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Curcumin-phospholipid supramolecular complex for transdermal application

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ABSTRACT

The objective of this work was to develop a transdermal therapeutic system loaded with Curcumin-Phospholipid Supramolecular Complex (CMN-PLC) for systemic delivery of Curcumin (CMN). The phospholipid complexation technique was investigated to overcome the solubility and stability problem of CMN to deliver it transdermally. Differential Scanning Calorimetry (DSC) and Scanning Electron Microscopy (SEM) study were performed to investigate the interaction of drug and PL. The CMN-PLC was incorporated in polymeric matrix of EudragitRS100 and EudragitRL100 of different ratio. The films were evaluated physicochemically. The drug permeation study was performed across excised pig ear epidermis. Surface morphology of transdermal films were studied by SEM before and after permeation study. The optimized formulation was evaluated for Anti-inflammatory efficacy on wistar rats by carrageenan induced rat paw edema method. Stability study of formulations was performed at ambient and accelerated conditions. The transdermal formulations showed good physicochemical properties like drug content, thickness, film folding endurance, moisture content and moisture uptake. The permeation study showed that the formulation followed zero order permeation kinetics. Minute irregularities and a few holes were observed in the photomicrograph of film which suggested the drug release was by simple diffusion mechanism. The optimized formulation CF5 showed significant anti-inflammatory efficacy than the oral control group ($p < 0.05$). Stability study data suggested the formulations loaded with CMN-PLC possessed maximum stability. The results of the experiments showed that the CMN can be effectively delivered by transdermal route by complexing it supramolecularly with PL and incorporating within transdermal matrix systems for sustained action and prolonged use.

Key words: Supramolecular, Transdermal, Permeation, Anti-inflammatory, Stability.

INTRODUCTION

Curcumin is chemically Diferuloyl methane, an active ingredient obtained from the rhizome of *Curcuma longa*, belongings to family Zingiberaceae. It has been used by the asian countries for more than 200 years in cookery, dying, medicine and cosmetics. Curcumin is having wide range of medicinal properties like anti-inflammatory, anti-oxidant, chemopreventive and chemotherapeutic activity [1]. Despites of its diverse therapeutic activity, use of curcumin in clinical practice is still not wide enough due to its short half-life and low bioavailability following oral administration and poor water solubility.

Formulations like microspheres [2], solid lipid nanoparticles [3], polymeric nanoparticles [4], topical gel formulations [5] and transdermal patches using penetration enhancers [6] have already been developed. A number of research works have been performed to increase the bioavailability of curcumin orally, among them phospholipid complexation of curcumin is a relatively easier and effective method [7, 8]. The curcumin phospholipid complex has been reported to have increased aqueous solubility and stability than pure curcumin and superior to liposomal and neosomal formulations of curcumin [9]. Some reports suggest the phospholipid complexes can be administered topically and transdermally [10, 11]. So attempt has been made to deliver curcumin transdermally for constant and prolonged action. The phopspholipid moiety envelops the drug molecule and is supramolecularly complexed with it providing the drug a good skin penetrating power and good stability. The transdermal therapeutic system is a promising mean for delivering the drug in a controlled manner across the skin. EudragitRS100 and EudragitRL100 are used in different ratio to achieve the desired drug release rate [12].

Aim of the present study was to develop a transdermal therapeutic system loaded with CMN-PLC, to study its drug permeation profile, therapeutic efficacy and stability profile. The CMN-PLC was prepared, characterized and the prepared complex was then incorporated into polymeric films. The films were evaluated for their physicochemical properties. To establish the transdermal route for the CMN-PLC, the polymeric films containing pure CMN and films containing physical mixture of CMN and PL and film loaded with complex were prepared and evaluated. The physicochemical parameters and maximum cumulative drug release profile were studied. The drug permeation study was performed through excised pig ear epidermis. Carrageenan induced rat hind paw edema method was performed to study the Anti-inflammatory efficacy of the transdermal films. Stability study at ambient and accelerated conditions was performed. The first order degradation rate constant of the three batches of formulations were determined and compared to investigate the effect of complexation on stability of the formulation.

MATERIALS AND METHODS

The Phospholipid was purchased from ACROS Organics, New York, USA. Curcumin was purchased from Himedia Laboratories Pvt. Ltd., Mumbai, India. EudragitRL100 and EudragitRS100 were purchased from Rohm Pharma, Germany. Dichloromethane, methanol, n-Hexane, Polyvinylalcohol, Di-n-butylphthalate and other chemicals were procured from Himedia Laboratories Pvt. Ltd., Mumbai, India.

Preparation of Curcumin-Phospholipid Supramolecular Complex (CMN-PLC)

The CMN-PLC was prepared by the method used by Maiti *et al.* (2007) with a slight modification [7]. The complex was prepared by taking stoichiometric ratio (1:1) of curcumin (74mg) and Phospholipid (150 mg) in a round bottom flask and refluxed with dichloromethane (20 ml) at a temperature of 50°C for 3 hours. Then the complex was evaporated slightly up to 10 ml and n-Hexane (5 ml) was added in two lots with continuous agitation to enhance the precipitation and remove traces of dichloromethane. The complex was then evaporated completely and again vacuum dried. The yield of the complex was determined to be 82%. The prepared complex was then stored in amber coloured glass bottle in a desiccator.

Determination of curcumin content in the complex

The content of curcumin in the prepared complex was determined spectrophotometrically [13]. Accurately weighed 5 mg of the complex was added to 10 ml of methanol and stirred in a magnetic stirrer for 2 hour for the complex to dissolve completely. 1 ml of the sample was withdrawn, diluted suitably and quantified spectrophotometrically (SPECTRASCAN UV 2600, Thermoscientific, India) at 421 nm.

Characterization of CMN-PLC

The prepared complex was characterized by Scanning Electron Microscopy (SEM) and Differential Scanning Calorimetry (DSC) [14].

Scanning Electron Microscopy

The CMN-PLC were coated with gold and their surface morphology was viewed and photographed with Scanning Electron Microscope (JSM-6360, Jeol, Japan) [15,16].

Differential Scanning Calorimetry (DSC)
The DSC study of CMN, PL, physical mixture of CMN and PL and the prepared CMN- PLC was performed. The samples were packed in aluminium crimp cells and heated with a rate of 10°C/min from 30 - 250°C with the help of Jade DSC, Perkin Elmer, USA. The transition peaks were observed for each sample and compared to identify any possible interaction.

Preparation of Matrix type Transdermal films
Matrix type transdermal films were prepared by solvent evaporation method. Eudragit RL100 and Eudragit RS100 were used as the film forming polymer [12] and di-n-butylphthalate was used as plasticizer. Polymer ratio of 1 : 1, 1 : 2, 1 : 3, 2 : 1 and 3 : 1 of Eudragit RS100 and Eudragit RL100 were selected respectively, for the preparation of film by taking a total polymer weight of 500mg (**Table 1**). The polymers were first dissolved in 5ml of dichloromethane, and then 30% V/W of polymer weight of plasticizer was added and stirred for 1 h. Then the CMN-PLC was added to the polymeric solution and stirred slowly for 30 minute for complete dissolution of the complex. The polymer mixture containing CMN-PLC was then poured uniformly on an aluminium mould containing previously prepared polyvinyl alcohol (5% W/V) backing membrane and allowed for controlled evaporation. After complete drying the films were wrapped with aluminium foil and stored in an amber coloured, air tight glass container until use.

Transdermal films loaded with pure CMN and films loaded with physical mixture of CMN and phospholipid were prepared as separate batch for comparison study by taking the same polymer ratio, solvent system, plasticizer and equivalent amount of drug.

Table 1. Formulations loaded with CMN-PLC.

Formulation code	Polymer ratio (Eudragit RL100 : EudragitRS100)	Percent of plasticizer Di-n-Butyl phthalate (%v/w)	Weight equivalent of CMN-PLC (mg)
CF1	1:1	30	25
CF2	1:2	30	25
CF3	1:3	30	25
CF4	2:1	30	25
CF5	3:1	30	25

Physicochemical evaluation of the transdermal films
The transdermal films were evaluated for their thickness, drug content, % moisture content, % moisture uptake and folding endurance.

Measurement of thickness of the films
The thickness of the patches was measured at nine different points using a screw gauge and average thickness was recorded.

Determination of drug content in the films
Drug contents in the films were estimated by placing a 1 cm^2 patch in a 10 ml volumetric flask. 5 ml of methanol was added to the flask and the flask was shaken for 2 hours in a water bath shaker for extraction of the drug from the film. The volume was made up to 10 ml with methanol. The resulting solution was analysed spectrophotometrically at 421nm.

Determination of % Moisture content of the films
The films were weighed and kept in a desiccators containing fused silica for 36 h until it showed a constant weight. The moisture content was calculated from the difference between the constant weight taken and the initial weight [17].

Determination of % Moisture uptake of the films
The films were weighed accurately and exposed to 84% relative humidity created by saturated solution by Potassium chloride. After 3 days, the films were weighed until it showed constant weight. The study was performed at room temperature [18].

Determination of Film Folding endurance
This was determined by repeatedly folding the film at the same place until it broke. The number of times the film could be folded at the same place without breaking or cracking gave the value of folding endurance. Films of 2 cm^2 area were cut from each formulation and folding endurance was measured thrice for each formulation and noted with Standard Deviation for all the formulations [19].

***Ex-vivo* skin permeation study**
The comparative permeation study was performed for all the three batches of formulations mentioned previously. The permeation profile of the prepared films were determined using Franz type diffusion cell containing full thickness excised pig ear epidermis, which is generally accepted model of permeation study across human skin [20, 21, 22] . The prepared epidermis was so placed that the dorsal surface attached to the drug matrix side. The holder containing the skin and the formulation was then placed on the reservoir compartment of the diffusion cell containing 50% PEG400 maintained at 37°C thermostatically and stirred by a magnetic stirrer. One ml sample was withdrawn at regular interval and fresh receptor fluid solution was added upon each removal. Absorbance of samples were read spectrophotometrically against blank. Cumulative amount of drug permeated per unit area was calculated for all the formulations and compared.

Surface Morphology Study by Scanning Electron Microscopy (SEM)
SEM is a well known method for study of surface behaviour of films, including the presence or absence of impurities on the surface and prediction of elastic nature of films [17]. The surface morphology of the transdermal film before and after skin permeation experiment was analysed by SEM (JEOL-JSM 6360, Japan).

***In Vitro* Anti-inflammatory efficacy study by Carrageenan induced Rat hind paw edema method**
The protocol for anti-inflammatory study was approved by the Institutional Animal Ethical Commettee, Department of Pharmaceutical Sciences, Dibrugarh University (Registration No. 1576/ Go/a/11/CPCSEA, Approval No: IAEC/DU/19). The studies were performed on wistar rats of both sex and are within the weight range of 130 – 150g. The animals after being procured were provided normal food and water *ab libitum* for 10 days and were kept in 12 hour light and dark cycle each for the animals to get adopted with the local environmental conditions.

The animals were divided into four different groups each containing six rats. The hair from the back of the rat was removed with the help of a marketed depilatory preparation 12 hour prior to the beginning of experiment. All the animals were injected with 100 µL of 1% homogeneous suspension of carrageenan in double distilled water into the sub-plantar region of the right hind paw beyond the tibia tarsal region and the paw were marked properly. Test group of rats were treated with the transdermal formulation (CF5) by securely adhering the patch on dorsal abdominal skin one hour prior to carrageenan injection. At the same time, control group received the vehicle (saline), while the oral control group were orally treated with pure curcumin. The placebo control group was treated with blank formulations without any drug. The paw volume was measured at 0, 1, 2, 4, 8, 12 and 24h after carrageenan administration by volume displacement method using a Digital Plethysmometer (Orchid Scientific, PLM 01, Nashik, India). The percentage edema rate and inhibition percentage of edema were calculated for each animal group from the mean volume with respect to vehicle treated control group [17, 23].

Stability study
The best formulations of the three batches were subjected to stability study at ambient condition and at accelerated condition according to International Conference on Harmonization (ICH) guidelines. Formulation CF5, PF5 and DF5 were selected from each batch. The drug content of each formulation was determined at 0, 30, 45, 60 and 90 days. The degradation rate constant of each formulation was determined to predict the stability. The log % drug remained against time (month) curve was plotted and slope was determined [6, 24, 25]. The first order degradation rate constant was calculated by the following formula and stability of formulations was studied.

$$slope = -k/2.303,$$

where, k = degradation rate constant.

Statistical Analysis
The data obtained in this study have been expressed as Mean ± S.D (Standard Deviation). The data were subjected to statistical analysis and assessed by one way Analysis of Variance (ANOVA) following Dunnett's t – test. p value of less than 0.05 was considered as evidence of a significant difference.

RESULTS AND DISCUSSION

Preparation and drug content study in CMN-PLC
The method of preparation of the CMN-PLC was simple and reproducible. The CMN content as determined by the spectrophotometric method was 32.6%.

Characterization of CMN-PLC
The complex formation was confirmed by SEM study and DSC study.

Scanning Electron Microscopy study
The surface morphology from the photomicrograph appeared as amorphous particles arranged in clusters, with spherical bulging outs, no impurities or crystalline substance on the surface and probably the drug molecule was uniformly dispersed on surface or entrapped within the phospholipid molecule [**Fig.1**].

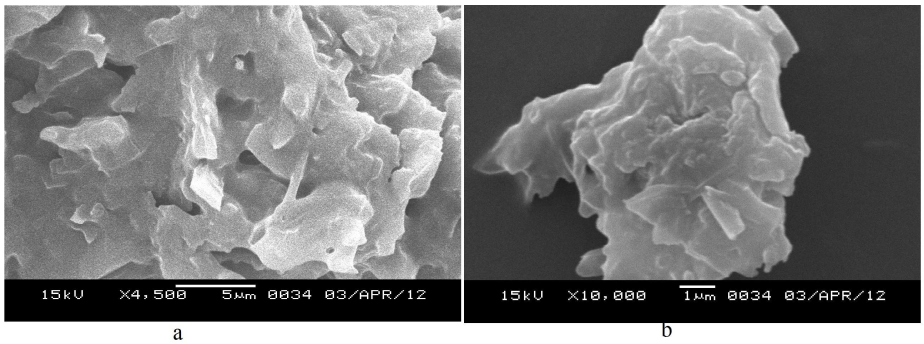


Fig.1. Photomicrograph of CMN-PLC at a magnification 4,5000 × (a) and 10,000 × (b).

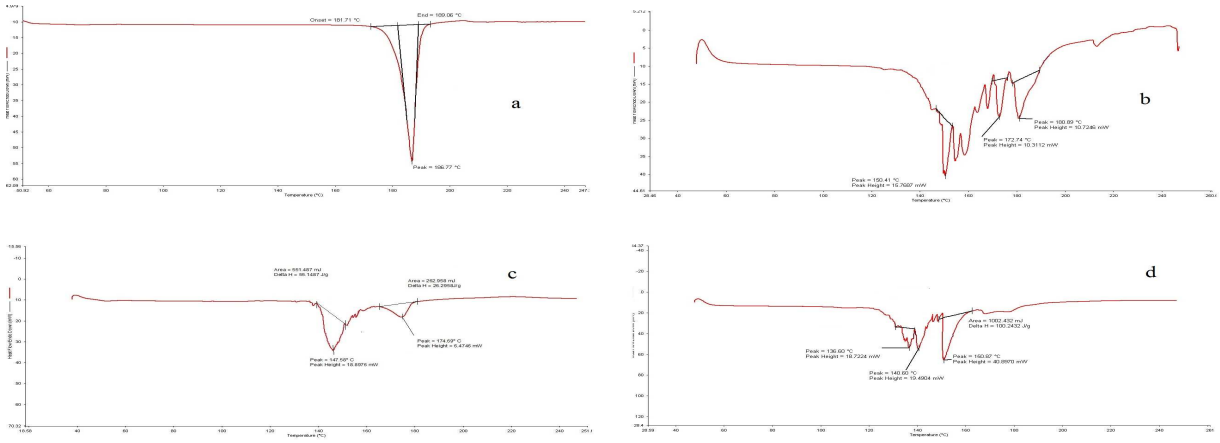


Fig.2. DSC Thermogram of pure CMN (a), PL (b), physical mixture of CMN and PL (c) and CMN-PLC (d).

Differential Scanning Calorimetry Analysis
The DSC provides maximum information about the possible interactions between two substances. DSC thermogram of pure CMN showed a sharp crystalline peak at 186.77°C, with an onset temperature of 181.71°C. The phospholipid shows multiple sharp peaks within a temperature range of 150.41 to 180.89°C, which was due to phase transition from gel to liquid crystalline state with the melting of non-polar

hydrocarbon tail of phospholipids [9, 15]. The thermogram of physical mixture showed two distinct peaks at 147.58°C, which might be due to phase transition of PL and a broad and blunt peak at 174.69°C, which was due to the drug moiety solubilised in melted PL to some extent and lost its crystallinity [7]. The thermogram of CMN-PLC showed different peaks than the physical mixture. Appearance of two new peaks at 136.60°C and 140.60°C were observed. The peak of drug was absent which was very prominent in the thermogram of pure CMN and physical mixture [**Fig.2**]. It was clear from the thermograms that the original peaks of drugs and PL were changed in case of the CMN-PLC, which indicated an interaction to have occurred in the CMN-PLC, which might be a supramolecular bonding involving hydrophobic interaction or Hydrogen bonding or both regarding the chemical structure of both the moieties [26].

Physicochemical evaluation of prepared transdermal films

The prepared CMN-PLC was incorporated into the transdermal film at different polymer ratio and evaluated for their physicochemical parameters. The thicknesses of films were within a range of 0.23-0.34 mm. The formulated films showed enough folding endurance. Moisture content and moisture uptake values were sufficiently less and were dependent upon the concentration of Eudragit RL100. This indicated that the formulation could resist microbial contamination and was less bulky and less brittle [27]. The Eudragit RL100 is having more quaternary ammonium groups, so more prone to hydration [28]; hence moisture uptake and moisture content were more for formulations having higher concentration of Eudragit RL100. The percentage drug content values were between 94.0 – 96.2%, which was good enough for all formulations (**Table 2**).

Table 2. Physico-chemical characterization of the formulation loaded with CMN-PLC.

Formulation code	Thickness (Mean ± S.D) mm	Folding endurance (Mean ± S.D)	% Moisture content (Mean ± S.D)	% moisture Uptake (Mean ± S.D)	% drug content (Mean ± S.D)
CF1	0.25 ± 0.03	260 ± 21	4.576 ± 0.481	7.432 ± 0.681	94.8 ± 1.2
CF2	0.23 ± 0.01	268 ± 18	4.441 ± 0.785	7.402 ± 0.563	96.2 ± 1.0
CF3	0.31 ± 0.02	280 ± 15	4.346 ± 0.609	6.720 ± 0.939	95.6 ± 1.6
CF4	0.29 ± 0.03	257 ± 12	4.800 ± 0.967	7.961 ± 0.925	94.0 ± 2.1
CF5	0.34 ± 0.02	266 ± 16	5.337 ± 1.015	8.129 ± 0.872	94.8 ± 1.1

S.D = Standard deviation, n = 6.

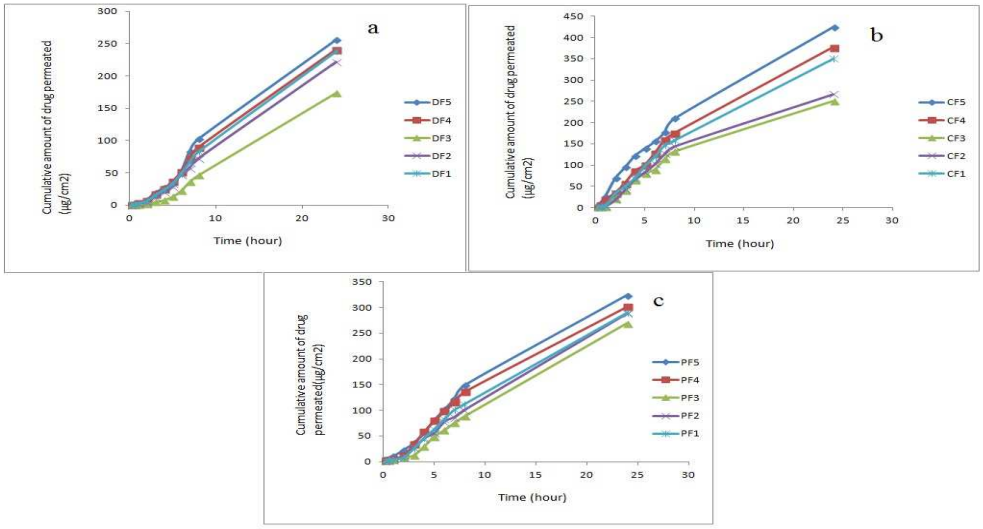


Fig. 3. Zero order permeation profile of the formulations loaded with Pure CMN (a), formulation loaded CMN- PLC (b), formulation loaded with Physical mixture (c).

***In vitro* skin permeation study**

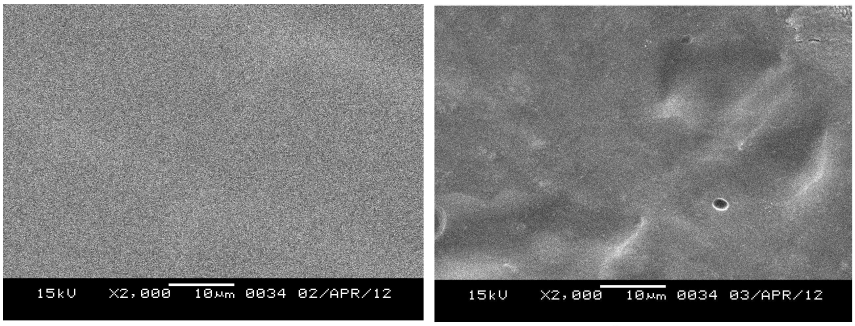
The *In-vitro* permeation study is the most important tool to predict the drug release behaviour of formulations *in vivo*. The permeation profile of all the three batches of transdermal formulations (Films

loaded with pure CMN, Physical mixture of CMN & PL and CMN-PLC) indicated that the CMN-PLC loaded films were superior to the other batches. The formulation loaded with CMN-PLC showed maximum % cumulative release after 24 hour. The steady state flux was determined from the slope of the zero order permeation kinetics study. The value of flux was found to be superior for films loaded with CMN-PLC. The formulation CF5 was having maximum % cumulative drug release (**Fig. 3**).

This clearly indicated that the increase in flux and % cumulative release of the formulation loaded with the complex was due to higher concentration of more hydrophilic polymer concentration and increased solubility of the CMN-PLC than pure CMN, where the solubility factor served much for this improvement. The process of drug release in controlled and sustained release formulations follows diffusion mechanism. When the matrix patch comes in contact with the eluting fluid medium thermodynamically compatible with the polymer, the fluid is absorbed and dissolution of polymer begins [29], which causes change in the entanglement of drug with the polymer chain by mobilization and transport of drug molecule across the skin adhered to the matrix patch. Molecular diffusion through polymers is an effective, simple and reliable mean to design sustained or controlled release formulations of various drug moeities [30] and diffusion of drug molecule in such multipolymeric matrix depends on structural and morphological parameters of the polymeric blend. So the Eudragit RL100 and Eudragit RS100 at different proportion were selected to observe the diffusivity, since the variation in the three dimensional network of the polymer chain will control the release of the drug molecule [31]. **Fig.3** illustrates the zero order permeation rates of the formulations of each batch. Comparing the zero order permeation kinetics profile it can be predicted that the improved permeation profile of the formulations loaded with CMN-PLC was due to the higher aqueous solubility as well as more permeability property of the CMN-PLC through the excised porcine epidermis [32]. The polymer ratio of 3 : 1 of Eudragit RL100 : Eudragit RS100 was shown to have good film forming as well as drug release properties.

Surface Morphology Study of the films

The surface morphology of the transdermal films loaded with CMN-PLC before and after skin permeation study was scanned. **Fig 4.a** shows the uniform distribution of the complex in the polymer matrix. The photomicrograph revealed that the complex was molecularly dispersed in the matrix showing no irregularities or any sorts of impurities on the surface. **Fig 4.b** shows the behaviour of the film after permeation study. The films showed some depressions along with a few holes but still the surface was observed to be elastic enough [33]. The SEM study indicated the drug release pattern is by simple diffusion mechanism.



a b

Fig. 4. SEM micrograph of Transdermal film Loaded with CMN-PLC; Before permeation study (a) and After permeation study (b).

Anti-inflammatory Efficacy study

The CF5 formulation was selected regarding its maximum flux rate and maximum cumulative percentage permeation in *in vitro* permeation study. This formulation was compared with oral control, to detect whether the curcumin upon complexation helpful in increasing therapeutic activity by transdermal route or not. The percentage edema rate and percentage edema inhibition rate were calculated (**Table 3**). The obtained data were analysed statistically and the result revealed that the oral control group was not significantly different from the control group ($p > 0.05$), where as, the test formulation was significantly

different from the control and oral control group ($p < 0.05$). The placebo control group was also found insignificant with the control group ($p > 0.05$), which indicates that the blank formulation has negligible effect on reduction of inflammation.

Table 3. *In Vitro* Anti-inflammatory efficacy study by Carrageenan induced Rat hind paw edema method.

Group	N	Edema Rate (%)[a] [Inhibition Rate (%)]						
		0 h	1 h	2 h	4 h	8 h	12 h	24 h
Control	6	0 ± 0.03	41.30 ± 0.7	49.12 ± 0.9	54.13 ± 1.0	56.24 ± 0.5	54.21 ± 1.1	48.27 ± 1.1
Oral[b]	6	0 ± 0.02 [0]	41.22 ± 0.8 [0.19]	46.97 ± 0.6 [4.37]	51.28 ± 0.6 [5.26]	52.64 ± 0.9 [6.40]	50.86 ± 1.0 [6.17]	46.66 ± 0.6 [3.30]
Placebo[c]	6	0 ± 0.01 [0]	41.29 ± 0.8 [0.02]	48.87 ± 1.1 [0.50]	54.08 ± 1.1 [0.09]	56.01 ± 0.5 [0.90]	54.15 ± 0.8 [0.11]	47.60 ± 1.3 [1.38]
Test[d]	6	0 ± 0.03 [0]	39.12 ± 1.1 [5.27]	43.10 ± 0.9 [12.23]	46.54 ± 1.2 [14.01]	44.86 ± 0.7 [20.23]	37.13 ± 0.8 [31.5]	17.20 ± 0.9 [64.36]

N = Number of animal in each group.; [a] = values are Mean ± S.D.; [b] = Analysis of Variance (ANOVA) analysis showing the Oral control group was not significantly different from control group ($p > 0.05$).; [c] = Analysis of Variance (ANOVA) analysis showing the placebo control group was not significantly different from control group ($p > 0.05$).; [d] = Analysis of Variance (ANOVA) analysis showing the test group was significantly different from control group and Oral control group ($p < 0.05$).

The experiment showed the increased response of CMN-PLC transdermally was possibly due to the major contribution of increased permeability and stability in the systemic circulation for a longer period than the uncomplexed CMN which was administered via oral route. The CMN is reported to have high systemic metabolism as such and often a higher dose of CMN is needed for achieving the therapeutic response upon oral administration. The CMN upon phospholipid complexation needs lesser amount of drug to produce the therapeutic response by virtue of its increased systemic stability and possesses an excellent penetration power across the stratum corneum.

Stability Study of the transdermal films

The stability of CMN-PLC in the systemic environment was predictable from the pharmacological study. The effect of phospholipid complexation on the stability of CMN in the transdermal formulation in *in vitro* condition was studied at ambient and accelerated conditions. The concentration of drug degraded and log % remained were calculated at each point of time during the stability study. The curves of log % drug remained against the time (months) were plotted. Straight lines were obtained in all the cases (R^2=0.9745 - 0.9931), which indicated that the degradation of drug in the transdermal therapeutic system followed first order rate. The first order drug degradation rate constants (k) were determined at both ambient and accelerated conditions from the slopes (**Table 4**). The values indicated that the formulation CF5 possessed a slower degradation rate than the other two formulations. As it is clear from the shelf-life determination equation, the shelf-life and rate constant are inversely proportional to each other [24]. The CF5 formulation had a degradation rate constant of 1.151×10^{-3} and 2.303×10^{-3} at ambient and accelerated condition respectively, which were the least value among all the test formulations. Hence, it can be stated that the CF5 formulation had a maximum shelf-life. The complexed CMN possesses better stability profile than the uncomplexed CMN and physical mixture in a transdermal therapeutic system. The physical properties of the formulations were also retained after the stability study.

Table 4. Comparative stability study of the best formulations of each batch.

Formulations	Temperature (Kelvin)	R^2	Slope	$K \times 10^{-3}$ ($Month^{-1}$)
Film Loaded with pure CMN (DF5)[a]	298	0.984	-0.0011	2.533
	313	0.978	-0.0022	5.066
Film Loaded with Physical mixture of CMN and PL (PF5)[a]	298	0.983	-0.0009	2.072
	313	0.993	-0.0019	4.375
Film loaded with CMN-PLC (CF5)[a]	298	0.985	-0.0005	1.151
	313	0.974	-0.001	2.303

[a] = the drug content was determined as Mean ± S.D (n = 6) and first order degradation curve was plotted.

The CMN is a potent anti-inflammatory agent possessing similar activity like NSAIDS but not having any adverse effects. Its oral bioavailability is very less due to excessive faecal elimination. Topical and transdermal approaches for delivering pure CMN are difficult because of its high lipophilicity. But, the CMN upon supramolecular complexation showed an increased stability in the transdermal films and it provides sufficient hydrophilicity to the drug for transdermal use. The transdermal therapeutic system is a novel method for controlled drug delivery and is well known for maintaining therapeutic drug level in blood more steadily than any other therapeutic systems and carrier mediated systems. The systemic effect of the drug is retained after complexation, besides that the phospholipids have their own beneficial effect to the body. CMN upon supramolecular complexation may be applicable for systemic delivery of CMN to achieve the successful clinical treatment of many other life threatening diseases by transdermal therapeutic system.

CONCLUSION

The experiments on the complexation of CMN with PL and to deliver it through transdermal route were observed to be possible by incorporating the prepared CMN-PLC within a matrix of EudragitRL100 and EudragitRS100 of suitable proportion. The polymers were having good film forming properties. The formulations incorporated with the CMN-PLC showed a good release kinetics and sound physicochemical and stability profile as compared to the films loaded with pure CMN and physical mixture of CMN and PL. Apart from that the CMN-PLC incorporated transdermal therapeutic system was having better Anti-inflammatory efficacy on wistar rats than the oral route. From this comparative study it has been made clear that the solubility and stability of CMN is improved markedly apart from the good skin penetrating property upon complexation with PL. No interaction of the CMN-PLC with the polymers, plasticizers, casting solvent and backing membrane was observed. The formulations were more stable at room temperature. The Phospholipid complexation may possibly create new path for formulating transdermal therapeutic system of number of phytoconstituents and synthetic pharmaceutically active molecules.

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