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Formulation, Development and Evaluation of Niosome for the Treatment of Psychosis

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Abstract
The present study was aimed to overcome the problems associated with the drug such as bioavailability, to reduce the dosage regimen, half–life, and to determine the appropriateness of niosomal formulation as a drug carrier. The niosomal suspension was prepared by Ether injection method, by varying ratios of span 60 and cholesterol and varying the concentration of span 60. The prepared nine formulations were evaluated for various parameters. The FTIR and DSC observation confirmed the purity and authenticity of the Haloperidol. The niosomal dispersion was off-white in color, odourless and fluid in nature. It was stable and did not show sedimentation. The pH was found in the range of 4.6-5.4. The drug content was found in the range of 89.13 to 99.52. The optimized formulation had a vesicular size of 2.52 - 3.42 µm. The Entrapment efficiency was found in range of 79.05 to 98.24. The highest entrapment efficiency was 98.24%. The values of zeta potential were found in a range 20.29 to -30.55mV. The maximum drug release (98.55 %) at the end of 24th hour. The present study concludes that the prepared niosomal suspension is a convenient and efficiency carrier for the delivery of antipsychotic drug. Besides this, it provided controlled delivery of drug.

Keywords: Niosomes, Cholesterol, Ether injection method, Vesicular size, Controlled drug delivery.

Introduction

Niosomes are microscopic lamellar structures formed by mixture of cholesterol and single alkyl chain non-ionic surfactant following hydration in aqueous media. Niosomes are competent for both hydrophilic and hydrophobic API's. [1] The surfactant used in the manufacturing of Niosome is chemically stable, accurate in composition and having low cost. Niosome has superior stability than liposome and prolong the release of the encapsulated API. Niosome can be deliver via various routes i.e. intravenous, intramuscular, subcutaneous, ocular, oral and transdermal. [2]

1.1 Structure of Niosome

Niosome contains vesicle making amphiphile i.e. non-ionic surfactant which is stabilized by inclusion of cholesterol and a little quantity of anionic surfactant which also helps in stabilizing the vesicle. [3]

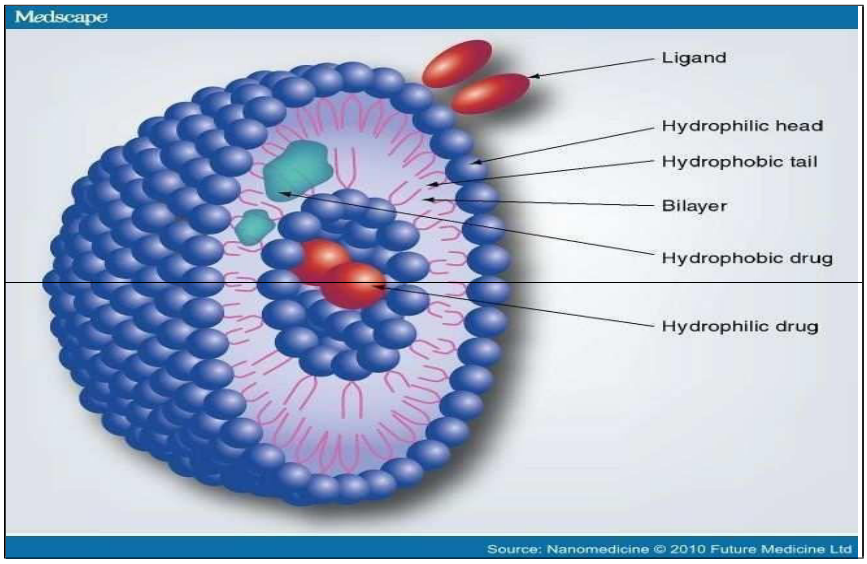


Fig. 1: Structure of Niosome[3]

1.2 Pros[4]

- Greater patient compliance
- Use for variety of API's
- Vesicle can be modified as per requirement
- Act as depot to release the drug steadily which allow controlled release
- Highly stable and osmotically active
- Increase the bioavailability of API's
- Does not require any special storage condition
- Enhance the permeation of API's
- Biodegradable, biocompatible and non-immunogenic
- Target drug delivery

1.3 Cons[4]

- Physical instability

- Aggregation
- Fusion
- Flow of embedded drugs
- Hydrolysis of encapsulated drugs limits the shelf life of the dispersion.

1.4 Composition[5]

The two major components used for the preparation of niosomes are,

1. Cholesterol
2. Nonionic surfactants

1.5 Manufacturing methods[6]

The manufacturing method should be chosen as per the use of the niosome as it effects no. of bilayer, size, size distribution, entrapment efficiency and permeability.

1. Ether injection method
2. Hand shaking method (thin film hydration technique)
3. Sonication Method
4. Micro fluidization Method
5. Multiple membrane extrusion method
6. Reverse Phase Evaporation Technique (REV)

1.6 Application[4]

- Drug targeting
- Used in cancer therapy, dermal and Mucocutaneous infections
- Deliver peptide API's
- Used for studying Immune response
- as a carrier for hemoglobin
- Used in various drug delivery systems, e.g. transdermal, ophthalmic
- Used in SR and cosmetics to increase the safety and efficacy of API.

2. Drug Profile

2.1 Haloperidol

Haloperidol, a first-generation typical antipsychotic, is commonly used worldwide to block dopamine D2 receptors in the brain and exert its antipsychotic action. The medication is used to manage the positive symptoms of schizophrenia, including hallucinations and delusions. [7]

2.2 Mechanism of Action[8]

Haloperidol, a first-generation typical antipsychotic, exerts its antipsychotic effects by blocking dopamine D2 receptors in the brain. This drug reaches its maximum effectiveness when 72% of dopamine receptors are blocked. Haloperidol's effects are not limited to the D2 receptor, as it also exerts blocking action on noradrenergic, cholinergic, and histaminergic receptors. The blocking of these receptors is associated with various adverse drug reactions.

2.3 Adult Dosage[7-8]

2.3.1 Psychosis: For psychosis, the oral and IM forms can be used. For moderate symptomology, the recommended dosage ranges from 0.5 to 2 mg orally, administered 2 to 3

times daily. In certain resistant cases, haloperidol dosages of up to 30 mg/d might be required. Acute agitation can be rapidly controlled with 2 to 5 mg IM injections every 4 to 8 hours. The maximum recommended IM dosage should not exceed 20 mg/d.

2.3.2 Schizophrenia: For moderate symptoms linked to schizophrenia, the recommended dosing involves oral administration of 0.5 to 2 mg of haloperidol, taken 2 to 3 times a day. For severe symptoms, the prescribed dosage is 3 to 5 mg of haloperidol administered orally to patients 2 to 3 times a day. The maximum recommended oral dosage should not exceed 100 mg/d.

3. Materials and Methods

3.1 Preformulation Study of Drug

Preformulation testing is the first step in the rationale development of finished dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The altogether intension of preformulation study is to gather data beneficial for the formulator in developing stable and bioavailable dosage forms, which can be mass- produced.

3.2 Determination of λmax by UV spectroscopy[9]

Haloperidol is weighed accurately and transferred to a 100 ml volumetric flask; the volume was adjusted to 100 ml with methanol, to get a 1000 µg/ml stock solution, further stock solution was diluted suitably to get 100 µg/ml solution. Further diluted suitably to get concentration of 5 µg /ml and 5 µg /ml of Haloperidol. The absorbance of the solution was scanned in the range of 200 to 400 nm in UV-visible double beam spectrophotometer in medium scanning speed against methanol as a blank. Repeat the abovementioned procedure for concentration of 10 µg/ml of Haloperidol.

3.3 Melting point determination[9]

It was obtained by using capillary tube technique. The perceived value was compared with the reference value.

3.4 FTIR spectroscopy[10]

The IR spectra of Haloperidol was recorded using Fourier transform infrared spectrophotometer with diffuse reflectance principle. Sample preparation involved mixing the sample with potassium bromide (KBr), triturating in glass mortar and finally placing in the sample holder. The spectrum was scanned over a frequency range 4000 – 400 cm-1.

3.5 Loss on Drying[10]

A sample of 0.1g of Haloperidol was weighed in a vessel. The sample containing vessel was then placed in a hot air oven at 100oC for 4 h. The sample was cooled in a desiccator and weighed.

3.6 DSC study[11]

The DSC thermogram of Haloperidol was recorded using Differential scanning calorimeter. Approximately 2 to 5 mg of sample was heated in a closed pierced aluminum pan from 30ºC to 180ºC at a heating rate of 5 ºC /min under a stream of nitrogen at a flow rate of 50ml/min.

3.7 Saturation solubility[12]

The shake flask technique was utilized to determine saturation solubility of Haloperidol in different solvent (i.e. Methanol, 0.1N HCl pH 1.2,Phosphate buffer pH 6.8 and Phosphate buffer pH 7.2). Excess quantity of Haloperidol was added separately in 10 ml of different solvent which were then mixed in vortex mixture at 37°C and at 100 rpm for 24 h. Solutions were filtered using whatman filter paper. The filtrates were diluted suitably and solutions were analyzed using UV-visible spectrophotometer against methanol, 0.1N HCl pH 1.2, Acetate buffer pH 4.5, Phosphate buffer pH 6.8 andPhosphate buffer pH 7.2 as a blank.

3.8 % Purity[12]

For % purity, 100 mg of Haloperidol was weighed and transferred to a 100 ml of volumetric flask. Then the volume was made up to100 ml mark with methanol. The flask was kept on a sonicator individually for 5min. Solution was then filtered using a whatmann filter paper. Then aliquot 10 ml from the filtered solution and dilute it up to 100 ml using methanol. Then absorbance of the resulting solution was measured at the λmax 247.5 nm using UV-Visible double beam spectrophotometer against methanol as blank. The linearity equation obtained from calibration curve was used for estimation of purity of Haloperidol.

3.9 Powder characterization (Physical properties) [13]

3.9.1 Angle of Repose

Angle of repose has been defined as the maximum angle possible between the surface of pile of powder and horizontal plane. The angle of repose for the Powder was determined by the funnel method.

Angle of repose was then calculated with the use of the following formula:

$$\tan \theta = h / r$$

Where,

θ= angle of repose
h= height of the pile
r = average radius of the powder cone

3.9.2 Bulk density

Bulk density of the powder was determined by pouring gently 10gms of sample through a glass funnel into a 50ml graduated cylinder. The volume occupied by the sample was recorded. The bulk density was calculated as follows:

$$\text{Bulk density (g/ml)} = \frac{\text{Weight of sample in g}}{\text{Volume occupied by the sample}}$$

3.9.3 Tapped density[13]

10 grams of sample was poured gently through a glass funnel into a 50ml graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping was recorded and tapped density was calculated as follows:

$$\textbf{Tapped density (g/ml)} = \frac{\text{Weight of sample in g}}{\text{Volume occupied by the sample (after tapping)}}$$

3.9.4 Carr's index[13]

One of the important measures that can be obtained from bulk and tapped density determinations is the percent compressibility or the Carr's index (I), which is determined by the following equation**:**

$$\textbf{Carr's compressibility index} = \frac{\text{Tapped density} - \text{Bulk density} \times 100}{\text{Bulk density}}$$

3.9.5 Hausner's ratio

Hausner's ratio is defined as a ratio of a tapped density to bulk density. It is measures of relative importance of inter particulate interactions.

Tapped density and bulk density were measured and the Hausner's ratio was calculated using the formula,

$$\textbf{Hausner's ratio} = \text{Tapped density} / \text{Bulk density}$$

3.10 Preparation of standard curve of Haloperidol [14]

3.10.1 Preparation of standard curve of Haloperidol in phosphate buffer (pH 6.8)at 247.5 nm

Preparation of standard stock solution (1000µg/ml):

Accurately weighed 100 mg of Haloperidol was dissolved in 100 ml of phosphate buffer (pH 6.8) to get a concentration 1000 µg/ml. This course of action was then used for arranging working standard plan.

Preparation of working standard solution (100µg/ml):

10 ml standard stock solution of Haloperidol was transferred to a 100 ml volumetric flask and volume was adjusted to 100 ml with phosphate buffer (pH 6.8) to get a concentration of 100 µg/ml.

Preparation of dilutions for calibration curve

Aliquots of 5,10,15,20,25,30,35 and 40 ml of working standard solution were pipetted out into 50 ml volumetric flasks. The volume was made up to the mark with phosphate buffer (pH 6.8). These dilutions gave 5,10,15,20,25,30,35 and 40µg/ml concentration of Haloperidol respectively. The absorbance of prepared solutions of Haloperidol in phosphate buffer (pH 6.8) was measured at wavelength maximum 247.5 nm using Shimadzu UV-1800 spectrophotometer against phosphate buffer (pH 6.8) as blank. The experiment was performed in triplicate and based on average absorbance the equation for the best line was generated.

3.11 Preparation of Drug loaded niosomal dispersions

Medicated Niosomes was prepared by using following process flow chart.

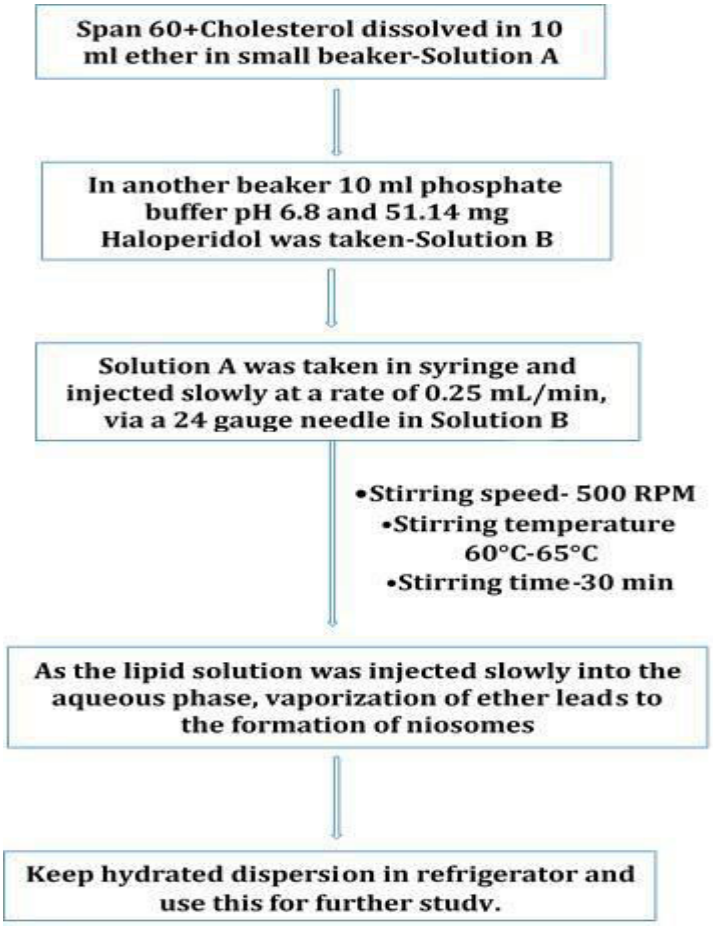


Fig. 2: Process flow chart for formulation of Medicated Niosome

Table 1: Formulations of Haloperidol loaded Niosomes

Sr. No.	Formulation Code	Haloperidol (%)	Span 60 (%)	Cholesterol (%)
1	F1	1	0.5	1
2	F2	1	1	1
3	F3	1	1.5	1
4	F4	1	2	1
5	F5	1	2.5	1
6	F6	1	3	1
7	F7	1	3.5	1
8	F8	1	4	1
9	F9	1	4.5	1

Note: All formulation contains 10 ml diethyl ether.

3.12 Evaluation parameters for Medicated Niosomes[15-17]

3.12.1 Organoleptic properties

The drug loaded dispersion was evaluated for colour, odour and appearance.

3.12.2 pH

The pH of niosome dispersion was checked by digital pH meter.

3.12.3 Total drug content

Assay of drug loaded niosomal dispersions were carried out by U.V. method.

2 ml of niosomal dispersion was dissolved into 50 ml Phosphate buffer solution having pH 6.8. The sample was stirred at 100 rpm to break the niosomes. Drug content was determined using UV spectrophotometer at respective absorption maxima.(20, 21)

3.12.4 Mean particle size and Polydispersibility index

The particle size analysis of the formulation (F7) was determined using Beckman particle size determination technique..

3.12.5 Entrapment efficiency[15]

Unentrapped drug from niosomal dispersion was separated by centrifugation method. Niosomes were centrifuged at 20,000 rpm at controlled temperature of 40°C for 60min. By using UV

spectroscopy unentrapped drug was quantified at respective absorption maxima. The results of Haloperidol loaded niosome were shown in Table

3.12.6 Zeta potential (ζ) [16]

Zeta potential of the dispersion was determined by Malvern zetameter. Time duration for zeta potential determination was 60 seconds and charge was find out.

3.12.7 In-Vitro Drug Release Studies[17]

The release of Haloperidol from niosomes was determined by using membrane diffusion technique. The niosomal formulation equivalent to 51.14 mg of Haloperidol was placed in a glass tube of diameter 2.5 cm with an effective length of 8 cm which was tied with previously soaked cellulose membrane (12,000-14,000 Da Molecular weight cut off), which acts as a donor compartment. The glass tube was placed in a beaker containing 100 ml of phosphate buffer (pH 6.8), acting as a receptor compartment. The whole assembly was fixed in such a way that the lower end of tube containing suspension was just touching (1-2 mm depth) the surface of diffusion medium. The temperature of receptor medium was maintained at 37 ± 5° C and was agitated at the speed of 100 rpm using magnetic stirrer. Aliquots of 5ml sample were withdrawn periodically and after each withdrawal same volume of medium was replaced. The collected samples were analyzed at 247.5 nm in double beam UV-VIS spectrophotometer using Phosphate Buffer (pH 6.8) as blank.

4.Result & Discussion

4.1 Characterization of Pure API

Table 2: Results of characterization of pure drugs

Sr. No	Test Parameters		Observation
1	Physical Appearance		A white powder.
2	λmax by UV spectroscopy Methanol		247.5 nm
	67 mM phosphate buffer pH 6.8 with 0.5 % SDS		247.5 nm
3	Melting point		150ºC -152ºC
4	Loss on Drying		0.41 % (NMT 0.5%)
5		Methanol	0.653
		Water	0.160

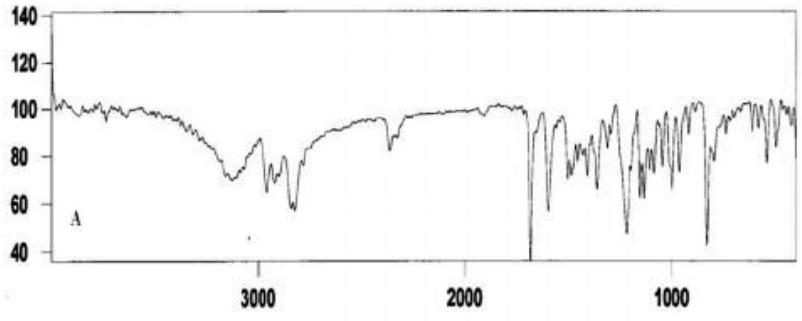
	Equilibrium solubility study (mg/ml)	0.1 N HCl, pH 1.2	0.081
		Phosphate buffer, pH 6.8	1.321
		Phosphate buffer, pH 7.4	1.384
6	% Purity		99.86 % (98.0 % to 102.0%)
7	Powder characterization		
	Angle of Repose (°)		16.46
	Bulk density (g/ml)		0.4137
	Tapped density (g/ml)		0.5578
	Carr's index		42.361
	Hausner's ratio		1.7328

From the above results it was concluded that all the practical results were complied with theoretical values. The melting point of Haloperidol was found to be 150°C - 152°C, which complies with theoretical values thus indicating purity of obtained drug sample. The solubility test indicates that Haloperidol has poor solubility in 0.1N HCl but its permeability was found to be more towards acidic side. Hence further emphasis was given to evaluate the drug dissolution atthis particular media along with pH 6.8 buffer as its solubility was found to be comparatively more at this particular media. From the solubility study data Haloperidol also shows lower solubility in water. Powder characteristics indicate that both the drug has good flowability.

4.2 FTIR spectroscopy

The FTIR spectrum disclosed characteristic peaks of haloperidol ν(C=O), ν(C-F) and ν(C-Cl) bands appeared at 1658, 1226 and 740 cm-1, respectively.

Fig. 2: FTIR Spectrum of Haloperidol pure drug



4.3 Differential scanning Calorimetry (DSC) study

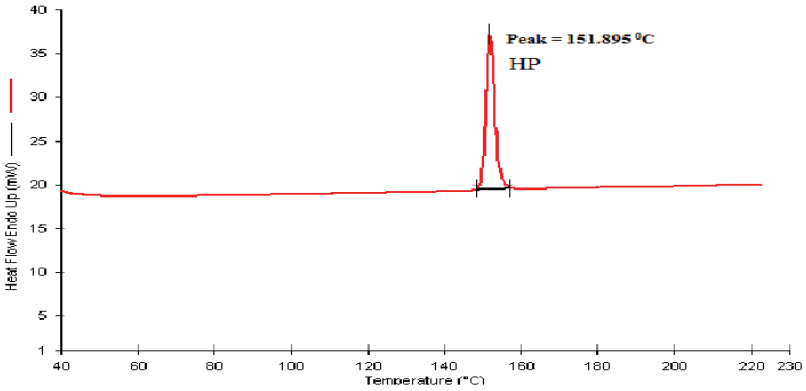


Fig. 3: DSC thermogram of Haloperidol pure drug

DSC thermogram of Haloperidol was recorded in the range of 20-180℃. The DSC thermogram of Haloperidol showed sharp endothermic peak at its melting point of 151.89℃.This observation confirmed the purity and authenticity of the Haloperidol.

4.4 Standard calibration curve

Table 3: Standard calibration curve data of Haloperidol in phosphate buffer (pH 6.8)at λmax 247.5 nm

Sr. No.	Concentration (ug/ml)	Absorbance			Absorbance (Mean*± SD)
1	5	0.103	0.102	0.104	0.103 ± 0.001
2	10	0.215	0.219	0.219	0.217 ± 0.0023
3	15	0.319	0.318	0.321	0.319 ± 0.0015
4	20	0.454	0.456	0.453	0.454 ± 0.0015
5	25	0.592	0.59	0.592	0.592 ± 0.0012
6	30	0.763	0.762	0.76	0.761 ± 0.0015
7	35	0.92	0.92	0.921	0.920 ± 0.0005
8	40	1.234	1.233	1.235	1.234 ± 0.001

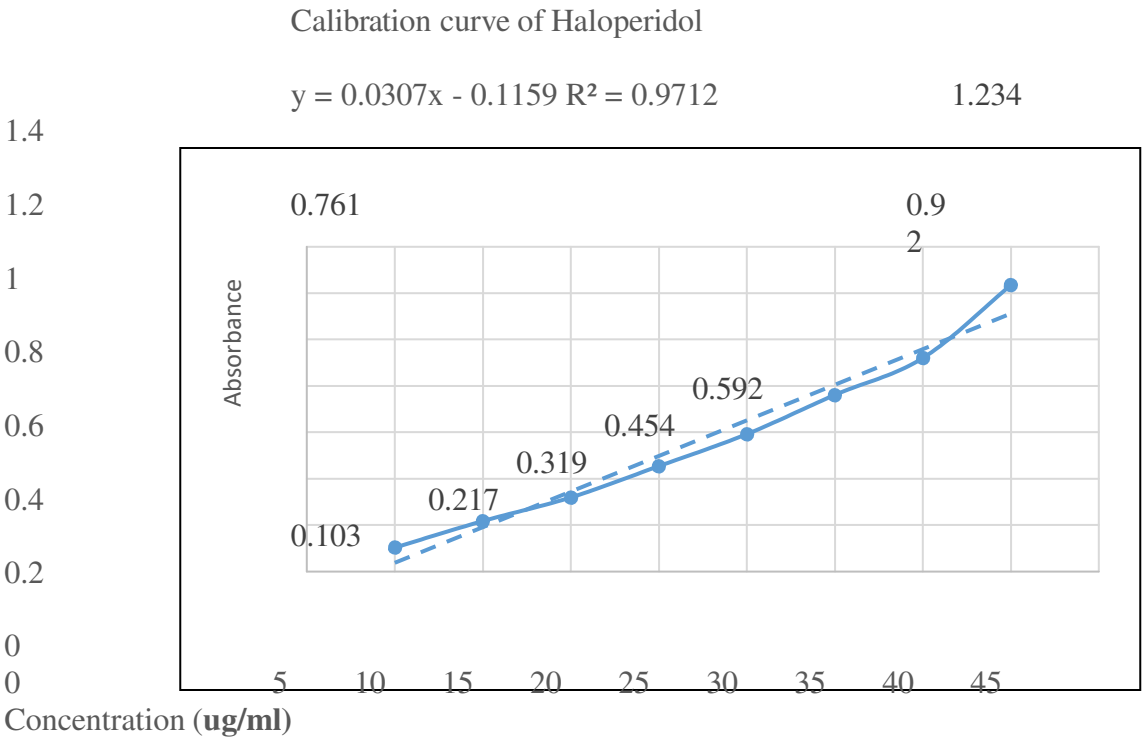


Fig. 4: Standard calibration curve of Haloperidol in phosphate buffer (pH 6.8)

4.5 Evaluation parameters for Medicated Niosomes

4.5.1 Organoleptic properties

The results of Organoleptic properties i.e. Appearance, Colour and Odour for all the nine formulations are summarize in below table.

Table 4: Organoleptic properties of medicated niosome

Sr. No.	Batch No	Appearance/Colour	Odour
1	F1	Milky white	Odourless
2	F2	Milky white	Odourless
3	F3	Milky white	Odourless
4	F4	Milky white	Odourless
5	F5	Milky white	Odourless
6	F6	Milky white	Odourless
7	F7	Milky white	Odourless
8	F8	Milky white	Odourless
9	F9	Milky white	Odourless

The Haloperidol niosomal dispersion was off-white in color, odourless and fluid in nature.

It was stable and did not show sedimentation.

4.5.2 pH

The results of pH value for all the nine formulations are summarize in below table

Table 5: pH of medicated niosome

Sr. No.	Batch No	pH (Mean*± SD)
1	F1	4.7±0.057
2	F2	4.6±0.051
3	F3	5.1±0.049
4	F4	4.9±0.035
5	F5	4.7±0.053
6	F6	5.2±0.041
7	F7	5.4±0.038
8	F8	5.1±0.045
9	F9	4.8±0.056

SD: Standard deviation, *: Mean of each 3 reading

The pH was found in the range of 4.6-5.4.

4.5.3 Total drug content

The results of drug content for all the nine formulations are summarize in below table

Table 6: Total drug content of medicated niosome

Sr. No.	Batch No	Drug content (%)(Mean*± SD)
1	F1	89.23 ± 1.75
2	F2	90.20 ± 0.61
3	F3	89.13 ± 0.79
4	F4	95.41 ± 0.90
5	F5	97.76 ± 1.50
6	F6	97.29 ± 0.59
7	F7	99.52 ± 0.97
8	F8	97.93 ± 1.25
9	F9	98.45 ± 1.19

SD: Standard deviation, *: Mean of each 3 readings

The drug content was found in the range of 89.13 to 99.52

4.5.4 Entrapment efficiency

The results of Entrapment efficiency for all the nine formulations are summarize in below table

Table 7: Entrapment efficiency of medicated niosome

Sr. No.	Batch No	Entrapment efficiency (%)(Mean*± SD)
1	F1	85.52 ± 1.13
2	F2	83.60 ± 1.39
3	F3	79.05 ± 1.14
4	F4	89.60 ± 2.26
5	F5	88.09 ± 1.94
6	F6	84.84 ± 1.60
7	F7	98.24 ± 1.50
8	F8	93.24 ± 2.25
9	F9	90.16 ± 1.03

The Entrapment efficiency was found in range of 79.05 to 98.24.

4.5.5 Mean particle size and Polydispersibility index

The results of Mean particle size and Polydispersibility index for all the nine formulations are shown in table

Table 8: Mean particle size and Polydispersibility index of medicated niosome

Sr. No.	Batch No.	Polydispersibility index	Particle size(µm)(Mean*± SD)
1	F1	0.411	2.76 ± 0.84
2	F2	0.389	2.99 ± 0.97
3	F3	0.42	3.24 ± 0.86
4	F4	0.385	3.08 ± 0.55
5	F5	0.325	3.20 ± 0.90
6	F6	0.37	3.42 ± 0.77
7	F7	0.387	2.52 ± 1.50
8	F8	0.404	2.90 ± 0.60
9	F9	0.395	3.32 ± 0.61

SD: Standard deviation, *: Mean of each 3 readings

The mean vesicle size of drug loaded niosomes of the different batches ranged between 2.52 - 3.42 µm. The polydispersibility index (PdI) was in the range of 0.325 – 0.420 for drug loaded niosomes which indicates a narrow vesicle size distribution.

4.5.6 Zeta (ζ) Potential Determination

The results of Zeta potential for all the nine formulations are shown in table

Table 9: Zeta (ζ) Potential of medicated niosome

Sr. No.	Batch No.	Zeta potential (Mv) (Mean*± SD)
1	F1	-27.77 ± 1.55
2	F2	-24.84 ± 0.79
3	F3	-20.29 ± 1.03
4	F4	-25.44±0.92
5	F5	-21.07±1.75
6	F6	-24.57±0.16
7	F7	-25.69 ± 1.87
8	F8	-28.27±0.28
9	F9	-30.55±0.28

SD: Standard deviation, *: Mean of each 3 readings

The values of ζ potential of the drug loaded niosomal formulation were in the range of-20.29 to -30.55mV. Values of zeta potential showed that the drug loaded niosome had sufficient charge and mobility to inhibit aggregation of vesicles.

4.5.7 In-Vitro drug release studies

The results of In-Vitro drug release studies for all the nine formulations are shown in table

Table 10: In-Vitro drug release data of medicated niosome

Sr. No.	Time (Hr)	% Cumulative drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	2	4.45	5.02	4.22	5.25	4.45	5.24	6.45	3.45	3.56
3	3	8.34	9.56	7.23	8.64	7.54	8.02	9.56	7.55	6.28
4	4	10.11	12.11	10.25	11.43	10.96	12.89	15.23	9.95	9.25
5	5	14.43	16.34	14.43	14.56	12.53	15.04	18.25	13.56	12.43
6	6	24.21	24.5	22.58	23.41	19.96	20.48	26.95	21.11	19.55
7	7	32.23	34.16	30.23	30.54	29.78	32.11	34.11	28.24	26.65
8	8	39.55	40.11	36.55	37.78	38.57	40.67	42.56	42.05	33.43
9	12	62.45	64.78	60.44	62.65	63.98	65.43	68.45	63.45	60.23
10	18	82.61	83.49	82.54	86.56	85.46	88.9	92.36	78.59	75.43
11	24	90.26	87.67	88.21	91.55	90.23	92.45	98.55	85.65	82.25

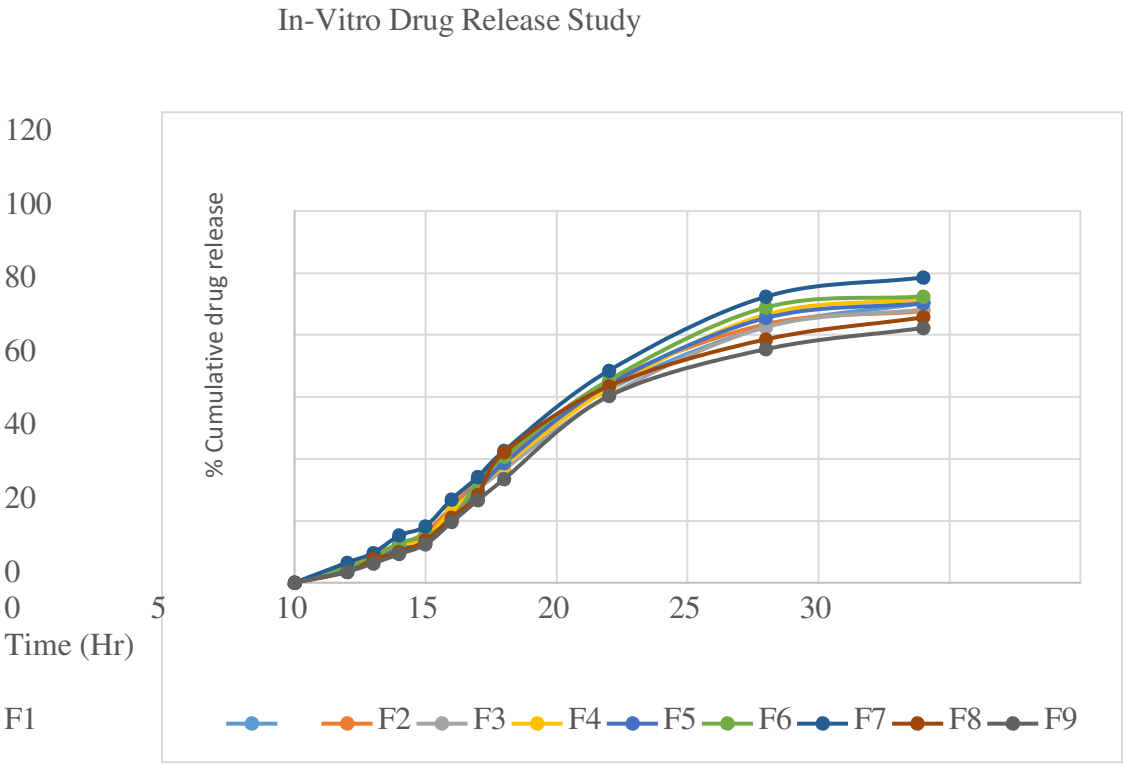


Fig. 5: In-Vitro drug release data of niosome formulations

For all the nine formulations there was no initial burst release but the release was constant in a controlled manner for a period of time upto 24 hrs. The results of in- vitro drug release revealed that the drug was released in a controlled manner from all the formulations and F7 showed maximum drug release (98.55 %) at the end of 24th hour.

5. Conclusion

The present study concludes that the prepared niosomal suspension is a convenient and efficiency carrier for the delivery of antipsychotic drug to conquer the troubles associated with it, like the poor solubility, low bioavailability, and half-life of the drug, thereby increasing the duration of

action and thereby increasing the half-life. The pre- formulation studies were carried out; from the study, it was clear that it satisfy the entire characteristic for oral drug delivery. The niosomal dispersion was off-white in color, odourless and fluid in nature. It was stable and did not show sedimentation. The pH was found in the range of 4.6-5.4. The drug content was found in the range of 89.13 to 99.52. The optimized formulation had a vesicular size of 2.52 - 3.42 µm. The Entrapment efficiency was found in range of 79.05 to 98.24. The highest entrapment efficiency was 98.24%. The values of zeta potential were found in a range 20.29 to -30.55mV. The maximum drug release (98.55 %) at the end of 24th hour. On the basis of result it was concluded that F7 was found the best formulation among all the nine formulations.

References

1. Okore, V. C., Attama, A. A., Ofokansi, K. C., Esimone, C. O. & Onuigbo, E. B. (2021) Formulation and Evaluation of Niosomes. *Indian Journal of Pharmaceutical Sciences*. 4(2). 21-29.
2. Mishra, N., Srivastava, V., Kaushik, A., Chauhan, V., Srivastava, G. (2014). Formulation and in-vitro evaluation of Niosomes of Aceclofenac. *Journal of Scientific and Innovative Research*. 3. 245-251.
3. Singh, R.P., Narke, R.M., Jadhav, V. (2020). Formulation and Evaluation of Asenapine Maleate Loaded Niosomes for the Treatment of Schizophrenia. *Indian Journal of Pharmaceutical Education and Research*. 54 (2). 128-139.
4. Kumar, B.S., Krishna, R.L., Vasudev, D., Nair, T.S. (2017) Formulation and Evaluation of Niosomal Suspension of Cefixime. *Asian Journal of Pharmaceutical and Clinical Research*. 10 (5). 195-201
5. Katrolia, A., Chauhan, S. B., Shukla, V. K. (2019). Formulation and evaluation of Metformin Hydrochloride -loaded Curcumin–Lycopene Niosomes. *SN Applied Sciences*. 17. 68-78.
6. Thabet, Y., Elsabahy, M., Eissa, N.G. (2022). Methods for preparation of niosomes: A focus on thin-film hydration method. Methods. *Elsevier*. 199. 9-15.
7. Drug Bank https://go.drugbank.com/drugs/DB00502
8. Food and Drug Administration (FDA) https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/018701s059lbl.pdf.
9. Beeravelli, S., Akondi, V., Nimmathota, M. (2022). Formulation Development and In vitro-Ex vivo Assessment of Simvastatin Niosomal Buccal Films. *Recent Patents on Nanotechnology. Bentham Science Publishers*. 16 (3). 235-249.
10. Kaur, D. and Kumar, S. (2018). Niosomes: present scenario and future aspects. *Journal of Drug Delivery and Therapeutics*. 8(5). 35-43.
11. Pei, L. Y., Chooi, L. L., Soi, M. C., Anna, P. K. L., Rhun, Y.k. (2018)
12. Niosomes: a review of their structure, properties, methods of preparation, and medical applications. *Asian Biomed (Res Rev News)*.11(4). 301–14.
13. Mujoriya, R., Bodla, R.B., Dhamande, K., Singh D. and Patle L. (2021) Niosomal Drug Delivery System: The Magic Bullet. *Journal of Applied Pharmaceutical Science*. 01 (09). 20-23.
14. Kaur, D. (2022). Niosomes: A New Approach to Targeted Drug Delivery. *International Journal of Pharmaceutical and Phytopharmacological Research*. 2(1). 53-59.
15. Ali, N., Harikumar, SL., Kaur, A. (2022). Niosomes: an excellent tool for drug delivery. *International journal of research in pharmacy and chemistry*. 2(2). 479-487.
16. Lambert T. Selecting patients for long-acting novel antipsychotic therapy. Australas

Psychiatry. 2006;14(1):38-42.
17. Conley RR, Kelly DL. Management of treatment resistance in schizophrenia. Biol Psychiatry. 2001;50(1):898-911.
18. Bartelds R, Nematollahi MH, Pols T, Stuart MCA, Pardakhty A, Asadikaram G. Niosomes, an alternative for liposomal delivery. PLoS One. 2018;13(4):e0194179