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Preparation Of Deep Eutectic Mixture Gel Containing Prednisolone For Skin Delivery

Alka Sharma[1], Sheetal Sharma[2*], Shikha Kumari[3], Vaishali Sharma[4], Prerna Thakur[5], Aman Kumar Sharma[6], Bhartendu Sharma[7]

[1]Assistant Professor, School of Pharmacy and Emerging Sciences, Baddi University of Emerging Sciences & Technology, Baddi Makhnumajra- 173205, H.P. India.

[2*]Assistant Professor, School of Pharmacy and Emerging Sciences, Baddi University of Emerging Sciences &Technology, Baddi Makhnumajra- 173205, H.P. India.

[3]Assistant Professor, KC Institute of Pharmaceutical Sciences, UNA-174303, H.P. India.

[4, 5]Assistant Professor, School of Pharmaceutical Sciences, Bahra University Shimla Hills, Waknaghat- 173234, H.P. India.

[6]Research Scholar, School of Pharmacy and Emerging Sciences, Baddi University ofEmerging Sciences & Technology, Baddi Makhnumajra- 173205, H.P. India.

[7]Associate Professor, School of Pharmacy and Emerging Sciences, Baddi University ofEmerging Sciences & Technology, Baddi Makhnumajra- 173205, H.P., India.

CorrespondingAuthor: Sheetal Sharma

ABSTRACT

The Development and Characterization of a Deep Eutectic Mixture-Based Topical Gel for Sustained Delivery of Prednisolone Topical Drug Delivery Systems offer advantages such as localized treatment and avoidance of hepatic first-pass metabolism, yet their efficacy is often limited by the stratum corneum and the poor solubility of many potent drugs. This thesis addresses the low aqueous solubility of prednisolone, a widely used corticosteroid, by developing a specialized topical formulation for sustained drug release. The primary objective was to enhance prednisolone solubility and incorporate it into an optimized topical gel. This was achieved through the innovative use of a Deep Eutectic Mixture (DES), specifically prepared with Choline Bitartrate and Benzoic acid. The resulting Deep Eutectic Mixture System (DESM) successfully solubilized the prednisolone, making it suitable for dermal application. The DESM was then integrated into a topical gel using Carbopol 934P as the gelling agent. Various formulations were prepared and rigorously evaluated for critical physicochemical properties, including pH (optimally ranging from 7.18 \pm 0.015 to 7.36 \pm 0.021), spread ability, and viscosity. The optimized formulation, designated F18, demonstrated superior performance, achieving a significant drug release of 86.94 \pm 1.23\% over 24 hours in in vitro studies. Kinetic modelling confirmed that the drug release from the optimized gel followed the Higuchi model (R^2=0.996), which is characteristic of a sustained-release mechanism. The results indicate that the combination of DESM technology with a topical gel formulation is a highly effective strategy for creating a novel and stable delivery system that significantly enhances the solubility and provides sustained bioavailability of poorly water-soluble drugs like prednisolone for improved therapeutic outcomes.

KEYWORDS: *Deep Eutectic Mixture (DES), Topical Drug Delivery, Sustained Release, Stratum Corneum, Deep Eutectic Mixture System (DESM), Higuchi Model, Solubility Enhancement.*

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1. INTRODUCTION

Topical drug delivery systems are localized drug delivery system for local delivery of therapeutic agents via skin to treat the cutaneous disorder. These systems are generally used for local skin infection. The formulations are available in different

forms, like from solid through semisolid to liquid. If the drug substance in the solution has a favorable lipid/water partition coefficient and if it is a non-electrolyte, then drug absorption is enhanced via the skin. Dermatological products have various formulation and range in consistency though the most popular derma products are semisolid dosage forms. Dermal products applied topically are categorized based on those applied to produce local effects and systemic effects. These systems are generally used for local skin infections whereas other route of drug administration fails (Ashara K *et al.,* 2017). Drug molecules with low doses delivered through topical route effectively that are limited to a small area anywhere in the body. Stratum corneum is lipid-rich in nature composed of 40% lipids, 40% protein, and only 20% water. Lipophilic character of the drug is best suited for topical delivery whose transport is aided by dissolution into intercellular lipids around the cells of the stratum corneum. However, hydrophilic drugs are difficult to transport to the stratum corneum layer because of its low water content. These molecules are absorbed into the skin through "pores" or openings of the hair follicles and sebaceous glands that restricts drug absorption. Percutaneous absorption is an ideal factor considered in topical drug delivery systems in order to achieve and maintain a uniform, systemic, therapeutic levels throughout the duration of use. The drug delivered passively via skin should have adequate lipophilicity and a molecular weight of less than 500 Da. Drugs applied via dermally reaches the area in optimum concentration by reducing the side effects and by increasing bioavailability and patient compliance (Kaur J and Gupta G *et al.,* 2016).

In topical drug delivery, the skin is one of the main and accessible organs on the human body. Stratum corneum forms a major penetration barrier to penetrate the drugs into and through the skin. However, this layer makes selective towards the delivery system. A key aspect of topical drug delivery is to make skin as a target organ for diagnosis and treatment. This review has more concerned with all detailed information regarding the conventional and current advances in topical drug delivery (Bhowmik D *et al.,* 2012)

1.1 Topical Drug Classification System (TCS)

Based on qualitative & quantitative composition, TCS provides a framework for classifying topical drug products. Topical drug products are classified into 4 classes. With the purpose to formulate an efficient and effective topical preparation, considerations are mainly concerned with the site of action of the drugs and its effect (Shah VP et al., 2015). Topical preparations may be used produce:

1.1.2 Advantages of topical drug delivery systems (Prausnitz *et al.*, 2008)

• Targeted Treatment
• Localized Effect Convenient to use and easy to apply.
• Reduced Systemic Side Effects.
• Convenience and Ease of Use
• Non-Invasive Route
• Avoidance of primary pass metabolism. Suitability for Dermatological Conditions Self-medication.
• Suitable for Specific Populations
• Avoids fluctuation in drug levels and risks.
• A large area of application compared to others route.
• Easily to terminate the medications

1.1.3 Disadvantages of topical drug delivery systems (Kute S *et al.*, 2013)

• The major disadvantage of the topical route is that the drugs having poorly lipid-soluble and high molecular weight are not absorbed by the skin or mucous membranes.
• Rapid onset of action may not be possible as the drug takes some time to penetrate (absorb).
• Patients feel uncomfortable, as staining or messing of clothes is often associated with the use of ointments, creams, pastes, and gels.
• Another disadvantage of the topical route is that it has no dosing accuracy.
• It is difficult to formulate with different drugs and ingredients or excipients.
• It is not suitable for all patients; some patients may face local skin irritation or allergenic reactions.

1.1.4 Factors Affecting Topical Drug Delivery System

The success of topical drug delivery is dependent on the interplay among various factors (Flynn GL, Hollinger MA, Kydonieus AF and Behl CR *et al.,* 2004)

• Physiological factors
• Physicochemical properties of the drug
• Formulation components and their interactions

Physiological factors concern mainly the properties of the skin such as thickness, hydration level and hair follicle density. These properties can demonstrate high individual variability depending on the age, gender, race, anatomical site, general health and environment condition such as temperature and humidity. In order to minimize the effects of such physiological

variability, the rate-limiting step for topical drug delivery should reside in the formulation instead of the biological barrier. The drug physicochemical properties almost invariably influence its ease of diffusion through the topical vehicle as well as permeation through the skin or mucosal surfaces. Properties of great significance include the molecular size as reflected by the molecular weight, partition coefficient between the vehicle and skin, melting point, stability, and chemical functionality which influence ionization potential, binding affinity and drug solubility in the vehicle. The role of vehicle formulation is evident through its effect on the drug as well as the site of application. The effect on the drug encompasses drug diffusion, thermodynamic activity, stability and degree of ionization of weakly acidic or basic drugs. The effect on the site of application is associated with modification of barrier property via chemical changes imparted by simultaneous uptake of formulation components and physical occlusion. These processes promote skin hydration or changes that increase drug penetration. The formulation factor also has an impact on vehicle consistency and viscosity which in turn, determine the adhesion and retention properties of the vehicle.

2. AIM AND OBJECTIVE

Preparation of deep eutectic mixture gel containing prednisolone for skin delivery.

Rationale

Prednisolone is a medicine that belongs to a group of medicines called corticosteroids. Corticosteroids are synthetic (manufactured) versions of a natural body chemical called cortisol. This medicine helps reduce inflammation in your body or suppress your immune system. Prednisone is a different medicine that is related to prednisolone and works in the same way to treat inflammatory diseases. Your doctor will prescribe the medicine and dose that is most suitable for your condition.

Topical corticosteroids are an essential tool for treating inflammatory skin conditions such as psoriasis and atopic dermatitis. Topical corticosteroids are classified by strength and the risk of adverse effects such as atrophy, striae, rosacea, telangiectasias, purpura, and other cutaneous and systemic reactions. The risk of adverse effects increases with prolonged use, a large area of application, higher potency, occlusion, and application to areas of thinner skin such as the face and genitals. When prescribing topical corticosteroids for use in children, lower potencies and shorter durations should be used. Topical corticosteroids can work safely and effectively in patients who are pregnant or lactating. They are available in formulations such as ointments, creams, lotions, gels, foams, oils, solutions, and shampoos. The quantity of corticosteroid prescribed depends on the duration of treatment, the frequency of application, the skin location, and the total surface area treated. Correct patient application is critical to successful use. Patients may be taught application using the fingertip unit method (Stacey *et al.,* 2008).

Prednisolone is a medicine used to treat a wide range of health problems including allergies, blood disorders, skin diseases, inflammation, infections and certain cancers and to prevent organ rejection after a transplant. It helps by reducing swelling (inflammation) and can also calm down your immune system. This helps autoimmune conditions, like rheumatoid arthritis, where your immune system mistakenly attacks its own tissue Prednisolone is a steroid or corticosteroid medicine. Corticosteroids are not the same as anabolic steroids. In addition to being painless, it enables both local and systemic delivery of therapeutics in a safe and controlled manner for a prolonged period of time, with the option of discontinuing treatment at any point. Skin has certain advantages over other non-invasive routes such as oral delivery which suffers from hepatic first pass metabolism, low oral absorption/bioavailability requiring frequent intake of large doses, or drug-dependent gastrointestinal irritation. In this study, we present a carrier system as a novel transdermal delivery material that can significantly improve penetration of drug through the skin. Deep eutectic mixture (EM) is a mixture of more than one substance that does not interact individually to create a new entity but in a particular ratio that exhibits a lower range of melting point than it had in individual. Deep eutectic solvents derivatives (DESDs) and Deep eutectic solvents (DESs) have low toxicity characteristics. As well as it increases drug solubility, bioavailability and permeability. Thus, it plays a significant role in drug delivery (Smith E.L *et al.,* 2014). The aim of the present study was to prepare a eutectic mixture formulation of Prednisolone to improve the drug solubility and the skin permeability.

3. MATERIALS AND METHODS

2.1 Materials and Method

Table 2.1: List of materials used

Sr. No.	Material	Source

1.	Prednisolone	Anant Pharmaceuticals Pvt. Ltd.
2.	Choline Bitartrate	Spectrum Chemical, United States
3.	Urea	Fischer Scientific
4.	Phenol	Qualikems
5.	Lactic Acid	Qualikems
6.	Benzoic Acid	Central Drug House
7.	Citric Acid	lobachemie
8.	Menthol	lobachemie
9.	Rescorcinol	lobachemie
10.	Carbapol 934P	lobachemie

Table 2.2: List of Equipments Used

Sr. No.	**Name of equipment**	**Manufacturer**
1.	UV Spectrophotometer	Shimadzu, Japan
2.	Magnetic Stirrer	REMI Equipment, Mumbai
3.	pH meter	Ohaus, USA
4.	Digital Balance	Shimadzu, Japan
5.	Melting Point Apparatus	Remi Equipment, Mumbai
6.	Vortex mixer	REMI Equipment, Mumbai
7.	Cooling Centrifuge	REMI Equipment, Mumbai
8.	FTIR Spectrometer	Perkin Elmer

9.	Water Bath Shaker	NSW India
10.	Vortex Shaker	REMI Equipment, Mumbai

4. METHODOLOGY

3.1.1. Pre-formulation studies

Pre-formulation is an integral part of the entire development process. It is the study of the physical and chemical properties of the drug prior compounding process. These studies focus on those physicochemical properties of the drug that could affect its performance and development of an efficacious dosage form. A thorough understanding of these properties may ultimately provide a rationale for formulation design, or support the need for molecular modification. In the simplest case, these pre-formulation investigations may merely confirm that there are no significant barriers to the compound's development. These studies are indispensable protocol for development of safe, effective and stable dosage form. The obtained drug sample was identified by various analytical techniques such as IR spectroscopy, UV spectroscopy, melting point etc (Ali J *et al*., 2008 and Acharya PC *et al*., 2018).

3.1.2. Organoleptic Properties

The organoleptic studies like general appearance like nature, colour, Odor etc. were performed by visual observations.
Color: Small quantity of drug was taken in butter paper and viewed in well illuminated place.
Odor: Very less quantity of drug was smelled to get the odor.

3.1.3. Melting Point

The melting point of the solid is defined as the temperature at which solid and liquid are at equilibrium at a total pressure. Melting point apparatus is used for the determination of melting point of the drug. A few amounts of the drug were placed in a thin-walled capillary tube 10-15 mm long, about 1 mm inside diameter, and closed at one end. The capillary, which contains the sample, was suspended to heat the samples slowly and evenly and thermometer placed to check the temperature. The temperature range over where the sample is observed to melt is taken as the melting point of the drug (Williams RL *et al*., 2006).

3.1.4 UV absorption maxima of Prednisolone

UV-visible spectrophotometer is generally used for structural information of various drugs to obtain specific information on the chromophoric part of the molecules in solution when exposed to light in the visible/ultraviolet region of the spectrum absorb light of particular wavelength depending on the type of electronic transition associated with the absorption. The UV spectrum is generally recorded as a plot of absorbance versus wavelength.
Double beam UV-visible spectrophotometer (Shimadzu, UV-1800, Japan) was used to know the λmax of drug. 36µg/ml solution of Prednisolone was scanned in the range of 200-400 nm (Kashyap *et al*., 2012).

3.2 Estimation of Prednisolone by UV-visible spectrophotometer

3.2.1. Preparation of Stock Solution

Standard stock solution of Prednisolone was prepared by dissolving 10mg of Prednisolone in 10ml of methanol which gives 1000µg/ml. 10ml of this stock solution was taken and was diluted up to 100ml by using methanol (solvent) to produce a concentration of 100µg/ml solution.

3.2.2. Preparation of Working Solution

The standard stock solution of Prednisolone (100µg/ml) was prepared in methanol. This solution was diluted with methanol, to obtain various dilutions from 6-36 µg/ml. Absorbance of these solutions was recorded at 243nm against methanol as blank using UV-visible spectrophotometer and standard curve was plotted against concentration. From the calibration curve intercept, slope, straight line equation and correlation coefficient were obtained.

5. SOLUBILITY STUDIES

The spontaneous interaction of two or more substances to form a homogenous molecular dispersion is called solubility.
For quantitative solubility study, excess amount of drug was taken in thoroughly cleaned culture tubes containing 3 ml of different solvents and Culture tubes were tightly closed. These Culture tubes were shaking on water bath shaker at 25°C for 24 h at room temperature. After 24 h each sample was centrifuged 15,000 rpm and supernatant was withdrawal.

After that Page 52 supernatant was filtered and filtrates was suitably diluted and determined spectrophotometrically (Zakeri-Milani *et al*., 2011).

4.1.1 Partition Coefficient of Drug

Partition coefficient (oil/water) is a measure of a drug's lipophilicity/hydrophilicity and an indication of drug's ability to cross cell membranes. It is defined as the ratio of unionized drug distributed between the organic and aqueous phases at equilibrium. Partition coefficient provides a means of characterizing the lipophilic/hydrophilic nature of the drug. Drugs having values of P much greater than 1 are classified as lipophilic, where as those with values much less than 1 are indicative of a hydrophilic drug. The partition coefficient is commonly determined using an oil phase of n-octanol and water. In the case n-octanol and water:

P o/w = C n-octanol/C water

The partition coefficient (Po/w) therefore is the quotient of two concentrations of drug in noctanol (Cn-octanol) and water (Cwater) respectively and is usually given in the form of its logarithm to base 10 (log P) (https://www.cdek.liu.edu/api/108755/pricing/prednisolone).

4.1.2. FTIR of Prednisolone and Excipients

The FT-IR (Fourier Transform Infrared) spectra of a substance or medication can reveal the groups that are present. For structure investigation, FT-IR spectroscopy was employed. For the purpose of identifying any potential medication interactions with excipients, an FT-IR spectrum of a mixture of Prednisolone and other ingredients was recorded. The FT-IR chamber received 1-2 mg of Prednisolone. The region between 4000 and 400 cm-1 of the infrared spectrum was observed (A Khaled *et al*., 2008).

4.1.3 Drug-excipients Compatibility Study by FTIR

The compatibility of drug with excipients was ascertained by FT-IR. FTIR was used as tool to detect any physical and chemical interaction between drug and excipients. Drug and various excipients were mixed thoroughly in ratio of 1:1. Samples were scanned by FTIR under the range of 400-4000 cm-1. The spectra of pure drug and drug with excipients were compared to check any incompatibility and physical changes.

4.1.4. Preparation of Deep Eutectic Solvent Mixture of Prednisolone

Choline chloride & Choline Bitartrate with a few chosen carboxylic acids were combined with aqueous media (5ml) at various ratios to create Deep Eutectic Solvent Derivatives (DESD). When homogenous solutions had formed, the mixtures were placed in vials and sealed. The oven temperature was set at 75°C. These samples were then kept at room temperature, and only those that continued to be liquid under testing conditions were evaluated as room-temperature solvents for model poorly soluble medicines. Due to their insufficient aqueous solubility, prednisolone was chosen as the model medication for the solubility experiment. A specific quantity of medication was given to a blank DESD solvent, followed by vigorous vortexing until the surplus solid remained undissolved, in order to establish the drug's solubility in DESDs. To achieve equilibrium, the final solution containing extra medication was allowed standing for 24hour (Farooq *et al*., 2020).

Table 4.1.4: Screening of Carboxylic Acid for Deep Eutectic Solvent Mixture of Prednisolone

Sr. No	Formulation Code	Carboxylic Acid Used	Ratio	Drug Prednisolone(mg)	Choline Chloride(mg)	Choline Bitartrate	Carboxylic Acid
1.	F1	Benzoic acid	1:1	10mg	10mg	-	10mg
2.	F2	Menthol	1:1	10mg	10mg	-	10mg
3.	F3	Citric acid	1:1	10mg	10mg	-	10mg

4.	F4	Phenol	1:1	10mg	10mg	-	10mg
5.	F5	Urea	1:1	10mg	10mg	-	10mg
6.	F6	Benzoic acid	1:1	10mg	-	10mg	10mg
7.	F7	Menthol	1:1	10mg	-	10mg	10mg
8.	F8	Citric acid	1:1	10mg	-	10mg	10mg
9.	F9	Phenol	1:1	10mg	-	10mg	10mg
10.	F10	Urea	1:1	10mg	-	10mg	10mg

6. EVALUATION OF DEEP EUTECTIC SOLVENT MIXTURE OF PREDNISOLONE

5.1 pH of the Solution

For pH measurements, the freshly prepared solutions were kept at 25 ± 2 °C for a period of 30 min. After pH was measured at this temperature, each solution was placed in a water bath and heated gradually up to 60 °C. The pH was determined using digital pH meter (Skulcova *et al*., 2018).

Drug Solubility

The most popular shake-flask method was employed for the drug solubility experiment. Here, drug was solubilized in each DESD by stirring at room temperature and then, placed in a temperature-controlled water bath for 24 hrs to attain equilibrium. Later, the sample solutions were filtered before they attained the maximum solubility of drug in DESDs. The clear solutions were then assayed using a double beam spectrophotometer to measure the absorbance spectra, which depict drug solubilization (Li, Z and Lee *et al*., 2016).

Drug Content

Once the solubility is being measured, the solution containing both the drugs was filtered through a Millex 69 PES syringe filter unit with a 0.22 µm membrane. The drug concentration in the filtered DESD supernatant was determined spectrophotometrically on a UV-Vis spectrophotometer. The absorbance of Prednisolone was measured by diluting the filtered aliquots in methanol (Hayyan *et al*., 2023).

5.2 Formulation of topical gel of DESM of Prednisolone

The optimized formulation (F13) containing 1:2 ratio of Choline Bitartrate and Benzoic Acid was found to be effective and was selected as best formulation for the conversion of topical gel formulation. Carbopol 934 was used to prepare the gel base. In a certain volume of optimized formulation, the carbopol 934P was added to the desired concentration. Accordingly, different percentages of gel were prepared to obtain the appropriate concentration of the gel. The common percentage of carbopol gel making material is between 1%, 1.5% and 2%. After complete dispersion, it was placed at room temperature till the carbomer powder completely dissolved for 24 hours. 1N of NaOH solution was added it dropwise to take care of the pH. The developed topical gel was evaluated for various parameters (Madan *et al*., 2019).

5.3 Physical appearance

The prepared gel was examined for color, homogeneity and appearance.

5.3.1 pH

2.5 g of gel were accurately weighed and dispersed in 25 ml of water. The pH of the dispersion was measured by employing a digital pH meter (Huang *et al*., 2021).

5.3.2 Spreadibility

Spreadability of gel was determined by laboratory fabricated apparatus that had two glass slides, the lower slide fixed to a wooden plate and the upper one attached to a balance by a hook. One gram of gel was placed on lower slide and weight was applied to the upper slide. On applying weight, the upper slide moved linearly in the direction of applied weight and the time required for complete displacement of the upper slide was recorded. Using the weight required for displacement spreadability was calculated by using Equation 1,

$S = m\ l / t$ …….Eq (1)

S is spreadability, m is the weight tied to the upper slide, l is the length of the glass slide and t is the time taken.

5.3.3 Drug content

The drug content of the prepared gel was administered by dissolving accurately weighed quantity of gel (1g) in 100 ml volumetric flask and volume was made up to 100 ml with solvent. The content was filtered through Whatman paper. 5 ml of above solution was taken into a 25 ml volumetric flask and volume was made up to mark with solvent. The content of both the drugs were estimated spectrophotometrically on a UV-VIS spectrophotometer.

5.3.4 In-Vitro Drug Release Study

This study was performed through dialysis membrane using Franz diffusion cell apparatus. The dialysis membrane is previously treated with 40% ethanol solution and soaked overnight. The treated membrane was placed in diffusion cell between the donor and acceptor compartments. About 1gm of gel was added to the treated membrane and the receptor compartment of the diffusion cell was filled with 7.4 pH phosphate buffer. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 100 rpm, the temperature was maintained at 37 ±0.50°C. The samples of 1 ml were withdrawn at time interval of 0.25 to 24 hrs analyzed for drug by using UV method. The receptor phase was replenished with an equal volume of 7.4 pH buffer at each time of sample withdrawal (Lu, W., and Chen, H. *et al*., 2022).

5.3.5 Drug release kinetic studies

Numerous mathematical operations that serve as the cornerstone of model-dependent techniques explain the release profile. Once a suitable function has been selected, the model parameters that were acquired are used to evaluate the release profiles. The results from the ex vivo permeation studies were visualised using the following methods of data treatment; (Dash S et al., 2010 and Islam M et al., 2010 and Shreeraj H *et al*., 2009)

- Zero Order model
- First Order model
- Higuchis Model
- Korsmeyer-Peppas model

5.3.6 Zero order kinetics

It can be used to explain the dissolution of a variety of modified release pharmaceutical dosage forms, including certain transdermal systems, matrix tablets with coated low soluble medicines, osmotic systems, etc. The simplest way to describe a zero order release is as follows:

$Q0 - Qt = K0t$

Where Q0 represents the initial concentration of the drug in the solution (typically, Q0= 0), Qt represents the amount of drug dissolved in time t, K0 represents the zero order release constant represented in units of concentration/time. Data from in vitro drug permeation tests were shown as the cumulative amount of drug released vs time to analyse the release kinetics.

5.3.7 First order kinetics

It can be used to describe how pharmaceuticals dissolve in pharmaceutical dosage forms, such as those that incorporate porous matrices that contain water-soluble medications. The equation can be used to describe the drug's first order kinetics-based release:

$\log C = \log C0 – K.t / 2.303$

Where k is the first order rate constant, t is the time, and C0 is the starting drug concentration. When the data are plotted as log cumulative percentage of medicine remaining vs. time, a straight line with a slope of K/2.303 results from the data.

5.3.8 Higuchi's Model

This model predicted the matrix system's drug release. Prior to being expanded to other geometrical and porous systems, it was mostly regarded for planar systems. This model is predicated on the following hypotheses: I initial drug concentration in the matrix is significantly higher than drug solubility; (ii) drug diffusion occurs only in one dimension (edge effect must be negligible); (iii) drug particles are much smaller than system thickness; (iv) matrix swelling and dissolution are negligible; (v) drug diffusivity is constant; and (vi) perfect sink conditions are always attained in the release environment. Higuchi was the first to create an equation to express the square root of a time-dependent process based on Fickian diffusion as the release of a medication from an insoluble matrix. Following is the simplified Higuchi equation;

Qt = KH (t) 0.5

Where Qt is the drug's release rate constant according to the Higuchi model, and KH is the drug's release rate constant over time. The data provides a straight line when the cumulative drug release is plotted against the square root of time, showing that the drug was released by diffusion mechanism. The slope is equal to 'KH'.

5.3.9 Korsmeyer-Peppas Model

The drug release from a polymeric system was described by Korsmeyer using a straightforward connection. The equation put forth by Korsmeyeret a can be used to characterise the release rates from controlled release polymeric matrices.

Q = K.tn

Where, Q is the percentage of drug released at time't' K is a kinetic constant incorporating structural and geometric characteristics of the tablets and 'n' is the diffusional exponent indicative of the release mechanism.

For Fickian release, n=0.45 while for anomalous (Non-Fickian) transport, n ranges between 0.45 and 0.89 and for zero order release, n = 0.89. The Korsmeyer-Peppas model was plotted between log cumulative % drug releases versus log time.

7. RESULTS AND DISCUSSIONS

6.1 Result of preformulation study of drug

•FT-IR spectra the aim of preformulation studies is to examine the physical and chemical properties of a drug substance. The selected drug Prednisolone was subjected for investigation of physical characterization parameters such as:
•Organoleptic properties
•Melting point
•UV-visible spectra
•Solubility
•Partition coefficient

6.1.1 Organoleptic properties

Organoleptic properties of drug Prednisolone found to be as per literature (Barth, J. *et al*., 1992)

6.1.2 Melting Point

The temperature at which a substance transitions from its solid to liquid state under a single atmosphere of pressure is known as the melting point of that substance. The drug's purity is implied by the melting point determination. Prednisolone's melting point was established using the capillary tube method, and it was discovered to be remarkably similar to the previously reported melting point.

Table 6.1: Melting Point of Prednisolone

Drug	Reference M.P.	Observed M.P.
Prednisolone	240°C	239.3°C±0.577

6.1.3. UV Spectroscopy

A double beam UV-visible spectrophotometer was used for quantitative analysis of the drug. A 36 µg/ml solution of Prednisolone in methanol was scanned in the range of 200-400 nm. The result of UV spectrum of Prednisolone shown in Figure. 6.1

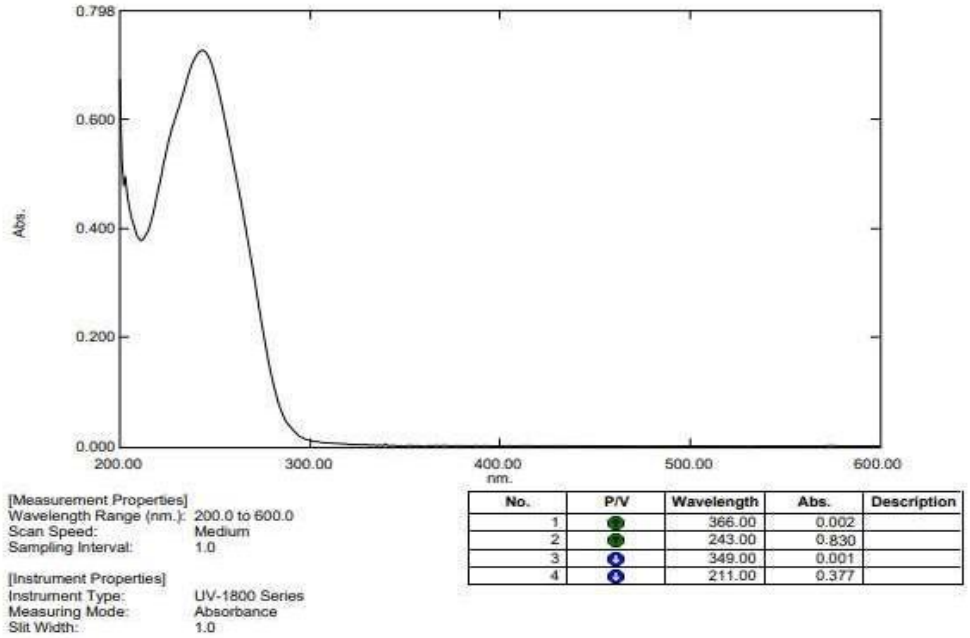

Figure 6.1: UV Spectrum of Prednisolone

6.1.4 Solubility studies

Solubility of drug in various solvents, were carried out in order to screen for the components to be used for formulation development. Analysis of the drug was carried out on UV Spectrophotometer.

Table 6.2: Solubility studies of Prednisolone for different solvents

Sr. No.	Solvent	Solubility in (mg/ml) (mean±SD)
1	Methanol	97.382±0.727
3	Ethanol	82.47±0.363
4	Acetone	11.30±0.03
5	Water	0.15±0.19
6	PB pH 7.4	0.10±0.005

* Each value is average of three independent determinations

6.1.5 Partition coefficient determination

Partition coefficient of the Prednisolone was determined using n-octanol and water. Log P greater than one indicates that the drug is lipophilic in nature, whereas those with partition coefficients less than one are indicative of a hydrophilic drug. This indicated the lipophilicity and purity of drug.

Table 6.3: Partition coefficient determination of Prednisolone

Partition coefficient of drug	Solvent system	Log P Values
Prednisolone	n-octanol:water	1.002±0.004

Value is expressed as mean ± SD; n = **3**

8. SUMMARY AND CONCLUSION

A wide variety of pharmaceutical dosage forms can be used in the delivery system for topical drugs. The topical delivery with gels can increase the resistance time of the drug on the skin and improve the delivery and release of the substance by increasing the residence time at the site.

In present investigation we have DESM of prednisolone to increase the residence time, bioavailability and onset of action.

On physicochemical evaluation, melting point of prednisolone was found to be 239.3°C±0.577. On UV spectrophotometer analysis absorption maxima of prednisolone were found to be 243 nm in methanol solvent. The partition coefficient of prednisolone in n-Octanol: Water was found to be 1.002±0.004. This indicates that the drug prednisolone is lipophillic in nature. As far as solubility profile is concerned, prednisolone the drug was found highly soluble in acetone, chloroform and methanol. On FTIR spectroscopy analysis there was no interaction between drug and polymer.

The DESM of prednisolone was prepared. The method of preparation of was found to be simple and reproducible. The physical appearance of all the formulation wars evaluated and was successfully able to have a transparent appearance with addition of drugs. The solubility study of drug revealed that F13 was having maximum prednisolone solubility. Further, upon altering the ratios, F13 have maximum drug solubility 16.17±0.555mg/ml was found. The drug content of the formulation F13 was found to contain 98.433±1.04% of prednisolone.

The optimal formulation was selected to preparation of topical gel with Carbapol 934P in different concentration. The pH of the prepared topical gel was found to be in the range from 7.18±0.015 to 7.36±0.021. Upon spreadibility study, the gels were found to have optimum results. Percentage drug content was obtained in all formulations with gel formulation was found to be in a range of 92.21±0.908 % to 99.76±0.343 % prednisolone The drug release from the topical gel prepared in formulation F18 achieved respective amount of individual drug release contributing 86.94±1.23% within 24 hr.

The best fit model has Higuchi as per high regression coefficient value. Hence from all aspects; we concluded that the release of drugs can be sustained release by proper designing of the formulation and selection of a suitable method of preparation. In this study we successfully produced sustained released drug delivery systems for the simultaneous drug release of prednisolone. This was achieved by processing them into DESM using Choline Bitartrate and Benzoic acid. The data reported herein clearly demonstrate that the drug solubility of poorly water-soluble drug enhanced by various folds, making it an ideal candidate to formulated into a topical gel.

REFERENCES

[1] Ashara K, Soniwala M, Shah K. Emulgel: A novel drug delivery system. Journal of Pakistan Association of Dermatology. 2017 Mar 29;26(3):244-9.
[2] 2. Kaur J, Kaur J, Jaiswal S, Gupta G. Recent advances in topical drug delivery system. Pharmaceutical Research. 2016;6(07):6353-69.
[3] 3. Bhowmik D. Recent advances in novel topical drug delivery system. The Pharma Innovation. 2012 Nov 1;1(9).
[4] 4. Shah VP, Yacobi A, Rădulescu FŞ, Miron DS, Lane ME. A science based approach to topical drug classification system (TCS). International journal of pharmaceutics. 2015 Aug 1;491(1-2):21-5.
[5] 5. Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. Nature biotechnology, 26(11), 1261-1268.
[6] 6. Kute S, Saudagar R. Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2013 Oct;3(4).
[7] 7. Flynn GL., et al. “Parameters of skin condition and function. In: Kydonieus AF, Berner B, editors. Transdermal delivery of drugs”. Volume II. Boca Raton: CRC Press (1987): 3-17.
[8] Ranade VV and Hollinger MA. “Transdermal drug delivery. In: Kydonieus AF, Berner B, editors. Transdermal delivery of drugs”. Volume I. Boca Raton: CRC Press (2004): 207-248.
[9] Kydonieus AF. “Fundamentals of transdermal drug delivery. In: Kydonieus AF, Berner B, editors. Transdermal delivery of drugs”. Volume I. Boca Raton: CRC Press (1987): 3-16.
[10] Behl CR., et al. “In vivo and in vitro skin uptake and permeation studies. In: Shah VP, Maibach HI, editors. Topical drug bioavail- ability, bioequivalence and penetration”. New York: Plenum Press (1993): 225-259
[11] Bos JD, Meinardi MM. The 500 Dalton rule for the skin penetration of chemical compounds and drugs. Experimental Dermatology: Viewpoint. 2000 Jun;9(3):165-9.
[12] Bajaj S, Singla D, Sakhuja N. Stability testing of pharmaceutical products. Journal of applied pharmaceutical science. 2012 Mar 24;2(3):129-38
[13] Andrews SN, Jeong E, Prausnitz MR. Transdermal delivery of molecules is limited by full epidermis, not just stratum corneum. Pharmaceutical research. 2013 Apr;30(4):1099-109.

[14] Bouwstra JA, Gooris GS. The lipid organisation in human stratum corneum and model systems. The Open Dermatology Journal. 2010 Apr 23;4(1).
[15] Abbott A.P., Capper G., Davies D.L., Rasheed R.K., Tambyrajah V. Novel solvent properties of choline chloride/urea mixtures. Chem. Commun. 2003:70–71. doi: 10.1039/b210714g. [PubMed] [CrossRef] [Google Scholar]
[16] Chakraborty, S., Chormale, J. H., & Bansal, A. K. (2021). Deep eutectic systems: An overview of fundamental aspects, current understanding and drug delivery applications. International Journal of Pharmaceutics, 610, 121203.
[17] Zhang Q., De Oliveira Vigier K., Royer S., Jérôme F. Deep eutectic solvents: Syntheses, properties and applications. Chem. Soc. Rev. 2012;41:7108–7146. doi: 10.1039/c2cs35178a. [PubMed] [CrossRef] [Google Scholar]
[18] Smith E.L., Abbott A.P., Ryder K.S. Deep Eutectic Solvents (DESs) and Their Applications. Chem. Rev. 2014;114:11060–11082. doi: 10.1021/cr300162p. [PubMed] [CrossRef] [Google Scholar]
[19] Martins M.A.R., Pinho S.P., Coutinho J.A.P. Insights into the Nature of Eutectic and Deep Eutectic Mixtures. J. Solut. Chem. 2019;48:962–982. doi: 10.1007/s10953-018-0793-1.
[20] Hammond O.S., Bowron D.T., Edler K.J. Liquid structure of the choline chloride-urea deep eutectic solvent (reline) from neutron diffraction and atomistic modelling. Green Chem. 2016;18:2736–2744. doi: 10.1039/C5GC02914G. [CrossRef] [Google Scholar]
[21] Harifi-Mood A.R., Buchner R. Density, viscosity, and conductivity of choline chloride+ethylene glycol as a deep eutectic solvent and its binary mixtures with dimethyl sulfoxide. J. Mol. Liq. 2017;225:689–695. doi: 10.1016/j.molliq.2016.10.115. [CrossRef] [Google Scholar]
[22] Shekaari H., Zafarani-Moattar M.T., Mohammadi B. Thermophysical characterization of aqueous deep eutectic solvent (choline chloride/urea) solutions in full ranges of concentration at T=(293.15–323.15)K. J. Mol. Liq. 2017;243:451–461. doi: 10.1016/j.molliq.2017.08.051. [CrossRef] [Google Scholar]
[23] Ghaedi H., Ayoub M., Sufian S., Shariff A.M., Murshid G., Hailegiorgis S.M., Khan S.N. Density, excess and limiting properties of (water and deep eutectic solvent) systems at temperatures from 293.15K to 343.15K. J. Mol. Liq. 2017;248:378–390. doi: 10.1016/j.molliq.2017.10.074. [CrossRef] [Google Scholar]
[24] Ghaedi H., Ayoub M., Sufian S., Hailegiorgis S.M., Murshid G., Farrukh S., Khan S.N. Experimental and prediction of volumetric properties of aqueous solution of (allyltriphenylPhosphonium bromide—Triethylene glycol) deep eutectic solvents. Thermochim. Acta. 2017;657:123–133. doi: 10.1016/j.tca.2017.09.025. [CrossRef] [Google Scholar]
[25] Sánchez P.B., González B., Salgado J., José Parajó J., Domínguez Á. Physical properties of seven deep eutectic solvents based on l-proline or betaine. J. Chem. Thermodyn. 2019;131:517–523. doi: 10.1016/j.jct.2018.12.017. [CrossRef] [Google Scholar]
[26] Leron R.B., Wong D.S.H., Li M.-H. Densities of a deep eutectic solvent based on choline chloride and glycerol and its aqueous mixtures at elevated pressures. Fluid Phase Equilib. 2012;335:32–38. doi: 10.1016/j.fluid.2012.08.016. [CrossRef] [Google Scholar]
[27] Abbott A.P. Application of Hole Theory to the Viscosity of Ionic and Molecular Liquids. ChemPhysChem. 2004;5:1242–1246. doi: 10.1002/cphc.200400190. [PubMed] [CrossRef] [Google Scholar]
[28] Abbott A.P., Capper G., Gray S. Design of Improved Deep Eutectic Solvents Using Hole Theory. ChemPhysChem. 2006;7:803–806. doi: 10.1002/cphc.200500489. [PubMed] [CrossRef] [Google Scholar]
[29] Patil PB, Datir SK, Saudagar RB. A Review on Topical Gels as Drug Delivery System. Journal of Drug Delivery and Therapeutics. 2019 Jun 15;9(3-s):989-94.
[30] Alvarez-Soria M.A., Herrero-Beaumont G, Moreno-Rubio J.et al.: " Long-term NSAID treatment directly deceases COX-2 and Mpges-1 production in the articular cartilage of patients with osteoatheritis,"ostroartherities and cartilage, 2008,16(12);1484-1493.
[31] Li.L,Rossoni G, Sparatore A, Lee L.C. Del Soldato P and MooreP.K. "Anti-inflammoraty and gastrointestinal effects of a novel diclofenac derivative, "Free Radial Bioalogy and Medicine, 2007,42(5);706-719.
[32] Karande P,Mitragotri S:Enhancement of transdermal drug delivery via synergistic action of chemicals, Biochemica et Biophysica Actas,2009, 1788:2362-2373
[33] Williams AC,Barry BW:Penetration enhancers,Advanced Drug Delivery via Reviews 2004,5:603-618.
[34] Barry BW: Novel mechanism and devices to enable successful transdermal drug delivery, European journal of pharmaceutical sciences,2001,14:101-114.
[35] Devi R .S, Narayan S, Vani G, and Shymala Devi C.S.: "Gastroprotective effect of Terminalia arjuna bark on diclofenac sodium induced gastric ulcer", Chemical-biological interactions,2007,167(1);71-83.
[36] Zatz JL., et al. "Pharmaceutical dosage form: Disperse system". Marcel Dekker (2005): 399-421.As delivery systems for orally administered drugs.
[37] Loyd VA., et al. "Ansel's pharmaceutical dosage forms and drug delivery systems. 9th ed. Philadelphia:

Lippincott Williams & Will- dns; (2011).
[38] Niyaz BB., et al. “Formulation and evaluation of Gel containing Fluconazole-Antifungal agent”. International Journal of Drug Devel- opment and Research 3.4 (2011): 109-128.
[39] Goyal S., et al. “Novel Anti-Inflammatory Topical Herbal Gels Containing Withania somnifera and Boswellia serrata”. International Journal of Pharmaceutical and Biological Archives 2.4 (2011): 1087-1094.
[40] Jones D. “Pharmaceutics-Dosage Form and Design”. 1st ed. London: Pharmaceutical Press (2008).
[41] Cevc G, Schatzlein A, Blume G. Transdermal drug carriers: Basic properties, optimization and transfer efficiency in case of epicutaneously applied peptides. J. Control. Rel.1995; 36:3-16.
[42] Columbus PS., et al. “Borden, Inc., assignee. Thixotropic adhesive gel”. United States patent US RE35144 E (1986): 9
[43] Pickup, M. E. (1979). Clinical pharmacokinetics of prednisone and prednisolone. Clinical pharmacokinetics, 4, 111-128.
[44] https://pubchem.ncbi.nlm.nih.gov/substance/49864708
[45] Journal of Microbiology, Epidemiology and Immunology. Vol. (9), Pg. 14, 1979.
[46] National Center for Biotechnology Information (2023). PubChem Substance Record for SID 135551856, 87-67-2, Source: Tractus. Retrieved September 4, 2023 from https://pubchem.ncbi.nlm.nih.gov/substance/135551856.
[47] https://en.wikipedia.org/wiki/Choline_bitartrate
[48] Lillard, Benjamin (1919). "Troches of Benzoic Acid". Practical Druggist and Pharmaceutical Review of Reviews.
[49] Experiment 2: Using Bomb Calorimetry to Determine the Resonance Energy of Benzene Archived 9 March 2012 at the Wayback Machine
[50] "Concise International Chemical Assessment Document 26: BENZOIC ACID AND SODIUM BENZOATE"
[51] Anwer, M.K.; Aldawsari, M.F.; Iqbal, M.; Almutairy, B.K.; Soliman, G.A.; Aboudzadeh, M.A. Diosmin-Loaded Nanoemulsion-Based Gel Formulation: Development, Optimization, Wound
[52] Mr. Umakant Sharma*1 , Saurabh Arjariya2 , Dr. Rajendra Chouksey3 , Dr. Neeraj Sharma4. Formulation and Evaluation of Pharmaceutical Gel Journal of Pharmaceutical Negative Results ¦ Volume 13 ¦ Special Issue 1 ¦ 2022
[53] Sokolova MP, Smirnov MA, Samarov AA, Bobrova NV, Vorobiov VK, Popova EN, Filippova E, Geydt P, Lahderanta E, Toikka AM. Plasticizing of chitosan films with deep eutectic mixture of malonic acid and choline chloride. Carbohydrate polymers. 2018 Oct 1;197:548-57.
[54] Liu C, Hu J, Sui H, Zhao Q, Zhang X, Wang W. Enhanced skin permeation of glabridin using eutectic mixture-based nanoemulsion. Drug delivery and translational research. 2017 Apr 1;7(2):325-32.
[55] DE BEULE, Karel; VAN GESTEL, Jef. Pharmacology of itraconazole. Drugs, 2001; 61(1): 27-37.
[56] HARIA, Malini; BRYSON, Harriet M.; GOA, Karen L. Itraconazole. Drugs. 1996;51(4): 585-620.
[57] Pharm AG, Pharm SM, Pharm SS, Pharm SP, Pharma NT, Shrestha JR, Pharm MB. Formulation & Evaluation of Fluconazole Gel for Topical Drug Delivery System. American Scientific Research Journal for Engineering, Technology, and Sciences (ASRJETS). 2021 Feb 14;76(1):124-37
[58] Lakshmi VS, Manohar RD, Mathan S, Dharan SS. Formulation and Evaluation of Ufasomal Topical Gel Containing Selected Non Steroidal Anti Inflammatory Drug (NSAIDs). Journal of Pharmaceutical Sciences and Research. 2021;13(1):38-48.
[59] Puri D, Mishra A, Singh AP, Gaur PK, Singh M, Yasir M. Formulation Development of Topical Preparation Containing Nanoparticles of Povidone-Iodine for Wound Healing. ASSAY and Drug Development Technologies. 2021 Feb 3.
[60] Tiwari A, Bag P, Sarkar M, Chawla V, Chawla PA. Formulation, validation and evaluation studies on metaxalone and diclofenac potassium topical gel. Environmental Analysis Health and Toxicology. 2021 Jan 11;36(1):e2021001.
[61] Shah P, Goodyear B, Dholaria N, Puri V, Michniak-Kohn B. Nanostructured Non-Ionic Surfactant Carrier-Based Gel for Topical Delivery of Desoximetasone. International Journal of Molecular Sciences. 2021 Jan;22(4):1535.
[62] Kumar B, Sahoo PK, Manchanda S. Curcumin Loaded Ethosomal Gel for Improved Topical Delivery: Formulation, Characterization and Ex-vivo Studies. Pharmaceutical Nanotechnology. 2021 Feb 8.
[63] Shameem S, Nithish N, Bhavitha M, Kumar S, Sahithya K. Formulation and Evaluation of Lawsone Loaded Nanosponge Gel for Topical Delivery. Future Journal of Pharmaceuticals and Health Sciences. 2021 Jan 18;1(1):29-36.
[64] Mane PK. Formulation and Evaluation of Peel-Off Gel Formulation Containing Fenugreek. Pharmaceutical Resonance. 2021; 3(2): 99-104
[65] Latha AM, Kumar JS, Sojana N, Mounika N, Priyanka G, Venkatesh A. Design and Optimization of Clotrimazole Emulgel by using various Polymers. Asian Journal of Pharmacy and Technology. 2021 Feb 1;11(1):41-7.
[66] Kaur M, Nagpal M, Singh M, Singh TG, Aggarwal G, Dhingra GA. Improved antibacterial activity of topical gel-based on nanosponge carrier of cinnamon oil. BioImpacts: BI. 2021;11(1):23.
[67] Gupta S, Tiwari S, Prajapati RN, Yadav RD, Chanchal DK, Mansoori MF. Pamam Dendrimer-Based Luliconazole Gel Formulation and Efficiency Evaluations. European Journal of Molecular & Clinical Medicine. 2021 Jan

30;7(8):4881-94.
[68] Redhu S, Pawar N. Development and characterization of microsponge gel for topical delivery of oregano oil. International Journal of Pharmaceutical Sciences and Research. 2021; 12(2): 1060-1073.
[69] Janakiraman KK, Paramaguru R, Janakiraman Kunchithapatham F. Optimization and Characterization of Novel Modified Release Gel Formulation of Dexibuprofen Using Full Factorial Design..(2020). Int. J. Life Sci. Pharma Res.;10(5):178-90.
[70] Agarwal S, Gautam G. Formulation, Development and Evaluation of Atorvastatin Ethosomal Gel. International Journal of Pharmaceutical Investigation. 2020 Dec 10;10(4):452-5.
[71] Gunjan VS. Enhanced Anti-Analgesic Morphine Based Gel: Formulation, Characterization, In-Vitro and In-Vivo Evaluation. Journal of Natural Remedies. 2020 Dec 8;21(8):94-102.
[72] Khan J, Norfarhani S, Sahu RK, Ruhi S, Kaleemullah M, Al-Dhalli S, Rasny M, Budiasih S, Baber S, Ng CH, Shamiha NN. Development and Evaluation of topical Emulgel of Aspirin using different Polymeric Bases. Research Journal of Pharmacy and Technology. 2020 Dec 1;13(12):6300-4.
[73] Al-Nima AM, Qasim ZS, Al-Kotaji M. Formulation, evaluation and anti-microbial potential of topical Licorice root extract gel. Iraqi Journal of Pharmacy. 2020 Dec 31;17(1):37-56.
[74] Parameters on Topical Gel Loaded With Povidone Iodine, Honey and Aloe Vera.(2020). Int. J. Life Sci. Pharma Res.;10(5):P111-117.
[75] Sujitha YS, Muzib YI. Preparation of Topical Nano Gel Loaded With Hesperidin Emusomoes: In vitro and in vivo Studies. International Journal of Pharmaceutical Investigation. 2020 Dec 10;10(4):500-5.
[76] Lad AS, Rodge P, Khandelwal KR. Formulation Development of Antimicrobial Gel Using Chia Seed Mucilage. Journal of Pharmaceutical Sciences and Research. 2020 Dec 1;12(12):1489-95.
[77] Syal S, Pandit V, Ankalgi AD, Verma CP, Ashawat MS. Formulation and Evaluation of Microsponges Gel of Havan Ash for the Treatment of Acne. Journal of Drug Delivery and Therapeutics. 2020 Nov 15;10(6):74-85.
[78] Patel DK, Kesharwani R, Kumar V. Etodolac loaded solid lipid nanoparticle based topical gel for enhanced skin delivery. Biocatalysis and Agricultural Biotechnology. 2020 Oct 1;29:101810.
[79] Arora D, Khurana B, Nanda S. Statistical development and in vivo evaluation of resveratrol-loaded topical gel containing deformable vesicles for a significant reduction in photo-induced skin aging and oxidative stress. Drug Development and Industrial Pharmacy. 2020 Nov 1;46(11):1898-910.
[80] Gupta S, Wairkar S, Bhatt LK. Isotretinoin and α-tocopherol acetate-loaded solid lipid nanoparticle topical gel for the treatment of acne. Journal of Microencapsulation. 2020 Nov 16;37(8):557-65.
[81] Chen J, Ma Y, Tao Y, Zhao X, Xiong Y, Chen Z, Tian Y. Formulation and evaluation of a topical liposomal gel containing a combination of zedoary turmeric oil and tretinoin for psoriasis activity. Journal of liposome research. 2020 Apr 16:1-5.
[82] Gujjar S, Madhavi BL, Karki R. Formulation and Evaluation of Topical Gel Containing Nanostructured Lipid Carriers Dispersion of an Antifungal Drug. ACTA Pharmaceutica Sciencia. 2019;57(4).
[83] Thomas MA. Formulation and evaluation of ethosomal gel of tazarotene for topical delivery. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm. 2019 Feb 9;13(01).
[84] Kasar PM, Kale KS, Phadtare DG. Formulation and evaluation of topical antifungal gel containing itraconazole. CDR. 2018 Jul 1;1(F2):F3.
[85] https://www.healthdirect.gov.au/prednisolone
[86] Stacey, S. K., & McEleney, M. (2021). Topical corticosteroids: choice and application. American Family Physician, 103(6), 337-343.
[87] Ali J, Khar R, Ahuja A. A textbook of dosage form design. Birla publications Pvt Ltd, Delhi; 3rd edition; 2008: 100-107.
[88] Acharya PC, Shetty S, Fernandes C, Suares D, Maheshwari R, Tekade RK. Preformulation in Drug Research and Pharmaceutical Product Development. InDosage Form Design Considerations 2018 Jan 1 (pp. 1-55). Academic Press.
[89] Williams RL, Team P, Staff US. Official USP Reference Standards: Metrology concepts, overview, and scientific issues and opportunities. Journal of pharmaceutical and biomedical analysis. 2006 Jan 23;40(1):3-15.
[90] Kashyap, R., Subrahmanyam, E. V. S., & Sharbaraya, A. R. (2012). Development and validation of UV spectroscopy method for the estimation of prednisolone in bulk and dosage form. Journal of chemical and pharmaceutical research, 4(2), 1090-1096.
[91] Zakeri-Milani, P., Nezhadi, S. H., Barzegar-Jalali, M., Mohammadi, L., Nokhodchi, A., & Valizadeh, H. (2011). Studies on dissolution enhancement of prednisolone, a poorly water-soluble drug by solid dispersion technique. Advanced Pharmaceutical Bulletin, 1(1), 48.
[92] https://www.cdek.liu.edu/api/108755/pricing/prednisolone
[93] A Khaled, K., A Sarhan, H., A Ibrahim, M., & W Naguib, Y. (2008). Controlled-release prednisolone poly (dl-lactide) microspheres: impact of formulation parameters, characterization and release mechanism. Bulletin of Pharmaceutical Sciences. Assiut, 31(1), 49-67.

[94] Farooq, M. Q., Abbasi, N. M., & Anderson, J. L. (2020). Deep eutectic solvents in separations: Methods of preparation, polarity, and applications in extractions and capillary electrochromatography. Journal of Chromatography a, 1633, 461613.
[95] Skulcova, A., Russ, A., Jablonsky, M., & Sima, J. (2018). The pH behavior of seventeen deep eutectic solvents. BioResources, 13(3), 5042-5051.
[96] Li, Z., & Lee, P. I. (2016). Investigation on drug solubility enhancement using deep eutectic solvents and their derivatives. International journal of pharmaceutics, 505(1-2), 283-288.
[97] Hayyan, M. (2023). Versatile applications of deep eutectic solvents in drug discovery and drug delivery systems: Perspectives and opportunities. Asian Journal of Pharmaceutical Sciences, 18(2).
[98] Madan, S., Nehate, C., Barman, T. K., Rathore, A. S., & Koul, V. (2019). Design, preparation, and evaluation of liposomal gel formulations for treatment of acne: in vitro and in vivo studies. Drug Development and Industrial Pharmacy, 45(3), 395-404.
[99] Huang, C., Chen, X., Wei, C., Wang, H., & Gao, H. (2021). Deep eutectic solvents as active pharmaceutical ingredient delivery systems in the treatment of metabolic related diseases. Frontiers in Pharmacology, 12, 794939.
[100] Lu, W., & Chen, H. (2022). Application of deep eutectic solvents (DESs) as trace level drug extractants and drug solubility enhancers: State-of-the-art, prospects and challenges. Journal of Molecular Liquids, 349, 118105]
[101] Dash S, Murthy PN, Nath L, Chowdhury P. (2010). Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 67(3): 217-23.
[102] Islam M, Reza S, Rahman H. In vitro Release Kinetics Study of Diltiazem Hydrochloride from Wax and Kollidon SR Based Matrix Tablets. Iranian Journal of Pharmaceutical Research. 2010; 7:101-8.
[103] Shreeraj H, Patil JKS, Patil NV. Gastroretentive drug delivery systems with potential herbal drugs for helicobacter pylori eradication: a review. J Chinese Integrative Med 2009; 7(10): 976-82.
[104] Barth, J., Damoiseaux, M., Möllmann, H., Brandis, K. H., Hochhaus, G., & Derendorf, H. (1992). Pharmacokinetics and pharmacodynamics of prednisolone after intravenous and oral administration. International journal of clinical
[105] pharmacology, therapy, and toxicology, 30(9), 317-324.
[106] Tatheer, F., Mazahir, R., & Anshul Kumar, S. (2015). Development and characterization of prednisolone liposomal gel for the treatment of rheumatoid arthritis. Int Res J Pharm, 6, 1-5.
[107] Das Tama, Manna Mahuli and Rudra Anandamoy. Formulation and characterization of papaya leaf gel. GSC Biological and Pharmaceutical Sciences. 2020; 10(03): 089–094.