CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.21264841

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

DESIGN, PREPARE AND CHARACTERIZATION OF DONEPEZIL LIPOSOMAL DRUG DELIVERY SYSTEM

A. Gopireddy*[1], Peechara Srividya[2], Rouhtu Divya[3]

[1]Professor, Department of Pharmaceutical Chemistry, Sana College of Pharmacy, Kodad, Telangana 508206.

[2]Assistant Professor, Department of Pharmaceutical Analysis, Sana College of Pharmacy, Kodad, Telangana 508206

[3]Assistant Professor, Department of Pharmaceutics, Sana College of Pharmacy, Kodad, Telangana 508206

Abstract:

The drug release from Liposomes depends on many factors including the composition of Liposomes, the type of drug encapsulated and nature of the cell. Once it is released a drug that normally crosses the membrane of a cell will enter the cell, other drugs will not enter. Donepezil is a drug with narrow therapeutic index and short biological half-life. This study aimed at developing and optimizing liposomal formulation of Donepezil in order to improve its bioavailability. In evaluation study the effect of the varying composition of lipids on the properties such as encapsulation efficiency, particle size and drug release were studied. Phase transition study was carried out to confirm the complete interaction of Donepezil with bilayer structure of liposome. Moreover, the release of the drug was also modified and extended over a period of 8 hr in all formulations. F2 emerged as the most satisfactory formulation in so far as its properties were concerned. Further, release of the drug from the most satisfactory formulation (F2) was evaluated through dialysis membrane to get the idea of drug release.

Keywords: *Liposomes, Donepezil , bioavailability, thin film hydration technique, in vitro drug release studies.*

Corresponding author:

A.Gopireddy,

Professor, Department of Pharmaceutical Chemistry,
Sana College of Pharmacy,
Kodad, Telangana 508206.

QR CODE

Please cite this article in press ***A.Gopireddy*** *et al.,* **Design, Prepare And Characterization Of Donepezil Liposomal Drug Delivery System**, *Indo Am. J. P. Sci, 2026; 13(07).*

1.INTRODUCTION:

Liposomes are biocompatible as well as biodegradable bilayer vesicles comprising of a hydrophilic aqueous core and are made of phospholipids. From the last several years the liposomal vesicles have been extensively considered as carrier of preference for the delivery of various potential drug candidates that are lipophilic as well as hydrophilic.[1] Generally, the the liposomes used in clinical practice have the size with diameter in the range of 50 to 300 nm.[2] The membranes of liposomal vesicle are linked with the plasma memebrane, and are consisting of bilayers made up of phospholipids. Instinctively, vesicles formation occurs upon hydration by means of aqueous media from phospholipids as a consequence of tails of hydrophobic fatty acid, and a head group of hydrophilic phosphatidyl that exist in the typical amphiphilic molecular structure.[3] In the liposomal membrane cholesterol (CH) can be simply incorporated just as plasma membrane in the matching style which stabilizes the membrane and adjust the release of the drug.[4]The drugs hydrophilic in nature are enclosed inside internal aqueous phase, whereas, in the bilayer area of the lipid tail the hydrophobic drugs are located. Liposomal membranes are fluidic in nature like the bio membranes and therefore, the enclosed drugs may be leaked out or released by the liposomes. The release rate is reliant on the components present in the membrane of liposome, like types of phospholipid's fatty acid acyl chain, degree of unsaturation, charge on lipid and inclusion of CH.[5] These nanocarriers can offer significant advantages as drug delivery systems which are as fallows. Entirely biodegradable, biocompatible, flexible, nonimmunogenic, non-toxic, drug delivery system for non-systemic and systemic administrations. Donepezil is used to treat dementia (a brain disorder that affects the ability to remember, think clearly, communicate, and perform daily activities) in people who have Alzheimer's disease. The present study involves preparation and evaluation of liposome containing Donepezil by using thin film hydration technique.

2.1 MATERIALS

Donepezil was collected as a gift sample from Aurobindo Laboratories Ltd Hyderabad, polymers,excipients were purchased from Vijaya Chemicals, HYD, Hyd.

2.2 METHODODOLOGY:

Formulation development

Table-1: Formulation table

Ingredients	F1	F2	F3	F4
Phosphatidylcholine	300	400	500	600
Cholesterol	10	20	30	40
Solvent (Methanol)	50	50	50	50
Donepezil	10	10	10	10
Phosphate buffer pH 7.4	100	100	100	100

Preparation of liposomes

Method

Liposomes were prepared by physical dispersion method using different ratio of lipids.

In this method the lipids were dissolved in chloroform. This solution of lipids in chloroform was spread over flat bottom conical flask. The solution was then evaporated at room temperature without disturbing the solution. The hydration of lipid film form was carried out with aqueous medium phosphate buffer (pH 7.4). For this the flask was inclined to one side and aqueous medium containing drug to be entrapped was introduced down the side of flask and flask was slowly returned to upright orientation. The fluid was allowed to run gently over lipid layer and flask was allowed to stand for 2 h at 37^0C for complete swelling. After swelling, vesicles are harvested by swirling the contents of flask to yield milky white suspension. Then formulations were subjected to centrifugation. Different batches of liposomes were prepared in order to select an optimum formula. All batches of liposomes were prepared as per the general method described.

Drug excipient compatibility studies[9]

Drug excipients compatibility studies were performed to know the compatibility of excipient with drug at accelerated conditions. The study was conducted by preparing homogenous mixture of excipients with drug and filled in HDPE bags and LDPE bags. Glass vials were exposed to 600 C and 400C/75 %RH for 4 weeks and LDPE bags were exposed to 400C±75 %RH for 4 weeks. Samples were observed periodically for any physical change.

Evaluations of liposomes[10,11,12]

Particle size analysis

All the prepared batches of liposomes were viewed under microscope to study their size. Size of liposomal vesicles from each batch was measured at different location on slide by taking a small drop of liposomal dispersion on it and average size of liposomal vesicles were determined.

SEM analysis

The morphology of liposomes was studied by a scanning electron microscope. For this purpose, the sample was lyophilized and placed on aluminum stubs and the surface was coated with a layer of gold particles using a sputter coater. The shape of the liposomes was determined by scanning electron microscopy (SEM) (XL30, Philips, the Netherlands) at 15 kV and 750 mA.

Drug entrapment efficiency of liposomes

Entrapment efficiency of liposomes were determined by centrifugation method. Aliquots (1 ml) of liposomal dispersion were subjected to centrifugation on a laboratory centrifuge (Remi R4C) at 3500 rpm for a period of 90 min. The clear supernatants were removed carefully to separate non

entrapped Donepezil and absorbance recorded at 238 nm. The sediment in the centrifugation tube was diluted to 100 ml with phosphate buffer pH 7.4 and the absorbance of this solution was recorded at 238 nm.

Amount of Donepezil in supernatant and sediment gave a total amount of Donepezil in 1 ml dispersion. % Entrapment of drug was calculated by the following formula

% Drug Entrapped (PDE) = Amount of drug in sediment/ Total amount of drug X 100

***In Vitro* Drug release study**

The release studies were carried out in 10 ml Franz diffusion cell containing 10 ml Phosphate buffer. Phosphate buffer pH 7.4 (10ml) was placed in a 10 ml beaker. The beaker was assembled on a magnetic stirrer and the medium was equilibrated at 37±5^{0}C. Dialysis membrane was taken and one end of the membrane was sealed. After separation of non-entrapped Donepezil liposomal dispersion was filled in the dialysis membrane and other end was closed. The dialysis membrane containing the sample was suspended in the medium. 1ml of aliquots were withdrawn at specific intervals, filtered after withdrawal and the apparatus was immediately replenished with same quantity of fresh buffer medium.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile.

The prepared Donepezil liposomes were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2^{o}c and refrigerator 2-8^{o}c for a period of 90 days.

3.RESULTS AND DISCUSSION:

Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and the selected lipid and other excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-lipid mixture, which confirmed the absence of any chemical interaction between the drug, lipid and other chemicals.

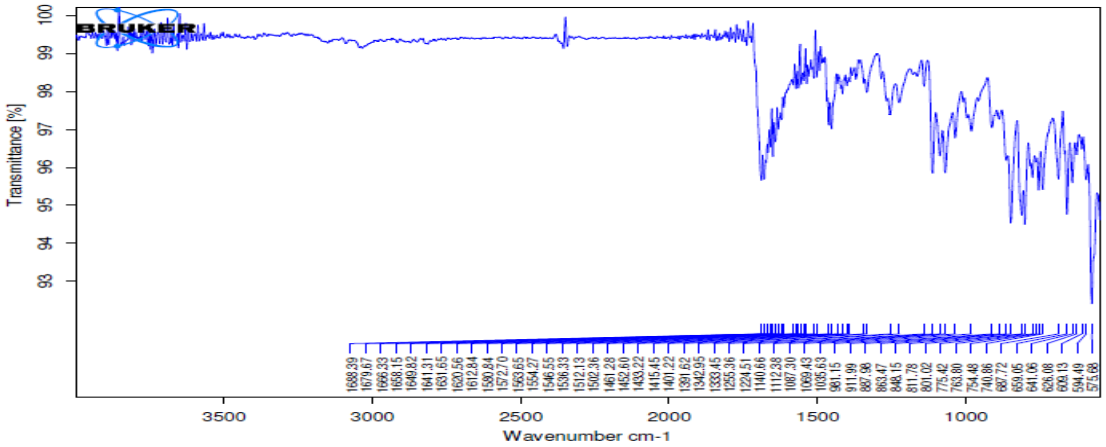

Fig-1: FTIR Studies of Pure Drug (Donepezil)

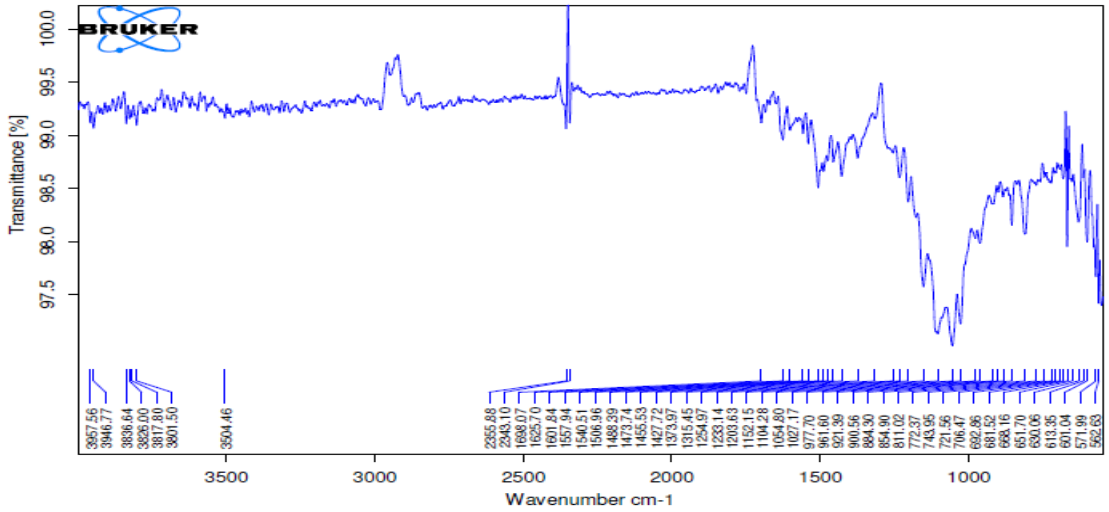

Fig -2: FTIR Studies of Donepezil and phosphotidylcholine

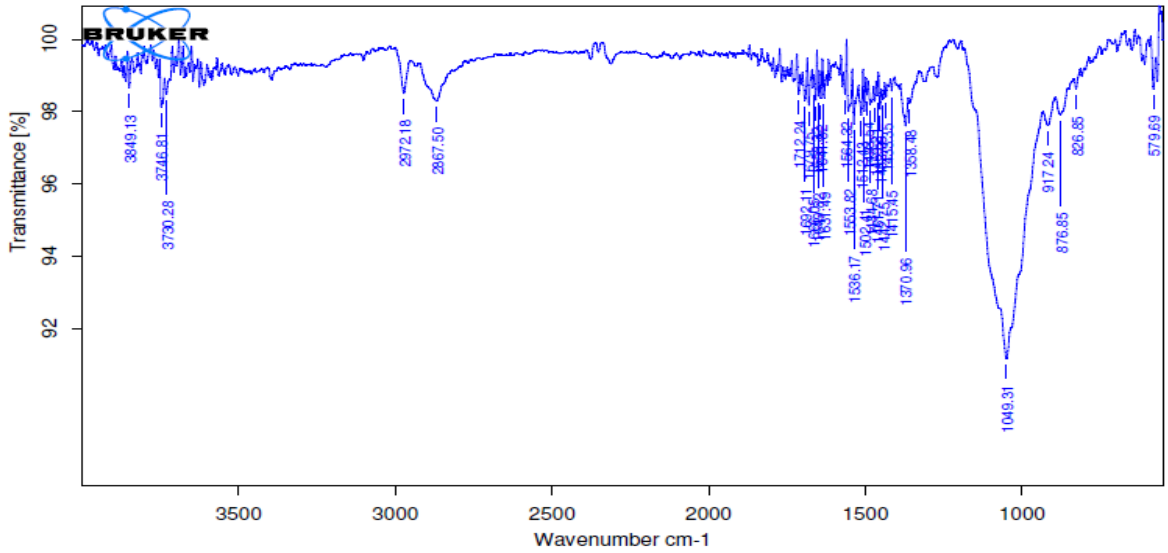

Fig-3:FTIR Studies of Donepezil and cholesterol

Particle size

Vesicle shape: Vesicle shape of the prepared formulation was found to be spherical from the SEM(scanning electron microscope) analysis at 15.00kV

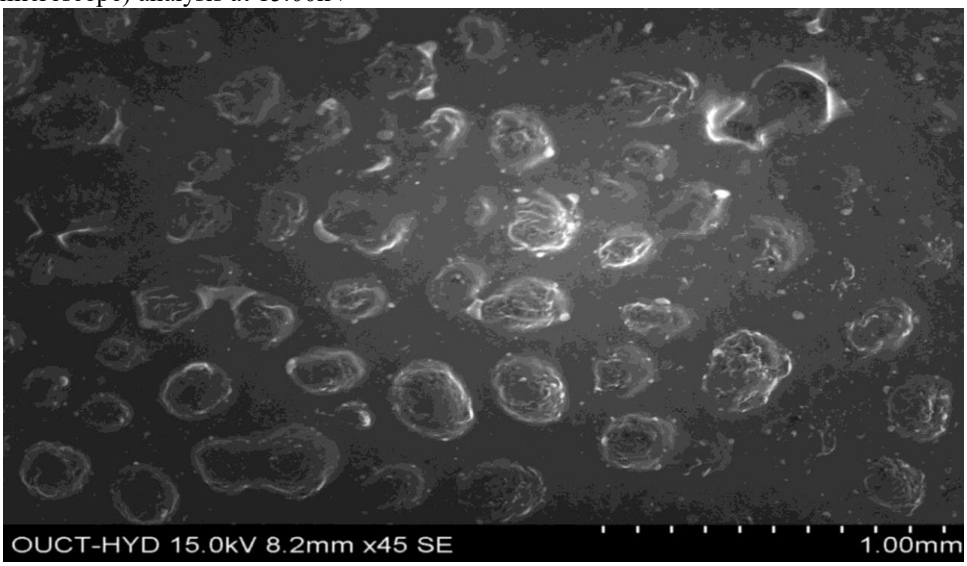

Fig-4: particle size of Donepezil liposomes

Table-2: Mean particle size (mps) of different formulation of liposomes

Sr. No	Formulation No.	Particle size
1	F1	10.11
2	F2	11.10
3	F3	11.25
4	F4	12.21

Drug entrapment efficiency

Table- 3: Different batches of liposome made by using different ratio of lipids

Sr. No	Formulation no.	DEE
1	F1	92.22
2	F2	98.25
3	F3	96.32
4	F4	92.51

Drug release studies

Table-4: Cumulative percentage drug release from various formulation of liposomes

Time	F1	F2	F3	F4
0	0	0	0	0
1	23.96	24.88	23.59	22.21
2	35.49	36.95	35.25	34.18
3	45.57	44.28	42.81	41.19
4	58.18	56.93	50.27	52.24
5	60.24	62.38	63.34	62.15
6	71.52	76.19	72.59	70.18
7	81.38	87.59	85.15	82.24
8	94.52	97.65	95.85	94.12

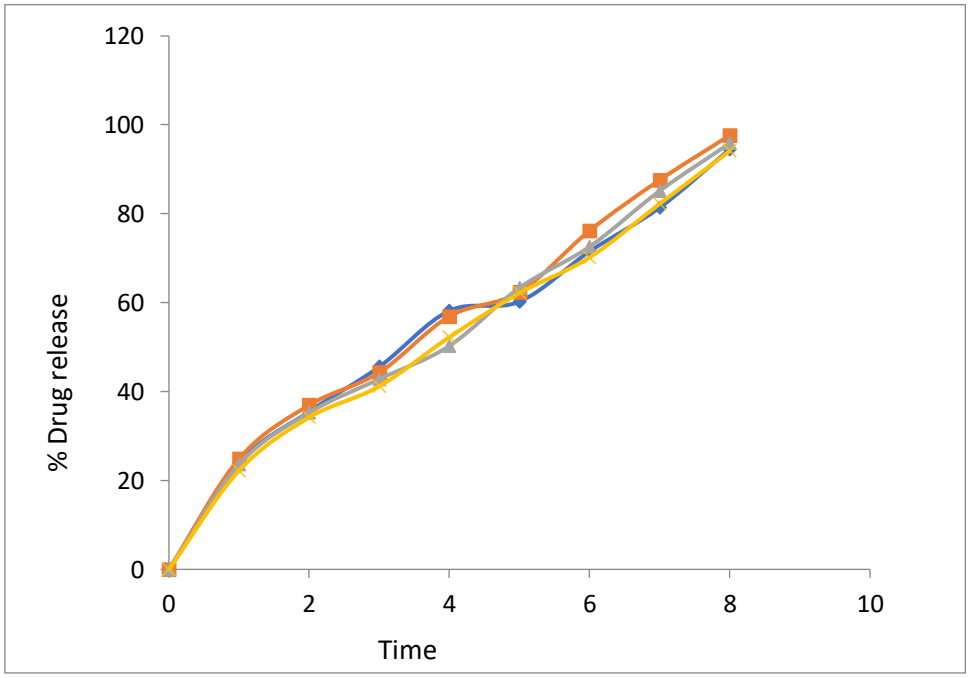

Fig-5 : *In vitro* drug release of (F1-F4) formulations

All the four batches of formulation F2 were found to release the drug in 8 h. The cumulative percentage release was found to be 97.65%.

Stability studies

There was no significant change in physical and chemical properties of the tablets of formulation F-2 after 3 months. Parameters quantified at various time intervals were shown;

Table-5: Results of stability studies of optimized formulation F-3

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-2	**25^{0}C/60%RH % Release**	97.65	97.45	96.85	95.63	**Not less than 85 %**
F-2	**30^{0}C/75% RH % Release**	97.65	97.10	96.72	95.52	**Not less than 85 %**
F-2	**40^{0}C/75% RH % Release**	97.65	96.99	96.51	94.99	**Not less than 85 %**

4. CONCLUSION:

From the performed work it was concluded that:

1. Donepezil possesses all requisite qualities required for liposomal drug delivery.
2. Among the various formulation, the combination F2 was found to be most suitable because of high encapsulation efficiency with smaller particle size.
3. The formulation F2 comprising phosphatidylcholine, cholesterol, fulfills the requirement of good liposomal formulation. *In vitro* drug release up to 8 hrs and more than 97.65% drug released. It shows encapsulation efficiency of 98.25 % .

5.REFERENCES:

1. Benita S. Microencapsulation Method and Industrial Application, Drug and The Pharmaceutical sciences. Vol.73 2002. p. 213.
2. Fuji G. Vesicles, Realization of the Drug Delivery Concept. Vol.62 1996. New York p. 491-495.
3. Bangham AD, Standish MM. Diffusion of univalent ions across the lamella of swollen Phospholipids. J. Mol. Biol. 1965; 13: 238-252.
4. Vyas SP, Khar RK. Targeted and controlled Drug Delivery, Novel Carrier system, CBS Publishers and distributors. 2002. p. 249.
5. Gregoriadis G. Liposome technology, Liposome preparation and related techniques, 3rd edition, vol. l 2007. p. 21.
6. Singh S, Gulati M. Advances in liposomal therapeutics, Targeting of drugs to lipid bilayer in liposomes: an approach for the success of liposomes as delivery systems. CBS Publishers and distributors. New Delhi. 2001. p. 4-34.
7. Scherphof G, Morselt H, Regts J. The involvement of the lipid phase transition in the plasma-induced dissolution of multilamellar phosphatidylcholine vesicles. Biochem. Biophys. Acta.1979; 556:196–207.
8. Jain NK. Controlled and novel drug Delivery, CBS Publishers and distributors.2002. p. 305,326,330.
9. Bangham AD. Techniques in life Science, lipid membrane biochemistry. Elsevier scientific publications. Ireland. 1982 p.1-25.
10. Drummond DC, Meyer O, Hong K. Pharmacokinetic study of liposome encapsulated drug. Pharmacological reviews 1999; 51(4): 691-743.11.
11. Lasic DD. Stealth liposomes, Microencapsulation Method and Industrial Applications. Vol. 73 1996 p. 297-311.