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Formulation and Evaluation of Secnidazole Transferosomal Gel for the Treatment of Vaginosis

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ABSTARCT: The focus of this research was to formulate a transfersomal gel formulation for transdermal delivery of Secnidazole. Secnidazole is a BCS class 3 drug which is high solubility and low permeability. Secnidazole is nitroimidazole class drug, which is used to treat fungal and yeast infections. Transferosomes are supra-molecular aggregates that are ultra-flexible and have a high ability to penetrate mammalian skin intact. Drug encapsulation in various transfersomal formulations containing various ratios of different phospholipid and surfactant ratio and Carbopol-934 is being researched for use as a transferosomal gel. Results: Entrapment efficiency (EE %), drug content, in-vitro skin permeation tests, and stability investigations were performed on the produced formulations.The vesicles were spherical in shape, as confirmed by Transmission Electron Microscopy. Secnidazole was successfully pinned with a standardised drug content in all formulations, according to the results, the transfersomal gel formulation (SG 2) showed better results having maximum drug content (87.8 ± 3.10) and cumulative percent drug release (79.8%) in 8 hrs. Conclusion: According to this report, transferosomes are a promising long-term delivery mechanism for Secnidazole and have reasonably good stability. This study suggests that transferosomes containing Secnidazole may be used as a transdermal drug delivery tool for the treatment of bacterial vaginosis infections.

Keywords: Transferosomal gel, Secnidazole, Bacterial vaginosis, Topical drug delivery, Transferosomes.

I. INTRODUCTION:

Bacterial vaginosis:

Bacterial vaginosis is a polymicrobial syndrome in which the normal vaginal lactobacilli, particularly those producing hydrogen peroxide, are replaced by a variety of anaerobic bacteria and mycoplasmas.The wide range of possible aetiologies is reflected in the variation in symptoms associated with bacterial vaginosis: these include grey, homogenous vaginal discharge; odorous discharge (fishy smell); increased discharge without an inflammatory response; yellow discharge; abdominal pain; intermenstrual bleeding; menorrhagia or prolonged menses.[1,2] Bacterial vaginosis is the most common cause of vaginitis, affecting over 3 million women in the United States annually.[3] Depopulation of lactobacilli from the normal vaginal flora and overgrowth of Gardnerella vaginalis and other anaerobic species are the presumed etiology. To date, no scientific evidence shows that bacterial vaginosis is a sexually transmitted disease. Malodorous vaginal discharge is the most common symptom. Differential diagnoses include trichomoniasis, moniliasis, and allergic or chemical dermatitis.[4,5]

The diagnosis is confirmed when at least three of the following four findings are present (Amsel's criteria)

1) thin, homogenous discharge, 2) pH greater than 4.5, 3) positive amine test, and 4) presence of clue cells.

Several risk factors studies for bacterial vaginosis have focused on whether it is a sexually transmitted infection. Although some studies have recorded associations between bacterial vaginosis and numbers of sexual partners and age at first intercourse, no consistent patterns have emerged.[6]

II. MECHANISM OF ACTION:

Nitroimidazoles (eg, metronidazole, secnidazole) are highly effective for treating Trichomonas vaginalis infections and bacterial vaginosis. 5- nitroimidazoles enters the bacterial cell as an inactive prodrug where the nitro group is reduced by bacterial enzymes to radical anions. It is believed that these radical anions interfere with bacterial DNA synthesis of susceptible isolates.[10]

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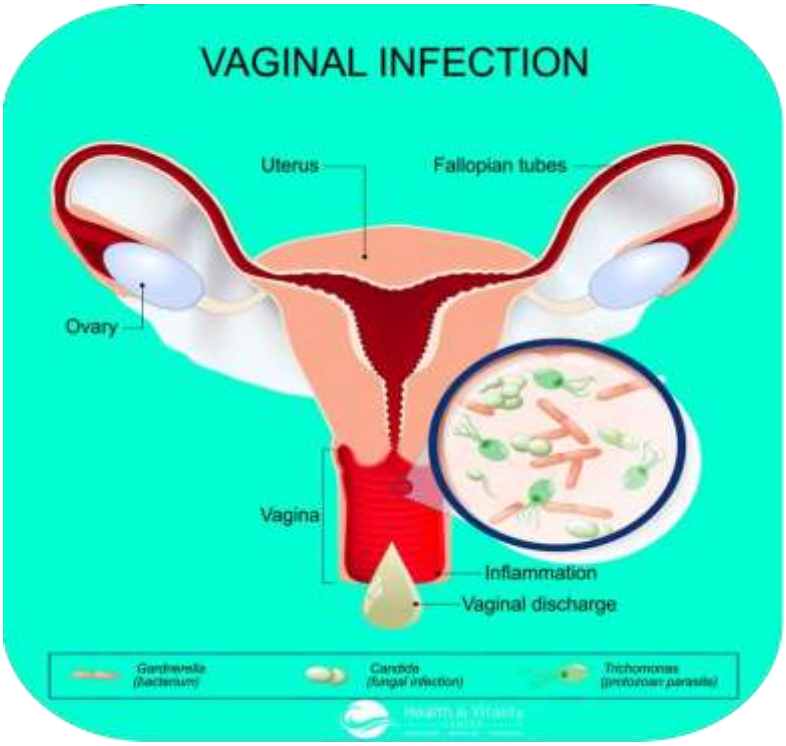

Fig 1. Bacterial vaginosis

The structure of a transferosome is seen in Fig. 1.

III. STRUCTURE OF TRANSFEROSOMES:

Transferosomes, even called as ultra deformable vesicles for applying to skin holding a lipid bilayer with phospholipids and edge activator along with aqueous layer. Based on the lipophilicity the active substance is enclosed with in core or amongst the bilayer. In comparison to liposomes, transferosomes are having a great capacity to touch whole deeper areas of skin once applied topically.[9]

These are a complex aggregate that is extremely adaptive and stress resistant. The vesicle is both self- regulating and self-optimizing because of its local composition and bilayer shape independence. This enables transferosomes to efficiently traverse various transport barriers before acting as a drug carrier for non-invasive targeted medication administration and therapeutic agent sustained release.[8]

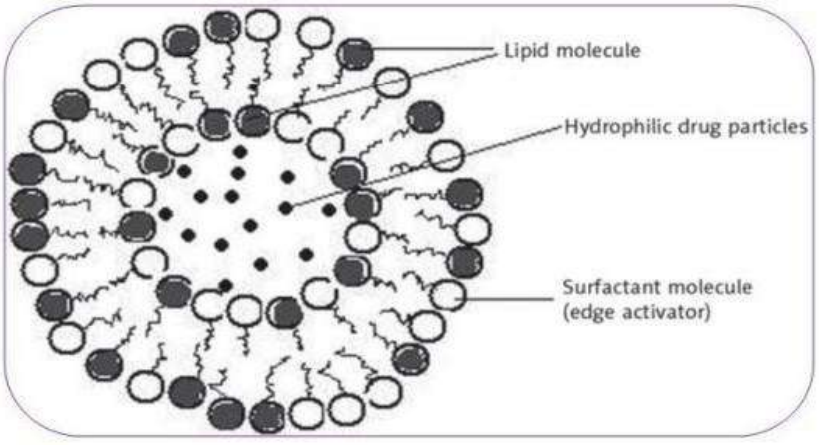

Fig 2. Structure of Transferosome

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IV. METHOD OF PREPARATION:

Preparation of transferosomes begins with the hydration of a surfactant and lipid mixture at elevated temperatures, followed by optional niosome size reduction to obtain a colloidal suspension

A. Preparation of small unilamellar vesicles:

I. Sonication
II. Micro fluidization

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:

I. Multiple membrane extrusion method
II. The "bubble" method
III. Emulsion method
IV. Lipid injection method

IV. TOPICAL GEL:

Topical drug delivery are dosage formthat involves drug transport to viable epidermal and or dermal tissues of the skin for local therapeutic effect while a very major fraction of the drug is transported into the systemic blood circulation. [15]

Topical administration of therapeutic agents offers many advantages over conventional oral drug delivery.Several important advantages of topical drug delivery are the limitation of hepatic first-pass metabolism, enhancement of therapeutic efficiency, and maintenance of steady plasma level of the drug.Topical gel preparations are intended for superficial skin application or to some mucosal surfaces for local action or skin penetration of medicament or for their soothing or protective action. [16]

METHOD AND MATERILAS:

Preparation for Secnidazole loaded Transferosome:

Step 1: Dissolve Ingredients like drug, surfactant, and phospholipid in selected organic solvent
Step 2: By using a vacuum rotary evaporator, organic solvent was removed at room temperature
Step 3: Formation of dry thin film on the surface of the flask wall
Step 4: The vesicles were formed by rehydrating the dry surfactant film with the help
of a rotary evaporator without vacuum with 15 ml phosphate buffer saline pH 7.4 which contained the drug and was kept at 60°C to eliminate any traces of organic solvent
Step 5: The finished transferosomal suspension was kept in the refrigerator for further investigation. [7,8]

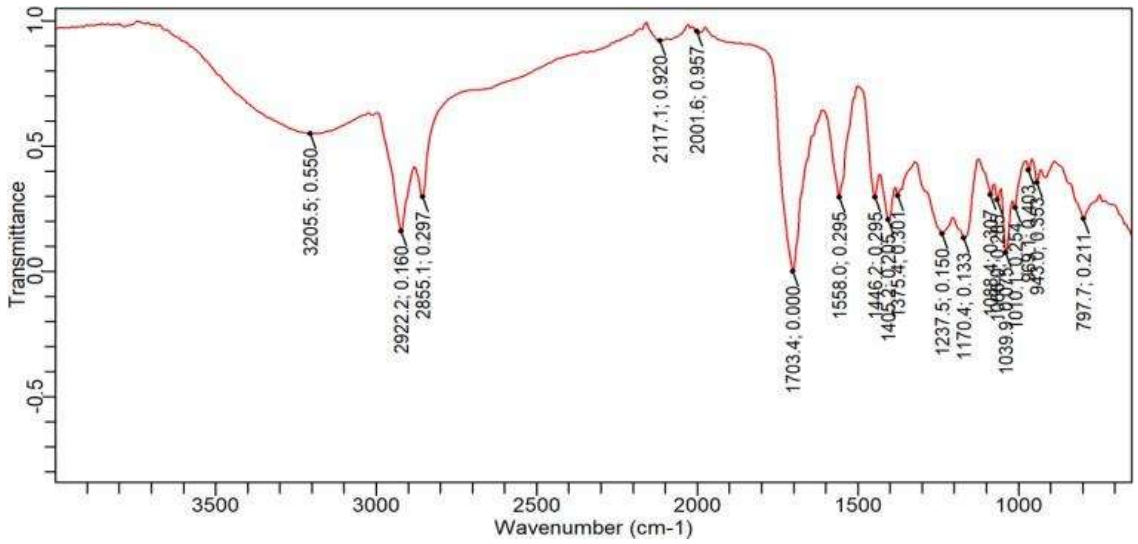

Fig 3. Identification of Drug by FT-IR study

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V. ORGANOLEPTIC PROPERTIES OF SECNIDAZOLE:

Table 1 Organoleptic properties of Secnidazole

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

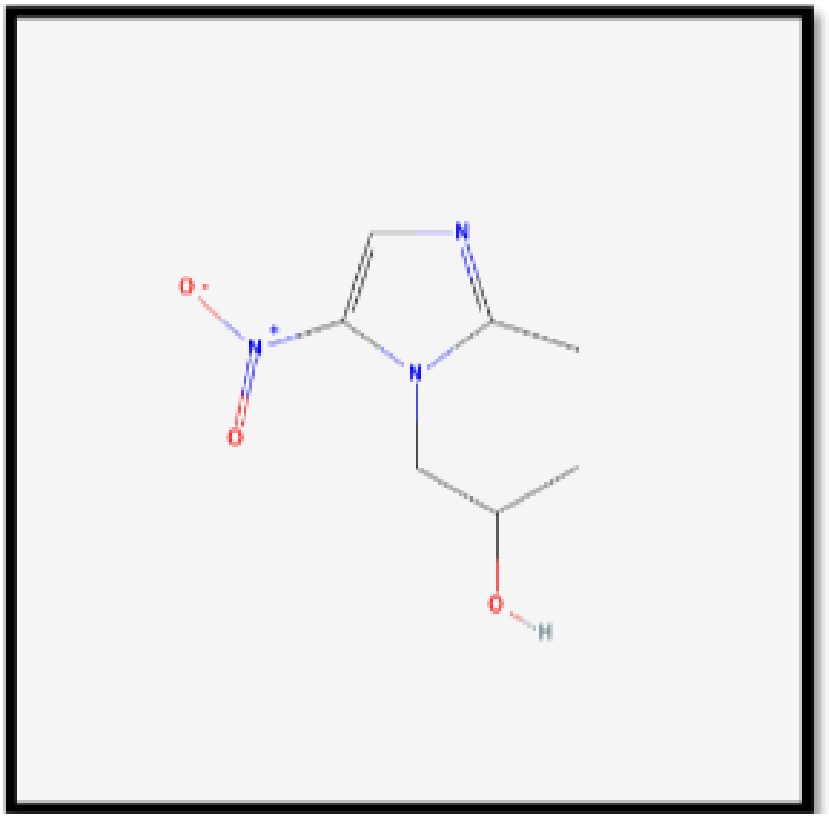

Fig 4. Chemical structure of Delafloxacin

Melting point secnidazole

Table 2 Melting point Secnidazole

Drug	Reported value	Observed values n=3; Mean (±SD)
Secnidazole	70-78 ^{0}C	76 ± 0.44 ^{0}C

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Linearity plot of Secnidazole

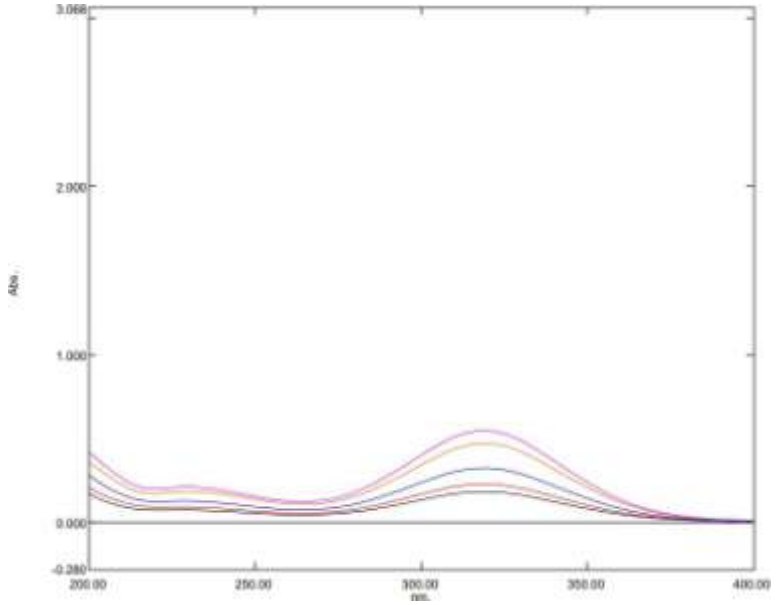

Fig 5. Linearity plot of Secnidazole

Table 3 Standard calibration curve of Secnidazole

Sr. no.	Concentration (µg/ml)	Absorbance (nm) (Mean±S.D) (n=3)
1.	2	0.216 ± 0.07
2.	4	0.304 ± 0.05
3.	4	0.376 ± 0.09
4.	6	0.434 ± 0.07
5.	10	0.518 ± 0.010

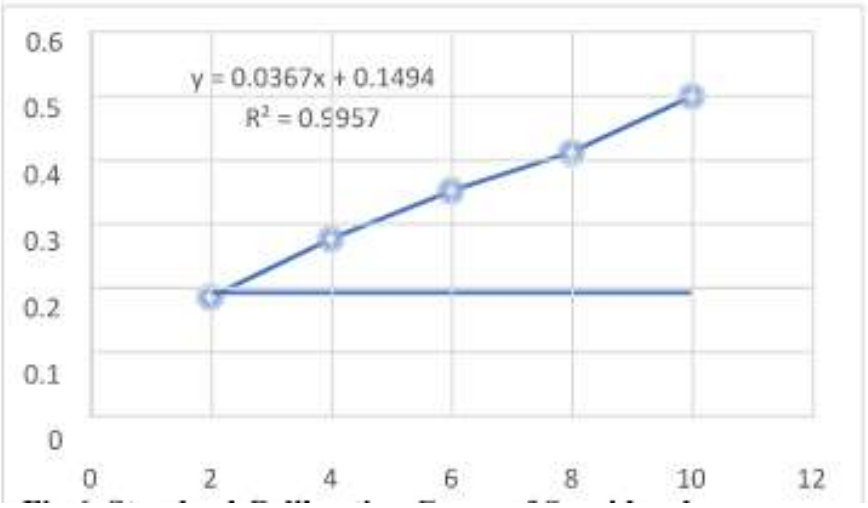

Fig 6. Standard Calibration Curve of Secnidazole summary

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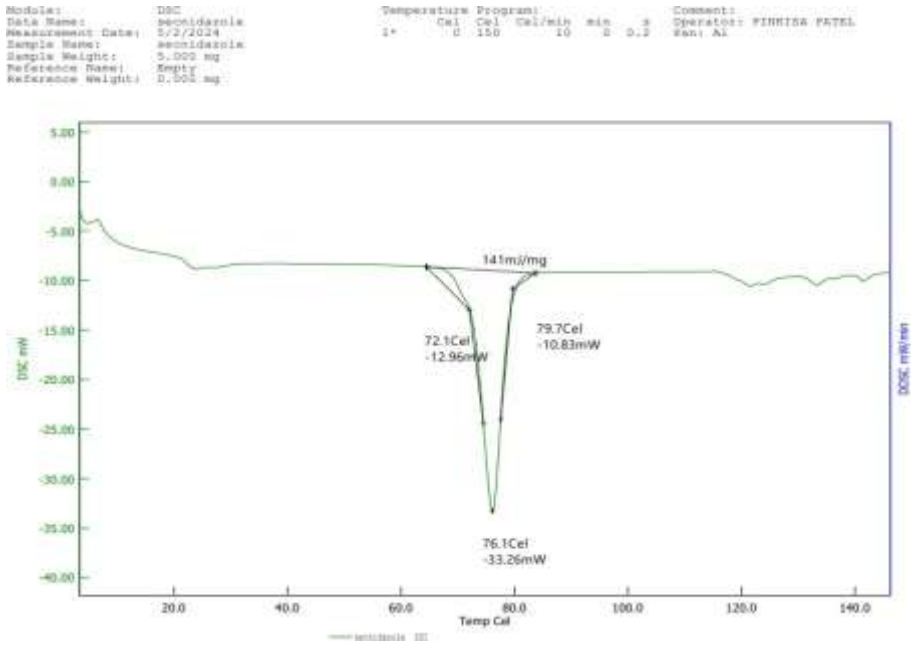

Fig 7. DSC Thermal analysis results of Secnidazole

Table 4 Transferosomes batches

Formulation code	Secnidazole (mg)	Soya lecithin (mg)	Sodium deoxycholate (mg)	Chloroform: methanol
S1	100	100	100	3:1
S2	100	100	50	3:1
S3	100	100	80	3:1
S4	100	100	120	3:1
S5	100	100	150	3:1
S6	100	100	200	3:1

Evaluation of transferosomes

Table 5 Evaluations of transferosomes for % drug content and Entrapment efficiency

Formulation code	%Drug content	% entrapment efficiency
S1	72.54 ± 3.54	70.90 ± 3.10
S2	64.5 ± 1.87	62.8 ± 2.56
S3	69.90 ± 1.54	67.4 ± 1.84
S4	82.7 ± 2.45	81.5 ± 2.7
S5	87.8 ± 3.10	86.8 ± 2.16
S6	84.3 ± 2.8	82.3 ± 3.7

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Surface Morphology of transferosomes

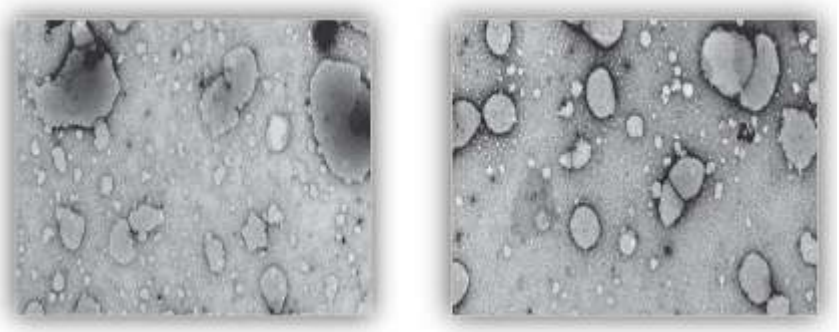

Fig 8. TEM of Transferosome

VI. DISCUSSION

The morphological characteristics of a dispersed system can be examined using TEM analysis. As seen in the TEM images of the representative spherical shape in the figure, the particle size was similar to the results of the particle size analysis

Table 6 Evaluations of transferosomes for zeta potential and vesicle size

Formulation code	Zeta potential (mV)	Vesicle size (nm)	PDI
S4	-36.9 ± 3.25	244.1 ± 50.7	0.729
S5	-32.7 ± 5.25	254.9 ± 53.5	0.674
S6	-22.7 ± 5.28	247.8 ± 57.2	0.698

VII. EVALUATION OF TOPICAL TRANSFEROSOMAL GEL:

Physical Appearances

The optimized transferosomal gel was found to be white, homogenous, and smooth in texture and no phase separation was observed

Measurement of pH

The pH of the formulated transferosomal gel was measured. It was found to be **6.84±0.1464**.

Table 7 Measurement of pH, Viscosity, Spreadability

Sr. No	Formulation	pH	Viscosity (cps)	Spreadability (gm.cm/sec)
1	**SG1**	**6.8**	5154	6.56
2	**SG2**	**6.9**	5597	6.27
3	**SG3**	**6.8**	5960	6.01

Viscosity

The viscosity of the optimized transferosomal gel was tested with a digital Brookfield viscometer. The viscosity of transferosomal gel formulations was found to be **5597(±0.08)** cps

Spreadability

The Spreadability of transferosomal gel is determined by placing 0.5 g of respective gel within a circle of diameter 1 cm, pre marked on a glass plate over which a second glass plate is placed a weight of 500 g is allowed to rest on the upper glass for about 5 min

The Spreadability was found to be **6.56 gm.cm/sec**

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In-Vitro % Drug Release Study

Sr. no.	Time (hr)	% CDR (SG1)	% CDR (SG2)	% CDR (SG3)
1.	1	9.4	11.5	10.2
2.	2	18.5	21.6	19.6
3.	3	27.4	32.4	30.4
4.	4	34.6	39.6	36.8
5.	5	42.2	48.7	45.6
6.	6	51.9	59.2	55.9
7.	7	62.1	68.4	63.7
8.	8	70.7	79.8	73.6

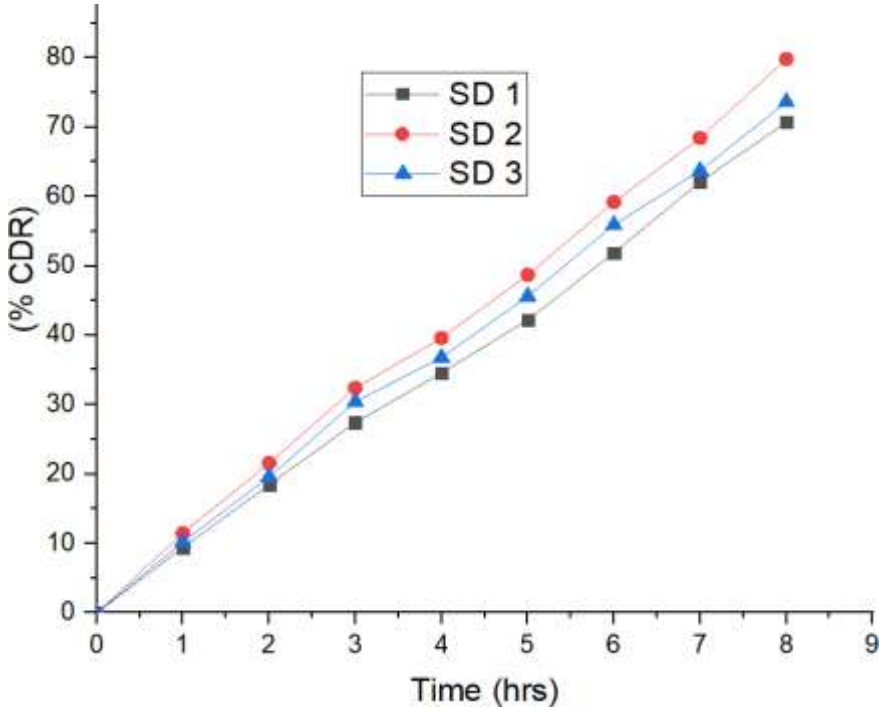

Fig 9. In-vitro Drug release

Stability studies

Table 8 Stability study

Sr. No.	Evaluation parameters	Optimized batch(SG2)	
		Day 0	Day 30
1	Physical appearance	White Smooth texture No phase separation was observed	White Smooth texture No phase separation was observed
2	pH	**6.9**	**7.05**
3	Viscosity(cps)	5597	5789
4	Spreadability	6.27 gm/s	6.56 gm/s
5	%Entrapment efficiency	82.3%	81.6%

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VIII. CONCLUSION:

It is concluded from the study that transfersomal gel formulated using sodium deoxycholate, soya lecithin, Carbopol, chloroform and methanol along with the pure drug Secnidazole can be used to improve the site specificity, increase the transdermal flux and prolong the release of the drug. Secnidazole could be entrapped into Transferosomes for penetration into skin pores much narrower than the vesicle diameter. The optimized transferosome formulation S5 containing 0.1 g Secnidazole showed promising results having higher entrapment efficiency (86.8 ± 2.16) when compared to other formulations with concentrations of drug being the only variable factor. Similarly, the transfersomal gel formulation (SG2) showed better results having maximum drug content (87.8 ± 3.10) and cumulative percent drug release (79.8%) in 8 hrs. Transferosomes can alternatively be used as carriers for other transdermal drug delivery system as they possess simple scale up and can also act as a penetration enhancer by itself with easy production. Finally, it is confirmed that transfersomal gel formulation of Secnidazole is therapeutically effective for the treatment of local skin infections and can be developed successfully as a commercial product to improve the antifungal activity of the drug and to treat vaginosis. use in the management of protozoal

REFERENCES:

[1]. Krohn M, Hillier S, Eschenbach D. Comparison of methods for diagnosing bacterial vaginosis among pregnant women. J Clin Microbial 1989; 27:1266±1271.

[2]. Hillier S, Critchlow C, Stevens C, et al. Microbiological, epidemiological and clinical correlates of vaginal colonisation by Mobiluncus species. Genitourin Med 1991; 67:26±31.

[3]. Holst E, Wathne B, Hovelius B, Mardh P. Bacterial vaginosis: microbiological and clinical findings. Eur J Clin Microbiol 1987; 6:536±541.

[4]. Woodrow N, Lamont RF. Bacterial vaginosis: its importance in obstetrics. Hospital Medicine 1998; 59:447±450.

[5]. Amsel R, Totten P, Spiegel C, Chen K, Eschenbach D, Holmes K. Nonspecific vaginitis: diagnostic techniques and microbial and epidemiologic associations. Am J Med 1983; 74:14±22.

[6]. June 2001. BJOG An International Journal of Obstetrics & Gynaecology 108(5):439-50.

[7]. Shukla KV, Meshram R, Yadav M. Formulation, development and evaluation of transfersomal gel of metronidazole. Journal of Drug Delivery and Therapeutics. **2019** Aug 30;9(4-A):642-5.

[8]. Gayathri, H., & Sangeetha, S. (2022). Pharmaceutical development of metronidazole loaded transferosome gel for skin delivery. International Journal of Health Sciences, 6(S7), 2258–2274.

[9]. Abd El Aziz MA, Sharifipour F, Abedi P, Jahanfar S, Judge HM. Secnidazole for treatment of bacterial vaginosis: a systematic review. BMC women's health. **2019** Dec;19(1):1-2.

[10]. Gillis JC, Wiseman LR. Secnidazole: a review of its antimicrobial activity, pharmacokinetic properties and therapeutic infections and bacterial vaginosis. Drugs.**1996** Apr;51:621-38.

[11]. Singh S, Verma D, Mirza MA, Das AK, Anwer MK, Sultana Y, Talegaonkar S, Iqbal Z. Development and optimization of ketoconazole loaded nano-transfersomal gel for vaginal delivery using Box- Behnken design: In vitro, ex vivo characterization and antimicrobial evaluation. Journal of Drug Delivery Science and Technology. **2017** Jun 1;39:95-103.

[12]. Livengood III CH. Bacterial vaginosis: an overview for 2009. Reviews in obstetrics and Gynecology. **2009**;2(1):28.

[13]. Bagnall P, Rizzolo D. Bacterial vaginosis: A practical review. Jaapa. **2017** Dec 1;30(12):15-21.

[14]. Narayana RC, NM H, Prabhakara P, Singh AK, EVS S. Formulation and in vitro evaluation of in situ gels containing secnidazole for vaginitis. Yakugaku Zasshi. **2009** May 1;129(5):569-74.

[15]. Mansukhlal PA, Narkhede Kantilal B, Prajapati Anuradha P, Narkhede Sachin B. formulation development and evaluation of pH based insitu vaginal gel of secnidazole. Vol-7 Issue-2 **2021** 2395-4396