. Biocatalyst thermostability permits a better operation temperature that is clearly advantageous attributable to a better reactivity (higher reaction rate, lower diffusional restrictions), higher stability, higher process yield (increased solubility of substrates and product and favorable equilibrium displacement in endothermic reactions), lower viscosity and fewer contamination issues. [48, 49, 50].

Gilatinase enzyme

In biology and chemistry Gelatinase may be a proteolytic enzyme that permits a living organism to hydrolyze gelatin into its sub compounds (polypeptides, peptides, and amino acids) that can cross the cytomembrane and be utilized by the organism. It's pepsin. Forms of gelatinases are expressed in several bacteria including Pseudomonas aeruginosa and Serratia marcescens. In humans, the genes for gelatinases areMMP2 and MMP9.[51]

Chitinase enzyme

Chitinases have associate huge potential. Chitinolytic enzymes have wide-ranging applications like preparation of pharmaceutically vital chitooligo-saccharides and N-acetyl d-glucosamine, preparation of single-cell protein, isolation of protoplasts from fungi and yeast, management of morbific fungi, treatment of pathogenic fungi, treatment of chitinous waste, and control of malaria [52].

Antimicrobials

Particularly, Streptomyces species produce around 7600 compounds, several of that are secondary metabolites that are potent antibiotics, which has created streptomycetes the first antibiotic-producing organisms exploited by the pharmaceutical industry [53, 54]. The antibiotics from Actinobacteria are differentiated into several major structural categories, like aminoglycosides (e.g., streptomycin and kanamycin), ansamycins (e.g., rifampin), anthracyclines (e.g., doxorubicin), β-lactam (cephalosporins), macrolides (e.g., erythromycin), and tetracycline. One of the first antibiotics used is streptomycin produced by Streptomyces griseus [55]. Some Actinobacteria produce more than one antibiotic substance (e.g., S. griseus), as well as the same antibiotic may be produced by different species of Actinobacteria (e.g, actinomycin, streptothricin) (Table 2).

Table.2: List of antibiotics produced from Actinobacteria

Antibiotic compound	Application	Actinobacteria
1,8-Dihydroxy-2-ethyl-3 methylanthraquinone	Antitumor	*Streptomyces* sp.
1-Hydroxy-1-norresistomycin	Antibacterial; anticancer	*Schisandra chinensis*
2-Allyloxyphenol	Antimicrobial; food preservative; oral disinfectant	*Streptomyces* sp.
Anthracyclines	Antitumor	*S. galileus*
Arenicolides A–C	Mild cytotoxicity	*Salinispora arenicola*
Arenimycin	Antibacterial; anticancer	S. arenicola
Avermectin	Antiparasitic	Streptomyces avermitilis
Bafilomycin	ATPase inhibitor of microorganisms, plant and animal cells	S. griseus, Streptomyces halstedii
Bisanthraquinone	Antibacterial	Streptomyces sp.
Butenolides	Antitumor	Streptoverticillium luteoverticillatum
Carboxamycin	Antibacterial; anticancer	Streptomyces sp.
Chinikomycins	Anticancer	Streptomyces sp.
Chloramphenicol	Antibacterial, inhibitor of protein biosynthesis	Streptomyces venezuelae
Cyanospraside A	Unknown	Solieria pacifica
Daryamides	Antifungal; anticancer	Streptomyces sp.
Frigocyclinone	Antibacterial	S. griseus
Glaciapyrroles	Antibacterial	Streptomyces sp.
Hygromycin	Antimicrobial, immunosuppressive	Streptomyces hygroscopicus
Lajollamycin	Antibacterial	Streptomyces Nodosus
Lincomycin	Antibacterial, inhibitor of protein	Streptomyces lincolnensis

	biosynthesis	
Marinomycins A–D	Antimicrobial; anticancer	Marinispora
Mechercharmycins	Anticancer	Thermoactinomyces sp.
Mitomycin C	Antitumor, binds to doublestranded DNA	Streptomyces lavendulae
Pacificanones A & B	Antibacterial	S. pacifica
Piericidins	Antitumor	Streptomyces sp.
Proximicins	Antibacterial; anticancer	Verrucosispora sp.
Rapamycin	Immunosuppressive, antifungal	S. hygroscopicus
Resistoflavin methyl ether	Antibacterial; antioxidative	Streptomyces sp.
Saliniketal	Cancer chemoprevention	S. arenicola
Salinispyrone	Unknown	S. pacifica
Salinispyrone A & B	Mild cytotoxicity	S. pacifica
Salinosporamide A	Anticancer; antimalarial	Salinispora tropica
Salinosporamide B & C	Cytotoxicity	S. tropica
Sesquiterpene	Unknown	Streptomyces sp.
Staurosporinone	Antitumor; phycotoxicity	Streptomyces sp.
Streptokordin	Antitumor	Streptomyces sp.
Streptomycin	Antimicrobial	S. griseus
Streptozotocin	Diabetogenic	S. achromogenes
Tetracyclines	Antimicrobial	Streptomyces achromogenes Streptomyces rimosus
Tirandamycins	Antibacterial	Streptomyces sp.
Valinomycin	Ionophor, toxic for prokaryotes and eukaryotes	S. griseus
ZHD-0501	Anticancer	Actinomadura sp.
Elaiomycins B and C	Antitumor	Streptomyces sp.
BK 190 N-[2-hydroxyphenyl)-2-phenazinamine (NHP),	Anticancer; antifungus	Nocardia dassonvillei
Chromomycin B, A2, A3	Antitumor	Streptomyces coelicolor
1,4-dihydroxy-2-(3-hydroxybutyl)-9, 10-anthraquinone 9, 10-anthrac	Antibacterial	Streptomyces sp. RAUACT-1

Enzymes for industrial use

Wide styles of biologically active enzymes are created by both marine and terrestrial Actinobacteria (Table 3). They secrete amylases to the skin of the cells that helps them to hold out extracellular digestion. This accelerator is of nice significance in biotechnological applications like food business, fermentation, and textile to paper industries owing to their ability to degrade starch [56]. Another necessary aspect of Actinobacteria is the production of cellulases that are a set of hydrolytic enzymes that hydrolyze the glucosidic bonds of polyose and connected cello-digosaccharide derivatives. Lipase is created from varied Actinobacteria, bacteria, and fungi and is employed in detergent industries, foodstuff, oleochemical, diagnostic settings, and conjointly in industries of pharmaceutical fields [57]. Many Actinobacteria are isolated from varied natural sources, still as in plant tissues and rhizospheric soil. Similarly, Actinobacteria are unconcealed to be a superb resource for L-asparaginase, which is produced by a variety of Actinobacteria, mainly those isolated from soils, such as S. griseus, Streptomyces karnatakensis, Streptomyces albidoflavus, and Nocardia sp. [58, 59]. The roots and rhizomes of many Thai healthful plants like lemon grass (Cymbopogon citratus) and ginger (Zingiber officinale) have long been utilized in Thai ancient medication for abdomen ache and respiratory disorder treatment [60].

Table.3: Enzymes and their industrial applications

Enzyme	Actinobacteria	Use	Industry of application
Protease	Thermoactinomyces sp.	Detergents	Detergent
	Nocardiopsis sp.	Cheese making	Food
	Streptomyces pactum	Clarification- low calorie beer	Brewing
	Streptomyces thermoviolaceus	Dehiding	Leather
	Streptomyces sp.	Treatment of blood clot	Medicine
Cellulase	Streptomyces sp.	Removal of stains	Detergent
	Thermobifida halotolerans	Denim finishing, softening of cotton	Textile
	Streptomyces sp.	Deinking, modification of fibers	Paper and pulp
	Thermomonospora sp.		
	Streptomyces ruber		
Lipase	Streptomyces griseus	Removal of stains	Detergent
		Stability of dough and conditioning	Baking
		Cheese flavoring	Dairy
		Deinking, cleaning	Textile
Xylanase	Actinomadura sp.	Conditioning of dough	Baking
	Streptomyces spp.	Digestibility	Animal feed
		Bleach boosting	Paper and pulp
Pectinase	Streptomyces lydicus	Clarification, mashing	Beverage
		Scouring	Textile
Amylase	Streptomyces sp.	Removal of stains	Detergent
	Streptomyces erumpens	Softness of bread softness and volume	Baking
	Nocardiopsis sp.	Deinking,drainage improvement	Paper and pulp
	Thermobifida fusca	Production of glucose and fructose syrups	Starch industry
	Nocardiopsis sp.	Removal of starch from woven fabrics	Textile
Glucose oxidase	Streptomyces coelicolor	Strengthening of dough	Baking
Keratinase	Nocradiopsis sp. SD5	Feather degradation	Animal feed
Phytase	Streptomyces luteogriseus R10	Phytate digestibility	Animal feed

Vitamins

Vitamin B12 because it exists in nature could also be created by microorganism or Actinobacteria [61]. Isolation of vitamin B12 from Actinobacteria fermentations [62, 63] excited sizeable interest in potential production of vitamin by microbial fermentations. Addition of cobalt salts to the media apparently acts as a precursor for all Actinobacteria to produce vitamin. As cobalt is a rather effective bactericidal agent, this precursor must be added carefully. The fermentations manufacturing the antibiotics streptomycin, aureomycin, grisein, and neomycin will produce some vitamin B12 [64].

Control of plant diseases

The agro industries show a marked interest for Actinobacteria as a source of agroactive compounds of plant growth– promoting rhizobacteria (PGPR) and of biocontrol tools [65, 66]. About 60% of the new insecticides and herbicides reported in the past 5 years originate from Streptomyces [66]. Kasugamycin is a disinfectant and antifungal metabolite discovered in Streptomyces kasugaensis [67], which acts as an inhibitor of protein biosynthesis in microorganisms however not in mammals, and its toxicological properties are excellent. To promote the systemically active kasugamycin is for control of rice blast Pyricularia oryzae and bacterial Pseudomonas diseases in many crops. Polyoxin B and D were isolated as metabolites of Streptomyces cacaoi var. asoensis in 1965 by Isono et al [68] as a new class of natural fungicides. . The ability of the polyoxins to interfere with the fungal cell membrane synthesis by specifically inhibiting chitin synthase [69] makes them acceptable with respect to environmental concerns. Polyoxin B found application against number of fungal pathogens in fruits, vegetables, and ornamentals. Polyoxin D is marketed by many companies to control rice sheath blight caused by Rhizoctonia solani. Validamycin A was found to be a prodrug that is converted within the fungal cell to validoxylamine A, an extremely strong inhibitor of trehalase [70]. Table 6 represents some of the antibiotics produced by the Actinobacteria that suppresses various plant diseases.

Table.6: Plant disease suppression by antibiotics produced by Actinobacteria

Disease	Actinobacteria	Antibiotic produced
Potato scab	Streptomyces melanosporofaciens EF-76 and FP-54	Geldanamycin
Grass seedling disease	Streptomyces violaceusniger YCED9	Nigericin and guanidylfungin A
Root rot of Pea	Streptomyces hygroscopicus var. geldanus	Geldanamycin
Asparagus root diseases	Streptomyces griseus	Faeriefungin
Rice blast disease	Streptomyces kasugaensis	Kasugamycin
Broad range of plant diseases	Streptomyces griseochromogenes	Blasticidin S
Sheath blight of rice	Streptomyces hygroscopicus var. limoneus No. T-7545	Validamycin
Brown rust of wheat	Streptomyces hygroscopicus	Gopalamycin
Phytophthora blight of pepper	Streptomyces violaceusniger	Tubercidin
Phytophthora blight of pepper	Streptomyces humidus	Phenylacetic Acid
Damping-off of cabbage	Streptomyces padanus	Fungichromin
Rice sheath blight	Streptomyces cacaoi var. asoensis	Polyoxin B and D
Powdery mildew	Streptoverticillium rimofaciens	Mildiomycin
Rice root disease	Micromonospora sp. SF-1917	Dapiramicin
Rice blast	Micromonospora sp. M39	2,3-dihydroxybenzoic acid, phenylacetic acid, cervinomycin A1 and A2
Blotch of wheat	Streptomyces malaysiensis	Malayamycin
Powdery mildew of cucumber	Streptomyces sp. KNF2047	Neopeptin A and B

Enhancement of plant growth

Merriman et al [71] according the use of S. griseus for seed treatment of barley, oat, wheat, and carrot to extend their growth. The isolate was originally selected for the biological control of Rhizoctonia solani. Though the S. griseus isolate did increase the average grain yield, dry foliage weight, tiller number, and advanced head emergence for wheat and oat over controls, the variations weren't statistically important. As a seed treatment for carrot, the isolate was additional productive. El-Abyad et al [72] described the use of 3 Streptomyces spp. within the control of bacteria, Fusarium and Verticillium wilts, early blight, and bacterial canker of tomato. The isolates used were Streptomyces pulcher, Streptomyces canescens, and Streptomyces citreofluorescens.

CONCLUSION

Actinobacteria is one amongst the dominant groups of microorganisms that produced industrially necessary secondary metabolites. A wide range of antibiotics within the market is obtained from Actinobacteria. Merchandise like enzymes, herbicides, vitamins, pigments, larvicides, phytohormones, and surfactants area unit produced by these many genera of Actinobacteria, which are of great commercial value. They're capable of degrading a good range of hydrocarbons, pesticides, and feather waste, and their metabolic potential offers a strong area for analysis and research work. However, several of the rare genera of Actinobacteria are neither discovered from unknown locations nor used for their biotechnological and industrial potential. Thus, studies on distinctive ecological environments may yield molecules that might become future harbingers of green technology.

ACKNOWLEDGMENTS

The authors are thankful to Department of Biotechnology & Bioinformatics, Sambalpur University for providing necessary facilities and guidance for the review. This is a part of my PhD thesis work.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

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