A REVIEW ON INDUSTRIALLY IMPORTANT METABOLITES FROM ACTINOMYCETES

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ABSTRACT
Microbial biotic compounds such as enzymes, pigments, antibiotics play an important function as metabolites, resulting in a wide range of applications and uses in a variety of sectors. Nowadays, the entire world is migrating away from synthetic and chemical products in favor of natural ones. Actinomycetes are a major microbial population found in soil, plant tissues, fresh water, and marine settings. Many useful extracellular enzymes, pigments, antibiotics, and antibacterial compounds are produced by Actinomycetes. Enzymes like cellulases from Streptomyces albus; pigments like Violacein from Streptomyces violaceus; antibiotics like Tetracycline from Streptomyces aureofaciens, produced by Actinomycetes and applied in different industries. Actinomycetes found in severe conditions are known to create novel bioactive compounds with high industrial potential. This article attempts to summarize Actinomycetes ability to create bioactive secondary metabolites from Actinomycetes and its applications in various industries.

KEYWORDS: Actinomycetes, Antibiotic, Enzyme, Industries, Pigments.

INTRODUCTION
Actinomycetes are large group of bacteria found in soil, and marine environments. They are well-known for producing a wide range of bioactive secondary metabolites, such as antibiotics, antifungal agents, anticancer medicines, and immunosuppressant’s, as well as a variety of enzymes, pigments and other bioactive substances (Roohiet al., 2019). Many of which have found use in the pharmaceutical, agricultural, food, cosmetics and other commercial industries(Araujo-Melo R. 2016).
The Actinomycetes are gram-positive bacteria. There is a growing need to learn more about the industrially relevant metabolites produced by Actinomycetes. Because of their ability to create varied and complex chemicals, Actinomycetes are seen as a possible source of industrially relevant metabolites. However, discovering and developing these metabolites can be a time-consuming and difficult process that requires considerable screening, isolation and characterization of bioactive compounds. However, because of the potential benefits of these metabolites, Actinomycetes are a significant field of research for industrial applications.

BACKGROUND:
Selman Waksman, who got the Nobel Prize in Medicine for his work on antibiotics, identified the first Actinomycetes, *Streptomyces griseus*, in 1914. Over 10,000 different Actinomycetes species have been found since then, and they continue to be a major source of novel medication leads and other physiologically active chemicals. Actinomycetes are well-known for producing antibiotics, which are critical for treating bacterial infections in humans, animals, and plants. *Streptomycin*, *erythromycin*, *tetracycline*, and *vancomycin* are some of the most well-known antibiotics generated by Actinomycetes. Since their discovery, many of these chemicals have become crucial instruments for contemporary medicine, saving many lives (Berdy J. 2012).

Actinomycetes produce antibiotics with a wide range of biological activity that have been used to treat bacterial, fungal, and some parasitic illnesses. *Streptomycin*, *erythromycin*, *tetracycline*, *vancomycin*, and *rifampicin* are examples of clinically important antibiotics generated by Actinomycetes (Berdy J. 2012).

In addition to antibiotics Actinomycetes can produce a number of enzymes having industrial applications such as proteases, amylases, lipases, cellulases, chitinases, and xylanases. Actinomycetes produce a wide range of enzymes that have biotechnological applications in a variety of sectors. Because of their ability to degrade a range of organic materials, proteases are frequently utilized in the food, detergent, and leather industries. Other enzymes, such as amylases and lipases, are used to make Biofuels and medicines (Kurosawa & Ghiviriga, 2014).

Actinomycetes are also recognized for producing a range of enzymes such as amylases, proteases, and cellulases. These enzymes have numerous industrial applications, including the manufacture of Biofuels, paper, textiles, and food goods. Furthermore, Actinomycetes are known to create a variety of colors with potential applications in the food and cosmetic industries (Chaudhary and Gupta 2020).

Antibiotics are one of the most important metabolites which can produce by Actinomycetes. These metabolites are used to treat bacterial infections in humans and animals, as well as it could be used in agricultural growth promoters. Antibiotics from Actinomycetes are more than two-thirds of all antibiotics used in human medicine. Actinomycetes are a key source of antibiotics and over 70% of all clinically effective antibiotics are produced from Actinomycetes. Actinomycetes produce antibiotics with a wide range of biological activity that have been used to treat bacterial, fungal, and some parasitic illnesses. *Streptomycin*, *erythromycin*, *tetracycline*, *vancomycin*, and *rifampicin* are examples of clinically important antibiotics generated by Actinomycetes (Berdy J. 2012).

Actinomycetes are also a rich source of colors used in the culinary, cosmetic, and textile industries.
Some of these pigments have also been proven to have anticancer and antioxidant effects. Actinomycetes are also known to create a variety of pigments used in the food, textile, and cosmetic sectors. Many Actinomycetes produce pigments of various colors, such as red, yellow, orange, brown and purple which are often more stable than synthetic dyes (Berdy J, 2005). These pigments are having antioxidant characteristics and have been demonstrated to offer possible health advantages (Favela-Torres et al., 2019).

Immunosuppressive drugs: Immunosuppressive compounds such as rapamycin and FK506 are abundant in Actinomycetes and are used clinically to prevent transplant rejection and treat autoimmune diseases. These drugs work by suppressing T lymphocyte activation, which is important in the immunological response (Koul et al., 1998). Finally, Actinomycetes have been revealed to produce a variety of additional industrially relevant metabolites, such as immune modulators and plant growth regulators, such as gibberellins and cytokinin’s.

Actinomycetes produce a diverse spectrum of additional bioactive chemicals with potential applications in a variety of sectors. Some Actinomycetes, for example, create antifungal chemicals with agricultural applications, while others produce indole-3-acetic acid, a plant growth hormone with agricultural and horticultural applications (Koul et al., 1998; Khamna et al., 2009).

INDUSTRIAL APPLICATIONS OF ENZYME, ANTIBIOTICS, AND PIGMENTS FROM ACTINOMYCETES:

A class of bacteria called Actinomycetes is well-known for its extensive metabolic capabilities and ability to produce a wide range of bioactive substances. Due to their special qualities, Actinomycetes' generated antibiotics, enzymes, and pigments have a wide range of industrial applications. Some of them are here:

**ANTIBIOTICS:**

- One of the first medicines to successfully treat infections caused by bacteria, streptomycin was found in the Actinomycetes *Streptomyces griseus* (Waksman, S. A., & Schatz, A., 1944).
- Erythromycin is an antibiotic used to treat a variety of bacterial illnesses. It is produced by several species of *Streptomyces*. In the pharmaceutical sector, it has been frequently utilized (McGuire J.M. et al., 1952).
- Avilamycin is a potent antibiotic isolated from the Actinomycetes *Streptomyces nodosus* that is used to necrotic enteritis (NE) control in poultry and for some bacterial illnesses that are resistant to other antibiotics. (Isogai Y. et al., 1983).
- Tetracyclines: A class of antibiotics called actinomycetes-derived tetracycline is used to treat a range of illnesses including bacterial, chlamydial, and mycoplasmal infections. (Gottlieb D. et al., 1967).

**ENZYMES:**

- Amylases are enzymes that convert starch into more digestible sugars. Actinomycetes generate them. These enzymes are used in the food business to breakdown starch and make sugars, as well as in the textile industry to resize fabrics (Manivasagan P. et al., 2014).
- Actinomycetal proteases are used in the food, leather, and detergent industries, while amylases...
are used in the production of beer, textiles, and paper. Proteins are broken down into smaller peptides and amino acids by the action of proteases enzyme. The processing of food (meat tenderization, dairy processing) and laundry detergents (stain removal) all require proteases that are generated from actinomycetes (Lee et al., 2005).

- Actinomycetes produce cellulases, which can split cellulose into glucose molecules. The Biofuel business uses these enzymes to transform cellulosic biomass into Biofuels, while the textile industry uses them to bio finish fabrics (Chaudhary and Gupta 2020).

- Lipases: lipases from actinomycetes are used in the food industry to hydrolyse lipids, which produces fatty acids and enhances flavour of food products. Due to their capacity to eliminate grease stains, they are also utilized in the detergent industry (Rathi P. et al., 2001).

PIGMENTS:

- Actinorhodin: Actinorhodin is a blue coloured pigment produced by Streptomyces coelicolor and it is used as a natural food colouring agent. (Rigali S. et al., 2018).

- While some actinomycetes can also produce Violacein. Violacein shows antibacterial and anticancer qualities, and it is useful in the cosmetic and pharmaceutical industries (Parihar A. et al., 2019).

- Prodigiosin: is a red pigment produced by numerous Streptomyces species that is used in food colouring and cosmetics due to its antibacterial qualities (Gerber N. N. and Stahly D. P. 1975).

- Actinomycetes can create pigments called melanin, which have potential benefits in the fields of cosmetics, medicine, and even environmental remediation like the removal of heavy metals (Araujo-Melo2016).

- Carotenoids: Some actinomycetes create pigments called carotenes that have antioxidant characteristics and are used in the food, cosmetics, and pharmaceutical industries (Gerber N. N. and Stahly D. P. 1975).

Actinomycetes are having potential for the synthesis of enzymes, antibiotics, and pigments that are used in a variety of industrial processes including food processing, medicines preparation, textiles processing (Roohi et al., 2019). Overall, actinomycetes represent a valuable source of industrially important metabolites, and now a day’s research is focused on discovering new compounds and developing more efficient methods for their production and isolation.

REVIEW

Ramendra S.P. et al., (2016) studied on pigment producing Actinomycetes and concluded that the isolation of Actinomycetes was done from different regions of Madhya Pradesh. Out of 85 Actinomycetes only 5 Actinomycetes showed pigment producing ability but he elected one Actinomycetes AR-ITM02 on the basis of morphological observation such as fast growth and pigment diffusion ability in media. Then he tested antimicrobial activity by agar overlay method on bacteria, fungi and yeast. The antimicrobial activity was shown by Actinomycetes against many pathogenic microorganisms. Kiran R.K.et al., (2009) studied that the antibacterial substances from Actinomycetes which was isolated from marine environment of Lonar crater and characterized. Out of the 24 isolates 12 isolates
were active against *Bacillus subtilis*, 13 against *Staphylococcus aureus*, 7 against *Escherichia coli*, 3 against *Proteus vulgaris* and 4 against *Salmonella typhi*. Metabolites in the yeast extract malt extract broth of 2 days grown *Streptomyces* spp. Shows that they have antimicrobial and cytotoxic activity against human lung carcinoma cell A549. Pachaiyappan S.K. *et al.*, (2012) studied total 35 isolates on the basis of colony characteristics on *Actinomycetes* isolation agar. Study showed that among the isolate *Actinomycetes Actinobacterium loyola* shows good antibacterial activity. Charu Singh *et al.*, (2016) studied that antifungal metabolites from *Actinomycetes* which were isolated from different regions of Madhya Pradesh. Total 80 strains of *Actinomycetes* isolated from the soils of different habitats of Chambal’s region of Madhya Pradesh and they were evaluated for their ability to inhibit plant pathogens *Macrophomina phaseolina*, *Fusarium oxysporum*, *Collectotrichum truncatum*, *Rhizoctonia solani* in vitro. Entire isolates were screened for their antifungal activity by agar overlay method against phytopathogenic fungi. After screening, out of these only one *Actinomycetaceae ACITM-1* showed antifungal activity against *Macrophomina phaseolina* and *Collectotrichum truncatum*. Salma Mukhtar *et al.*, (2017) works on *Actinomycetes* and explain how industries are looking for new microbial strains, including *Actinomycetes* in order to produce novel enzymes to fulfill the current requirements because up till now, only 20 enzymes produced by microorganisms are utilized by various industries. *Actinomycetes* are of great significance since they have ability to produce and secrete variety of extracellular hydrolytic enzymes that are safe for the environment. However, many of the rare genera of *Actinomycetes* have been neither manipulated nor explored for their biotechnological potential. Studies on the microbial potential of extreme environments can be utilized to produce novel enzymes that can become future harbingers of green biotechnology.

**CONCLUSION**

The review highlights the importance of *Actinomycetes* as a significant source of industrially significant metabolites, such as pigments, enzymes, and antibiotics. These metabolites have numerous uses in industries like biotechnology, agriculture, and medicine. Antibiotics developed from *Actinomycetes* have transformed modern medicine and remain a major area of study in microbiology. These bacteria produce enzymes that are used in a variety of sectors, including the generation of Biofuels and food processing. Additionally, the food, textile, and cosmetic industries use *Actinomycetes* pigments. Despite the availability of antibiotics, the rise of bacteria that are resistant to them calls for the investigation of novel antibiotics, with *actinomycetes* being a top contender because of their genetic variety. For the purpose of finding novel metabolites with therapeutic and commercial applications, *Actinomycetes* untapped potential must be discovered in the post-genomic era. *Actinomycetes* that have been genetically modified can now manufacture new compounds with enhanced properties, opening the door to the possibility of safer and more efficient biologically active chemicals. To fully understand metabolite
creation mechanisms and unlocked the entire spectrum of Actinomycetes potential applications, more study is essential. Overall Actinomycetes continue to be a promising source of industrially relevant metabolites, and further research in this area has the potential to yield innovative and beneficial products for industrial and medical uses.

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## ACTINOMYCETES SOURCE OF METABOLITES-ANTIBIOTICS

Table 01: Antibiotics - Commercially important Antibiotics produced by Actinomycetes, their characteristics and potential uses

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Actinomycetes</th>
<th>Antibiotic</th>
<th>Key Details</th>
<th>use</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Streptomyces coelicolor</em></td>
<td>Actinorhodin</td>
<td>Blue-pigmented</td>
<td>Actinorhodin is a potent, bacteriostatic, pH-responsive antibiotic and used for managing oxidative damage, protein damage and selected forms of DNA damage.</td>
<td>Hopwood, D. A., Bibb, M. J., <em>et al.</em>, (1985)</td>
</tr>
<tr>
<td>3</td>
<td><em>Streptomyces aureofaciens</em></td>
<td>Tetracycline</td>
<td>Broad-spectrum antibiotic</td>
<td>Used to treat bacterial infections. Inhibits protein synthesis by binding to the 30S ribosome subunit.</td>
<td>Gottlieb, D., &amp; Everett, K. D. (1967)</td>
</tr>
<tr>
<td>4</td>
<td><em>Streptomyces nodosus</em></td>
<td>Avilamycin</td>
<td>Glycopeptides antibiotic</td>
<td>Used in food animals for necrotic enteritis (NE) control in poultry.</td>
<td>Isogai, Y., Hasegawa, T., <em>et al.</em>, (1983)</td>
</tr>
<tr>
<td>5</td>
<td><em>Streptomyces nodosus</em></td>
<td>Niddamycin</td>
<td>Macrolide antibiotic</td>
<td>Used for the treatment of numerous infections, including but not limited to septicemia, intra-abdominal infections, lower respiratory infections</td>
<td>Nishizawa, K., Iwami, M., <em>et al.</em>, (1986)</td>
</tr>
<tr>
<td>6</td>
<td><em>Streptomyces erythraeus</em></td>
<td>Erythromycin</td>
<td>--</td>
<td>Used to treat respiratory tract infections, skin infections, and sexually transmitted infections. Inhibits protein synthesis by binding to the 50S ribosome subunit.</td>
<td>McGuire, J.M., Corcoran, J.W., <em>et al.</em>, (1952)</td>
</tr>
<tr>
<td>9</td>
<td><em>Streptomyces kanamyceticus</em></td>
<td>Kanamycin</td>
<td>--</td>
<td>Used to treat bacterial infections. Inhibits protein synthesis by binding to the 30S ribosome subunit.</td>
<td>Hara, O., Beppu, T., <em>et al.</em>, (1957)</td>
</tr>
</tbody>
</table>
Table 02: Enzyme- Commercially important enzymes produced by Actinomycetes, their characteristics and potential uses

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Actinomycetes Strain</th>
<th>Enzyme Produced</th>
<th>Function</th>
<th>Industrial Applications</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Streptomyces griseus</em>, <em>Streptomyces thermoviolaceus</em>,</td>
<td>Protease</td>
<td>Breaks down proteins</td>
<td>Food processing, detergent production</td>
<td>Lee et al., (2005)</td>
</tr>
<tr>
<td></td>
<td><em>Streptomyces pactum</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><em>Streptomyces rubiginosus</em></td>
<td>Amylase</td>
<td>Breaks down starch into sugars</td>
<td>Baking, brewing, biofuel production</td>
<td>Manivasagananet al. (2014)</td>
</tr>
<tr>
<td>3</td>
<td><em>Streptomyces ruber</em>, <em>Thermobifidahalotolerans</em>,</td>
<td>Cellulase</td>
<td>Breaks down cellulose into sugars</td>
<td>Biofuel production, paper industry</td>
<td>Chaudhary and Gupta (2020)</td>
</tr>
<tr>
<td></td>
<td><em>Streptomyces albus</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><em>Streptomyces rimosus</em></td>
<td>Lipase</td>
<td>Breaks down lipids into fatty acids and glycerol</td>
<td>Detergent production, biodiesel production</td>
<td>Rathi P. et al., (2001)</td>
</tr>
<tr>
<td>5</td>
<td><em>Streptomyces exfoliatius</em></td>
<td>Xylanase</td>
<td>Breaks down xylan into xylose and other sugars</td>
<td>Food processing, biofuel production</td>
<td>Kumar et al., (2013)</td>
</tr>
<tr>
<td>6</td>
<td><em>Actinomadurakeratinilytica</em></td>
<td>Keratinase</td>
<td>Keratin</td>
<td>Leather</td>
<td>Priya et al., (2012)</td>
</tr>
<tr>
<td>7</td>
<td><em>Streptomyces thermoviolaceus Nocardiopsisprastina</em></td>
<td>Chitinase</td>
<td>Colloidal chitin</td>
<td>Textile, Leather</td>
<td>Hussain et al., (2002)</td>
</tr>
<tr>
<td>8</td>
<td><em>Streptomyces lydicus</em></td>
<td>Pectinase</td>
<td>Polygalacturonic acid</td>
<td>Beverage</td>
<td>Rajasekar A. et al., (2010)</td>
</tr>
</tbody>
</table>
**Table 03: Pigments- Commercially Important Pigments Produced by Actinomycetes, their Characteristics and Potential uses.**

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Actinomycetes Strain</th>
<th>Pigment Produced</th>
<th>Industrial Importance</th>
<th>Details</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td><em>Streptomyces lividans</em></td>
<td>Blue pigment</td>
<td>Antitumor agent</td>
<td>Blue pigment produced in aerial mycelium</td>
<td>Wu et al., (2018)</td>
</tr>
<tr>
<td>3</td>
<td><em>Streptomyces griseus</em></td>
<td>Prodiginine</td>
<td>Antibiotic, anticancer, immunosuppressant</td>
<td>Red pigment produced in submerged mycelium</td>
<td>Singh et al., (2018)</td>
</tr>
<tr>
<td>5</td>
<td><em>Actinokineospora sp.</em></td>
<td>Naphthoquinone</td>
<td>Antibacterial, antifungal</td>
<td>Red pigment produced in submerged mycelium</td>
<td>Becher et al., (2019)</td>
</tr>
<tr>
<td>7</td>
<td><em>Streptomyces lividans</em></td>
<td>Blue pigment</td>
<td>Antitumor agent</td>
<td>Blue pigment produced in aerial mycelium</td>
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<tr>
<td></td>
<td><em>Streptomyces griseus</em></td>
<td>Prodiginine</td>
<td>Antibiotic, anticancer, immunosuppressant</td>
<td>Red pigment produced in submerged mycelium</td>
<td>Singh et al., (2018)</td>
</tr>
<tr>
<td>8</td>
<td><em>Streptomyces violaceus</em></td>
<td>Violacein</td>
<td>Antitumor agent, antimicrobial</td>
<td>Purple pigment produced in submerged mycelium</td>
<td>Parihar A. et al., (2019)</td>
</tr>
<tr>
<td>9</td>
<td><em>Actinokineospora sp.</em></td>
<td>Naphthoquinone</td>
<td>Antibacterial, antifungal</td>
<td>Red pigment produced in submerged mycelium</td>
<td>Becher et al., (2019)</td>
</tr>
<tr>
<td>10</td>
<td><em>Streptoverticillium rubrireticuli</em></td>
<td>Prodigiosin</td>
<td>Red</td>
<td>—</td>
<td>N. N. Gerber and D. P. Stahly, (1975)</td>
</tr>
<tr>
<td>11</td>
<td><em>Streptomyces echinoruber</em></td>
<td>Rubrolone</td>
<td>Red</td>
<td>—</td>
<td>(Gerber N., N. and Stahly D. P. 1975)</td>
</tr>
</tbody>
</table>