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Research Article

Effect of edge actuators on the formulation and characterization of tolnaftate proniosomes

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ABSTRACT

This article is to investigate the effectiveness of formulating proniosomes as the transdermal drug delivery system for tolnaftate. Proniosomes are the dry formula tions of water soluble carrier particles coated with surfactant and rehydrated to form niosomal dispersions exhibiting therapeutic response. Topically proniosomes increase the duration of action when applied thereby reducing the systemic absorption of drug. Tolnaftate is an antifungal agent used for topical fungal diseases. Different formulations of Tolnaftate proniosomes (F1 -F12) were prepared by slurry method with varying amounts of surfactant, cholesterol and mannitol and were evaluated for parameters li ke solubility, melting point, particle size, drug entrapment and *in vitro* drug release. All the formulations showed high solubility but the maximum solubility and *in vitro* drug release (in pH 7.4) was exhibited by F4 formulation with drug and span 60 as an edge actuator. The best fit model indicating mechanism of dissolution from the formulation showing the highest release was found to be Higuchi matrix release. It revealed that the release mechanism from the formulation could be diffusion. The present study confers that Tolnaftate Proniosomes are suitable for the transdermal drug delivery and can be formulated with span-60 as an edge actuator for exhibiting maximum drug release.

Keywords: Proniosomes; Tolnaftate; Niosomes; Cholesterol; Coacervation.

INTRODUCTION

Nanotechnology has created a revolution in the field of sciences with the development of novel dosage forms like niosomes, liposomes and proniosomes. Proniosomes are the water soluble carrier particles coated with surfactant which upon hydration form niosomes. (Walve, J.R., 2011, 743-50). This proniosomal drug delivery have concerned towards transdermal delivery because surfactants themselves act as penetration enhancers and are environmental, harmless, amphiphillic, have property of encapsulation and they can entrap both hydrophilic as well as lipophillic drugs in the vesicular membrane of cholesterol. (Neeraj, B., 2012, 10-26). It was reported to attain better stability than liposomes and niosomes. It can prolong the circulation of the entrapped drugs and enhances the penetration into target tissue and reduce toxicity. (Radha, G.V., 2013, 42-48)

Proniosomes prove their efficiency by converting themselves to niosomes on hydration. (Chein, Y. W., 1992).

Proniosomes → (hydration) → Niosomes

The hydration can happen more over by the skin or by the adding of aqueous solvents. Proniosomes preserve trap together hydrophilic as well as lipophilic drugs. (Venkatesh, D.N., 2014, 178-182)

Methods of preparation of proniosomes

1. Spraying method.
2. Slurry method.
3. Coacervation phase separation method.

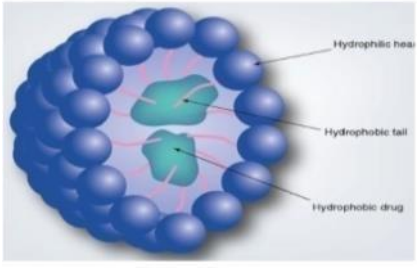

Figure 1: Structure of proniosome

1. Spraying method

Formation of Proniosomes by spraying method involves the mixing of surfactant with the organic solvent and then spraying this mixture onto sorbitol powder followed by evaporation of the solvent. As the sorbitol

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carrier is soluble in the organic solvent, it is essential to repeat the process until the preferred surfactant load has been achieved. The so obtained carrier has very thin surfactant coating around it and hydration of this coating allows the formation of multilamellar vesicles. (Kumar, K., 2011,71-74)

2. Slurry method

Proniosomes uses mannitol as a carrier. The time required for the formation of proniosomes by the slurry method is independent of the ratios of surfactant and carrier used. In this method, the entire quantity of surfactant solution is added to mannitol powder in a biological oxygen demand (BOD) shaker, until the powder appears to be dry and free flow. (Baillie, A.J., 1985, 863-868).

3. Coacervation phase separation method

Accurately weighed or required amount of surfactant, carrier (lecithin), cholesterol and drug are taken in a clean and dry wide mouth glass vial (5 ml) and solvent is added to it. The mixture is then heated with continuous stirring on water bath at 60-70ºC for 5 min, till the surfactant gets dissolved completely. The above dispersion is allowed to cool down to room temperature, so that the dispersion gets converted to gel i.e. proniosomal gel. (Shwetha, V., 2015, 25-30)

Mechanism of drug transport through skin

There are three main pathways for a drug molecule to penetrate the stratum corneum.

Hydrophilic drugs permeate by Intercellular pathway and the Lipophilic drugs by Intracellular (Transcellular) mechanism. Both the drugs can penetrate the stratum corneum through the transcellular route. (Ijeoma Uchegbu, F., 1998, 33-70).

1. ***Transcellular mechanism*:** In this pathway hair follicles and sweat ducts offers pores that by pass the stratum corneum.
2. ***Intercellular mechanism*:** In this type of route drug directly goes to the systemic circulation via lipid matrix between keratocytes.
3. ***Intracellular mechanism*:** In this route drug molecule penetrates directly across the stratum corneum by diffusion method. Stratum corneum is the main barrier for drug molecules from transdermal drug delivery system. (Mithun, B., 2013, 636-641).

Materials and Methods

Materials and Sources

Tolnaftate was supplied as a gift sample by Yarrow Chemicals Pvt. Ltd**.** Cholesterol and chloroform were purchased from Finar Chem. Ltd, Ahmadabad. Mannitol, Tween-80 and Methanol were purchased from Merck Specialties Pvt.Ltd., Mumbai. Span-20 and Tween-20 were purchased from Moly Chemicals Pvt. Ltd and Oxford Laboratory Reagent, Mumbai respectively.

Construction of Calibration curve

100mg of Tolnaftate was weighed accurately and dissolved in methanol and made up to 100ml in a volumetric flask (1st stock solution 1000µg/ml).

From this 10ml of solution was pipetted out and made up to 100ml. this gives 2nd stock solution (100µg/ml).

From the above stock, 0.2ml was pipetted out and made up to 10ml in 10ml volumetric flask. From this the aliquots were prepared whose concentration ranges from 2-16 µg/ml and the absorbance was measured at 258nm against the reagent blank.

Preparation of Tolnaftate Proniosomes

Proniosomes were prepared by the slurry method. As per the method, surfactants, cholesterol solution and Tolnaftate dissolved in chloroform and methanol were added to a 250ml conical flask containing the mannitol carrier. Additional chloroform: methanol (2:1) solution added to form slurry in the case of lower surfactant loading. The flask was attached to a BOD (Biological Oxygen Demand) incubator shaker to evaporate solvent at 60 to 70 rpm, a temperature at 45 ± 2ºC, until the mass in the flask had become a dry free flowing product. This dry preparation is referred to as proniosomes and used for further studies on powder properties. These proniosomes were stored in a tightly closed container at refrigerator temperature until further evaluation. (Mohamed N., 2010, 85-89).

RESULTS AND DISCUSSION

A successful attempt was made to formulate proniosomes of Tolnaftate using different surfactants, stabilizers, carriers. Effect of these substances on the formulations was assessed. In the present work, twelve formulations were formulated whose composition is mentioned in Tables 5-6. The formulated proniosomes were characterized for various physicochemical parameters.

Evaluation of Tolnaftate proniosomes

Determination of Melting point

The melting point of Tolnaftate was found to be 110-111.5^{o}C which complied with the BP standards.

Determination of Solubility

Solubility of Tolnaftate in various solvents reveals that it was soluble in methanol, chloroform, and acetone. It is insoluble in water, sparingly soluble in ether, slightly soluble in alcohol.

Morphology

Shape and surface morphology of proniosomes was studied using scanning electron microscopy (SEM). Proniosomes were mounted on an aluminum stub with double sided adhesive carbon tape. The vesicles were

Table 1: Calibration Curve data for Tolnaftate at 257nm

S.No	Concentration in µg/ml	Absorbance at 257nm
1.	0	0
2.	2	0.138
3.	4	0.264
4.	6	0.385
5.	8	0.498
6.	10	0.62
7.	12	0.736
8.	14	0.868
9.	16	0.992

nm = nanometres

µg/ml = microgram per milliliter

Table 2: Composition of Proniosomes of Tolnaftate (F1 to F6)

INGREDIENTS	F1	F2	F3	F4	F5	F6
Tolnaftate (mg)	100	100	100	100	100	100
Cholesterol (mg)	10	20	50	10	20	50
Mannitol (mg)	100	90	80	100	90	80
Span- 20 (mg)	90	80	50	-	-	-
Span- 60 (mg)	-	-	-	90	80	50
Tween- 20 (mg)	-	-	-	-	-	-
Tween- 80 (mg)	-	-	-	-	-	-
Chloroform (ml)	10	10	10	10	10	10
Methanol (ml)	5	5	5	5	5	5

Table 3: Composition of Proniosomes of Tolnaftate (F7 to F12)

INGREDIENTS	F7	F8	F9	F10	F11	F12
Tolnaftate (mg)	100	100	100	100	100	100
Cholesterol (mg)	10	20	50	10	20	50
Mannitol (mg)	100	90	80	100	90	80
Span- 20 (mg)	-	-	-	-	-	-
Span- 60 (mg)	-	-	-	-	-	-
Tween- 20 (mg)	90	80	50	-	-	-
Tween- 80 (mg)	-	-	-	90	80	50
Chloroform (ml)	10	10	10	10	10	10
Methanol (ml)	5	5	5	5	5	5

F = Formulation

mg = microgram

ml = millilitres

then sputter- coated with gold/palladium using a vacuum evaporator and examined with the scanning electron microscope equipped with a digital camera at 10kv accelerating voltage. (Tamizharasai, S., 2013, 517 - 523).

Particle size

Particle size analysis showed that the sizes of different formulations were in the range of 412nm to 920nm, indicating that these vesicles were all of a small size.

Drug Content

Drug content uniformity was determined as triplicate by dissolving the proniosomes in methanol and dissolved proniosomes were undergone centrifugation at 3000rpm for 5min. The solution was diluted to Beer's range and observed in UV-Specrophotometer. The value ranges from 89% to 94%. (Tamer, M.S., 2015, 375-383).

Entrapment Efficiency

Entrapment efficiency of proniosomes was determined by centrifugation method. 100mg of proniosomes powder were subjected to centrifugation on a laboratory centrifuge (Remi R4C) at 3500rpm for a period of 90min. The sediment in the centrifugation tube as diluted to 100ml with methanol and the absorbance of this solution was recorded at 257nm. Amount of Tolnaftate in supernatant and sediment gave a total amount of Tolnaftate in 1ml dispersion. Percentage

Table 4: Entrapment efficiency, Particle size, Drug content, Zeta potential of all Formulations

S.No.	Formulation Code	Particle Size (nm)	Drug Content (%)	Entrapment Efficiency (%)	Zeta Potential (mV)
1	F1	686	90	48.2	**-32**
2	F2	760	91	55.38	**-35.6**
3	F3	412	89	68.98	**-30**
4	F4	796	94	71.17	**-34**
5	F5	829	93	72.04	**-33**
6	F6	910	91	82.03	**-33.2**
7	F7	691	90	69.71	**-38.1**
8	F8	725	92	68.43	**-36.9**
9	F9	770	89	64.57	**-34.3**
10	F10	481	90	63.96	**-40**
11	F11	856	89	60.68	**-33.5**
12	F12	920	89	57.04	**-33.2**

mV = microvolts
F = Formulation
nm = nanometers

Table 5: in-vitro diffusion data for formulations F1 to F6

S. No	Time (h)	% Cumulative drug release					
		F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	0
2	0.5	5.06	11.36	5.42	10	6.16	8.9
3	1	14.86	18.29	15.71	18.46	17.5	16.4
4	2	26.12	28.7	26.71	27.6	26.97	26.1
5	4	30.08	33.53	31.79	31.79	33.05	31.4
6	6	35.32	38.4	35.72	38.06	40.36	37.6
7	8	41.83	47.87	45.71	43.09	53.54	42.1
8	10	47.18	55.15	54.59	48.16	68.72	47.9
9	12	52.58	57.96	59.93	65.6	79.75	54.4
10	24	90.12	76.38	80.63	94.51	92.52	89.5

Table 6: invitro diffusion data for formulations F7 to F12

S. No	Time (h)	% Cumulative drug release					
		F7	F8	F9	F10	F11	F12
1	0	0	0	0	0	0	0
2	0.5	9.3	9.87	14.3	9.52	13.4	10.7
3	1	15.7	17.38	23.2	17.74	20.3	19.1
4	2	25.5	24.96	35.1	26.15	32.9	27.6
5	4	33.02	35.08	43.7	29.94	41.1	30.2
6	6	38.16	39.13	50.6	36.11	48.2	37.7
7	8	43.36	44.45	60.3	42.35	57.7	42.9
8	10	49.8	51.06	67.1	46.29	63.8	49.1
9	12	56.3	58.96	71.03	52.62	67.8	54.4
10	24	91.9	90.39	86.26	89.95	83.2	70.42

entrapment of drug was calculated by the following formula.

$$\text{Entrapment efficiency} = \frac{\text{Amount of entrapped drug}}{\text{Total amount of drug}} \times 100$$

The entrapment efficiency ranges from 48.2% to 82.03%. As per the obtained results it is concluded that as the concentration of cholesterol increases the particle size also increases and entrapment efficiency decreases. (Sharda, S., 2012, 236-245).

Zeta Potential

The Zeta potential of a proniosome preparation can help to predict the fate of proniosomes invivo. The zeta potential values for the Tolnaftate Proniosomal formulations lie between values -30mV to -40mV.

Table 7: invitro Release Profile of Higuchi Model for Formulations F1 to F6

S. No	Square root of time	F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	0
2	0.70711	5.06	11.36	5.42	10	6.16	8.9
3	1	14.86	18.29	15.71	18.46	17.5	16.4
4	1.41421	26.12	28.7	26.71	27.6	26.97	26.4
5	2	30.08	33.53	31.79	31.94	33.05	31.4
6	2.44941	35.32	38.4	35.72	38.06	40.36	37.6
7	2.82843	41.83	47.87	45.71	43.09	53.54	42.8
8	3.16228	47.18	55.15	54.59	48.16	58.72	47.9
9	3.4641	52.58	57.96	59.93	55.6	69.75	54.4
10	4.89898	90.12	76.38	80.63	94.51	92.52	89.5

Table 8: invitro Release Profile of Higuchi Model for Formulations F7 to F12

S. No	Square root of time	F7	F8	F9	F10	F11	F12
1	0	0	0	0	0	0	0
2	0.70711	9.3	9.87	14.3	9.52	13.4	10.7
3	1	15.7	17.38	23.2	17.74	20.3	19.1
4	1.41421	25.5	24.96	35.1	26.15	32.9	27.6
5	2	33.02	35.08	43.7	29.94	41.1	30.2
6	2.44941	38.16	39.13	50.6	36.11	48.2	37.7
7	2.82843	43.36	44.45	60.3	42.35	57.7	42.9
8	3.16228	49.8	51.06	67.1	46.29	63.8	49.1
9	3.4641	56.3	58.96	71.03	52.62	67.8	54.4
10	4.89898	91.9	90.39	86.26	89.95	83.2	70.42

Table 9: Invitro Release Profile of Korsmeyer- Peppas model for Formulations F1 to F6

S. No	Log time	Log Cumulative % drug release					
		F1	F2	F3	F4	F5	F6
1	-0.30102	0.73399	1.05537	0.73399	0.94939	0.78958	0.70415
2	0	1.196176	1.26221	1.196176	1.21484	1.24303	1.17201
3	0.30102	1.42667	1.45788	1.42667	1.4216	1.43088	1.41697
4	0.60205	1.50229	1.52543	1.50229	1.49692	1.51917	1.47827
5	0.77815	1.55291	1.58433	1.55291	1.57518	1.60595	1.54802
6	0.90308	1.66001	1.68006	1.66001	1.63144	1.72867	1.62148
7	1	1.73711	1.74154	1.73711	1.68033	1.76878	1.67375
8	1.07918	1.77764	1.76312	1.77764	1.73559	1.84354	1.72082
9	1.38021	1.95727	1.8829	1.90649	1.95182	1.96623	1.95482

***In vitro* diffusion studies**

In vitro diffusion studies of all the formulations of tolnaftate proniosomes were carried out in pH 7.4 phosphate buffer. The study was performed for 24hrs, and cumulative percentage drug release was calculated at different time intervals. The *invitro* drug release profiles for the formulations (F1-F6), (F7-F12) were tabulated in Table 5 and Table 6. The plot of time Vs cumulative % drug release for formulations (F1-F6) and (F7-F12) were plotted and depicted in Figures 9-10. Effects of various polymers and their concentration on drug release were studied.

Curve fitting analysis

In order to describe the kinetics of the release process of drug in all formulations, various equations were

Table 10: Invitro Release Profile of Korsmeyer- Peppas model for Formulations F7 to F12

S. No	Log time	Log % Cumulative drug release					
		F7	F8	F9	F10	F11	F12
1	-0.30102	1.02938	1.15533	1.05537	0.96848	0.99431	0.97863
2	0	1.28103	1.36548	1.26221	1.19589	1.24004	1.24895
3	0.30102	1.4409	1.5453	1.45788	1.40654	1.39724	1.41747
4	0.60205	1.48	1.64048	1.52543	1.51877	1.54505	1.47625
5	0.77815	1.57634	1.70415	1.58433	1.5816	1.5925	1.55762
6	0.90308	1.63245	1.78031	1.68006	1.63708	1.64787	1.62685
7	1	1.69108	1.82672	1.74154	1.69722	1.70808	1.66548
8	1.07918	1.73559	1.85144	1.76312	1.7505	1.77055	1.72115
9	1.38021	1.96331	1.95612	1.93580	1.95400	1.92012	1.84769

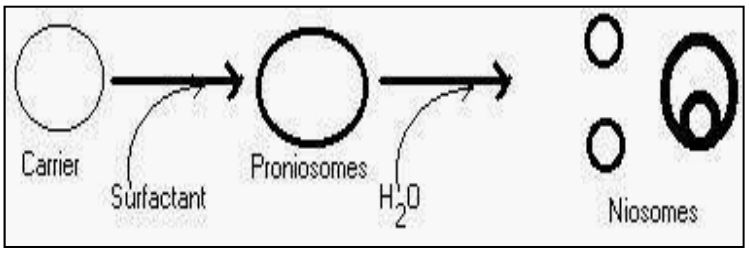

Figure 2: Formation of niosomes from proniosomes

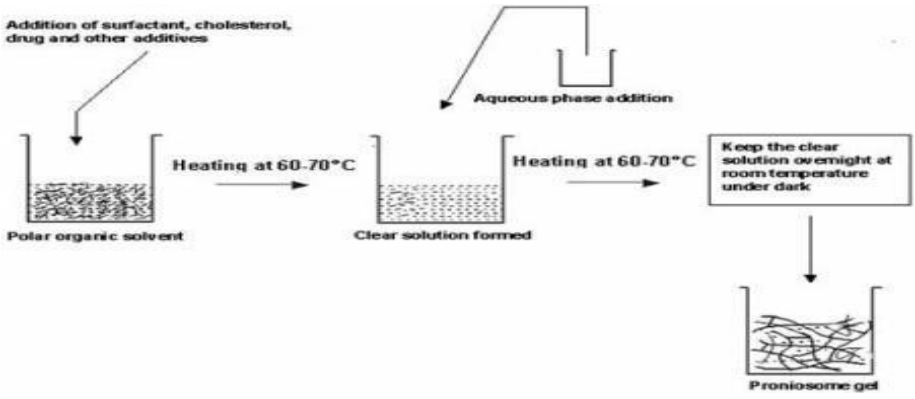

Figure 3: Diagrammatic representation of coacervation phase separation method

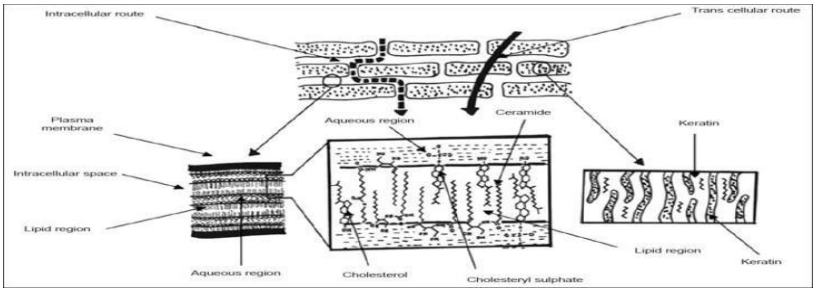

Figure 4: Mechanism of Drug transport through skin

used, such as zero-order rate equation, which describe the system where release rate is independent of the concentration of the dissolved species. The first-order equation describes the release from the systems where dissolution rate is dependent on the concentration of the dissolving species.

Higuchi square root equation describes the release from system where solid drug is dispersed in insoluble matrix, and the rate of drug release is related to the rate of diffusion. The Korsmeyer-peppas equation is used to analyze the release of pharmaceutical polymeric dosage forms, when the release mechanism is not well known or when more than one type of release

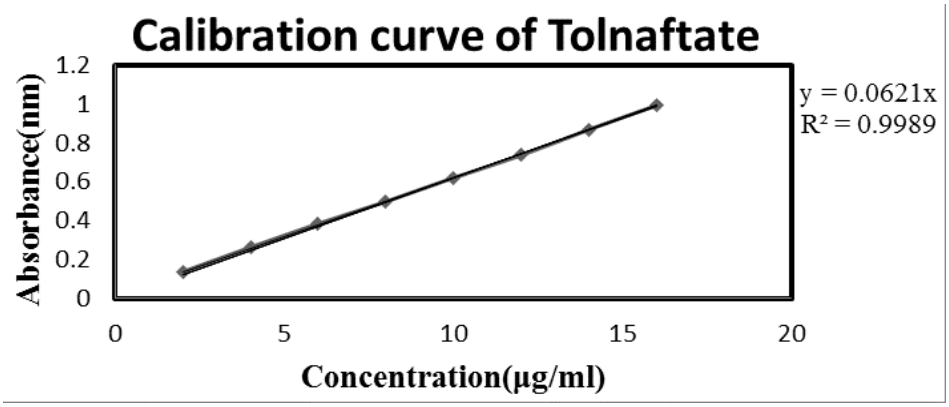

Figure 5: Calibration curve of Tolnaftate

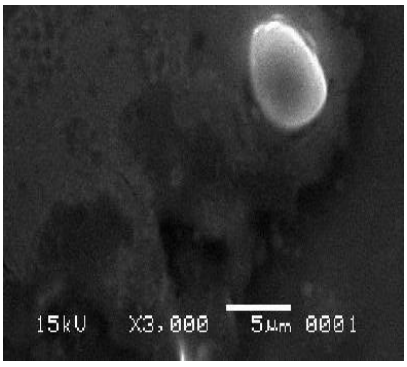

Figure 6: Morphology of Proniosomes

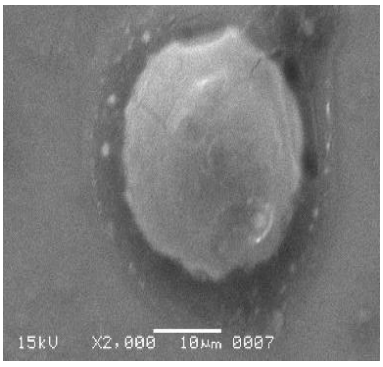

Figure 7: Morphology of Proniosomes

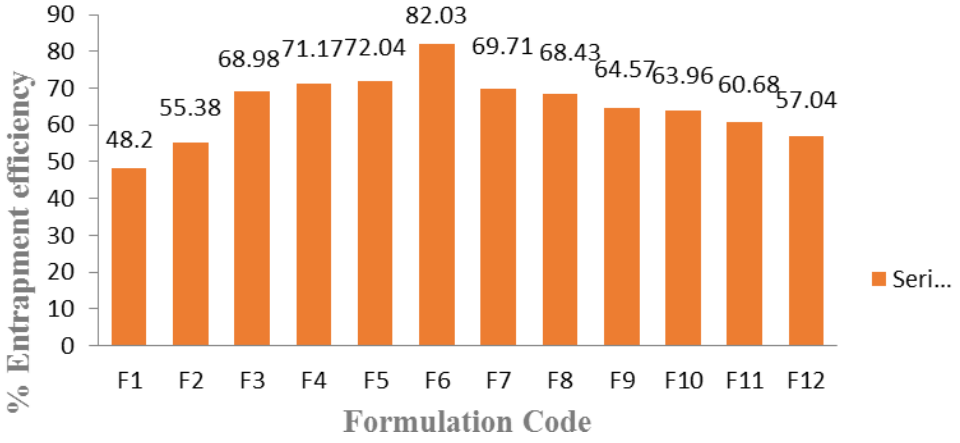

Figure 8: Graph showing Entrapment Efficiency

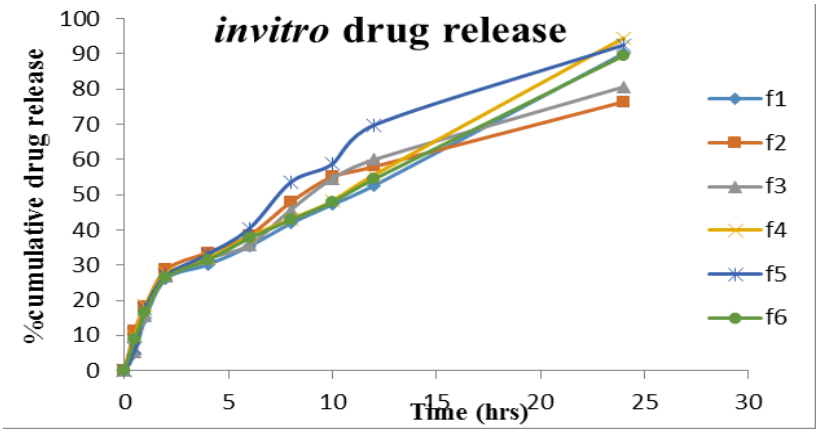

Figure 9: invitro diffusion studies for F1 to F6

Table 11: InVitro Release Profile of First Order for Formulation F1 to F6

S. No	Time(h)	Log % Cumulative drug retained					
		F1	F2	F3	F4	F5	F6
1	0	2	2	2	2	2	2
2	0.5	1.977	1.947	1.975	1.954	1.972	1.959
3	1	1.93	1.912	1.925	1.911	1.916	1.922
4	2	1.868	1.853	1.865	1.859	1.863	1.866
5	4	1.844	1.822	1.833	1.832	1.825	1.836
6	6	1.81	1.789	1.808	1.791	1.775	1.791
7	8	1.764	1.717	1.734	1.755	1.667	1.757
8	10	1.722	1.651	1.657	1.714	1.615	1.716
9	12	1.675	1.623	1.602	1.647	1.48	1.658
10	24	0.994	1.3732	1.2871	0.739	0.873	1.021

Table 12: InVitro Release Profile of First Order for Formulation F7 to F12

S. No	Time(h)	Log % Cumulative drug retained					
		F7	F8	F9	F10	F11	F12
1	0	2	2	2	2	2	2
2	0.5	1.957	1.954	1.932	1.956	1.937	1.95
3	1	1.925	1.917	1.885	1.915	1.901	1.907
4	2	1.872	1.875	1.812	1.868	1.826	1.859
5	4	1.825	1.812	1.75	1.845	1.77	1.843
6	6	1.791	1.784	1.693	1.805	1.714	1.794
7	8	1.753	1.744	1.598	1.76	1.626	1.756
8	10	1.7	1.689	1.517	1.73	1.558	1.706
9	12	1.64	1.613	1.461	1.675	1.507	1.658
10	24	0.908	0.982	1.137	1.002	1.225	1.470

Table 13: Release Kinetics Data of the Formulations F1 to F12

Formulation Code	Zero order R^2	First order R^2	Higuchi's R^2	Korsmeyer-peppas	
				N	R^2
F1	0.948	0.940	0.969	0.647	0.942
F2	0.856	0.970	0.989	0.476	0.983
F3	0.888	0.987	0.986	0.631	0.935
F4	0.942	0.906	0.966	0.538	0.976
F5	0.861	0.986	0.987	0.643	0.951
F6	0.947	0.949	0.978	0.642	0.934
F7	0.949	0.942	0.981	0.491	0.968
F8	0.937	0.962	0.988	0.465	0.984
F9	0.796	0.968	0.974	0.493	0.985
F10	0.952	0.936	0.968	0.544	0.986
F11	0.806	0.963	0.978	0.52	0.988
F12	0.854	0.959	0.987	0.479	0.974

phenomena could be involved**.** The data obtained from *in-vitro* diffusion studies were fitted to zero-order (ta- bles 5-6), first-order (tables 11-12), Higuchi (tables 7-8) and Korsmeyer–Peppas (tables 9-10) equations.

The diffusion data obtained were plotted as Time versus cumulative percent drug released as zero order (fig 9-10), Time versus log cumulative percent drug remain- ing as First order release kinetics(fig 15-16), Square root of time versus cumulative percent drug released as Higuchi equation(fig 11-12) and Log time versus log cumulative percent drug released as per Korsmeyer-Peppas equation (fig 13-14).

Identification of Tolnaftate

The IR spectrum of pure drug was found to be similar to that of standard spectrum of Tolnaftate. The spectrum of Tolnaftate shows the following groups at their

frequencies shown in 1298, 1481, 1626, 1900 -2100, 2927cm^{-}1.

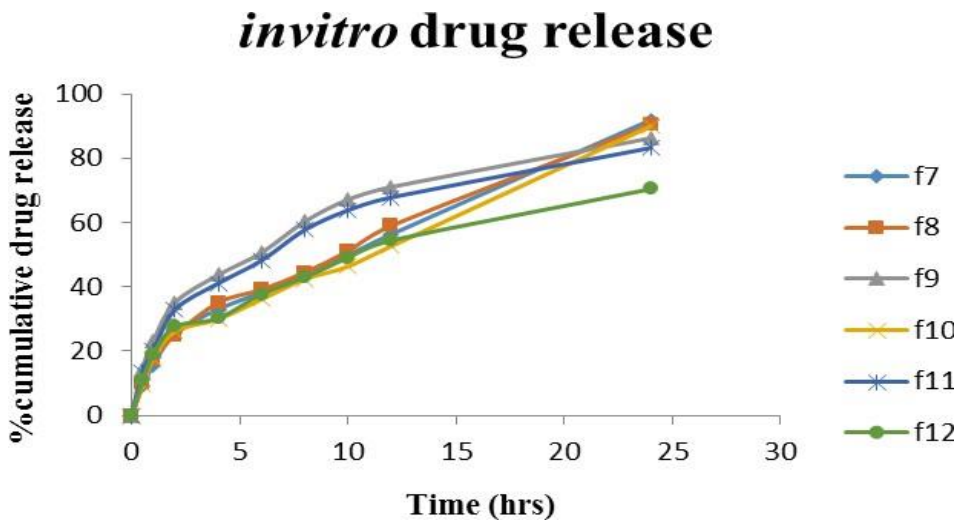

Figure 10: invitro diffusion studies for F7 to F12

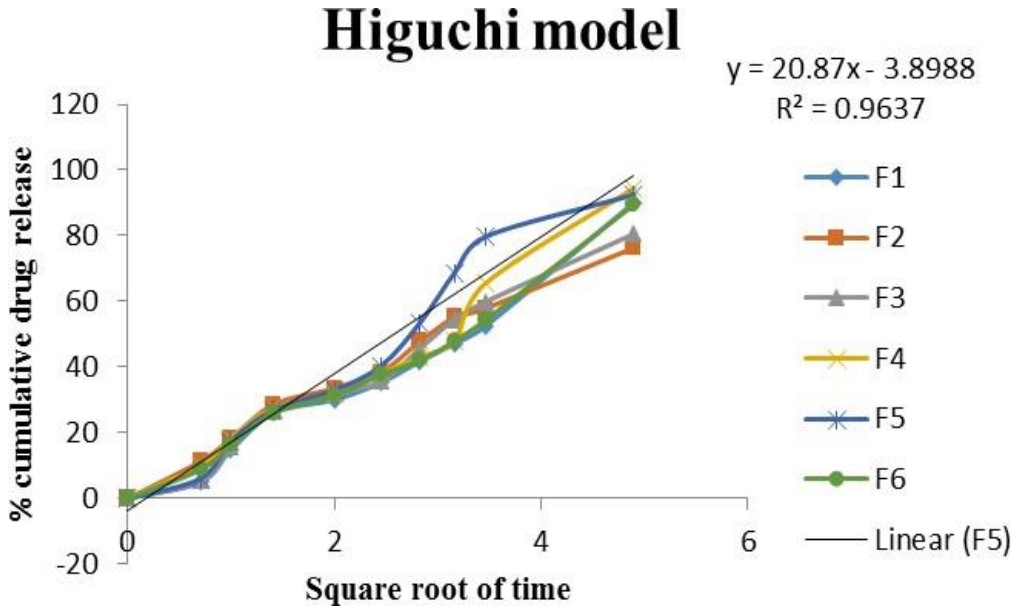

Figure 11: Square Root of Time Vs Cumulative % Drug Released (Higuchi's Release Mechanism) of Formulation F1 to F6

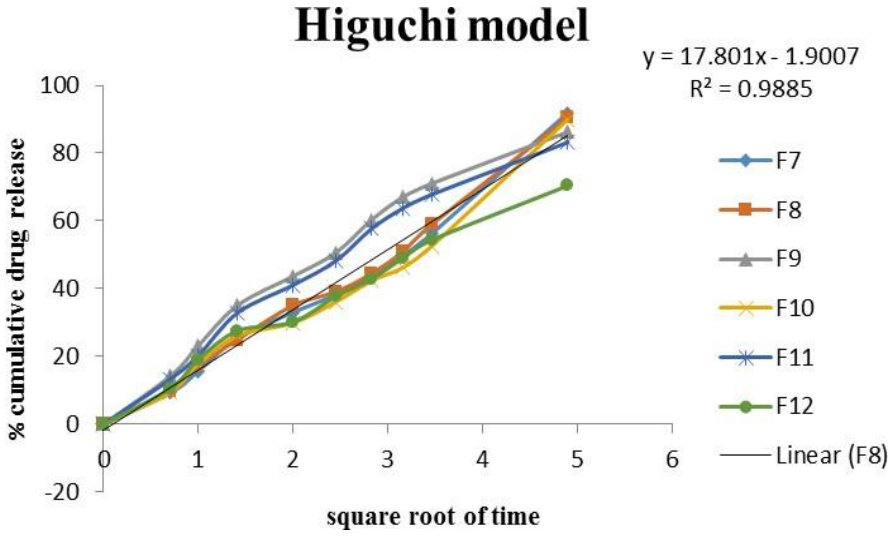

Table 14: Functional groups of Infrared spectroscopy

Polymers	Groups		Assigned		
	C-H Stretch	C-N (Carbomate) Stretch	C-N Stretch	C=S Stretch	C=C Stretch
Tolnaftate (Pure drug)	2927	1481	1298	1900-2100	1626
Tolnaftate+Cholesterol+ Mannitol+Span-60	2835.57	1477.72	1299.3	2002.3	1626.8

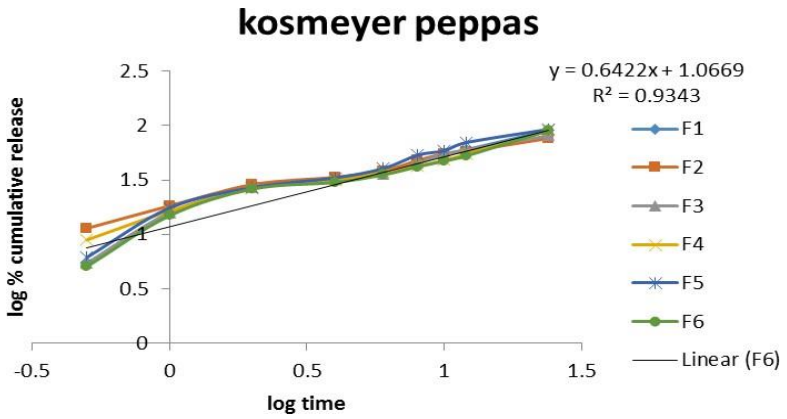

Figure 13: Log Time Vs Cumulative % Drug Released (Korsmeyer- Peppas Release Mechanism) of Formulation F1 to F6

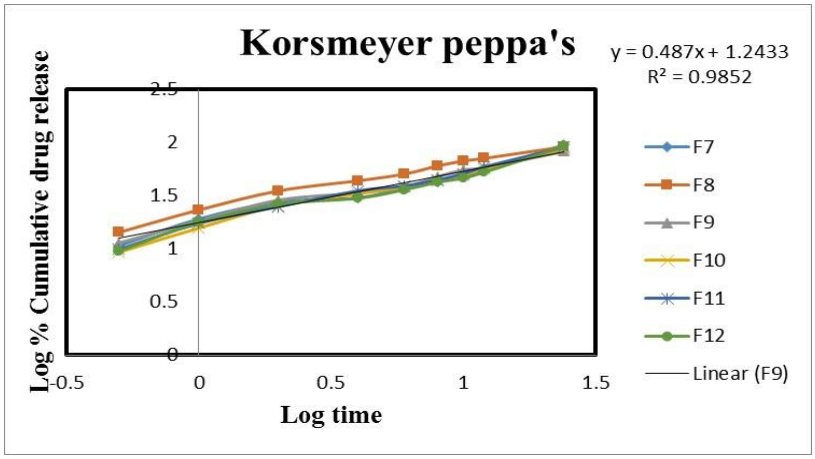

Figure 14: Log Time Vs Cumulative % Drug Released (Korsmeyer- Peppas Release Mechanism) of Formulation F7 to F12

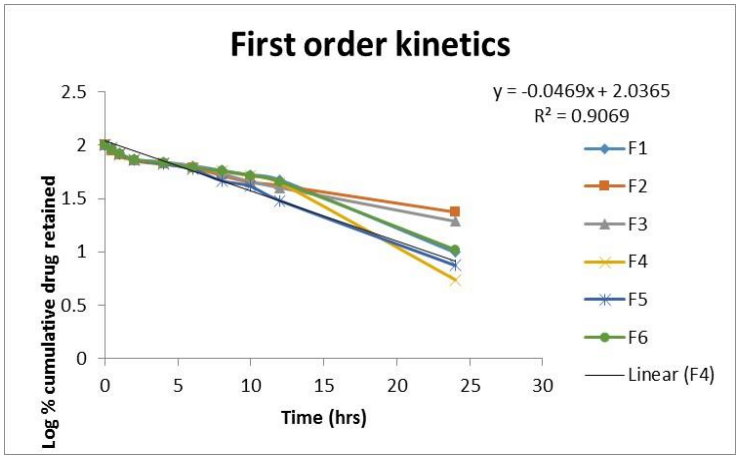

Figure 15: Time Vs Log Cumulative % Drug Retained (First Order Kinetics) of Formulations F1 to F6

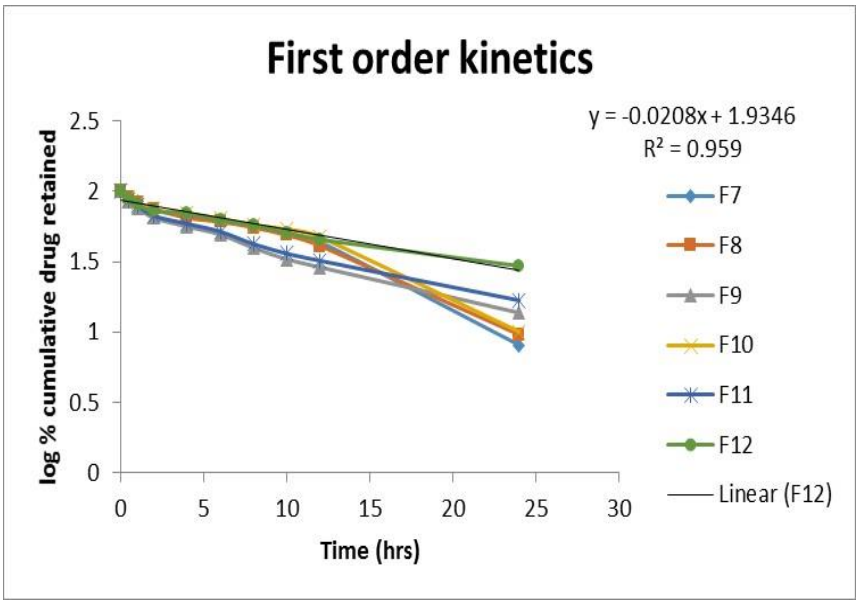

Figure 16: Time Vs Log Cumulative % Drug Retained (First Order Kinetics) of Formulations F7 to F12

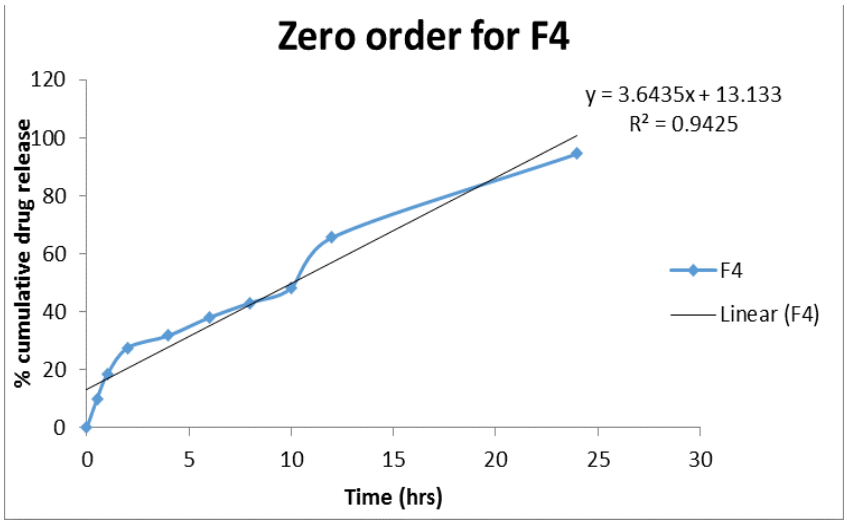

Figure 17: Time Vs Cumulative % Drug Released (Zero order kinetics) of Formulation F4

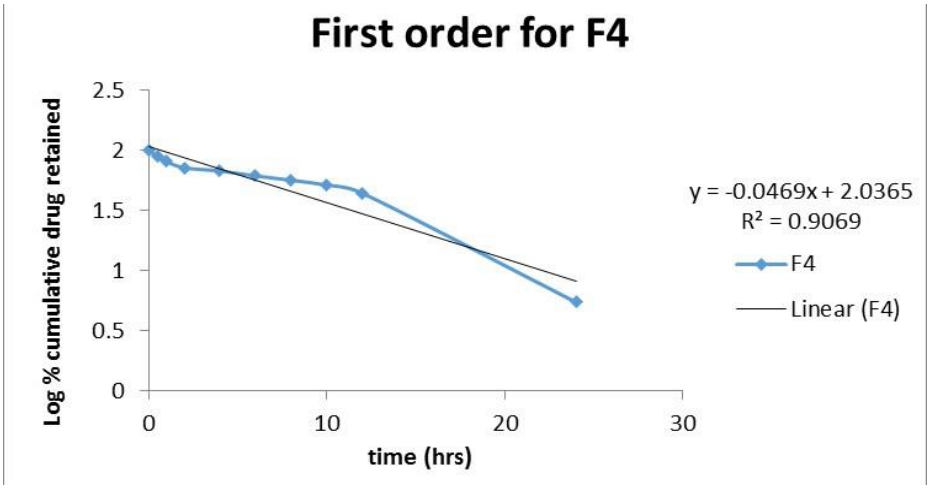

Figure 18: Time Vs Log Cumulative % Drug Retained (First order kinetics) of Formulation F4

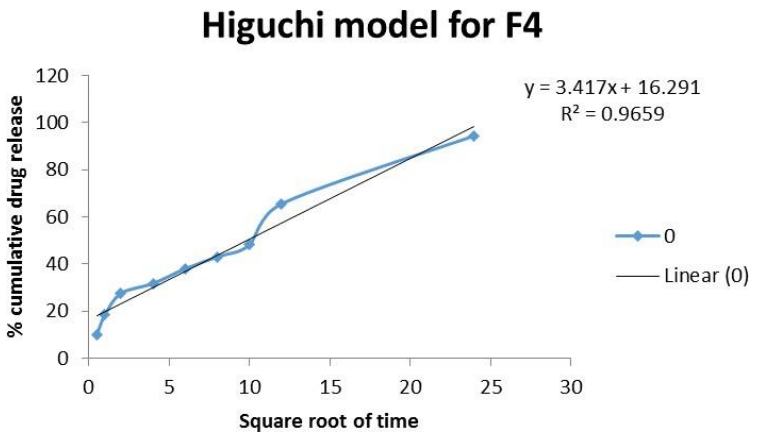

Figure 19: Square root of time Vs Cumulative % drug released (Higuchi's release mechanism) of Formulation F4

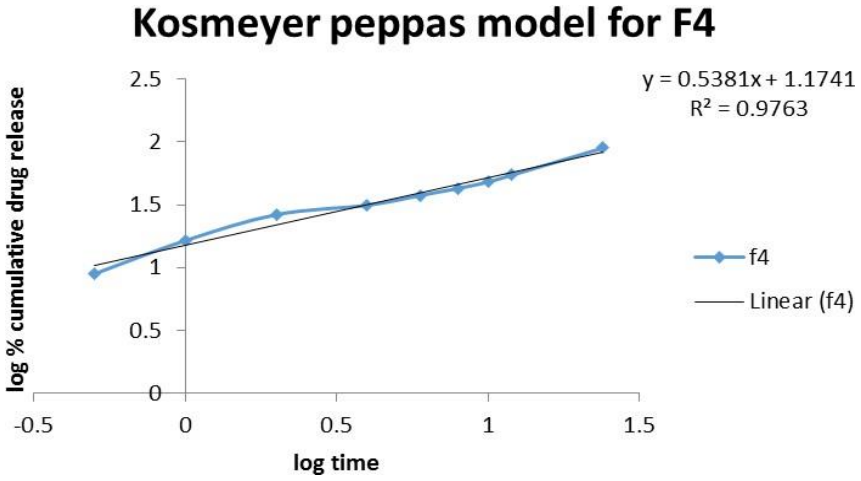

Figure 20: Log time Vs Log cumulative % drug released (Korsmeyer-peppas release mechanism) of Formulation F4

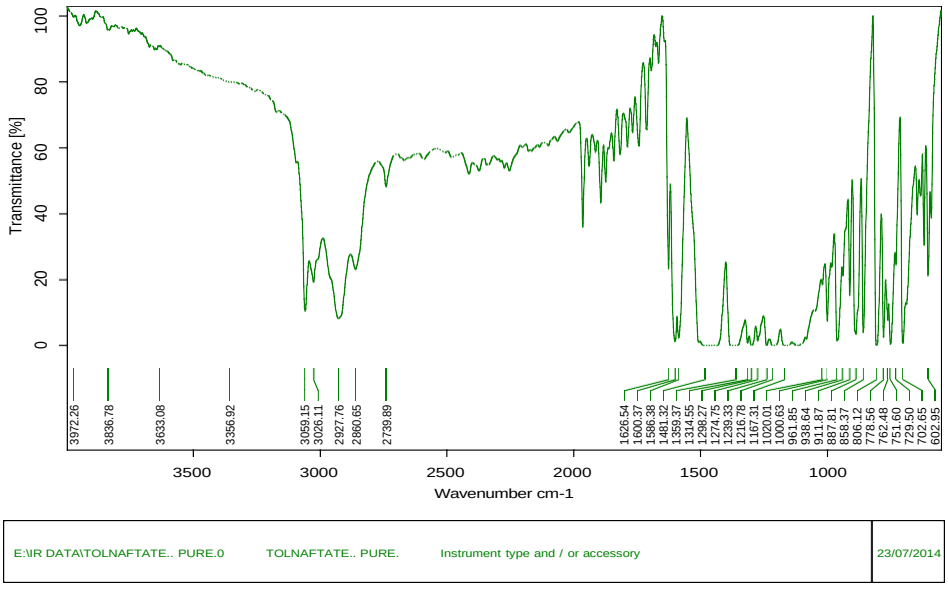

Figure 21; IR spectra of Pure Tolnaftate

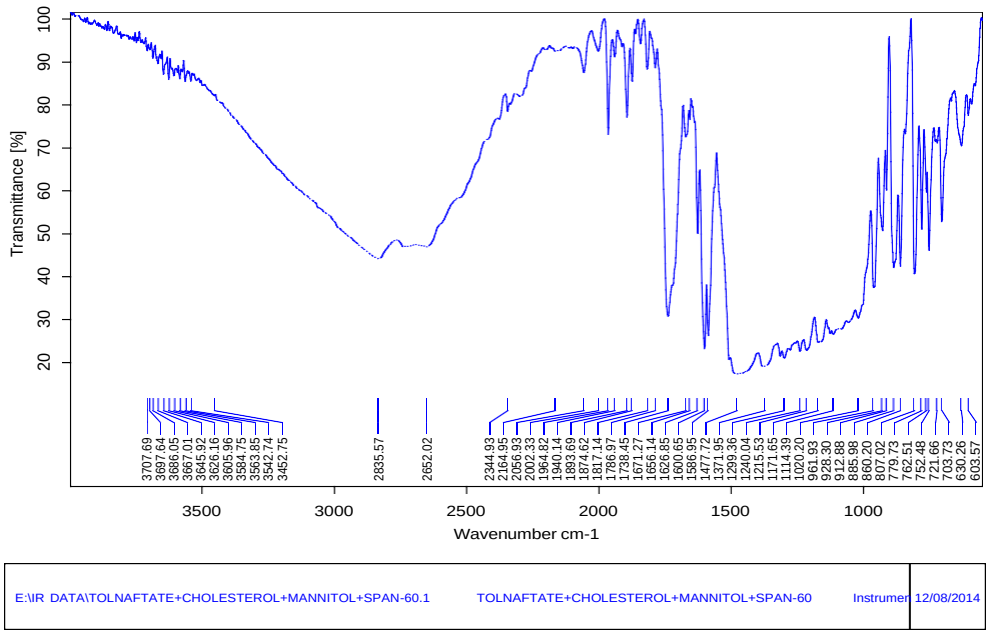

Figure 22: IR spectra of Tolnaftate + Cholesterol + Mannitol + Span-60

Drug – Polymer compatibility studies

Compatibility studies of pure drug Tolna ftate with lipids were carried out prior to the formulation of proniosomes. IR spectra of pure drug and lipids was taken, which are depicted in Figures 21-22. The characteristic peak of Tolnaftate was present in spectra at respective wavelength. Thus, indicating compatibility between drug and polymers. It shows that there was no significant change in the chemical integrity of the drug.

CONCLUSION

The current research is made to formulate proniosomes as transdermal drug delivery system bearing Tolnaftate, as an anti-fungal agent. The results obtained clearly indicate the potential of proniosomal formulation in the treating fungal infections through penetration of drug across the skin barriers. The results shows that the type of surfactant, amount of cholesterol used affect the encapsulation efficiency and rate of release from proniosomes. Of all the formulations, F4 is found to be the optimized and shows maximum drug release from the prepared proniosome. With the data obtained from current experimental work we can expect the proniosome formulations to be safe and effective for systemic and topical drug delivery.

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