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Formulation and Characterization of Liposomes containing Clindamycin and Green tea for Anti Acne

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ABSTRACT:
Novel drug delivery carriers such as liposomes are very versatile to suit the delivery of various drug molecules. Clindamycin is generally considered the most effective antibiotic in treatment of acne. Topical clindamycin are used less often due to lower efficacy or increased side effects. Thus, liposomes have been selected for the present work assuming that incorporation of Clindamycin into liposomes may reduce the side effects associated with it. To overcome the potential risk of adverse effects and antibiotic resistance from prescription medications, traditional herbal medicines have been extensively studied as alternative treatments for many diseases. Green tea is one of the best herbal remedies known to treat acne because of its antibacterial properties. Liposomes with drug were prepared using lipid film hydration method and the optimum ratios of the components were determined. The liposomes were characterized for their vesicle size, shape, encapsulation efficiency, drug content and *in-vitro* drug release study. Highest encapsulation efficiency (69.5% and 66.2%) and *in-vitro* drug release (82.5 % and 82.2%) was achieved with formulation F1 and F6 respectively, containing lipid: cholesterol in the ratio of 1:1. Liposomal formulations have been incorporated into carbopol gel base and comparison of that has been made with non liposomal marketed gel. The non liposomal marketed gel showed higher release (90.5%) than liposomal gel of clindamycin (77.5%) and green tea (74.8%) within 24 hours. MIC of formulated liposomal green tea was comparable with the marketed non liposomal gel. Clindamycin found to be more superior against *Micrococcus luteus* than green tea.

KEYWORDS: Liposomes, Clindamycin, Green tea, Anti Acne.

INTRODUCTION:

In recent years, the scientists have channelised their research efforts in development of new drug delivery systems that direct the drug to the specific site in order to improve the therapeutic efficacy and reduce the adverse effects of the drug. Targeting drugs through carrier system has been a control theme of research in therapeutics.

Targeting the drug is usually attained by utilizing a carrier eg. Albumin conjugates, antibodies, lectins, glycoprotein DNA, dextran, polysaccharides, nanoparticle and liposome.

Liposomal drug delivery system [1]

Several researchers are working towards developing novel drug delivery systems like mouth dissolving tablets, sustained and extended release formulations, mucoadhesive systems, transdermal dosage forms, microparticles, microcapsules, nanoparticles, implants, phytosome, liposomes, microspheres etc. of herbs [2]. Liposome, first described in 1965 and initially as models for studying the biological membranes have been considered more frequently as drug carriers for several drugs to reduce toxicity or to deliver the drug at site of action**.** Liposomes are now finding application in commercial development as dosage form. When phospholipids are dispersed in an aqueous phase, hydration of the polar head group of the lipids results in a heterogeneous mixture of structures generally referred to as vesicles, most of which contain multiple lipid bilayers forming concentric spherical shells. These vesicles are known as liposomes.

Liposomes are microscopic vesicles which consist of one or more concentric phospholipid bilayers surrounding an aqueous membrane. This allows a wide range of materials to be incorporated since hydrophilic drugs are entrapped in the aqueous regions and hydrophobic materials are located in the hydrocarbon region. Liposomal system allows for a high accumulation of drug in the skin, with relatively low permeation flux as compared to the conventional dosage system. This will no doubt continue to use of old drug with better and established therapeutic index with minimum side effect. Green tea has been found to have inhibitory effects on the chemical-induced lung tumorigenesis[2]. Liposomes are the lipid vesicles prepared from a variety of natural and synthetic phospholipids are being considered as drug carrying structures. They may serve as a solubilization matrix, as local depot for sustained release of dermally active compounds, as permeation enhancers, or as a rate-limiting membrane barrier for the modulation of systemic absorption of drugs via the skin [3]. Qualities of green tea as an antioxidant, anti mutagenic and anti–carcinogenic, and its role in hypertension prevention, cardiovascular risk modification, ultraviolet radiation protection, body weight management and oral health improvement [4]. Plant are provided source of inspiration novel, drug compound as plant are medicine plant it is important to human health and wellbeing and various drug that produce from trees.Medicinal plant is important for different disease condition like anemia, malaria,diabetes [5]. Clindamycin sensitive both in vivo and in invitro and the strain does not typically become clindamycin resistant during therapy [6]. Infections produced by Staphylococcus aureus are commonly treated by various antibiotics. Clindamycin is one of the potent antibiotics commonly used in the medical management for the effective treatment of infections caused by Staphylococcus [7]. Medical interest in green tea is centred on chemicals known as polypheones (poly-fenols), which have antioxidant properties. It contains more vitamins and minerals than black tea and produces many effects that can fight infection and disease in human bodies [8]. The story of success of liposomes was initiated by Banghum and his colleagues in the early 1960s who observed that smears of egg lecithin reacted with water to form quite intricate structures. These more or less homogenous lipid vesicles were first called smectic mesophases. Later, a colleague of Banghum termed them-more euphoniously-liposomes [9].

Methods of preparation [10]

There are several methods to prepare liposomes each depending on the type of liposome desired (SUV, MLV or LUV). Some commonly used procedures are:

- Thin film hydration
- Sonication
- Extrusion
- French pressure
- Injection of water immiscible solvent
- Injection of water miscible solvents
- By alternative water miscible solvents
- By pH adjustment.
- Detergent Dialysis method
- Reverse phase evaporation.

Mechanism of liposome formation [11]

In order to understand why liposomes are formed when phospholipids are hydrated, it requires a basic understanding of physicochemical features of phospholipids. Phospholipids are amphipathic (having affinity for both aqueous and polar moieties) molecules as they have a hydrophobic tail and a hydrophilic or polar head. In aqueous medium the molecules in self - assembled structures are oriented in such a way that the polar portion of the molecule remains in contact with the polar environment and at the same time shields the non-polar part. Molecules of phosphatidyl choline (PC) are not soluble (rather dispersible) in aqueous medium in the physical chemistry sense, as in aqueous media they align themselves closely in planer bilayer sheets to minimize the unfavourable interactions between the bulk aqueous phase and long hydrocarbon fatty acyl chain. Such interactions are completely eliminated when the sheets fold over themselves to form closed, sealed and concentric vesicles. Lipid vesicles are formed when thin lipid films or lipid cakes are hydrated and stacks of liquid crystalline bilayers become fluid and swell. The hydrated lipid sheets detach during agitation and self close to form large, multilameller vesicles (MLVs). Once these vesicles are formed, a change in the vesicle shape and morphology requires energy input in the form of sonic energy (sonication to get small unilamellar vesicles, SUVs) and mechanical energy (extrusion to get large unilamellar vesicles, LUVs).

Characterization of liposomes [12]

Liposomal formulations after their formulation and processing for a specified purpose are characterized to ensure their predictable *in-vitro* and *in-vivo* performances. The characterization parameters for the purpose of evaluation could be classified into three broad categories, which include physical, chemical and biological parameters. Physical characterization evaluates various parameters including size, shape, surface features, lamellarity, phase behaviour and drug release profile. Biological characterization parameters are helpful in establishing the safety and suitability of the formulations for the *in- vivo* use for therapeutic applications. Some of the parameters characterized in liposome product development are size distribution, surface topology, capture volume, lamellarity and *in-vivo* drug release profile.

Acne Vulgaris [13]

Acne vulgaris, commonly termed acne, is an extremely common disease. It can be found in nearly all teenagers to some degree as well as in women in their 30s. Regardless of severity, acne often has a greater psychologic effect than cutaneous effect. Indeed, most patients overestimate the severity of their disease, while most physicians underestimate its impact on their patients. Studies have shown that people with severe acne as teens are less employable as adults and that self-esteem is low. When combined with other adolescent tensions, acne can be a difficult disease to treat. Acne vulgaris is a disorder of the pilosebaceous unit resulting in the formation of comedones, inflammatory papules, pustules, nodules, cysts and scars. It affects the face and trunk, most commonly presenting in puberty. In a cross-sectional study of 16-year-olds, acne prevalence was 94.4% for males and 92% for females, with 14% having moderate to severe acne. The prevalence of acne after 25 years of age is10% and after 40, 1% in men and 5% in women.[6]Intensive research is focused on antibiotics entrapped in liposomes to enhance their antibacterial activity and pharmacokinetic properties**.**[7] Lipid vesicles as drug carriers significantly influence on drug distribution and reduce toxic side effects during antibiotic therapy. One of the most serious problems of current medicine is the increase in drug resistance among bacterial pathogens, which limits conventional therapy. Many researchers are making efforts to discover new classes of antibacterial drugs, but some studies are focused on improving currently available antibiotics in a new form (liposomal formulations).

MATERIALS AND METHODS:

Instruments Used:

Electronic balance BL-220H, Centrifuge apparatus C- 30BL, UV-VISIBLE spectrophotometer 2202, Orbital Shaker CIS 24BL, Incubator HIS TC 102, Microscope BM- 800, Digital pH meter LT-11

Materials Used:

Clindamycin hydrochloride- Medrich Pharmaceutical Ltd, Bangalore (Gift sample), Green tea leaves- Korakundah, Niligris estate, Tamilnadu, Cholesterol- Hi-Media laboratories Pvt. Ltd, Soya Lecithin- Hi- Media laboratories Pvt. Ltd, Carbopol 940- Ranbaxy chemicals Pvt. Ltd, Triton X- 100-SD fine Chemicals, Mumbai, Methyl hydroxyl Benzoate and Triethanol amine- SD fine Chemicals, Mumbai, Chloroform- Hi- Media laboratories Pvt. Ltd, Hydrochloric acid-Ranbaxy chemicals Pvt. Ltd

METHODOLOGY:

1. Determination of λ_{max} of Clindamycin Hydrochloride

2. Determination of λ_{max} of Green tea

3 Formulation of Liposomes [14]

Preparation of liposomes containing Clindamycin hydrochloride:

- Five liposomal formulations were prepared by thin film hydration method using clindamycin hydrochloride, soya lecithin, and cholesterol.
- The soya lecithin: cholesterol: clindamycin were used in a ratio of 50:50:20 (F1), 60:40:20 (F2), 70:30:20 (F3), 80:20:20 (F4) and 90:10:20 (F5) as shown in table 4.
- Clindamycin hydrochloride was used in each preparation. Clindamycin hydrochloride being water- soluble was incorporated along with aqueous phase.
- A 10 ml solution of chloroform containing cholesterol and soya lecithin was dissolved and kept for evaporation until depositing a thin layer of the solid admixture on the walls of the flask.
- The dried lipid film was hydrated with 10ml of distilled water containing clindamycin by shaking it in vibrator for about 1 hour to disperse the film in form of poly dispersed liposomes.

Preparation of liposomes containing Green tea:

- Five liposomal formulations were prepared by thin film hydration method using green tea, soya lecithin, and cholesterol.
- The soya lecithin: cholesterol: green tea were used in a ratio of 50:50:20 (F6), 60:40:20 (F7), 70:30:20 (F8), 80:20:20 (F9) and 90:10:20 (F10) as shown in the table 4.
- Green tea was used in each preparation. Green tea being water- soluble was incorporated along with aqueous phase.
- A 10 ml solution of chloroform containing cholesterol and soya lecithin was dissolved and kept for evaporation until depositing a thin layer of the solid admixture on the walls of the flask.
- The dried lipid film was hydrated with 10ml of distilled water containing drug by shaking it in vibrator for about 1 hour to disperse the film in form of poly dispersed liposomes.

Table 1: Formulation table of liposomes

Drug Used	Formulations	Formulation Ratios (Lipids: Cholesterol: Drug)
Clindamycin	F_1	50:50:20
	F_2	60:40:20
	F_3	70:30:20
	F_4	80:20:20
	F_5	90:10:20
Green Tea	F_6	50:50:20
	F_7	60:40:20
	F_8	70:30:20
	F_9	80:20:20
	F_{10}	90:10:20

Characterization of Liposomes:

1. Determination of the average size and size distribution in liposomes [15]:

2. Determination of shape of the liposome

3. Drug content [16]

4. Encapsulation efficiency [17]

5. Stability of liposomal suspension [18]

Stability of the selected suspension formulation were carried out at 25^{0}C±2^{0}C / 60% RH±5% RH for 3 months. Effects of temperature and RH on the vesicle size and drug content were studied.

***6.In-vitro* drug release study [19]**

Preparation of Liposomal Gels [20]

Formula:

Carbopol 940	: 2% w/w
Triethanolamine	: q.s.
Methyl hydroxy benzoate	: 0.15 % w/w
Distilled water	: 95.8 % w/w

Procedure:

1. Preparation of Carbopol 940 Gel Base:

Carbopol 940 were sprinkled slowly to 5 ml of water as medium and the medium were continuously stirred to get a uniform dispersion of carbopol. The methyl hydroxy benzoates were pre dissolved in separate portion of water (5 ml) and added to carbopol dispersion. Final volumes were adjusted with water and pH brought to neutral by using the triethanolamine. This preparation were kept overnight, till the carbopol becomes uniform in texture and appearance and the air bubbles are removed.

2. Incorporation of Liposomes into Gel Base:

The drug loaded liposomes were incorporated into gel base (carbopol 940) in such a way that final formulation contained 1 % w/w (0.2 g/10ml liposomal suspension was levigated with 10g of gel base) drug.

Evaluations of Liposomal gel and Marketed Gel:

Prepared liposomal gels and marketed gel (ACNESOL) were evaluated as per follows

Physical Evaluations:

Preliminary evaluations of formulations were carried out as follows:

pH, Viscosity, Spreadability, *In*-vitro drug release, Stability study

RESULTS:

Characterization of Liposomes:

Determination of Average Particle Size of Liposomal Formulation:

The average particle size of liposome was carried out by using the microscopic method. The results are given in tables 2 and 3 and figures 1 and 2.

Tab 2: Size Analysis of Liposomal Formulations (F1)

Size Range		Mid value (d)	Particles (n)*	nd
Eye Piece Division	µm			
0-2	0 - 6.25	3.125	109	340.6
2-4	6.25-12.50	9.375	39	365.6
4-6	12.5-18.75	15.600	2	31.2
6-8	18.75-25	21.870	0	0

*Average of three determinations
Average particle size = ∑ nd = 737.445 =4.91 µm.

∑n 150

In the similar way average particle size of other formulations was calculated.

Table 3: Data of Average Particle Size Determinations

S. No	Formulations	Average Particle Size* (µm±SD)
1	F1	4.91±0.015
2	F2	5.20±0.016
3	F3	5.75±0.0137
4	F4	5.79±0.0205
5	F5	6.25±0.024
6	F6	4.26±0.0127
7	F7	4.57±0.0214
8	F8	5.29±0.0205
9	F9	5.87±0.0169
10	F10	6.58±0.025

* Value represented mean ± S.D, n = 3

Fig 1: Size distribution of clindamycin liposomes

Fig 2: Size distribution of green tea liposomes

Drug content:

Drug content of liposomal formulation were determined according to the procedure. The liposomal suspension were centrifuged and washed three times with distilled water then it was lysed using 1% v/v solution of triton X- 100 by centrifuged for 1 hour at 2000 rpm and 0.5 ml supernatant was separated and analyzed.

Encapsulation efficiency:

The amount of drug entrapped in the liposomes was determined by complete vesicle disruption followed by extraction with 1% v/v solution of triton X- 100. The percentage of entrapped drug in the liposomal formulations is shown in table 4.

Table 4: Table showing the drug content and Encapsulation Efficiency

Formulation	Drug Content* (%)	Encapsulation Efficiency*
F1	71.2±0.71	69.5±0.98
F2	64.2±0.23	56.4±0.37
F3	57.8±0.65	52.6±0.58
F4	53.5±0.77	48.2±0.41
F5	49.3±0.47	45.7±0.95
F6	69.9±0.39	66.2±0.34
F7	56.3±0.87	54.3±0.46
F8	51.5±0.58	47.6±0.74
F9	48.3±0.44	44.4±0.65
F10	43.7±0.37	40.1±0.54

*Value represented mean± S.D, n = 3.

***In-vitro* drug release study:**

The *in-vitro* drug release study was carried out using egg membrane. The release studies were done for continuous 8 hours and then last sample was withdrawn at 24 hours to determine whether drug release was still continued. The results are shown in following tables 5and 6 and figures 3 and 4.

Table 5: *In-vitro* drug release of clindamycin liposomal formulations

Time in Hours	Percentage Cumulative Release				
	F1	F2	F3	F4	F5
1	18.5	26.0	21.9	23.9	26.0
2	26.5	28.2	23.6	25.6	30.5
3	33.5	31.5	32.8	36.8	48.6
4	45.2	39.7	38.4	49.7	57.6
5	52.1	49.2	47.9	57.1	62.2
6	55.7	57.05	56.4	64.3	68.7
7	58.5	59.7	67.2	69.7	72.3
8	60.2	63.6	70.3	73.8	75.6
24	82.5	85.41	89.3	93.5	97.5

Table 6: *In-vitro* drug release of green tea liposomal formulations

Time in Hours	Percentage Cumulative Release				
	F6	F7	F8	F9	F10
1	19.9	19.8	18.4	17.1	19.7
2	28.5	25.2	26.8	28.2	24.8
3	37.5	34.6	36.7	38.9	41.2
4	45.2	44.7	46.3	48.8	52.8
5	48.5	49.6	52.1	56.8	63.1
6	52.3	54.5	55.7	61.9	68.5
7	55.7	56.8	59.1	68.7	74.7
8	57.5	59.3	64.7	71.9	77.8
24	82.2	85.4	88.1	93.3	96.7

Fig 3: Graph showing *in-vitro* drug release of clindamycin liposomal formulations

Fig 4: Graph showing *in-vitro* drug release of green tea liposomal formulations

Stability study of liposomal suspension:

The effect on vesicle size and drug content during stability studies was done at 25^{0}C±2^{0}C / 60%RH±5%RH and results are given in the table7.

Table 7: Effect on vesicle size and drug content during stability

Parameter	Clindamycin suspension [F1]		Green tea suspension [F6]	
	Initial	Final	Initial	Final
Vesicle size	4.91±0.015	5.06±0.018	4.26±0.012	4.75±0.016
Drug content (%)	71.2±0.71	70.2±0.97	69.9±0.39	68.2±0.29

*n=3

Evaluations of Liposomal Gel and Marketed Gel:

Prepared liposomal gels and marketed gel (ACNESOL) were evaluated as per follows

Table 8: Table showing results of physical evaluations

Formulations	pH *	Viscosity* (cps)	Spreadability* (g.cm/sec)
F1	6.6±0.25	9750±23	2.93±0.012
F2	6.8±0.27	8752±24	3.19±0.017
F3	6.8±0.31	7450±41	3.19±0.018
F4	6.2±0.15	2510±29	3.56±0.011
F5	6.5±0.18	2452±25	3.99±0.016
F6	6.8±0.11	6770±26	2.73±0.014
F7	6.2±0.23	6016±28	3.05±0.015
F8	6.6±0.36	4433±21	3.27±0.013
F9	6.3±0.22	4520±28	3.25±0.017
F10	6.9±0.41	7752±23	3.82±0.016
Marketed gel (ACNESOL GEL)	6.6±0.35	9398±29	2.85±0.014

*Value represented mean± S.D, n = 3.

***In-vitro* drug release:**

The *in-vitro* drug release studies were done for F1 and F6 since these formulations have smaller particle size so the penetrations of drug might be increased. The formulation F1 and F6 suspension was incorporated into the gel and *in-vitro* drug release study was done. For this study topical liposomal gel containing 1% drugs was prepared and compared with the marketed non liposomal gel containing 1% of clindamycin. The *in-vitro* drug release was studied using a diffusion cell. The cell consists of two compartments, the donor compartment and receptor compartment. The donor compartment and receptor compartment was in contact with ambient condition of atmosphere. The receptor compartment was in contact with a (100 ml) solution in the receptor compartment (distilled water) was stirred by a rod shaped magnetic bead driven by a magnetic stirrer. The results are given in table 9 and figure 5.

Table 9: *In-vitro* drug release data of formulated liposomal gel and marketed non liposomal gel

Time in Hours	Percentage Cumulative Release		
	Liposomal Green Tea Gel	Liposomal Clindamycin Gel	Marketed Non Liposomal Clindamycin Gel
1	10.6	13.8	18.3
2	16.2	18.5	25.3
3	21.8	23.8	31.2
4	24.3	27.2	39.7
5	29.7	32.6	44.5
6	33.9	35.8	48.3
7	38.3	40.2	55.4
8	43.7	45.6	59.7
24	74.8	77.5	90.5

Fig 5: Graph showing *in-vitro* drug release of formulated liposomal gel Vs marketed non liposomal gel

Stability study of gel:

The effect on viscosity, spreadibility and *in-vitro* drug release during stability was done at 25^{0}C±2^{0}C / 60%RH±5%RH and results are given in the table10.

Tab 10: Effect on viscosity, spreadibility and *in-vitro* drug release during stability

Parameters	Clindamycin liposomal gel [F1]		Green tea liposomal gel [F6]	
	Initial	Final	Initial	Final
Viscosity	9750±23	9790±31	6770±26	6796±31
Spreadability	2.93±0.012	3.01±0.022	2.73±0.014	2.81±0.017
In-vitro drug release	74.8	75.3	77.5	78.1

*n=3

DISCUSSION:

Characterization of Liposome:

Determination of average particle size of liposomal formulation:

The average particle size of liposome was carried out by using the microscopic method. The results are given in table 2 and 3 and figure 1 and 2. The size of liposomal formulations ranged from 4µm – 18.75µm and the average diameter was found to be in the range of 4.91µm – 6.75µm. The influence of liposome size seems to be important parameter. Furthermore, the membranes of MLV are more flexible, and due to their heterogeneity some budding of the liposome bilayer can occur, which could result in better adaptation to the surface of the skin and enable some infiltration of bilayer into the pores in stratum corneum lamellae. Integration of phospholipid molecules with the skin lipids might have served further, to help retain the drug molecules within the skin, thus leading to prolonged presence of drug molecules at the receptor site and localized drug action in the skin. These conclusions suggested the possible use of the prepared formulations as local depots for sustained release of incorporated drug over a prolonged period of time.

Shape of liposomes:

Prepared liposomes were viewed under microscope to study the lamellarity and shape. Most of the vesicle was found to be spherical in shape.

Drug content:

Drug content of liposomal formulation was determined according to the procedure. The result showed (Table-4) 43.7 - 71.2% drug content in the formulation that means there is no degradation of the drug in the process. The drug bearing capacity of liposomes was found to be invariably dependent on drug - lipid ratio employed in the liposomal composition.

Encapsulation efficiency:

The amount of CMP entrapped in the liposomes was determined by complete vesicle disruption followed by extraction with 1% v/v solution of triton X- 100. The percentage of entrapped drug in the liposomal formulations is shown in table 4. The encapsulation efficiency of liposomes constituted from varying concentrations of lipids and cholesterol for loading drug are compared. The encapsulation efficiency of the liposomes was significantly influenced by the presence of cholesterol and its drug to lipid ratio. Liposomes consisting of cholesterol showed significantly increased encapsulation efficiency. The percentage entrapment of clindamycin was found to be maximum with formulation F1 and green tea was found to be maximum with formulation F6. The entrapment efficiency of drug decreased when molar ratio of lipid to cholesterol was changed from 1:1. This may be due to increasing concentration of Cholesterol which may increases lipophilic properties of lipid bilayer hence increase entrapment of drugs, and liposomes with less amount of cholesterol, the lipid bilayer become more fragile which lead to decrease in entrapment efficiency because of leaking of drug during shaking.

***In-vitro* drug release study:**

The *in- vitro* drug release study in distilled water was carried out using egg membrane. The results are shown in tables 5 and 6 and figures 3 and 4. Comparison of results obtained from *in- vitro* drug release studies for all ten formulations has been done. It was found that formulations F1 and F6 shows less drug release rate than other formulations. This may be due to higher drug entrapment. The liposomes prepared by phosphatidyl choline and cholesterol may therefore be used for sustain release. The proportion of cholesterol is important factor in liposome formulation as it influences integrity, stability as well as hydrophilic drug entrapment in liposome. Multilamellar liposomal formulation produced sustained release of drug because of the presence of several lipid bilayers that release the drug slowly over prolonged period of time.

Stability study of liposomal suspension:

Stability of liposomal suspension was carried out for 3 months at temperatures as per ICH guidelines. The results are given in the table7. The accelerated high level temperature and more relative humidity may degrade the liposomal formulations so the stability studies were done at room temperature with ambient humidity. At 25^{0}C ± 2^{0}C/60% RH ±5% RH, insignificant change was observed on drug content and vesicle size. Slight increase in the vesicle size (insignificant) was observed which might be attributed to very slight fusion of the liposomes.

Evaluations of Liposomal Gel and Marketed Gel

pH:

The pH of the formulation from F1 to F5 and F6 to F10 was in between 6.2 to 6.8 and 6.2 to 6.9 respectively, which lie in the normal pH range of the human skin. The results were depicted in Table 8. The pH of the developed formulations was in accordance with that of human skin pH rendering them more acceptable. The developed formulations had pH near to that of skin. So, we can conclude that prepared liposomal gel was suitable for topical application.

Viscosity:

The rheological behaviour of the different formulations of gel was studied using Brookfield viscometer. The results were depicted in Table 8. The results indicated that torque and shear stress increases where as viscosity decreases.

Spreadability:

A comparative study of viscosity and spreadability showed that the viscosity of the formulations increases, spreadability decreases and vice versa. Lesser the time taken for separation of the two slides, better the Spreadability. The results were depicted in Table 8.

***In-vitro* drug release study:**

The *in-vitro* drug release studies were done for F1 and F6 since these formulations have smaller particle size so the penetrations of drug were increased. The formulation F1 and F6 suspension was incorporated into the gel and *in-vitro* drug release study was done. For this study topical liposomal gel containing 1% drugs was prepared according to the procedure and compared with the marketed non liposomal gel containing 1% clindamycin. It was found that non liposomal gel shows higher release than liposomal gel. Release of drug from liposomes embedded into the gel base was significantly slower than the release from liposomal suspension, which confirmed that encapsulation of drug into liposomes, resulted in a prolonged drug release rate. Lower release rate from liposome gel systems compared to basic liposome dispersion could be a result of the influence of the viscosity of the gel matrix followed by slower drug penetration. The results are given in table 10 and figure 5.

Stability study of gel:

Stability of liposomal dispersion was carried out for 3 months at temperatures as per ICH guidelines. The results are given in the table10. The accelerated high level temperature and more relative humidity may degrade the liposomal formulations so the stability studies were done at room temperature with ambient humidity. No significant change was observed on spreadability, viscosity and *in-vitro* drug release at 25^{0}C±2^{0}C / 60% RH±5% RH.

CONCLUSION:

Clindamycin hydrochloride is an antibacterial drug which is used mainly in topical treatment of acne. The marketed clindamycin gel has many limitations such as skin irritation with concomitantly low tolerability and difficulties with patient compliance. Topical clindamycin are used less often due to lower efficacy or increased side effects. Thus the problems associated with these formulations made us to design the novel drug delivery system for Clindamycin. Thus, liposomes have been selected for the present work assuming that incorporation of Clindamycin into liposomes may reduce the side effects associated with it. To overcome the potential risk of adverse effects and antibiotic resistance from prescription medications, traditional herbal medicines have been extensively studied as alternative treatments for many diseases. Green tea is one of the best herbal remedies known to treat acne because of its antibacterial properties. Liposome containing clindamycin and green tea was prepared using different ratio of lipid and cholesterol by thin film hydration method in order to achieve a controlled and prolonged release of drug, when administered by topical route.

The formulation containing lipids and cholesterol with 1:1 ratio is found to be better when it's characterized for various pharmaceutical characters. The drug entrapment study also showed that the significant amount of drug was entrapped in liposomal vesicle. Selected liposomal clindamycin and green tea formulations showed prolonged release even upto 24 hours. So, prepared formulations will be an added advantages, when patients apply these product at bed time. The patient may get better therapeutic effects in terms of permeation and prolongation. Topical formulation of liposome containing Clindamycin and green tea showed much greater antibacterial activity compared to non liposomal marketed formulation in terms of MIC. The MIC of formulated liposomal green tea was comparable with the marketed non liposomal gel. In conclusion, the clindamycin hydrochloride and Green tea containing liposomes have real potential for treatment of Acne vulgaris. Further studies using animal model will throw more light on the effectiveness of the formulation *in- vivo.*

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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