IJPSR (2023), Volume 14, Issue 8 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 07 December 2022; received in revised form, 22 February 2023; accepted 02 May 2023; published 01 August 2023

FORMULATION AND EVALUATION OF BOSWELLIC LOADED TRASFEROSOMES HYDROGEL TO TREAT PSORIASIS

Surbhi Sirswal * and Sanjay Singh

Siddhartha Institute of Pharmacy, Veer Madho Singh Bhandari Uttrakhand Technical University, Dehradun - 248001, Uttrakhand, India.

Keywords:

Transferosomes, Psoriasis, Anti-inflammatory, Herbal drug

Correspondence to Author:
Surbhi Sirswal

Assistant Professor, Department of Pharmaceutical Sciences, Siddhartha Institute of Pharmacy, Veer Madho Singh Bhandari Uttrakhand Technical University, Dehradun - 248001, Uttrakhand, India.

E-mail: Surbhisirswal23@gmail.com

ABSTRACT: Transfersomes, which may penetrate mammalian skin, are notably ultra deformable (ultraflexible) lipid supramolecular aggregates. A type of formulation carrier system called a transfersome can transport medications with both low and high molecular weights transdermally. Transfersomes enter the underlying viable skin in an undamaged state through skin's stratum corneum pores that are smaller than its size. The major goal of the transferosome in treating the condition psoriasis is drug penetration through the skin. However, the stratum corneum is the most formidable defence against drug penetration via the skin. In order to assist penetrate the stratum corneum barrier, the use of lipid vesicles like transfersomes in delivery systems has attracted increasing interest in recent years. The current study set out to statistically improve the vesicular formulations (Transfersomes) of a model medicine, boswellic acid which is obtained from *Boswellia serreta* known as for the treatment of psoriasis.

INTRODUCTION: Most of the time, it is impossible to establish an effective, successful therapeutic treatment. This is frequently because of a variety of factors, including the occurrence of hepatic first-pass metabolism, unfavorable side effects, the rejection of invasive treatments, and low patient compliance [1]. Various medication delivery systems have been created and researched to solve these issues over the years. Transdermal delivery systems are a viable strategy because they are minimally invasive and have no first-pass effects. However, addressing the skin's barrier function is necessary, which prohibits or muffles the transdermal transport of medicinal substances [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(8).4054-60

This article can be accessed online on www.ijpsr.com

DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(8).4054-60

The barrier function of the top layer of skin is the biggest difficulty for transdermal delivery methods. Ionized substances and molecules with molecular weights larger than 500 Da typically cannot penetrate through skin. As a result, this route can only be used to provide a small number of medications. One potential solution to this issue is to encapsulate the medications in transfersomes. In contrast to traditional liposomes, they feature a bilayered structure that makes it easier to encapsulate hydrophilic, lipophilic, and amphiphilic drugs.

Because they are naturally elastic, transfersomes can deform and compress through tiny pores much smaller than their own size [3]. Transferosomes are a successful drug delivery carrier for transdermal applications because, in contrast to liposomes, they may transmit larger quantities of active compounds to intact deeper parts of the skin after topical administration Phosphatidylcholine (C18).

A unique kind of artificial vesicle called a transferosome, a new drug delivery device, contains phosphatidylcholine and an edge activator. Phosphatidylcholine makes up the majority of transferosomes and is the most prevalent lipid in cell membranes, which is well tolerated by skin, lowering the likelihood of side effects such hypersensitivity reactions. A specific kind of composite body, known as a transferosome, has been developed under the theory of the rational membrane to solve the problem of penetration across skin barriers and a transcutaneous moisture gradient. It is a synthetic vesicle that may deform more than regular liposomes by many orders of magnitude. These have greater elasticity than regular liposomes. For efficient transdermal medication administration, transferosomes have been employed extensively as a new carrier Surfactants like Tween® 80, Span® 80, and sodium deoxycholate are the most popular edge activators [4-6]. Conventional liposomes have drawbacks as well, including a poor ability to encapsulate hydrophilic medicines, an unstable membrane that causes leaky behaviour, and a brief half-life. Other unique vesicles, including niosomes, sphingosomes, bilosomes, chitosomes, transfersomes, ethosomes and invasomes have been discovered and developed as a result of these significant challenges [7]. An herbal extract obtained from the *Boswellia serrata* tree is called Boswellia, often known as Indian frankincense. In Asian and African traditional medicine, Boswellia extract resin has been utilised for generations. More than 200 bioactive substances can be found in *Boswellia species*. Among these, boswellic acid (BA) has been demonstrated to have significant anti-inflammatory effects, which has demonstrated significant pharmacological efficacy in treating several inflammatory illnesses, including rheumatoid arthritis, osteoarthritis, and asthma. Active substances are currently administered to psoriatic and eczematous patients topically [8-10].

MATERIALS AND METHODS:

Materials:

Active Ingredient: Boswellic acid grade quality with the lot number SB1W0030 and PDR-No. 30076166 was acquired from LobaChemPvt. Ltd in India. It has a mean particle size of around 25 µm, a melting range of 184-186°C and a distinctive odour. It is a white, crystalline powder. This sample meets the standard of current Indian Pharmacopeia (IP) and United State Pharmacopoeia (USP).

Inactive Ingredients: Span 80 and Tween 80, Triton and Lecithin x-1200, 6-carboxyfluorescein provided from Aglowmed Limited, Roorkee India.

Analytical Reagents: Acetonitrile (ACN), triethylamine, potassium phosphate monobasic and orthophosphoric acid were procured from Aglowmed limited, Roorkee India. All reagents used were of grade analytical Sodium hydroxide.

Methods:

Preparation of transfersome: By using the lipid film hydration methodology and a handshaking technique, the transfersome was formed. As a modified handshake, the ingredients and composition are listed in **Table 1**.

TABLE 1: COMPOSITION FOR THE FORMULATION

Edge activator	Formulation code	LC:TS*	Solvent
TWEEN 80	NAV1	95:05	Ethanol
	NAV2	85:15	
	NAV3	95:05	Isopropyl Alcohol
	NAV4	85:15	
SPAN 80	NAV1	95:05	Ethanol
	NAV2	85:15	
	NAV3	95:05	Isopropyl Alcohol
	NAV4	85:15	

*LC = Lacithin and TS = Tween 80 and Span 80

The medication boswellic acid and the edge activator will be dissolved in a 1: 1 ratio before making the mixture. The organic solvent will be eliminated by evaporation with the aid of handshaking above the 42°C transition temperature. A thin film will form on the flask's inner layer due to the rotator's motion. A thin coating of the produced formulation is set aside for at least 24 hours to ensure that the organic solvent completely evaporates. With the aid of a pH 7.4 phosphate

buffer, the preparation's film is hydrated. The suspension is then further hydrated for an hour at temperatures ranging from 2 to 80 ° C[2].

Formulation Optimization: For the preparation and formulation qualities, many transferome preparation processes are used. Procedures for formulation and preparation are well-validated and optimised. Boswellic acid-containing trans-ferosome formulation involves a number of variable processes, including effects of the Lecithin: Surfactant ratio (95:05, 85:15), effects of the formulation's solvents (ethanol, isopropyl alcohol), and changes brought about by surfactants like Span 80 and Tween 80. The drug is then entrapped in the transferosomes, and the efficacy of entrapment is assessed and improved. Other preparatory variables were kept constant when the transferosomes system was being developed.

Data Interference Study: The interference investigation for the drug-polymer, drug diluents, and drug lubricants, which were used as additives in the formulation, was conducted using the FTIR method.

Characterization of Transferosome Formulation: Photomicroscopy will be used to characterize the transferosome formulation, and electron microscopy will also be used in this row. In essence, there are the electron microscopes that Philips manufactures. This microscope will be utilised to do more characterisation research.

Calculation of the Entrapment Efficacy of Transferosomes: The centrifugation method will be used to assess the effectiveness of the formulation of transferosomes with boswellic acid at entrapping particles. The prepared transferomes will be placed into the centrifuge, the speed will be set to 1400 rpm, and the procedure will last 30 minutes. The liquid's top layer is removed, and after it has been diluted with phosphate buffer (pH 7.4), the amount of untrapped boswellic acid will be measured using an ultraviolet spectrophotometer at a wavelength of 427.2 nm. Before measuring absorbance, the upper layer of sample should be diluted by 100 parts. This technique will demonstrate the formulation's entrapment effectiveness, finalizing the entrapment effectiveness by the upper layer's boswellic acid content. The percentage of drug trapped is used to calculate the efficiency of entrapment [11].

The trapped drug will be further measured using a UV spectrophotometer and phosphate buffer with a pH of 7.4. After the vesicles have been washed three to four times with phosphate buffer, the values will be analyzed [12].

Zeta Potential Value, Vesicle size Value and size Distribution Determination: For the analysis of zeta potential value, vesicle size value, and size distribution determination, the MalvenZetasizer DTS version 4.90 from the United Kingdom was used. This instrument is used to estimate the permeation of the tranferosomes with the aid of colloidal property and vesicle stability.

Topical Hydrogel Formulation: Carbopol hydrogel has been prepared to integrate transferosomes as a vehicle. To create a topical hydrogel, an improved boswellic acid transfersomes aqueous dispersion was used in **Table 2**.

TABLE 2: FORMULATION OF TOPICAL HYDROGEL

Hydrogel Ingredients	Topical Hydrogel formulation			
	NAV1	NAV2	NAV3	NAV4
Transfersome	Eqv. to 2% of drug	Eqv. to 2% of drug	Eqv. to 2% of drug	Eqv. to 2% of drug
Carbopol971P	0.50%	1.00%	1.50%	2.00%
Propylene glycol	10%	10%	10%	10%
Glycerol	30.5%	30.5%	30.5%	30.5%
Distilled Water		QS		

For the dispersion of optimal transferosomes, the equivalent of 200 milligrammes of pure medication was taken into consideration. The topical hydrogel controlled release formulation hydrogel was created using carbopol 972P, a hydrogel formulation polymer. With care taken to prevent any lumping, the known amount of carbopol 972P powder (0.5g, 1g 1.5g, and 2 g) was well swirled by a magnetic stirrer with distilled water before being left to hydrate for four to five hours. The

dispersion was neutralized to change the pH with 10% (w/v) aqueous sodium hydroxide solutions.

Parameters to Evaluate Topical Hydrogel:

pH Determination: The pH will be calculated at room temperature using a digital pH metre manufactured in Shimazdu, Korea.

Skin Permeation Studies *In-vitro*: Franz diffusion cell, an instrument with a compartment volume of 50 ml and an effective area of 2.45 cm^2, was used for the study. Goat skin was studied using phosphate buffer solution with a pH of 7.4. Fresh goat skin from the slaughterhouse was purchased and gathered for the experiment. After the hair was removed, the skin was preserved in a saline solution while the layer of fatty tissues was also removed using an abrasive substance. Skin was preserved in isopropyl alcohol solution between 0 to 40^oC.

The stratum corneum side of the treated skin was exposed to the Franz diffusion cell donor compartment, while the treated skin was horizontally positioned on the receptor compartment. 50ml could fit in the receptor compartment, and 2.50 cm^2 of the donor compartment was exposed to intense penetration. A magnetic stir bar was used to stir the 50ml of phosphate buffered saline (pH 7.4) in the receptor compartment at 100rpm while it was kept at 37°C.

The skin was treated with a hydrogel formulation (equal to 10 mg of medication), and the top of the diffusion cell was covered. To maintain sink conditions, 1 ml aliquots of the receptor medium were removed at the proper intervals and promptly replaced with an equivalent volume of brand-new phosphate buffers (pH 7.4).

When calculating the release profile, correction factors for each aliquot were taken into account. At max 427.2nm in **Fig. 1**, the samples were examined spectrophotometrically.

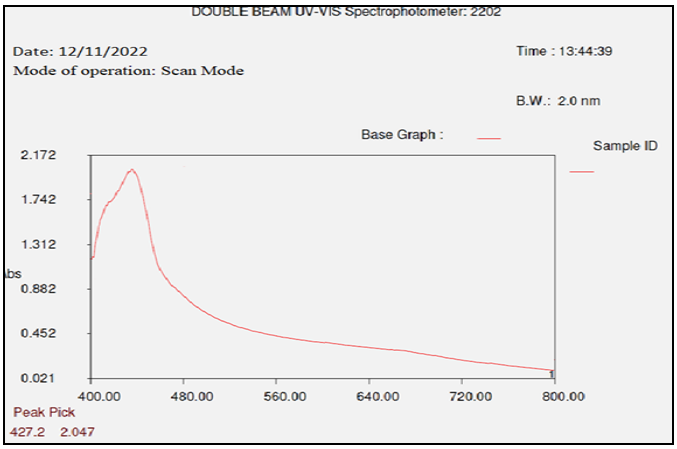

FIG. 1: DETERMINATION OF ABSORPTION MAXIMA (AMAX) IN PBS (pH 7.4)

Studies on Skin Deposition of Optimized Formulation: The skin surface was cleansed five times with ethanol: PBS pH 7.4 (1:1), then with water to remove any remaining drug from the surface at the culmination of the permeation trials (after 24 hours). After that, the skin was diced apart.

The tissue was then further homogenised in an ethanol: buffer solution (1:1) with a pH 7.4 and left at room temperature for 6 hours. Boswellic acid concentration was determined using a UV visible spectrophotometric technique following appropriate dilutions with phosphate buffer solution (pH 7.4) at 427.2nm and shaking for 5 minutes while centrifuging at 5000 rpm. Using a student's t-test, the result was contrasted with the control group.

TABLE 3: ENTRAPMENT EFFICIENCY OF DIFFERENT FORMULATION

Molar ratio (LC:TS)*	Formulation Code	Entrapment Efficiency*(%)
	Tween 80	
95:05	NAV1	67.3±0.073
85:15	NAV2	72.4±0.020
95:05	NAV3	74.3±0.016
85:15	NAV4	76.4±0.084
	Span 80	
95:05	NAV1	72.6±0.032
85:15	NAV2	79.1±0.045
95:05	NAV3	80.9±0.011
85:15	NAV4	89.4 ±0.050

*All values are mean ± S.D. for n=3, LC = Lecithin, TS = Tween 80 & Span 80

TABLE 4: *IN-VITRO* RELEASE STUDY OF TOPICAL HYDROGEL FORMULATIONS (NAV1-NAV4)*

Time in hours	% drug Permeated				
	NAV1	NAV2	NAV3	NAV4	CONVENTIONAL GEL
0	0	0	0	0	0
1	8.87±0.01	8.32±0.03	7.47±0.01	7.01±0.03	3.34±0.02
2	16.49±0.03	16.05±0.02	15.95±0.03	15.53±0.01	5.12±0.05
4	20.80±0.01	20.11±0.02	19.65±0.02	19.32±0.05	8.55±0.01
6	22.30±0.02	21.96±0.04	21.02±0.06	20.78±0.03	13.24±0.02
8	25.04±0.07	25.01±0.05	24.57±0.01	23.51±0.02	16.86±0.03
10	26.30±0.01	25.99±0.05	25.09±0.04	24.59±0.01	20.34±0.07
24	50.62±0.02	49.12±00.01	48.89±0.06	48.54±0/05	33.52±0.01

*All values are mean ± S.D. for n=3

RESULT AND DISCUSSION: Transferosome formulation delivers non-invasive medication across the skin layers. Transferosomes are known as elastic liposomes because of their flexibility characteristics and improved penentration; for this reason, the formulation of transferosomes was carried out.

Characterization of Transfersomes: Electron microscopes and optical microscopes were employed to determine surface morphology. The results were shown in **Fig. 2** & **3.**

FIG. 2: OPTICAL MICROPHAGE OF BOSWELLIC ACID LOADED TRANSFEROSOMES AT 10X

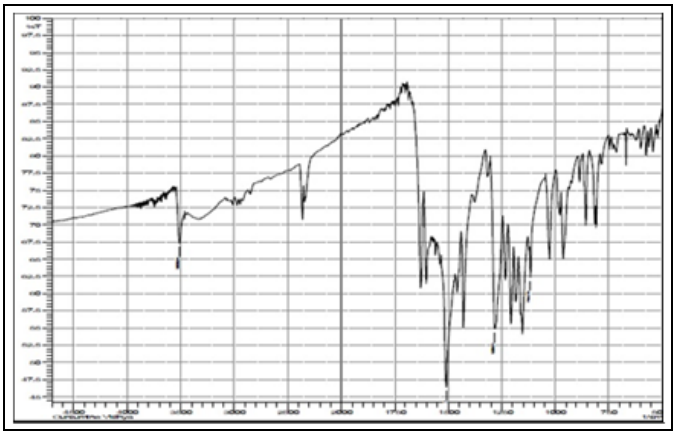

FIG. 3: IR SPECTRA OF BOSWELLIC ACID WITH PREPARED FORMULATION

Study of Interference: Interference of drug to polymer is tested under drug diluents. The drug and the lubricants used in the formulation result in the decision that there is no drug intraction in the formulation, which is shown in **Fig. 4.**

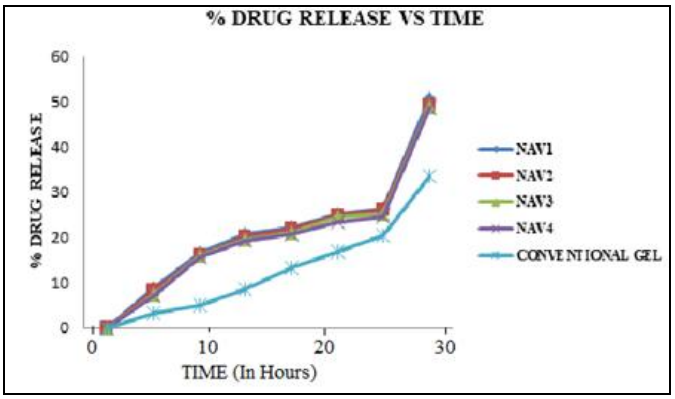

FIG. 4: *IN-VITRO* DRUG RELEASE STUDY OF TOPICAL HYDROGEL FORMULATION

Efficacy of Entrapment: Deformable vescicles entrapment efficacy was found to be in range of 68.2±0.074 to 89.6±0.049 Table C. Entrapment efficacy of the T8 was shown maximum which was (89.6±0.049 for T8). Comparison of encapsulated aqueous volume with lipid volume in the vesicles and the effect of edge activator and the phospholipid have positive effect on the boswellic acid but when we increase the surfactant quantity in the formulation than the entrapment efficacy of formulation decreases concentration but have certain limit of PC:EA.

Zeta Potential, Vesicle Size Value and Size Distribution Value: Malvern Zetasizer instrument was employed for the present study by the help of the light scattering method; the values of vesicle size, size distribution and zeta potential were analyzed with boswellic acid loaded formulation T8 and the mean size of the vesicles was found to be 336.4 nm in **Fig. 3** and **4.** Normal size

distribution was found by analyzing the size distribution curve. Transferoisomal vesicles containing ethanol were large because ethanol is highly soluble in water compared with isopropyl alcohol. Edge activator effect on vesicles as of Span 80 was small compared to tween 80; both were of the same size with the same solvent system.

pH Estimation of Boswellic Acid Loaded Transferosomes: The pH value of topical boswellic acid loaded transferosomes was measured by using digital pH meter of Schimazdu Korea at the room temperature. The value of pH of topical boswellic acid loaded transferosomes NAV1, NAV2, NAV3 and NAV4 were found 6.5±0.22, 6.3±0.24, 6.4±0.12 and 6.7±0.35 respectively.

***In-vitro* Release Study of Boswellic Acid Loaded Transferosomes:** Boswellic acid loaded transferosomes topically release *in-vitro* study is done and analyzed by the instrument Franz diffusion cells which were processed for time of 24 hours with phosphate buffer at the pH 7.4 with temperature range between 37 degree celcius to 37.5 degree celcius and 100 rpm in the sinked form all the data of dissolution shown in the Table. The result of dissolution profiles showed that the concentration of gelling agent (Carbopol 971P) in the range of 0.5% to 2.0% affects the release rate slightly. Regarding the formulation NAV1 to NAV4, the values of drug release after 24 hrs were found to be 50.62%, 49.12%, 48.89% and 48.54% respectively.

The values of drug release of the formulations NAV1 to NAV4 after 4 hour were found to be 20.80%, 20.11%, 19.65% and 19.32% respectively. This result of the dissolution profile showed slight initial burst release. This is probably caused by the Release of drug absorbed on the transfersome surface or precipitated from the superficial lipid layer. Prolonged Release in the later stage can be attributed to the slow diffusion of the drug from the lipid vesicle.

Kinetic Analysis of Dissolution Data: The drug release data were explored for the type of release mechanism followed. Release kinetic study of all formulations (NAV1 to NAV4) was studied in Table E for different kinetic equations (zero order, first order, and Higuchi equation). The best fit with higher correlation ($r^2 > 0.99$) was found with Higuchi's equation for all the formulations, which means that the Release of boswellic acid from the lipid layer vesicles was due to diffusion. The kinetic release study was again verified by putting the values of release data in modern biopharmaceutics software MB-V6 and found that all the formulations follow the Higuchi model. Hence, we can state that the Release of boswellic acid from the lipid bilayer system was mainly due to the diffusion mechanism.

CONCLUSION: A popular and effective natural anti-inflammatory medication is boswellic acid. Its action is comparable to that of NSAIDs in the treatment of inflammatory pain. When used orally, the main issue with boswellic acid is its poor bioavailability due to decreased GI absorption. Since it is a herbal medication, it has no side effects such as hepatotoxicity, upper GIT haemorrhage, or other adverse reactions. Approximately 25 to 85% of orally supplied boswellic acid is excreted in the faeces unabsorbed. Due to limited permeability through skin, its topical application is extremely tough.

Transfersomes, a vesicular drug delivery device, are designed to distribute Boswellic acid over skin in order to solve this issue. A possible method to increase the permeability of boswellic acid over time is to manufacture transfersomes from TS: Span80 in the ratio 85:15 (in mmol). Finally, we come to the conclusion that boswellic acid gel with transfersome entrapment provides superior penetration than plain drug gel. Transdermal distribution necessitates a higher permeability because the drug dose is so high. Due to this characteristic, transdermal administration of boswellic acid via a transfersomal formulation is more effective.

ACKNOWLEDGEMENT: I am very thankful to Dr. Sharad Visht (Professor, Tishk International University, Erbil, Iraq) and Dr. Sanjay Singh (Principal of Siddhartha Institute of Pharmacy, Dehradun, India) for their constant support.

CONFLICTS OF INTEREST: There is no conflict of interest.

REFERENCE:

1. Chaurasiya P, Ganju E, Upmanyu N, Ray SK and Jain P: Transfersomes: A novel technique for transdermal drug delivery. Journal of Drug Delivery and. Therapeutics 2019; 9: 279–285.
2. Jain AK: Kumar F: Transfersomes: Ultradeformable vesicles for transdermal drug delivery, Asian Journal of Biomaterial and Research 2017; 3: 1–13.
3. Shakthi ATO, Varin T and Romchat C: Transfersomes: A promising nanoencapsulation technique for transdermal drug delivery. National Libraby of Medicines 2020; 12(9): 855.
4. Raquel FG, Aikaterini L, Larry S, Francisco BF, Ballesteros MP and Dolores RS: Transferosomes as nanocarriers for drugs across the skin: Quality by design from lab to industrial scale. International Journal of Pharmaceutics 2020; 573: 118817.
5. Abhay K: Transferosome: A recent approach for transdermal drug delivery. Journal of Drug Delivery and Therapeutics 2018; 8(5): 100-104.
6. Lovely C, Anuj P, Sakshi G and Gargi G: Topical drug delivery of ketoconazole entrapped transferosomal gel with design and enactment. International Journal of Pharmaceutics and Research 2021; 12(12): 6615-6616.
7. Ge X, Wei M, He S and Yuan W: Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery. Pharmaceutics 2019; 11: 55.
8. Moncivaiz A: Overview-Boswellia (Indian Frankincense), Healthline, 2018; 1-2 (https://www.healthline.com/health/boswellia).
9. Nair AS and Paliwal A: Systems pharmacology and molecular docking strategies prioritize natural molecules as anti-inflammatory agents, Inflammation anf Natural Products- Science Direct 2021; 283-319.
10. Ganpeng Y, Wang X, Tianqing Z, Liuting Z, Kailin Y and Jun L: Effectiveness of Boswellia and Boswellia extract for osteoarthritis patients: A systematic review and meta-analysis, BMC Complementary Medicine and Therapies 2020; 20: 225.
11. Pravalika R and Bindu EH: Formulation and Evaluation of Transferosomes Loaded with an Anti-Hyperlipidemic Drug, J of Scientific Res and Reports 2021; 21(6): 65-71.
12. Yadav D, Sandeep K, Pandey D and Dutta RK: Liposomes for drug delivery. Journal of Biotechnology and Biomaterial 2017; 7: 1–8.

How to cite this article:
Sirswal S and Singh S: Formulation and evaluation of boswellic loaded trasferosomes hydrogel to treat psoriasis. Int J Pharm Sci & Res 2023; 14(8): 4054-60. doi: 10.13040/IJPSR.0975-8232.14(8).4054-60.