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Review Article

# Important antiviral properties of *Streptomyces* species compounds

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ABSTRACT

*Streptomyces* species, a subgroup of Actinomycetes bacteria, have been analysed for their antiviral properties. These bioactive secondary metabolites, which have a broad spectrum of chemical structures and strong biological activity, offer a promising opportunity for new antiviral therapeutics against various viral infections. These metabolites target different stages of viral replication or interactions with host cells, making them important for biological research and pharmaceutical development. *Streptomyces* bacteria contain numerous antiviral mechanisms that inhibit viral infections at different stages of the viral life cycle. *Streptomyces* and other actinomycetes can improve the health of people with viruses, and recent research suggests that combining *Streptomyces* with other bacterial species could improve overall health and regulate infections. This emphasises the importance of comprehensive approaches to combating viral infections and research into natural products. Further research into multispecies combinations of *Streptomyces* and other bacterial species is needed to fully utilise their therapeutic potential against viral diseases.



## 1. Introduction

The investigation natural compounds from *Streptomyces* species; a subgroup of Actinomycetes bacteria, for antiviral properties offers a possible way to combat viral infections. *Streptomyces* species produce various bioactive secondary metabolites, some of which have antiviral effects.[1] These microbial metabolites offer a promising opportunity for new antiviral therapeutics against a variety of viral infections. Several *Streptomyces* species produce bioactive secondary metabolites that exhibit a broad spectrum of chemical structures and potent biological activity. These chemicals show potential for fighting viral infections by targeting various stages of viral replication or interactions with host cells.[2] These metabolites, with their various chemical structures and biological activity, present promising pathways for the creation of new antiviral treatments. Harnessing the antiviral capability of *Streptomyces*-derived chemicals is a huge step forward in the ongoing battle against viral infections, underscoring the necessity of looking to natural sources for novel solutions to global health problems.[3] The antiviral properties of these metabolites make them important for biological research and pharmaceutical development. These chemicals are promising in the fight against influenza viruses, herpes viruses and HIV by targeting viral replication or interactions between host cells. *Streptomyces* species produce bioactive secondary metabolites that are not only of biomedical, but also of economic and industrial use.[4,5] The diverse chemical compositions and potent biological properties of Actinomycetes have applications in pharmacy, agriculture and biotechnology,

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all of which aim to improve human health and well-being by utilizing microbial diversity. Actinomycetes are therefore important partners in humanity's ongoing endeavors' to harness the potential of microbial ecosystems for societal progress. The use of actinomycete-derived molecules emphasizes their central role in various fields and highlights their indispensable contribution to the search for solutions that benefit both human well-being and global progress.[6] *Streptomyces* species are known for their ability to synthesise a wide range of natural products that exhibit remarkable structural diversity. These compounds include macrolides, tetracyclines, aminoglycosides, glycopeptides, ansamycins and terpenes.[7,8] *Streptomyces hygroscopicus* in particular stands out as an outstanding producer, secreting around 180 metabolites with different bioactivities. These metabolites hold immense potential for various applications in medicine, agriculture and industry and contribute to advances in drug development, agricultural solutions and industrial processes.[9] Current research highlights the importance of *Streptomyces* as a source of bioactive chemicals and their potential to improve human health by tapping into the chemical diversity found in nature.

## 2. *Streptomyces* as a Natural Healer

*Streptomyces* bacteria stand out as natural healers, possessing a remarkable ability to produce bioactive compounds with therapeutic potential. These microorganisms have garnered attention for their diverse repertoire of secondary metabolites, many of which exhibit powerful medicinal properties. *Streptomyces*-derived compounds have been instrumental in the development of numerous antibiotics, such as streptomycin and erythromycin, which have revolutionized the treatment of bacterial infections.[10] Beyond antibiotics, *Streptomyce*s metabolites also demonstrate activity against other pathogens, including viruses and fungi, making them valuable candidates for antiviral and antifungal therapies. Moreover, these bioactive compounds hold promise in combating cancer, inflammation, and other complex diseases, showcasing the versatility of *Streptomyces* in medical research. By tapping into the natural capabilities of *Streptomyces*, researchers continue to uncover novel therapeutic agents with diverse mechanisms of action and improved efficacy. As such, *Streptomyces* emerges not only as a natural healer but also as a source of inspiration for the development of innovative medicines to address a wide range of health challenges.[8,11] *Streptomyces bacteria* show different behaviours when confronted with viral infections, demonstrating their exceptional adaptability and defensive capabilities. These chemicals can interfere with various stages of viral replication, such as viral entry, genome replication and assembly, thereby preventing the replication and spread of the virus. In addition, *Streptomyces* species use sophisticated quorum sensing mechanisms to communicate and coordinate their responses to viral threats (Sarveswari and Solomon, 2019). This communication network allows them to alter their gene expression and metabolic processes in real time, enhancing their ability to fight viral infections.

*Streptomyces* bacteria can also influence the host's immune response to viral infections and thus possibly strengthen the host's defences against invading viruses.[5,8] The bacteria help the host to build a strong antiviral defence by increasing the production of antimicrobial peptides, enhancing phagocytosis and controlling the production of cytokines. They compete with viruses for important nutrients and resources in their environment. The bacteria have potential to reduce the viral load in their environment by competing with viruses for these nutrients.[11,12] They may also have built-in or learned methods to fight viral infections, such as restriction modification systems, CRISPR-Cas systems or the production of viral defence proteins. These processes provide additional layers of defence against viral threats and demonstrate the plasticity and tenacity of *Streptomyces* bacteria in the fight against viral infections. *Streptomyces*' broad set of behaviours highlights their importance as beneficial friends in the ongoing war against viral infections.[3,13]

## 3. Potential Antiviral Compounds from *Streptomyces*

*Streptomyces* bacteria contain a wealth of potentially antiviral chemicals, including a variety of secondary metabolites that promise efficacy against viral infections. These chemicals, derived from different *Streptomyces* species, have a variety of mechanisms that target different stages of viral replication or the host cell. Many viruses, including herpesviruses, HIV-1 and influenza A virus, can be killed by compounds derived from *Streptomyces*.[8] These include polyene antibiotics (such as streptovaricins) and cyclic depsipeptides (such as azalomycins).[14] Many complex polyketides, such as napyradiomycins, and antibiotics, such as salinomycin, have the potential to prevent viral entry or replication.[15] The discovery of these antiviral molecules underscores the need to look to nature for novel drugs, and *Streptomyces* is emerging as a promising option for the development of new antiviral drugs. Among these compounds are:

To fully exploit the potential of these molecules, their mode of action, efficacy and safety profile need to be further investigated the in treating viral infections and addressing global health concerns. The bacteria represent a rich source of potential antiviral compounds, with numerous secondary metabolites showing promising activity against viral infections (Table 1, Figure 1).

**Table 1:** List of natural compounds and its role against viral pathogens

| Compounds | *Streptomyces* sp. | Role against virus | References |
|---|---|---|---|
| Avilamycin | *Streptomyces viridochromogenes* | Inhibit the transcription in HIV-1 and other retroviruses | 16,17 |
| Azalomycin | *Streptomyces hygroscopicus* | These compounds are cyclic depsipeptides show its antiviral activities against Herpes simplex virus (HSV) -1 and -2 | 18–20 |
| Herboxidiene | *Streptomyces chromofuscus* | Inhibits the replication of HIV-1 | 21,22 |
| Madumycin | *Streptomyces venezuelae* | Inhibit the DNA replication in HSV-1 | 23,24 |
| Napyradiomycins | *Streptomyces kebangsaanensis* WS-68302 | Blocking the entry of HIV-1 in host cell | 25 |
| Nourseothricin | *Streptomyces noursei* | Inhibiting protein synthesis in adenoviruses, herpesviruses, and poxviruses during infection | 26–28 |
| Salinomycin | *Streptomyces albus* | Restrict the growth of RNA viruses, including influenza A virus and Zika virus | 29,30 |
| Streptovaricins | *Streptomyces griscus* | Exhibit antiviral activity against herpes simplex virus (HSV) and vaccinia virus by disrupting viral membrane integrity | 31,32 |

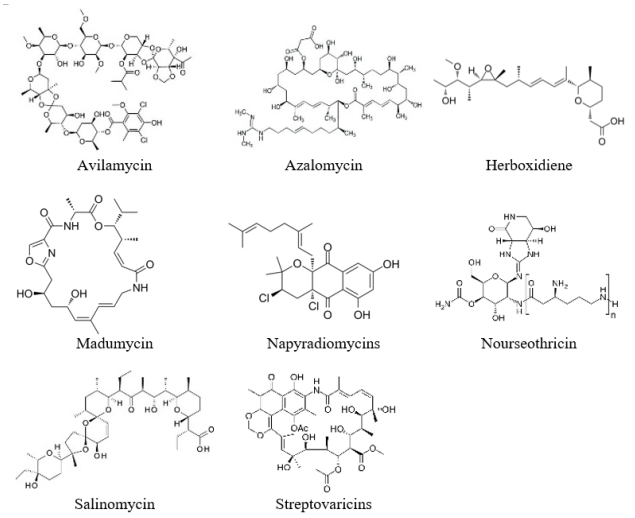


**Figure 1:** Compounds (Table 1)

## 4. Antiviral Mechanism of Secondary Metabolites from *Streptomyces*

The secondary metabolites of *Streptomyces* have numerous antiviral mechanisms that inhibit viral infections at different stages of the viral life cycle. *Streptomyces*-derived secondary metabolites are known to have a broad spectrum of structures and potent biological activity.[2] They could be used for the production of new antiviral drugs (Figure 2). Preventing viruses from entering host cells is one of the most important antiviral mechanisms. To prevent viruses from attaching to and entering cells, some secondary metabolites produced by *Streptomyces* species bind to specific proteins or receptors on their surface. These chemicals block the initial stages of infection where the virus attempts to infect the host cells, preventing the virus from replicating and spreading. They can also target the pathways that the virus uses to replicate in the infected cells. These substances have the potential to block viral enzymes that are essential for processes such as genome replication, transcription and protein synthesis.[33] To illustrate, there are *Streptomyces* compounds that can interfere with the process of viral particle formation by interfering with viral DNA polymerase and RNA-dependent RNA polymerase. This can interfere with viral nucleic acid synthesis. These drugs effectively suppress viral replication and spread and interfere with essential processes of viral replication. These agents not only directly target viral components, but also enhance the host's innate immune response to viral infections through immunomodulatory actions. By acting on antiviral signalling pathways, these chemicals can promote the synthesis of interferons and other antiviral cytokines that inhibit viral replication.[34] In addition, certain *Streptomyces* metabolites increase the phagocytic activity of immune cells, which helps the body to remove virus-infected cells and viral particles. The compounds also cause apoptosis in infected cells.[35] These chemicals inhibit the replication and spread of the virus in the host by triggering apoptosis, which eliminates virus-infected cells before viral replication can take place. This process not only eliminates virus-infected cells but also prevents the release of new infectious virus particles. In combination with conventional antiviral drugs, the secondary metabolites obtained from *Streptomyces* can have additive or synergistic effects.[36] This method of combination therapy has the potential to increase antiviral efficacy, reduce drug resistance and increase antiviral activity against a variety of viral infections. The

metabolites have a multi-pronged attack against viruses, targeting their entry, replication, immune evasion, survival of infected cells and dissemination. The processes described here show that *Streptomyces*-derived drugs are promising for new antiviral treatments due to their broad spectrum of activity and low risk of resistance.

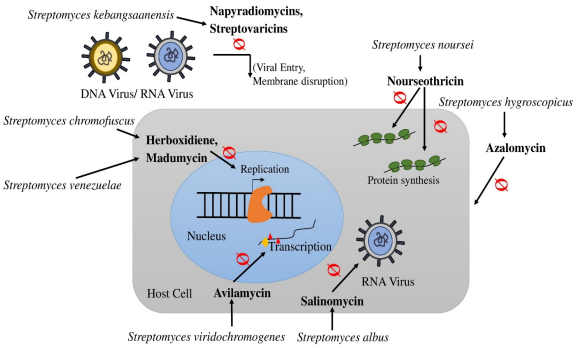


**Figure 2:** Inhibitory mechanism of natural compounds against viral pathogens

## 5. Futuristic Prospects of *Streptomyces* in Viral Infection

Members of the actinomycete class, especially *Streptomyces*, are often neglected, although the metabolites of many bacterial species are widely studied and used in the treatment of viral infections.[37] New research has shown that *Streptomyces* and other actinomycetes can improve the health of people who are sick with viruses. *Streptomyces*, whether studied individually or in combination, has been the main focus of previous research. Nevertheless, a number of original studies published recently have highlighted multi-species techniques as important environmentally friendly solutions for infection management. *Streptomyces* is a bacterial species, but it has the potential to unlock new health benefits and natural chemicals when combined with other bacterial species. A more holistic approach is needed to combat viral infections, and this trend towards using mixtures of different species is bringing to light the untapped potential of actinomycetes in medicine.

## 6. Conclusion

Actinomycetes, especially *Streptomyces*, are usually neglected in the treatment of viral infections, although many bacterial metabolites have been studied. Recent research suggests that combining *Streptomyces* with other bacterial species could improve overall health and regulate infections. Earlier studies focused on single or multiple *Streptomyces* strains, while today's work focuses on multiple species. This emphasises the importance of comprehensive approaches to fighting viral infections and exploring natural products. By using actinomycetes in combination therapies, unimagined health benefits can be discovered and environmentally sustainable approaches to treating viral infections can be created. Therefore, it is necessary to conduct further research on multispecies combinations of *Streptomyces* and other bacterial species to fully exploit their therapeutic potential against viral diseases.

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## 8. Conflict of Interest

None

## 9. Ethical Clearance

None

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