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Formulation and Evaluation of Transferosomes Loaded with an Anti-Hyperlipidemic Drug

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The primary goal of this research is to create transferosome formulations that contain an anti-hyperlipidemic medication. Simvastatin, the medication employed in the formulation, has a low bioavailability of 60% and undergoes substantial hepatic degradation. These are the deformable nano-vesicles which can deliver both hydrophilic and hydrophobic drugs through transdermal route to enhance the Bioavailability of drugs which undergoes extensive hepatic metabolism when given through oral route which can increase patient compliance. Transferosomes are prepared and characterized by various evaluation tests like SEM analysis, vesicular size, surface morphology. After all evaluations done, Out of 12 formulations F2 formulation showed more entrapment efficiency. The reason for this is that there are more phospholipids present, and as the surfactant concentration rises, medication release becomes more rapid. Our main goal is to improve bioavailability, which can be accomplished by optimising the concentrations of phospholipid and surfactant in this drug delivery system, resulting in a controlled release of drug.

Keywords: Transferosomes; soyalecithin; Tween 60; Tween 80; Span 60; Span80.

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1. INTRODUCTION

Several drug delivery techniques have been identified for the treatment of acute and chronic diseases for many years, and the most commonly available dosage forms in the market for the treatment of these diseases are tablets, capsules, suppositories, pills, ointments, liquids, aerosols, and ointments. Though these dosage forms increase patient compliance and release the drug at more predictable rates, the frequency of administration is a limitation in using them to get the drug to therapeutic levels and deliver the drug in an efficient manner because the patient does not feel comfortable administering the dosage forms as often as prescribed by the physician There is a need for the development of innovative approaches that can improve patient compliance while also safely and effectively administering the medicine at therapeutic concentrations [1].

The concept beyond targeting the drug is to deliver the drug to a specific target site exclusively in order to maximize the therapeutic effect of a drug at that particular site where it needs. By this approach side effects that may occur due to drug can also be decreased. By this type of drug delivery system drug exposure to the non specific tissues is reduced [2].

Concept of Controlled release drug delivery systems goes beyond of Sustained release drug delivery system where it releases the drug at a constant rate. The drug release kinetics through these drug delivery systems indicates predictability and reproducibility. The release of drug in controlled drug delivery systems is predictable [3] kinetically and also the result obtained would be reproducible from one unit to another.

Carriers that are used in Targeted drug delivery system:

1.1 Colloidal Carriers

a) Vesicular Carriers
   Liposomes, Niosomes, Tranferosomes [4], Aquasomes, Ethosomes

b) Micro particulates
   Nanoparticles, Microparticles

- Cellular Carriers : Resealed erythrocytes, Monoclonal Antibodies
- Supra Molecular delivery systems : Micelles, Lipoproteins
- Polymer systems : Bioadhesive, Biodegradable, Bioerodible, Soluble synthetic polymers
- Macromolecules : Proteins

1.2 Transferosomes as Drug Delivery Agents

Drug delivery through vesicles is having a very great importance to release the drug in a controlled and constant way [5].

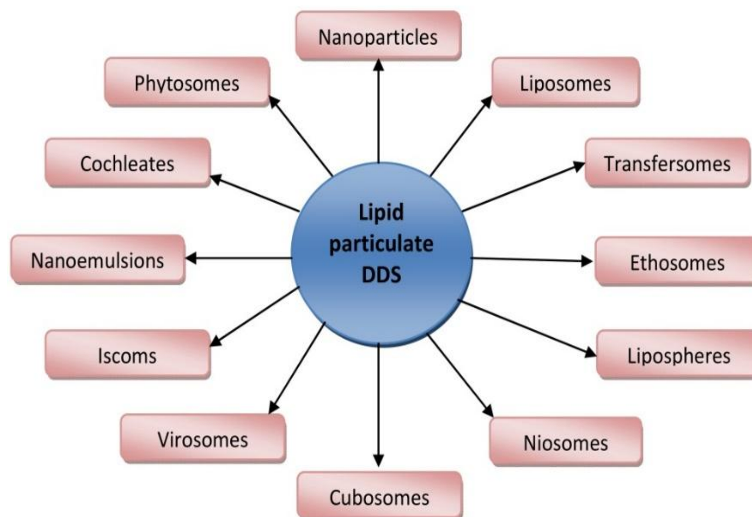

Fig. 1. Carriers used in Targeted drug delivery system

1.3 Structure of Transferosomes

Transferosomes are the vesicular carriers containing a hydrophilic liquid core in the inner surface and the outer surface is composed of lipids and surfactants. Due to the presence these two hydrophilic and lipophilic portions it can entrap both the hydrophilic and lipophilic drugs. Hydrophilic drug entrapped in the hydrophilic core while the lipophilic drug gets entrapped in the lipophilic portion because of the action of electrostatic or hydrophobic forces [6].

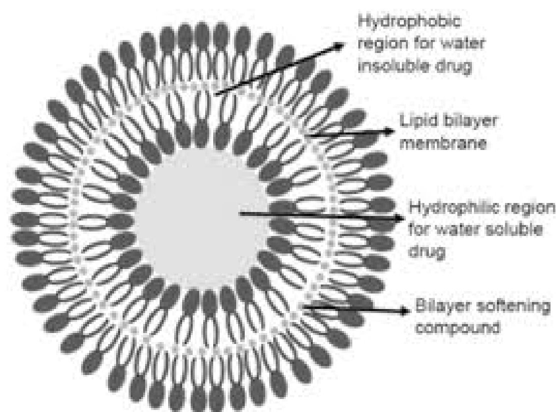

Fig. 2. Structure of Transferosomes

2. MATERIALS AND METHODS

simvastatin is obtained as a gift sample from aurobindho labs hyderabad., Soya lecithin, Span 60, Span 80, Tween 60, Tween 80 are obtained from Yarrow chemicals. All the chemicals used are of analytical grade.

2.1 Methodology

2.1.1 Preparation of transferosomes

Transferosomes are made by dissolving phospholipids and surfactants in Methanol and chloroform in a 1:1 ratio. The resultant is fed into a rotary evaporator, where the organic solvent is evaporated, resulting in the production of a thin film, which is then mixed with phosphate buffer.and hydrated for 24 hrs the resultant vesicular dispersions results in the formation of Transferosomes [7]. The tranferosomes formulation were given in Table 1.

2.1.2 Drug excipient compatibility studies

The compatibility between the drug and excipients are checked by using the FTIR spectroscopy [8] through KBR pellet technique. By comparing the peaks at particular wavelengths of the functional groups of the molecules, compatibility between drug and excipient is known through FT-IR interpretation.

2.1.3 Physical appearance

The Prepared formulations are checked for their clarity by visual inspection by keeping them against a black and white background.

2.1.4 pH

pH of the formulations were checked by using the digital pH meter.

2.1.5 Shape of the vesicles

Vesicle shape is determined by employing Scanning Electron Microscopy method (SEM) [9]

2.1.6 Entrapment efficiency

Entrapment efficiency [10] is determined by taking the vesicular suspension and centrifugation is carried out for the vesicular suspension. The drug that left is evaluated by collecting the remaining supernatant fluid after centrifugation process.

It is calculated by using the formula

%EE = Drug Loading/Theoritical Drug Loading * 100

2.1.7 Drug content

The amount of drug present in the vesicular structure is determined by using the UV Spectroscopic method.

2.1.8 In Vitro diffusion studies

In vitro diffusion studies [11,12] are conducted by using the franz diffusion cell. It consists of two compartments upper donor compartment and lower receptor compartment. Vesicular suspension is taken in donor compartment and phosphate buffer is taken in receptor compartment. The whole set is placed on the magnetic stirrer. Samples were withdrawn from the receptor compartment at a pre determined intervals and it is replaced with the fresh buffer. Samples withdrawn are analyzed by using the uv-Spectrophotometer at 237nm.

Table 1. Formulation Table of Transferosomes

Formulation Code	Drug (mg)	Soya Lecithin (mg)	Tween80 (mg)	Tween60 (mg)	Span80 (mg)	Span60 (mg)
F1	10	90	10	-	-	-
F2	10	85	15	-	-	-
F3	10	80	20	-	-	-
F4	10	90	--	10	-	-
F5	10	85	-	15	-	-
F6	10	80	-	20	-	-
F7	10	90	-	-	10	-
F8	10	85	-	-	15	-
F9	10	80	-	-	20	-
F10	10	90	-	-	-	10
F11	10	85	-	-	-	15
F12	10	80	-	-	-	20

3. RESULTS AND DISCUSSION

Transferosomes were prepared using the thin film hydration approach in the current investigation. Transferosomes are vesicular structures that are uniquely engineered to transport drugs through the skin.

The recognized UV analytical method was used in this study to estimate the concentration of simvaststin. The maximum wavelength for simvaststin was found to be 245nm. Beers law was followed between the ranges of 5-40µg/ml.

The zeta potential of all the formed transfersomes varied in the range --31.8±1.9 to -48.3± 2.4 mV and -40.8±1.3 mV for F4 as shown in Fig. 6.

3.1 FT-IR Studies

The purpose of this research was to confirm the drug-excipient interaction. The preformulation study involving drug and excipient interactions is must . FTIR spectroscopy is used extensively in this research to achieve it. On an FTIR spectrophotometer, the FTIR spectra were recorded (Bruker, USA). The resolution was $1cm^{-1}$ and the scanning range was 4000 to 600 cm^{-1}.

SIMVASTSTIN:

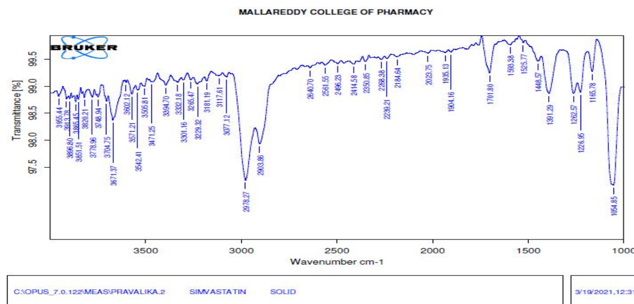

Fig. 3. FTIR of pure drug

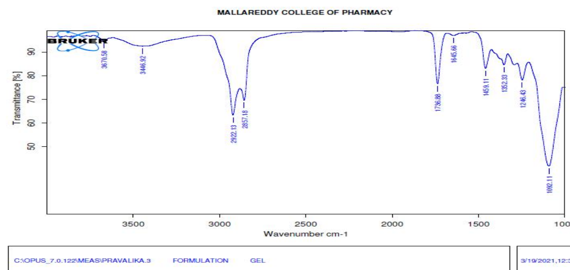

Fig. 4. FTIR of formulation

3.2 Entrapment Efficiency

As the Phospholipids concentration increases entrapment efficient also increases and there is no interference with the surfactant concentration.

3.3 Shape of the Vesicles

From all the evaluation studies as F2 Formulation is considered as the optimized formulation SEM and Zeta potential studies were carried out for F2 Formulation from SEM studies it was found that the vesicle size is 2µm.The transfersomes morphology was analysed by scanning electron microscope. The transfersomes were found to be spherical with good structural composition having a definite boundary as shown in the Fig. 5.

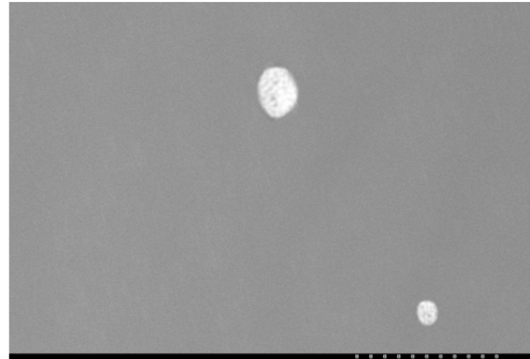

Fig. 5. Surface morphology for F2 formulation

3.4 Drug Content

The amount of drug present in the vesicular structure is determined by using the UV Spectroscopic method.

Table 2. Entrapment Efficiency of F1-F12 formulations

Formulation Code	Percentage of Drug Entrapment
F1	34.3
F2	**65.75**
F3	38.9
F4	43.15
F5	47.58
F6	40.61
F7	55.31
F8	59.35
F9	32.64
F10	42.19
F11	33.55
F12	36.51

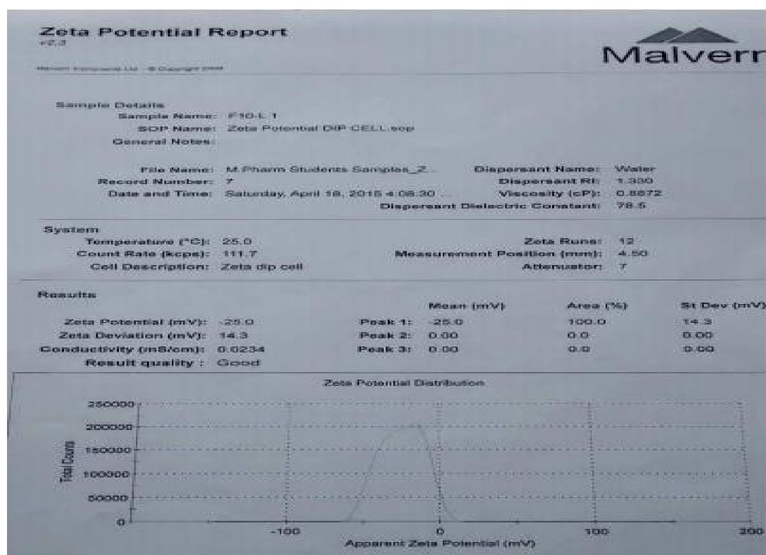

Fig. 6. Zeta potential for F2 formulation

Table 3. Drug Content of F1-F12 Formulation

Formulation Code	Drug Content
F1	92.2
F2	**97.14**
F3	90.1
F4	93.5
F5	92.5
F6	94.5
F7	89.9
F8	95.2
F9	94.3
F10	96.1
F11	92.8
F12	91.5

Table 4. *In-Vitro* Drug Dissolution Studies for Formulations F1-F12

Time (hrs)	% Cumulative drug release 12 formulations(F1-F12)											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	11.4	17.5	13.5	15.0	12.5	12.3	14.5	11.1	15.2	15.7	09.5	08.9
1	22.4	26.2	21.7	24.0	19.0	20.0	21.5	19.0	22.8	22.0	18.5	15.0
2	26.1	33.6	32.3	27.0	25.0	24.1	29.0	25.5	29.8	28.2	26.0	22.9
3	31.5	39.5	39.1	34.0	38.5	37.2	34.5	31.9	37.7	34.3	37.5	30.7
4	39.2	45.8	43.1	41.5	42.9	41.1	41.2	36.2	42.3	39.2	42.6	36.5
5	45.8	56.3	57.3	48.3	51.3	43.3	47.3	42.3	45.3	45.3	49.3	41.3
6	57.3	62.9	63.4	54.3	56.7	51.7	53.8	49.6	51.8	54.2	55.2	47.5
7	61.4	68.2	66.5	61.5	64.7	59.2	62.8	57.8	58.3	61.7	63.2	55.5
8	73.6	74.5	72.9	70.9	69.6	68.7	66.7	64.6	65.9	68.7	68.7	61.7
9	76.5	85.2	79.5	85.5	72.8	73.0	71.0	70.9	71.6	74.9	74.8	68.4
10	85.3	98.2	84.4	90.6	86.6	86.5	81.8	78.5	80.6	82.5	83.9	73.6

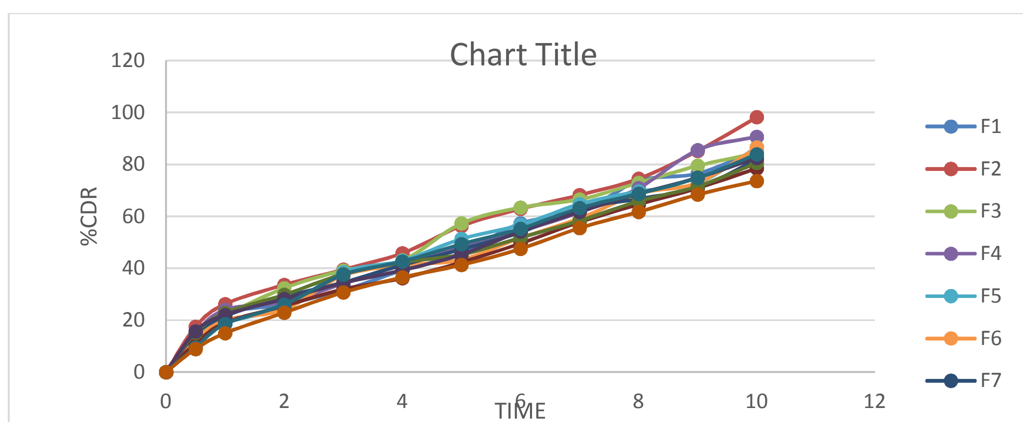

Fig. 7. In-Vitro Drug Diffusion Studies for Formulations F1-F12

3.5 *In Vitro* Diffusion Studies

In vitro diffusion studies are conducted by using the franz diffusion cell. It consists of two compartments upper donor compartment and lower receptor compartment. Vesicular suspension is taken in donor compartment and phosphate buffer is taken in receptor compartment. The whole set is placed on the magnetic stirrer. Samples were withdrawn from

the receptor compartment at a pre determined intervals and it is replaced with the fresh buffer. Samples withdrawn are analyzed by using the uv-Spectrophotometer at 245nm.

4. CONCLUSION

Transferosomes are the novel drug delivery systems where one can deliver both hydrophilic and lipophilic drug and as this system is used to deliver the drug through the transdermal route it can improve the patient compliance too.since this delivery system is designed for topical administration , ideal formulation should show slow drug release for a sufficient time to avoid frequent application and to reduce systemic absorption so based on the entrapment efficiency values and drug release studies formulation F2 was selected as best formulation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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