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Abstract: Emulgel for dermatological use has several favorable properties such as being greaseless, thixotropic, non-staining, emollient, easily removable, easily spreadable, longer shelf life, bio-friendly, water-soluble, transparent and pleasing appearance. Emulgel is used to treat aches and pains caused by colds, muscle aches, headaches, arthritis, backaches, psoriasis and other conditions and injuries. Emulgel has appear as one of the most absorbing topical delivery systems as it has binary release control system i.e. emulsion and gel. When emulsion and gel are used in combined form, the dosage form are referred as emulgel. The use of emulgel based systems as topical drug delivery vehicles is analyzed, with particular significance being placed on recent developments and future directions.

Keywords: Emulgel, Mefenamic acid, Gelling agents, Topical drug delivery, Skin diseases

INTRODUCTION:
Topical drug delivery systems have been used for centuries for the treatment of local skin disorders and relieve the pain. One side the topical applications of the drug offer the potential advantages of delivering the drug directly to the site of action and delivering the drug for an extended period of time at the affected site that mainly acts at related regions. On the other hand, the topical delivery system increases the contact time and mean resident time of the drug. The most common side effect of some oral dosage forms is a gastrointestinal irritation. The long term use of such drugs is associated with severe gastrolatry. Over the last decades the treatment of illness has been accomplished by administering drug to human body via various routes namely oral, sublingual, rectal, parental etc. The topical drug delivery system is generally used where these systems of drug administration fails or in local skin infection like fungal infection. Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorder.

Dermatological products applied to skin are diverse in formulation and range in consistency from liquid to powder but the most popular products are semisolid preparation. Within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations [1-4]. In recent year the focus of pharmaceutical researches gradually shifting to the development of drug delivery systems rather than finding newer chemical entities for an around improve mentation drug therapy. Now a day’s scenario pharmaceutical researches work is focused to fulfill the therapeutic needs of patients. Most widely used drugs when given by oral route have side effects like gastric irritation, nausea, bleeding in gastrointestinal tract etc. In order to minimize such side effects and systematic toxicities and also achieve better therapeutic effects one of the promising method is to administered drug via skin or, in short by topical drug delivery system.

Topical DDS is a localized drug delivery system anywhere in the body through ophthalmic rectal vaginal & skin as topical routes [5]. Topical drug delivery system has several advantages such as ability to deliver drug more selectively to a specific site, avoidance of gastro intestinal incompatibility and metabolic degradation associated with oral administration more over topical deliveries provide increased bio-availability by avoiding first pass metabolism by liver and consistent delivery for extended period.

Topical drug delivery system has several advantages such as ability to deliver drug more selectively to a specific site, avoidance of gastro-intestinal incompatibility & metabolic degradation associated with oral administration.
Moreover topical deliveries provide an increased bioavailability by avoiding first pass metabolism by liver and a consistent delivery for extended period. In topical drug delivery system drug diffuses out of the delivery system, reaches to the site of action and gets absorbed by the skin [6, 7, 8].

**Formulation Considerations** [9,10]
The challenges in formulating topical preparations are
1. Determining systems that are non-toxic, non-irritating, non-comedogenic and non-sensitizing.
2. Formulating cosmetically elegant preparation.
3. The formulation must have low allergic potential, good physiological compatibility and high biocompatibility

**Emulgel: Emulsion + Gel** [11-14]
As the name suggest, they are the combination of emulsion and gel. Both water-in-oil and oil-in-water type of emulsion used as a vehicle to deliver various drugs to the skin. They also have a high ability to penetrate the skin. The presence of the gelling agent in water phase converts a emulsion into an emulgel. Emulgel for dermatological use has several favorable properties such as being greaseless, thixotropic, emollient, non-staining, easily spreadable, easily removable, longer shelf life, bio-friendly, water-soluble, transparent and pleasing appearance.

Molecules can basically penetrate into the skin by three routes: through intact stratum corneum, sweat ducts, or sebaceous follicle. The surface of the stratum corneum presents more than 99.9% of the total skin surface available for percutaneous drug absorption. Passage through this outermost layer is the rate limiting step for percutaneous absorption. The major steps involved in percutaneous absorption include the establishment of a concentration gradient, which provides the driving force for drug movement across the skin, release of drug from the vehicle (partition coefficient), and drug diffusion across the layers of the skin (diffusion coefficient).

**Advantages** [15, 16]
1. Avoidance of first pass metabolism.
3. More selective to a specific site.
4. Improve patient compliance.
5. Suitability for self-medication.
6. Providing utilization of drug with short biological half-life and
7. Narrow therapeutic window.
8. Ability to easily terminate medication when needed.
9. Convenient and easy to apply.
10. Incorporation of hydrophobic drugs
11. Better loading capacity
12. Better stability
13. Production feasibility and low preparation cost
14. Controlled release
15. No intensive sonication

**Disadvantages**
1. Skin irritation on contact dermatitis.
2. The possibility of allergenic reactions.
3. The poor permeability of some drug through the skin.
4. Drug of large particle size not easy to absorb through the skin.
5. The occurrence of the bubble during formation of emulgel.
**Physiology of Skin [17]**

Most of the topical preparations are meant to be applied to the skin. So basic knowledge of the skin and its physiology function are very important for designing topical. Skin is the soft outer covering of vertebrates. In humans, it is the largest organ of the integumentary system. The skin has multiple layers of ectodermal tissue and guards the underlying muscles, bones, ligaments and internal organs. The skin has several layers. The overlying outer layer is called epidermis; the layer below the epidermis is called dermis. They dermis contain a network of blood vessels, hair follicle, sweat gland and sebaceous gland. Beneath the dermis are subcutaneous fatty tissues. Bulbs of hair project into these fatty tissues. Human skin is known to contain an average of 40-70 hair follicles and 200-300 sweat ducts on every square cm of the skin. The pH of skin varies from 4- 5.6. Sweat and fatty acid secretions from sebum influence the pH of skin surface. The skin of an adult body covers a surface area approximately 2m² and receives about one third of blood circulation through the body.

![Fig. No. 1: Structure of skin](image)

The skin of an average adult body covers a surface area approximately and receives about one third of the blood circulating through the body. An average human skin surface is known to contain, on the average 40-70 hair follicles and 200-300 sweat ducts on every square centimeter of the skin. The pH of the skin varies from 4 to 5.6. Sweat and fatty acid secreted from sebum influence the pH of the skin surface.

**Epidermis:**
The epidermis is the outermost layers of the skin. It forms a protective barrier over the body's surface, responsible for keeping water in the body and preventing pathogens from entering, and is a stratified squamous epithelium, composed of proliferating basal and differentiated suprabasal keratinocytes. The epidermis also helps the skin regulate body temperature [18]. Keratinocytes are the major cells, constituting 95% of the epidermis, while Merkel cells, melanocytes and Langerhans cells are also present. The epidermis can be further subdivided into the following strata or layers (beginning with the outermost layer) Stratumcorneum, Stratum lucidum, Stratum granulosum, Stratum spinosum, Stratum germinativum [19].

**Basement membrane**
The epidermis and dermis are separated by a thin sheet of fibers called the basement membrane, and is made through the action of both tissues. The basement membrane controls the traffic of cells and molecules between the dermis and epidermis but also serves, through the binding of a variety of cytokines and growth factors, as a reservoir for their controlled release during physiological remodeling or repair processes [20].

**Dermis**
The dermis is the layer of skin beneath the epidermis that consists of connective tissue and cushions the body from stress and strain. The dermis provides tensile strength and elasticity to the skin through an extracellular matrix composed of collagen fibrils, micro fibrils, and elastic fibers, embedded in proteoglycans.
It also contains the hair follicles, sweat glands, sebaceous glands, apocrine glands, lymphatic vessels and blood vessels. The blood vessels in the dermis provides nourishment and waste removal from its own cells as well as for the epidermis.

The dermis is tightly connected to the epidermis through a basement membrane and is structurally divided into two areas: a superficial area adjacent to the epidermis, called the papillary region, and a deep thicker area known as the reticular region [21].

**Papillary region**
The papillary region is composed of loose areolar connective tissue. This is named for its finger like projections called papillae that extend toward the epidermis. The papillae provide the dermis with a "bumpy" surface that interdigitates with the epidermis, strengthening, and the connection between the two layers of skin [22].

**Reticular region**
The reticular region lies deep in the papillary region and is usually much thicker. It is composed of dense irregular connective tissue, and receives its name from the dense concentration of collagenous, elastic, and reticular fibers that weave throughout it. These protein fibers give the dermis its properties of strength, extensibility, and elasticity. Also located within the reticular region are the roots of the hair, sebaceous glands, sweat glands, receptors, nails, and blood vessels.

**Hypodermis**
The hypodermis is not part of the skin, and lies below the dermis. Its purpose is to attach the skin to underlying bone and muscle as well as supplying it with blood vessels and nerves. It consists of loose connective tissue and elastin. The main cell types are fibroblasts, macrophages and adipocytes (the hypodermis contains 50% of body fat). Fat serves as padding and insulation for the body. Another name for the hypodermis is the subcutaneous tissue [23].

**Subcutaneous connective tissue:**
The subcutaneous tissue or hypodermis is not actually considered a true part of the structured connective tissue which is composed of loose textured, white, fibrous connective tissue containing blood and lymph vessels, secretory pores of the sweat gland and cutaneous nerves. Most investigators consider drug is permeating through the skin enter the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug [23, 24].

**Factors to be considered when choosing a topical preparation [24, 25]**
1. Effect of the vehicle e. g. an occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient or protective action.
2. Match the type of preparation with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.

3. Match the type of preparation with the site. (e.g., gel or lotion for hairy areas)

4. Irritation or sensitization potential. Generally, ointments and w/o creams are less irritating, while gels are irritating. Ointments do not contain preservatives or emulsifiers if allergy to these agents is a concern.

**Drug delivery across the skin:** [26-27]

The epidermis is the most superficial layer of the skin and is composed of stratified keratinized squamous epithelium which varies in thickness in different parts of the body. It is thickest on with elastic fibers. The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. Blood vessels are distributed profusely beneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries. In the most exposed areas of the body—the hands, feet, and ears blood is also supplied to the plexus directly from the small arteries through highly muscular arterio-venous and astomoses.

A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment. The skin acts as a two-way barrier to prevent absorption or loss of water and electrolytes.

There are three primary mechanisms of topical drug absorption: Transcellular, intercellular, and follicular. Most drugs pass through the tortuous path around corneocytes and through the lipid bilayer to viable layers of the skin. The next most common (and potentially under recognized in the clinical setting) route of delivery is via the pilosebaceous route. The barrier sides in the outer most layer of the epidermis, the stratum corneum, as evidenced by approximately equal rates of penetration of chemicals through isolated stratum corneum or whole skin.

Creams and gels that are rubbed into the skin have been used for years to deliver pain medication and infection fighting drugs to an affected site of the body. These include, among other gels and creams for vaginal yeast infections, topical creams for skin infections and creams to soothe arthritis pain.

New technologies now allow other drugs to be absorbed through the skin (transdermal). These can be used to treat not just the affected areas (for example, the skin) but the whole body (systemic).

**Emulgel preparation:**

1. **Aqueous material:**
   This forms the aqueous phase of the emulsion. Commonly used agents e.g. water, alcohols.

2. **Oils:**
   These agent forms the oily phase. For externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffin’s are widely used.

3. **Emulsifier:** Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life. e.g. Polyoxyethylene 40 stearate, Sorbitan mono-oleate (Span 80) Polyoxyethylene sorbitanmonoooleate (Tween 80), Stearic acid, Sodium stearate.
4. **Preservatives:**
E.g. Propyl paraben, methyl paraben, Benzalkonium chloride, Benzoic acid, Benzyl alcohol etc.

5. **Antioxidants:**
E.g. Butylated Hydroxy Toluene (BHT), Ascorbylpalmitate, Butylated Hydroxy anisole (BHA), etc.

6. **Humectant:**
E.g. Glycerin, Propylene glycol, etc.

7. **Gelling agents:**
These are the agents used to increase the consistency of any dosage form can also be used as thickening agent. E.g. Carabopol 934, carabopol 940, HPMC, HPMC-2910, sodium CMC.

8. **Permeation enhancer:**
These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. E.g. Oleic acid, lecithin, isopropyl myristate, urea, eucalyptus oil, chenopodium, oil, pyrroldione, laurocapran, dimethyl sulphoxide, linoleic acid, menthol.

**Properties of penetration enhancer:**
- They should be non-toxic, non-irritating and non-allergenic.
- They would ideally work rapidly and the activity and duration of effect should be both predictable and reproducible.
- They should have no pharmacological activity within the body i.e. should not bind to receptor sites.
- The penetration enhancers should work unidirectional i.e. should allow therapeutic agents into the body whilst preventing the loss of endogenous material from the body.
- The penetration enhancers should be appropriate for formulation into diverse topical preparations, thus should be compatible with both excipients and drugs.
- They should be cosmetically suitable with an appropriate skin ‘feel’.

![Fig no 4: Penetration of Emulgel](Image)

**Mechanism of Penetration enhancer** [28]
Penetration enhancers may act by one or more of three main mechanisms:
1. Disruption of the highly ordered structure of stratum corneum lipid.
2. Interaction with intercellular protein.
3. Improved partition of the drug, co-enhancer or solvent into the stratum corneum.

**Formulation of Emulgel:**

**Determination of Mefenamic Acid solubility in selected oils** [29]:
Mefenamic Acid solubility test was performed to select the oil for preparation of micro emulsion. The 1 g of ibuprofen was added into each flask containing 5ml of selected oils such as castor oil, oleic acid, isopropyl myristate, liquid paraffin and the mixtures were shaken for 24 hours at temperature 250 C and next were centrifuged at 3000 rpm during 5 min. In the supernatant Mefenamic Acid content was determined by UV spectrophotometric method.

**Pseudo ternary phase diagram** [30]:
Mefenamic Acid showed maximum solubility in oleic acid as compared to other oils; hence, it was selected for further studies. Tween 80, as a surfactant, and ethanol, as surfactant, showed better solubility for Mefenamic Acid and good emulsifying properties with oleic acid. Pseudo ternary phase diagrams were
constructed using water titration method. Surfactant and co surfactant (Smix) were mixed in different weight ratios (1:1, 1:2, and 1:3, 2:1 and 3:1). Oil and Smix mixture were mixed thoroughly in different weight ratios (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1). Distilled water was added drop wise to the different mixtures of oil/Smix until cloudy dispersion was obtained. Pseudo ternary plots were constructed using Chemix School Software and micro emulsions were prepared based on ternary phase diagram [31,32].

**Method of Preparation:**
Different formulations were prepared using varying amount of gelling agent. The method only differed in process of making gel in different formulation. The preparation of emulsion was same in all the formulations. The gel bases were prepared by dispersing Carbopol 934 and in distilled water separately with constant stirring at a moderate speed using mechanical shaker. Formulations F1 were prepared by using carbopol 934 as a gelling agent with different concentration and formulation f2 were prepared by using xanthum gum as a gelling agent with different concentration and formulation f3 were prepared by combination of both i.e. carbopol 934 and xanthum gum with different concentration. The gel were prepared by dispersing the gelling agent in heated distilled water (75°C) and the dispersion was cooled and left overnight. The pH of all the formulations was adjusted to 5.5 to 6.5 using tri ethanol amine (TEA). The oil phase of the emulsion was prepared by dissolving methyl and propyl parabens in ethanol and it was added to oleic acid. Then Mefenamic Acid was added to oil phase. The aqueous phase was prepared by incorporating Tween-80 into distilled water, then both phase were mixed using constant stirring to get micro emulsion. The obtained emulsion was mixed with the gel in 1:1 ratio with gentle stirring to obtain the emulgel [33,34,35].

**Materials and Equipment’s:**

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Materials</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Mefenamic acid</td>
<td>Concept pharmaceutical, Aurangabad</td>
</tr>
<tr>
<td>2.</td>
<td>Oleic acid</td>
<td>Research-lab fine industries, Mumbai</td>
</tr>
<tr>
<td>3.</td>
<td>Tween 80</td>
<td>Thomas Baker chemical, Mumbai</td>
</tr>
<tr>
<td>4.</td>
<td>Xanthan gum</td>
<td>Lobalchemie</td>
</tr>
<tr>
<td>5.</td>
<td>Ethanol</td>
<td>Chinachagshu Yangyuan chemical</td>
</tr>
<tr>
<td>6.</td>
<td>Methyl paraben</td>
<td>Thomas Baker chemical, Mumbai</td>
</tr>
<tr>
<td>7.</td>
<td>Propyl paraben</td>
<td>Thomas Baker chemical, Mumbai</td>
</tr>
<tr>
<td>8.</td>
<td>Carbopol 934</td>
<td>Local chemical</td>
</tr>
<tr>
<td>9.</td>
<td>Tri ethanolamine</td>
<td>Thomas Baker chemical, Mumbai</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Name of Instruments</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Magnetic stirrer</td>
<td>Omega scientific industries</td>
</tr>
<tr>
<td>2.</td>
<td>Heating mantle</td>
<td>Shital scientific industries, Mumbai</td>
</tr>
<tr>
<td>3.</td>
<td>Electronic balance</td>
<td>Citizen, Mumbai</td>
</tr>
<tr>
<td>4.</td>
<td>UV-spectrophotometer</td>
<td>Agilent cary 630 Spectrophotometer</td>
</tr>
<tr>
<td>5.</td>
<td>Hot air oven</td>
<td>Shital scientific</td>
</tr>
<tr>
<td>6.</td>
<td>Centrifuge</td>
<td>Central scientific</td>
</tr>
<tr>
<td>7.</td>
<td>Stability chamber</td>
<td>Sky lab industries and engineering pvt.ltd</td>
</tr>
<tr>
<td>8.</td>
<td>Brookfield viscometer</td>
<td>Digital viscometer, USA</td>
</tr>
<tr>
<td>9.</td>
<td>Hot plate</td>
<td>Dolphin Mumbai</td>
</tr>
<tr>
<td>10.</td>
<td>Mechanical stirrer</td>
<td>Remi motor Ltd</td>
</tr>
<tr>
<td>11.</td>
<td>IR</td>
<td>Shimazdunavi Mumbai</td>
</tr>
<tr>
<td>12.</td>
<td>Franz diffusion cell</td>
<td>Glass work new Delhi</td>
</tr>
</tbody>
</table>
Evaluation of Emulgel: [35-44]

Physical examination
The Prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency and phase separation.

Determination of pH:
pH of the formulation was determined by using digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3 times.

Viscosity:
Viscosity is the most important parameter in the evaluation as it governs many properties of the formulation such as spreadability, pourability of the product from the container etc. As there are various factors which can affect the viscosity like change in temperature, change manufacturing conditions, quality of raw materials etc. The viscosity of emulgel was determined by LVT Brookfield viscometer. The sample was placed in a clean and dried container and viscosity was checked as per standard operating procedure of viscometer by using spindle no. 4 at speed 30 rpm. After recording the dial reading viscosity was calculated in the centipoises (cps). Following formula is used for the calculation of the viscosity:

\[
\text{Viscosity in centipoises (cps)} = \text{Dial reading} \times \text{Factor.}
\]

For calculation of viscosity put the factor value corresponding to the speed and the spindle number.

Spreadability
To determine spreadability of the gel formulations, two glass slides of standard dimensions were selected. Formulation whose spreadability was to be determined was placed over one slide and the other slide was placed over its top such that the gel is sandwiched between the two slides. The slides were pressed upon each other so as to displace any air present and the adhering gel was wiped off. The two slides were placed onto a stand such that only the lower slide is held firm by the opposite fangs of the clamp allowing the upper slide to slip off freely by the force of weight tied to it. 20 g weight was tied to the upper slide carefully. The time taken by the upper slide to completely detach from the lower slide was noted.

Ex vivo diffusion study:
Cellophane membrane previously soaked in the respective dissolution medium overnight was used as the permeation membrane. 200 ml of Phosphate buffer pH7.4 was placed in a beaker (receptor compartment). An accurately weighed quantity (1 g) of the formulated Emulgel was then uniformly spread on the cellophane membrane (donor compartment) and this membrane was tied to the diffusion tube (a hollow tube open on both sides). One side of the cellophane membrane was kept in contact with the medium (Phosphate Buffer pH 7.4). The medium was constantly agitated using a magnetic stirrer and the temperature was maintained at a constant of 37 ± 1 °C throughout the operation. Samples of 10 ml volume were then withdrawn from the receptor compartment at intervals of 1 hour over a period of 8 hours and the amount withdrawn was replaced with fresh volume of the medium. The samples withdrawn were then analyzed for the amount of mefenamicacid released by UV spectrophotometric method by measuring the absorbance of the samples at 280 nm against Phosphate Buffer pH 7.4 taken as blank.

Skin irritation test:
A 0.5 g sample of the test article was then applied to each site (two sites per rabbit) by introduction under a double gauze layer to an area of skin approximately 1” x 1” (2.54 x 2.54 cm²)

Stability studies:
The Gellified Emulsion was applied on the skin of a rabbit. Animals were returned to their cages. After a 24 h exposure, the Gellified emulsion is removed. The test sites were wiped with tap water to remove any remaining test article residue. The prepared emulgels were packed in aluminium collapsible tubes (5 g) and subjected to stability studies at 5 °C, 25 °C/60% RH, 30 °C/65% RH, and 40 °C/75% RH for a period of 3
mo. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.

**Rheological Studies:**
Rheological properties (study of deformation and flow of matter) are required in various pharmaceutical areas. Some of the reasons for determining these properties are:
1. It helps in understanding the physicochemical nature of vehicle and quality control of ingredients, test formulations and final products, together with the manufacturing process such as mixing pumping and filling.
2. It reflects the effects such as temperature and storage time on the products.
3. It helps to assess a topical formulation with respect to the patient usage e.g. removal of preparation from jar or tube without spillage or spreadability and adherence to skin.
4. Finally, it helps to monitor the effects of vehicles consistency on the release of drug from the preparation and its subsequent percutaneous absorption. Rheological techniques may be used to study the conditions operating during the application of preparation to the skin.

**RESULTS & DISCUSSION:**

**Solubility of Mefenamic Acid:**

**Table no.3: Detection of solubility**

<table>
<thead>
<tr>
<th>Solvents</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distilled water</td>
<td>Insoluble</td>
</tr>
<tr>
<td>Dichloromethane</td>
<td>Soluble</td>
</tr>
<tr>
<td>Chloroform</td>
<td>Soluble</td>
</tr>
<tr>
<td>Methanol</td>
<td>Soluble</td>
</tr>
<tr>
<td>Acetone</td>
<td>Soluble</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Soluble</td>
</tr>
</tbody>
</table>

The solubility of pure drug in 10mg/ml of solvent was carried out and it reveals that it is soluble in methanol; acetone and insoluble in distilled water.

**Physical appearance & Melting point determination:**

**Table no.4: Physical appearance & Melting point determination**

<table>
<thead>
<tr>
<th>Properties</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>White</td>
</tr>
<tr>
<td>Odour</td>
<td>Slight</td>
</tr>
<tr>
<td>Appearance</td>
<td>Microcrystalline Powder</td>
</tr>
<tr>
<td>M.P.</td>
<td>228-230</td>
</tr>
</tbody>
</table>

The physical characters was found to be as per standard drug, so drug used in formulation was found to be pure according to I.P. specification. The melting point of pure mefenamic acid was found to be 228-230°C so drug used in formulation was found to be pure according to I.P. specification.
FTIR study of mefenamic Acid:

![FTIR of The Drug (Mefenamic Acid)](image1)

**Fig no. 5: FTIR of The Drug (Mefenamic Acid)**

**Determination Of λ max:**
Mefenamic Acid showed the maximum wavelength at 285 nm, which matches with the standard. Hence drug used in formulation was found to be pure according to I.P. specification.

![Determination of λ Max of the Drug](image2)

**Fig no.6: Determination of λ Max of the Drug**

**Calibration Curve of Mefenamic Acid:**

**Table no.5: Calibration Curve of Mefenamic Acid**

<table>
<thead>
<tr>
<th>Concentration(µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.747</td>
</tr>
<tr>
<td>1</td>
<td>0.595</td>
</tr>
<tr>
<td>1.5</td>
<td>0.585</td>
</tr>
<tr>
<td>2</td>
<td>0.599</td>
</tr>
<tr>
<td>2.5</td>
<td>0.660</td>
</tr>
</tbody>
</table>

![Determination of calibration Curve](image3)

**Fig no.7: Determination of calibration Curve**
Assay of Mefenamic Acid:
By titrimetric method the percent purity of mefenamic Acid was found to be 98% which is acceptable as per the IP standards.

Solubility in selected oils:
Mefenamic Acid showed the maximum solubility in oleic acid among the selected oils, so it was considered as an oil phase for the preparation of emulsion.

Pseudo ternary phase diagram:
From all following phase diagrams i.e. 1:1, 1:2, 2:1 and 3:1 the ratio of 2:1 S/Cos concentration showed good self-micro emulsifying region hence selected for formulation of micro emulsion. Right part from boundary line in phase diagram shows us the region in which self-micro emulsifying region exists. A larger micro emulsion region is responsible for the higher micro emulsifying potential of the combination. Thus, it is helpful in finding regions having better ability at lower proportion of surfactants and having higher drug loading potential.

Phase separation:
Emulsion is thermodynamically unstable system, which may separate when subjected to physical stresses like centrifugation. Though micro emulsions are homogeneous single phase system, they were subjected to centrifugation to confirm the absence of phase separation. Micro emulsion did not show any sign of phase separation when subjected to centrifugation, which confirms physical stability of micro emulsion.

Method of preparation of emulgel:
The emulgels were prepared by the procedure as mentioned in the experimental work under method of preparation.

Physical appearance of emulgel formulation:
The prepared emulgel formulations were inspected visually for their color, homogeneity and consistency.

<p>| Table no 6: Determination of physical properties of formulated emulgels |
|---------------|-------|---------|---------|------------------|
| Formulation  | Colour         | Homogeneity | Consistency          | Phase separation |
| F1           | Milky white    | Homogeneous | Cream like semisolid | No               |
| F2           | Milky white    | Homogeneous | Cream like semisolid | No               |
| F3           | Milky white    | Homogeneous | Cream like semisolid | No               |
| F4           | Yellowish creamy | Homogeneous | Cream like semisolid | No               |
| F5           | Yellowish creamy | Homogeneous | Cream like semisolid | No               |
| F6           | Yellowish      | Homogeneous | Cream like           | No               |</p>
<table>
<thead>
<tr>
<th>Formulation</th>
<th>pH (mean±SD)</th>
<th>Spreadability(gm./s) (mean±SD)</th>
<th>Extrudability</th>
</tr>
</thead>
<tbody>
<tr>
<td>F7</td>
<td>6.58±0.07</td>
<td>22.5±0.57</td>
<td>Very good</td>
</tr>
<tr>
<td>F8</td>
<td>6.57±0.07</td>
<td>34.61±0.57</td>
<td>Excellent</td>
</tr>
<tr>
<td>F9</td>
<td>6.45±0.01</td>
<td>19.56±0.57</td>
<td>Very good</td>
</tr>
<tr>
<td>F10</td>
<td>6.44±0.05</td>
<td>22.5±0.57</td>
<td>Excellent</td>
</tr>
<tr>
<td>F11</td>
<td>6.30±0.07</td>
<td>20.05±0.85</td>
<td>Good</td>
</tr>
<tr>
<td>F12</td>
<td>6.05±0.02</td>
<td>16.97±0.39</td>
<td>Good</td>
</tr>
<tr>
<td>F13</td>
<td>6.46±0.06</td>
<td>28.12±1.1</td>
<td>Excellent</td>
</tr>
<tr>
<td>F14</td>
<td>6.30±0.07</td>
<td>20.05±0.85</td>
<td>Good</td>
</tr>
<tr>
<td>F15</td>
<td>6.05±0.02</td>
<td>16.97±0.39</td>
<td>Good</td>
</tr>
</tbody>
</table>

Extrudability:- a) 90%-100% = Excellent, b) 80%-90% = Very good (n=3)

**Spreadability:**

Spreadability is the term expressed to denote the extent of area to which the gel readily spreads on application to the skin. One of the essential criteria for an emulgel is that it should have good spreadability. It depends upon the type and concentrations of polymers used in the formulation. More viscous formulation would have poor spreadability. The formulation F2 showed more spreading coefficient, i.e. 34.61, as compared to other formulations, this is because formulation contained optimum concentration of Carbopol 934, i.e. 1.5.

**Viscosity:**

Rheological behavior of the emulgel formulations exhibited non-Newtonian shear thinning pseudo plastic type of flow, i.e. decreases in viscosity at increasing shear rates. As the shear stress is increased, the
disarranged molecules of the gelling material are caused to align their long axes in the direction of flow. Viscosity for respective emulgels was found to be

![Bar graph showing viscosity of formulated emulgel](Image)

**Fig no.9: Bar graph showing viscosity of formulated emulgel**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>RPM</th>
<th>Viscosity (cps)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>F2</td>
<td>12</td>
<td>34</td>
</tr>
<tr>
<td>F3</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>F4</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>F5</td>
<td>64.5</td>
<td>89.5</td>
</tr>
<tr>
<td>F6</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>F7</td>
<td>64.5</td>
<td>91.5</td>
</tr>
<tr>
<td>F8</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>F9</td>
<td>8342</td>
<td>21012</td>
</tr>
</tbody>
</table>

**Table no.8: Determination of viscosity of formulated emulgels**

Rheological Studies:
The rheograms depict that all formulations F1 to F9 show the thixotropic behaviours, since the down curve shifted to the left of the up curve when r.p.m. plotted against dial reading. Thus, formulations F1 to F9 are shear thinning systems. The shear thinning systems indicate that the breakdown of structure is not reformed immediately when the stress is removed. The phenomenon is thixotropic and is exhibited by only shear thinning systems. Shear thinning nature for topical preparations are desired because they can spread easily on the affected area. Viscosity at higher temp.is slightly decreased but rheological property remains thixotropic.

![Rheological behavior of F1, F2 & F3](Image)

**Fig no.10: Rheological behavior of F1, F2 & F3**
Drug content determination:
All formulations showed drug content in between the range of 70%-95%. The drug content of all formulations is tabulated as under:

Table no.9: Determination of Drug content of formulated emulgels

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug Content (%) (mean ± SD), n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>71.70±0.12</td>
</tr>
<tr>
<td>F2</td>
<td>92.30±2.50</td>
</tr>
<tr>
<td>F3</td>
<td>75.18±0.95</td>
</tr>
<tr>
<td>F4</td>
<td>90.85±1.02</td>
</tr>
<tr>
<td>F5</td>
<td>80.75±0.35</td>
</tr>
<tr>
<td>F6</td>
<td>73.64±0.45</td>
</tr>
<tr>
<td>F7</td>
<td>89.55±0.19</td>
</tr>
<tr>
<td>F8</td>
<td>65.85±0.90</td>
</tr>
<tr>
<td>F9</td>
<td>90±0.65</td>
</tr>
</tbody>
</table>

In vitro drug release:
The release of active pharmaceutical ingredient (Mefenamic Acid) from the emulgel was varied according to polymer concentration. The drug release from its emulsified gel formulation can be categorized in the following ascending order: F9 < F8 < F7 < F6 < F5 < F4 < F3 < F2 < F1. The progressive augment in the amount of drug diffusion through membrane from formulation credited to gradual dwindling in the
concentration of polymer. It has been recapitulated that, if we amplify the concentration of polymer, the diffusion of drug through the membrane also diminishes. The cumulative % of drug release profile of all the formulation batches has been shown below

**Table no.10: In-vitro% cumulative drug release of formulations F1 to F4**

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.5</td>
<td>12.58</td>
<td>14.25</td>
</tr>
<tr>
<td>2</td>
<td>16.55</td>
<td>18.73</td>
<td>19.22</td>
</tr>
<tr>
<td>3</td>
<td>29.60</td>
<td>24.23</td>
<td>25.73</td>
</tr>
<tr>
<td>4</td>
<td>42.55</td>
<td>35.85</td>
<td>29.15</td>
</tr>
<tr>
<td>5</td>
<td>58.88</td>
<td>67.95</td>
<td>51.23</td>
</tr>
<tr>
<td>6</td>
<td>70.17</td>
<td>90.30</td>
<td>61.97</td>
</tr>
</tbody>
</table>

**Table no11: In-vitro% cumulative drug release of formulations F5 to F9**

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22.3</td>
<td>22.75</td>
<td>22.95</td>
<td>17.23</td>
<td>14.12</td>
</tr>
<tr>
<td>2</td>
<td>28.35</td>
<td>28.31</td>
<td>27.95</td>
<td>21.35</td>
<td>22.13</td>
</tr>
<tr>
<td>3</td>
<td>31.95</td>
<td>32.25</td>
<td>37.41</td>
<td>27.12</td>
<td>27.35</td>
</tr>
<tr>
<td>4</td>
<td>38.13</td>
<td>38.45</td>
<td>49.79</td>
<td>31.0</td>
<td>32.03</td>
</tr>
<tr>
<td>5</td>
<td>48.25</td>
<td>49.35</td>
<td>68.23</td>
<td>40.82</td>
<td>43.42</td>
</tr>
<tr>
<td>6</td>
<td>78.17</td>
<td>78.17</td>
<td>75.50</td>
<td>53.01</td>
<td>58.13</td>
</tr>
</tbody>
</table>

**In-vitro release profile of all formulations (F1-F9):**
These figures indicate that formulated emulgel gave higher flux and permeation.

**Fig no.13: % Cumulative drug release of F1, F2, F3, F4**
**Fig no.14:** % Cumulative drug release of F5, F6, F7, F8 & F9

**Determination of Total Microbial Count (TMC):**
There was no microbial growth found on any formulation on the day of preparation and after stability study also. Thus, the prepared emulgel formulations does not contain any microbial contamination.

**Stability study:**
The stability test was carried out for three months and results revealed that all the emulgel showed better stability at 40°C and 30°C. And all the parameter obtained are satisfactory.

**CONCLUSION:**
From the result and summary we have conclude that the formulation F2 which contain carbopol 394 1.5% shows the satisfactory result as compare to other batches Hence the objective of this study i.e.

- To achieved local application
- Avoiding first pass effect
- Increase patient compliance
- Reduction of dose

Was achieved through this investigation as a successfully one.

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36. Bhanu VP, Shanmugam V, Lakshmi PKDevelopment and optimization of novel diclofenac sodium


