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Preparation, Characterization and Evaluation of Anti-inflammatory Activity of Dexamethasone Topical Liposomal Gel Formulation

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ABSTRACT

The aim of the study was to prepare and evaluate topical gels incorporating liposomes of Dexamethasone base. Multilamellar vesicular (MLVs) liposomes were prepared using thin film hydration method. By subjecting MLVs to sonication using Ultra homogenizer, SUVs were formed. Liposomes were composed of soya lecithin, cholesterol, and dexamethasone. Using these method different concentrations of dexamethasone liposomes were prepared and were successfully incorporated in 1% carbopol gels. Liposomes were characterized for their particle size using zeta sizer and entrapment efficiency by dialysis method. SUVs were evaluated for *in vitro* release. Viscosity of gel formulations was measured using Brookfield viscometer, Drug lipid compatibility was performed using FTIR spectroscopy. Liposomal gels were evaluated for *in vitro* release studies, ex-vivo permeation studies and pharmacodynamic studies (Anti-inflammatory activity). Results showed more localized and sustained effect with Liposomal dexamethasone gels than dexamethasone gel formulation.

Keywords: Dexamethasone, Liposomal gel, Multilamellar vesicles, Small unilamellar vesicles, Anti-inflammatory activity.

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INTRODUCTION

As of today drugs are administered topically or applied to the skin for their action at the site of application. A topical dermatological product is designed to deliver drug into the skin treating dermal disorders with the skin as target organ¹. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. The main challenge in topical drug delivery is to overcome the inherent barrier of the skin, the rate limiting step in topical transport generally occurs at the stratum corneum, the outermost layer of the skin. Liposomes had been intensively studied as drug carrier systems for topical delivery² since they have the potential to enhance drug penetration in to skin, increase therapeutic effectiveness and decrease side effects and act as local depot for sustained release of dermally active component³. One reason of the penetration enhancing effect of liposomes may be caused by the interactions between the intracellular lipid in the skin and the liposome bilayer. The extent of enhancement depends on the liposome size, lipid composition, the lipophilic nature of the drug and on the nature on the skin. However, the liposomes are difficult to directly administered onto the skin for the desired effect. On the other hand, these can be incorporated in to gels and applied on to the skin. It has been found that liposomes incorporated gels are stable⁴. Topical liposomal gel formulations can be used to manipulate the barrier function of the skin and availability of drugs to the viable skin tissues and intended to serve local action and such are formulated to provide prolonged local contact with minimal absorption. Usually it is impossible to incorporate intact liposomes in creams because of interactions between the surface active surfactants and the liposomal layers. Hydrogels are clinically acceptable system which possess good tissue compatibility and suitable rheological properties⁵ resulting in long residue times at the site of application and provide sustained drug concentration and provides localized drug reservoirs for continuous drug delivery, and convenience in handling and ease of application as compared to conventional gels and creams. More over carbopol gels are anionic hydrogels with good buffering capacity, which may contribute to maintain the Skin p^H . Hence Liposomes are incorporated in carbomer hydrogels to obtain semisolid liposomal gel formulation. In this study such an application for Dexamethasone base has been investigated. Dexamethasone ($C_{22}H_{29}FO_5$) is a potent synthetic glucocorticoidal steroidal drug used to treat various inflammatory and autoimmune conditions like Rheumatoid arthritis, oedema, nasal and eye allergies. It has a half-life of 30-52 hours and 70% of protein binding. Oral usage of glucocorticoids causes numerous adverse and toxic effects like stomach upset, disturbances in electrolytic balance, muscle atrophy, negative protein balance (catabolism),

increased appetite leading to significant weight gain etc., and also dexamethasone undergoes first pass metabolism. Hence dexamethasone administration by alternate routes other than oral is preferable. Carrier systems for topical delivery have the potential to enhance the drug penetration into the skin, improve therapeutic effectiveness and decrease side effects. Liposomal carriers can act as a local depot for sustained release of dermally active components. Liposomes seem to be well suited for use on inflamed and damaged skin². Incorporation of liposomes in to gels and further their administration topically have been suggested and investigated. One of the limitations of conventional topical dosage forms on the skin is relatively short residence time of the drug at the site of application. Because a controlled release and prolonged retention on the skin is often required for the desired therapeutic effect. Dexamethasone gels to treat postoperative inflammation after cataract surgery (Dexagel®) are available in the market. Liposomal dexamethasone-diclofenac combinations for local osteoarthritis treatment as reported⁶, Dexamethasone Liposomal topical gel preparations are not in the market. The issue of topical delivery dexamethasone has been investigated by several novel delivery approaches. So in this study, we aimed to prepare liposomes of dexamethasone and incorporate them in to a gel and further evaluate their anti-inflammatory activity.

MATERIALS AND METHOD

Dexamethasone Base purchased from Yarrow Chem. Products, Mumbai. Carbapol 934 gifted by Genuine Chemical Co., Mumbai, Soya lecithin and Cholesterol from Hi Media Laboratories Pvt. Ltd, Chloroform and Methanol from Finar Chemicals, Ahmedabad, Propylene glycol and Carrageenan from S.D. Fine chem. Ltd, Mumbai. The other chemical were of analytical reagent grade.

Preparation of Dexamethasone Liposomes

Multi lamellar liposomes (MLV) consisting of dexamethasone were prepared using the thin film hydration method. Dexamethasone, soya lecithin, cholesterol were dissolved in mixture of chloroform and methanol (9:1) in a round bottom flask. A thin layer of lipid containing drug was allowed to form on the walls of the flask by evaporating the mixture of organic solvents under reduced pressure using a rotary evaporator (Laborota 4000, Heidolph, Germany), for 8 min, at a temperature 80°C and 30 rpm, The obtained thin film layer was dried overnight in a vacuum oven to ensure the complete removal of organic solvent. Then thin film layer was hydrated with 20ml of saline phosphate buffer (7.4), while vortexing the flask, which was maintained at a temperature of 70°C and 90rpm for 45 minutes. The Liposomal suspension was then centrifuged at 3000rpm for

30 min, to separate the free drug and then pellet of MLVs was resuspended in 10ml volume of saline buffer and centrifuged the suspension to form a pellet. To the pellet formed in second centrifuge add 5ml of saline buffer. The resulting suspension was subjected for sonication for 15min(3min each cycle,5 cycles, 150V/T Probe) using a Ultra-homogenizer(Biologics inc.,USA) to get small unilamellar vesicles(SUVs).The lipid dispersion should begin to clarify to yield a slightly hazy transparent solution. Temperature was maintained at around 65°C.So formed SUVs liposomal solution contains free drug also along with drug encapsulated in SUVs, Dialysis method is employed for SUVs to remove the free drug contents from the SUVs solution. To enhance the drug encapsulation, the surface area occupied by phospholipids and drug was optimized by adding glass beads in the round bottom flask and the MLVs were prepared. MLVs thus prepared were used to prepare SUVs. There is an increase in encapsulation with increase in surface area with addition of glass beads. For the current study three batches of liposomes were prepared and composition is shown in Table (1)

Table 1: Formulation Ingredients of Dexamethasone Base Liposomes

Formulations	Ingredients		
	Dexamethasone	Soyalecithin	Cholesterol
I	15mg	100mg	5mg
II	30mg	100mg	5mg
III	60mg	100mg	5mg

- 1) Saline phosphate buffer-20ml,
- 2) Organic solvent: Chloroform-9ml, Methanol-1ml;

Formulation of Gel for Liposomal Dispersion⁷

As a vehicle for incorporation of dexamethasone liposomes for topical delivery anionic carbopol hydrogel was made. Carbopol934(1g) was dispersed in demineralized water (88ml) by stirring at 800rpm (Remi, Mumbai India) for 60 minutes. Then propylene glycol (10ml) was added and the mixture was neutralized by drop wise addition of 10% NaOH⁸. Mixing was continued until a transparent gel appeared, while the amount of the base was adjusted to achieve a gel with pH 6.5.

Incorporation of dexamethasone Liposomes in to the gel

Liposomes containing dexamethasone were mixed into the 1% (w/w) Carbopol hydrogel by an electrical mixer 25rpm for 5min to get Dexamethasone liposomal gel(DEXLG)

Characterization of Dexamethasone Liposomal gel (DEXLG)

Physicochemical properties of DEXLG⁹

The liposomal enriched hydrogels were characterized for their Physicochemical Properties such as colour, odour and pH.

Microscopy

Prepared liposomes (MLVs and SUVs) were observed under Binocular microscope (PZRM-700, Quasmo, India) at suitable magnification.

Particle size and zeta potential of liposome enriched hydrogels

The mean size, polydispersity index of the size distribution and zeta potential of liposomes was determined by photon correlation spectroscopy (PCS) using Zetasizer 3000 HAS (Malvern Instruments, Malvern, UK). The DEXL'S were diluted 1:1000 with the aqueous phase of the formulation to get a suitable kilo counts per second (kcps). Analysis was performed at 25°C with an angle of detection of 90°C. Each value reported is the¹⁰ average of three measurements. The poly dispersity index measures the size distribution of the liposome population.

Entrapment efficiency

Separation of untrapped drug from prepared liposome was carried out by Dialysis bag method. In this method liposomal suspension was taken in a dialysis bag which suspended in 200ml of phosphate buffer (7.4) and maintained with stirring at 100rpm throughout the experiment. At fixed time intervals 15,30,45,60 min. & then for every hour for 24hrs replace volume of 100ml buffer every time point to maintain sink conditions. Measure the absorbance. Note the time when absorbance started to decrease& calculate the amount released till a decrease in the release is noted. This is the amount of the free drug present in the SUVs. This was subtracted from the drug amount that is there in liposomal suspension obtained from MLVs supernatant absorbance value.

$$\% \text{Entrapment efficiency} = \frac{\text{Entrapped drug (mg)}}{\text{Total drug Added (mg)}}$$

***In vitro* release studies of DEXG and DEXLG**

In vitro release studies for DEXLG were performed using dialysis membrane method. Dialysis was soaked in warm water at 45°C for 30minutes before using it for release study. To the membrane DEXLG were applied with some friction. This membrane was clamped carefully clamped to one end of the hollow glass tube and considered as the donor compartment¹¹. The dissolution medium i.e., saline phosphate buffer (7.4) (100ml) was taken in the receiver compartment. The donor compartment was immersed in the receiver compartment. The rpm of the system was maintained by using magnetic stirrer and bead. Samples (10ml) were removed from the receptor compartment at predetermined intervals and replaced with fresh medium to maintain sink conditions immediately. As the dexamethasone is an hydrophobic drug accurate estimation amount of drug release at regular interval can be estimated by vortexing the specified quantity of aliquots samples with excess amount methanol(because dexamethasone soluble in methanol) .The samples were

analyzed using UV-Visible spectrophotometer at 240.4nm. Using a mixture of saline buffer and methanol as a blank solution. Data obtained from the *in vitro* release studies were fitted to various kinetic equations to find out the mechanism of dexamethasone release from liposomal gel¹²

***Ex vivo* Permeation studies**

Preparation of skin

The abdominal hair of Wister rats, weighing 140 ± 20 g, was trimmed using trimmer 24hr before treatment. After anaesthetizing the rat with ether, the abdominal skin was surgically removed from the animal and adhering subcutaneous fat was carefully cleaned. To remove extraneous debris and leachable enzymes, the dermal side of the skin was in contact with a saline solution for 1hr before starting the diffusion experiment. All surgical and experimental procedure were reviewed and approved by the animal and ethics review committee, Vaagdevi College of pharmacy, Warangal, Andhra Pradesh, India. A system employing improved Franz diffusion cells with a diffusion area of 4.15cm^2 was used for permeation studies. The excised rat skin was set in a place with the stratum corneum facing the donor compartment. Dexamethasone gel and (0.5ml of liposomal suspension in 6gm) was applied to the skin surface in the donor compartment and the receptor compartment was filled with saline phosphate buffer pH 7.4(24ml). During the experiments, the diffusion cell was maintain at $37 \pm 0.5^\circ\text{C}$ and stirred at 500 rpm. After application of the test formulation on the donor side, at fixed intervals, 5 ml of aliquots were withdrawn from receiver compartment through side tube and analyzed by UV-Visible spectrophotometer at 240.4nm.

Rheological Behaviour

The rheological measurements were performed on a Brookfield Programmable Rheometer LVDV-III + CP 230 equipped with a cone and plate test geometry (plate diameter 20 mm, cone angle 4°C). All measurements were carried out at a temperature of $20 \pm 0.1^\circ\text{C}$. The rheological properties of the developed hydrogels¹³ containing liposomes dexamethasone loaded were studied by continuous shear investigations, which were performed in order to evaluate the shear rate [1/s] as function of shear stress [Pa]. This study started applying 0 Pa up to a maximum shear stress of 100 Pa and the resulting shear rate was measured¹⁴

Drug- Excipient Compatibility Study

Dexamethasone base, soya lecithin, and dexamethasone liposomes were subjected to FTIR analysis so as to predict if there is any interaction is possible between the drug and the polymer.

Pharmacodynamic Studies: Anti-inflammatory Activity by Carrageenan induced rat hind paw edema method¹⁵. The animals used for *in vivo* experiments were adult male Wister rats (140–160

gm) purchased from the Mahaveer Enterprises (Hyderabad, India). The animals were kept under standard laboratory conditions, at $25 \pm 1^{\circ}\text{C}$ and $55 \pm 5\%$ relative humidity with a 12 hr light/dark cycle. The animals were housed in polypropylene cages, with free access to a standard laboratory diet and water. The study was approved by the Institutional Animal and Ethics Committee (Vaagdevi College of Pharmacy, Warangal, and Andhra Pradesh, India). Registration number-1047/ac/07/CPCSEA, 24-04-2007 Carrageenan induced paw edema method was used to study the *in vivo* performance of the prepared drug delivery system. Rats were fasted for 12hrs prior to experiment while allowing access to water throughout the experiment.

Group I: served as control, administered normal saline solution orally.

Group II: served as Standard, administered 0.6 mg/kg of dexamethasone solution orally.

Group III: received dexamethasone gel topically. (6gm of gel with 3.3 mg of dexamethasone).

Group IV: received dexamethasone liposomal gel formulation I topically(6gm of gel with 0.73mg of dexamethasone loaded liposomes).

Group V: received dexamethasone liposomal gel formulation II topically(6gm of gel with 1.754 mg of dexamethasone loaded liposomes).

Group VI: received dexamethasone liposomal gel formulation III topically(6gm of gel with 4.875mg of dexamethasone loaded liposomes).

Anti-inflammatory activity was determined by measuring change in the volume of inflamed paw, produced by injection of carrageenan (0.1 ml of 1% w/v) using plethysmometer (INCO, India). Male wistar rats selected for the study were weighed and marks were made on the right hind paw just behind tibia-tarsal junction on each animal. Thus, every time the paw was dipped in the plethysmograph (mercury displacement method) up to the fixed mark to ensure constant paw volume. Wister rats were divided into six groups including one controlled group with each group comprising of 3 animals. The paw volume was noted at 0, 1, 2, 3, 4, 6, 8, and 24 hr. The formulation was applied topically to the albino rats of respective groups, near the right hind paw by rubbing 20times excluding the animals of controlled group¹⁶. The controlled group animals were injected with saline (0.9% NaCl) containing no drug. After 30 min of topical application of formulations, 0.1 ml of 1% w/v carrageenan (in 0.9% normal saline) was injected in the sub planter region of the right hind paw of rats. The initial reading just after injection and subsequent paw volumes was measured up to 24 h. The percent inhibition of edema induced by carrageenan was calculated for each group using the following equation:

$$\% \text{ inhibition of edema} = 100(1 - (a-x/b-y))$$

Where a = mean paw volume of treated animals after carrageenan injection

x = mean paw volume of treated animals before carrageenan injection

b = mean paw volume of control animals after carrageenan injection

y = mean paw volume of control animals before carrageenan injection

RESULTS AND DISCUSSION

Dexamethasone Liposomal Gels: Preparation, Characterization and *in vivo* Evaluation

Physicochemical Properties

The liposome suspensions were white in colour, odourless and fluid in nature. Gels loaded with liposome suspensions were colourless, odourless with smooth appearance.

Microscopy

All the batches of the liposomes prepared were viewed under binocular compound microscope. Figure 1 shows the Microscopic view of dexamethasone multilamellar vesicular liposomes. The SUVs incorporated into the gels were of nanorange size and could not be seen even under 100X of the microscope.



A (10 X)



B (40 X)

Figure 1: Microscopic view of Dexamethasone base Multilamellar vesicular liposomes

Particle size and Zeta potential

Particle size, Poly dispersity index (PDI) and Zeta potential values of the liposomes incorporated in gels were found to be DEXLG I----- 249.8, 0.282, -46.3 ± 9.61 ,

DEXLG II-----171.9, 0.334, -30.8 ± 11.7 , DEXLG III-----142.8, 0.432, -28.0 ± 10.8 .

Entrapment Efficiency

The Entrapment efficiency values were determined for three batches of liposomes were observed as 49.26%, 58.48%, 81.2%.

In Vitro Release studies

The % Cumulative amount release of dexamethasone from DEXLGI, DEXLGII, DEXLGIII s were investigated for period of 24hr; each sample was analyzed. Figure (2) shows the *in vitro* release profile of DEXLs. DEXLGI, DEXLGII, DEXLGIII could prolong the drug release by the fact that the drug molecules are entrapped in the lipid matrix. The amount of drug release at the end of 24hr in DEXG, DEXLGI, DEXLGII, and DEXLGIII formulations was found to be 0.22mg, 0.78mg, 1.48mg, and 3.22mg respectively. All the three liposomal formulations showed controlled drug release and also an increase in release rate was observed after 24hr. The log percent cumulative drug released was plotted as a function of log time and the slope of the curves was determined as values of diffusional release exponent (η). The values of diffusional release exponent (η) from the straight lines were noted to be 0.596, 0.6955, and 0.7278 in liposomal gel formulations of DEXLGI, DEXLGII, DEXLGIII respectively which showed that release pattern of drug from the formulations follows a non Fickian pattern. Thus the formulations with higher drug contents show the higher release rate constants.

EX Vivo Permeation studies

The cumulative amount of dexamethasone permeated from DEXLGI, DEXLGII, DEXLGIII, and DEXG were investigated for a period of 24 hr. Figure 3 shows the *ex vivo* permeation profile of DEXLGI, DEXLGII, DEXLGIII, and DEXG formulations respectively. The release kinetics was established by determining the diffusional release exponent from the plot of cumulative drug permeated versus log time. This plot yielded straight line from which diffusional release exponent (η) were calculated.

In liposomal gel and drug dispersed formulations respectively, which showed that the cumulative amount of drug permeated in 24hr were 207.36, 450.755, 1449.5, 3143.52 $\mu\text{g}/\text{cm}^2$ for DEXLGI, DEXLGII, DEXLGIII and DEXG formulations respectively. The release kinetics was established by determining the diffusional release exponent from plot yielded a straight line from which diffusional rate exponent (η) were calculated and found to be 0.667, 0.734, 0.867 in liposomal gel

formulations of DEXLGI,DEXLGII,DEXLGIII respectively. This showed that release of drug from these formulations followed a non Fickian pattern.

Rheological Behaviour

The rheological status of a semisolid drug carrier system is a very important physical parameter. Rheology measurements provide essential information about different aspects concerning semisolid preparations. Moreover, rheological measurements are valuable tools in quality control of ingredients and final products. Concerning application and performance on skin they provide essential information. Furthermore, drug release from semisolid vehicles is influenced by the rheological behaviour. The rheological behaviour of hydrogels loaded with liposomes and drug dispersed gel were evaluated and the flow curve of the gels was shown in Figure (4) and (5).Formulations with different concentrations of drug loaded liposomal gels and drug dispersed gel showed the similar rheological behaviour.

Pharmacodynamic studies

The *in vivo* performance of DEXLG s and DEXG were carried out using carrageenan induced rat paw edema method. Formulations DEXLG s under study decreased the inflammation. In DEXLGII formulation the maximum inhibition was observed at 6th hr with higher value 82.9%, and even after 24hr, 32.2% inhibition was observed .In DEXLGIII formulation the maximum inhibition was observed at 4hr with higher value 84.2%,and even after 24hr, 38.4% inhibition was observed. However, in case of oral administration, inhibition was displayed at 2hr with magnitude of 79.4% and just after 4hr it scored below 40% and in case of DEXG administration, inhibition was displayed at 3 hr with magnitude of 75.4% and just after 6hr scored below 50% Figure (6) In comparison to orally administered DEX and DEXG, the formulations DEXLGII, DEXLGIII which applied topically gave good results. The maximum inhibition for DEXLGII, DEXLGIII was observed at 6hr, 4hr and the inhibition was maintained up to an 8hr and also even after 24hr inhibition observed. The Anti-inflammatory activities of the formulations DEXLGII, DEXLGIII were maintained for longer time due to slow release of the drug and localised action. This was attributed to gel structure and the surface active properties of the gel.

Drug-Excipient Compatibility study

The IR spectral analysis of dexamethasone alone showed that the principal peaks were observed at wave numbers of 3471.99, 2939.27, 1704.78, 1618.55, 1407.08, 1057.11 and 893.1. In the spectra of the dexamethasone liposomes 1739.86, 1071.62 were observed for the dexamethasone. However, some additional peaks were observed with physical mixtures, which could be due to the presence of polymer. These results suggest that there is no interaction between the drug and

polymer used in the polymer used in the present study. FTIR Profiles of dexamethasone, soya lecithin, cholesterol, and placebo liposomes and the drug and polymer were in (Figure 7, 8 and 9)

Table 2: *In vitro* release of Dexamethasone base gel and Dexamethasone Liposomal gels

Time	DEXG	DEXLGI	DEXLGII	DEXLGIII
0.5	0.50949	0.033	0.0613	0.225
1	0.65934	0.0429	0.084	0.301
2	0.8924	0.06	0.114	0.437
3	1.172	0.068	0.1565	0.524
4	1.59	0.08	0.189	0.625
5	1.83	0.093	0.2318	0.732
6	2.02	0.1055	0.269	0.832
7	2.3	0.117	0.306	0.952
8	2.34	0.135	0.348	1.104
9	2.53	0.157	0.374	1.14
10	2.667	0.192	0.425	1.234
11	2.92	0.197	0.46	1.339
12	3.086	0.201	0.503	1.453
24	3.226	0.22	0.522	1.48

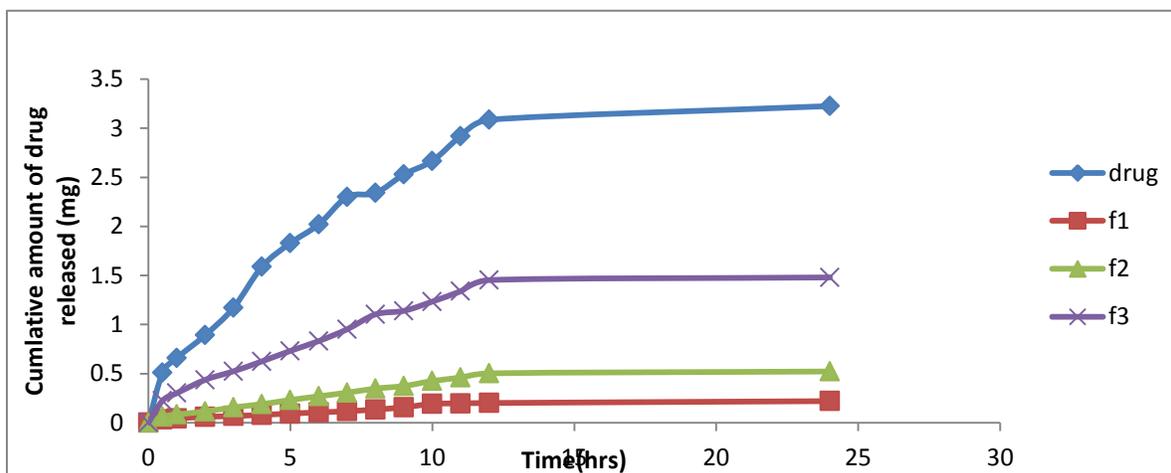


Figure 2: *In vitro* release of Dexamethasone gel and from Liposomal gels

Table 3: *Ex vivo* permeation of Dexamethasone base gel and from gels enriched with Liposomes

Time	DEXG	DEXLGI	DEXLGII	DEXLGIII
1	509.49	25.44	63.2	184.68
2	755.91	30.72	73.4	214.5
3	972.36	41.7	108.62	321.75
4	1215.45	67.68	147.168	90.75
5	1545.12	80.88	190.612	591.5
6	1961.37	95.52	232.4	680.8
7	2171.16	120.4	299.36	887.2
8	2534.13	150.2	374.92	1036.7
24	3143.52	207.36	517.42	1449.5

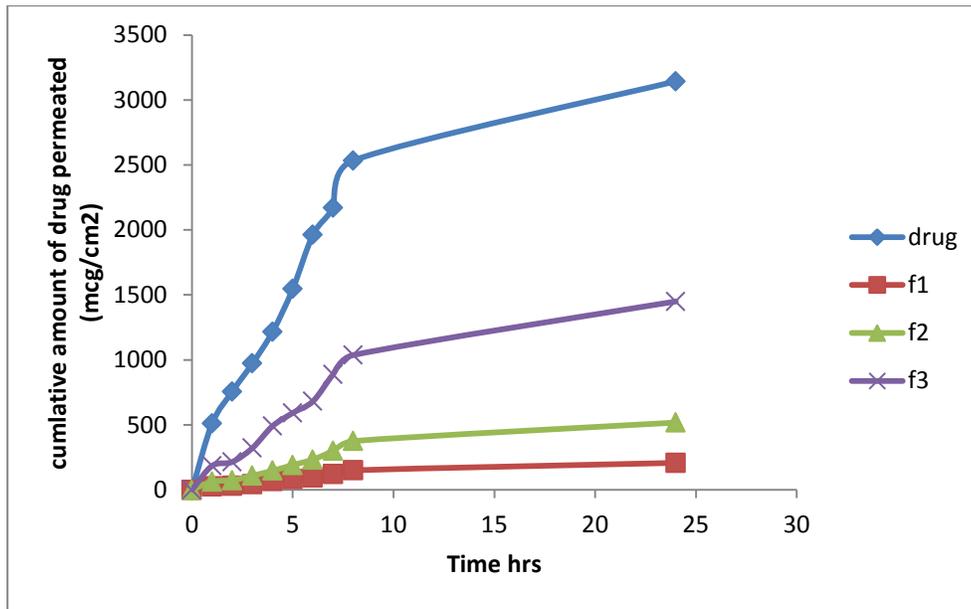


Figure 3: Ex vivo permeation of Dexamethasone base gel and from gels enriched with Liposomes

Table 4: Shear rates of liposomes containing hydrogels as a function of shear stress

Shear Stress (Pa)	Shear rate (1/s)
1	10.3
2	13.1
4	17.1
5	19.1
10	23.7
20	27.1
50	31.3
100	34.1

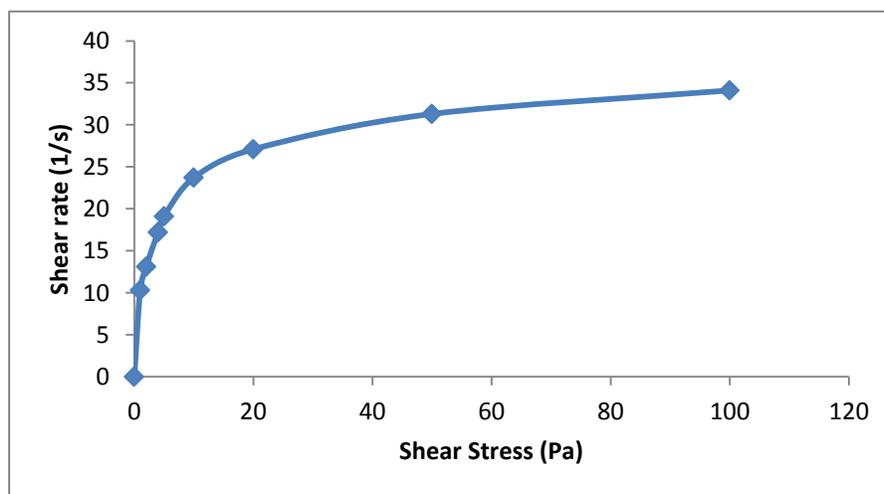
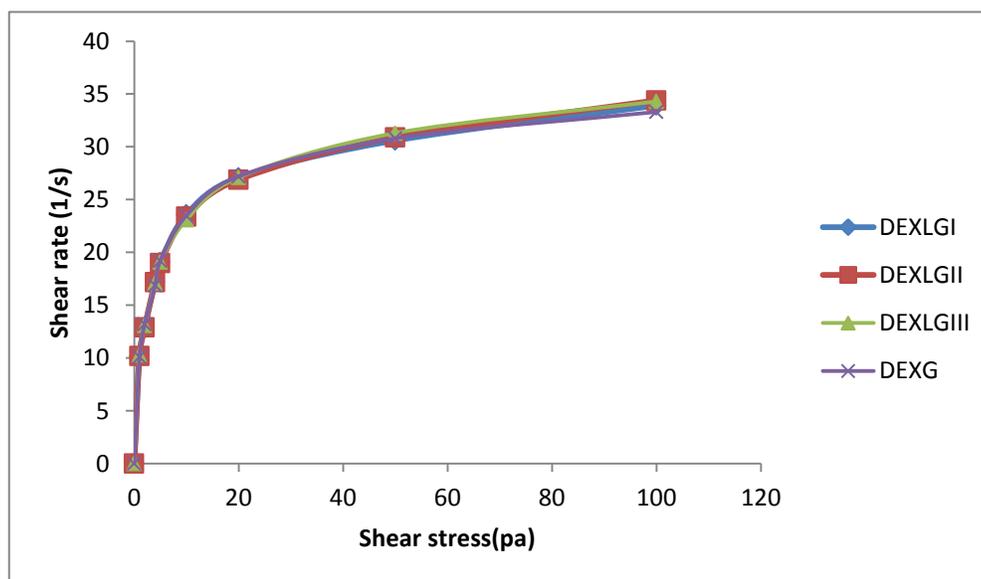


Figure 4: Shear rates of Liposomes containing hydrogels as a function Of shear stress

Table 5: Shear rates of liposomes containing hydrogels and drug containing gel as a function of shear stress

Shear stress	DEXLGI	DEXLGII	DEXLGIII	DEXG
0	0	0	0	0
1	10.2	10.2	10.3	10.1
2	12.9	12.9	13.1	13.2
4	17.2	17.2	17.1	16.9
5	19.1	19	19.1	19.2
10	23.6	23.4	23.1	23.5
20	27.1	26.9	27.1	27.2
50	30.6	30.9	31.3	30.8
100	33.9	34.4	34.3	33.3

**Figure 5: Shear rates of Liposomes containing hydrogels as a function of shear stress****Table 6: Anti-inflammatory activity of Dexamethasone liposome enriched hydro gels after topical application in comparison to oral administration and Dexamethasone base gel in carrageenan induced rat paw edema (n=3)**

Time	DEXG	Oral	DEXLGI	DEXLGII	DEXLGIII
1	63.8	58.6	48.6	42.8	52.7
2	70.2	76.4	60.2	57.4	63.2
3	75.4	64.6	76.8	74.8	79.4
4	56.8	52.8	79.2	80.4	84.2
6	49.4	40.6	82.5	84.9	80.6
8	34.6	29.8	75.9	72.9	78.3
24	18.8	12.7	29.5	32.6	38.4

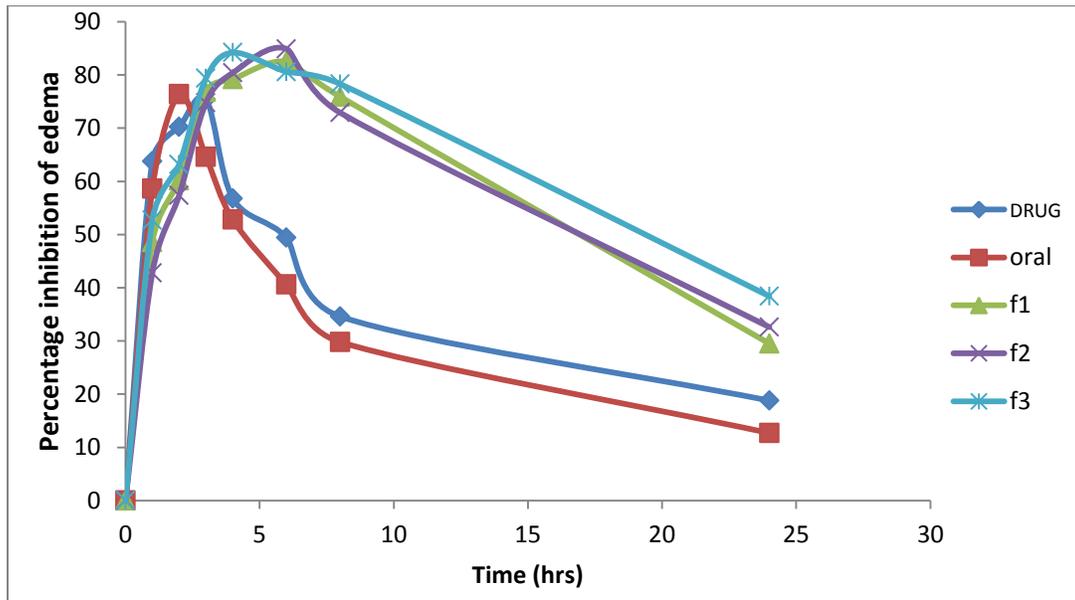


Figure6: Anti-inflammatory activity of Dexamethasone liposome enriched hydrogels after topical application in comparison to oral administration and Dexamethasone base gel in carrageenan induced rat paw edema (n=3)

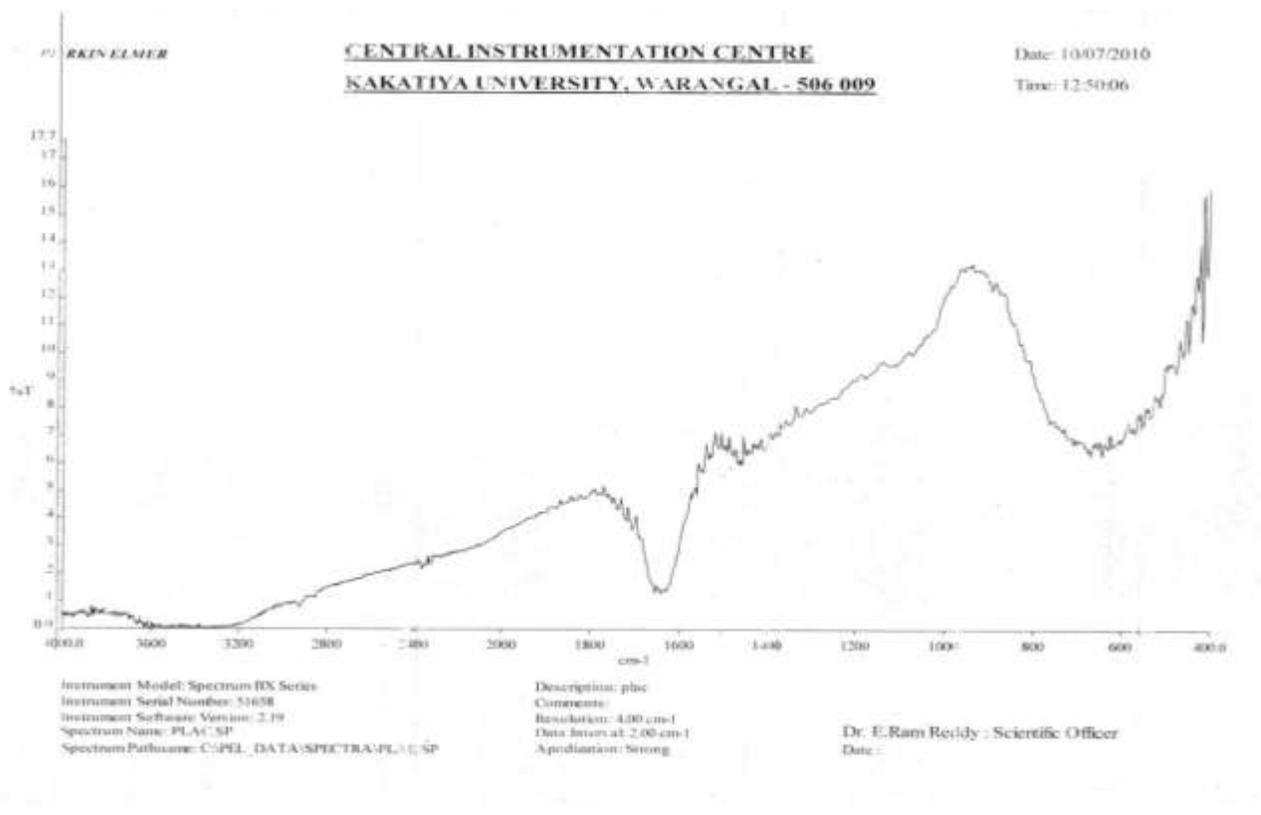


Figure 7: FTIR Spectra of Placebo Liposome

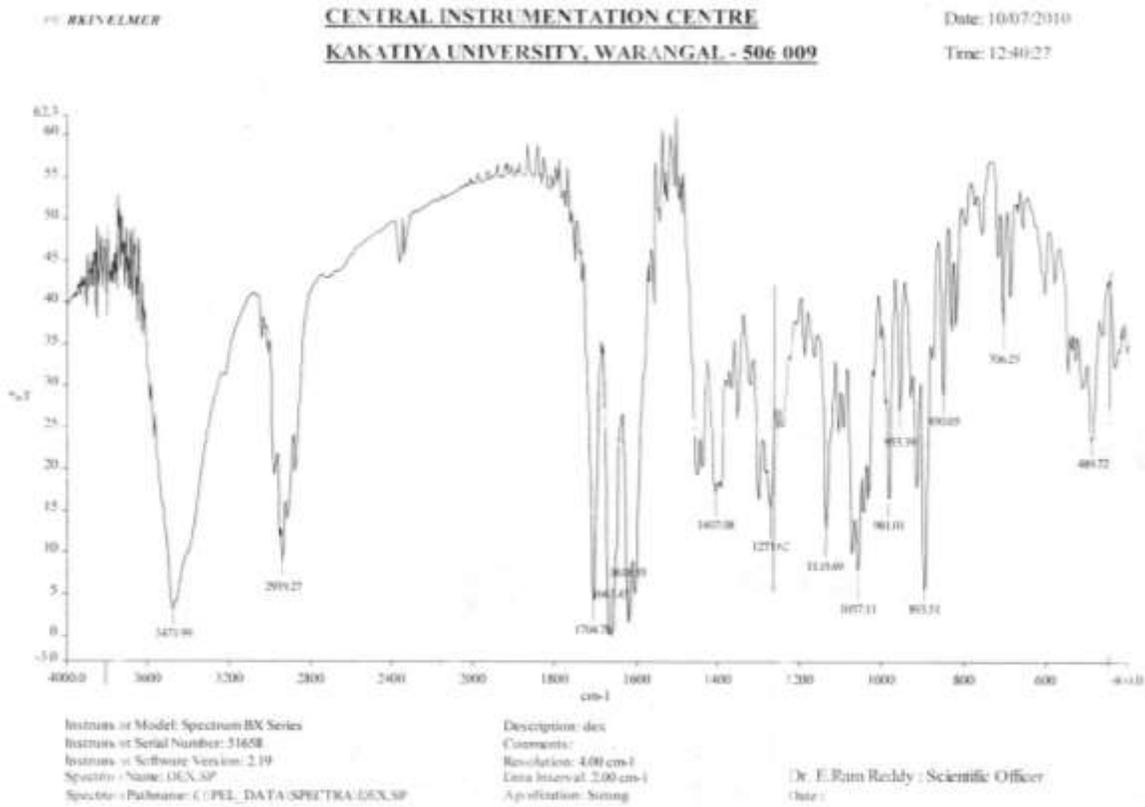


Figure 8: FTIR Spectra of Dexamethasone Base

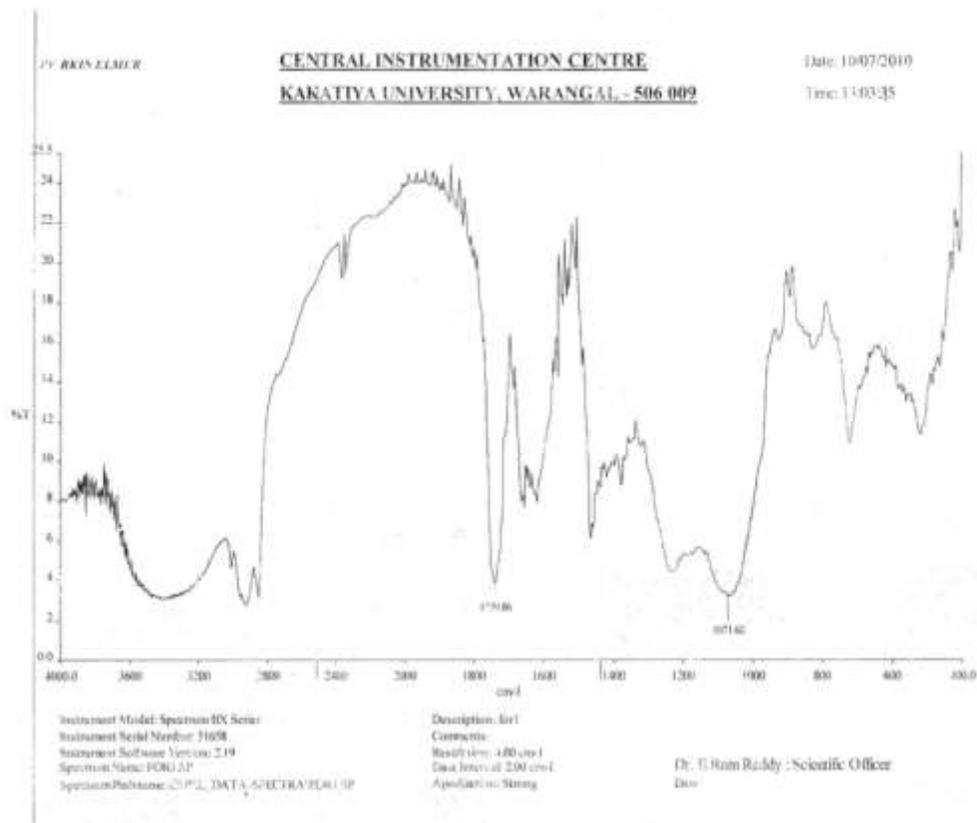


Figure 9: FTIR Spectra of Dexamethasone base loaded Liposomes

CONCLUSION

Dexamethasone being a hydrophobic drug having high first pass metabolism and severe side effects upon oral administration. To avoid first pass metabolism and to enhance the localized drug action, Dexamethasone liposomes were prepared by film hydration method and successfully incorporated into carbopol gel for topical delivery. Gels enriched with liposomes possessed a localized drug release over a period of 24 hrs. Topical administration of Dexamethasone liposomal gels shows good anti-inflammatory activity in comparison to oral and conventional gel administration.

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