International Journal of Agriculture and Biosciences 2026 15(2): 614-620.
https://doi.org/10.47278/journal.ijab/2025.185

RESEARCH ARTICLE
eISSN: 2306-3599; pISSN: 2305-6622

# Physical and Chemical Characterization of the Polyene Antibiotic Roseofungin Isolated From *Streptomyces Roseoflavus V. Roseofungini As-20*

Baiken Baimakhanova [1], Amankeldi Sadanov [1], Asya Balgimbayeva [1], Lyudmila Trenozhnikova [1], Vladimir Berezin [1], Olga Lakh [1], Saltanat Orazymbet [1], Andrey Bogoyavlenskiy [1], Erik Shorabaev [1], Gul Baimakhanova [1], Alma Amangeldi [1], Aibat Ibraimov [1], Aigul Amitova [3] and Gulzat Aitkaliyeva [2,*]

[1]Research and Production Center for Microbiology and Virology LLC, Kazakhstan
[2]Satbayev University, Kazakhstan
[3]Astana International University, Astana, Kazakhstan
*Corresponding author: g.aitkaliyeva@satbayev.university

## ABSTRACT

The purpose of this study was to investigate the physicochemical properties of the polyene antibiotic Roseofungin, isolated from Streptomyces roseoflavus var. roseofungini AS-20.14, to assess its potential as an antifungal agent. Roseofungin was characterized using UV–VIS spectrophotometry, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), infrared (IR) spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy. These techniques were employed to analyze the antibiotic's thermal stability, absorption spectra, and molecular structure. The UV-VIS spectra revealed two maxima at 260nm and 362nm, typical of carbonyl-conjugated pentaenes. TGA and DSC analyses indicated low thermal stability, with significant mass loss at higher temperatures. The IR spectrum confirmed the presence of hydroxyl and carbonyl groups, while NMR spectroscopy supported the structural assignment of Roseofungin. The antibiotic demonstrated broad-spectrum antifungal activity and lower toxicity compared to other polyenes. The study confirms the potential of Roseofungin as an effective antifungal agent, particularly against dermatophytes and molds. Its physicochemical properties and lower toxicity position it as a promising candidate for further research and development in antifungal therapies, especially for drug-resistant fungal infections.

**Keywords:** Antifungal activity; Dermatophytes; Molds; Polyenes; Roseofungin structure.

**Article History**
Article # 25-407
Received: 18-Sep-23
Revised: 23-Sep-23
Accepted: 14-Oct-25
Online First: 03-Nov-25

## INTRODUCTION

Bacteria of the genus *Streptomyces* are known for their ability to produce antibiotics, are responsible for 99% of known antimicrobial compounds, and dominate the production of antimicrobial drugs (Odumosu et al., 2017; Alam et al., 2022; Donald et al., 2022).

Polyene antibiotics are a well-studied class of antifungal drugs used in clinical practice today (Vanreppelen et al., 2023; Ngece et al., 2024; Quinn & Dyson, 2024). The most well-known polyene antimycotics included in the World Health Organization's List of Essential Medicines are amphotericin B, nystatin and natamycin (World Health Organization, 2019; Haro-Reyes et al., 2022; Akinosoglou et al., 2024).

The structure of polyene antibiotics contains a hydrophobic polyene "tail" and a hydrophilic "head" with a polyol chain (Zotchev, 2003), where hydroxyl groups give the molecule an amphipathic character (Guo et al., 2021; Haro-Reyes et al., 2022). Depending on the number of conjugated double bonds, polyenes can be divided into trienes, tetraenes, pentaenes, hexaenes, heptaenes, etc (Li et al., 2021; Maia et al., 2021; Zhao et al., 2022).

Polyenes have a wide spectrum of antifungal activity against yeasts, filamentous fungi and endemic dimorphic fungi. *Candida, Cryptococcus, Aspergillus, Mucor, Rhizopus, Histoplasma, Coccidioides* and *Blastomyces* are sensitive to the action of polyenes (Johnson, 2021; Jauregizar et al., 2022; Akinosoglou et al., 2024).

It is generally accepted that the primary antifungal mechanism of polyene drugs depends on interactions between antibiotic molecules and fungal cell membrane ergosterol via the polyene region of the macrolactone core (Anderson et al., 2014; Cafrey et al., 2016; Kim et al., 2018; Pham et al., 2019; Guo et al., 2021; Maji et al., 2023).

**Cite this Article as:** Baimakhanova B, Sadanov A, Balgimbayeva A, Trenozhnikova L, Berezin V, Lakh O, Orazymbet S, Bogoyavlenskiy A, Shorabaev E, Baimakhanova G, Amangeldi A, Ibraimov A, Amitova A and Aitkaliyeva G, 2026. Physical and chemical characterization of the polyene antibiotic roseofungin isolated from *Streptomyces Roseoflavus V. Roseofungini As-20*. International Journal of Agriculture and Biosciences 15(2): 614-620. https://doi.org/10.47278/journal.ijab/2025.185

A Publication of Unique Scientific Publishers

Roseofungin is a pentaene antibiotic from the subgroup of carbonyl-conjugated pentaenes. A number of previous reports (Ermakova et al., 2001; Sadanov et al., 2016a; Sadanov et al., 2020; Abdukhakimova et al., 2021; Bogoyavlenskiy et al., 2023; Yelubayeva et al., 2024) have shown the effectiveness of roseofungin (in concentrations of 0.5-12.5 μg/mL) in suppressing a wide range of pathogens of superficial and deep mycoses - trichophytosis, microsporia, favus, candidiasis, cryptococcosis, sporotrichosis, chromomycosis, aspergillosis, etc., as well as against pathogens of a number of viral infections (Sadanov et al., 2016b; Berezin et al., 2019).

Current research in this article is aimed at the physical and chemical characterization of *roseofungin* isolated from the mycelium of the producer strain Streptomyces roseoflavus v. *roseofungini AS-20.14*.

## MATERIALS & METHODS

The antibiotic roseofungin was obtained by cultivating the streptomycete strain Streptomyces roseoflavus v.roseofungini AS-20.14 (Sadanov et al., 2016b). Fermentation was performed under submerged conditions in a standard actinomycete medium at 28°C for 7 days. The culture broth was filtered, and the biomass was extracted using ethanol. Crude extracts were purified by silica gel column chromatography and recrystallized to yield dry roseofungin. The final product was dried under vacuum at 40°C to constant weight.

Absorption spectra were measured on a UV2600I UV–VIS spectrophotometer (Shimadzu, Japan) using ethanol solutions of roseofungin at concentrations ranging from $2.6 \cdot 10^{-6}$ to $1.2 \cdot 10^{-5}$ mol·L$^{-1}$. Thermogravimetric analysis (TGA) was conducted using a NETZSCH STA 409 instrument at temperatures from 50 to 900°C, with a heating rate of 10 K/min. Differential scanning calorimetry (DSC) was implemented using an SKZ1052B instrument. Heating was performed up to 300°C at a rate of 15°C/min under nitrogen atmosphere.

Infrared spectroscopy measurements were performed on ALPHA II between the range 4000 and 500cm$^{-1}$. NMR spectra of the obtained product were determined on a JNM-ECZS spectrometer.

All experiments were conducted in triplicate using independently prepared batches of roseofungin to ensure reproducibility. No in vitro or in vivo biological assays were carried out in this study; the focus was solely on physicochemical and structural characterization.

### Statistical Analysis

Linear regression analysis was applied to UV-VIS absorption data using Microsoft Excel 2019 to establish the correlation between absorbance and concentration. The regression equation was calculated in the form Y = A + B·X, with a correlation coefficient ($R^2$) of 0.9816 and molar absorptivity (ε) determined to be 6279L·mol$^{-1}$·cm$^{-1}$. All measurements were performed in triplicate, and average values were used for plotting. Standard deviations were calculated for absorbance values, with variability not exceeding 5%.

## RESULTS AND DISCUSSION

The absorption spectra in the UF/VIS region of roseofungin solutions in ethanol (2,6·10-6 to 1,2·10-5 mol·L-1) have two maxima at 260 and 362nm (Fig. 1), which is characteristic of the group of carbonyl-conjugated pentaenes (Hamilton-Miller, 1973).

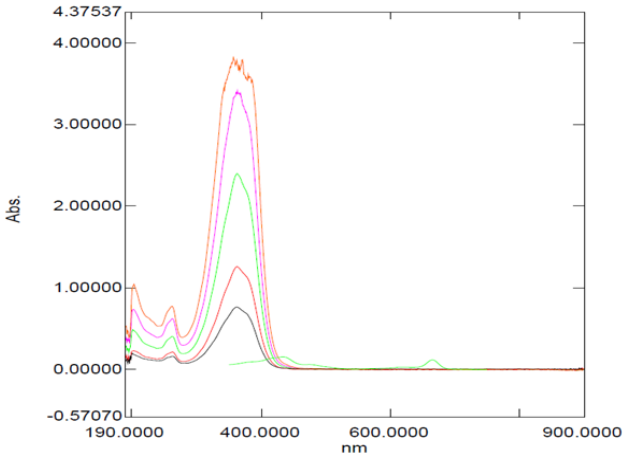


**Fig. 1:** Absorption spectra of the obtained product.

Following the approach described by Brescansin et al. (2013), calibration curves were constructed to assess the relationship between concentration and absorbance, and molar absorption coefficients (ε) were calculated. For this purpose, the corresponding values were calculated for the most intense peak recorded at 362nm using Excel.

Our findings on the two absorption maxima at 260 and 362nm are in agreement with those reported for other polyene macrolides. For example, Zhao et al. (2022) demonstrated that characteristic UV peaks are determined by the conjugated double-bond system and serve as key markers for identifying polyenes. Similarly, Guo et al. (2021) confirmed that such spectral features are closely linked to the amphiphilic nature of these molecules, which enables their interaction with ergosterol in fungal membranes. Thus, the spectral properties of roseofungin are consistent with the modern understanding of polyene structure and mechanism of action.

Linear regression results were established for type Y=A+B*X with a correlation coefficient of 0.9816 and a molar absorptivity (ε) of 6279 l ·mol$^{-1}$ ·cm$^{-1}$ (Table 1).

**Table 1:** Linear regression data of the UV–VIS calibration curve of roseofungin (absorbance vs. concentration, n=3)

| Parameters | Value | Description |
|---|---|---|
| A | 0.0068 | Regression intercept |
| B | 6279 L·mol$^{-1}$·cm$^{-1}$ | Molar absorptivity |
| $R^2$ (Correlation coefficient) | 0.9816 | Determined by linear regression analysis (Microsoft Excel 2019) |

Note: The correlation coefficient ($R^2$) was obtained from a linear regression of absorbance vs. concentration using triplicate measurements.

TGA and DSC methods were used to evaluate the thermal characteristics of the obtained product.

From TGA data it is evident that the obtained product undergoes complex chemical changes upon heating. When the temperature was increased up to 150°C, only

insignificant mass changes were observed on the curve. Changes in the mass of the sample up to 21 % are explained by thermal cracking of polyene chains. The significant mass loss (about 58%) between 300 and 475°C may be due to crosslinking of polyenes (Jia et al., 2016). At 475°C, the thermal processes are almost completed, but the mass loss does not correspond to 100% (Fig. 2).

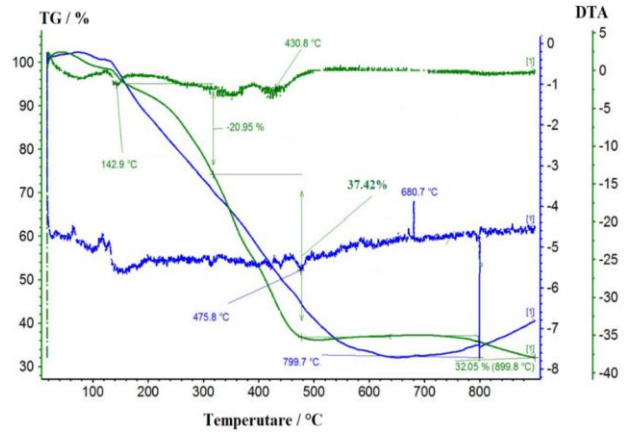


**Fig. 2:** TG analysis of Roseofungin.

In general, the TGA curve of roseofungin indicates a mass loss in the temperature range from 30 to 900°C in the amount of about 68%, indicating low thermostability of the product when exposed to heat, which is probably due to the polyfunctional nature of the structure of the polyene molecule (Łubkowski et al., 1989).

The only one endothermic peak is observed at ~ 45°C, which may indicate the semi-crystalline lattice of the sample. Comparable shifts in UV–Vis absorption maxima were observed by Svirkin et al. (2022) for amphotericin B formulations, highlighting that molecular environment and formulation conditions can significantly influence spectral behavior and stability.

The reduced thermal stability observed in our study corresponds well with recent findings on related macrolide compounds. Pielichowski et al. (2023) reported that thermal degradation of polyenes is typically associated with the breakdown of conjugated double bonds and subsequent crosslinking. At the same time, Maji et al. (2023) showed that even polyenes with limited thermal stability can be effectively stabilized through optimized excipient systems and formulation strategies. These comparisons suggest that the relatively low thermostability of roseofungin does not preclude its clinical application, provided that suitable storage and formulation approaches are applied.

The IR spectrum of the sample (Fig. 3) shows absorption bands in the 1200-700cm$^{-1}$ region which includes 704, 745, 843, 890, 940, 1005, 1090 and 1147cm$^{-1}$ due to different C-C and C-C-H vibrations.

C-C valence vibrations are characteristic of the 1625-1340cm$^{-1}$ range: bands at 1571, 1457 and 1341cm$^{-1}$ are observed for the Roseofungin sample (Agatonovic-Kustrin et al., 2021). The presence of symmetric and asymmetric valence vibrations of alkyl groups CH3 and CH2 is confirmed by intense absorption bands in the range 3000 - 2800cm$^{-1}$ (Aitkaliyeva et al., 2022; Shams et al., 2023): 2923 and 2853cm$^{-1}$. A less intense peak at 1615cm$^{-1}$ is characteristic of the C=C bond in alkenes, which corresponds to the structural formula of roseofungin.

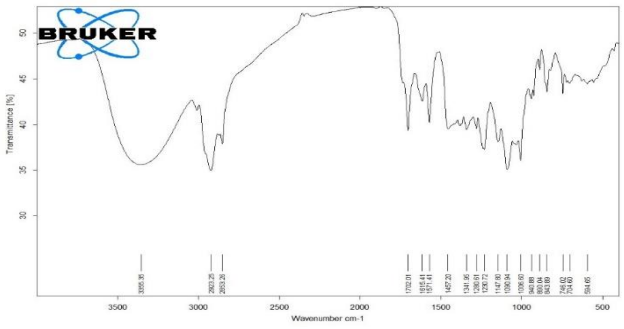


**Fig. 3:** IR spectrum of Roseofungin.

The absorption bands in the region of 1230 and 1280cm$^{-1}$ are characteristic of the vibrations of the C-O group. The intense band at 1702cm$^{-1}$ also indicates the content of carbonyl groups. A broad absorption band at 3355cm$^{-1}$, confirms the presence of OH-group in the composition of roseofungin.

The IR spectral data are confirmed by the results of $^{1}$H and $^{13}$C NMR spectroscopy.

Table 2 summarizes the chemical shift of the $^{1}$H and $^{13}$C signals of Roseofungin.

**Table 2:** $^{1}$H NMR and $^{13}$C NMR data of roseofungin in DMSO

| No. | $^{1}$H NMR | $^{13}$C NMR |
|---|---|---|
| 1 | 1.28m | 19.09s |
| 2 | 1.49 t, 1.67m | 40.00m |
| 3 | 2.94s | 56.56s |
| 4 | 3.80s | 70.31s |
| 5 | 3.87d, 4.81s | 60.72s |

The peak at 1.49ppm is a triplet (Fig. 4) that integrates to 3 protons and correspond to a methyl group. The signal at 1.67ppm indicates a methylene group. The peak at 2.94ppm can be attributed to hydrogen bonded to the –C=O group. The presence of an intense peak at 3.8 and a doublet at 3.87ppm confirms the hydrogen content in the OH group (Wang et al., 2017). The peak at 4.81ppm was due to the presence of protons of the primary hydroxyl group (Sasaki et al., 2000). The results obtained are consistent with the data of $^{13}$C NMR spectroscopy (Fig. 5). Similarly, Hogan et al. (2024) demonstrated that glycoanalogue polyenes with sugar moieties can modulate ergosterol binding and toxicity, suggesting that the structural features of roseofungin, such as hydroxyl substitutions, may also contribute to its favorable safety profile.

The confirmation of hydroxyl and carbonyl groups in the roseofungin structure is consistent with modern structural studies of polyene antibiotics. Maia et al. (2021) emphasized that the number and spatial distribution of hydroxyl groups strongly influence the amphiphilicity and biological activity of polyenes. Furthermore, Jauregizar et al. (2022) highlighted that functional groups directly affect solubility and the interaction of polyenes with fungal membranes. Taken together, our findings reinforce the idea that roseofungin possesses a favorable set of

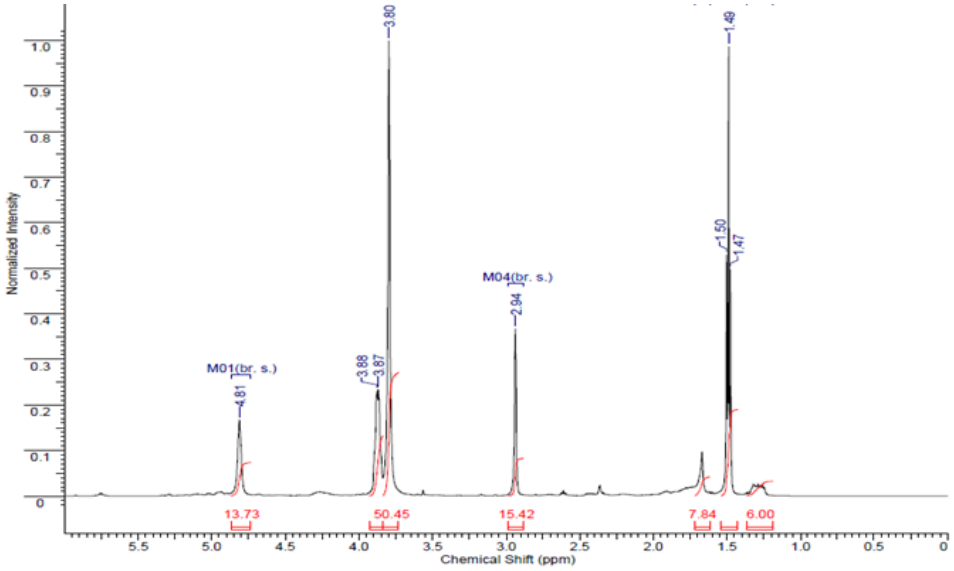


**Fig. 4:** $^{1}H$ NMR spectrum of Roseofungin.

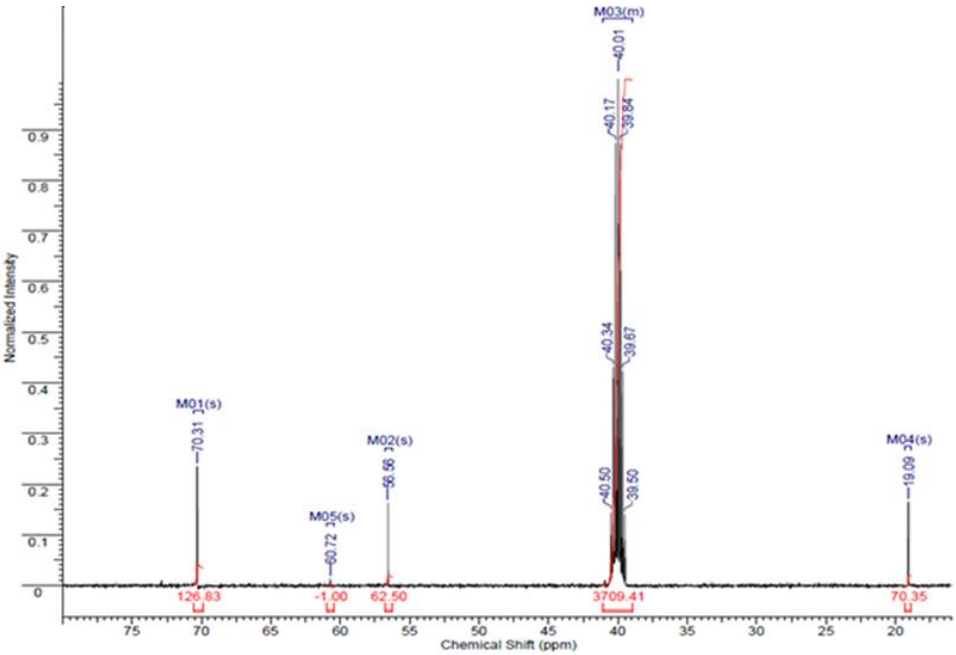


**Fig. 5:** $^{13}C$ NMR spectrum of in DMSO. X-axis: chemical shift (δ, ppm); Y-axis: relative intensity (arbitrary units).

structural features that support effective ergosterol binding and antifungal activity. The increasing prevalence of fungal infections and growing drug resistance pose a serious threat to human health (Zhu et al., 2023).

Despite the fact that most polyene antibiotics used in medicine are active mainly against yeast fungi, roseofungin is also highly active against dermatophytes, mold fungi, and pathogens of tropical mycoses (Brescansin et al., 2021). In addition, it has been found that Roseofungin is more stable, less toxic than other polyene antibiotics, and exhibits antiviral activity against a number of viruses (Brescansin et al., 2013; Sadanov et al., 2016b; Abdukhakimova et al., 2021).

The analysis of physicochemical properties of the antibiotic roseofungin confirmed the presence of carbonyl and hydroxyl groups in the structure of the molecule and it's belonging to carbonyl-conjugated pentaenes. Since it is known that natural and bioengineered polyene macrolide antibiotics and a number of their semi-synthetic derivatives represent a unique basis for studying the relationship between their structure and antifungal activity (Tevyashova et al., 2013), our studies are of scientific interest for further investigation of the mechanism of action of the antibiotic roseofungin.

The physicochemical analysis of Roseofungin reveals crucial insights into its potential as a therapeutic agent, particularly in light of the rising incidence of drug-resistant fungal infections. The UV-VIS absorption peaks at 260 and 362nm, consistent with the spectral signatures of carbonyl-conjugated pentaenes, reinforce its structural classification and functional similarity to other polyene macrolides such as amphotericin B and nystatin (Smitherman, 2016). This spectral behavior, coupled with the intense IR bands corresponding to hydroxyl and carbonyl groups, suggests strong amphiphilic properties, which are known to mediate the insertion of polyenes into fungal membranes and disrupt ergosterol-rich lipid bilayers (Akkerman et al., 2023).

The thermal analysis indicates relatively low thermostability, with major decomposition occurring

between 300–475°C. This is aligned with previous findings on polyene antibiotics, where thermal degradation correlates with the breakdown of conjugated double bonds and the onset of polymer crosslinking (Pielichowski et al., 2023). While low thermal stability might pose formulation challenges, it is not necessarily a limiting factor in clinical settings, where storage conditions are controlled and shelf life can be extended with protective excipients.

NMR data further support the assignment of Roseofungin's structural features, particularly the distribution of hydrogen and carbon atoms in relation to functional groups critical for biological activity. Of particular interest is the presence of the primary hydroxyl group, which may participate in hydrogen bonding and influence solubility and membrane permeability (Grushevenko et al., 2023).

Recent clinical observations confirm the urgent need for antifungal drugs with broader activity profiles. Ngece et al. (2024) reported that many conventional polyenes remain highly effective against Candida spp. but are much less active against dermatophytes and molds. Similarly, Quinn and Dyson (2024) pointed out that increasing resistance among non-Candida pathogens necessitates the development of new molecules with wide-ranging activity. Against this backdrop, our results on roseofungin highlight its potential as a promising candidate for the treatment of dermatophytoses and mold infections, where therapeutic options are currently limited.

Roseofungin's broader spectrum of antifungal activity, especially its effectiveness against dermatophytes and molds, positions it favorably compared to conventional polyenes, which often exhibit limited activity beyond Candida spp. (Ngece et al., 2024). Its reported lower toxicity is significant, given the dose-limiting nephrotoxicity of amphotericin B (Abdel-Hafez et al., 2022). This feature enhances its candidacy for both topical and systemic applications, particularly in immune-compromised patients.

Importantly, the emerging antiviral potential of Roseofungin, as suggested in previous studies and hinted at by structural analogies with known dual-action compounds, opens new research avenues in the context of co-infections and broad-spectrum prophylactic therapy (Gabbianelli et al., 2023).

Equally important is that the reduced toxicity of roseofungin aligns with recent trends in polyene research. Abdel-Hafez et al. (2022) demonstrated the dose-dependent nephrotoxicity of amphotericin B, which continues to limit its therapeutic use. In contrast, Yelubayeva et al. (2024) reported that roseofungin exhibits a more favorable safety profile in preclinical testing. Additionally, Akinosoglou et al. (2024) showed that structural modification of polyenes can effectively lower their cytotoxicity while preserving antifungal activity. These findings support the conclusion that roseofungin meets the key modern criteria for safer antifungal therapy.

Overall, these findings emphasize the therapeutic promise of Roseofungin and justify further exploration into its pharmacodynamics, formulation strategies, and clinical translation, as was underscored by Cavassin et al. (2024), who reported ongoing safety and tolerability challenges with different amphotericin B regimens in clinical practice, highlighting the importance of identifying safer alternatives such as roseofungin.

**Conclusion**

The study provides a comprehensive physicochemical characterization of the compound, highlighting its significant antifungal activity. Authors' results confirm the presence of key functional groups, including hydroxyl and carbonyl groups, and establishe Roseofungin as a carbonyl-conjugated pentaene. The results also demonstrate the compound's relatively low thermal stability and amphipathic nature, which enables its interaction with fungal cell membrane ergosterol, thus disrupting membrane integrity and leading to cell death.

Roseofungin shows a broad spectrum of activity against various fungal pathogens, including yeasts, dermatophytes, and molds, while exhibiting lower toxicity and greater stability compared to other polyene antibiotics. This positions it as a promising candidate for addressing fungal infections, including those caused by drug-resistant strains. Given the increasing prevalence of fungal infections and drug resistance, the findings of this study contribute valuable insights into the potential therapeutic applications of Roseofungin, warranting further exploration into its mechanism of action and clinical efficacy. The study emphasizes the need for continued research in developing effective antifungal therapies based on polyene macrolide structures.

Further research on Roseofungin should investigate its pharmacokinetics, delivery strategies, and mechanisms of antifungal and antiviral action. Evaluation of its efficacy against resistant strains is also necessary.

## DECLARATIONS

**Funding:** The authors declare that no funding was received for this study.

**Acknowledgment:** This research was funded by the Science Committee of the Ministry of Education and Science of the Republic of Kazakhstan, grant number BR21882248, Development and organization of original domestic medicines production according to GMP standards.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Data Availability:** Data available upon request from the corresponding author.

**Ethics Statement:** This study did not involve experiments on humans or live animals. All laboratory procedures were restricted to the physicochemical and structural characterization of the antibiotic Roseofungin derived from Streptomyces roseoflavus var. roseofungini AS-20.14. The microbial strain used in this study is maintained in the

institutional culture collection under standard biosafety conditions at the Research and Production Center for Microbiology and Virology LLC, Kazakhstan under approval reference No. 03-3005/24, dated 20 May 2024.

**Author's Contribution:** AI designed the study. BB, AS and AB (Asya Balgimbayeva) organized the experimental work and collected samples. LT and VB performed laboratory analyses and data processing. OL, AB (Andrey Bogoyavlenskiy), contributed to statistical analysis and interpretation of results. ES, GB, AA prepared the initial draft of the manuscript. GA supervised the project and critically revised the manuscript. All authors read and approved the final version.

**Generative AI Statement:** The authors declare that no Gen AI/DeepSeek was used in the writing/creation of this manuscript.

**Publisher's Note:** All claims stated in this article are exclusively those of the authors and do not necessarily represent those of their affiliated organizations or those of the publisher, the editors, and the reviewers. Any product that may be evaluated/assessed in this article or claimed by its manufacturer is not guaranteed or endorsed by the publisher/editors.

## REFERENCES


Abdel-Hafez, Y., Siaj, H., Janajri, M., Abu-Baker, Y., Nazzal, Z., Hamdan, Z., Adwan, R., Aiesh, B.M., & Anaya, A.I. (2022). Tolerability and epidemiology of nephrotoxicity associated with conventional amphotericin B therapy: A retrospective study in tertiary care centers in Palestine. *BMC Nephrology, 23*, 132. https://doi.org/10.1186/s12882-022-02770-2

Abdukhakimova, D., Markhametova, Z., Shamkeeva, S., Zhulamanova, A., Trenozhnikova, L., Berezin, V., & Azizan, A. (2021). Characterization of extremophilic actinomycetes strains as sources of antimicrobial agents. In C. Barreiro, & J.-L. Barredo (Eds.), Antimicrobial therapies (pp. 59-75). New York: Humana. https://doi.org/10.1007/978-1-0716-1358-0_4

Agatonovic-Kustrin, S., Balyklova, K.S., Gegechkori, V., & Morton, D.W. (2021). HPTLC and ATR/FTIR characterization of antioxidants in different rosemary extracts. *Molecules, 26*(19), 6064. https://doi.org/10.3390/molecules26196064

Aitkaliyeva, G., Yelubay, M., Yerzhanova, D., Ismailova, A., & Massakbayeva, S. (2022). The use of polyethylene terephthalate waste as modifiers for bitumen systems. *Eastern-European Journal of Enterprise Technologies, 3*(6), 117. http://dx.doi.org/10.15587/1729-4061.2022.257782

Akinosoglou, K., Rigopoulos, E.A., Papageorgiou, D., Schinas, G., Polyzou, E., Dimopoulou, E., Gogos, C., & Dimopoulos, G. (2024). Amphotericin B in the Era of New Antifungals: Where Will It Stand?. *Journal of Fungi (Basel, Switzerland), 10*(4), 278. https://doi.org/10.3390/jof10040278

Akkerman, V., Scheidt, H.A., Reinholdt, P., Bashawat, M., Szomek, M., Lehmann, M., Wessig, P., Covey, D.F., Kongsted, J., Müller, P., & Wüstner, D. (2023). Natamycin interferes with ergosterol-dependent lipid phases in model membranes. *BBA Advances, 4*, 100102. https://doi.org/10.1016/j.bbadva.2023.100102

Alam, K., Mazumder, A., Sikdar, S., Zhao, Y.M., Hao, J., Song, C., Wang, Y., Sarkar, R., Islam, S., Zhang, Y., & Li, A. (2022). Streptomyces: The biofactory of secondary metabolites. *Frontiers in Microbiology, 13*, 968053. https://doi.org/10.3389/fmicb.2022.968053

Anderson, T.M., Clay, M.C., Cioffi, A.G., Diaz, K.A., Hisao, G.S., Tuttle, M.D., Nieuwkoop, A.J., Comellas, G., Maryum, N., Wang, S., Uno, B.E., Wildeman, E.L., Gonen, T., Rienstra, C.M., & Burke, M.D. (2014). Amphotericin forms an extramembranous and fungicidal sterol sponge. *Nature Chemical Biology, 10*(5), 400-406. https://doi.org/10.1038/nchembio.1496

Berezin, V., Abdukhakimova, D., Trenozhnikova, L., Bogoyavlenskiy, A., Turmagambetova, A., & Issanov, A. (2019). Antiviral activities of extremophilic actinomycetes extracts from Kazakhstan's unique ecosystems against influenza viruses and paramyxoviruses. *Virology Journal, 150*, 16. https://doi.org/10.1186/s12985-019-1254-1

Bogoyavlenskiy, A.P., Alexyuk, M.S., Sadanov, A.K., Berezin, V.E., Trenozhnikova, L.P., & Baymakhanova, G.B. (2023). Draft genome sequence data of Streptomyces anulatus, Strain K-31. *Data, 8*(8), 131. https://doi.org/10.3390/data8080131

Brescansin, E.G., Portilho, M., & Pessine, F. (2013). Physical and chemical analysis of commercial nystatin. *Acta Scientiarum Health Sciences, 35*(2), 215-221. https://doi.org/10.4025/actascihealthsci.v35i2.12769

Brescansin, F. N., Prochnow, C., Guilardi, L. F., Kleverlaan, C. J., Bacchi, A., Valandro, L. F., & Pereira, G. K. R. (2021). Effect of different surface treatments on optical, colorimetric, and surface characteristics of a lithium disilicate glass–ceramic. Journal of Esthetic and Restorative Dentistry, 33(7), 1017–1028. https://doi.org/10.1111/jerd.12793

Cafrey, P., De Poire, E., Sheehan, J., & Sweeney, P. (2016). Polyene macrolide biosynthesis in streptomycetes and related bacteria: Recent advances from genome sequencing and experimental studies. *Applied Microbiology and Biotechnology, 100*(9), 3893-3908. https://doi.org/10.1007/s00253-016-7474-z

Cavassin, F.B., Magri, M.M.C., Vidal, J.E., Carlesse, F.A.D.M.C., Falci, D.R., Baú-Carneiro, J.L., & Queiroz-Telles, F. (2024). Effectiveness, tolerability, and safety of different amphotericin b formulations in invasive fungal infections: a multicenter, retrospective, observational study. *Clinical Therapeutics, 46*(4), 322-337. https://doi.org/10.1016/j.clinthera.2024.01.011

Donald, L., Pipite, A., Subramani, R., Owen, J., Keyzers, R.A., & Taufa, T. (2022). *Streptomyces*: Still the Biggest Producer of New Natural Secondary Metabolites, a Current Perspective. *Microbiology Research, 13*(3), 418-465. https://doi.org/10.3390/microbiolres13030031

Ermakova, O.S., Tolmacheva, V.P., Levandovskaya, S.V., Khudyakova, S.S., Bogoyavlensky, A.P., Makhmudova, N.R., Tustikbaeva, G.B., Berezin, V.E., Nikitina, E.T., & Daurenbekova, A.S. (2001). Antiviral properties of the pentaene antibiotic roseofungin. *Clinical Microbiology and Antimicrobial Chemotherapy, 3b*(1), 13-14.

Gabbianelli, R., Shahar, E., de Simone, G., Rucci, C., Bordoni, L., Feliziani, G., Zhao, F., Ferrati, M., Maggi, F., Spinozzi, E., & Mahajna, J. (2023). Plant-derived epi-nutraceuticals as potential broad-spectrum anti-viral agents. *Nutrients, 15*(22), 4719. https://doi.org/10.3390/nu15224719

Grushevenko, E.A., Rokhmanka, T.N., Borisov, I.L., Volkov, A.V., & Bazhenov, S.D. (2023). Effect of OH-group introduction on gas and liquid separation properties of polydecylmethylsiloxane. *Polymers, 15*(3), 723. https://doi.org/10.3390/polym15030723

Guo, X., Zhang, J., Li, X., Xiao, E., Lange, J.D., Rienstra, C.M., Burke, M.D., & Mitchell, D.A. (2021). Sterol sponge mechanism is conserved for glycosylated polyene macrolides. *ACS Central Science, 7*(5), 781-791. https://doi.org/10.1021/acscentsci.1c00148

Hamilton-Miller, J.M.T. (1973). Chemistry and biology of the polyene macrolide antibiotics. *Bacteriological Reviews, 37*(2), 166. https://doi.org/10.1128/MMBR.37.2.166-196.1973

Haro-Reyes, T., Díaz-Peralta, L., Galván-Hernández, A., Rodríguez-López, A., Rodríguez-Fragoso, L., & Ortega-Blake, I. (2022). Polyene antibiotics physical chemistry and their effect on lipid membranes; Impacting biological processes and medical applications. *Membranes, 12*(7), 681. https://doi.org/10.3390/membranes12070681

Hogan, M., Song, Y., Muldoon, J., & Caffrey, P. (2024). Generation of New Glycoanalogues of Polyene Antibiotics by Synthetic Biology—Testing Current Technical Boundaries. *SynBio, 2*(1), 31-55. https://doi.org/10.3390/synbio2010003

Jauregizar, N., Quindós, G., Gil-Alonso, S., Suárez, E., Sevillano, E., & Eraso, E. (2022). Postantifungal effect of antifungal drugs against Candida: What do we know and how can we apply this knowledge in the clinical setting? *Journal of Fungi, 8*(7), 727. https://doi.org/10.3390/jof8070727

Jia, P.Y., Feng, G.D., Hu, Y., & Zhou, Y.H. (2016). Synthesis and evaluation of a novel N--P-containing oil-based fire-retardant plasticizer for poly(vinyl chloride). *Turkish Journal of Chemistry, 40*(1), 65-75. https://doi.org/10.3906/kim-1503-2

Johnson, M.D. (2021). Antifungals in clinical use and the pipeline. *Infectious Disease Clinics of North America, 35*(2), 341-371. https://doi.org/10.1016/j.idc.2021.03.005

Kim, H.J., Han, C.Y., Park, J.S., Oh, S.H., Kang, S.H., Choi, S.S., Kim, J.M., Kwak, J.H., & Kim, E.S. (2018). Nystatin-like Pseudonocardia polyene B1, a novel disaccharide-containing antifungal heptaene antibiotic. *Scientific Reports, 8*, 13584. https://doi.org/10.1038/s41598-018-31801-y

Li, J., Sang, M., Jiang, Y., Wei, J., Shen, Y., Huang, Q., Li, Y., & Ni, J. (2021). Polyene-producing Streptomyces spp. from the fungus-growing

termite Macrotermes barneyi exhibit high inhibitory activity against the antagonistic fungus Xylaria. *Frontiers in Microbiology*, *12*, 649962. https://doi.org/10.3389/fmicb.2021.649962

Łubkowski, J., Błazejowski, J., Czerwinski, A., & Borowski, E. (1989). Thermal behaviour and stability of amphotericin B. *Thermochimica Acta, 155*, 29-37. https://doi.org/10.1016/0040-6031(89)87133-3

Maia, L.F., De Oliveira, V.E., Edwards, H.G.M., & De Oliveira, L.F.C. (2021). The diversity of linear conjugated polyenes and colours in nature: Raman spectroscopy as a diagnostic tool. *ChemPhysChem, 22*(3), 231-249. https://doi.org/10.1002/cphc.202000818

Maji, A., Soutar, C.P., Zhang, J., Lewandowska, A., Uno, B.E., Yan, S., Shelke, Y., Murhade, G., Nimerovsky, E., Borcik, C.G., Arango, A.S., Lange, J.D., Marin-Toledo, J.P., Lyu, Y., Bailey, K.L., Roady, P.J., Holler, J.T., Khandelwal, A., SantaMaria, A.M., Sanchez, H., & Burke, M.D. (2023). Tuning sterol extraction kinetics yields a renal-sparing polyene antifungal. *Nature*, *623*(7989), 1079–1085. https://doi.org/10.1038/s41586-023-06710-4

Ngece, K., Ntondini, T.L., Khwaza, V., Paca, A.M., & Aderibigbe, B.A. (2024). Polyene-based derivatives with antifungal activities. *Pharmaceutics, 16*(8), 1065. https://doi.org/10.3390/pharmaceutics16081065

Odumosu, B.T., Buraimoh, O.M., Okeke, C.J., Ogah, J.O., & Michel, F.C. (2017). Antimicrobial activities of Streptomyces ceolicolor strain AOB KF977550 isolated from a tropical estuary. *Journal of Taibah University for Science, 11*(6), 836-841. https://doi.org/10.1016/j.jtusci.2017.01.006

Pham, J.V., Yilma, M.A., Feliz, A., Majid, M.T., Maffetone, N., Walker, J.R., Kim, E., Cho, H.J., Reynolds, J.M., Song, M.C., Park, S.R., & Yoon, Y.J. (2019). A review of the microbial production of bioactive natural products and biologics. *Frontiers in Microbiology, 10*, 1404. https://doi.org/10.3389/fmicb.2019.01404

Pielichowski, K., Njuguna, J., & Majka, T.M. (2023). Thermal degradation of polymeric materials: conclusions and future outlook. In Thermal degradation of polymeric materials (2nd ed.) (pp. 347-360). Elsevier. https://doi.org/10.1016/B978-0-12-823023-7.00011-3

Quinn, G.A., & Dyson, P.J. (2024). Going to extremes: progress in exploring new environments for novel antibiotics. *Publisher: Nature Publishing Group* 2(1), 8. https://doi.org/10.1038/s44259-024-00025-8

Sadanov, A. K., Berezin, V. E., Balgimbayeva, A. S., & Trenozhnikova, L. P. (2016a). A drug with antifungal and antiviral activity in the form of an ointment and a method for its preparation. Patent of the Republic of Kazakhstan No. 31491 of September 15, 2016. Ministry of Justice of the Republic of Kazakhstan.

Sadanov, A.K., Berezin, V.E., Trenozhnikova, L.P., Balgimabayeva, A.S., & Ultanbekova, G.D. (2016b). Human mycoses and antifungal drugs: Monograph. Almaty: Kausar Studio, 292 p. (in Russian).

Sadanov, A.K., Ibragimova, L.N., Trenozhnikova, L.P., Tugelbay, G.E., Berezin, V.E., & Turlybaeva, Z.Z. (2020). Suppositories with antifungal and antiviral activity for the treatment of vaginal candidiasis. Utility model Patent No. 5056 of October 9, 2020. Ministry of Justice of the Republic of Kazakhstan.

Sasaki, T., Nose, H., Hosoya, A., Yoshida, S., Kawaguchi, M., Watanabe, T., Usui, T., Ohtsuka, Y., Shomura, T., Takano, S., & Tatsuta, K. (2000). PF1163A and B, new antifungal antibiotics produced by Penicillium sp. II. Physico-chemical properties and structure elucidation. *The Journal of Antibiotics, 53*(1), 38-44. https://doi.org/10.7164/antibiotics.53.38

Shams, S., Lima, C., Xu, Y., Ahmed, S., Goodacre, R., & Muhamadali, H. (2023). Optical photothermal infrared spectroscopy: A novel solution for rapid identification of antimicrobial resistance at the single-cell level via deuterium isotope labeling. *Frontiers in Microbiology, 14*, 1077106. https://doi.org/10.3389/fmicb.2023.1077106

Smitherman, L. (2016). In brief: Antifungal drugs. *Pediatrics in Review, 37*(6), 267-268. https://doi.org/10.1542/pir.2015-0171

Svirkin, Y., Lee, J., Marx, R., Yoon, S., Landrau, N., Kaisar, M.A., Qin, B., Park, J.H., Alam, K., Kozak, D., Wang, Y., Xu, X., Zheng, J., & Rivnay, B. (2022). Amphotericin B release rate is the link between drug status in the liposomal bilayer and toxicity. *Asian Journal of Pharmaceutical Sciences*, *17*(4), 544-556. https://doi.org/10.1016/j.ajps.2022.04.007

Tevyashova, A.N., Olsufyeva, E.N., Solovieva, S.E., Printsevskaya, S.S., Reznikova, M.I., Trenin, A.S., Galatenko, O.A., Treshalin, I.D., Pereverzeva, E.R., Mirchink, E.P., Isakova, E.B., Zotchev, S.B., & Preobrazhenskaya, M.N. (2013). Structure-antifungal activity relationships of polyene antibiotics of the amphotericin B group. *Antimicrobial Agents and Chemotherapy, 57*(8), 3815-3822. https://doi.org/10.1128/AAC.00270-13

Vanreppelen, G., Wuyts, J., Van Dijck, P., & Vandecruys, P. (2023). Sources of antifungal drugs. *Journal of Fungi, 9*(2), 171. https://doi.org/10.3390/jof9020171

Wang, W., Song, T., Chai, W., Chen, L., Chen, L., Lian, X.Y., & Zhang, Z. (2017). Rare polyene-polyol macrolides from mangrove-derived Streptomyces sp. ZQ4BG. *Scientific Reports, 7*(1), 1703. https://doi.org/10.1038/s41598-017-01912-z

World Health Organization (WHO) (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization.

Yelubayeva, A.E., Baimakhanova, B.B., Sadanov, A.K., Balgimbaeva, A.S., Berezin, V.E., Baimakhanova, G.B., Turlybayeva, Z.Z., Massirbayeva, A.D., & Doolotkeldieva, T.D. (2024). Pre-clinical studies of the anti-fungal drug "Rozeofungin-AS, ointment 2%". *Microbiology and Virology*, 2(45), 215–230. https://doi.org/10.53729/MV-AS.2024.02.13

Zhao, W., Jiang, H., Liu, X.-W., Zhou, J., & Wu, B. (2022). Polyene Macrolactams from Marine and Terrestrial Sources: Structure, Production Strategies, Biosynthesis and Bioactivities. *Marine Drugs, 20*(6), 360. https://doi.org/10.3390/md20060360

Zhu, P., Li, Y., Guo, T., Liu, S., Tancer, R.J., Hu, C., Zhao, C., Xue, C., & Liao, G. (2023). New antifungal strategies: Drug combination and co-delivery. *Advanced Drug Delivery Reviews, 198*(2016), 114874. https://doi.org/10.1016/j.addr.2023.114874

Zotchev, S.B. (2003). Polyene macrolide antibiotics and their applications in human therapy. *Current Medicinal Chemistry, 10*(3), 211-223. https://doi.org/10.2174/0929867033368448