BULETINUL INSTITUTULUI POLITEHNIC DIN IAŞI
Publicat de
Universitatea Tehnică „Gheorghe Asachi” din Iași
Volumul 72 (76), Numărul 1, 2026
Secţia
CHIMIE şi INGINERIE CHIMICĂ
DOI: 10.5281/zenodo.20120434

ANTIFUNGAL EVALUATION OF A GEL FORMULATION WITH NYSTATIN-LOADED LIPOSOMES

BY

CODRIN PAUL FUIOAGA[1,2,*], DELIA MIHAELA RATA[2], LEONARD IONUT ATANASE[1,2,3], TUDOR MOCANU[2], XENIA PATRAS[2] and ANCA NICULINA CADINOIU[2]

[1]"Gheorghe Asachi" Technical University of Iași, "Cristofor Simionescu" Faculty of Chemical Engineering and Environmental Protection, Iași, Romania
[2]Faculty of Medicine, Apollonia University of Iași, Romania
[3]Academy of Romanian Scientists, Bucharest, Romania

Received: September 14, 2025
Accepted for publication: March 10, 2026

Abstract. This study explores the development of a novel liposomal formulation of Nystatin for transmembrane administration aimed at treating oral mycoses. Traditional Nystatin, though effective, presents systemic toxicity risks. By encapsulating it in cationic liposomes (DPPC/DOTAP/CHOL) and embedding them into alginate hydrogels, the researchers achieved controlled drug release, improved bioavailability, and reduced side effects. The formulations were synthesized via lipid film hydration, characterized by zeta potential, size distribution, and encapsulation efficiency, and evaluated *in vitro* for antifungal efficacy using *Candida albicans* ATCC 10231. Results indicated dose-dependent antifungal activity with promising inhibition zones. This liposomal approach offers a safer, targeted alternative to systemic antifungals, particularly beneficial for patients with compromised mucosal barriers or immunosuppression. Future directions include broader microbiological evaluations and optimization of liposomal drug loading.

Keywords: Liposomal Nystatin, antifungal therapy, transmucosal delivery, alginate hydrogel, *Candida albicans*.

---

[*]Corresponding author; *e-mail*: codrin_paul@ymail.com

1. Introduction

The concentration of various Candida species, especially *Candida albicans*, in the oral cavity reaches a percentage of 10-50% in healthy individuals. The abundant presence of yeasts in the saliva of patients undergoing prophylactic administration of broad-spectrum antibiotics, especially before laborious surgical interventions, predisposes to the occurrence of oral mycoses or even broncho-pulmonary mycoses, in the case of long-term endotracheal intubation (Di Cosola *et al.*, 2021).

Hyposalivation is also a condition that favors the multiplication of yeasts in the oral cavity and the appearance of mycoses because the saliva secreted in reduced volume fails to remove microorganisms from the various anatomical structures and thus favors their colonization. In addition to the reduction of salivary flow, hyposalivation is also accompanied by a reduction in pH to values below 6.5. The acidic environment thus created is beneficial for the multiplication of various yeast species (Buranarom *et al.*, 2020).

Some acrylic prosthetic devices (totally/partially removable prostheses) provide excellent support for the adhesion and multiplication of yeasts, becoming true "microorganism-generating deposits" in the case of poor hygiene (Ribeiro *et al.*, 2024). In addition, blastospores and filaments of *Candida albicans* adhere to host tissues, this phenomenon being possible following the interaction between yeast mannoproteins, with the role of adhesin, and some surface glycoproteins with the role of receptors. *Candida albicans* also has the ability to bind to some matrix proteins such as fibronectin, laminin and collagen (Jørgensen, 2024).

In this context, reducing the yeast load in the oral cavity can provide the premises for a judicious prevention of oral mycoses. Since the use of antifungals in prophylaxis is inopportune for many reasons (the risk of developing resistance to antifungals, the rather negligible toxicity of such products, patient reluctance, etc.), the establishment and observance of rigorous oral hygiene measures, as well as the use of antiseptic solutions - such as mouthwashes, can bring important benefits in the prevention of oral fungal infections in patients at risk: diabetics, pregnant women, HIV-positive patients, acrylic denture wearers, patients undergoing broad-spectrum antibiotic therapy/prophylaxis and radiotherapy, patients with malignant hemopathies, with autoimmune syndromes or sialoadenopathies.

This study analyzed the possibility of obtaining a new liposomal formulation for encapsulating nystatin for use in the treatment of fungal infections in the oral cavity.

Liposomes are bilayer-coated spheres, vesicles obtained from phospholipids filled with liquid which could be loaded with therapeutic agents and used to protect and deliver drugs throughout the body (Cadinoiu *et al.*, 2019). The bilayer structure of liposomes is almost identical to the bilayer construction of cell membranes that surround each of the cells in the human body. This is due

to the unique composition of phospholipids. The phosphate end of the phospholipid is hydrophilic, and the fatty acid tails (lipids) are hydrophobic. When phospholipids are in a water-based solution, the hydrophobic tails move rapidly to distance themselves from the liquid, so all the tails turn inward and all the ends turn toward the liquid (outside or inside), forming a bilayer membrane, with all the tails pointing toward each other and the ends pointing either outside or inside the sphere they have formed (Cadinoiu *et al.*, 2021).

Nystatin, having the chemical structure presented in Fig. 1, is a polyene antibiotic obtained by biosynthesis, being a metabolite of the species *Streptomyces noursei*.

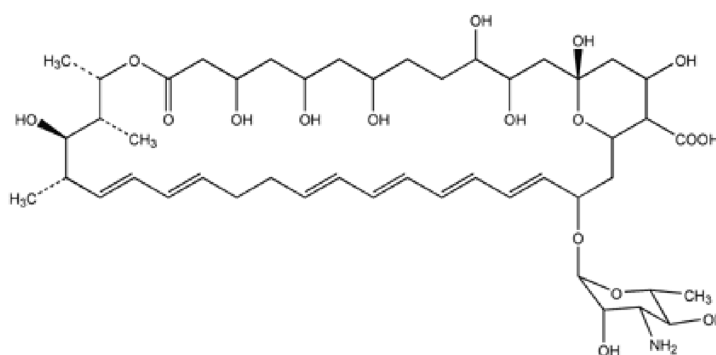

Fig. 1 – Chemical structure of nystatin.

Nystatin has an antifungal effect due to its action on the cell membrane of the micromycete, the structure of which it permeabilizes by combining with its sterols. The most pronounced effect is exerted on yeast-like fungi in full multiplication phase (Sousa *et al.*, 2023).

Nystatin therapy is indicated in mycoses located at the level of various mucous membranes (oral, oesophageal, gastro-enteric, nasal, pharyngeal, ocular, vulvovaginal) but also in those affecting the skin, whose causative agent is sensitive to this antifungal (especially *Candida*, rarely *Geotrichum* or *Cryptococcus*). Nystatin is also recommended for prophylactic purposes, in subjects with diminished general resistance, or in those who are subject to long-term therapies with antibiotics, corticosteroids or immunosuppressive drugs (Rai *et al.*, 2022).

Similar to other polyene antifungal agents, Nystatin binds to ergosterol in the fungal membrane. This binding disrupts the osmotic integrity of the Asadi fungal membrane, resulting in leakage of intracellular potassium, magnesium, sugars, and metabolites and subsequent cell death. The lipid carrier of liposomal nystatin does not alter this basic mode of action (Asadi *et al.*, 2024).

When Nystatin is incorporated into liposomes, *in vitro* activity is maintained. Liposomal Nystatin is composed of Nystatin encapsulated in liposomes containing dimyristoyl phosphotidyl choline and dimyristoyl phosphotidyl glycerol. Some lipids form membranes that self-assemble to form liposomes. In principle, liposomes could be created using a single lipid, such as DPPC alone. However, some compounds, such as cholesterol (CHOL), are added to improve stability or other structural properties. Apparently, cholesterol has the effect of making the membrane less permeable by filling in holes or gaps (Tseng *et al*., 2007; Yang *et al.*, 2016).

In order to reduce the systemic toxicity of Nystatin, liposomal nystatin was first developed in 1987 (Mehta *et al.*, 1987). It is manufactured by AronexPharmaceuticals under the generic name liposomal Nystatin and under the trade name Nyotran™. It is in late phase III clinical trials.

Liposomal Nystatin is active against a wide range of yeasts and molds, including *Candida* spp., *Cryptococcus neoformans*, and *Aspergillus* spp. (Asadi *et al*., 2024; Giamberardino *et al.*, 2024). Comparison of minimal inhibitory concentrations (MICs) of nystatin and liposomal Nystatin yields variable results. Nystatin and liposomal nystatin MICs are either similar (Arikan *et al.*, 2002) or the MIC of liposomal Nystatin is lower (Oakley *et al.*, 1999). The mechanism by which liposomal Nystatin generates lower MICs is unknown, and some authorities prefer that these tests be simply performed using the parent compound (Nystatin) alone.

The liposomal formulation enhances the activity of the drug by allowing the drug to be trapped in the reticuloendothelial system and delivered specifically to the site of infection. Thus, the improved final activity of the lipid formulation compared to the parent compound nystatin is most likely not a result of enhanced "*in vitro*" activity, but rather is an improved "*in vivo*" efficacy. Thus, the significance of susceptibility testing for liposomal nystatin is unknown.

In clinical trials conducted to date, liposomal nystatin has been administered intravenously at doses of 0.25 to 4 mg/kg/day (Offner *et al.*, 2004). Typical doses are not yet known.

Unlike Nystatin, serious toxic reactions due to systemic administration of liposomal Nystatin are less likely to occur. The most common side effect is hypokalemia. Nephrotoxicity also occurs, although details regarding the frequency of this side effect are not yet available (Semis *et al.*, 2012).

Contrary to the liposomal form of Nystatin is administered intravenously, our study aims to obtain a liposomal product that can be administered topically with the same pharmacological effect and with reduced side effects.

2. Materials and methods

2.1. Materials

The following materials were used in this study: 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) and 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP) used in this study to obtain liposomes were received as a gift samples from Lipoid GmbH, Germany, for the author to carry out the present studies. Cholesterol (CHOL) (purity 95%) used to obtain liposomes was obtained from Alfa Aeser. Sodium alginate used to obtain gels was purchased from Alfa Aeser. The viscosity of a 1% solution is 1000-1500 cPs. Nystatin (purity min. 85%, 90% of particles 45 μm) used in this study was obtained from Antibiotice, Iași, Romania. Chloroform and methanol were obtained from Chemical Company, Romania. All other chemicals used were of analytical grade.

2.2. Methods

2.2.1. Liposome's preparation method

Cationic liposomes loaded with nystatin were prepared by the lipid film hydration method using three types of lipids: DPPC, DOTAP and CHOL. Briefly, lipids, in different ratios DPPC:CHOL:DOTAP (Table 1) together with nystatin, were dissolved in 10 mL chloroform/methanol mixture (2/1 volume ratio).

Table 1
Experimental plan used for the synthesis of cationic liposomes

Sample code	DPPC (mg)	CHOL (mg)	DOTAP (mg)	Nystatin (mg)	Physiological serum (mL)
L-1	22	2	1	1.25	5
L-2	21	2	2	1.25	5
L-3	19	4	2	1.25	5
L-4	17	4	4	1.25	5

The organic solvents were evaporated (using a Heidolph rotoevaporator, at 150 rpm, 40°C and 300 mbar pressure) from the round bottom flask (250 mL) leading to the formation of a thin film on the walls of the flask. To dry completely, the lipid membrane was kept under a constant flow of argon for 15 minutes. Then, the lipid film was hydrated with 5 mL of physiological saline solution at 42°C. After vigorous stirring using a DLab Variable Speed Vortex, a spontaneous formation of MLVs occurred. The obtained dispersion was placed in a sonicator bath for 10 minutes at 45°C in order to break up the existing aggregates. Finally, the liposomes suspension was incubated for 1–2 hours at a temperature above the lipid transition temperature (at 42 °C) to alleviate membrane structural defects.

2.2.2. Gel's preparation method

Alginic acid was first isolated and named by a Scottish scientist, E.C.C. Stanford, in 1883. Since then, alginic acid and its derivatives have been used as a hydrocolloid in a variety of applications, such as food additives, pharmaceuticals, cosmetics and the textile industry. Alginate is known for its biocompatibility, biodegradability, and non-toxicity (Rață *et al.*, 2025) and also has a protective effect on the mucosa of the upper gastrointestinal tract when administered orally (Traserra *et al*., 2023).

Sodium alginate, the most widely used derivative of alginic acid, forms gels in contact with divalent ions such as Ca^{2+} ions. Crosslinking of alginate occurs by replacing Na^{+} ions with Ca^{2+} ions. Calcium ions are able to crosslink alginates because they can form two bonds, unlike sodium ions which are monovalent (Hu *et al.*, 2022). The gel used in this study for liposome immobilization was obtained by crosslinking sodium alginate with calcium chloride following an experimental plan detailed in Table 2.

Table 2
Experimental plan for obtaining alginate gel

Sample code	Concentration of sodium alginate solution, (%)	Mass ratio
G-1	2	20/1

Sodium alginate was left to dissolve in distilled water overnight, at a temperature of 25°C and a stirring speed of 500 rpm. Over 20 mL of alginate solution, 400µL of $CaCl_2$ solution (5%) were added dropwise, under vigorous stirring, to obtain the gel. The gel thus obtained was subjected to centrifugation (5 minutes, 5000 rpm) to eliminate the air entrapped during stirring.

2.2.3. Preparation of liposomal formulations

To obtain liposomal formulations, a suspension of nystatin-loaded liposomes was added to the sodium alginate solution prior to the addition of calcium chloride (Fig. 2). The final concentration of the drug loaded liposomes formulation was 0.5% (w/v).

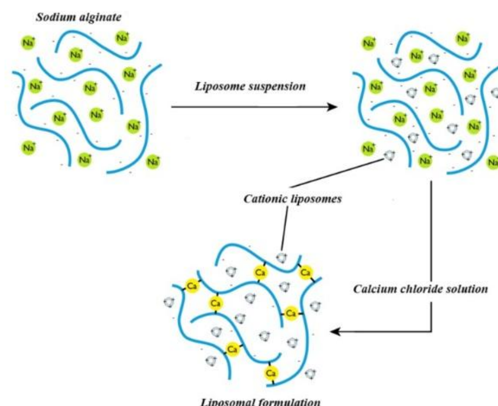

Fig. 2 – Schematic representation of obtaining liposomal formulations.

2.3. Characterization methods

The average diameter of the liposomes was determined by laser light diffractometry (Malvern ZetasizerNanoZS) at a concentration of 0.1% (w/v) in ultrapure water, at 25°C.

Zeta potential was measured by laser Doppler microelectrophoresis at 25°C after dilution in hydration medium at an appropriate counting rate using a Malvern Zetasizer Nano ZS.

The drug encapsulation efficiency was determined using the equation:

$$E\% = \frac{m_{Np}}{m_{Nt}} \times 100$$

where: E% – encapsulation efficiency; m_{Np} – experimentally determined amount of nystatin in MLV; m_{Nt} – theoretical amount of nystatin.

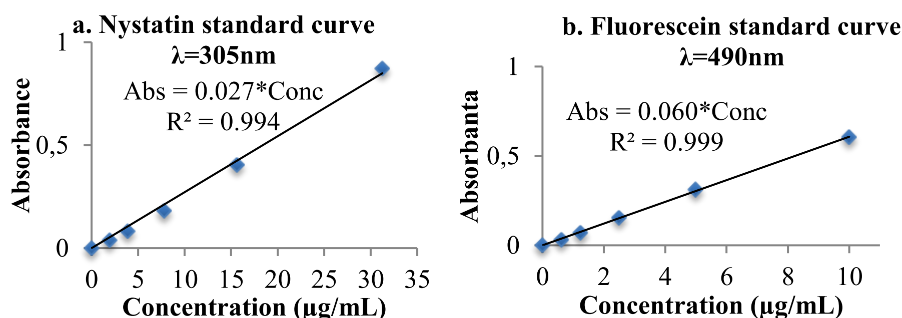

Fig. 3 – Standard curve of nystatin in methanol/water mixture (a) and fluorescein in water (b).

200µL of liposome suspension was added to 1.8 mL of methanol to disrupt the liposomal membrane and solubilize the drug. The amount of drug encapsulated in the liposomes was then evaluated spectrophotometrically (T60 Spectrophotometer, manufactured by PG Instruments) taking into account the equation of the standard curve (Fig. 3a).

The *in vitro* release of nystatin from liposomal formulations was studied spectrophotometrically. Since nystatin is not soluble in aqueous medium, hydration of the lipid film with a fluorescein solution was chosen to facilitate characterization of liposomal encapsulation and stability. 100 mg of gel with incorporated liposomes were immersed in 20 mL PBS (pH=6.8), in covered containers, and incubated at 37°C, in a thermostated bath, under shaking (50 rpm). It should be noted that for each experiment the samples were prepared in triplicate. At predetermined durations, the amount of each active principles released was monitored spectrophotometrically taking into account the equation of the standard curve (Fig. 3). The amount of fluorescein released was then correlated to the amount of nystatin in the liposomes.

The evaluation of antifungal activity was performed by the Kirby-Bauer disk diffusimetric method. Mueller-Hinton Agar supplemented with 2% glucose (Carl Roth GmbH, Germany) was used as the test medium. Candida albicans ATCC 10231 was used as the test strain. The strain was stored at -80ºC until use, then it was plated on YPD (Yeast Peptone Dextrose) Agar and incubated overnight at 36ºC. From the culture thus obtained, 4-5 typical colonies were selected and then suspended in sterile physiological serum to obtain a turbidity of 0.5 McFarland (approximately 106 CFU/mL). The suspension thus obtained was used to inoculate the test plate (200 µL/plate) within a maximum of 15 minutes of preparation. The inoculum was dispersed uniformly using a sterile swab, in three different directions. After drying the surface of the medium, under the protection of a class 2 biosafety hood, the two test products were spotted, in a volume of 10 µl each, in pre-established areas. The plate was incubated for 24 hours at 36ºC, then the diameters of the inhibition zones obtained for the two products were measured.

3. Results and discussion

3.1. Colloidal characteristics

The average diameter of the drug-free liposomes ranged from 2.27µm to 7.89 µm (Table 3). The size distribution of sample L-3-N is 8.59 µm. As can be seen from Table 3, the size of drug-loaded vesicles increases and is accompanied by a decrease in PDI, which may suggest a structural reorganization of the liposomal population upon Nystatin incorporation.

Table 3
Colloidal characteristics of liposomes

Sample code	Size (nm)	Dimensional polydispersity index	Zeta potential (mV)
L-1	7890±156	0.406±0.011	16.2±0.2
L-2	5810±131	0.229±0.009	27.1±0.5
L-3	6140±142	0.419±0.013	22.1±0.9
L-3-N	8590±185	0.245±0.008	15.9±0.3
L-4	2270±105	0.836±0.030	22.9±0.1

The zeta potential was determined to reveal the surface charge of the liposomes. For all four samples the zeta potential was positive (Fig. 4).

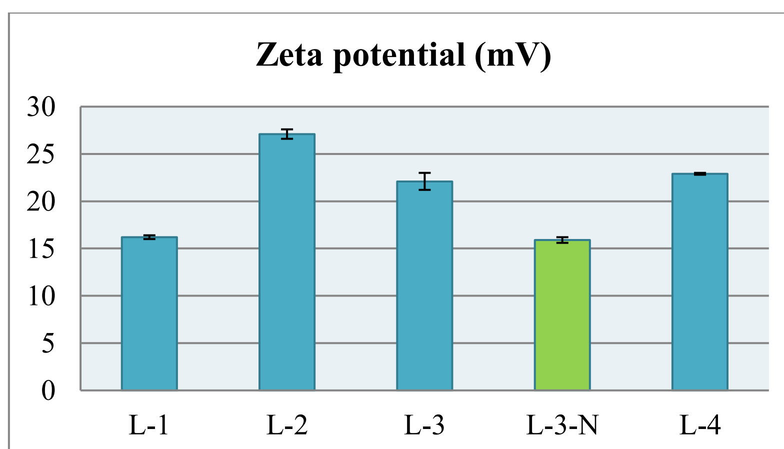

Fig. 4 – Zeta potential values for the analyzed samples.

3.2. Drug encapsulation efficiency

The encapsulation efficiencies of nystatin and fluorescein were evaluated spectrophotometrically. The values obtained are presented in Table 4.

Table 4
Encapsulation efficiencies of nystatin and fluorescein

Sample code	Nystatin encapsulation efficiency (%)	Fluorescein encapsulation efficiency (%)	Loaded Nystatin amount(µg) /mL liposomal suspension	Loaded fluorescein amount (µg) /mL liposomal suspension
G3-L-1	82.34±1.54	22.81±0.51	411.70±7.7	114.05±2.55

3.3. *In vitro* release of nystatin and fluorescein from liposomal formulations

Nystatin, a hydrophobic active principle, and fluorescein, a hydrophilic active principle, were encapsulated in large MLV-type liposomes (DPPC/CHOL/DOTAP). The liposomes loaded with fluorescein and nystatin were then immobilized in alginate gels cross-linked with calcium chloride. The release kinetics of fluorescein and nystatin from these gels are shown in Fig. 5.

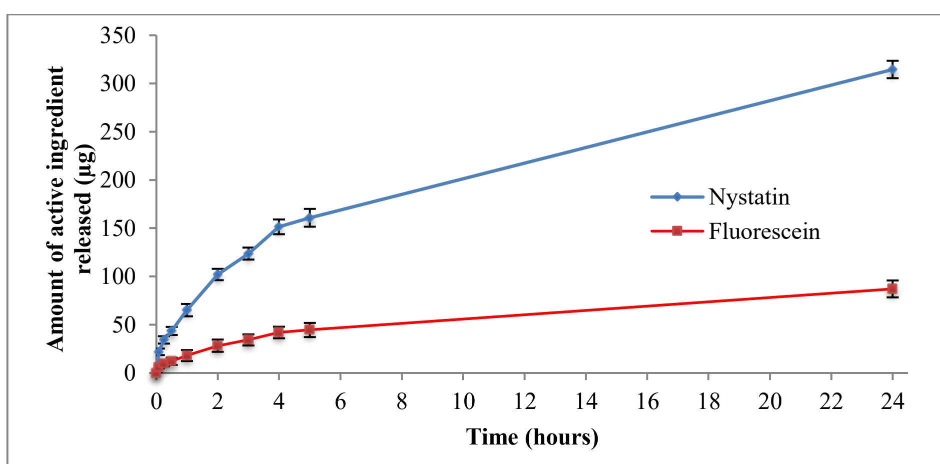

Fig. 5 – Release kinetics of fluorescein and nystatin.

3.4. "*In vitro*" antifungal effect of the synthesized gel

The disk diffusion method (Kirby-Bauer) showed an anti-candidiasis activity as evidenced by the zones of inhibition (Fig. 6 and Table 5).

Fig. 6 – Diameter of the inhibition zones for the two tested products: liposome suspension (left) – 18 mm; hydrogel with liposomes (right) – 15 mm.

This is a preliminary evaluation on a standard strain of *Candida albicans* ATCC 10231 which confirms that the tested products - both the liposome suspension with nystatin - L-1 (final concentration of the active substance of 0.5%) and the liposome gel with nystatin - G-L-1 (final concentration of the active substance of 0.5%) - are in the sensitive, dose-dependent sensitive spectrum.

Therefore, a significant antifungal activity is observed for the liposomal product, but for the liposome-based gel with Nystatin, a larger amount of Nystatin will need to be loaded for greater inhibition to enter the sensitivity range of the antifungal assay.

Table 5

Recommendations for interpreting susceptibility to liposomal Nystatin

Sensitive	Dose-dependent sensitivity	Resistant
>17mm	15mm	<13mm

We note that these "*in vitro*" antifungal evaluations were performed preliminary to prove the possible direct anti-candida effect. In the future, the research team will continue the evaluation steps through more elaborate tests (diffusimetric method, antifungal sensitivity testing with E-Test strips, etc.) and on several types of *Candida* strains or other yeasts.

The technology for synthesizing these medicinal products is under continuous evaluation and development because it represents a very good alternative for producing new medicinal forms. The controlled release of the active principle is ideal from a pharmacological point of view, therapeutic efficacy, bioavailability and safety of the medical act.

4. Conclusions

There is a complex pathology related to oropharyngeal fungal infections determined either by an increasingly lower resistance of the body or by an increase in the aggressiveness of candidal pathogens. The drug arsenal is limited, new antifungals have not appeared and then the solution is to obtain new drug forms that increase the efficiency of the existing ones. Obtaining liposomal gel that includes Nystatin can offer an effective, convenient anti-candidiasis treatment option with reduced side effects. The lipid carrier of liposomal nystatin does not change the basic mode of action, when nystatin is incorporated into liposomes, the *in vitro* activity is maintained, demonstrated in our work. As a result, the active principle, Nystatin, encapsulated in liposomes offers a much improved bioavailability (delivery into the blood), as well as better delivery into individual cells. This was one of the reasons why the author proposed the use of encapsulation for transmucosal administration of nystatin in the therapy of oral candidiasis.

REFERENCES

Arikan S., Ostrosky-Zeichner L., Lozano-Chiu M., Paetznick V., Gordon D., Wallace T., Rex J. H., *In vitro activity of nystatin compared with those of liposomal nystatin, amphotericin B, and fluconazole against clinical Candida isolates.* J. Clin. Microbiol., **40**, *4*, 1406, https://doi.org/10.1128/JCM.40.4.1406-1412.2002 (2002).

Asadi M., Toofani-Milani A., Bahman Soufiani K., *Nystatin Encapsulated Nanoliposomes: Potential Anti-infective against Candida Spp. Isolated from Candidiasis Patients*. Adv. Biomed. Res., **13**, *56,* 1, https://doi.org/10.4103/abr.abr_65_23 (2024).

Buranarom N., Komin O., Matangkasombut O., *Hyposalivation, oral health, and Candida colonization in independent dentate elders*, PLoS One. **15**, *11*, e0242832, https://doi.org/10.1371/journal.pone.0242832 (2020).

Cadinoiu A.N., Rata D.M., Atanase L.I., Daraba O.M., Gherghel D., Vochita G., Popa M., *Aptamer-Functionalized Liposomes as a Potential Treatment for Basal Cell Carcinoma*, Polymers, **11**, 1515, https://doi.org/10.3390/polym11091515 (2019).

Cadinoiu A.N., Rata D.M., Atanase L.I., Mihai C.T., Bacaita S.E., Popa M., *Formulations Based on Drug Loaded Aptamer-Conjugated Liposomes as a Viable Strategy for the Topical Treatment of Basal Cell Carcinoma—In Vitro Tests*, Pharmaceutics, **13,** 866, https://doi.org/10.3390/pharmaceutics13060866 (2021).

Di Cosola M., Cazzolla A.P., Charitos I.A., Ballini A., Inchingolo F., Santacroce L., *Candida albicans and Oral Carcinogenesis. A Brief Review*, J. Fungi, **7**, 476, https://doi.org/10.3390/jof7060476 (2021).

Giamberardino C. D., Schell W. A., Tenor J. L., Toffaletti D. L., Perfect J. R., *Efficacy of Liposomal Nystatin in a Rabbit Model of Cryptococcal Meningitis*. J. Fungi, **10**, *8*, 520, https://doi.org/10.3390/jof10080520 (2024).

Hu C., Lu W., Sun C., Zhao Y., Zhang Y., Fang Y. *Gelation behavior and mechanism of alginate with calcium: Dependence on monovalent counterions.* Carbohydr. Polym., **294**, 119788, https://doi.org/10.1016/j.carbpol.2022.119788 (2022).

Jørgensen M.R., *Pathophysiological microenvironments in oral candidiasis,* APMIS **132**, *12*, 956-973, https://doi.org/10.1111/apm.13412 (2024).

Mehta R.T., Hopfer R.L., Gunner L.A., Juliano R.L., Lopez-Berestein G., *Formulation, toxicity, and antifungal activity in vitro of liposome-encapsulated nystatin as therapeutic agent for systemic candidiasis*, Antimicrob. Agents Chemother. **31***, 12,* 1897-1900, https://doi.org/10.1128/aac.31.12.1897 (1987).

Oakley K.L., Moore C.B., Denning D.W., *Comparison of in vitro activity of liposomal nystatin against Aspergillus species with those of nystatin, amphotericin B (AB) deoxycholate, AB colloidal dispersion, liposomal AB, AB lipid complex, and itraconazole,* Antimicrob. Agents Chemother., **43**, *5*, 1264-6, https://doi.org/10.1128/aac.43.5.1264 (1999).

Offner F., Krcmery V., Boogaerts M., Doyen C., Engelhard D., Ribaud P., Cordonnier C., de Pauw B., Durrant S., Marie J., Moreau P., Guiot H., Samonis G., Sylvester R., Herbrecht R., *Liposomal Nystatin in Patients with Invasive Aspergillosis Refractory to or Intolerant of Amphotericin B*. Antimicrob Agents Chemother., **48,** *12*, 4808, https://doi.org/10.1128/aac.48.12.4808-4812.2004 (2004).

Rai A., Misra S.R., Panda S., Sokolowski G., Mishra L., Das R., Lapinska B., *Nystatin Effectiveness in Oral Candidiasis Treatment: A Systematic Review & Meta-Analysis of Clinical Trials*. Life, **12**, 1677, https://doi.org/10.3390/life12111677 (2022).

Rață D.M., Cadinoiu A.N., Grădinaru L.M., Fuioaga P.C., Vochita G., Delaite C., Atanase L.I., *Design and characterization of curcumin-loaded electrospun nanofibers based on poly(vinyl alcohol) and sodium alginate*. eXPRESS Polym. Lett., **19**, *3*, 233-245, https://doi.org/10.3144/expresspolymlett.2025.18 (2025).

Ribeiro A.B., Pizziolo P.G., Clemente L.M., Aguiar H.C., Poker B.d.C., Silva A.A.M.e., Makrakis L.R., Fifolato M.A., Souza G.C., Oliveira V.d.C., Watanabe E., Lovato da Silva C., H. *Strategies for Preventing and Treating Oral Mucosal Infections Associated with Removable Dentures: A Scoping Review*, Antibiotics, **13**, *3*, 273, https://doi.org/10.3390/antibiotics13030273 (2024).

Semis R., Nili S.S., Munitz A., Zaslavsky Z., Polacheck I., Segal E. *Pharmacokinetics, tissue distribution and immunomodulatory effect of intralipid formulation of nystatin in mice*, J. Antimicrob. Chemother. **67**, *7*, 1716-1721, https://doi.org/10.1093/jac/dks117 (2012).

Sousa F., Nascimento C., Ferreira D., Reis S., Costa P., *Reviving the interest in the versatile drug nystatin: A multitude of strategies to increase its potential as an effective and safe antifungal agent*, Adv. Drug Deliv. Rev. **199**, 114969, https://doi.org/10.1016/j.addr.2023.114969 (2023).

Traserra S., Cuerda H., Vallejo A., Segarra S., Sabata R., Jimenez M. *Gastroprotective Effects of Oral Glycosaminoglycans with Sodium Alginate in an Indomethacin-Induced Gastric Injury Model in Rats*, Vet. Sci., **10**, *12*, 667, https://doi.org/10.3390/vetsci10120667 (2023).

Tseng L.P., Liang H.J., Chung T.W., Huang Y.Y., Liu D.Z., *Liposomes Incorporated with Cholesterol for Drug Release Triggered by Magnetic Field*, J. Med. Biol. Eng. **27**, *1*, 29-34 (2007).

Yang S.T., Kreutzberger A.J.B., Lee J., Kiessling V., Tamm L.K., *The role of cholesterol in membrane fusion*, Chem. Phys. Lipids, **199**, 136-143, https://doi.org/10.1016/j.chemphyslip.2016.05.003 (2016).

EVALUAREA ANTIFUNGICĂ A UNUI GEL CU LIPOZOMI ÎNCĂRCAȚI CU NISTATINĂ

(Rezumat)

Acest studiu explorează dezvoltarea unei noi formulări lipozomale de nistatină pentru administrare transmembranară, menită să trateze micozele orale. Nistatina tradițională, deși eficientă, prezintă riscuri de toxicitate sistemică. Prin încapsularea acesteia în lipozomi cationici (DPPC/DOTAP/CHOL) și încorporarea acestora în hidrogeluri de alginat, cercetătorii au obținut eliberarea controlată a medicamentului, biodisponibilitate îmbunătățită și efecte secundare reduse. Formulările au fost sintetizate prin hidratarea filmului lipidic, caracterizate prin potențial zeta, distribuția dimensiunilor și eficiența încapsulării și evaluate in vitro pentru eficacitatea antifungică utilizând

Candida albicans ATCC 10231. Rezultatele au indicat o activitate antifungică dependentă de doză, cu zone de inhibare promițătoare. Această abordare lipozomală oferă o alternativă mai sigură și mai țintită la antifungicele sistemice, benefică în special pentru pacienții cu bariere mucoase compromise sau imunosupresie. Direcțiile viitoare includ evaluări microbiologice mai ample și optimizarea încărcării medicamentului lipozomal.