WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 5, 1801-1819. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF PRONIOSOMAL GEL OF AMOROLFINE HYDROCHLORIDE

Jayadev N. Hiremath*[1], Parkash G. Yaragatti[2], Nagond Mukund M.[2] and Avinash S.G.[2]

[1,2]Department of Pharmaceutics, H.S.K. College of Pharmacy Bagalkot, Karnataka, India.

Article Received on
20 March 2021,

Revised on 09 April 2021,
Accepted on 30 April 2021

DOI: 10.20959/wjpr20215-20432

***Corresponding Author**
Jayadev N. Hiremath
Department of Pharmaceutics, H.S.K. College of Pharmacy Bagalkot, Karnataka, India.

ABSTRACT

The aim of this work was to formulate and evaluate antifungal Proniosomal gel containing Amorolfine Hydrochloride. Proniosomes were prepared by coacervation phase separation method using nonionic surfactant (span 60), cholesterol, soya lecithin and other ingredients at different concentrations. All the proniosomal gel formulations were converted to niosomal suspensions and evaluated for entrapment efficiency, reproducibility, spontaneity, vesicular diameter, shape and size distribution, microphotography, FTIR studies and *in vitro* drug release. The results suggested that increasing the cholesterol concentration from 10% to 30% in the formulations increases the entrapment efficiency. In formulations with lecithin, entrapment efficiency decreased with increase in its concentration. The sizes of proniosomes were found to be uniform and spherical in shape. The IR spectral analysis suggested that there was no interaction between the drug and formulation additives. The kinetic parameters were studied using dissolution software PCP DISSOV.2. Proniosomal gel with 30% of cholesterol/lecithin formulations provided better controlled release over period of 15 hrs.

KEYWORDS: Proniosomal gels, Amorolfine Hydrochloride, Cholesterol, Lecithin and Span 60.

1. INTRODUCTION

From early 1980's niosomes[1-2] have gained wide attention by researchers for their use as drug targeting agents, drug carriers to have variety of merits while avoiding demerits associated with the conventional form of drugs. Niosomes were studied as better alternatives to liposomes for entrapping both hydrophilic and hydrophobic drugs.[3-4] The

additional merits with niosomes are low toxicity due to non ionic nature, no requirement of special precautions and conditions for formulation and preparation.[5]

Proniosomes are vesicular systems, in which the vesicles are made up of non- ionic surfactants, cholesterol and other additives. Semisolid liquid crystal gel (proniosomes) prepared by dissolving the surfactant in a minimal amount of an acceptable solvent, namely ethanol and then hydration with least amount of water to form a gel. These structures are liquid crystalline compact niosomes hybrids that can be converted into niosomes immediately upon hydration[6-7] or used as such in the topical/transdermal applications. Use of proniosome gel in topical/dermal delivery does not require hydration prior to application, but they can be applied as such or loaded on a base material of emulsion, gel, ointment, etc. prior to application. The base material helps in the application of the formulation to the skin and dilution of the active material. Proniosomes are nowadays used to enhance drug delivery in addition to conventional niosomes. They are becoming popular due to their semisolid/ liquid crystalline compact nature when compared to niosome dispersion. Proniosomal gels are generally present in transparent, translucent or white semisolid gel texture, which makes them physically stable during storage and transport.[8] Addition of water leads to interaction between water and polar groups of the surfactant resulting in swelling of bilayers. When the concentration of solvent is increased above a limited value, the bilayers tend to form random spherical structures, i.e., multilamellar, multivesicular structures. When shaken with water i.e. the aqueous phase of water, complete hydration takes place leading to the formation of niosomes. The beauty of these proniosomes lies in their ability to rearrange as stable noisomal suspensions, on hydration with water.[9]

2. MATERIAL AND METHODS

Materials

Amorolfin Hydrochloride was received as gift sample by (Curetech Skincare), Cholesterol (Specrochem Mumbai), Lecithin soya (Himedia Mumbai), Span60 (SDFCL Mumbai), Ethanol (Changshu Hongsheng Fine Che Co.), Glycerol (SQ Thermofischers Mumbai), Potassium dihydrogen orthophosphate (SDFCL Mumbai), di-Sodium hydrogen orthophosphate dehydrate (SDFCL Mumbai) were used for the formulation of proniosomes. All reagents and chemicals used are analytical grades.

Methods

Development of UV spectroscopic method

Preparation of calibration curve

The standard calibration curve was prepared in the concentration range of 4-20µg/ml. For this stock solution was prepared by dissolving 10 mg of accurately weighed Amorolfine Hydrochloride in 10 ml of methanol 1mg/ml (stock solution 1). From this stock solution, pipette out 1 ml and dilute to 10 ml with methanol it gives 100µg/ml (stock solution 2). From this stock solution pipette out 0.4,0.8,1.2,1.6 and 2.0ml into a series of 10 ml volumetric flask and volume was made up to 10ml with methanol to get 4, 8, 12, 16 and 20µg/ml solutions of Amorolfine Hydrochloride respectively. The optical density values of resulting solutions were measured at 221nm and recorded in table 1 with statistical data. Concentration versus optical density values are plotted and given in the figure 1.

Preparation of proniosomal gel

Coacervation phase separation method

This method is widely adopted to prepare proniosomal gel. Precisely weighed amounts of surfactant, lipid and drug are taken (as shown in table 2) in a clean and dry wide mouthed glass vial of 5.0 ml capacity and ethanol (1.0ml) is added to it. After warming, all the ingredients are mixed well with a glass rod; the open end of the glass bottle is covered with a lid to prevent the loss of solvent from it and warmed over water bath at 60-70°C for about 5 min until the surfactant mixture is dissolved completely. Then the aqueous phase (0.1% glycerol solution) is added and warmed on a water bath till a clear solution was formed which is then converted into proniosomal gel on cooling.

Characterization of Proniosomal gel

FTIR studies

The compatibility between pure drug and surfactants, cholesterol, lecithin was detected by FTIR spectra obtained on Shimadzu FT-IR8400/8900. The potassium bromide pellets were prepared on KBr press. To prepare the pellets the solid powder sample were ground together in a mortar with 100 times quantity of KBr. the finely grounded powder was introduced into a stainless steel die. The powder was pressed in the die between polished steel anvils at a pressure of about $10t/in^2$. For liquid samples thin film of sample liquid is made on pellet. The spectra's were recorded over the wave number of 3900^{-1} to 450 cm^{-1}.

Preparation of niosomes from proniosomal gel

Prepared proniosomal gel is weighed and filled in vials. Saline buffer pH 5.5 is added to the vials, which are then put into an Ultra Solicitor (EQUITER-8442.060.53H) and agitated for 2 min to get niosomal suspension.

Characterization of niosomes prepared from proniosomal gel

Entrapment efficiency

Free drug was separated from noisome entrapped drug by centrifugation. When a 1 ml aliquot of noisome was centrifuged at 18000×g, a stiff, floating fraction containing the niosome formed at the bottom of the tube, and a clear niosome free solvent fraction remained at the top. The clear fraction was used for determination of the free drug.

Calculate the entrapment efficiency by using following equation.

$$\textbf{Entrapment efficiency} = \frac{\textbf{Amont}\ of\ entrapped\ drug}{total\ amount\ of\ drug} \times 100$$

Rate of Spontaneity

Approximately 10 to 20 mg of proniosomal gel was transferred to the bottom of a clean stoppered glass bottle and spread uniformly around the wall of the glass bottle with the help of a glass rod, 2 ml of phosphate saline was added carefully along the walls of the glass bottle and left in a glass bottle after 20 minutes, a drop of this dispersion was withdrawn and placed on Neubaures chamber to count the number of vesicles. The numbers of niosomes eluted from proniosomes were counted.

Vesicular size distribution and average particle size determination

Particle size analysis was carried out using an optical microscope (compound microscope) with a calibrated eye piece micrometer.

Calibration of eye piece micrometer

A standard stage micrometer was used for calibration. Each division value on stage is 10µ. The eye piece micrometer consists of 100 divisions. Calibration was undertaken to find out the measure of each division using the standard stage micrometer. After calibration, the eye piece micrometer was used for particle size determination. A suspension of proniosomal gel was prepared in saline buffer pH 5.5. A drop of the suspension was mounted on a slide and observed under the microscope. About 100 niosomes were measured individually with the

help of eye piece micrometer, average was taken and their size distribution range, mean diameter was calculated.

***In vitro* release studies**

The release of Amorolfine Hydrochloride from proniosomal gel formulations were determined using membrane diffusion technique. The proniosomal gel formulation equivalent to 1250 µg of Amorolfine Hydrochloride was converted to niosomal suspension and taken in a Himedia Dialysis membrane bag having a diameter 14.3 mm with an effective length of 10 cm that was previously soaked in PBS, which acts as a donor compartment. The Dialysis Bag was placed in a beaker containing 50 ml of saline buffer pH 5.5, which acts as receptor compartment. The temperature of receptor medium maintained at 37 ± 10^{0}C and the medium was agitated at 100 rpm speed using magnetic stirrer. Aliquots of 2ml sample were withdrawn periodically and after each withdrawal same volume of medium was replaced. The collected samples were analyzed at 221 nm in Double beam UV-VIS spectrophotometer using saline buffer pH5.5 as blank. The *in vitro* drug release was studies by using PCP-DISSOV2.

Antifungal activity of proniosomal gel by disc diffusion method

The antifungal activity was screened by disc diffusion method. Candida albicans was grown on SDA. Broth was then prepared from pure culture of Candida albicans. Solution of the compound was prepared by dissolving 10 mg of compound in 1 ml of buffer/distilled water. Sabouraud′s dextrose agar plates were prepared. A thin lawn of Candida albicans was prepared on SDA. Two wells were punched on the plate. 50µl of compound and 50µl of Fluconazole was added in two wells. The plates were incubated at 37ºc for 24 hours. After 24 hours the plates were taken and zone of inhibition was noted.

Stability Studies

The stability of vesicles to retain the drug (Drug Retention Behavior) was assessed by keeping the proniosomal gel at three different temperature conditions, i.e., Refrigeration Temperature (4-8^{0}C), Room Temperature (25 ± 2^{0}C) and oven (45 ± 2^{0}C). Throughout the study, proniosomal formulations were stored in aluminum foil-sealed glass vials. The samples were withdrawn at different time intervals over a period of 1-45 days and drug content was analyzed spectrophotometrically.

3. RESULT AND DISCUSSION

The present work aimed to formulate and evaluate antifungal proniosomal gel formulations. The proniosomal gels were prepared with various surfactants, cholesterol and lecithin concentrations using ethanol as carrier. The Amorolfine Hydrochloride drug and prepared formulation were characterised for Entrapment efficiency, Rate of Spontaneity, Vesicular size, shape and size distribution, FTIR studies, *In vitro* Drug Release, Antifungal Activity and Stability Studies.

Entrapment efficiency

The entrapment efficiency of niosomes prepared at varied concentration of surfactant (Span60), Lecithin and Cholesterol concentrations are shown in table 3.The percent Entrapment Efficiency of a drug in the niosomes prepared from proniosomal gel using Span 60 and Cholesterol was in the range of 82.10±0.22and 91.28±0.42for FCS1, FCS2, FCS3, FCS4 and FCS5 formulations. The percent Entrapment Efficiency of a drug in the niosomes prepared from proniosomal gel using Span 60 and Lecithin was in the range of 10.24±0.47 and 64.64±0.48for FLS1, FLS2, FLS3, FLS4 and FLS5 formulations.

Span 60 (C_{18}-alkyl chain) having high phase transition temperature (gel to liquid transformation) of about 53^0 C and having critical packing parameter (CPP)ranging from 0.5 to 1 entraps the drug molecule by forming vesicles. The only drawback of span 60 was, drug leakage from the vesicles because of high phase transition temperature and the release was also rapid. A concentration of about 30% to 50% cholesterol was optimum to get stable vesicle by abolishing the phase transition temperature resulting in stable niosomes without drug leakage.

Rate of Spontaneity

For spontaneity studies, the formulations data is shown in Table 4.

- Rate of spontaneity studies of a drug in the niosomes prepared from proniosomal gel using Span 60 and Cholesterol was in the range of 16.10±0.63(mm^3X1000) and 27.65±0.44 (mm^3X1000) for FCS1,FCS2,FCS3,FCS4 and FCS5 formulations.
- Rate of spontaneity studies of a drug in the niosomes prepared from proniosomal gel using Span 60 and Lecithin was in the range of 19.95±0.28(mm^3X 1000)and 47.07±0.22 (mm^3X 1000) for FLS1, FLS2, FLS3, FLS4 and FLS5 formulations.

Vesicular size, shape and size distribution

The proniosomal gel was converted into niosomal suspension and the size of the niosomes was measured using an optical microscope with calibrated eyepiece micrometer. From every batch about 100 niosomes were measured for the diameter, the average diameter was calculated and shown in Tables 5 and 6. The average vesicle size of niosomes of all the batches was in the range of 56.18µm to104.39µm. The size distribution was in the range of 23.46µm to 211.14µm. The prepared niosomes were of uniform size and spherical in shape.

FTIR studies

FTIR spectrums of Amorolfine, span 60, cholesterol, lecithin and proniosomal gel formulations are shown in figure 2 to 7. FTIR spectrum of Amorolfine showed characteristic peaks at 2478 cm^{-1} and 2565 cm^{-1} which belongs to NH^{+} stretching vibration located at the nitrogen atom of morph line ring. The characteristic C-H stretching (aliphatic) vibration were observed at 2869 cm^{-1} and 2966 cm^{-1}. Aromatic C=C stretching vibrations are present at 1410 cm^{-1} to 1510 cm^{-1}. Span 60 in the pure form shows the presence of hydroxyl absorption at 3374 cm^{-1}, strong aromatic CH=CH stretching at 2916 cm^{-1} and a strong C=O of carbonyl ester is noticed at 1735 cm^{-1}. Similarly, cholesterol as expected shows the presence of hydroxyl absorption at 3662 cm^{-1} and C-H absorption from 2866 to 2932 cm^{-1}. IR spectrum of proniosomal formulations showed all characteristic peaks indicating proniosomes formed were not chemical reaction products, but exists in original form and available for the biological action.

***In vitro* Drug Release Studies**

The *in vitro* drug release from various Amorolfine Hydrochloride proniosomal gel formulations are shown in figures 8 and 9. In all the cases, 18% to 53% of drug is released in the first 6 hours, due to initial bursting of improper niosomes in the formulations. However, after 6 hours, the release was steady because the stable niosomes retain the drug and the release was extended up to 15 hours with sustained action.

To ascertain the drug release mechanism and release rate, data of the above formulations were model fitted by using PCP disso V2.0 dissolution software. The models selected were Zero order, First order, Higuchi Matrix, Korsemayer Peppas and Hixon crowel. The best fit model for all FCS1 to FLS5 except FLS4 formulations was found to be Peppas with ‘n’ value between 0.4485 to 0.9641.

Antifungal Activity

Antifungal activity of proniosomal formulations FCS3 and FCS4 were found to be promising. The antifungal activity was compared with Fluconazole as standard drug, which showed 40mm zone of inhibition. FCS3 and FCS4 showed 35mm as zone of inhibition are shown in table 8 and figure 10 to 13.

Stability Studies

The stability of niosomes prepared at varied concentration of surfactant (Span60), Lecithin and cholesterol concentrations are shown in table 7. The results showed that proniosomal gel formulation was quite stable at refrigeration and room temperatures as not much leakage of drug was found at these temperatures (See Table 7). Percent drug retained at 45 ± 2^{0} C might have decreased due to the melting of the formulation. Therefore, the proniosomal gel formulations can be stored at either refrigeration or room temperature.

Table 1: Calibration curve data of Amorolfine Hydrochloride in Methanol at 221nm.

Concentration (µg/ml)	Absorbance
0	0±0.000
4	0.214±0.004
8	0.393±0.007
12	0.549±0.003
16	0.730±0.005
20	0.903±0.008

*Average of three determination.

Table 2: Different formulae of Amorolfine Hydrochloride0.25w/w Proniosomal gel with various surfactants, cholesterol and lecithin concentrations using ethanol as carrier. Batch size: 4G.

Formulation Code	Drug	Surfactant Type	Surfactant Concentration	Cholesterol	Lecithin	Ethanol	Water
FCS1	10mg	Span60	3590mg	400mg	-	1.0ml	3.2ml
FCS2	10mg	Span60	3190mg	800mg	-	1.0ml	3.2ml
FCS3	10mg	Span60	2790mg	1200mg	-	1.0ml	3.2ml
FCS4	10mg	Span60	2390mg	1600mg	-	1.0ml	3.2ml
FCS5	10mg	Span60	1990mg	2000mg	-	1.0ml	3.2ml
FLS1	10mg	Span60	3590mg	-	400mg	1.0ml	3.2ml
FLS2	10mg	Span60	3190mg	-	800mg	1.0ml	3.2ml
FLS3	10mg	Span60	2790mg	-	1200mg	1.0ml	3.2ml
FLS4	10mg	Span60	2390mg	-	1600mg	1.0ml	3.2ml
FLS5	10mg	Span60	1990mg	-	2000mg	1.0ml	3.2ml

Table 3: Entrapment efficiency of proniosomal gel formulations prepared using span60, cholesterol and lecithin.

Formulation Code	Entrapment efficiency(±SD)*
FCS1	82.10 ±0.22
FCS2	82.20 ±0.38
FCS3	90.28±0.24
FCS4	90.20 ±0.16
FCS5	91.28±0.42
FLS1	64.64±0.48
FLS2	43.28±0.36
FLS3	20.40 ±0.64
FLS4	12.00 ±0.78
FLS5	10.24±0.47

*Average of three reading

Table 4: Rate of Spontaneity of Proniosomal gel Batches of FCS1 to FCS5 and FLS1 to FLS5.

Formulation Code	Rate of spontaneity (±SD)* (mm^3X1000)	Formulation Code	Rate of spontaneity (±SD)* (mm^3X1000)
FCS1	25.46±0.44	FLS1	19.95 ±0.28
FCS2	22.57 ±0.22	FLS2	41.38 ±0.36
FCS3	27.65±0.36	FLS3	47.07 ±0.22
FCS4	16.10 ±0.63	FLS4	33.68 ±0.32
FCS5	20.47 ±0.24	FLS5	36.22 ±0.44

*Average of three reading

Table 5: Particle size distribution and average particle size of FCS1, FCS2, FCS3, FCS4 and FCS5 formulations.

Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles
0-5µ	15	0-5µ	12	0-5µ	59	0-5µ	51	0-5µ	14
6-10 µ	53	6-10 µ	68	6-10 µ	38	6-10 µ	49	6-10 µ	70
11-15 µ	27	11-15 µ	19	11-15 µ	3	11-15 µ	0	11-15 µ	16
16-20 µ	5	16-20 µ	1	16-20 µ	0	16-20 µ	0	16-20 µ	0
Average: 104.39 µ		Average: 94.35 µ		Average: 63.34 µ		Average: 65.57 µ		Average: 93.95 µ	
Fig 4a Size Distribution FCS1		Fig 4b Size Distribution FCS2		Fig 4c Size Distribution FCS3		Fig 4d Size Distribution FCS4		Fig 4e Size Distribution FCS5	

Table 6: Particle size distribution and average particle size of FLS1, FLS2, FLS3, FLS4 and FLS5 formulations.

Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles	Size range inµ	No of Particles
0-5µ	32	0-5µ	39	0-5µ	19	0-5µ	56	0-5µ	67
6-10 µ	63	6-10 µ	60	6-10 µ	74	6-10 µ	43	6-10 µ	33
11-15 µ	5	11-15 µ	1	11-15 µ	7	11-15 µ	1	11-15 µ	0
16-20 µ	0	16-20 µ	0	16-20 µ	0	16-20 µ	0	16-20 µ	0
Average: 76.24 µ		**Average: 70.73 µ**		**Average: 86.09 µ**		**Average: 61.81 µ**		**Average: 56.18 µ**	

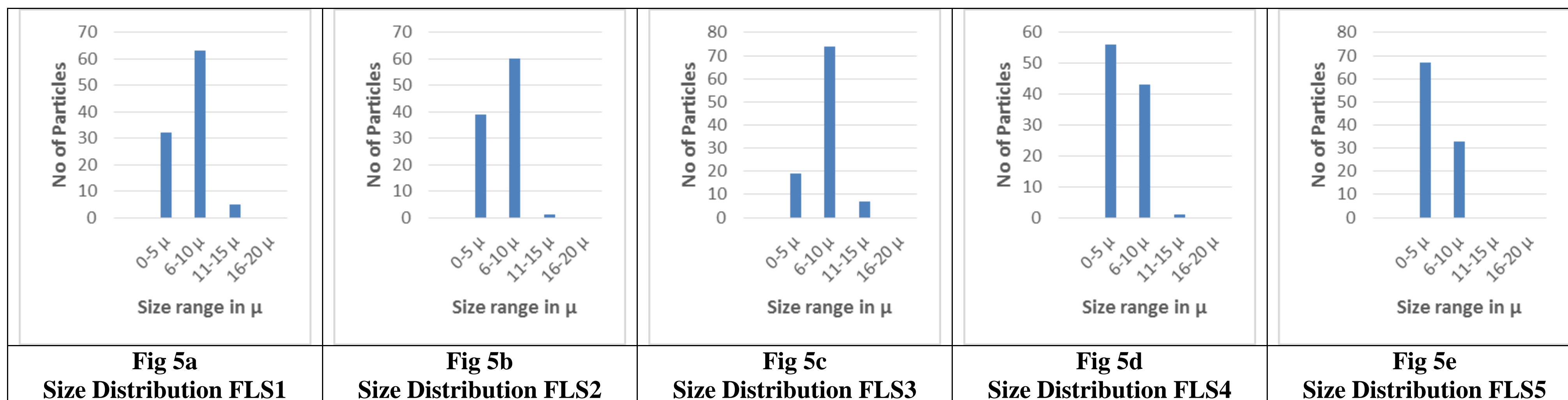

Fig 5a Size Distribution FLS1	Fig 5b Size Distribution FLS2	Fig 5c Size Distribution FLS3	Fig 5d Size Distribution FLS4	Fig 5e Size Distribution FLS5

Table 7: Stability Studies of proniosomal gel formulations prepared using span60, cholesterol and lecithin.

Days	In Room Temperature (25 ± 2^0c)				In Refrigeration Temperature ($4\text{-}8^0$c)				In Oven Temperature(45 ± 2^0c)			
	Batch Code	Entrapmt efficiency %(±SD)*	Batch Code	Entrapment efficiency %(±SD)*	Batch Code	Entrapment efficiency %(±SD)*	Batch Code	Entrapment efficiency %(±SD)*	Batch Code	Entrapment efficiency %(±SD)*	Batch Code	Entrapment efficiency %(±SD)*
ZERO DAY	FCS1	82.10	FLS1	64.64	FCS1	-	FLS1	-	FCS1	-	FLS1	-
	FCS2	82.20	FLS2	43.28	FCS2	-	FLS2	-	FCS2	-	FLS2	-
	FCS3	90.28	FLS3	20.40	FCS3	-	FLS3	-	FCS3	-	FLS3	-
	FCS4	90.20	FLS4	12.00	FCS4	-	FLS4	-	FCS4	-	FLS4	-
	FCS5	91.28	FLS5	10.24	FCS5	-	FLS5	-	FCS5	-	FLS5	-
FIFTEEN DAYS	FCS1	77.34	FLS1	60.43	FCS1	78.24	FLS1	63.86	FCS1	75.34	FLS1	55.35
	FCS2	78.17	FLS2	39.86	FCS2	78.97	FLS2	40.53	FCS2	76.10	FLS2	35.48
	FCS3	85.42	FLS3	17.96	FCS3	86.46	FLS3	18.24	FCS3	80.98	FLS3	11.96
	FCS4	86.56	FLS4	9.74	FCS4	87.10	FLS4	10.75	FCS4	80.23	FLS4	6.76
	FCS5	87.63	FLS5	7.79	FCS5	88.16	FLS5	7.49	FCS5	81.46	FLS5	4.69
THIRTYDAYS	FCS1	73.41	FLS1	57.23	FCS1	74.42	FLS1	61.53	FCS1	70.32	FLS1	51.44

	FCS2	74.12	FLS2	38.67	FCS2	74.86	FLS2	39.47	FCS2	71.13	FLS2	30.56
	FCS3	86.20	FLS3	15.42	FCS3	84.67	FLS3	16.32	FCS3	78.22	FLS3	8.87
	FCS4	87.34	FLS4	8.96	FCS4	84.43	FLS4	6.86	FCS4	79.36	FLS4	5.78
	FCS5	88.97	FLS5	6.84	FCS5	85.88	FLS5	5.98	FCS5	80.45	FLS5	3.56
FOURTY FIVE DAYS	FCS1	70.86	FLS1	52.65	FCS1	71.34	FLS1	55.65	FCS1	68.24	FLS1	48.67
	FCS2	71.65	FLS2	32.79	FCS2	71.98	FLS2	34.54	FCS2	69.68	FLS2	28.59
	FCS3	80.68	FLS3	13.34	FCS3	78.58	FLS3	11.69	FCS3	76.36	FLS3	6.98
	FCS4	81.24	FLS4	6.98	FCS4	79.86	FLS4	5.25	FCS4	76.98	FLS4	4.69
	FCS5	82.10	FLS5	5.23	FCS5	80.12	FLS5	4.87	FCS5	77.44	FLS5	2.96

Table 8: Antifungal activity of Amorolfine proniosomal gel formulations.

SI. No.	Candida albicans	Zone of Inhibition	Zone of Inhibition Fluconazole
1	FCS3	35mm	40mm
2	FCS4	35mm	45mm
3	FLS4	30mm	40mm

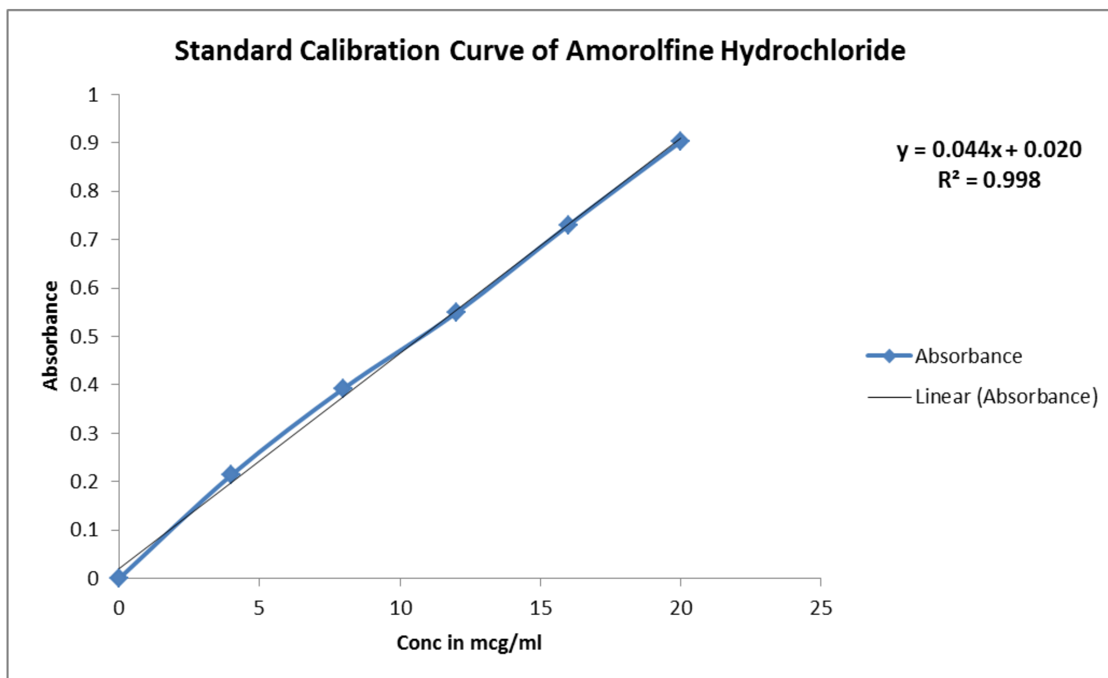

Figure 1: Calibration curve of Amorolfine Hydrochloride in Methanol at 221nm.

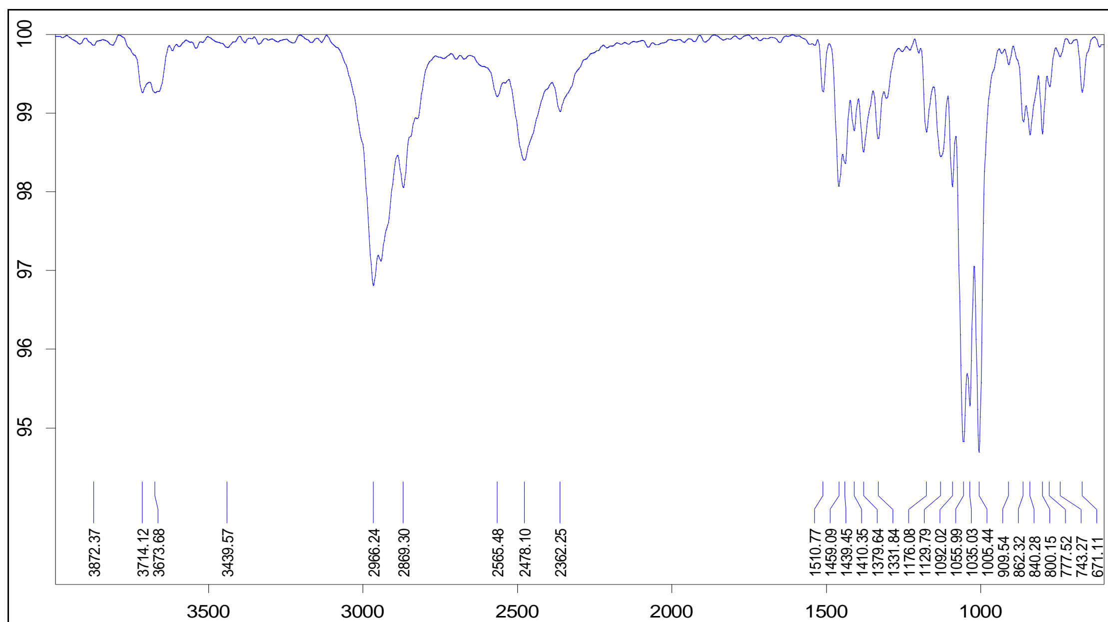

Figure 2: FTIR Spectra of Amorolfine Hydrochloride.

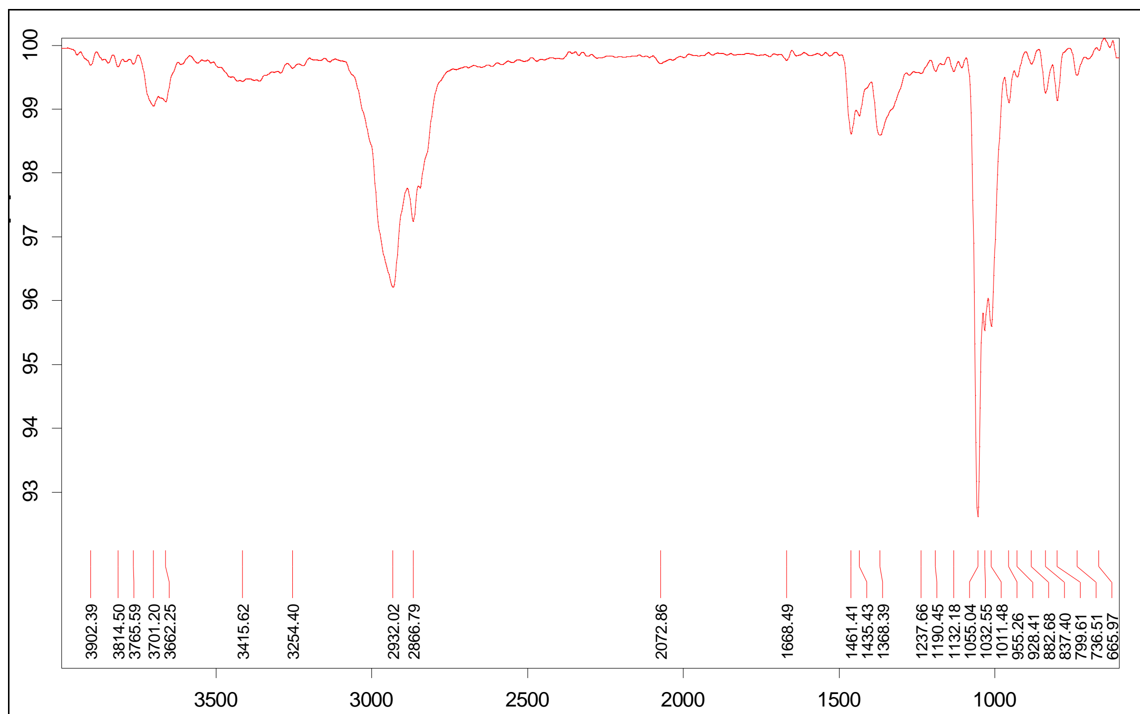

Figure 3: FTIR Spectra of Cholesterol.

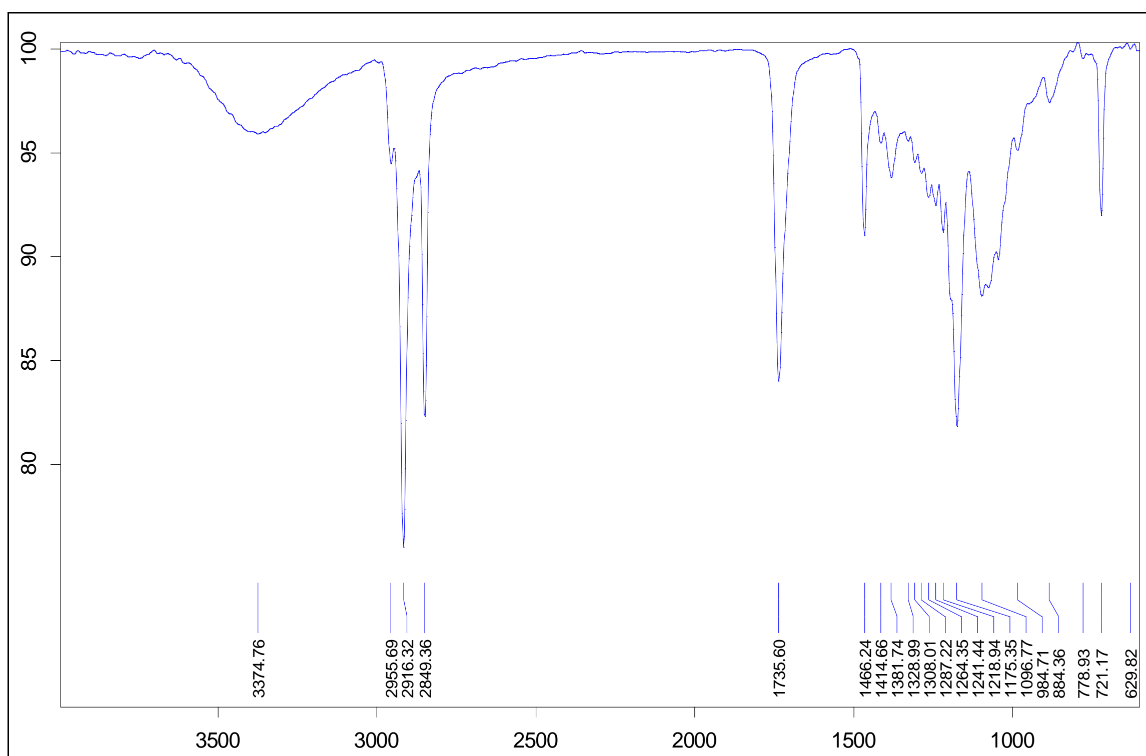

Figure 4: FTIR Spectra of Span 60.

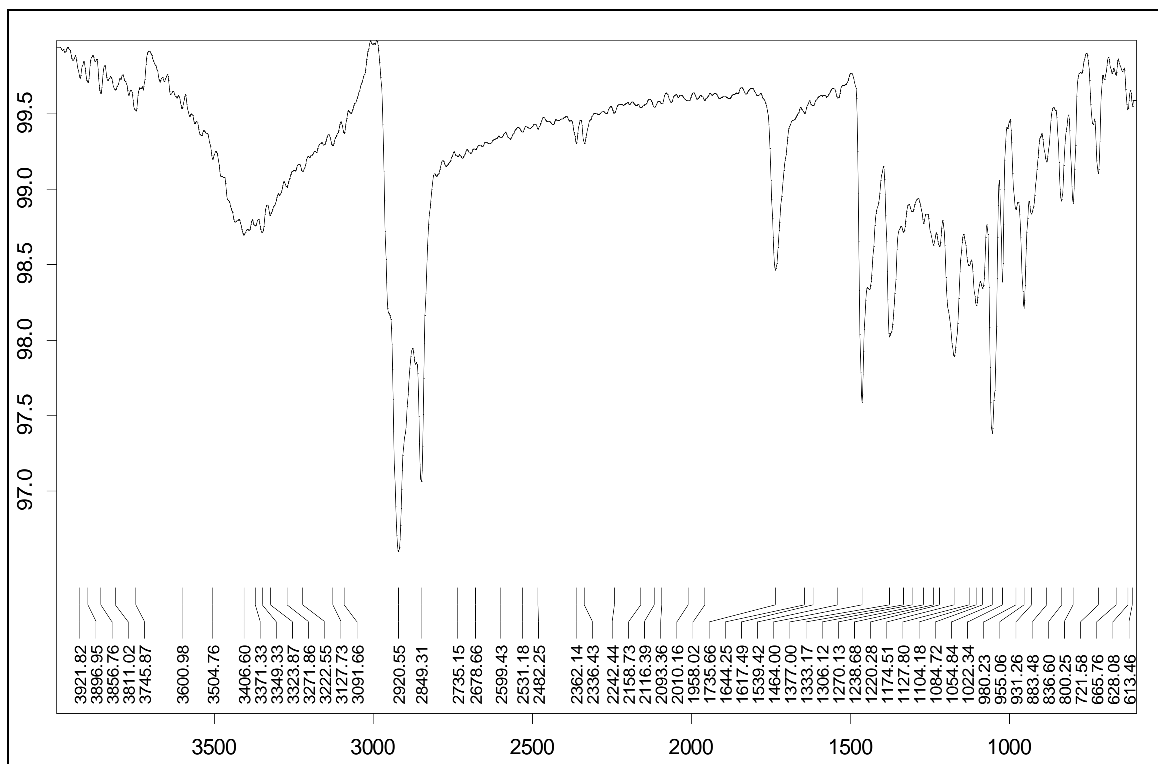

Figure 5: FTIR Spectra of Amorolfine Hydrochloride, Cholesterol, Span 60.

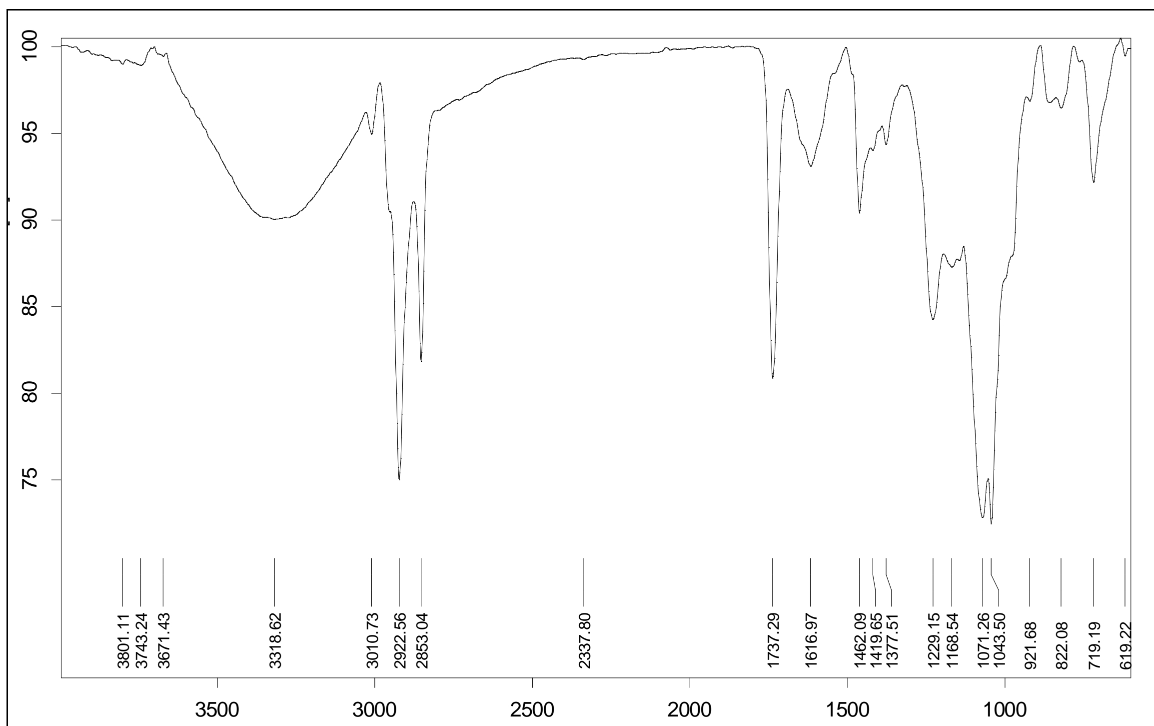

Figure 6: FTIR Spectra of Lecithin.

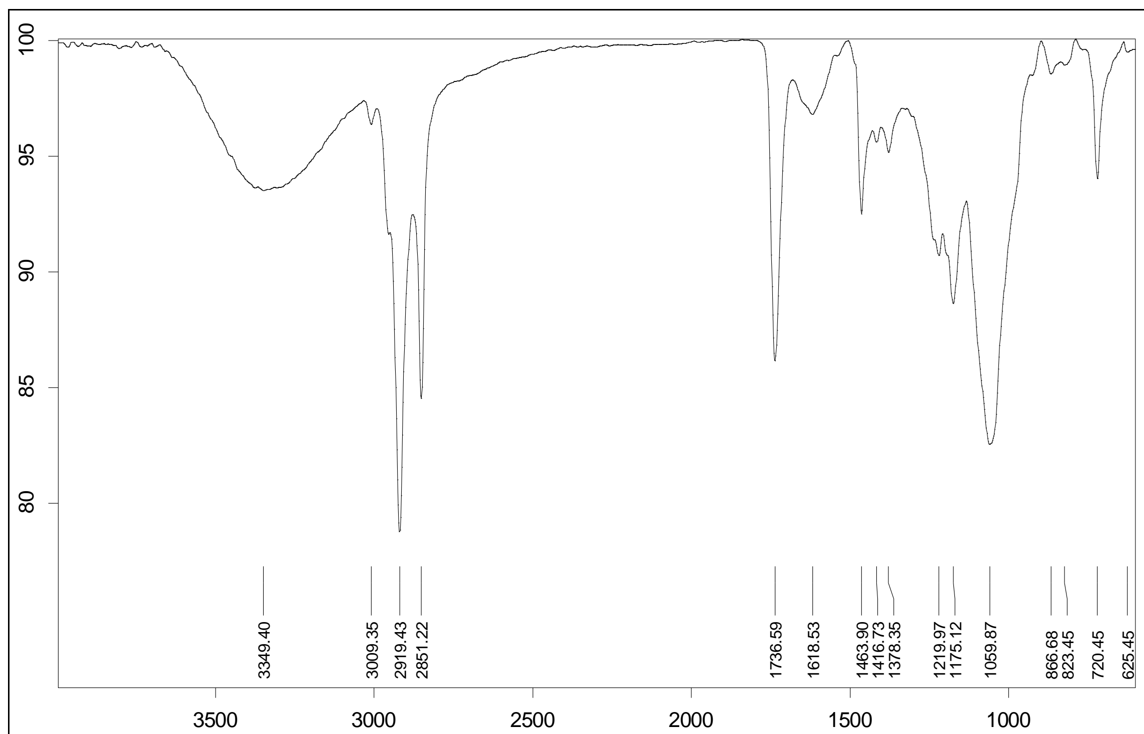

Figure 7: FTIR Spectra of Amorolfine Hydrochloride, Lecithin, Span 60.

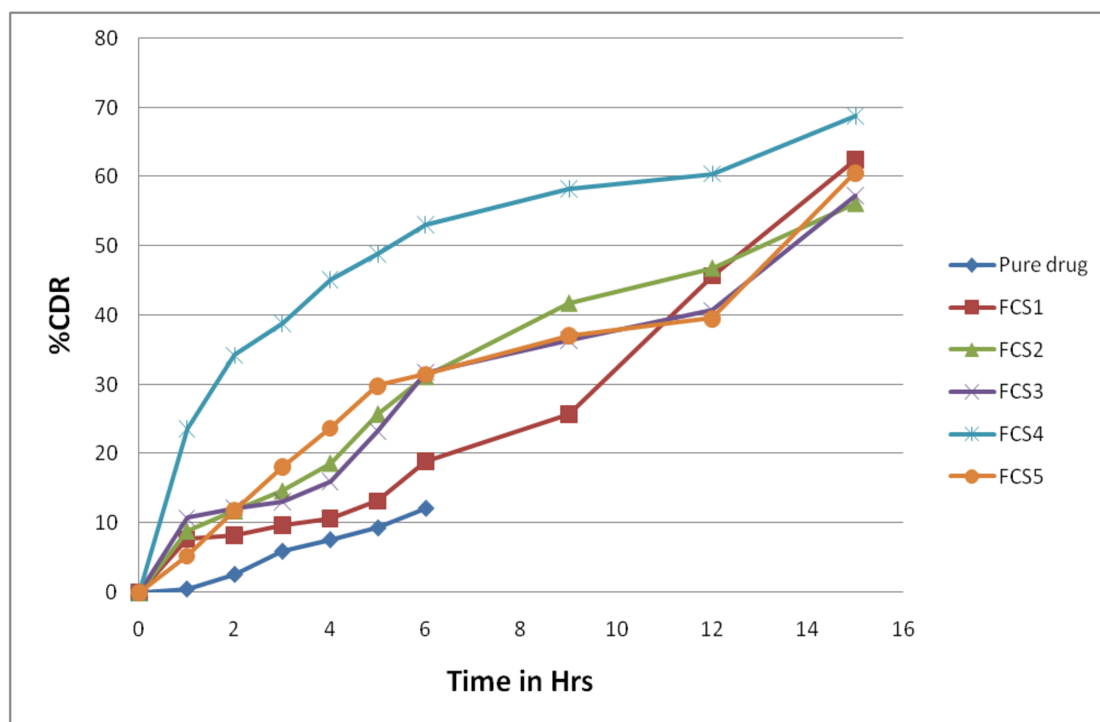

Figure 8: Comparison of dissolution profile of pure drug and batches FCS1, FCS2, FCS3, FCS4 and FCS5.

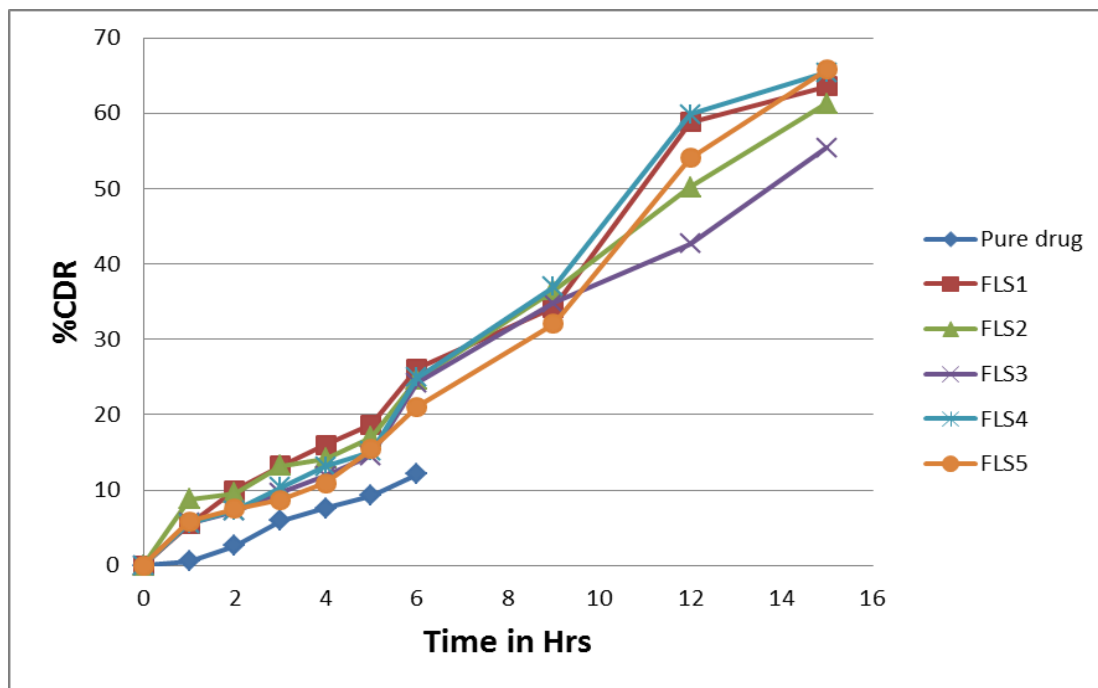

Figure 9: Comparison of dissolution profile of pure drug and batches FLS1, FLS2, FLS3, FLS4 and FLS5.

Figure 10: Zone of Inhibition for FCS3

Figure 11: Zone of Inhibition for FCS4

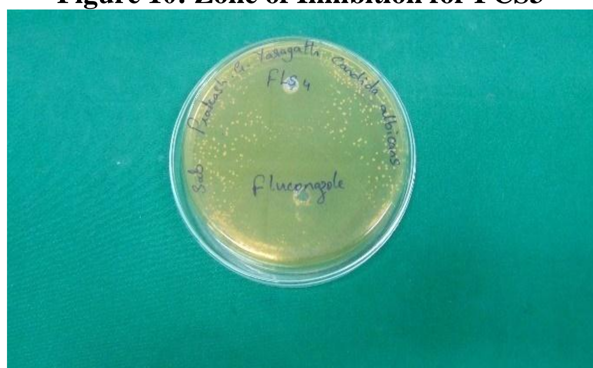

Figure 12: Zone of Inhibition for FLS4

Figure 13: Zone of Inhibition for FCS3, FCS4 and FLS4

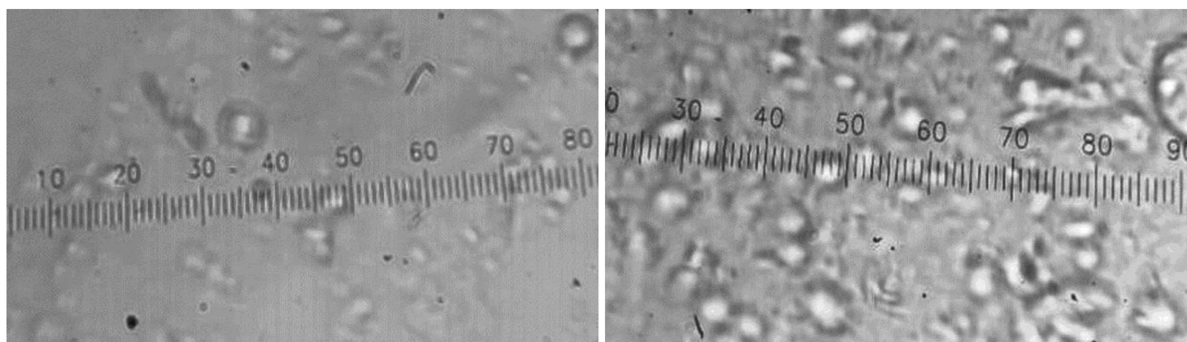

Figure 14: Microphotographs ofbatchFCS3 **Figure 15: Microphotographs of batchFLS5**

3. CONCLUSION

Proniosomal gel can be conveniently prepared by coacervation phase separation method using nonionic surfactants (span60), lecithin and cholesterol at different concentrations. The entrapment efficiency of proniosomal gel with span 60 increases as concentration of cholesterol increases from 10% to 30% and Entrapment Efficiency decreases with increase in Lecithin concentration. The optimum concentration of cholesterol was found to be 30%. In case of proniosomal gel formulations. The average vesicular size of niosomes of all the batches was measured in the range of 56.18µm to104.39µm.The size distribution was in the range of 23.46 to 211.14 µm.

The dissolution parameters were studied by using dissolution software PCP DISSO V.2 for niosome formulations. The drug release from vesicles is dependent on concentrations of cholesterol/Lecithin in proniosomal gel formulations with span 60 and it decreases with increase in their concentrations. It is mainly due to the influence of phase transition temperature and critical packing parameter of surfactant. For all the proniosomal gel formulations the release was extended up to 15 hours. Sustained release was observed with formulation containing 30% of cholesterol. The optimized formulation FCS3 showed maximum Entrapment of drug, 90.28±0.24 and the release from this formulation was more sustained 57.30±0.88 after 15hrs. The best fit model for allFCS1 to FLS5 formulations except FLS4 was found to be Peppas with 'n' value "between" 0.4485 to 0.9641 suggesting release is diffusion controlled. The antifungal activity of FCS3 and FCS4 were found to be promising with zone of inhibition 35mm. The antifungal activity was compared with Fluconazole as standard.

4. ACKNOWLEDGEMENT

I am thankful to the faculty members, Department of Pharmaceutics, H.S.K. College of Pharmacy, Bagalkot. For providing necessary facilities to carry out this research work.

5. REFERENCES

1. Schreier H, Boustra J. Liposomes and niosomes as topical drug carriers: dermal and transdermal drug delivery. J Control Release, 1994; 30: 1-15.
2. Baillie A, Florence A, Hume L, Muirhead G, Rogerson A. Preparation and properties of niosomes-nonionic surfactant vesicles. J Pharmacol, 1985; 37: 863-868.
3. Yoshioka T, Sternberg B, Florence AT. Preparation and properties of vesicles (niosomes) of sorbitan monoesters (span 20, 40, 60 and 80) and a sorbitan trimester (span 85). Int J Pharm, 1994; 105: 1-6.
4. Uchegbu IF, Vyas SP. Non-ionic surfactantbased vesicles (niosomes) in drug delivery. Int J Pharm., 1998; 172: 33-70.
5. Carafa M, Santucci E, Lucania G. Lidocane loaded nonionic surfactant vesicles: characterization and in vitro permeation studies. Int J Pharm., 2002; 231: 21-32.
6. Gupta A, Prajapati SK, Balamurugan M, Singh M, Bhatia D. Design and development of a proniosomal transdermal drug delivery systems for captopril. Trop J Pharm Res., 2007; 6: 687-693.
7. Tsai YH, Fang JY, Yu SY, Wu PC, Huang YB. In vitro skin preparation of estradiol from various Proniosomal formulations. Int J Pharm, 2001; 215: 91-99.
8. Tiddy GJT. Surfactant-water liquid crystal phases. Phys Rep., 1980; 57: 1–46.
9. Jain NK, Khopade AJ, Vora B. Proniosomes based transdermal delivery of levonorgesterol for effective contraception. J Control Release, 1998; 54: 149-165.