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DEVELOPMENT AND ASSESSMENT OF SECNIDAZOLE TRANSFEROSOMAL GEL FOR VAGINOSIS THERAPY

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ABSTRACT:
This study aimed to develop a transfersomal gel formulation for transdermal delivery of Secnidazole, a BCS class 3 drug known for its high solubility and low permeability. Secnidazole, a nitroimidazole-class drug, is used to treat fungal and yeast infections. Transferosomes, highly flexible supra-molecular aggregates capable of intact penetration through mammalian skin, were utilized for drug encapsulation. Various transfersomal formulations containing different ratios of phospholipids, surfactants, and Carbopol-934 were prepared and evaluated.Results included assessments of entrapment efficiency (EE %), drug content, in-vitro skin permeation studies, and stability tests. Transmission Electron Microscopy confirmed that the vesicles were spherical in shape. Secnidazole was successfully encapsulated with consistent drug content across all formulations. Among them, the transfersomal gel formulation (SG 2) demonstrated superior characteristics with the highest drug content (87.8 ± 3.10%) and cumulative percent drug release (79.8%) over 8 hours.Conclusion: This study concludes that transferosomes represent a promising approach for long-term delivery of Secnidazole, exhibiting satisfactory stability. The findings suggest that transferosomal formulations containing Secnidazole have potential as effective transdermal drug delivery systems for treating bacterial vaginosis infections.

KEYWORDS:
Transferosomal gel, Secnidazole, Bacterial vaginosis, Topical drug delivery, Transferosomes.
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INTRODUCTION:
Bacterial vaginosis (BV) is characterized as a polymicrobial syndrome where the normal vaginal lactobacilli, particularly those producing hydrogen peroxide, are displaced by various anaerobic bacteria and mycoplasmas. This condition exhibits a wide range of potential causes, which is reflected in its diverse symptoms. Common symptoms of BV include gray, homogenous vaginal discharge; a distinctive fishy odor; increased discharge without inflammation; yellow discharge; abdominal pain; intermenstrual bleeding; menorrhagia or prolonged menses [1,2]. BV is the leading cause of vaginitis, affecting more than 3 million women annually in the United States [3]. The reduction of lactobacilli from the normal vaginal flora and the proliferation of Gardnerella vaginalis and other anaerobic species are believed to be the underlying causes. Notably, there is no conclusive scientific evidence indicating that BV is a sexually transmitted disease, though malodorous vaginal discharge remains its most prevalent symptom. Trichomoniasis, moniliasis, and allergic or chemical dermatitis are among the differential diagnoses [4,5].

The diagnosis of BV is confirmed when at least three of the following four findings, known as Amsel's criteria, are present: 1) thin, homogenous discharge, 2) pH greater than 4.5, 3) positive amine test, and 4) presence of clue cells.

Research on the risk factors associated with BV has explored its potential as a sexually transmitted infection. While some studies have suggested links between BV and factors such as number of sexual partners and age at first intercourse, consistent patterns have not been established [6].

Mechanism of Action:

Nitroimidazoles, such as metronidazole and secnidazole, are potent agents used in the treatment of Trichomonas vaginalis infections and bacterial vaginosis. These compounds enter bacterial cells as inactive prodrugs, where bacterial enzymes reduce the nitro group to radical anions. It is hypothesized that these radical anions disrupt bacterial DNA synthesis in susceptible strains [10].

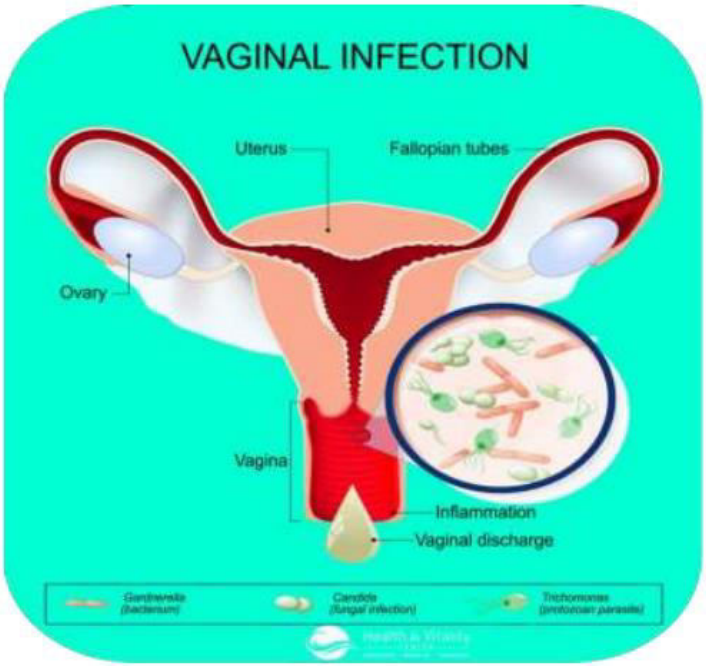

Fig 1: Bacterial vaginosis

Structure of Transferosomes:

Transferosomes, also known as ultra-deformable vesicles for skin application, consist of a lipid bilayer composed of phospholipids and edge activators surrounding an aqueous core. Depending on the lipophilicity of the active substance, it can be encapsulated within the core or integrated between the bilayers. Compared to liposomes, transferosomes have superior flexibility, allowing them to penetrate deeper layers of the skin upon topical application [9].

These complex aggregates are highly adaptable and resilient to stress. The vesicles are self-regulating and self-optimizing due to their local composition and bilayer structure, enabling them to efficiently navigate various transport barriers. This makes transferosomes effective as carriers for non-invasive targeted drug delivery and sustained release of therapeutic agents.

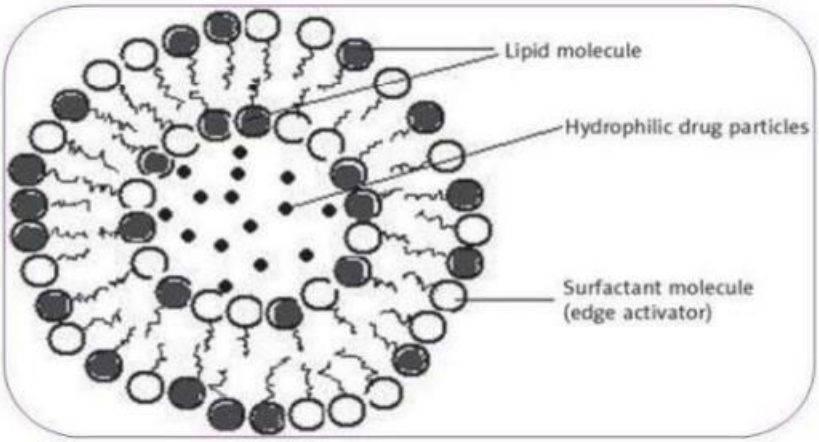

Fig 2. Structure of Transferosome

Method of Preparation:

Preparation of Transferosomes:

1. Hydration of Surfactant and Lipid Mixture:

○ Begin by hydrating a mixture of surfactant and lipid at elevated temperatures, followed by optional reduction of niosome size to achieve a colloidal suspension.

A. Preparation of Small Unilamellar Vesicles: I. Sonication II. Microfluidization

B. Preparation of Multilamellar Vesicles: I. Hand-shaking method II. Trans-membrane pH gradient drug uptake process

C. Preparation of Large Unilamellar Vesicles: I. Reverse phase evaporation technique II. Ether injection method

D. Miscellaneous Methods: I. Multiple membrane extrusion method II. Bubble method III. Emulsion method IV. Lipid injection method

Topical Gel: Topical drug delivery involves the transport of drugs to viable epidermal and/or dermal tissues of the skin for local therapeutic effects, while a significant portion of the drug may enter the systemic blood circulation [15].

Advantages of Topical Drug Delivery: Topical administration offers several advantages over conventional oral drug delivery, including bypassing hepatic first-pass metabolism, improving therapeutic efficacy, and maintaining steady plasma drug levels. Topical gel formulations are designed for superficial skin application or to mucosal surfaces for local action, penetration of drugs into the skin, or for their soothing or protective effects [16].

Method and Materials: Preparation of Secnidazole-Loaded Transferosomes:

Step 1: Dissolve the drug, surfactant, and phospholipid in a selected organic solvent. Step 2: Remove the organic solvent at room temperature using a vacuum rotary evaporator. Step 3: Form a dry thin film on the surface of the flask wall. Step 4: Rehydrate the dry surfactant film with 15 ml phosphate buffer saline (pH 7.4) containing the drug using a rotary evaporator without vacuum at 60°C to eliminate any remaining traces of organic solvent. Step 5: Store the final transferosomal suspension in the refrigerator for further investigation [7,8].

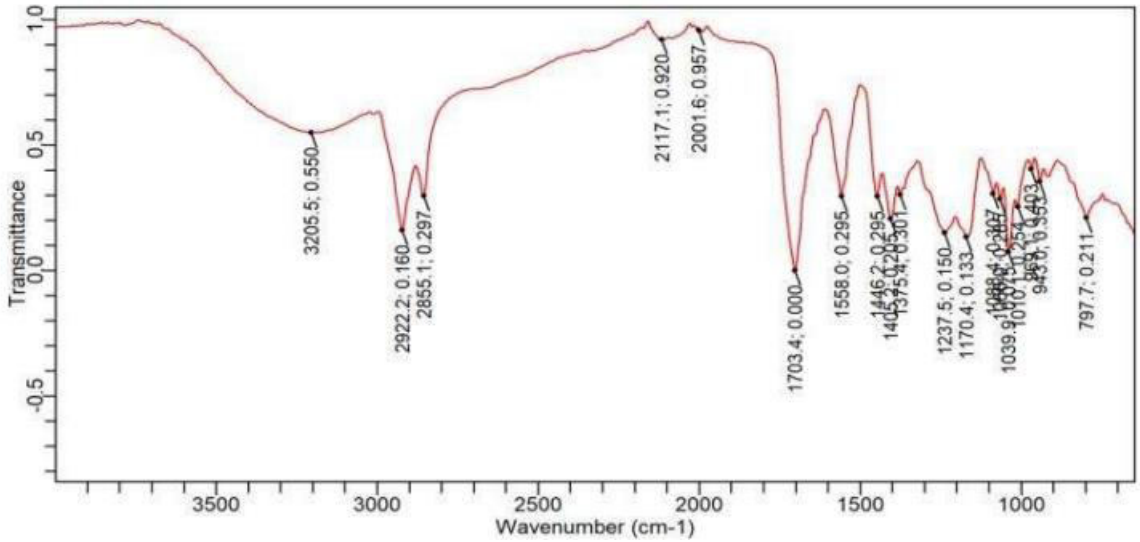

Fig 3. Identification of Drug by FT-IR study

ORGANOLEPTIC PROPERTIES OF SECNIDAZOLE

Table 1 Organoleptic properties of Secnidazole

Properties	Standard	Result
State	Solid	Solid
Color	White	White
Odor	Odourless	Odourless

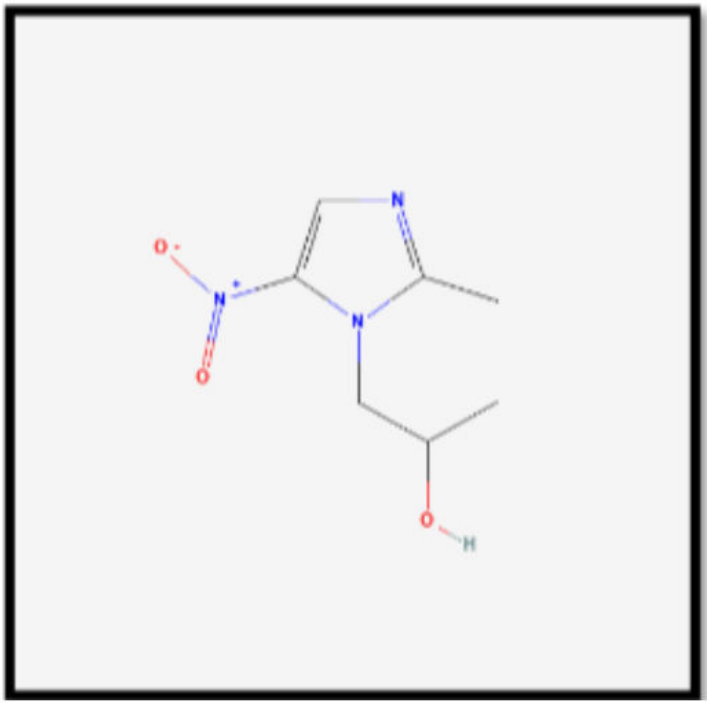

Fig 4. Chemical structure of Delafloxacin

CONCLUSION

Based on the findings of this study, it is concluded that the transfersomal gel, composed of sodium deoxycholate, soya lecithin, Carbopol, chloroform, and methanol, in combination with pure Secnidazole, effectively enhances site specificity, increases transdermal flux, and prolongs drug release. Secnidazole was successfully encapsulated within transferosomes, allowing penetration into skin pores significantly narrower than the vesicle diameter. The optimized transferosome formulation, S5, containing 0.1 g of Secnidazole, demonstrated superior entrapment efficiency (86.8 ± 2.16) compared to other formulations, where drug concentration was the sole variable factor. Similarly, the transfersomal gel formulation (SG2) demonstrated superior outcomes with maximum drug content (87.8 ± 3.10) and achieved a cumulative percent drug release of 79.8% within 8 hours. Transferosomes exhibit potential as carriers for various transdermal drug delivery systems due to their straightforward scalability and intrinsic capability to enhance penetration. This study confirms that the transfersomal gel formulation of Secnidazole is therapeutically effective for treating local skin infections and holds promise as a commercial product to enhance the drug's antifungal activity and address vaginosis, thereby aiding in protozoal management.

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