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Original Research Article

FORMULATION AND EVALUATION OF FELBINAC LOADED TRANSFEROSOMES GEL FOR ANTI-INFLAMMATORY EFFECT

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ABSTRACT

Inflammation is a process that occurs as a result of tissue damage, generating venule dilatation, increased vascular permeability, and infiltration of histamine, cytokines, and other inflammatory components. The strong medications frequently have off-target effects, which significantly reduces patient compliance. Furthermore, traditional nonsteroidal anti-inflammatory drugs face numerous formulation problems. The goal of this study is to development & evaluation of transferosomal gel of Felbinac for treating inflammation. The falbinac was first procured. The optimization of transferosome was performed for various parameters. Further transferosomal gel was prepared by standard methods. Results revealed that formulation F-12 have all ideal characteristics. The size & zeta potential for F-12 was noted to be 125.45nm & -38.12 mv respectively. The % Entrapment efficiency for the same was found to be 75.65%. The optimized transferososmal gel has Extrudability & Spreadability of 178±4 gm & 13.36±0.15 g.cm/sec respectively. The gel viscosity was estimated to be 3256±15 cps. In vitro drug release study of prepared gel formulation revealed that 96.65% of drug was released in 12 hr. The release kinetics data of optimized transferosomal gel suggested that it follows Korsmeyer model which is evident from R^2 value of 0.990. Stability study data revealed that the gel is stable for 3 months at 4.0 ±0. 2°C with average particle size of 236.45 nm & % Entrapment efficiency of 70.12. So, it can be concluded that the combined action of felbinac and transferosome for topical administration can be used in the treatment of inflammation.

Keywords: Infllammation, Transferosomal gel, Novel drug delivery, Transdermal druf delivery, Transferosomal gel, felbinac

INTRODUCTION

Inflammation is a vital biological reaction triggered by a variety of adverse stimuli such as viruses, bacterial infections, poisons, toxic chemicals, and tissue injury. Inflammatory cytokines and reactive oxygen species are generated during inflammation. Inflammatory cytokines bind to numerous receptors on target cells' plasma membranes. Internalisation of receptors and entry into early endosomes, where components of the signalling cascade might meet, is required to launch the signalling cascade and activate transcription factors. The receptor's subsequent cytoplasmic destiny is critical to the progression and course of inflammation (Ahmed, 2011; Medzhitov, 2008; Trowbridge *et al*., 1997).

Inflammation is treated with frequent drug administration and large doses of NSAIDs such as indomethacin, diclofenac, ibuprofen, celecoxib, and etorcoxib. These strong medications frequently have side effects that significantly reduce patient compliance. Furthermore, typical nonsteroidal anti-inflammatory drugs face numerous formulation issues such as limited solubility and permeability, poor bioavailability, gastrointestinal enzyme degradation, food interactions, and toxicity (Halliwell *et al*., 1998). To circumvent these obstacles, researchers have turned to topical medication administration, which has higher patient compliance and avoids the first past effect seen with conventional oral administration. Furthermore, nanosized carriers such as transferosomes have been devised to improve drug absorption through the layers of the skin and reach the site of inflammation. These drug delivery methods are non-toxic, have high drug encapsulation efficiency, and provide prolonged drug release (Vane and Botting, 1996).

Transferosomes are ultra-deformable vesicles with an aqueous core and a complex lipid bilayer. The bilayer's local composition and interdependence of shape make it self-regulating and self-optimizing. Transferosomes are suitable candidates for non-delivery of tiny, medium, and big sized ones due to their deformability. Transferosomes may deform and pass through constrictions 5-10 times smaller than their own diameter without significant loss' flexibility can be produced by combining appropriate surface active components in the proper ratios. The resultant flexibility of the transferosome membrane reduces the likelihood of full vesicle rupture in the skin and allows transferosomes to follow natural water gradients throughout the epidermis when applied under non-occlusive conditions. They overcome skin penetration by pressing themselves along the sratum corneum's internal lipids (Benson, 2006; Jain and Kumar, 2017).

Enhanced drug administration via the skin by an ultradeformable vesicular carrier presents new difficulties and potential for the development of newer, better therapeutics. As a result, it is possible to conclude that the new ultra-flexible drug carrier (transferosome) can overcome all of the problems associated with transdermal delivery because transferosomes are specially optimised vesicles capable of responding to external stress through rapid and energetically inexpensive shape transformations (Kumavat *et al*., 2013).

Felbinac is a medication used to treat muscle discomfort, arthralgia, and ankylosing spondylitis. Felbinac is an NSAID (nonsteroidal anti-inflammatory medication). It works by inhibiting the release of particular chemical messengers responsible for pain and inflammation (Hosie and Bird, 1994). The goal of this study is to development & evaluation of transferosomal gel of Felbinac for treating inflammation.

MATERIALS AND METHODS

Chemicals

Soya PC, ethanol, distilled water, Carbopol 934, propylene glycol were obtained from Loba chemie Mumbai pvt ltd. All chemicals used were of laboratory grade.

Preparation of Felbinac loaded Transfersomes

1. Dissolving Soya PC in ethanol: Soya PC is dissolved in ethanol at a concentration of 0.5% to 2% w/v. The exact amount of ethanol used ranges from 5 to 20 ml. This step is carried out in a closed vessel.
2. Heating the mixture: The ethanol solution containing Soya PC is heated to a temperature of 30 ± 1°C using a water bath. This temperature is maintained throughout the process.
3. Addition of distilled water or drug solution: Distilled water or a drug solution in distilled water (at a concentration of 1% w/v) is slowly added in a fine stream to the ethanolic lipid solution. The water or drug solution is also preheated to 30 ± 1°C.
4. Continuous mixing: The addition of water or drug solution is accompanied by continuous mixing using a magnetic stirrer at a speed of 900 rpm. Mixing is continued for 5 minutes to ensure proper dispersion of the components.
5. Cooling: After mixing, the resulting vesicular dispersion is left to cool at room temperature (25±1°C) for 45 minutes. During this time, the vesicles form and stabilize (Malakar *et al.*, 2012). Different transferosomal dispersions and their composition are shown in table 7.1-7.4.

Preparation of gel base

1. Dispersion of Carbopol 934: Accurately weigh Carbopol 934 (1% w/v) and disperse it into 80 ml of double distilled water in a beaker. Continuous stirring at 800 rpm is maintained for 1 hour to ensure proper dispersion of Carbopol 934 in water.
2. Addition of propylene glycol: After 1 hour of stirring, 10 ml of propylene glycol is added to the Carbopol 934 dispersion. This helps in enhancing the viscosity and consistency of the gel.
3. Adjustment of gel volume: The volume of the gel is adjusted to a total of 100 ml, likely by adding an additional 10 ml of double distilled water. This step ensures that the gel has the desired volume for further processing.
4. Incorporation of transferosomal preparation: The transferosomal preparation containing Felbinac, corresponding to a concentration of 3% w/w, is incorporated into the gel base. This step is performed to achieve the desired concentration of the drug in the gel base (Ghanbarzadeh *et al.*, 2013).

Characterization of Felbinac loaded Transfersomes

Surface charge and vesicle size

The vesicles size and size distribution and surface charge were determined by Dynamic Light Scattering method (DLS) (Malvern Zetamaster, ZEM 5002, Malvern, UK). Zeta potential measurement of the Transfersomes was

based on the zeta potential that was calculated according to Helmholtz–Smoluchowsky from their electrophoretic mobility. For measurement of zeta potential, a Zetasizer was used with field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9 % NaCl adjusted to a conductivity of 50 lS/cm (Wu *et a*l., 2019).

Entrapment efficiency

One milliliter of MIC Transfersomes suspension was centrifuged at 15.000 rpm for 1 h to allow the separation the entrapped drug from the un-entrapped drug. After removal of the supernatant, the sediment was lysed using methanol and then analysed spectrophotometrically at 246nm using a UV spectrophotometer (Labindia 3000+).

Characterization of Transfersomes containing gel

The physical properties of gel, such as colour, aroma, and texture, were examined first. The gel's pH was determined using a digital pH metre. The shearing force on a spindle revolving at a fixed, constant speed while immersed in the sample was evaluated using a Brookfield Viscometer. Excess gel was placed between two glass slides, and a 1000g weight was placed in the slides for 5 minutes to compress a sample to uniform thickness. The pan was filled with weight (80 gram). The time it took to separate the two slides was used to determine spreadability. The washability of gel was tested by applying the gel to a specific area of skin and then washing it with water. The amount of time required to completely remove the gel by washing was recorded. The extrudability test is used to determine how much force is required to extrude the gel from a collapsible tube. The drug content or percent assay of gel was evaluated by using spectrophotometer. The *in vitro* release of drugs from the formulations was studied through cellophane membrane.

Stability Studies

Stability study was carried out for drug loaded Transfersomes at two different temperatures i.e. refrigeration temperature (4.0 ±0. 2°C) and at room temperature (25-28±2°C) for 3 weeks. The formulation subjected for stability study was stored in borosilicate container to avoid any interaction between the formulation and glass of container. The formulations were analyzed for any physical changes and drug content.

Table 1: Optimization of lipid concentration

Formulation code	Soya PC (% w/v)	Ethanol	Drug (% w/v)	Average vesicle size (nm)	% entrapment efficiency
F1	0.5	10	1	312.25	73.32
F2	**1**	**10**	**1**	**285.65**	**78.85**
F3	1.5	10	1	345.85	69.98
F4	2	10	1	320.22	72.23

Table 2: Optimization of ethanol concentration

Formulation code	Soya PC (% w/v)	Ethanol	Drug (% w/v)	Average vesicle size (nm)	% entrapment efficiency
F5	1	5	1	285.65	69.98
F6	1	**10**	**1**	**245.23**	**73.25**
F7	1	15	1	296.85	68.85
F8	1	20	1	274.65	67.74

Table 3: Optimization of drug concentration

Formulation code	Soya PC (% w/v)	Drug (% w/v)	Ethanol (ml)	Average vesicle size (nm)	% Entrapment efficiency
F9	**1**	**1**	**10**	**148.85**	**73.32**
F10	1	1.5	10	162.23	69.98
F11	1	2	10	174.65	68.74

Table 4: Optimization of Stirrer time

Formulation code	Soya PC: (% w/v)	Drug (% w/v)	Stirrer time (min)	Average vesicle size (nm)	% Entrapment efficiency
F12	**1**	**1**	**5**	**125.45**	**75.65**
F13	1	1	10	110.25	71.12
F14	1	1	15	105.47	69.98

Table 5: Characterization of Optimized formulation of Transfersomes

Characterization	Average vesicle size (nm)	% Entrapment efficiency	Zeta Potential (mV)
F-12	125.45	75.65	-38.12

Table 6: Characterization of gel based formulation

Formulation	Viscosity (cps)	Assay* (%)	Extrudability (g)	Spreadability (g.cm/sec)
Optimized Gel	3256±15	99.15±0.25	178±4	13.36±0.15

Table 7: *In vitro* drug release study of prepared gel formulation

S. No.	Time (hr)	Root T	Log T	% Cumulative Drug Release	% Cumulative Drug Release Remain	Log % Cumulative Drug Remain to be Release	Log % Cumulative Drug Release
1	0.5	0.707	-0.301	24.45	75.55	1.878	1.388
2	1	1.000	0.000	36.65	63.35	1.802	1.564
3	2	1.414	0.301	48.85	51.15	1.709	1.689
4	4	2.000	0.602	65.58	34.42	1.537	1.817
5	6	2.449	0.778	73.32	26.68	1.426	1.865
6	8	2.828	0.903	89.98	10.02	1.001	1.954
7	12	3.464	1.079	96.65	3.35	0.525	1.985

Table 8: Release Kinetics of optimized gel of transferosomal gel

Formulation	Zero order	First order	Higuchi	Korsmeyer
Gel	0.909	0.976	0.981	0.990

Table 9: Stability Study of optimized formulation of Transfersomes

Characteristic	Time (Month)					
	1 Month		2 Month		3 Month	
Temperature	4.0 ±0. 2°C	25-28±2°C	4.0 ±0. 2°C	25-28±2°C	4.0 ±0. 2°C	25-28±2°C
Average particle size (nm)	220.12	285.45	225.65	296.65	236.45	325.65
% EE	74.23	63.32	71.25	60.15	70.12	52.12
Physical Appearance	Normal	High turbid	Normal	High turbid	Normal	High turbid and agglomeration

RESULTS AND DISCUSSION

The optimization of prepared transferosome was done for various parameters like lipid, ethanol concentration, drug concentration, stirrer time. From the optimization parameters it was noticed that formulation F-12 have all ideal characteristics. The size & zeta potential for F-12 was noted to be 125.45nm & -38.12 mv respectively. The % Entrapment efficiency for the same was found to be 75.65%. The optimized transferososmal gel has Extrudability & Spreadability of 178±4 gm & 13.36±0.15 g.cm/sec respectively. The spreadability and extrudability of the formulation was determined to be satisfactory. The spreadability number indicates that the gel is easily spreadable with a small degree of shear. The extrusion from the tube is critical for application and patient acceptance. The homogeneity of the various formulations was examined visually as well as by applying pressure between the thumb and index finger and was determined to be excellent. The gel viscosity was estimated to be 3256±15 cps. *In vitro* drug release study of prepared gel formulation revealed that 96.65% of drug was released in 12 hr. The release kinetics data of optimized transferosomal gel suggested that the it follows Korsmeyer model which is evident from R^2 value of 0.990. The models were created to show the release of semisolid dosage forms containing low solubility medicines.

Stability study data revealed that the gel is stable for 3 months at 4.0 ±0. 2°C with average particle size of 236.45 nm & % Entrapment efficiency of 70.12. We can use the combined action of felbinac and transferosome for topical administration in the treatment of inflammation.

CONCLUSION

The created formulation of transferosome included gel is a unique strategy for the treatment of inflammation via the Transdermal route, allowing the drug to permeate through the skin while also exhibiting sustained release characteristics. The felbinac in transferosomal gel format were found to have higher bioavailability, anti-inflammatory, and analgesic effectiveness when compared to the medications' existing forms. Transfersomes are effective medication carriers for penetrating skin tissues. The incorporation of transferosomal lidocaine into gel enhances drug permeability. Furthermore, embedding transferosomal vesicles in gel dosage form improves their stability. Certain skin permeation enhancers can be used with transferosomal lidocaine gel to increase medication permeation. This approach has the potential to be used to deliver multiple topical medications without affecting the skin's structure.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Ahmed, A.U. (2011) An overview of inflammation: Mechanism and consequences. *Frontiers in Biology*, 6, 274–281
- Medzhitov, R. (2008) Origin and physiological roles of inflammation. *Nature*, 454, 428–435
- Trowbridge, H.O., Emling, R.C. & Fornatora, M. (1997) Inflammation. A review of the process. *Implant Dentistry*, 6, 238
- Halliwell, B., Hoult, J.R. & Blake, D.R. (1988) Oxidants, inflammation, and anti-inflammatory drugs. *FASEB Journal*, 2, 2867–2873
- Vane, J.R. & Botting, R.M. (1996) Mechanism of action of anti-inflammatory drugs. *Scandinavian Journal of Rheumatology. Supplement*, 102 (Supplement 102), 9–21
- Benson, H.A. (2006) Transfersomes for transdermal drug delivery. *Expert Opinion on Drug Delivery*, 3, 727–737
- Jain, A.K. & Kumar, F. (2017) Transfersomes: Ultradeformable vesicles for transdermal drug delivery. *Asian J. Biomater. Res.*, 3, 1–3.
- Kumavat, S.D., Chaudhari, Y.S., Borole, P., Duvvuri, P., Bubera, N., Shenghani, K., Shah, P. & Mishra, P. (2013) Transfersomes: A promising approach for transdermal drug delivery system. *Asian Journal of Pharmaceutical Sciences and Research*, 3, 1–7.
- Hosie, G. & Bird, H. (1994) The topical NSAID felbinac versus oral NSAIDs: A critical review. *European Journal of Rheumatology and Inflammation*, 14, 21–28
- Ghanbarzadeh, S. & Arami, S. (2013) Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transfersomes. *BioMed Research International*, 2013, 616810
- Wu, P.S., Li, Y.S., Kuo, Y.C., Tsai, S.J. & Lin, C.C. (2019) Preparation and evaluation of novel transfersomes combined with the natural antioxidant resveratrol. *Molecules*, 24, 600