Pharmacophore 2016, Vol. 7 (2), 82-95 USA CODEN: PHARM7 ISSN 2229-5402

Pharmacophore

(An International Research Journal)

Available online at http://www.pharmacophorejournal.com/

Original Research Paper

FABRICATION AND EVALUATION OF RITONAVIR PRONIOSOMAL TRANSDERMAL GEL AS A VESICULAR DRUG DELIVERY SYSTEM

Minakshee Nimbalwar*, Kanchan Upadhye and Gouri Dixit

Department of Pharmaceutics Priyadarshini J. L. College of Pharmacy,

Electronic Zone Building, MIDC, Hingna Road, Nagpur-440016 Maharashtra, India

ABSTRACT

The aim of the study was formulation and evaluation of a proniosomal transdermal gel as vesicular drug delivery system for improving stability of formulation and sustaining drug release of Ritonavir, an HIV antiviral drug. Initial studies focussed on the formulation parameters that influence the manufacturing process by using non ionic surfactant and then evaluation parameters for optimization of formulation. The drug excipients compatibility studies were carried out by DSC studies and FTIR spectra revealed that the drug and excipients used were compatible with each other. The evaluation of proniosomes shows an entrapment efficiency range of 61.60±2.05 to 91.74±0.54%. The optimized batch shows the encapsulation efficiency 91.74±0.54%, vesicle size 246.48±3nm and drug content 96.41±0.74%. The drug release studies of proniosomal gel was carried out by diffusion through cellophane membrane % drug release was found to be 89.09±1.5%, Rate of spontaneity 14.54±0.95 mm^3x1000, pH 7.2±1.45, viscosity 4298±2.05 cp, spreadability 48±0.23 mm. The optimized formulation was evaluated for morphology and structure of proniosomes (SEM) shows spherical in shape, Zeta Potential was found to be -56.21. This study provided the evidence that the proniosomal vesicles are valuable as the transdermal drug delivery for ritonavir to sustaining the drug release and enhance the stability of formulation.

Keywords: Proniosomes, Transdermal Gel, Surfactant, Ritonavir, Vesicular drug delivery system.

INTRODUCTION

Drug delivery system using colloidal particulates carriers such as liposomes[1] and niosomes[2] have distinct advantages over conventional dosage forms. These carriers can act as drug reservoirs and modification of their composition or surface can Be used for drug targeting. In disperse aqueous system liposomes have problems associated with degradation by hydrolysis or oxidation as well as sedimentation, aggregation or fusion of liposomes during storage and problems in their sterilisation. Niosomes are unilamellar or multilamellar vesicles are capable of entrapping hydrophilic and hydrophobic solutes.[3] Niosomes are promising drug carriers as they posses greater stability and lack of many disadvantages associated with liposomes such as high cost and the variable purity problems of phospholipids. Large scale production of niosomes without the use of acceptable solvents.[4,5]

Proniosomes are recent development in novel drug delivery system. These are most advanced drug carrier in vesicular system in which these are made up of non-ionic based surfactants, cholesterol and other additives.[6] "Proniosomes are water soluble carrier particles that are coated with surfactant and can be hydrated to form niosomal dispersion immediately". It minimize problems of vesicular systems such as aggregation, fusion and leakage of drug and provide additional convenience in transportation, distribution, storage and dosing. The vesicles overcomes demerits of liposomes and niosomes.[7] Proniosomes are

hydrated by agitation in hot water for short period of time offer a versatile vesicular delivery concept with the potential for drug delivery via the transdermal route.[8]

Ritonavir is selected for current study which is a peptidomimetic inhibitor of both the HIV-1 and HIV-2 proteases. Ritonavir belongs to a group of HIV protease inhibitors (PIs). The drug has a short half life of 3 to 5 hours and is currently administered orally and parentally. However it has to be administered frequently and is associated with numerous some side effects due to which an alternate route is required. Transdermal delivery certainly appears to be an attractive route of administration to maintain drug blood levels of Ritonavir for extended period of time.[9]

The aim of this study is to investigate the feasibility of use of proniosome as proniosomal gel of Ritonavir in the transdermal delivery system. Vesicles prepared were characterized by vesicle size determination, scanning electron microscopy, zeta potential analysis, in-vitro drug release studies and stability studies under experimental conditions to investigate the leaking of drug during storage

MATERIALS AND METHOD

Materials

Ritonavir was provided as a gift sample from Cipla Ltd, Mumbai .All the other ingredients were of pharmaceutical grade**.**

Experimental Methodology

Preformulation studies

Solubility Studies

Solubility studies of Ritonavir (RnV) was carried out in various solvents such as water, methanol, isopropanol, phosphate buffer and ethanol.

Melting Point Determination

The Melting point was determined by using digital melting point apparatus by taking drug in the capillary.

Compatibility Studies

Infrared absorption spectra

The IR spectrum of ritonavir was recorded by using KBr pellet method. The pellet was scanned over range of 500-4000 cm^{-1} in FTIR and the spectrum was obtained.

DSC

DSC thermogram of drug, was separately recorded by placing the sample in aluminium pan with a reference pan heated at a rate of 20°C /min over a range of 0-300°C. Inert atmosphere was maintained with purge of nitrogen gas.

Formulation Development

Formulation of Proniosomes

Proniosomes were prepared by coacervation phase separation method by using different non ionic surfactants. In this method the drug was taken in a clean and dry wide mouthed glass vial and methanol was added to it. All the ingredients were mixed well with a glass rod. The open end of the glass vial was covered and warmed over water bath at 50-60°C for about 5 minutes. Then aqueous phase phosphate buffer pH 7.4 was added and warmed on a water bath until a clear solution was formed.[10]

Formulation of Proniosomal Transdermal Gel

The prepared proniosomes batches P1-P8 were incorporated into 1.5% Carbopol blank gel. In this 1.5% w/w of carbopol-934 use for the preparation of gel. The quantity of methyl paraben and propyl paraben equal to 0.2 and 0.02 g respectively in dispersion. The pH of gel was adjusted to 6.8-7.4 by addition of triethanolamine and NaOH. The gel was allowed to stand overnight under vacuum to remove the entrapped air.[11]

Characterisation of Proniosomes

Physical Observation of Proniosomes

The proniosomal dispersion was examined for physical characteristics such as colour and the state of dispersion.

Microscopic Examination

The proniosomal dispersion was examined for the structure and lamellarity under microscope at magnification powers of 10X and 45X and photomicrographs were recorded.

Entrapment Efficiency

The aqueous proniosomal suspension was centrifuged at 25,000rpm at 25^0C for 30 min to separate untrapped drug as supernatant. Supernatant was separated, filtered and sufficiently diluted with methanol to determine the concentration of untrapped drug spectrophotometrically at 240 nm.[12] The percentage of drug encapsulation was calculated by equation;

Entrapment efficiency (%) = [(t-f)/t] ×100

Where,

t is the concentration of total drug.

f is the concentration of free drug.

The entrapment efficiency of proniosomes is depend on the vesicle size.

Evaluation of Proniosomal Gel

Organoleptic Characters

The prepared proniosomal transdermal gels were inspected visually for clarity, colour and presence of any particles.

Drug Content

The drug content was determined by dissolving the proniosomal gel sample in ethanol and measuring the absorbance at 240 nm from which the drug content was calculated.

Viscosity

Viscosities of the formulated Proniosomal gels were determined using Brookfield Viscometer (DV-II + Pro) with T-Shaped spindle set using Spindle no. 96 The gel sample was taken in a beaker and the dial reading was noted at 100 rpm 25°C.

pH Measurement

The pH measurement of the proniosomal gels were determined by using a pH meter which was calibrated before use with standard buffer solutions at pH 4 and 7. The quantity of gel equal to 1 g was dispersed in 20 ml distilled water and the pH was measured gives different pH values.[13, 14]

Spreadability

The spreadability of vesicular gel formulation were 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 was placed. A weight of 500 g was allowed to rest on the upper glass plate for about 15 secs.[15]

Rate of Spontaneity

Rate of spontaneity is defined as number of niosomes formed after hydration of proniosomes for 15 min. 0.2g of proniosomal gel is transferred to bottom of the small Stoppered glass tube and then spread along the walls of the container uniformly. Further, 2 ml saline (0.154 M NaCl) is added carefully and keep aside for 15 min without agitation. A drop of this aqueous layer is withdrawn and placed over Neubaur's chamber and observe number of niosomes eluted from proniosomes in optical microscope.[16]

In-Vitro Drug Release Studies

In-vitro drug release study of proniosomal transdermal gel was carried out by using dialysis bag as donor compartment. Proniosomal transdermal gel equivalent to 10 mg was taken in dialysis bag, placed in buffer

containing phosphate buffer solution which acted as receptor compartments. A standard dialysis membrane soaked in pH 7.4 for 24 hours before use or soaked in warm water for 10 mins and both the end were sealed with closer clips by adding proniosomal gel formulation. The beaker was kept at magnetic stirrer with 100 rpm and maintained at 37±1^{0}C. At predetermined interval of 12 hrs sample were withdrawn and replaced with 1ml of fresh phosphate buffer solution sink condition was maintained throughout experiment. Sample withdrawn were diluted and analyzed by UV spectrophotometer at 240 nm.[17]

Optimization of Proniosomal Transdermal Gel

The optimization of proniosomal transdermal gel was done by considering all the evaluation parameters discussed above.

Evaluation of Optimized Formulation

The optimized formulation were evaluated for following parameters.

Morphology and structure of proniosomes (SEM)

The surface morphology (roundness, smoothness, and formation of aggregates) of proniosomes was studied by Scanning Electron Microscopy. Shape for the formulation was determined by scanning electron microscope (Motic image, Kolkatta). The formulation was spread uniformly on glass slide and observed under electron microscope for vesicular shape.[18]

Measurement of Vesicle Size

The mean particle size diameter and size distribution (polydispersity index, PI) was determined by Malvern zetasizer nano. Each sample was run 3 times and analysis was carried out at 25 ^{0}C with an angle of detection 173°.

Measurement of Zeta Potential

The zeta potential was analyzed for proniosomal formulation by Malvern Zetasizer in Sinhagad Institute of Pharmacy, Pune. Each sample was run 3 times and the analysis was carried out at 25 ^{0}c with an angle of detection 173°C.[19,20]

Skin Irritation Study

Skin irritation test was done on the human skin by applying approximately 1gm of proniosomal transdermal gel on the surface of skin 1cm^2 and sensitization can be performed on healthy human skin. The proniosomal transdermal gel was to be removed after some time and the skin was observed for any type of irritation.[21]

Stability Study

Stability studies were carried out by storing the optimized formulation at various temperature conditions as per ICH guidelines i.e. At refrigeration temperature (2°-8°C), Room temperature (25°± 0.5°c) for a period of two months. Drug content and variation in the average vesicle diameter were determined before and after the completion of 2 months.[22]

RESULT AND DISCUSSION

Preformulation Studies of RnV.

i. Solubility Studies of RnV

Solubility studies of RnV was carried out in various solvents. From the result of solubility of RnV in different solvents, it was observed that, RnV was insoluble in water, slightly soluble in isopropanol, soluble in ethanol and soluble in methanol .

ii. Melting Point Determination

From the result, melting point of RnV was found to be 121±2^0 C.

iii. Compatibility Studies

The drug-excipient interaction was performed by FT-IR and DSC.

a) Infrared Absorption Spectra (FT-IR)

FT-IR spectrum of RnV

The FT-IR spectrum of RnV was measured in solid state as potassium bromide dispersion. The characteristic peaks (cm-1) were assigned for respective functional groups. The FT-IR spectra of pure drug and excipients and physical mixture of drug with excipient is shown in figure below.

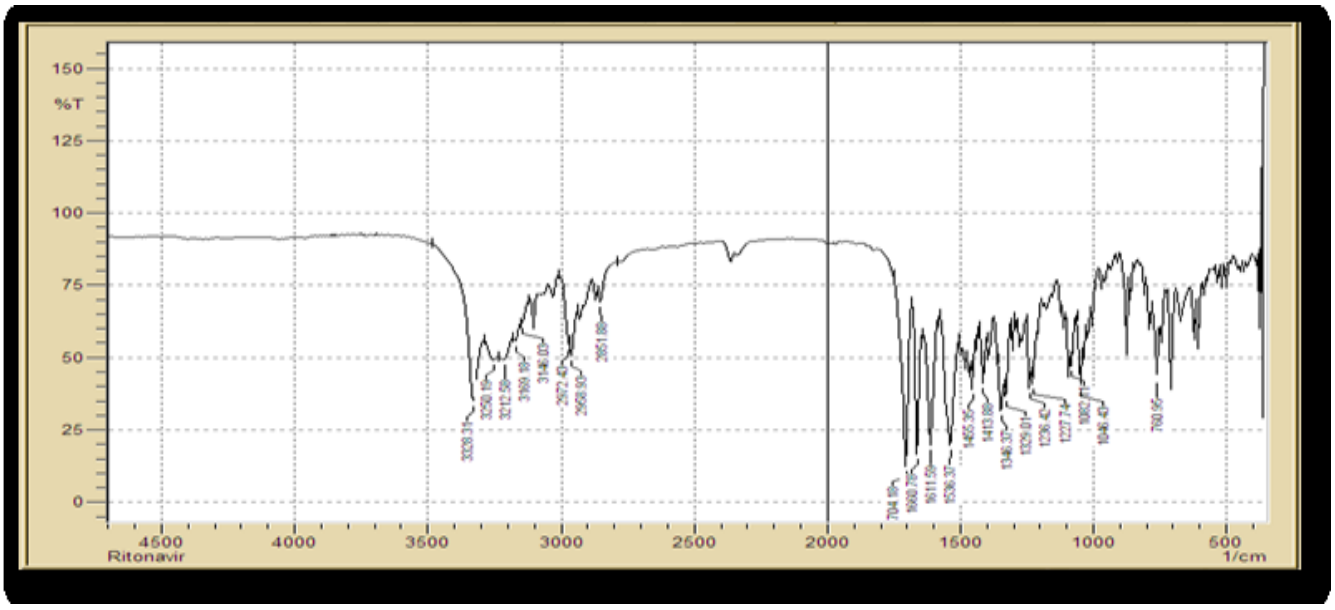


Figure 1: FT-IR spectrum of RnV

The presence of peaks at 672 cm^{-1} and 722cm^{-1} shows Ar-OH Phenol at plane deformation shows Alcohol/Phenol O-H Stretch, were characteristic to the lecithin used in the formulation.

FT-IR Spectrum of Drug and Excipients Mixture

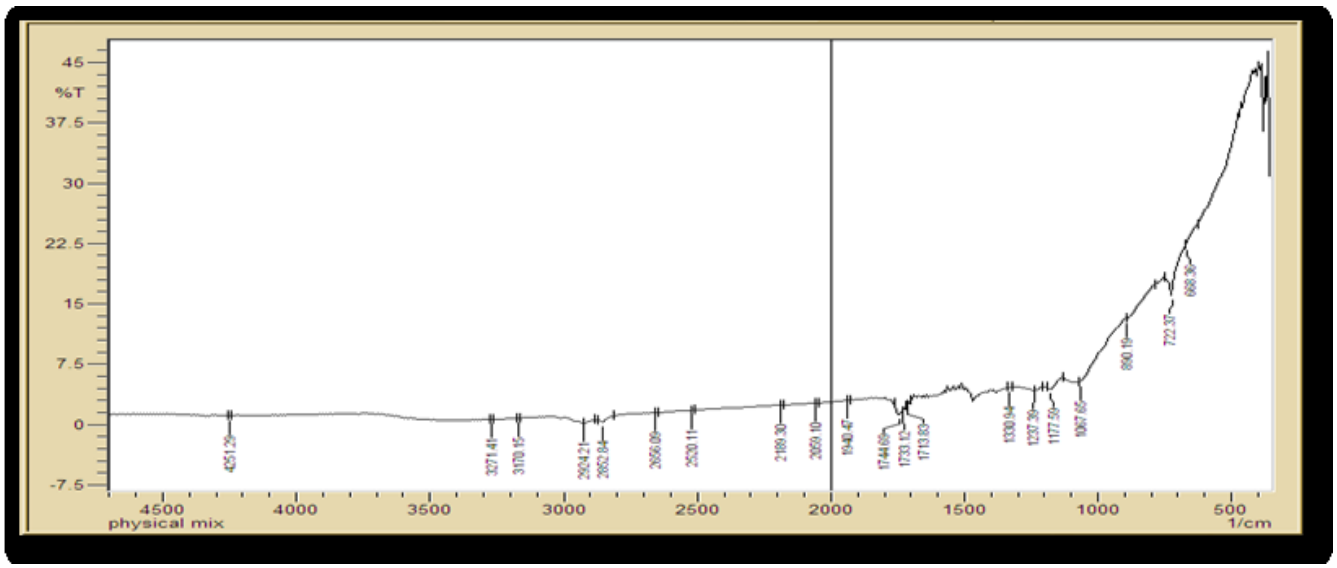


Figure 2: FTIR spectrum of drug and excipients mixture

The presence of peaks at 666 cm^{-1} shows Ar-OH Phenol plane deformation and CH=CH di-substitution of alkene plane deformation, 890 cm^{-1}(Aromatic C-H Bending), 1062 cm^{-1} and 1177 cm^{-1} (C-N stretching, C-O present), 1227 cm^{-1} and (O-H bending in-plane), 1713 cm^{-1} shows Aldehyde C=O Stretch, 2852 cm^{-1} and 2620 cm^{-1} (Carboxylic Acid O-H Stretch), 3146 cm^{-1} shows Alcohol/Phenol O-H Stretch, 3271 cm^{-1} shows Alcohol/Phenol O-H Stretch, 3250 cm^{-1} within range 3300-3250 cm^{-1}shows =CH-H Stretch, were characteristic to the physical mixture of drug and excipients.

IR spectrum of physical mixture of drug with excipients revealed that there was no appreciable change in position and intensity of peak with respect to IR spectrum of pure RnV and lecithin. IR analysis revealed that there was no known chemical interaction between drug and excipients.

b) Differential Scanning Colorimetry (DSC)

Diffential scanning colorimetry is performed for the compatibility study of drug and other excipient at different temperature.

DSC of Ritonavir

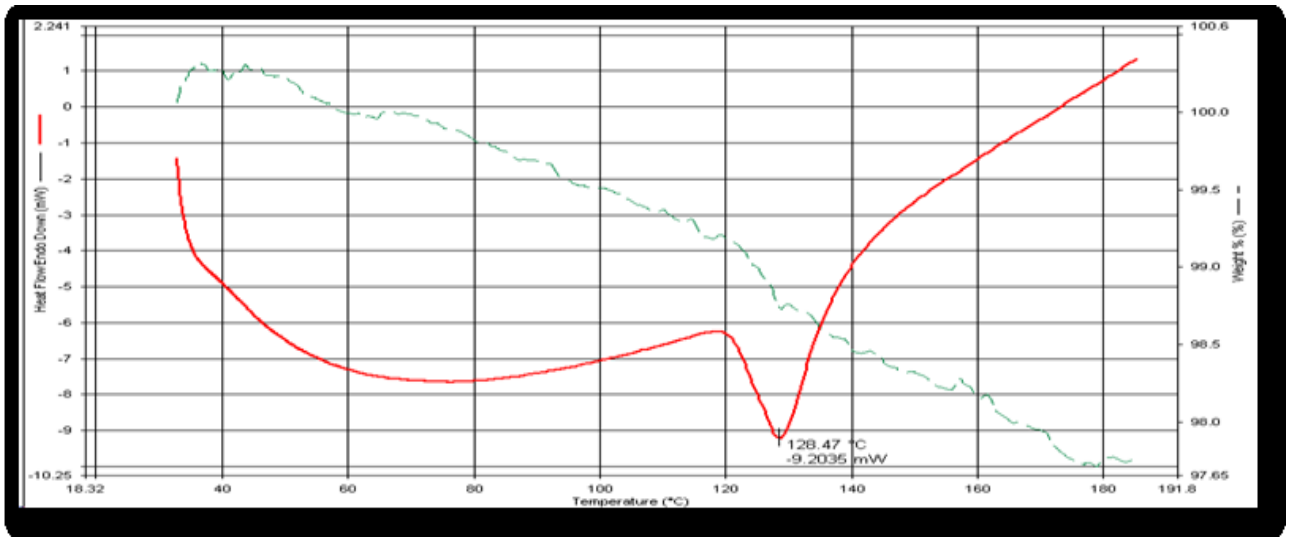


Figure 3: DSC of Ritonavir

DSC of Drug and Excipients Mixture

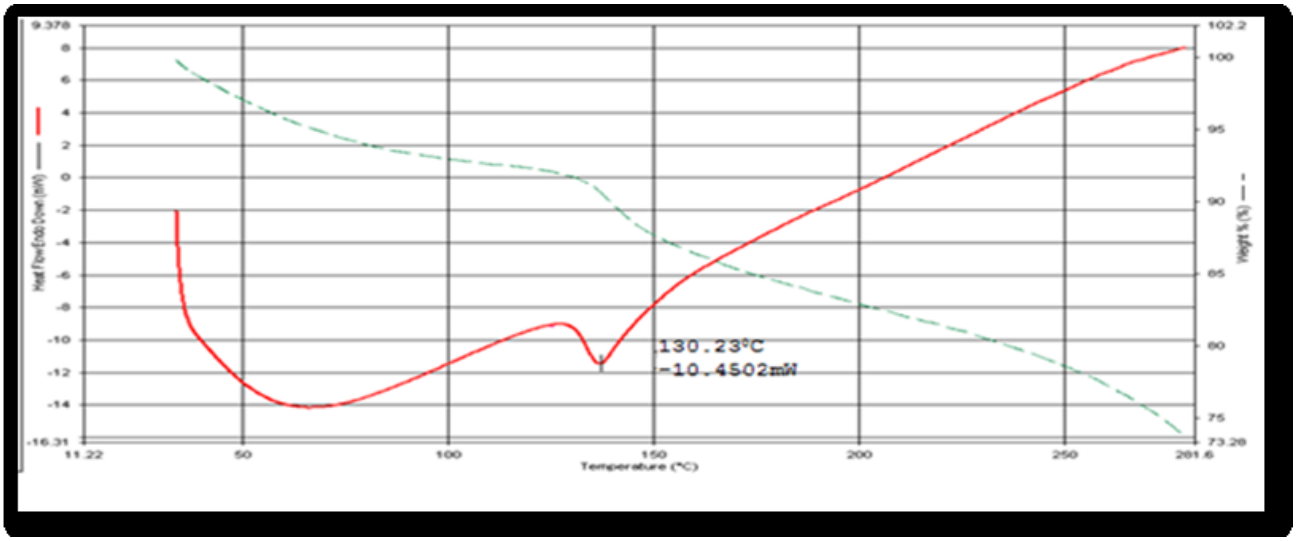


Figure 4: DSC of drug and excipients mixture

Early onset of endotherm for pure RnV (at 128^0 C) and for physical mixture (at 130^0 C) endotherm. These results indicated partial amorphisation and solubilisation of RnV due to the processing and absence of any additional peak indicated that there was no interaction between the drug and excipients used in the formulation.

Formulation of Proniosomes

The Proniosomes were prepared by Coacervation phase separation method by using different surfactants span 20, 40, 60, 80 and tween 20, 40, 60, 80, cholesterol and Lecithin the detailed procedure were described. The formation of proniosomal dispersion were done successfully.

Compositions of Preliminary Formulations

Table 1: Compositions of preliminary formulations

Batches	Surfactant Name	Surfactant	Cholesterol	Lecithin	RnV
P1	Span20	45.5%	5%	45%	1%
P2	Span40	45.5%	5%	45%	1%
P3	Span60	45.5%	5%	45%	1%
P4	Span80	45.5%	5%	45%	1%
P5	Tween20	45.5%	5%	45%	1%
P6	Tween40	45.5%	5%	45%	1%
P7	Tween60	45.5%	5%	45%	1%
P8	Tween80	45.5%	5%	45%	1%

Characterization of Proniosomes

i. Physical Observation of Proniosomes

Physical observation of proniosomes shown as given below.

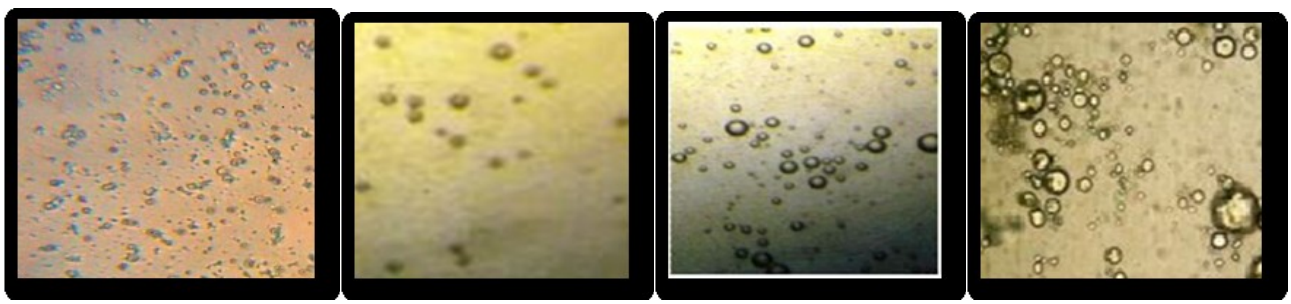
Table 2: Physical observation of proniosomes

Sr. No	Formulation	Appearance of Proniosomes
1	P1	White Semi-solid
2	P2	Brown Transparent Liquid
3	P3	Creamy White Semi-solid
4	P4	Creamish Liquid
5	P5	Creamish Liquid
6	P6	Brown Liquid
7	P7	Brownish semisolid
8	P8	Yellowish gel

These parameters were checked for proniosomes revealed that the proniosomes were white to brown in colour having White Semi-solid, Creamish Liquid in appearance and characteristic odour.

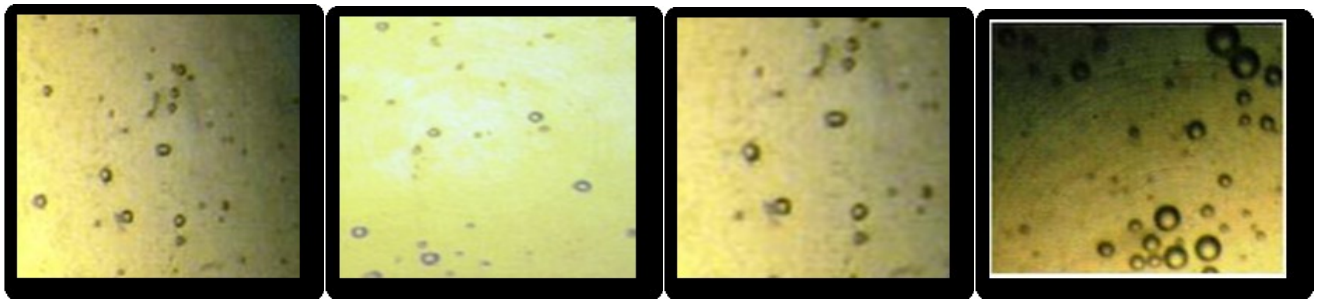
ii. Microscopic Examination

Microscopic examination of proniosomes at 10X magnification power. Photomicrographs were taken for proniosomes by using optical microscope .



P1 (Span20) P2 (Span40) P3 (Span60) P4 (Span80)

Figure 5: Photomicrographs of Formulations P1, P2, P3 and P4 Containing Span 20, 40, 60, 80 as a surfactant



P5 (Tween20) P6 (Tween40) P7 (Tween60) P8 (Tween80)

Figure 6: Photomicrographs of Formulations P5, P6, P7 and P8 containing Tween20, 40, 60, 80 as a surfactant

The photomicrographs of hydrated P1 to P8 proniosomal formulations shown in above figure which is composed of cholesterol, lecithin and span20, 40, 60, 80 ,tween20, 40, 60, 80. The photographs revealed that the proniosomes were bilayered structure having spherical shape and no aggregation or agglomeration was observed.

iii. Entrapment Efficiency

Encapsulation efficiency of proniosomal gel formulations of batches P1-P8 ranged were shown as follows.

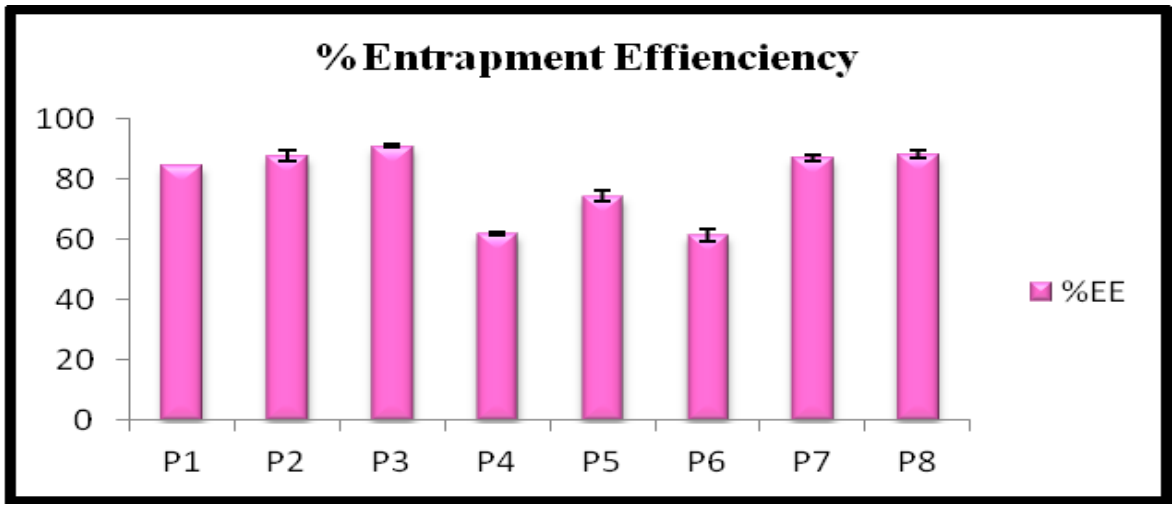


Figure 7: % Entrapment Efficiency of Proniosomal Formulations.

Entrapment efficiency was found to be in range of 80.40% to 92.20% formed from Span and tween surfactants. The cholesterol content of the formulation was increased, the encapsulation of drug also increased. The formulations (P3) containing span 60, soya lecithin, cholesterol showed high encapsulation efficiency compared to other formulations.

Formulation of Proniosomal Transdermal Gel

The transdermal proniosomal gel was prepared successfully by using Carbopol as gelling agent. Different batches of proniosomal gel of RnV were prepared by using Spans and Tweens as surfactant. Cholesterol and soya lecithin. Soya lecithin was selected over egg lecithin because the former gives vesicles of larger size, possibly due to differences in the intrinsic composition of soya and egg derived lecithin. The formulations prepared with Spans were smooth and homogenous with gel like appearance. No proper gel was obtained with Tweens. After formulation of proniosomes were dispersed in Carbopol 934 for formulation of proniosomal gel. The prepared proniosomal gel formulations (P1-P8) were kept in dark room or in cool condition for further use and characterisation.

Evaluation of Proniosomal Gel

The prepared proniosomal transdermal gel were evaluated for selection and optimization of batch fromP1-P8.

i. Organoleptic Characters

These parameters were checked by visual inspection of proniosomal transdermal gel.

Table 3: Organoleptic characters of gel

Sr. No.	Batches	Colour	Odour	Clarity	Particles
1	P1	Thick Light brownish	Characteristic	Opaque	No
2	P2	Pale yellow	Characteristic	Opaque	No
3	P3	Creamish	Characteristic	Opaque	No
4	P4	Light brownish gel	Characteristic	Opaque	No
5	P5	Yellow	Characteristic	Highly thick	No
6	P6	Yellow	Characteristic	Highly thick	No
7	P7	Brownish	Characteristic	Opaque	No
8	P8	Yellowish	Characteristic	Opaque	No

Proniosomal gel of ritonavir prepared with Span (40, 60) have pale yellow semi solid gel like appearance. Proniosomal gel produced from Span 20 have thick sticky gel like appearance and span 80 have light brownish gel like appearance. Proniosomal gel of tween 20 appears as Yellow highly viscous liquid form and proniosomal gel of Tween 80 appears as semisolid crystalline gel and it has characteristic odour.

ii. Drug Content

The drug content of the formulations shown below in table:

Table 4: Drug content

Sr. No.	Formulation	Drug content (%)
1	P1	86.52 ±1.05
2	P2	88.47 ±0.5
3	P3	96.41 ±0.74
4	P4	78.13 ±0.63
5	P5	76.27 ±0.8
6	P6	70.43 ±0.1
7	P7	84.24 ±1.0
8	P8	89.911 ±3.02

All values represent mean±standard deviations(SD), n=3 The results indicated that the process employed to prepare proniosomes was capable of producing formulations with consistent drug content. The drug content among all the batches was within the range from 65.43 ±0.1% to 96.41 ±0.74% (Table)

Characterization of Proniosomal Formulations for Physical Appearance, pH, Viscosity (cp) And Spreadability

Table 5: Characterization of proniosomal formulations for pH, Viscosity (cp), Spreadability and Rate of spontaneity

Batches	Viscosity (cp)	pH	Spreadability Using 50gm	Rate of spontaneity (mm^3 x
P1	5580 ±1	6.2 ±2	38±1.05	11.19±1.05
P2	4500 ±0.05	5.7 ±0.95	46±0.02	15.25±0.45
P3	4298 ±2.05	7.2 ±1.45	48±0.23	14.54±0.95
P4	5130 ±1.45	7.1 ±1	45 ±0.05	10.58±0.05
P5	3536±3.15	6.4±0.05	65±1.05	12.30±0.02
P6	3452±2	5.9±1.52	53±0.45	10.49±1.8
P7	3436 ±1.83	6.8 ±1	50 ±3.24	12.90±1
P8	3246 ±1.23	5.31 ±0.34	52 ±0.23	11.45±0.1

All values represent mean±standard deviations (SD), n=3

iii. In-Vitro Drug Release Studies

The *In-Vitro* drug release of all 8 batches (P1-P8) were show that thep3 batch sustains the drug release upto 12 hrs. Results are depicted in table and are presented in figure

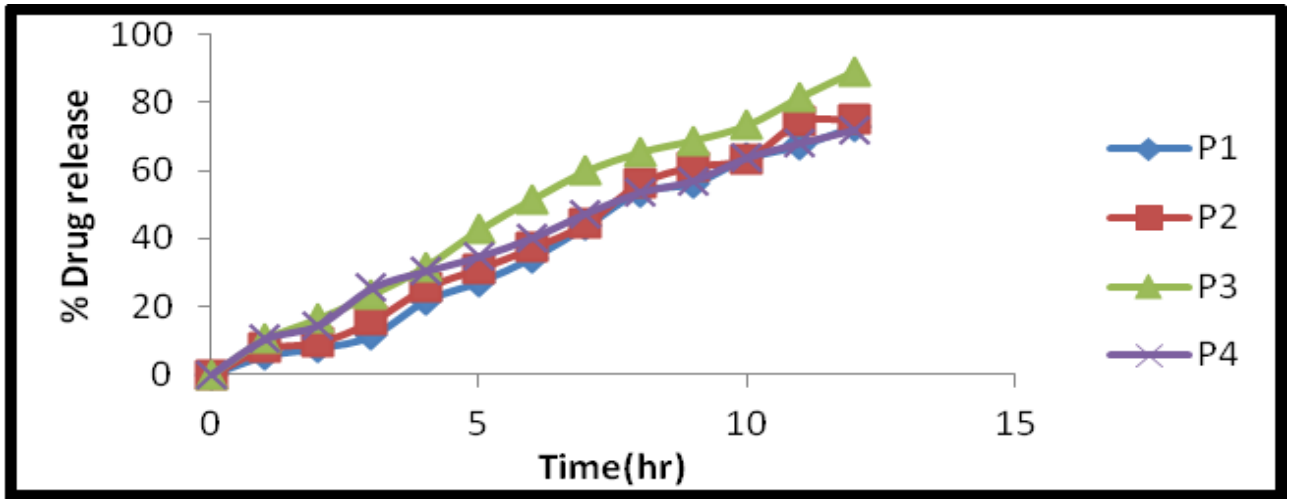


Figure 8: *In-vitro* drug release study of proniosomal gel of batches P1, P2, P3 and P4

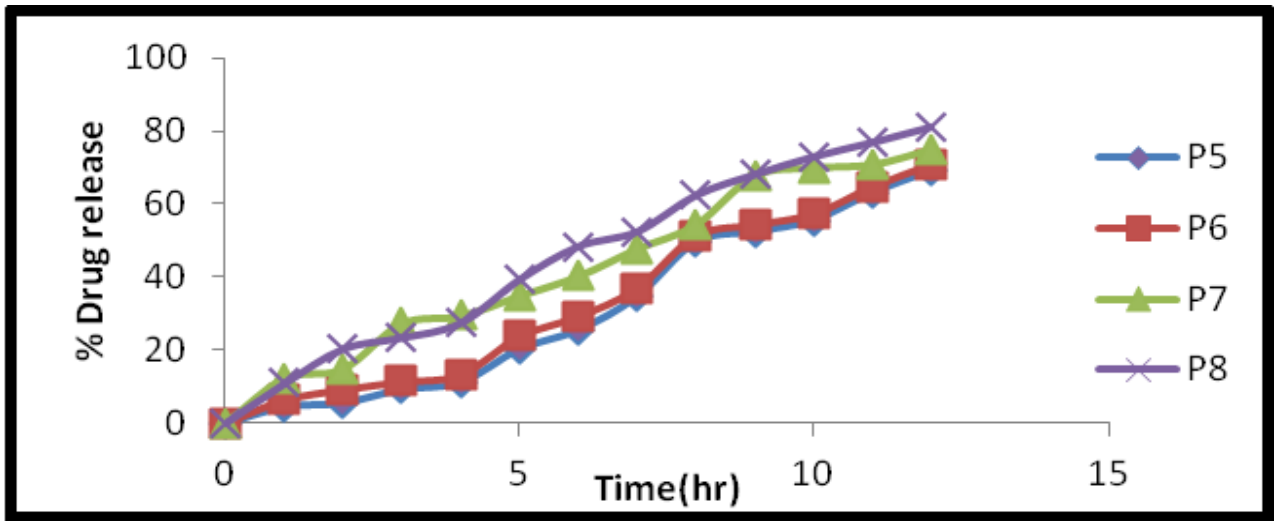


Figure 9: *In-vitro* drug release study of proniosomal gel of batches P5, P6, P7 and P8

Formulations which have higher cholesterol content (P1-P8) showed less drug release over a period of 12 hrs. Increase in cholesterol amount and use of different non ionic surfactant resulted in a more intact lipid bilayers as a barrier for drug release and decreased its leakage by improving the fluidity of the bilayers membrane and reducing its permeability, which led to lower drug elution from the vesicles and sustaining drug release.

The in-vitro drug release studies performed showed that P1-P8 released the drug shown in table for 12 hrs. The order of drug release was as follows: P3>P8>P7>P2>P1>P4>P5>P6. The proniosomal gel formation by using span 60 sustaining drug release and by considering all the evaluation parameter batch P3 shows best result and consider it as optimized formulation.

Optimization of Proniosomal Transdermal Gel

Optimization of proniosomal transdermal gel Formulation was based on the basis of evaluation parameters batch P3 was found to optimized batch and further it get evaluated for other parameters.

Evaluation of Optimized Formulation

Optimized formulation were evaluated for following parameters such as morphology of niosomes derived from proniosomal gel was studied using Scanning Electron Microscopy, Zeta potential, Skin irritancy test and Stability studies.

i. Morphology and Structure of Proniosomes (SEM)

Scanning Electron Microscopy were performed to observed the surface morphology of proniosomal gel.

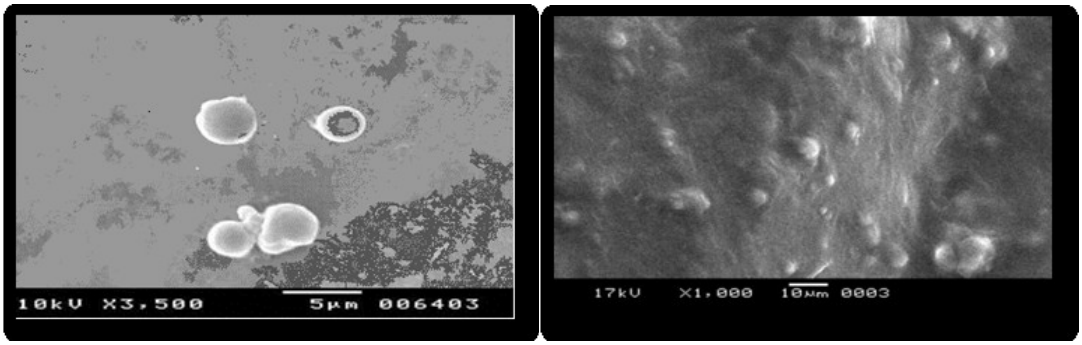


Figure 10: SEM images of optimized formulation (P3)

SEM imaging of RnV proniosomal transdermal gel revealed that the niosomes produced from hydration of proniosomes were spherical in shape and discrete with sharp boundaries having large internal aqueous space. SEM imaging of proniosomes produced from optimized formulation P3 was shown in above Figure.

ii. Measurement of Zeta Potential

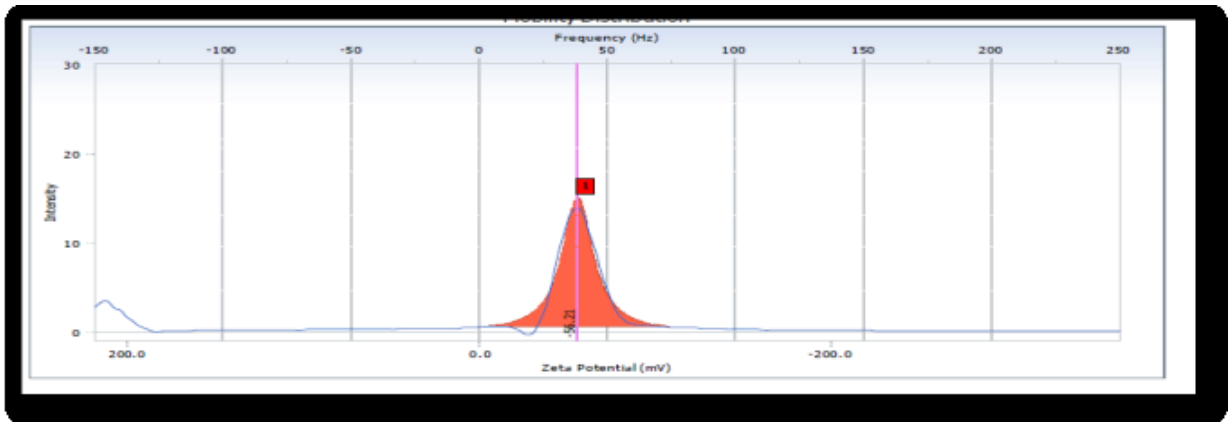


Figure 11: Measurement of zeta potential

Zeta potential of formulation was found to be -56.21mv . The ionization of surface groups may produce a surface charge. Physiologic surfactants are anionic surfactants and upon ionization it produces pH dependent net surface charge. The optimized formulation showed polydispersity index less than 1 which depicts a narrow size distribution. Niosomes prepared with Tween were significantly larger than those prepared with Span since Tween has lower hydrophobicity than Span. The formulation P3 was considered optimized since Span60 produced the vesicles of normal size with higher entrapment of drug. Moreover; it is found that the drug leakage from the vesicles composed of Span 60 is low, due to its high phase transition temperature. Result for Zeta Potential shown in table.

iii. Measurement of Vesicle Size

The mean particle size diameter and size distribution (polydispersity index, PI) was determined by photon cross-correlation spectroscopy

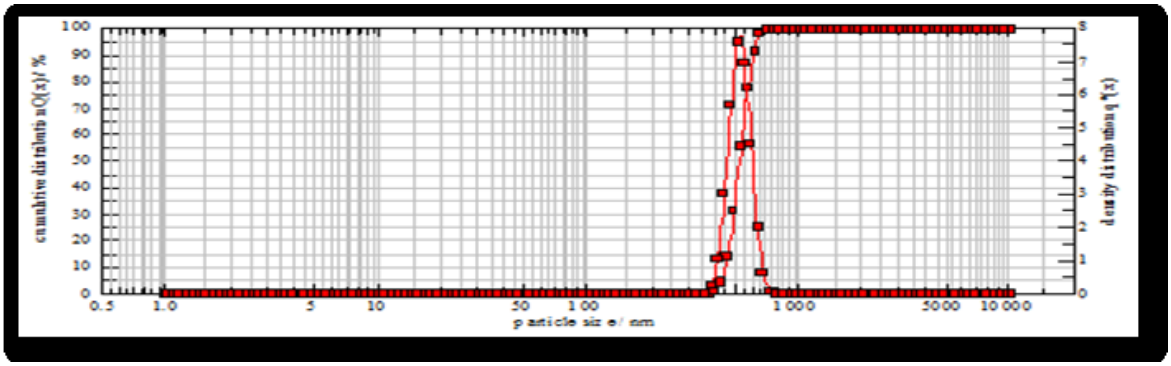


Figure 12: Graph for determination of vesicle size of batch P3

Vesicle size of RnV proniosomes of P3 batch was found to be 346.48nm, which indicated that vesicles formed with Spans were smaller in size than vesicles formed with Tweens. The relationship observed between niosome size and Span hydrophobicity has been attributed to the decrease in surface energy with increasing hydrophobicity, resulting in the smaller vesicles. Increasing the cholesterol content also contributed an increase in the hydrophobicity, with a subsequent slight reduction in vesicle size.

Skin Irritation Study

Skin irritation test was done on the human skin. The proniosomal transdermal gel is to be removed after some time and the skin is to be observed for irritation, there is no irritation or oedema on the skin it was observed by visually and sensitization was performed.

Stability Study

There was no significant change in relation to drug release and encapsulation efficiency. It shows that proniosomes has better stability.

Table 6: Stability study data of optimized formulation (P3)

Sr.No.	Temp. (^{0}c)	Initial		After 1months	
		Encapsulation efficiency*	Drug release	Encapsulation efficiency*	Drug release
1	4-8^0**c**	91±0.53	89.02±0.53	89.01±0.46	86.62±0.53
2	25±2^0**c**	90.61 ± 0.23	88.16± 0.23	87.32±0.56	88.06± 0.23
3	45±2^0**c**	89.01 ± 0.56	88.2 ± 0.56	85.73±0.32	83.2 ± 0.56

All values represent mean±standard deviations(SD), n=3

There was no significant change in physical characterization of formulation. It shows that proniosomes has better stability

Table 7: Physical characterization of batch P3 after 1 month

Sr. No.	Physical Characterization	Observation
1	Colour	Creamish
2	Odour	Characteristic
3	Clarity	Opaque
4	Particles	No

FTIR Spectrum of Proniosomal Formulation

The FTIR study of optimised batch shows that there is not any interaction between drug and other excipient. It shows that the proniosomal transdermal gel is stable.

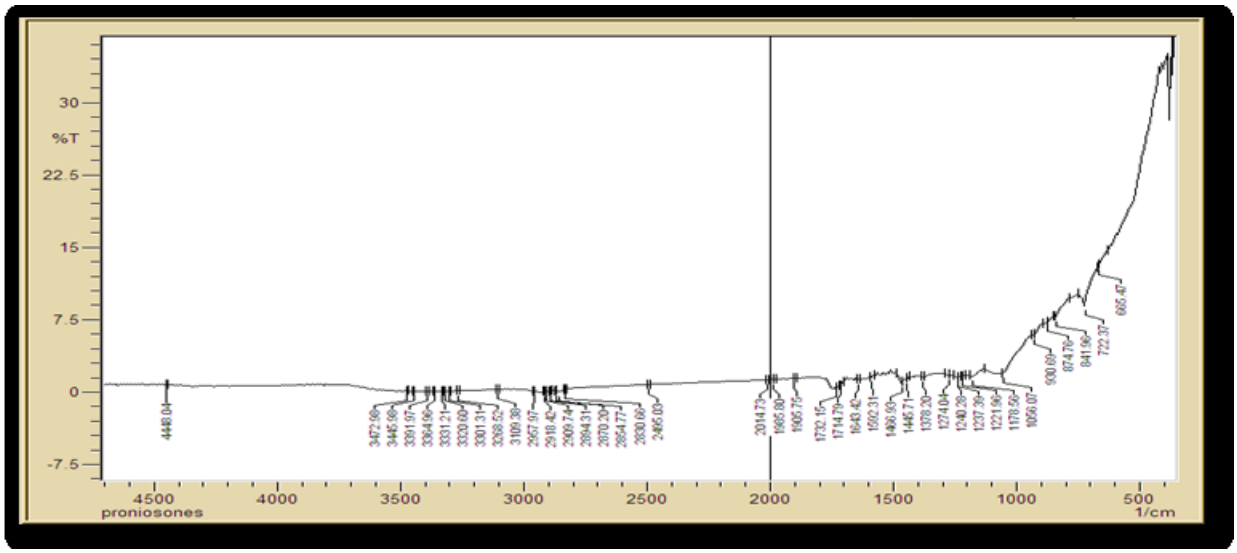


Figure 13: FTIR spectrum of proniosomal formulation

The presence of peaks at 665 cm^{-1} and 722 cm^{-1} Ar-OH Phenol plane deformation and CH=CH di-substitution of alkene plane deformation, 841 cm^{-1} and 874 cm^{-1}shows Aromatic C-H Bending, 1056 cm^{-1}, 1237 cm^{-1} and 1240 cm^{-1} shows C-N stretching, C-O present, 1330cm^{-1} shows O-H bending in-plane, 1714 and 1732 cm^{-1} shows Aldehyde C=O Stretch, 1905 and 1985cm^{-1} shows Substitution on benzene ring, 2857cm^{-1} and 2918cm^{-1} shows Carboxylic Acid O-H Stretch, 2909 cm^{-1} shows CH_3 & $-CH_2-$ in aliphatic compound, 2918cm^{-1} shows Alkyl C-H Stretch, were characteristic to the final formulation of proniosomal gel. IR spectrum of proniosomal transdermal gel showed that there was no appreciable change in position and intensity of peak with respect to IR spectrum of pure RnV and excipients, excipients and physical mixture of drug. Thus there is compatibility between drug and excipients after the formulation.

CONCLUSION

For the present study Ritonavir an antiviral BCS class II drug was selected as the drug candidate for the formulation of transdermal gel. The proniosomal gel could be an effective alternative vehicle for delivering drug through transdermal route. The results of present study indicate that Ritonavir proniosomes containing lecithin, cholesterol and surfactants sustained the release of drug over 12 hrs. The proniosomes containing span 60 shows best results, thus it helped to provide a sustained release effect by delivering it transdermally and helped to reduced side effect associated with other system. Thus proniosomal gel system shown potential for delivery of suitable drug candidate Ritonavir.

REFERENCE

1. Chiranjeevi, G; Muthukumaran, M and Krishnamoorthy, B (2013), "A review potency of vesicular system in transdermal drug delivery", ***RJPBCS***, Volume 4 (2), 156-170.
2. Chhotalal, K; Paun, J; Soniwala, M and Chawada, J (2014), "Vesicular drug delivery system: A. novel approach", ***MJPSMS***, Volume 3(3), 1-14.
3. Bharti, N; Loona, S and Khan, MM (2012), "Preparation and characterisation of metformin proniosomal gel for treatment of diabetes mellitus", ***Int. J. Pharm. Sci. Rev. Res.***, Volume 15(2), 108-144.
4. Benipal, G (2015), "Design development and evaluation of proniosomal gel of an antifungal drug – Ketoconazole", ***Int. J. Pharm Sci. Rej. Res***, Volume 31(2), 265- 272.
5. Kapil, kumar and Rai, AK (2011), "Development and evaluation of proniosomes encapsulated curcumin for transdermal administration", ***Trop J. of Pharma Res.***, Volume 10 (6), 697-703.
6. Kapil and Rai, AK (2011), "Development and evaluation of proniosomes as a promising drug carrier to improve TDDS", ***IRJP***, Volume 2(11), 71-74.
7. Singh, S; Chaudhari, Y and Singh, R (2015), "Proniosomes: a recent advancement in vesicular drug delivery system", ***WJPR***, Volume 4 (4), 1671-1689.
8. Udasi, T; Wankhede, V; Ingale, L and Atram, S (2013), "Proniosomes: A novel apporoach to vesicular drug delivery system", ***IJPPSR***, Volume 3(1), 1-6.
9. Gupta, A; Zhang, Y and Unadkat, J (2004), "MAO Q: HIV protease inhibitors are inhibitors but not substrates of the human breast cancer resistance protein (BCRP/ABCG2)", ***J Pharmacol Exp Ther.***, Volume 310 (1), 334-41.
10. S, Prajapati; M, Singh and D, Bhatia (2007), "Design and development of proniosomal transdermal drug delivery system for captopril", ***Int. J. Pharm Res.***, Volume 6(2), 687-693.
11. Gamal, M and Ahmed, A (2015), "Penetration enhancers in proniosomes as a new strategy for enhanced transdermal drug delivery", ***OSPJ***, Volume 23(1), 67-74.
12. Gupta, R; Santosh, kumar; Gupta, N and Prajapati, SK (2014), "The proniosomes development and optimization as a surrogated drug carriers for oral delivery of gliclazide, an overview", ***WJPPS***, Volume 3, 275-294.

13. Singla, S and Harikumar, SL (2012), "Proniosomes for effective topical delivery of clotrimazole development, characterisation and performance", ***Asn J Pharm Sci.***, Volume 7(4), 259-270.
14. Pinnika, P; Divya, A and Seetha, Devi (2014), "Formulation and evaluation ofcandensarten cilixetil transdermal proniosomal gel", ***JDDT***, Volume 4(2), 90-98.
15. Farooqui, N; Jaiswal, V and Kar, M (2014), "A review onproniosomal gel: potential carrier system in transdermal delivery for non-steroidal anti-inflammatory drugs", ***IJPLS***, Volume 5(10), 3939-3947.
16. Malarkodi, A and Shrilakshmi, Sanesan (2013), "Proniosomal gel: An effective novel therapeautic topical drug delivery system", ***Int. J. Pharm. Tech. Res.***, Volume 5 (4), 1754-1764.
17. Patil, H; Hardikar, S and Bhosale, A (2012), "Formulation development and evaluation of proniosomal gel of carvedilol", ***IJPPS***, Volume 4 (2), 191-197.
18. Ram, A; Thakur, A and Mithhal, V (2012), "Proniosomal provesicular for transdermal delivery of hydralazine for hypertension", ***AJPCR***, Volume 5 (3), 219-25.
19. Annakulla, D; Errabelli, M; Jukati, R and Banderi, S *et al*. (2010), "Provesicular drug delivery system: An overview and appraisal", ***Arc. Appl. Sci. Res***, Volume 2(4), 135-146.
20. Pankaj, MS; Rini, T and Dandagi, M (2013), "Formulation and evaluation of proniosome based drug delivery system of anti fungal drug clotrimazole", ***Int. J. Pharm. Sci. Nano***, Volume 6 (1), 1945-1951.
21. Hanan, Lithy EI; Shoukry, O and Mahran, L (2011), "Novel sugar esters of proniosomes transdermal delivery of vinpocetim of clinical and preclinical study", ***EJPB***, Volume 77, 43-55.
22. Ahmad, S Sabreesh; M, Patan; Rafi, Khan and Sai *et al.*, (2011) "Formulation and evaluation of lesinopril dihydrate proniosomal gel", ***JAPS***, Volume 1(8), 181-185.

Correspondence Author:
Minakshee Nimbalwar
Department of Pharmaceutics Priyadarshini J. L. College of Pharmacy, Electronic Zone Building, MIDC, Hingna Road, Nagpur-440016 Maharashtra, India

Cite This Article: Minakshee, Nimbalwar; Kanchan, Upadhye and Gouri, Dixit (2016), "Fabrication and evaluation of ritonavir proniosomal transdermal gel as a vesicular drug delivery system", ***Pharmacophore***, Vol. 7 (2), 82-95.