CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

NIOSOMES: A PROMISING VESICULAR DRUG DELIVERY SYSTEM FOR TUBERCULOSIS

Archana S. Magdum*, Y. R. Hundekar, Dr. R. M. Chimkode
SGMCP Mahagaon, Shivaji University, Kolhapur.

Abstract:
The drug ethambutol HCl is one of the first line antitubercular agent available in tablet form used in the treatment of pulmonary tuberculosis disease, for long term therapy but according to researcher the drug shows poor absorptivity in presence of food when administered orally & required higher dose of about 25mg/kg, also has short half life i.e.2-4 hrs., so to well utilization of drug as well as to minimize the side effects, there should have to modify the formulation in other suitable dosage form, like vesicular drug delivery system, in which incorporating the drug into system in the form of niosomes, and its characteristic action gives the sustained release of dose. So the present work of this research was to prepared and evaluate the niosomal drug delivery system by reverse phase evaporation method and were evaluated their particle size analysis, surface morphology, entrapment efficiency, in-vitro release profile etc.

Key word: *Ethambutol HCl, Niosomes, Tuberculosis, Vesicular drug delivery system, in-vitro release etc.*

Corresponding author:
Archana S. Magdum,
SGMCP Mahagaon, Shivaji University, Kolhapur.
Email: archurajmane@gmail.com

QR code

Please cite this article in press as Archana S. Magdum et al, ***Niosomes: A Promising Vesicular Drug Delivery System for Tuberculosis****, Indo Am. J. P. Sci, 2017; 4(08).*

INTRODUCTION:

For proper delivering of drug to the site of action with the aim of sustained and prolonged effect of medication, there is a number of drug delivery systems are available in medical science like that vesicular delivery system is one of them. It is preferred due to the presence of lipid vesicles in its structure which support as carrier system and such vesicles have some value in membrane biology, immunology and diagnostic technique as well in genetic engineering,to incorporate both lipophilic as well as hydrophilic drug for long term activity, leads to reduction of drug intake by improving bioavailability of medication,cause least side effects.There is number of lipid based vesicular drug delivery systems like virosomes, cubosomes, liposomes, niosomes, ethosomes, transferosomes etc. are available. Such delivery systems are used to delay drug elimination, complete metabolized drug and gives sustained activity with solves the instability, insolubility, rapid degradation problems and widely used in specialized areas like gene delivery, protein delivery, tumor targeting and targeting to brain etc [1,2].

Niosomes

These are type of vesicular drug delivery system, in which the specified medication is incorporated in a vesicle. The vesicle is composed of a bilayer of non-ionic surface active agent is known as niosomes. These are very small and microscopic in size also lies in the nanometric scale, structurally similar to liposomes, niosomes are mostly formed by incorporation of cholesterol with excipients, and these are more penetrating power than any emulsions [3].

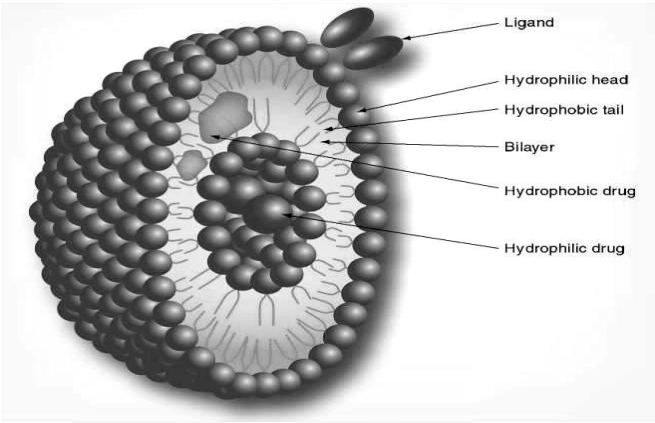


Fig 1: Structure of Niosomes

The above image of niosomes are shows lamellar structures, hydrophilic nonionic surfactant point outwards and hydrophobic ends face each other to form bilayer, constitute of stability based non-ionic surfactant polyoxyethylene ether class and cholesterol in aqueous medium. In generally the vesicular drug delivery system is mainly affected by type of surfactant used, nature of drug, temperature and use of lipids etc [4].

Advantage of Niosomes

- Due to water–based vehicle, niosomes offers high patient compliance compared to oily dosage forms.
- Due to presence of hydrophilic, amphiphilic and lipophilic moieties in its structurewhich facilitates drug incorporation as well as protectionto target the site of action in controlled as well sustained manner.
- Niosomes can modify the metabolic rate and half life of the drug, thus decreasing the side effects of the drugs by improving the bioavailability of poorly dissolved drugs [5].

Disadvantages of Niosomes

- Physically instable
- Aggregation
- Fusion
- Leakage of entrapped drug
- Due to hydrolysis of encapsulated drug limits the shelf-life of the dispersion.

Application of Niosomes

- Niosomes used as carriers for deliver drugs, hormones, vaccines at the site of action.
- As penetration enhancers, for systemic absorption of drugs through skin.
- Used to target drugs to the reticuloendothelial system.
- To treat tumors in animals, parasitic infections of the liver.
- Niosomes used to protect the peptides from gastrointestinal peptide breakdown.
- Due to their immune selectivity, low toxicity, good stability they are used to study the nature of the immune response provoked by antigens [6].

Tuberculosis

As the population increases there is number of diseases also increases in the world due to environmental pollution, improper cleanliness likewise diseases like Tuberculosis (TB) is one of them, itis an airborne infectious disease caused by organism *mycobacterium tuberculosis*,Which is generated by the coughing, sneezing, talking, or

singing of a person with pulmonary or laryngeal tuberculosis and spread by small airborne droplets [7], which affects the respiratory system as well as other organs like lymph node, pleura, bone, genitor urinary tract etc. which caused by number of death in the developing world. According to the World Health Organization one third of the world's population is suffered with *Mycobacterium tuberculosis [8,9]*.

Types of Tuberculosis:
Based on clinical manifestation after exposure and location of bacilli.

1. Primary infection: When infected droplet enters in the terminal of alveoli of lungs of the body, it shows first exposure to tubercle bacilli, and begins life cycle of bacilli in the lungs.
2. Secondary infection: It is occurs re-entry of organisms who is already hypersensitive due to earlier exposure [10].

For tuberculosis therapy there is number of drugs are available those are classified into two types-
1. First line drug: eg.- Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Streptomycin
2. Second line drug: eg. - Thiacetazone, Paraaminosalicylic acid, Ethionamide, Cycloserine, Kanamycin [11].

Currently Available treatment for tuberculosis:
Treatment of active tuberculosis with a single drug is notpossible andthis result may development of tuberculosis, as suggested by WHO treatment of TB requires multi-drug therapy and comprising of,

1) Beginning intensive phase of rifampicin (RIF), isoniazid (INH), pyrazinamide (PYZ), and ethambutol (ETB) daily for two months.
2) A continuation phase of RIF and INH for a further four months, either daily or 3 times per week, to be taken as per advise [12].

According to researcher, tuberculosis therapy is more difficult, due to the randomized structure and chemical composition of cell wall of mycobacterium organism, so the use of most antibiotics is ineffective. In actual TB requires long period treatment (around 6 to 24 months) to entirely eliminate mycobacteria from the body, almost all antitubercular drug shows poor absorption in presence of food and therapy may need long term. Sometimes poor patient compliance is the common reason for failure of TB therapy, these problems can be prevented by loading the drug by lipid coating. The lipid coating is destabilized when interaction with target cells, which results in the local release of the encapsulated drug such system is known asvesicular drug delivery system.

MATERIALS AND METHODOLOGY:

Materials:
Ethambutol Hcl, Polyoxyethylene (2) stearyl ether (Brij 72), Stearyl amine, Cholesterol, Potassium dihydrogen phosphate, Disodium hydrogen phosphate, Sodium chloride, Chloroform etc.

Preparation of Blank Niosomes [13]
To optimize the processing condition, excipients like Cholesterol and surfactant are dissolved in a mixture of ether and chloroform (1:1), thus a blank niosomes was prepared.

Preparation of Ethambutol HCl loaded Niosomes.
The comparative study formulation chart for Niosomes preparation is shown in following table. Niosomes of Ethambutol HCl prepared by Reverse phase evaporation method (REV), An aqueous phase (about 25ml) containing drug (100 mg) is added to prepared blank niosomes and the resulting two phases are sonicated at less temperature, by probe sonication by addition of a phosphate buffered saline (PBS) solution which form clear gel.Further niosomal suspension was diluted with PBS and stir for 10min to yield niosomes. The present organic phase was removed by rotary evaporator by applying suitable temperature.

Table 1: Formulation Table of Ethambutol Hydrochloride loaded Niosomes

Formulation	Drug(mg)	Cholesterol (mg)	Brij 72 (mg)	Stearyl amine (mg)
F1	100	500	400	4
F2	100	250	200	2
F3	100	250	400	2
F4	100	500	200	4
F5	100	500	400	2
F6	100	500	200	2
F7	100	250	400	4
F8	100	250	200	4

Evaluation and Characterization

Preformulation Studies:

The drug morphological, melting point, solubility studies.

Reverse Phase (RP) HPLC studies:

Analysis of drug by RP- HPLC method for standardization of maximum wavelength by obtaining standard calibration curve.

Drug Excipients Physical Compatibility Study (FTIR)

The active drug nature and drug-excipients compatibility study was done prior to the formulation of niosomes by Fourier transform infra-red (FTIR) by comparing spectral peaks in the spectra of Ethambutol drug and excipientswith standard reference spectra.

Differential Scanning Calorimetry (DSC)

DSC is one of the most used calorimetric techniques, employed to characterize the solubility and physical state of drug in the complex. Thermo grams of ethambutol HCl and one formulation of ethambutol HCl loaded niosomes was recorded using a DSC and were compared. The samples (5 mg) were hermetically sealed in flat bottomed aluminum pans and heated at a temperature of 100-300 °C using alumina as a reference standard.

Particle Size and Surface Morphology Analysis:

Particle size and surfacemorphological study wasanalyzedbyscanningelectronmicroscopy(SEM). Here, the cleaned brass specimen studs were used for sample mounting. Then wet solvent paint was applied on these studs and as the paint was wet, the pellets were placed on each stud and allowed for dry. Then the sample was observed in SEM and photographs were taken.

Determination of Percentage of Entrapment Efficiency (E.E):

Entrapment efficiency of Ethambutol HCl loaded niosoms was done by centrifugationmethod. The niosomalpreparationwere placed in centrifugation tube and applied 15000 rpm, for 30 min. The supernatant (1ml) content was taken and diluted with water. Then the unentrapped drug was determined by UV spectrophotometer at 360 nm. The free ethambutol HCl in the supernatant gives the total amount of unentrapped drug, and encapsulation efficiency is known as the percent of drug trapped and was calculated by following equation. Drug content was calculated from equation of straight line obtained for standard curve for ethambutol HCl.

$$\% \text{ E.E} = \frac{\text{Total amount of drug} - \text{Free dissolved drug}}{\text{Total amount of drug.}} \times 100$$

In vitro Drug Release Studies [14,15]

The *in vitro* drug release profile is an important tool that predicts in advance how a drug may behave *in vivo*. Release studies are required to predict the reproducibility of rate and duration of drug release.

Drug release

To determine the invitro drug release kinetics of niosomes, the dialysis method is used. Prepared niosomal content was placed in the dialysis pouch and sealed, then place the pouch in 200ml of buffer solution with constant stirring at 37 ºC. Samples were withdrawn at regular interval and drug content analysis is carried out by UV visible spectroscopical method.

Release kinetics

The data of In-vitrorelease study was fitted in to three different kinetics models namely zero order, first order, and higuchi's classical model. The drug release mechanism is defined statics in terms of co-relation co-efficient, the highest values of co-relation co-efficient shows the appropriate release mechanism.

RESULTS AND DISCUSSION:

Preformulation Studies:

The sample of Ethambutol HCl was found to bewhite to off white, odourless powder. And based on literature, the melting point of Ethambutol HClis200-202ºC, and by estimation it was found to be 196- 203ºC that indication isdrug purity.And was soluble in water and slightly soluble in methanol.

HPLC analysis for Determination of λ_{max}:

The λ_{max} of Ethambutol HCl was determined in water by RP-HPLC, It was found to be maximum wavelength 415nm. And the same shown in figure no. 2.

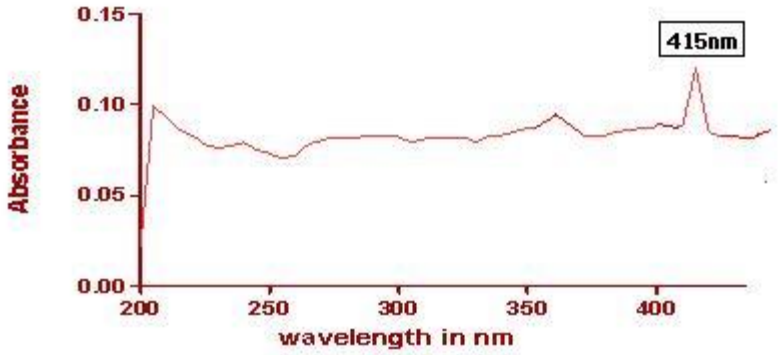


Fig 2: λ max of ethambutol HCl

Standard calibration curve for Ethambutol HCl in water.

Calibration curve for Ethambutol HCl was constructed using water as solvent at 415nm.The concentration selected was 10-50µ/ml**.** and data of calibration observed in table no. 2, with graphical representation in figure no. 3

Table 2: Calibration data for Ethambutol HCl

Concentration µg/ml	Absorbance*
10	0.093
20	0.172
30	0.280
40	0.365
50	0.430

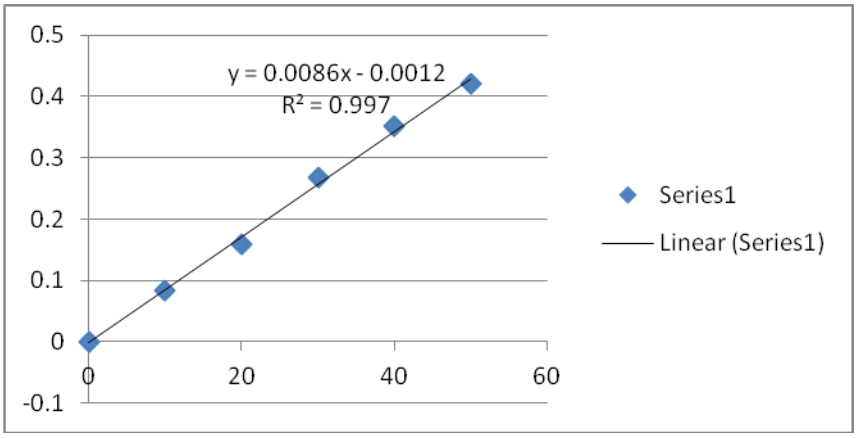


Fig 3: Standard calibration Curve of Ethambutol HCl

A straight line was obtained at R^2=0.997. Equation of straight was found to be y= 0.008 x -0.001

FTIR study

By FTIR study of ethambutol HCl, it was found to be the obtained spectral peaksof functional group present in drug were compared with standard reference peaks and found that drug is pure one. The obtained FTIR spectra of drug are shown in fig.no.4 and respective functional group shown in table no.3.

As well asthe obtained spectral peaks of functional group present in mixture of drug with brij 72 and cholesterol were compared with standard reference peaks and found that drug was miscible throughout the mixture. Obtained FTIR spectra of mixture of drug with excipients are shown in figure no. 5 and respective spectral functional group shown in table no.4

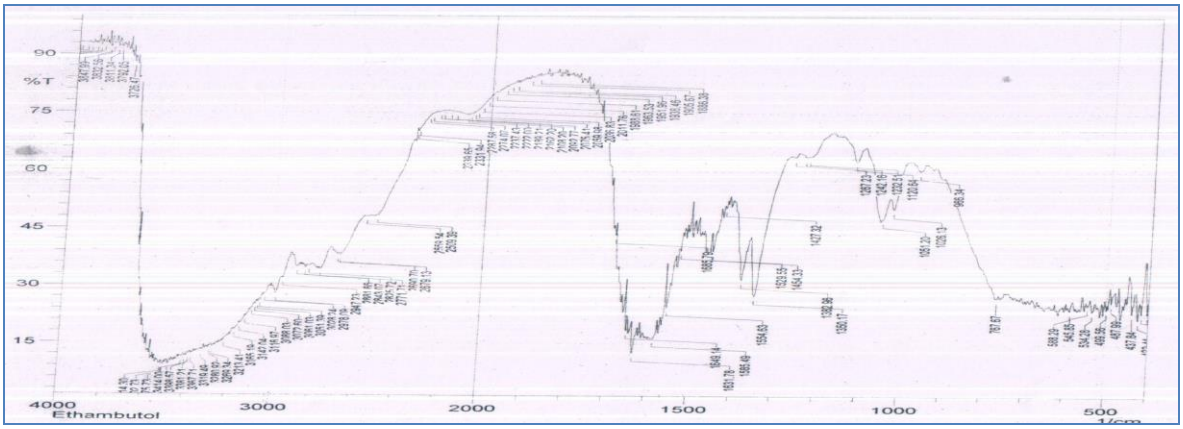


Fig.4: IR Spectra of Pure Ethambutol HCl

Table 3: Peaks (Cm^{-1}) and Functional Groups Present Ethambutol HCl.

Sr. No.	Peaks cm^{-1}	Functional group
1	2881.65	C-H ($CH_{3)}$
2	1350.17	O-H (Stre)
3	3280.92	N-H (Sed)
4	1529.55	C-H (def)

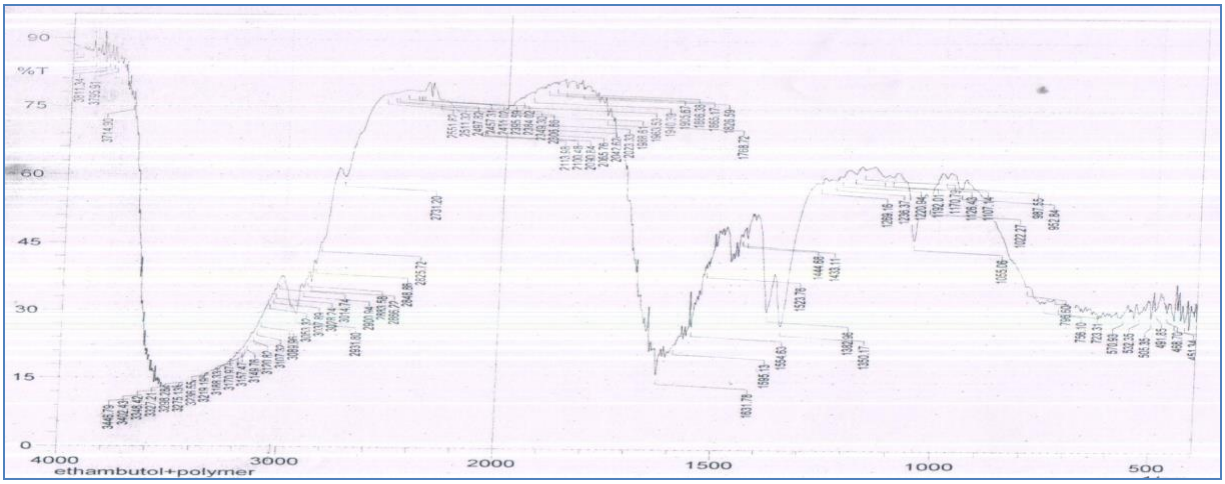


Fig 5: IR of mixture of Ethambutol HCl + Brij 72+Cholesterol.

Table 4: Peaks (Cm^{-1}) and Functional Groups Present in mixture of Ethambutol HCl + Brij72 + Cholesterol

Sr. No.	Peaks cm^{-1}	Functional group
1	2883.58	C-H
2	1350.17	O-H (Str)
3	3275.13	N-H (Sed)
4	1523.76	C-H (Def)

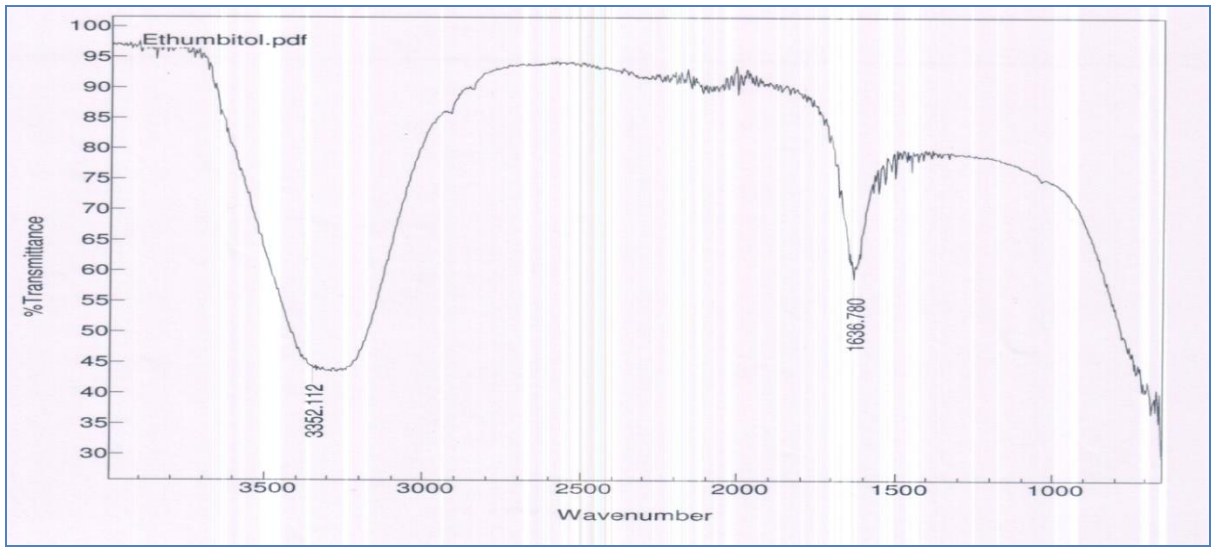


Figure no. 6: IR Spectra of Ethambutol HCl loaded Niosomes Formulation

Table no.5: Peaks (Cm^{-1}) and Functional Groups Present Niosomes formulation

Sr. No.	Peaks cm^{-1}	Functional group
1	3352.11	C-H(CH_3)
2	1636.78	C-H (Str)

FTIR gives thespectral peaks of ethambutol loaded niosomal formulation were compared with standard reference spectral peaks of functional group and found that the drug pure and is compatible with excipients which are used in formulation. Obtained FTIR spectra of drug loaded niosomes are shown in figure no.6 with respective functional group shown in table no.5.

Differential Scanning Calorimetry (DSC)

Using DSC analysis of drug, polymer and excipients the nature of the drug inside the polymer matrix can be assessed. The obtained DSC graph of formulation is shown in figure no. 7

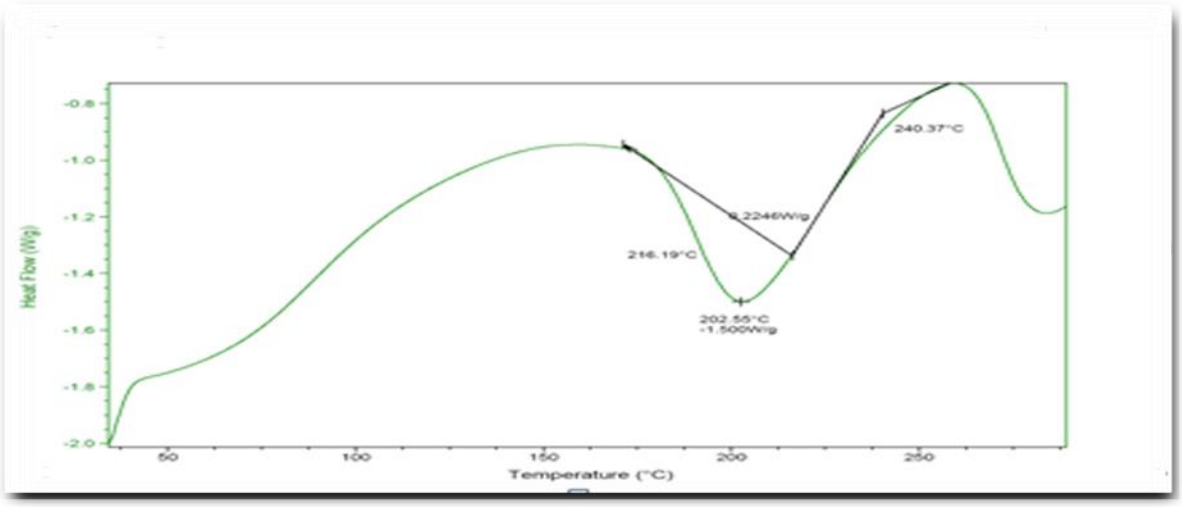


Fig 7 : DSC Thermogram Of Ethambutol Hcl Pure Drug

The DSC patterns of pure ethambutol shown a sharp endotherm at 202.55 °C with corresponding to its melting point. So there was a negligible change in the melting endotherms ofthe formulation compared to pure drug. This observation further supports the IR spectroscopy results, which shows the absence of interactions within the drug and the polymer complex.

Percentage of Drug Entrapment Efficiency

After niosomal preparation the percentage of entrapment efficiency of ethambutol HCl was found to be range from 72.26 to 86.73 %. It was observed thatwhen increased the lipid concentration caused by higher entrapment efficiency.Moreover, higher drug loading lowered the percentage of entrapment and encapsulation, which shown the wastage of drug during the micro encapsulation process.The % drug entrapment efficiency of the prepared Niosomes formulations are shown in table no.6 and displayed in figure no.8

Particle size Analysis:

Prepared niosomal mean particle sizefound that 200nm to 300nm. Actually the mean size was influenced by the concentration of lipid used in the formulation. As the volume of water varies, niosomes deformed to nonspheral shape and even broken and the effect of stirring speed was also observed for all formulations,as the stirring speed was increased there is decrease in average particle sizedue to high stress developed at the interface caused by creation of new surfaces which were stabilized by amphiphiles resulting in smaller particle size distribution. Mean particle size of all formulations are given in the table no. 6 and its graphical representation shown in the figure no. 9.

Table 6: Percentage of Drug entrapment efficiency, Particle size of niosomal preparation of ethambutol HCl.

Formulation code	%Drug entrapment efficiency*	Particle size* (nm)
F1	86.73	227.9
F2	74.58	227.3
F3	77.27	407.0
F4	81.92	202.4
F5	85.43	214.3
F6	79.53	212.5
F7	76.51	280.6
F8	72.26	201.3

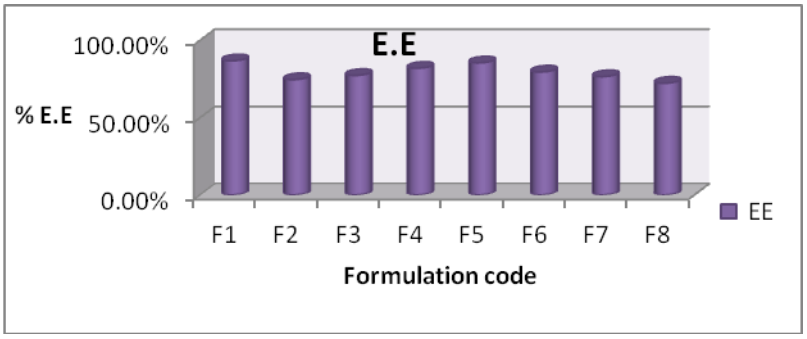


Fig 8: % of Entrapment efficiency (E.E) of different Formulations

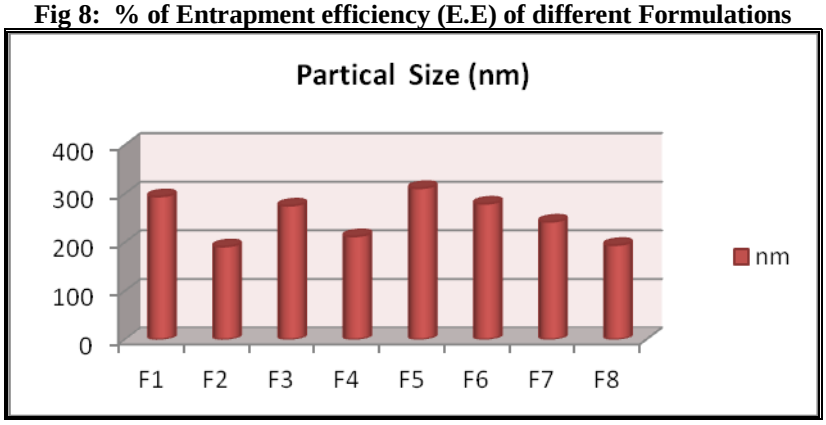


Fig 9: Average particle size of Formulations

Shape and Surface Morphology:
Morphology of the niosomal preparation was investigated by scanning electron microscopy and were spherical & irregular and their surface was smooth and devoid of cracks giving them good in appearance. In general, the Niosomes were well formed and in shape. The obtained SEM data are shown in figure no.10.

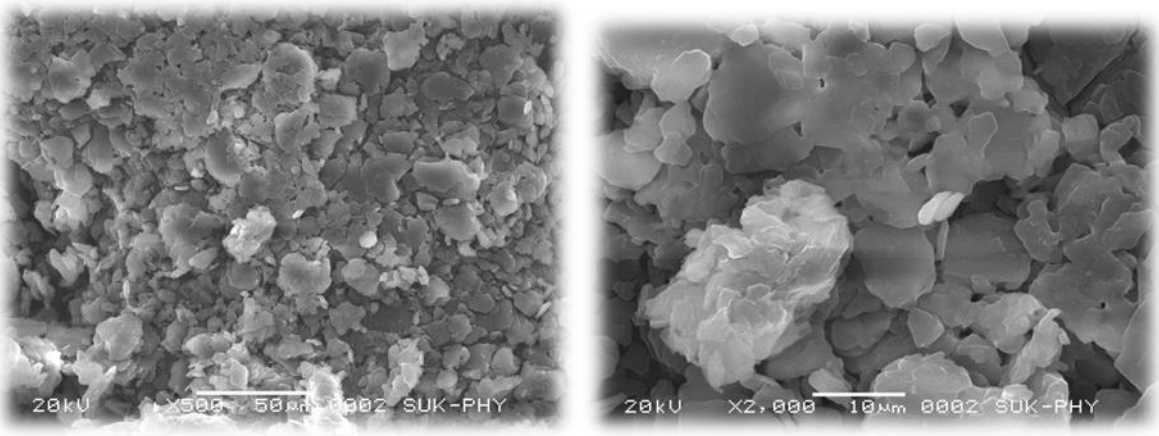


Fig10: SEM images of Ethambutol HCl loaded Niosomes

In Vitro Drug release of niosome of Ethambutol HCl using Dialysis bag method:

In vitro drug release studies of all the niosomal formulations were carried out in a phosphate buffer pH 7.4 using dialysis membrane. The study was performed for 12 hrs, and cumulative drug release (CDR) was calculated for different time intervals. The formulations F1, F2, F3, F4, F5, F6, F7, and F8 have shown the drug release of 85.50%, 91%, 88.80%, 87.70%, 84.41%, 86.61%, 88.80% and 92.09% respectively after 12 hrs. The drug release profile formulation F1 table no. 7 shown drug release kinetic data and cumulative drug release profile of all prepared formulations are shown in table no. 8

It was observed from the formulations that, *"the drug release profile slightly increases as the concentration of lipid of formulation increases. The data of dissolution study indicates that the drug release from niosome was slow and sustained up to 12hrs".*

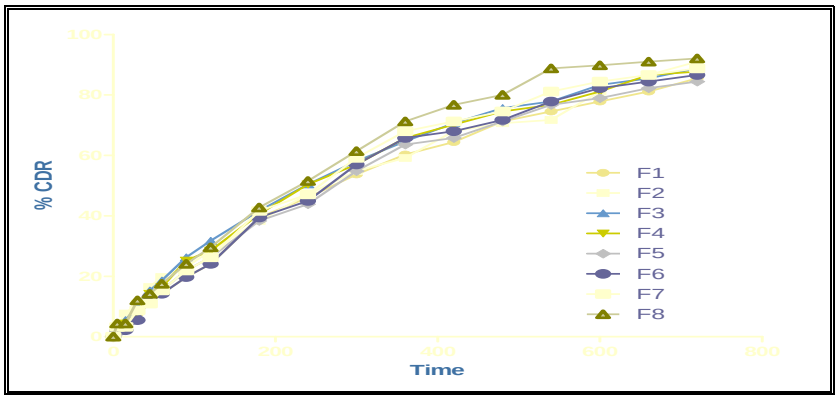
Table 7: In vitro Drug release profile of F1 formulation

Time(min)	Sq. root Time	Log time	Abs	CDR	% C D R*	Log % CDR	% Drug retained	Log % drug retained
0	0	0	0	0	0	0	100	2
5	2.236	0.698	0.002	2.18	2.18	0.33	97.82	1.99
15	3.872	1.176	0.004	4.37	4.37	0.64	95.63	1.98
30	5.477	1.477	0.007	7.67	7.67	0.88	92.33	1.96
45	6.708	1.653	0.010	10.96	10.96	1.03	89.04	1.93
60	7.745	1.778	0.013	14.24	14.24	1.15	85.76	1.93
90	9.486	1.954	0.018	19.72	19.72	1.29	80.28	1.90
120	10.954	2.079	0.022	24.11	24.11	1.38	75.89	1.88
180	13.416	2.255	0.036	39.46	39.46	1.59	60.54	1.78
240	15.491	2.380	0.042	46.04	46.04	1.66	53.96	1.73
300	17.320	2.477	0.049	53.72	53.72	1.73	46.28	1.66
360	18.973	2.556	0.055	60.29	60.29	1.78	39.71	1.59
420	20.493	2.623	0.061	64.41	64.41	1.80	35.59	1.55
480	21.908	2.681	0.065	71.26	71.26	1.85	28.74	1.45
540	23.237	2.732	0.068	74.54	74.54	1.87	25.46	1.40
600	24.494	2.778	0.071	77.83	77.83	1.89	22.17	1.34
660	25.690	2.819	0.074	81.13	81.13	1.90	18.87	1.27
720	26.832	2.857	0.078	85.50	85.50	1.93	14.50	1.16

Table 8: In vitro Drug release profile of F1 to F8 formulation

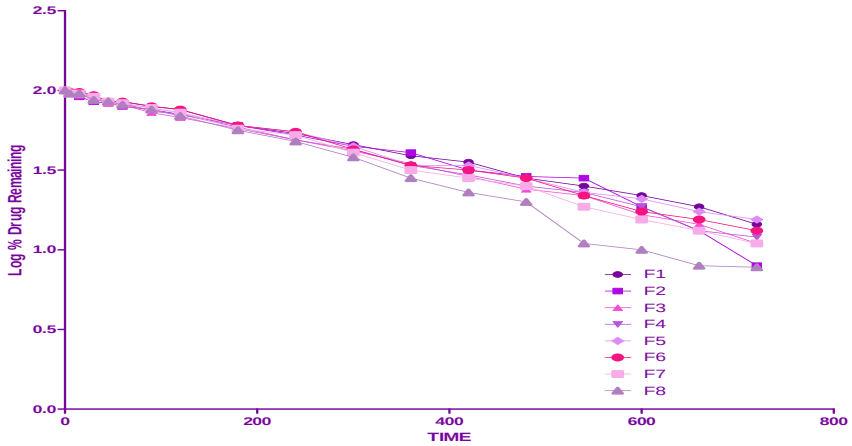
Time (min)	Sq. root Time	Log time	F1		F2		F3		F4		F5		F6		F7		F8	
			Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)	Abs	CDR* (% CDR)
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	2.236	0.698	0.002	2.18	0.003	3.28	0.002	2.18	0.002	2.18	0.001	1.09	0.002	2.18	0.003	3.28	0.004	4.37
15	3.872	1.176	0.004	4.37	0.007	7.67	0.005	5.48	0.004	4.37	0.002	2.18	0.002	2.18	0.003	3.28	0.004	4.37
30	5.477	1.477	0.007	7.67	0.010	10.96	0.009	9.85	0.007	7.67	0.005	5.48	0.005	5.48	0.008	8.76	0.011	12.05
45	6.708	1.653	0.010	10.96	0.015	16.44	0.014	15.34	0.013	14.24	0.012	13.23	0.012	13.15	0.010	10.96	0.013	14.24
60	7.745	1.778	0.013	14.24	0.018	19.72	0.017	18.63	0.015	16.44	0.014	15.34	0.013	14.24	0.014	15.34	0.016	17.53
90	9.486	1.954	0.018	19.72	0.021	23.02	0.024	26.30	0.023	25.20	0.020	21.92	0.018	19.72	0.020	21.92	0.022	24.11
120	10.954	2.079	0.022	24.11	0.026	28.50	0.029	31.78	0.026	28.50	0.024	26.30	0.022	24.11	0.024	26.30	0.027	29.59
180	13.416	2.255	0.036	39.46	0.035	38.37	0.038	41.65	0.037	40.56	0.035	38.37	0.036	39.46	0.038	41.65	0.039	42.74
240	15.491	2.380	0.042	46.04	0.043	47.13	0.046	50.42	0.046	50.42	0.040	43.85	0.041	44.94	0.043	47.13	0.047	51.52
300	17.320	2.477	0.049	53.72	0.050	54.81	0.053	58.09	0.052	57.00	0.050	54.81	0.052	57.00	0.054	59.20	0.056	61.39
360	18.973	2.556	0.055	60.29	0.054	59.20	0.059	64.68	0.060	65.78	0.058	63.58	0.060	65.78	0.062	68.00	0.065	71.26
420	20.493	2.623	0.061	64.41	0.062	68.00	0.064	70.66	0.054	70.16	0.060	65.78	0.062	68.00	0.065	71.26	0.070	76.74
480	21.908	2.681	0.065	71.26	0.064	70.66	0.069	75.64	0.068	74.54	0.065	71.26	0.066	71.72	0.068	74.54	0.073	80.02
540	23.237	2.732	0.068	74.54	0.066	71.72	0.071	77.83	0.070	76.74	0.070	76.74	0.071	77.83	0.074	81.13	0.081	88.80
600	24.494	2.778	0.071	77.83	0.074	81.13	0.076	83.31	0.074	81.13	0.072	78.93	0.075	82.25	0.077	84.41	0.082	89.89
660	25.690	2.819	0.074	81.13	0.079	86.61	0.078	85.50	0.079	86.61	0.075	82.22	0.077	84.41	0.079	86.61	0.083	91.00
720	26.832	2.857	0.078	85.50	0.083	91.00	0.081	88.80	0.080	87.70	0.077	84.41	0.079	86.61	0.081	88.80	0.084	92.09

***** Cumulative Drug Release



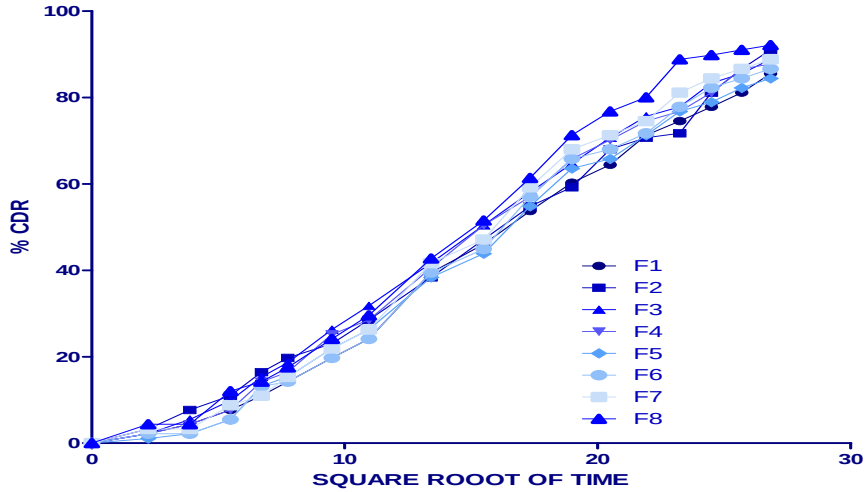
Zero order kinetic Model

Fig 11: % Cumulative Drug Release v/S. Time.



First order kinetic model

Fig 12: Log % Cumulative Drug Remaining v/s. Time.



Higuchi's classical diffusion model

Fig 13: % Cumulative Drug Released v/s. Square Root of Time.

Drug release kinetic data for niosome formulations:

To find out exact mechanism of drug elease from niosomes, data was fitted in three different kinetic models and various equations were used, such as zero-order rate equation, first-order and Higuchi's Classical Diffusion model.

Zero-order rate equation describes the release from system is independent of the concentration of the dissolved content. The first-order equation describes the release rate from the systems is dependent on the concentration of the dissolving species. Higuchi's Classical Diffusion model describes the release from system where drug solution is dispersed in insoluble matrix, and the rate of drug release is related to the rate of diffusion. Thus found that, the data obtained from *in vitro* drug release studies were fitted to zero-order, first-order and Higuchi's equations and is represented in figure no.11, 12 and 13. After performing statistical analysis for release study data the coefficient of correlation was found to favor zero order kinetics.

For studying the release kinetics, all formulations are fitted in the mathematical models. In order to describe the kinetics of the release process of drug in all formulations,

The drug release data obtained of niosome formulations were plotted in the following modes of data treatment. And kinetic modeling of drug release data shown in table no. 9

Zero Order Kinetics: - Time v/S. % Cumulative Drug Release.

First Order Kinetics: - Time v/S. Log % Cumulative Drug Remaining.

Higuchi Plot: - Square Root of Time v/S. % Cumulative Drug Released

Table 9: Kinetic modeling of drug release from Niosomes

Formulation code	Zero order		First order		Higuchi's equation	
	R^2	Slope	R^2	Slope	R^2	Slope
F1	0.9563	0.1219	0.9978	-0.0011	0.9873	3.536
F2	0.9663	0.1217	0.9596	-0.0012	0.9922	3.520
F3	O.9439	0.1246	0.9979	-0.0012	0.9936	3.651
F4	0.9448	0.1256	0.9966	-0.0012	0.9900	3.671
F5	0.9496	0.1233	0.9964	-0.0011	0.9874	3.590
F6	0.9513	0.1276	0.9967	-0.0012	0.9831	3.705
F7	0.9480	0.1302	0.9975	-0.0013	0.9842	3.789
F8	0.9455	0.1357	0.9894	-0.0016	0.9852	3.956

Values for regressions coefficient shown in table no.9 for different kinetic models. From the results it is cleared that the drug release mechanism from the formulations was found to follow First order kinetics. The dissolution process is purely defined by the total concentration of the drug present in the developed formulation, indicating that the total drug payloads play an important role in the release profile.

CONCLUSION:

In this work an attempt was made to prepared a vesicular drug delivery system in the form of niosomes for an antitubercular drug ethambutol HCl, for deliver at proper site to achieve and maintain the desired drug concentration for sustained activity and thus prevent repeated dose of drug which was proved by *in vitro* release study data, that all the formulations followed first order kinetic model. This implies that developed formulations have a potential to deliver the drug in controlled release manner.

However, TB is difficult to treat, due to the unusual structure and chemical composition of the mycobacterium cell wall, which makes many antibiotics ineffective, TB requires much longer periods of treatment (around 6 to 24 months) to entirely eliminate mycobacteria from the body. According to research found that almost all antitubercular drugs shows poor absorption in presence of food, need of multidrug regimens, poor patient compliance. These problems could possibly be prevented by shielding the drug from the extracellular environment by means of a lipid coating i.e. niosomes. The lipid coating is destabilized upon interaction with cells of the target site resulting in the local release of the encapsulated drug.

ACKNOWLEDGEMENTS

Regarding thankful to Dr. R. M. Chimkode, Principal and HOD of Pharmacognosy, as well as my colleague Mr. Y. R. Hundekar, Assist. Professor, Pharmaceutics department, SGMCP Mahagaon, for their constant support for making this research work and thankful to my other colleagues for their encouraging support. And finally I thankful to Lupin pharmaceuticals, Gujarat. for providing gift sample of Ethambutol Hcl, for my research work.

REFERENCES:

1.Ravi Kumar, Shivjee Kumar, Shyam Shankar Jha and Amit Kumar Jha. Vesicular System-Carrier for Drug Delivery. Pelagia Research Library. 2011; 2 (4):192-202

2.http://scialert.net/abstract/?doi=ajsr.2011.1.15

3.Kumar A., Pal J., JaiswalA., Singh V. Review on niosomes as novel drug delivery system. International Research Journal of Pharmacy. 2011; 2(5): 61-65.

4.Krishna Gopal Das, Alpana Ram. Niosome as a novel drug delivery system a review. International Journal of Applies Pharmaceutics 2014 ;6(1): 1-7.

5.Alok Pal Jain, Prabhakar Sharma, Prakash Pandey1, Ramchandra Gupta, Sunil Roshan, Ashish Garg, Apoorva Sahu, Alisha Jain. Niosome a novel approach for drug delivery system: an overview. Asian Journal of Pharmaceutical Sciences And Research. 2013; 3(5):18-30.

6.http://www,intechopen,com/books/recent-advances-in-novel-drug-carrier-system/the-role-of-carrier-in-drug-powder-inhaler

7.http://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf

8.Nusarat shafiq, Ritika Kondel, Samir Malhotra, Tuberculosis & nanotechnology, 10.5005/jp-Journals-10028-1084.

9.Tariq K. Almog, Arwa M. Elhagi, Nour Alhuda R. Ben Naji, Salah M. Bensaber, Microwaves assistant technique in spectrophotometric assay of isoniazid using it's schiff's base derivatives. International Journal of Pharmaceutical Science and Research. 2013; 4(2):644-649.

10.Harsh Mohan. Pathophisiology. 2015; (5): 205-206.

11.Christian Lienhardt. New Drugs for the Treatment of Tuberculosis. Journal of Infectious Diseases Advance. March 23, 2012

12.Viness Pillay, Lisa Claire du Toit and Michael Paul Danckwerts. Tuberculosis chemotherapy: current drug delivery approaches, BioMed Central. 2006

13.H H Willard; L LMerrit (Jr.); J A Dean. Instrumental Methods of Analysis, 7th Edition, CBS Publishers and Distributors, 1986, 287-320.

14.E F Fiese; T A Hagen. The Theory and Practice of Industrial Pharmacy, (L Lachman; H A Liebermann; J LKanig. Eds), 3rdEdition, 1987, 180.

15.Harinichowdaryvadlamudi, 1 m. sevukarajan. niosomal drug delivery system-a review. indoamerican journal of pharmaceutical research. 2012:2(9).