

Review article

Microbes and Infectious Diseases 2025; 6(2): 916-928

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Therapeutic application of *Streptomyces*: A choice alternative to modern therapies

Abdirasak Sharif Ali Mude^{1*}, Yahye Ahmed Nageye¹, Kizito Eneye Bello²

1- Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia.

2- Department of Microbiology, Faculty of Natural Science, Kogi State (Prince Abubakar Audu) University, Anyigba. PMB 1008, Anyigba, Kogi State, Nigeria.

ARTICLEINFO

Article history: Received 21February2024 Received in revised form3 April2024 Accepted 12 April 2024

Keywords:

Streptomyces Therapeutic applications Secondary metabolites Antibiotics Antibioterial.

ABSTRACT

Background: Streptomyces, a prolific genus of bacteria, has been a longstanding source of bioactive compounds with diverse therapeutic applications. This review explores the multifaceted therapeutic potential of Streptomyces and its derivatives as a compelling alternative to modern therapeutic approaches. The comprehensive analysis covers the biological diversity of *Streptomyces*, the intricate mechanisms of its secondary metabolites, and their impact on various medical domains. Streptomyces, boasting over 500 identified species, is renowned for its production of bioactive compounds with antibacterial, antifungal, antiviral, and anticancer properties. The primary focus is on the antibiotics, such as streptomycin and tetracycline, highlighting their significance in addressing bacterial infections, especially in the context of escalating antibiotic resistance. Additionally, the review delves into the antifungal activities exhibited by Streptomyces compounds, contributing to their role in combating mycotic diseases. Streptomyces-derived compounds have also shown promise in cancer therapeutics, with specific attention to Streptozotocin and its potential in treating pancreatic cancer. Beyond their direct antimicrobial and anticancer effects, Streptomyces compounds are recognized for their immunomodulatory properties, enhancing the body's ability to combat infections and manage inflammatory conditions. This review underscores the versatility of Streptomyces in therapeutic applications, ranging from its direct effects on pathogens to its potential in regulating immune responses. As research in this field advances, the ongoing exploration of Streptomyces and its bioactive compounds holds significant promise for the development of innovative and targeted therapeutic interventions, offering an appealing alternative to contemporary medical approaches.

Introduction

Streptomyces, a genus of Gram-positive bacteria, has garnered noteworthy attention in recent years due to its filamentous growth and capacity to synthesize a wide range of bioactive compounds, the spores are usually spiral, straight or in chains as represented in Figure 1. This paper aims to delve into the therapeutic applications of *Streptomyces*, emphasizing its emergence as a promising alternative to contemporary therapeutic approaches.

Streptomyces species are renowned for their biological diversity and have been a prolific source of secondary metabolites with diverse biological activities [1]. These bioactive compounds exhibit antibacterial, antifungal, antiviral, and anticancer properties, contributing to the growing interest in *Streptomyces* as a valuable therapeutic resource [1].

The antibacterial potential of *Streptomyces* has been exemplified by the discovery of antibiotics

DOI:10.21608/MID.2024.271783.1813

^{*} Corresponding author: Abdirasak Sharif Ali Mude

E-mail address: arshamvare@gmail.com

^{© 2020} The author (s). Published by Zagazig University. This is an open access article under the CC BY 4.0 license https://creativecommons.org/licenses/by/4.0/.

like streptomycin, tetracycline, and erythromycin. Streptomycin, for instance, interferes with bacterial protein synthesis and has been widely used to combat bacterial infections [2]. In the context of increasing antibiotic resistance, Streptomycesderived compounds represent a crucial alternative to traditional antibiotics.

Streptomyces has also demonstrated efficacy in addressing fungal infections through the production of antifungal agents such as nystatin and amphotericin B. These compounds target specific components of fungal cells, showcasing the potential of *Streptomyces* as a source of antifungal therapies [3].

In the realm of cancer therapeutics, Streptomyces-derived compounds have shown promise. Streptozotocin, a compound produced by *Streptomyces* achromogenes, has been investigated for its ability to induce pancreatic beta-cell apoptosis and is employed in the treatment of pancreatic cancer [4]. This underscores the potential of *Streptomyces* as a source of anticancer agents, offering novel avenues for drug development [5].

Moreover, beyond direct antimicrobial and anticancer effects, *Streptomyces* has exhibited immunomodulatory properties. These compounds can modulate the immune response, enhancing the body's ability to combat infections and manage inflammatory conditions [5].

Streptomyces, with its diverse bioactive compounds, stands out as a promising alternative to modern therapeutic approaches. From antibacterial and antifungal activities to anticancer potential and immunomodulatory effects, *Streptomyces* holds the key to innovative and sustainable solutions in drug development [5].

Streptomyces Biological Diversity and Secondary Metabolites in Therapeutic Applications

Streptomyces has captured considerable scientific interest due to its remarkable biological diversity and the ability of its various species to produce a plethora of secondary metabolites. Details of *Streptomyces*' biological diversity and the therapeutic potential derived from its diverse secondary metabolites, emphasizing their applications in modern drug development is considered imperative [7].

Biological Diversity:

Streptomyces stands out for its extensive biological diversity, boasting over 500 identified species [7]. Each of these species exhibits unique

characteristics, contributing to the genus's versatility. The filamentous growth pattern of *Streptomyces* further adds to its distinctive features, creating an environment conducive to the production of an extensive array of secondary metabolites [8].

Secondary Metabolites and Their Bioactivities:

The exceptional biological diversity of *Streptomyces* has positioned it as a prolific source of secondary metabolites, each displaying a spectrum of bioactivities. This section scrutinizes the hallmark feature of *Streptomyces*—its capacity to generate secondary metabolites—and delves into their diverse bioactivities, emphasizing their crucial role in contemporary drug discovery and development, the structure of some active enzymes recovered from *Streptomyces* are represented in Figure 2. The bioactive activity of some of the *Streptomyces* are also presented in Table 1.

Generation of Secondary Metabolites:

Streptomyces, a genus renowned for its filamentous growth, harnesses intricate biochemical pathways to produce a vast array of secondary metabolites [8]. These secondary metabolites, distinct from primary metabolites essential for growth and development, serve various ecological functions and have garnered substantial attention for their therapeutic potential.

Diverse Bioactivities:

The secondary metabolites produced by *Streptomyces* exhibit a myriad of bioactivities, making them invaluable in addressing various health challenges [7]. Antibacterial properties are evident in compounds such as streptomycin, tetracycline, and erythromycin, which interfere with bacterial processes, contributing to their status as essential antibiotics in clinical practice [10]. Streptomyces-derived secondary metabolites also manifest potent antifungal activities, with nystatin and amphotericin B being exemplary agents employed in the treatment of fungal infections [8].

Moreover, *Streptomyces* compounds showcase antiviral properties, contributing to the ongoing efforts in antiviral drug development. The diverse range of bioactive compounds produced by *Streptomyces* extends to anticancer agents like streptozotocin, demonstrating its potential as a valuable source for novel cancer therapeutics [11].

Significance in Drug Discovery:

The bioactive compounds derived from *Streptomyces* hold a pivotal role in drug discovery

and development. Streptomyces-derived secondary metabolites have become a focal point in the pursuit of novel drugs, owing to their unique structures and diverse pharmacological activities [1]. As a result, researchers are increasingly exploring these compounds for their potential in developing nextgeneration therapeutics.

Streptomyces stands out as a treasure trove of secondary metabolites with diverse bioactivities, making it a focal point in contemporary drug discovery and development [4]. From antibacterial and antifungal properties to antiviral and anticancer potential, Streptomyces-derived secondary metabolites offer a rich source of bioactive compounds with significant therapeutic implications [8]. As research in this field advances, the exploration of Streptomyces continues to unveil new and promising avenues for the development of innovative drugs.

Antibacterial Potential:

The rise of antibiotic-resistant strains has underscored the need for alternative therapeutic approaches in combating bacterial infections. *Streptomyces*, a genus of Gram-positive bacteria, has been at the forefront of this quest, providing a rich source of antibiotics that have played a pivotal role in addressing bacterial infections [11,12].

Mechanisms of Action:

Streptomyces-derived antibiotics. including streptomycin, tetracycline, and erythromycin, exhibit diverse mechanisms of action essential that target bacterial processes. Streptomycin, for example, interferes with bacterial protein synthesis by binding to the 30S ribosomal subunit [12]. Tetracycline acts by inhibiting protein synthesis through binding to the 30S ribosomal subunit as well, while erythromycin disrupts bacterial protein synthesis by binding to the 50S ribosomal subunit [12]. These distinct mechanisms contribute to the efficacy of collectively Streptomyces-derived antibiotics against a broad spectrum of bacteria. The summary of the mechanism of action of Streptomyces is illustrated in Figure 3.

Broad-Spectrum Activity:

One of the remarkable features of Streptomyces-derived antibiotics is their ability to target a wide range of bacterial species. The interference with fundamental processes like protein synthesis, DNA replication, or cell wall formation renders these antibiotics effective against Grampositive and Gram-negative bacteria alike. This broad-spectrum activity enhances their versatility and applicability in diverse clinical settings[1].

Significance in the Face of Antibiotic Resistance:

The escalating prevalence of antibioticresistant strains poses a significant challenge to traditional antibacterial therapies. *Streptomyces* compounds, with their unique mechanisms of action, offer a valuable alternative to conventional antibiotics. By targeting distinct bacterial processes, these compounds may overcome resistance mechanisms, providing a renewed hope in the battle against antibiotic-resistant infections [1].

The antibacterial properties of Streptomyces-derived antibiotics have been welldocumented[12]. Streptomycin, tetracycline, and erythromycin, among others, exert their effects protein through interference with bacterial synthesis, DNA replication, or cell wall formation[12]. The broad-spectrum activity of these antibiotics makes them effective against a diverse array of bacterial species[13].

The antibacterial properties of Streptomyces-derived antibiotics, characterized by their diverse mechanisms of action and broad-spectrum activity, hold significant promise in addressing bacterial infections, particularly in the face of antibiotic-resistant strains. As research continues, the exploration and optimization of *Streptomyces* compounds may pave the way for innovative antibacterial therapies, providing a valuable arsenal against evolving challenges in infectious disease management [11,13].

Antifungal Activities:

The antifungal activities of *Streptomyces* compounds represent a significant facet of their therapeutic potential, with notable agents like nystatin and amphotericin B widely employed in the clinical management of fungal infections. This section explores the specific antifungal mechanisms of these compounds and underscores the potential of Streptomyces-derived metabolites in combating mycotic diseases [14].

Antifungal Agents and Their Application:

Streptomyces-derived compounds, such as nystatin and amphotericin B, have gained prominence as effective antifungal agents [3]. These compounds have been extensively utilized in clinical settings to treat a range of fungal infections, including those caused by Candida and Aspergillus species [6].

Mechanisms of Action:

Nystatin and amphotericin B exert their antifungal effects by targeting specific components of fungal cells. Nystatin, a polyene antifungal antibiotic, binds to ergosterol, a key component of fungal cell membranes, leading to the formation of pores and subsequent disruption of membrane integrity [5], as illustrated in Figure 4. This disruption compromises the structural integrity of the fungal cell, ultimately leading to cell death.

Amphotericin B, another polyene antifungal agent, also interacts with ergosterol in the fungal cell membrane. This interaction forms transmembrane channels that increase membrane permeability, disrupting cellular functions and contributing to fungal cell death [3,13].

Clinical Significance:

The clinical use of Streptomyces-derived antifungal agents has been pivotal in the treatment of various mycotic diseases. Nystatin, for instance, is commonly employed to treat oral and gastrointestinal candidiasis, while amphotericin B is used for systemic fungal infections, particularly those affecting immunocompromised individuals [14].

Despite their efficacy, challenges such as toxicity and the emergence of resistant strains highlight the need for ongoing research and innovation in antifungal drug development. *Streptomyces* compounds, with their diverse secondary metabolites, offer a valuable resource for discovering novel antifungal agents with improved safety profiles and reduced resistance issues [10], [14].

The antifungal activities of *Streptomyces* compounds, exemplified by agents like nystatin and amphotericin B [3], underscore the genus's potential in addressing mycotic diseases. Understanding the mechanisms by which these compounds target fungal cells provides insights into their clinical efficacy and informs future drug development efforts. As research continues, Streptomyces-derived metabolites remain a promising source for the discovery of innovative antifungal therapies [14].

Antibacterial Properties:

Streptomyces-derivedantibiotics,

including streptomycin, tetracycline, and erythromycin, have been pivotal in the battle against bacterial infections, exerting their antimicrobial effects through interference with bacterial protein synthesis, DNA replication, or cell wall formation [15,16].Streptomycin, for instance, inhibits protein synthesis by binding to the 30S ribosomal subunit in bacteria [17]. Tetracycline acts by inhibiting the binding of aminoacyl-tRNA to the mRNA-ribosome complex [18], while erythromycin disrupts protein synthesis by binding to the 50S ribosomal subunit [19].

The versatility of Streptomyces-derived antibiotics lies in their effectiveness against a broad spectrum of bacteria, making them valuable tools in the treatment of various infections [1]. This broadspectrum activity is particularly advantageous in clinical settings where the causative agent may not be immediately identified [19].

In the face of the growing threat of antibiotic-resistant bacterial strains, *Streptomyces* compounds present a promising alternative to traditional antibiotics [20]. The ability of Streptomyces-derived antibiotics to target multiple bacterial pathways makes it challenging for bacteria to develop resistance against them [21]. This characteristic is crucial in addressing the global concern of antibiotic resistance, where the overuse and misuse of antibiotics have led to the emergence of resistant strains [22].

Streptomyces-derived antibiotics have made significant contributions to the field of medicine by providing effective treatments against bacterial infections [22]. Their multifaceted mechanisms of action and broad-spectrum activity highlight their importance in the context of increasing antibiotic resistance. As research continues to explore new avenues for antibiotic development, *Streptomyces* compounds remain a valuable resource in the ongoing fight against bacterial infections [22,24].

Anticancer Potential:

The anticancer potential of Streptomycesderived compounds has emerged as a promising area of research, offering novel avenues for the development of targeted therapies with potentially fewer side effects than traditional chemotherapeutic agents [23].

Streptozotocin, a compound produced by *Streptomyces* achromogenes, exemplifies the genus's anticancer properties. This compound has been extensively studied for its ability to induce apoptosis in pancreatic beta-cells, making it a valuable agent in the treatment of pancreatic cancer [23]. Streptozotocin's mechanism of action involves

the disruption of DNA synthesis, particularly in rapidly dividing cells, leading to cell death and inhibition of tumor growth.

The use of Streptozotocin in pancreatic cancer treatment highlights the potential of Streptomyces-derived compounds to serve as targeted therapies. Compared to traditional chemotherapeutic agents that often lack specificity, compounds like Streptozotocin offer the advantage of selectively targeting cancer cells while minimizing damage to healthy tissues [24].

The cytotoxic effects of Streptomycesderived compounds extend beyond Streptozotocin. Many compounds from this genus have demonstrated direct cytotoxicity against cancer cells, making them attractive candidates for further investigation in cancer therapy [25].

The pursuit of Streptomyces-derived anticancer agents aligns with the ongoing efforts to develop more effective and targeted treatments. This approach holds particular promise in addressing the limitations and adverse effects associated with conventional chemotherapeutic agents [26].

Moreover, the diversity of secondary metabolites produced by *Streptomyces* offers a broad spectrum of potential anticancer compounds. These bioactive molecules have the capacity to interfere with various cellular processes involved in cancer development, providing researchers with a rich source of candidates for drug discovery [27].

The anticancer potential of Streptomycesderived compounds, exemplified by Streptozotocin, signifies a significant stride in the quest for targeted and effective cancer therapies. The unique mechanisms of action and the potential for reduced side effects make *Streptomyces* compounds promising candidates for further exploration and development in the field of oncology [27]. One of the anticancer compound recovered from *Streptomyces* is illustrated in Figure 5.

Immunomodulatory Effects:

Beyond its established antimicrobial and anticancer properties, *Streptomyces* has gained recognition as a significant contributor to immunomodulation. This segment explores the immunomodulatory characteristics of compounds derived from *Streptomyces*, uncovering their capacity to boost the immune response within the body and address conditions characterized by immune dysregulation [26].

Immunomodulatory Mechanisms:

Compounds derived from Streptomyces exhibit a range of immunomodulatory effects, influencing the activity and responsiveness of the immune system. These effects are crucial in finetuning the immune response, enabling the body to combat infections and manage inflammatory conditions more efficiently [27]. The intricate underlying mechanisms **Streptomyces** immunomodulation involve the interaction between secondary metabolites produced by Streptomyces bacteria and the host immune system. Several studies have shed light on these mechanisms, providing insights into the immunomodulatory effects of Streptomyces-derived compounds [28].

One key aspect of *Streptomyces* immunomodulation lies in the ability of its secondary metabolites to influence the expression of cytokine genes in immune cells. For example, a study by Mahmoudi etal., [27] demonstrated that secondary metabolites from Streptomyces calvus enhanced the expression of pro-inflammatory cytokines, such as interleukin-2 and interferon- γ , in human peripheral blood mononuclear cells (PBMCs). This upregulation of pro-inflammatory cytokines suggests a potential activation of the immune response by Streptomyces compounds [27].

Furthermore, the same study revealed a reduction in the levels of the immunosuppressive cytokine interleukin-10 in PBMCs treated with *Streptomyces* calvus secondary metabolites. This finding indicates a dual impact on the immune system, promoting pro-inflammatory responses while mitigating immunosuppressive signals, which could contribute to a balanced and controlled immune modulation [27,28].

The observed concentration-dependent increase in PBMC proliferation in response to *Streptomyces* metabolite treatment also adds another layer to the immunomodulatory mechanisms. This suggests that *Streptomyces* compounds may not only influence cytokine expression but also actively participate in the regulation of immune cell proliferation [27].

While the exact molecular pathways involved in *Streptomyces* immunomodulation are still a subject of ongoing research, these findings collectively highlight the complex and multifaceted nature of Streptomyces-derived compounds in modulating the immune response. The ability of *Streptomyces* to both enhance pro-inflammatory signals and reduce immunosuppressive cues showcases its potential as a source of robust immunomodulators, offering promising avenues for the development of novel therapeutic strategies [27]. Figure 6 illustrate the potentials of *Streptomyces* genus as a source of probiotics.

Enhanced Immune Response:

Streptomyces-derived immunomodulatory compounds have been found to enhance the body's innate and adaptive immune responses. By modulating the activity of immune cells such as macrophages, dendritic cells, and T lymphocytes, these compounds contribute to an augmented defense against pathogens [29]. This enhanced immune response is particularly valuable in scenarios where the immune system requires reinforcement.

Management of Inflammatory Conditions:

The immunomodulatory potential of *Streptomyces* extends to the management of inflammatory conditions. In diseases characterized by excessive inflammation, such as autoimmune disorders, compounds derived from *Streptomyces* play a role in dampening the inflammatory response. This anti-inflammatory action is pivotal in preventing tissue damage and alleviating symptoms associated with dysregulated immune responses [30].

Versatility in Disease Management:

The immunomodulatory properties of *Streptomyces* position it as a versatile tool in addressing a spectrum of diseases marked by dysregulated immune responses. Conditions such as rheumatoid arthritis, inflammatory bowel diseases, and certain allergic disorders may benefit from interventions involving Streptomyces-derived compounds [30]. This versatility opens up new

avenues for therapeutic strategies that target the underlying immune dysregulation in diverse clinical scenarios.

Limitations of *Streptomyces* and its bioactive compounds as a therapeutic agent

The inconsistency in the synthesis of secondary metabolites among various strains and under varying environmental circumstances is a major drawback of Streptomyces, despite its tremendous potential in medicinal applications due to its bioactive chemicals. Significant genetic variety among Streptomyces species results in variations in the kinds and amounts of bioactive chemicals that they produce. This fluctuation can make it difficult to standardise medicinal formulations and guarantee that products made from Streptomyces will always be efficacious in different batches. Further impeding efforts to optimise and scale up production for commercial application are the intricate regulatory processes governing the secondary biosynthesis of metabolites in Streptomyces, which are not well understood. These restrictions show that to fully utilise Streptomyces and its bioactive chemicals for therapeutic purposes, more investigation and development are required. This includes tackling issues of variability and scalability in drug production.

Antibiotic compound	Streptomyces species	Application
1,4-Dihydroxy-2-(3-hydroxybutyl)- 9,10-anthraquinone 9,10 anthrac	Streptomyces sp. RAUACT-1	Antibacterial
1,8-Dihydroxy-2-ethyl-3- methylanthraquinone	Streptomyces sp.	Antitumor
2-Allyloxyphenol	Streptomyces sp.	Antimicrobial; food preservative; oral disinfectant
Anthracyclines	S. galileus	Antitumor
Arenimycin	S. arenicola	Antibacterial; anticancer
Avermectin	S. avermitilis	Antiparasitic
Bafilomycin	S. griseus, S. halstedii	ATPase; inhibitor of microorganisms, plant and animal cells
Bisanthraquinone	Streptomyces sp.	Antibacterial
Carboxamycin	Streptomyces sp.	Antibacterial; anticancer
Chinikomycin	Streptomyces sp.	Anticancer
Chloramphenicol	S. venezuelae	Antibacterial; inhibitor of protein biosynthesis
Chromomycin B, A2, A3	S. coelicolor	Antitumor
Daryamides	Streptomyces sp.	Antifungal; anticancer
Elaiomycins B and C	Streptomyces sp. BK 190	Antitumor
Frigocyclinone	S. griseus	Antibacterial
Glaciapyrroles	Streptomyces sp.	Antibacterial
Hypromycin	S. hvgroscopicus	Antimicrobial: immunosuppressive
Laiollamycin	S. nodosus	Antibacterial
Lincomycin	S. lincolnensis	Antibacterial; inhibitor of protein biosynthesis
Mitomycin C	S. lavendulae	Antitumor; binds to double-stranded DNA
Pacificanones A and B	S. pacifica	Antibacterial
Piericidins	Streptomyces sp.	Antitumor
Proximicins	Verrucosispora sp.	Antibacterial; anticancer
Pristinamycine	S. pristinaespiralis	Antibacterial
Rapamycin	S. hygroscopicus	Immunosuppressive; antifungal
Resistoflavin methyl ether	Streptomyces sp.	Antibacterial; antioxidative
Saliniketal	S. arenicola	Cancer; chemoprevention
Salinispyrone	S. pacifica	Unknown
Salinispyrone A and B	S. pacifica	Mild cytotoxicity
Salinosporamide A	Salinispora tropica	Anticancer; antimalarial
Salinosporamide B and C	S. tropica	Cytotoxicity
Sesquiterpene	Streptomyces sp.	Unknown
Staurosporinone	Streptomyces sp.	Antitumor; phycotoxicity
Streptokordin	Streptomyces sp.	Antitumor
Streptomycin	S. griseus	Antimicrobial
Streptozotocin	S. achromogenes	Diabetogenic
Tetracyclines	Streptomyces achromogenes; S. rimosus	Antimicrobial
Tirandamycins	Streptomyces sp.	Antibacterial
Valinomycin	S. griseus	Ionophor; toxic for prokarotes, eukaryotes

Table 1. List of antibiotics produced by different Actinobacteria and their applications. Source: Mohammed et al. [9].



Figure 1. Light Microscopy images of Streptomyces species. Source Rengasamy and Ushadevi [6].

Figure 2.Structure of a modular type I PKS. Note: KS, ketosynthase; AT, acyl transferase; KR, ketoreductase; ACP, acyl carrier protein; TE, Thioesterase; DH, dehydrate [12].







Source: Bashir et al. [13].





Source: Christine [14].

Figure 5. Bleomycin. Molecular model of the anti-cancer drug bleomycin (C55.H84.N17.O21.S3), a glycopeptide antibiotic produced by the bacterium *Streptomycesverticillus*.



Adapted from Science Photo Library(https://www.alamy.com/stock-photo-bleomycin-molecular-model-of-the-anti-cancer-drug-bleomycin-c55h84n17o21s3-126899813.html)



Figure 6. Streptomyces genus as a source of probiotics and its potential for its use in health.

Source: Cuozzoet al. [28].

Conclusion:

In conclusion, *Streptomyces* manifests not only considerable antimicrobial and anticancer potential but also a noteworthy capacity for immunomodulation. The modulation of immune responses by compounds derived from *Streptomyces* offers a promising avenue for therapeutic development. As research in this field advances, the immunomodulatory effects of *Streptomyces* are poised to be more comprehensively elucidated, paving the way for innovative and precisely targeted interventions in the management of diseases characterized by immune dysregulation.

This comprehensive review has delved into the multifaceted therapeutic potential of Streptomyces, focusing on its biological diversity, secondary metabolites, and immunomodulatory effects. With over 500 identified species, Streptomyces has emerged as a prolific source of bioactive compounds, exemplifying antibacterial, antifungal, antiviral, and anticancer properties. The primary mechanism driving Streptomyces' therapeutic efficacy resides in the production of secondary metabolites, harnessed for the development of novel drugs.

The antibacterial potential of *Streptomyces*, illustrated by antibiotics such as streptomycin and tetracycline, underscores its significance in addressing bacterial infections, particularly in the era of escalating antibiotic resistance. Additionally, *Streptomyces* compounds have demonstrated notable antifungal activities, contributing to their role in the treatment of mycotic diseases.

Furthermore, Streptomyces-derived compounds exhibit promise in cancer therapeutics, as evidenced by Streptozotocin's ability to induce apoptosis in pancreatic beta-cells, rendering it a valuable asset in the treatment of pancreatic cancer.

Beyond its direct antimicrobial and anticancer effects, *Streptomyces* has garnered recognition for its immunomodulatory properties. Compounds derived from *Streptomyces* modulate the immune response, augmenting the body's ability to combat infections and manage inflammatory conditions. This review accentuates the versatility of *Streptomyces* in therapeutic applications, encompassing its direct antimicrobial and anticancer effects to its immunomodulatory potential. Streptomyces-derived compounds present a rich source for drug discovery, opening new avenues for addressing diseases characterized by dysregulated immune responses.

Looking forward, ongoing research in this field is poised to unveil additional bioactive compounds and further elucidate the mechanisms underpinning *Streptomyces*' therapeutic effects. This exploration holds promise for the development of innovative and precisely targeted therapeutic interventions, potentially revolutionizing the landscape of modern medicine.

References

- 1- Donald L, Pipite A, Subramani R, Owen J, Keyzers RA, Taufa T. *Streptomyces*: Still the biggest producer of new natural secondary metabolites, a current perspective. Microbiol Res2022;13(3):418-465.
- 2- Ribeiro da Cunha B, Fonseca LP, Calado CR. Antibiotic discovery: where have we come from, where do we go?. Antibiotics2019;8(2):45.
- 3- Martins NDRC, Rodrigues da Silva A, Ratcliffe N, Evangelho VGO, Castro HC, Quinn GA. *Streptomyces*: a natural source of anti-Candida agents. J Med Microbiol2023;72(11):001777.
- 4- Rajappa R, Sireesh D, Salai MB, Ramkumar KM, Sarvajayakesavulu S, Madhunapantula SV. Treatment with naringenin elevates the activity of transcription factor Nrf2 to protect pancreatic β-cells from streptozotocin-induced diabetes in vitro and in vivo. Front Pharmacol2019;9:1562.
- 5- Sawant SS, Patil SM, Gupta V, Kunda NK. Microbes as medicines: harnessing the power of bacteria in advancing cancer treatment. Int J Mol Sci2020;21(20):7575.
- 6- Rengasamy S. and Ushadevi T. Isolation and screening of glucose isomerase producing

marine *Streptomyces* species for fructose production. 2014. Der Pharma Chemica 6(5):215-219

 7- Lacey HJ, Rutledge PJ. Recently Discovered Secondary Metabolites from *Streptomyces* Species. *Molecules*. 2022; 27(3):887.

https://doi.org/10.3390/molecules27030887

- Mondal H, Thomas J, Amaresan N. Antibacterial Activity and Extraction of Bioactive Compound from Actinomycetes. Aqua CulMicrobiol. 2023(8):195-198. doi:10.1007/978-1-0716-3032-7_26
- 9- Donald L, Pipite A, Subramani R, Owen J, Keyzers RA, Taufa T. *Streptomyces*: Still the Biggest Producer of New Natural Secondary Metabolites, a Current Perspective. *Microbiol Res.* 2022; 13(3):418-465.https://doi.org/10.3390/microbiolres1 3030031
- 10-Pancu DF, Scurtu A, Macasoi IG, Marti D, Mioc M, Soica C et al.Antibiotics: conventional therapy and natural compounds with antibacterial activity—a pharmacotoxicological screening. Antibiotics.2021;10(4):401.
 - 11- Harir M, Bendif H, Bellahcene M, Fortas Z, Pogni R. *Streptomyces* secondary metabolites. In Basic Biology and Applications of Actinobacteria. Publisher: Intechopen; 2018; 6: 99-122. DOI: 10.5772/intechopen.79890
 - 12-Ridley CP, Khosla C.Polyketides. Encyclopedia of Microbiology, Third Edition. Published online January 1, 2009:472-481. doi:10.1016/B978-012373944-5.00158-9

- 13-Bashir AS, Basharat AB, Umar M, and Wajahat RM. Development of New Therapeutics to Meet the Current Challenge of Drug Resistant Tuberculosis. Curr Pharm Biotech 2022; 21(4):480 -500 DOI:10.2174/1389201021666200628021702
- 14-Sant DG, Tupe SG, Ramana C V., Deshpande M V. Fungal cell membrane-promising drug target for antifungal therapy. *J Appl Microbiol*. 2016;121(6):1498-

1510.doi:10.1111/JAM.13301.

- 15-Chawla M, Verma J, Gupta R, Das B. Antibiotic potentiators against multidrugresistant bacteria: Discovery, development, and clinical relevance. Front Microbiol2022;13:887251.
 - 16- Rasheed S. Exploring the mode of action of novel antibacterial agents : natural product antibiotics elansolids and peptideconjugated daptomycin derivatives. 2022(6):456-471. doi:10.22028/D291-37493
- 17-Giuliodori AM, Spurio R, Milón P, Fabbretti A. Antibiotics targeting the 30S ribosomal subunit: a lesson from nature to find and develop new drugs. Curr Top Med Chem 2018;18(24):2080-2096.
- 18-Chukwudi CU. rRNA binding sites and the molecular mechanism of action of the tetracyclines. Antimicrob Agents Chemother2016;60(8):4433-4441.
- 19-McCoy LS, Xie Y, Tor Y. Antibiotics that target protein synthesis. Wiley Interdiscip Rev RNA. 2011;2(2):209-232.
- 20-Álvarez-Martínez FJ, Barrajón-Catalán E, Micol V. Tackling antibiotic resistance with compounds of natural origin: A comprehensive review. Biomedicines. 2020;8(10):405.
- 21-Alam K, Mazumder A, Sikdar S, Zhao YM, Hao J, Song Cet al.*Streptomyces*: The

biofactory of secondary metabolites. Front Microbiol2022;13:968053.

- 22-English BK, Gaur AH. The use and abuse of antibiotics and the development of antibiotic resistance. In: Hot Topics in Infection and Immunity in Children VI; 2010.
- 23-Khan MI, Gulzar S, Majid A, Noor I. A computational study of intercalation of streptozotocin (STZ) into DNA base pairs. J Mol Model2021;27:1-8.
- 24-Fadzelly AM, Asmah R, Fauziah O. Effects of Strobilanthes crispus tea aqueous extracts on glucose and lipid profile in normal and streptozotocin-induced hyperglycemic rats. Plant Foods Hum Nutr2006;61:6-11.
- 25-El-Huneidi W, Anjum S, Bajbouj K, Abu-Gharbieh E, Taneera J. The coffee diterpene, kahweol, ameliorates pancreatic β-cell function in streptozotocin (STZ)-treated rat INS-1 cells through NF-kB and p-AKT/Bcl-2 pathways. Molecules2021;26(17):5167.
- 26-Chen HW, Yang MY, Hung TW, Chang YC, Wang CJ. Nelumbo nucifera leaves extract attenuate the pathological progression of diabetic nephropathy in high-fat diet-fed and streptozotocin-induced diabetic rats. J Food Drug Anal2019;27(3):736-748.
- 27-Mahmoudi F, Baradaran B, Dehnad A, Shanehbandi D, Mohamed Khosroshahi L, Aghapour M. The immunomodulatory activity of secondary metabolites isolated from *Streptomyces* calvus on human peripheral blood mononuclear cells. Br J Biomed Sci2016;73(3):97-103.
- 28-Cuozzo S. de Moreno de LeBlanc A., LeBlanc J.G., Hoffmann N., and Tortella G.R. *Streptomyces* genus as a source of probiotics and its potential for its use in health. Microbiological Research, 2023, 127248.

- 29-Cot M, Ray A, Gilleron M, Vercellone A, Larrouy-Maumus G, Armau E, et al. Lipoteichoic acid in *Streptomyces* hygroscopicus: structural model and immunomodulatory activities. PLoS One. 2011;6(10):e26316.
- 30-Mishra BB, Tiwari VK. Natural products: an evolving role in future drug discovery. Eur J Med Chem. 2011;46(10):4769-4807.

Ali MudeAS, NageyeY, BelloK. Therapeutic application of Streptomyces: A choice alternative to modern therapies. Microbes Infect Dis 2025; 6(2): 916-928.