IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
October 2021 Vol.:22, Issue:3

Preparation and Optimization of Tinidazole Loaded Transfersomal Gel

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Supriya Gawai*; Smita Khedkar; Kedar Bavaskar; Ashish Jain

Shri D. D. Vispute College of pharmacy and research center, Department of Pharmaceutics, devad, India.

Submitted: 23 September 2021
Accepted: 29 September 2021
Published: 30 October 2021

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Non-Ionic Surfactant Vesicles, Tinidazole, Transfersomes, Transfersomal Gel, Vesicular Drug Delivery System

ABSTRACT

Transfersomes are vesicular carriers in drug delivery systems that are reported in the seventies. They are formed by self-assembly of non-ionic surfactant and soyalecithin upon hydration with aqueous media resulting in lamellar a structure that encapsulates both polar and non-polar drugs. In the present research work, Tinidazole transfersomes were prepared by using non-ionic surfactant span 60 and soyalecithin in 80:20 concentration by thin-film hydration method. The prepared Tinidazole transfersomes were incorporated into the gel prepared by varying concentrations of poloxamer 407. Transfersomal gels were evaluated for homogeneity, grittiness, pH, viscosity, spreadability, extrudability, drug content uniformity, *in-vitro* diffusion and stability study.

INTRODUCTION:

This research work aims to formulate Tinidazole transfersomal gel for Bacterial Vaginosis.

The creation of novel drug delivery mechanisms for existing drug molecules has reawakened interest in recent years. The development of a novel delivery system for existing drug molecules has enhanced the drug's performance in terms of safety and efficacy. Also, patient compliance has improved with overall therapeutic benefit to a significant extent.

Currently transdermal delivery is one of the most budding methods for drug application. Transdermal Drug Delivery System (TDDS) are defined as self-contained, discrete dosage forms which when applied to intact skin will deliver the drug through the skin at a controlled rate to the systemic circulation.[1] TDDS are dose formulations that are intended to administer a therapeutically beneficial volume of medication through the skin of a patient. [4]

Transfersomes are vesicular carrier structures with at least one inner aqueous compartment surrounded by a lipid bilayer and an edge activator. Transfersome is an ultra-deformable, highly flexible and stress-responsive complex system that possesses an aqueous core surrounded by lipid bilayer. The name Transfersome means "carrying body" and is derived from Latin word "transferred", meaning "to carry across", and Greek word "soma" for a "body". These are artificial vesicle designed to be cell-like vesicle engages in exocytosis, and thus make it suitable system for controlled and targeted drug delivery of the system via Transdermal route is an interesting option because this route is convenient, safe and offer several advantages over conventional routes. [2]

By squeezing themselves around the intracellular sealing lipid of the stratum corneum, this mechanism overcomes the difficulties of skin penetration. The flexibility of transferosomes is governed by mixing suitable surface active components in proper ratios with phospholipids, also the flexibility of transferosomes minimizes the risk of complete vesicle rapture in the skin and allows the Transfersomal system to follow natural water gradient across the epidermis under non-occlusive.[3]

Transfersomes is composed of phospholipids like phosphatidylcholine which self assembles into lipid bilaye in aqueous environment and closes to form a vesicle. A lipid bilayer softening compound is added to increase lipid bilayer flexibility and permeability and known as edge activator. Structural components of transfersomes include non-ionic surfactants, soya lecithin, additives and drug. [11]Tinidazole is an antibacterial and antiparasitic (antiprotozoal)

medication used to treat Giardiasis, Bacterial vaginosis and Amoebiasis infections. Tinidazole is ineffective following oral administration due to its poor water solubility and significant hepatic metabolism. Apart from that, Tinidazole has side effects, most of which occur in the gastrointestinal tract.[13] Furthermore, it causes diarrhoea during these outbreaks, increasing the risk of opioid loss before it takes effect. This issue can be solved by reshaping drug distribution to take place via a particular pathway, such as the skin.[14]

Bacterial vaginosis (BV) is the most common cause of vaginal discharge in women of reproductive age. For numerous years, oral metronidazole has been demonstrated to be an effective treatment for BV. Metronidazole, on the other hand, has a high risk of adverse effects, which might make sticking to a 7-day treatment plan difficult, ending in treatment failure. Oral tinidazole has been used to treat bacterial vaginosis for over 25 years, but in a range of dosage regimens.[6] Tinidazole has been found to enhance the cure rate in placebo-controlled studies on many occasions. Longer treatment courses (e.g., 1 g daily for 5 days) are more efficacious than a single oral dosage of 2 g. Oral tinidazole is equally effective as oral metronidazole, intravaginal clindamycin cream, and intravaginal metronidazole tablets in treating BV, according to comparative studies. Tinidazole, on the other hand, has better gastrointestinal tolerability and a less metallic flavor than oral metronidazole.[16]

The objective of this research is to formulate Tinidazole Transfersomes and uniformly disperse it in different gel base to make a Transfersomal gel (hydrogel). Several polymeric hydrogel transfersome systems have been produced and characterized in recent years, but Carbapol 934 and Poloxamer 407 have received a lot of attention for their use in the production of this transfersomal gel.

MATERIALS AND METHODS:

MATERIALS

All the materials and chemicals were of analytical grade and procured from authentic sources. Tinidazole was gifted by Aarti Drugs Ltd., Mumbai, India. Span 60, cholesterol, carbopol 934, poloxamer 407, propylene glycol, glycerol, triethanolamine, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, chloroform, methanol, dialysis membrane was purchased from Research-Lab Fine Chem Industries, Mumbai, India.

Method of preparation of Transfersome:

- **By Thin Film Hydration Method-**[5]

Transfersomal ingredients like non-ionic surfactant and soya-lecithin in different concentrations were dissolved in a volatile organic solvent like ethanol in a beaker and sonicated for complete solubilization of ingredients. In another beaker, drug was made solubilized in methanol. After complete solubilization both the solutions were mixed in a round bottom flask. The volatile organic solvent was removed by using rotary flash vacuum evaporator under vacuum reduce pressure (600 mmHg) at 60℃ temperature for about 1hr with the speed of 120rpm, leaving a thin film on the wall of flask. The dried layer was hydrated using aqueous media like phosphate-buffered saline (PBS) pH 4.5 with gentle shaking for about 1hr and the suspension was kept in desiccators (overnight) for hydration and complete removal of organic solvent. After hydration transfersomal dispersion was further sonicated to get uniform unilamellar vesicles.

Separation of unentrapped material

- **By Centrifugation-**[8]

The transfersomal suspension is centrifuged and the supernatant solution is separated. After separation, the pellet is washed and then resuspended to obtain a transfersomal suspension free from the unentrapped drug.

Formulation of transfersomal gel

The transfersomal suspension was dispersed into the gel of different concentrations. Poloxamer 407 and carbapol 934 were the gelling agents used. Transfersomal gel with poloxamer 407 was prepared using cold method while transfersomal gel using carbapol 934 was prepared with the help of dispersion method. Other excipients used are Propylene Glycol, Glycerol, methylparaben, propylparaben, triethanolamine and distilled water. During the preparation of transfersomal gel using cold method gelling agent was added in distilled water and kept at cold temperature for 24 hrs before incorporating transfersomal suspension into it, later preservatives were added and pH was adjusted using pH adjuster. In the dispersion method gelling agents and excipients were added in boiling water, to form a uniform viscous mixture whose pH is acidic, triethanolamine was added to make the system more viscous and adjust its pH to the optimum level. Later transferosomal dispersion is then

added to gel base and pH was adjusted using pH adjuster. Formulation codes and composition of Transfersomal Gel is given in **Table No. 1.**

Table No. 1: **Formulation codes and composition of Transfersomal Gel**

Formulation codes	Carbapol 934	Poloxamer 407	Propylene Glycol	Glycerol
TG1	0.5%	-	10%	30%
TG2	1%	-	10%	30%
TG3	-	20%	-	-
TG4	-	22%	-	-

Evaluation of transfersomal gel

1. Physical appearance:[10]

The prepared Transferosomal gel was evaluated for its color, odour, transparency, texture and flocculation by the visual inspection. After the addition of Transfersomal dispersion, the gel turns opaque.

2. pH: [8]

The pH of gel formulation was determined by using digital pH meter. The electrode is first calibrated with pH 4.0 and pH 7.0 solution, and then the readings were recorded on pH meter.

3. Homogeneity: [9]

The prepared Transferosomal gel formulation was checked for the presence of any floccules or sediment by visual inspection.

4. Spreadability: [7] [19]

The spreadability of the formulation was determined using the Spreadability apparatus. 1gm of gel was placed on glass slide which was fixed on a wooden block placed the second slide above the first. The thread was passed over the pulley whose one terminal was attached to slide while another was tied with weight. The time required to separate the two slides i.e. the time in which the upper slide slips over the lower slide is noted and taken as a measure of spreadability. The experiments were done in triplicate. The following formula is used to calculate the spreadability:

$$S = m \times \frac{l}{t}$$

Where, S is the Spreadability

m is the weight tied to the upper slide (g)

l is the length of glass slide (cm)

t is the time taken to separate the slide from each other (s)

5. Extrudability: [6]

Transferosomal gel was filled in collapsible aluminum tubes of 10gm and sealed. A collapsible tube was placed between two slides on which weight of 500gm was placed. The amount of gel extruded was noted and weighed.

6. Percent Drug content: [14]

To ensure uniform distribution of drug (entrapped in transfersomes) into the gel, fixed quantity of the gel samples was collected from a different location (top, middle and bottom) of the tube and weighed accurately 0.250 g of formulation and transferred in a 250 ml volumetric flask each and diluted with 100 ml methanol (as it also breaks the transfersomal structure). Flask was shaken vigorously for 30 min on the mechanical shaker to disperse the gel and sonicated for about 10 – 15 min for complete extraction of drug. Then this solution was filtered and was analyzed by a UV-Vis spectrophotometer. Drug content was determined from the standard calibration curve of drug.

7. *In-vitro* diffusion study: [12]

In-vitro diffusion study is also termed an *in-vitro* drug release study. This study is carried out by using diffusion cell and diffusion membranes. In-vitro diffusion studies of transfersomal gels were carried out by suing a set of Franz diffusion cells, to study the release rate of drug from the formulation. The receptor chamber was filled with receptor medium (PBS pH 4.5). The receptor medium was stirred continuously and its temperature was kept at 37°C ± 1°C by circulating water through a jacket surrounding the cell body throughout the experiment. A dialysis membrane which was already soaked in receptor medium for 12 hrs was clamped between two chambers. 1 g of the formulation was placed in the donor cell. Subsequently, 1 ml samples were collected after particular time interval from the receptor cell. The same

volume of fresh medium was added after each collection to keep the volume constant. The withdrawn samples were diluted if required and subjected to spectrophotometric analysis using fresh receptor medium as blank. The concentration of drug released at a particular time interval was determined by using an equation generated from standard calibration.

8. Stability Studies:[7]

The stability studies are under process and are carried out as per ICH guidelines. Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. Sample were withdrawn periodically and tested for various evaluation parameters mentioned above. Stable formulation must retain the evaluation parameters at specified storage conditions over a period of time.

RESULTS AND DISCUSSION:

Drug – Excipient Compatibility Study by Fourier Transform Infra-Red (FTIR) Spectroscopy -

IR spectrum of pure drug and excipients along with the mixture of drug and excipients were recorded by FTIR and the compatibility of drug and excipients was checked by comparing the spectra. The FTIR of all the samples is represented in **Figure 1** to **Figure 5** along with spectrum peaks in description. All the characteristic peaks were found in the sample. The FTIR study concluded that there was no interaction between Tinidazole and any of the excipient.

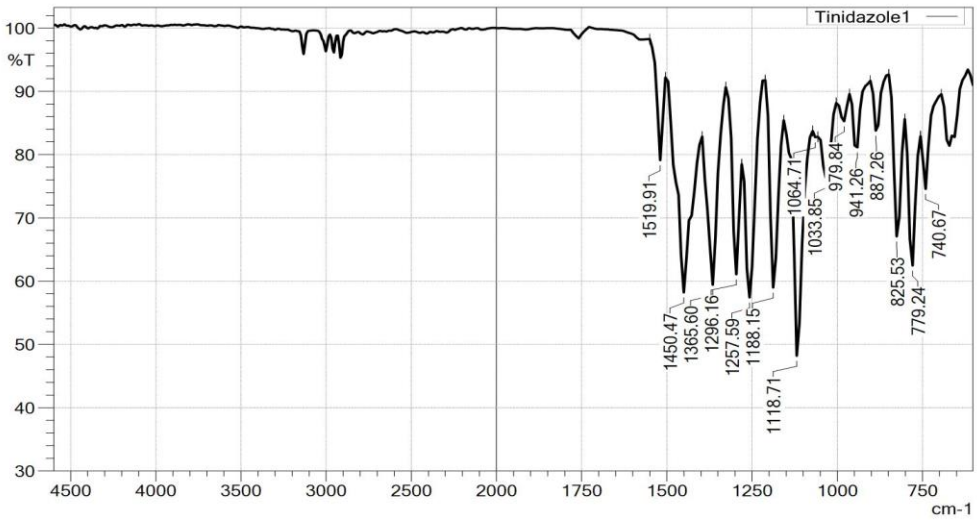

Figure No. 1: IR spectra of Tinidazole.

For IR spectrum the peak of tinidazole for C-H group was noted on 740.67, 779.24, 825.53, 887.26, 941.26, 979.84 cm^{-1} showing Alkenes (out-of-plane bend) ,Aromatics (out-of-plane bend) Type of Vibration with frequency of 1000-650,900-690 cm^{-1}.

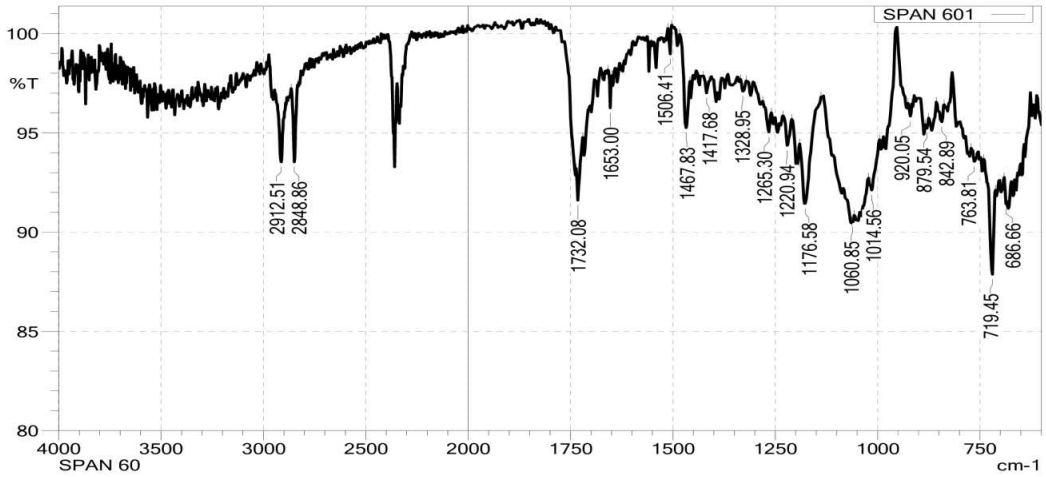

Figure No. 2: IR spectra of Span 60.

IR spectrum the peak of Span-60 for C-H group was noted on 719.45, 763.81, 842.89, 879.54 cm^{-1},showing Aromatics (out-of-plane bend) type of Vibration with frequency of 900 cm^{-1}. For C-O group peak was noted on 1014.56, 1060.85, 1176.58, 1220.94, 1265.30 cm^{-1}, showing Alcohols, Ethers, Esters type of Vibration with frequency of 1350 1000 cm^{-1}. For C-H group IR spectrum peak was noted on 1467.83 cm^{-1}, showing -CH2- (bend) type of Vibration with frequency of 1350 1467 cm^{-1}. For C=O group peak was noted on 1732.08cm^{-1}, showing Ester type of Vibration with frequency of 1750-1730cm^{-1} and for C-H group peak was noted on 2912.51 cm^{-1}, showing Alkanes (stretch) type of Vibration with frequency of 3000-2850 cm^{-1}.

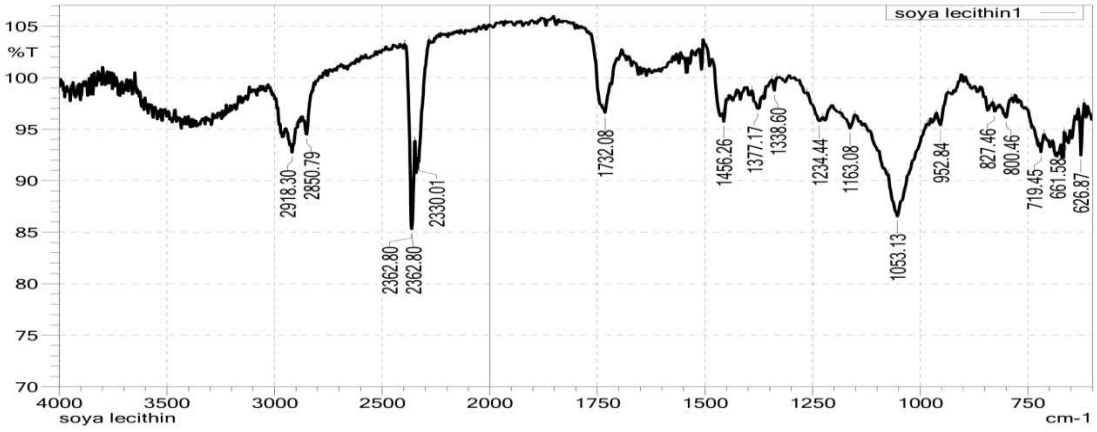

Figure No. 3: IR spectra of Soya lecithin

IR spectrum the peak of Soya lecithin for C-O group was noted on 1053.13, 1163.08 cm^{-1},showing C-O bonds type of Vibration with frequency of 1200-970 cm^{-1}. For C-H group peak was noted on 1456.26 cm^{-1}, showing -CH2- (bend) type of Vibration with frequency of 1456 cm^{-1}. For C=O group IR spectrum peak was noted on 1732.08 cm^{-1}, showing Carboxylic acids type of Vibration with frequency of 1765-1720 cm^{-1} and for C-H group peak was noted on 2918.30, 2850.79 cm^{-1}, showing Alkanes (stretch) type of Vibration with frequency of 3000-2850 cm^{-1}.

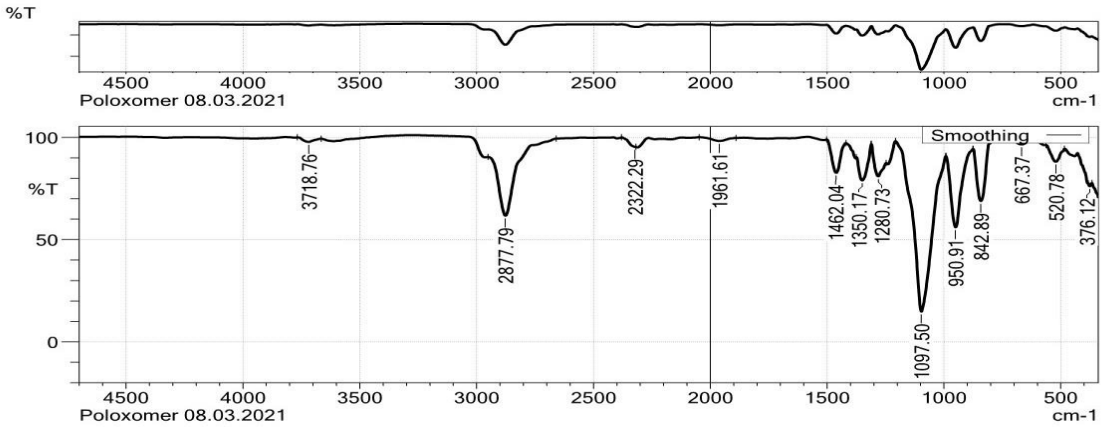

Figure No. 4: IR spectra of poloxamer 407

IR spectrum the peak of poloxamer 407 for C-H group was noted on 842.89,950.91 cm^{-1},showing Alkenes (out-of-plane bend) Aromatics (out-of-plane bend) type of Vibration with frequency of 1000-650 and 900-690 cm^{-1}. For C-O group peak was noted on 1097.50, 1280.73 cm^{-1}, showing - Carboxylic acids type of Vibration with frequency of 1300-1000 cm^{-1} and for C-H group peak was noted on 2877.79 cm^{-1}, showing Alkanes (stretch) type of Vibration with frequency of 3000-2850 cm^{-1}.

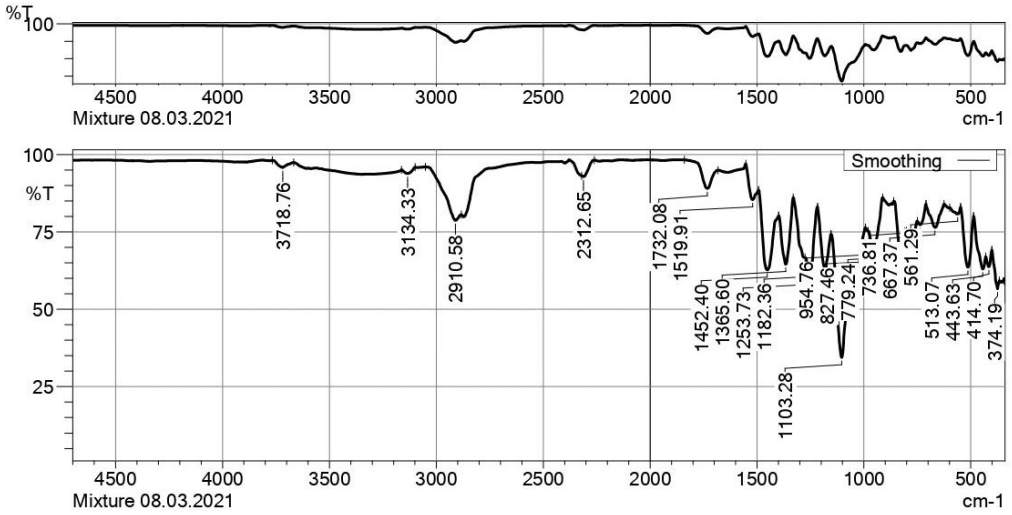

Figure No. 5: IR spectra of API and Excipients

IR spectrum the peak of API and Excipients for C-H group was noted on 736.81, 779.24, 827.46, 954.76 cm^{-1},showing Alkenes (out-of-plane bend) Aromatics (out-of-plane bend) type of Vibration with frequency of 1000-650 and 900-690 cm^{-1}. For C-O and C-N group peak was noted on 1182.36, 1253.73 cm^{-1} showing Alcohols, Ethers, Esters, Carboxylic acids, Amines type of Vibration with frequency of 1300-1000,1350-1000 cm^{-1}. For C=O group peak was noted on 1732.08 cm^{-1} showing Ester type of Vibration with frequency of 1750-1730 cm^{-1} and for C-H and O-H group peak was noted on 2910.58 cm^{-1}, showing Alkanes (stretch) Carboxylic acid type of Vibration with frequency 3000-2850 and 3400-2400cm^{-1}.

- **Transfersomal Gel**

The results of all the evaluation parameters (homogeneity, grittiness, pH, viscosity, spreadability, extrudability, drug content uniformity, and in-vitro diffusion study) of Transfersomal gels are tabulated in **Table 2.**

Table No. 2: Results of evaluation parameters of Transfersomal Gel.

Formulation Evaluation		TG1	TG2	TG3	TG4
Homogeneity		+++	++	++	+++
Grittiness		+++	++	++	+++
pH		4.52±0.05	4.49±0.05	4.51±0.05	4.54±0.05
Viscosity (cP)		35,060	41,480	30,740	49,530
Spreadability (g.cm/sec)		25	18.75	37.50	31.25
Extrudability (%)		94	96	93	95
Drug Content Uniformity(%)		81.26	84.21	85.29	90.41
In-vitro Diffusion (%)	0 hrs	7.95	5.96	6.95	8.94
1 hrs		22.51	19.42	18.42	20.50
2 hrs		31.10	28.96	22.87	23.97
3 hrs		36.65	40.54	34.43	33.54
4 hrs		41.47	43.41	40.22	39.31
5 hrs		47.39	52.54	52.20	47.21
6 hrs		59.50	56.25	53.26	56.29
7 hrs		65.77	65.77	67.52	68.57
8 hrs		75.18	73.15	79.01	78.06
9 hrs		79.70	78.64	86.65	86.70
10hrs		81.23	84.21	85.29	90.41
* n (number of observations) = 03					
+++ Excellent, ++ Good, + Satisfactory, - Poor, -- Fail					

TG1 and TG4were found to be best in case of homogeneity as compared to other Transfersomal gel. TG2and TG3 showed the presence of aggregates and lumps.

No appreciable particulate matter was seen in TG1 and TG4 under an optical microscope. Hence obviously it fulfills the requirement of freedom from particulate matter. TG2 and TG3 failed the test.

TG1 and TG4 were found to have appropriate viscosity suitable for topical application. TG2 was slightly more viscous. The viscosity of TG3 was found to be very low.

The spreadability of TG1 and TG4 was found to be good as compared to TG2 and TG3. Lesser the time taken for separation of two slides indicates more slip and better spreadability. Least resistance to the separation of the slides indicates good spreadability.

More quantity of transfersomal gel extruded indicates better extrudability. The Extrudability of TG1 and TG4 was found better as compared to other formulations.

Drug content uniformity of TG4 was found to be best represent the homogeneous distribution of drug (entrapped in transfersomes) throughout the gel.

In-vitro Drug release of all Formulations is shown in graphical format in **Fig no. 6.**

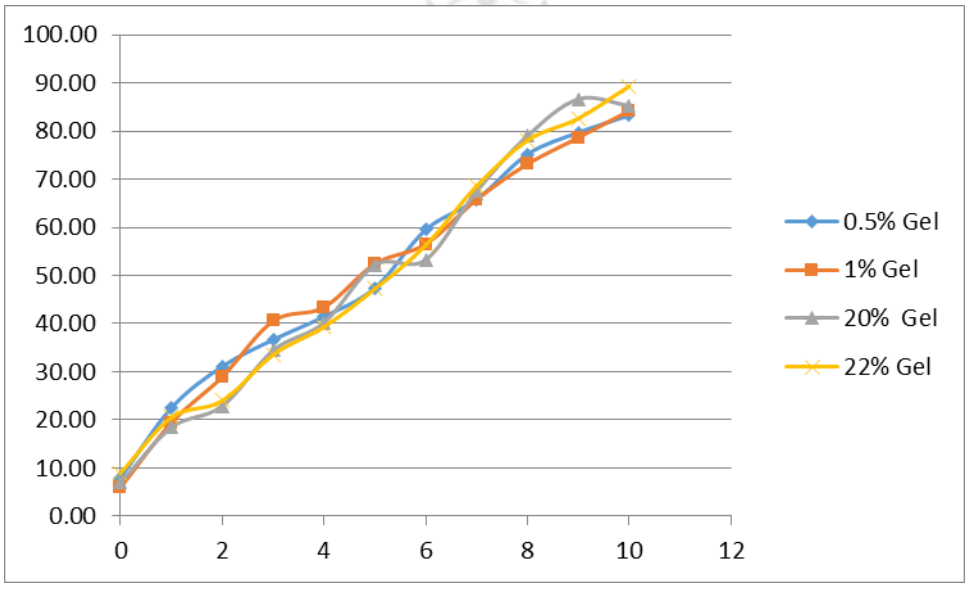

Figure No. 6: *In-vitro* Drug release of Formulation.

- **Drug Release Kinetic Modeling**

The in-vitro release data was fitted in various release kinetic models to predict the release mechanism of drug from the Transfersomal gel. From **Figure no. 7** to **Figure no. 11.**

Figure no. 7: Zero-order model kinetic release

Figure no. 8: First order model kinetic release

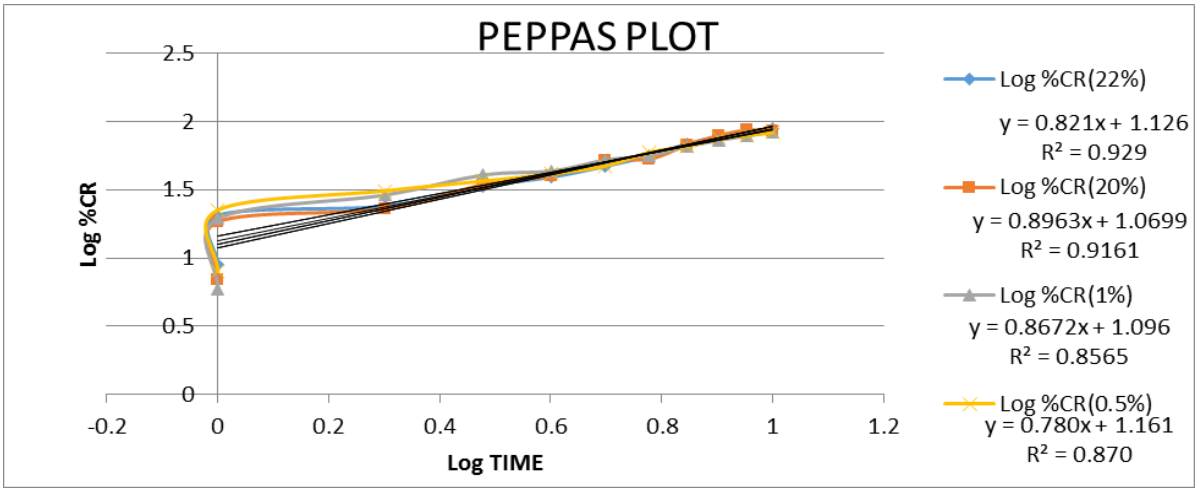

Figure no. 9: Korsmeyer-peppas model kinetic release

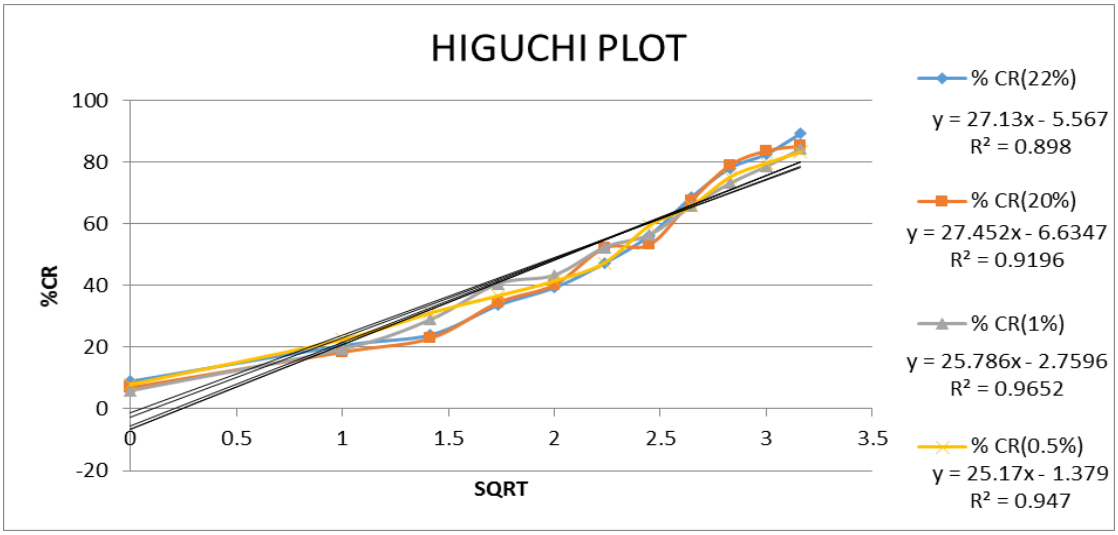

Figure no. 10: Higuchi model kinetic release

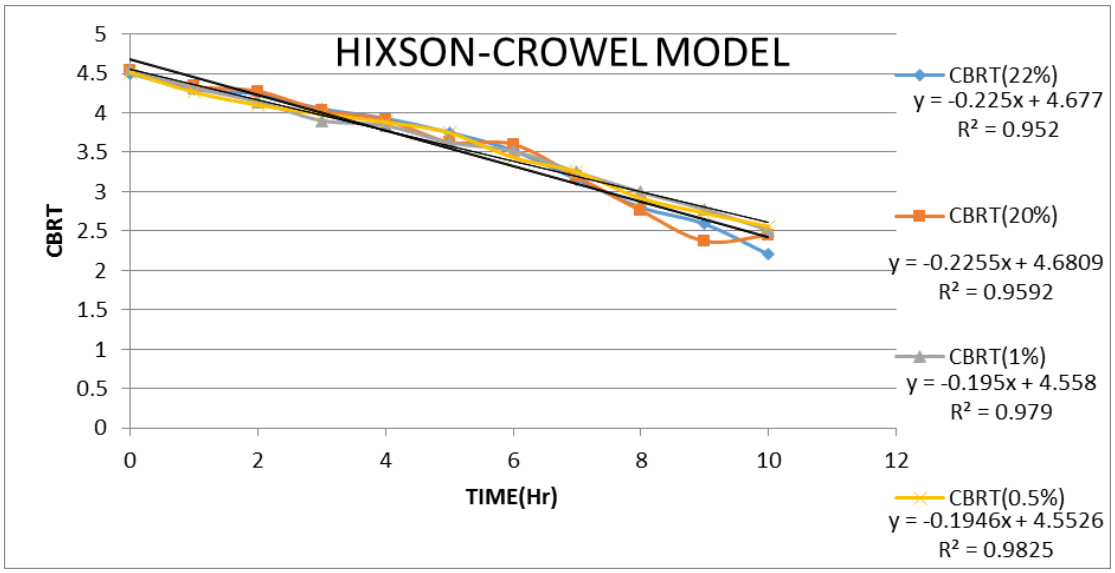

Figure no. 11: Hixson-Crowell model kinetic release

Table No. 3: R^2 values of formulations from the drug release kinetic models

Formulation / Kinetic models	TG1 (0.5%)	TG2 (1%)	TG3 (20%)	TG4 (22%)
Zero order model	0.983	0.984	0.985	0.992
First order model	0.825	0.782	0.869	0.913
Higuchi model	0.947	0.965	0.919	0.898
Korsmeyer-peppas model	0.870	0.856	0.916	0.929
Hixson-crowell model	0.982	0.979	0.959	0.952

The R^2 values of the formulations were tabulated in **table no. 3** respectively. The results revealed that all the formulations were best fitted in the zero-order release kinetic model as they showed the highest R^2 value among all the kinetic models. Hence, all the formulation follows the zero-order release. But the formulation F4TG4 showed the highest R^2 value among all the formulations indicating the best zero-order release kinetics. It indicates that a constant amount of drug is released per unit time from the Transfersomal gel

- **Stability Study**

The stability study of the Transfersomal gels was performed as per ICH guidelines. Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. The sample was withdrawn periodically and tested for various evaluation parameters. The results of the stability study are tabulated in **table no. 4** respectively.

Table No. 4: Stability Study of TG4Transfersomal Gel.

Formulation	**TG4**			
Storage condition	30℃ ± 2℃ / 65 % RH ± 5 % RH			
Time interval (days)	0	30	60	90
Homogeneity	+++	+++	+++	+++
Grittiness	+++	+++	+++	+++
pH	4.54±0.05	4.53±0.05	4.50±0.05	4.50 ±0.05
Viscosity (cP)	49,530	49,530	49,530	49,530
Spreadability (g.cm/sec)	31.25	31.25	28.84	28.24
Extrudability (%)	93	93	93	93
Drug content uniformity (%)	90.41	87.79	84.69	82.31
* n (number of observations) = 03				
+++ Excellent, ++ Good, + Satisfactory, - Poor, -- Fail				

There was not much more variation in the properties of transfersomal gel TG4 under stability study as the formulation retained all the properties when stored at specified storage conditions over a while, indicating that the transfersomal gel was very much stable.

- **Microbiological studies** [17,18]

Microbiological tests were performed on the improved formulation as well as a 2 % w/v plain drug solution to compare against microorganisms. The test microorganism will be *Staphylococcus aureus*. In the Petri-plate, a layer of nutrient agar (20 mL) was allowed to solidify before being seeded with the test micro-organism (0.2 mL). With the aid of a sterile borer with a 4 mm diameter, cups were formed on the solidified agar layer. The cups will then be filled with a volume of the optimized formulation. The Petri plate was kept at room temperature for 4 hours before being incubated at 37°C for 24 hours. The zone of inhibition was observed. Zone of inhibition of Optimized formulation is shown in **Fig no. 12.**

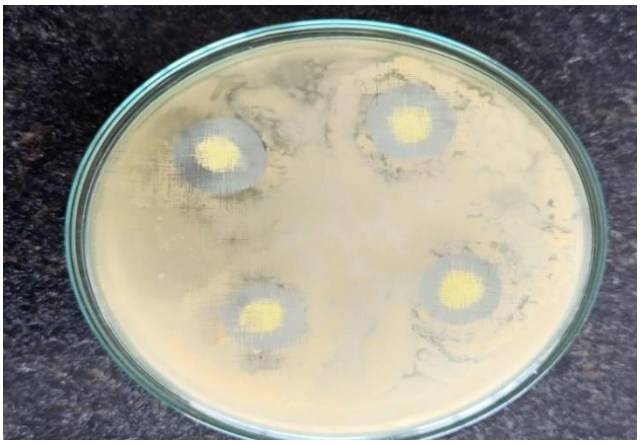

Fig no. 12: Zone of inhibition of Optimized formulation

- **Optical Microscopy**

The prepared and optimized sample of Tinidazole Transfersomes was observed for optical microscopy by using electron microscope under 100 X.Microscopic appearance of ultradeformable vesicle formulations obtained by electron microscopy is shown in **Fig no. 13.**

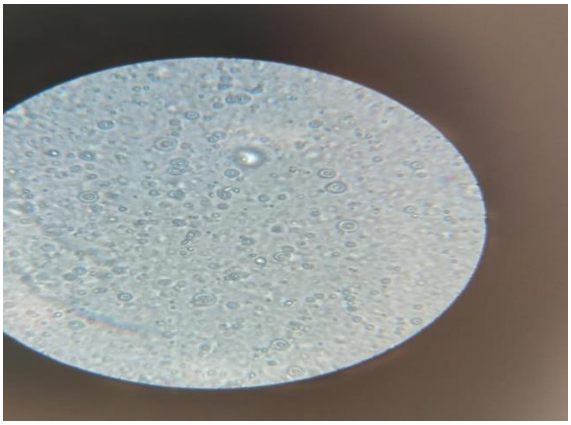

Fig no. 13: Microscopic appearance of ultradeformable vesicle formulations obtained by electron microscopy.

- **Transmission Electron Microscopy**

The prepared and optimized sample of Tinidazole Transfersomal Gel was sent for Transmission Electron microscopy and the result is mentioned in **Figure 14**.

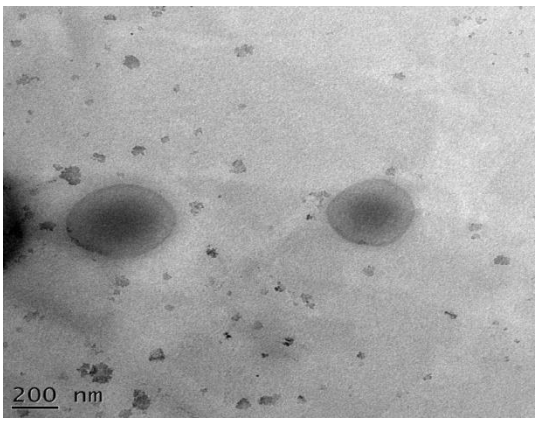

Fig no. 14: Microscopic appearance of ultradeformable vesicle formulations obtained by Transmission electron microscopy.

CONCLUSION:

In this experiment performed transferosomal suspension was dispersed in carbomer and Poloxamer gel, a tinidazole transferosomal gel was created for BV. After evaluation of both the gels, Tinidazole transfersomal gel having poloxamer as the gelling agent was found to have greater *in-vitro* drug release 90.41% along with the highest R^2 value among all the formulations and good stability for shelf life. Tinidazole Transfersomal gel formulation provided sustained and prolonged delivery of Tinidazole in controlled manner with constant release as it follows zero order release kinetics. The transfersomal gel formulation could be a

useful dosage form to reduce the unwanted and undesirable side effects associated with oral route.As a result, transfersomal gel may be regarded the ideal vesicular carrier for Tinidazole administration via the skin. The preparation process is quite simple and industrially viable. The transfersomal gel formulation has a lot of potentials, and its clinical implications can be investigated in the future.

ACKNOWLEDGEMENT

The corresponding author is thankful to Prof. Kedar Bavaskar (Research Guide), Dr. Bhushan Rane (HOD) and Dr. Ashish Jain (Principal) from Shri D. D. Vispute College of Pharmacy and Research Center, India for valuable guidance and for providing excellent facilities to conduct the research. Heartfelt thanks to my parents for their constant support and blessings.

REFERENCES

1. Bala P., Pal K., &Jathar S. Transdermal Drug Delivery System (TDDS) - A Multifaceted Approach for Drug Delivery. Journal of Pharmacy Research. 2015; (8) 1805-1835.
2. Modi C.D., Bharadia P.D. Transfersomes: New dominants for Transdermal delivery. Am. J. pharmTech Res. 2012; 2(3).
3. Bangham A.D. Physical structure and behavior of lipids and lipid enzymes. Adv Lipid Res. 1963; 1:65-104.
4. Solanki D, Kushwah L. Transfersome-A Review. World journal of pharmacy and pharmaceutical sciences. 2016; vol-5,435-449.
5. Bakliwal .S., Rane .B., Jain .A. Transfersomes. A Glimpse of novel drug delivery system, 1ST Edition, nirali prakashan, 2017 pg no-7.1-7.10.
6. Armstrong N, Wilson J. Tinidazole in the treatment of bacterial vaginosis. *Int J Womens Health*. 2009;1:59-65
7. Rane S., Rane B.R., Jain. Formulation development and evaluation of niosomal gel loaded with tinidazole niosomes. World journal of pharmaceutical research. 2018; (15)817-837.
8. Gawai S, Khedkar S, Bavaskar K, Dr. Jain A. Niosome –A Novel Drug Delivery System.' Journal of pharmaceutical chemistry and drug formulation. 2020; vol-2, issue-2 44-59.
9. Thakur N. Thakur P. and Jain V. Development and evaluation clindamycin phosphate transfersomal gel. Journal of Drug Delivery and Therapeutics. 2018; 8(5):168-177.
10. Bala, T.S, Navya, S. Formulation and in vitro evaluation of topical ethosomal gels of miconazole nitrate. World J. Pharm. Res. 2017; 6(8), 1882-1898.
11. Chaurasiya P, Ganju E, Upmanyu N, ray S. K, and Jain P. Transfersome: a novel technique for transdermal drug delivery. Journal of Drug Delivery and Therapeutics. 2019; 9(1):279-285.
12. Sajid S., Gudipati M., Nadendla R. Development and characterization of Micinazole Nitrate Transfersomal gel. International journal of research in pharmaceutical sciences and technology. 2020; 1(4), 109-116
13. National Center for Biotechnology Information. Pub Chem Compound Summary for CID 5479, Tinidazole. https://pubchem.ncbi.nlm.nih.gov/compound/Tinidazole. Accessed Sept. 5, 2021.
14. Patel J, Patel B, Banwait H, Parmar K, Patel M. Formulation and Evaluation of Topical Aceclofenac Gel Using Different Gelling Agent. Int. J. Drug Dev. Res. 2011; 3(1): 156-164.
15. Packard R. S. Tinidazole: a review of clinical experience in anaerobic infections. The Journal of antimicrobial chemotherapy, 10 Suppl A. 1982; 65–78. https://doi.org/10.1093/jac/10.suppl_a.65
16. Heikkinen, J., &Vuopala, S. Anaerobic vaginosis: treatment with tinidazole vaginal tablets. Gynecologic and obstetric investigation. 1989; *28*(2), 98–100. https://doi.org/10.1159/000293524

17. Hatefi, A., &Amsden, B. Biodegradable injectable in situ forming drug delivery systems. Journal of controlled release: official journal of the Controlled Release Society. 2002; 80(1-3), 9–28. https://doi.org/10.1016/s0168-3659(02)00008-1
18. Vernon, B. L., Fusaro, F., Borden, B., & Roy, K. H. Partition-controlled progesterone release from waterborne, in situ-gelling materials. International journal of pharmaceutics. 2004; *274*(1-2), 191–200. https://doi.org/10.1016/j.ijpharm.2004.01.017
19. Rathod H.J, & Mehta D.P A Review on Pharmaceutical Gel. International Journal of Pharmaceutical Sciences. 2015; 1. 33-47.

	Supriya Madhukar Gawai* B-Pharm Shri. D.D. Vispute college of pharmacy and research center, New Panvel.
	Smita Khedkhar B-Pharm Shri. D.D. Vispute college of pharmacy and research center, New Panvel.
	Kedar Bavaskar (Asst Professor) M-Pharm Shri. D.D. Vispute college of pharmacy and research center, New Panvel.
	Dr. Asish Jain (Principal) M-Pharm, PhD. Shri. D.D. Vispute college of pharmacy and research center, New Panvel.