"Formulation development and evaluation of emulgel drug delivery system for the treatment of psoriasis"

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Abstract

Many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels. When gels and emulsions are used in combined form the dosage form is referred as Emulgel in recent years, there has been great interest in the use of novel polymers. A suitable method of analysis of drug was UV spectrophotometric. Mometasone furoate showed maximum absorption at a wavelength of 260nm. Various formulations (F1-F8) were developed by using Carbopol 940 for local release of Mometasone furoate for the treatment of topical infections by using penetration enhancer Tween 80. Developed formulations of Mometasone furoate were evaluated for the physiochemical parameters such as drug content, viscosity, spread ability, in vitro diffusion. Viscosity studies of various formulations revealed that formulation F4 is better compare to others. Release of drug from Mometasone furoate emulgel was significantly slower, which confirmed that slight prolonged drug release rate. Incorporation of carbomer affected the release rate of the drug. By increasing the amount of carbomer, the release rate of the drug decreased, which could be related to the increased rigidity of the formulation, followed by its de-creased permeability for the drug. In vitro drug release from the semisolid preparation of Mometasone furoate emulgel optimized formulation F4 shows significantly improved in drug release rate as compare to marketed preparation. It was concluded that developed formulations deliver the drug for the treatment of fungal disease. Hence it could be concluded that the carbomer based semisolid preparation would providing local onset of action without need of any device for their application on skin. The preparation of emulgel has potential advantages over marketed preparation as they improved patient compliance rapid local onset of action for longer period with cost effectiveness. The pediatric and geriatric populations are the primary ones whose problems are easily targeted.

Keywords: Psoriasis, Emulgent, Mometasone, FTIR Spectroscopy, λmax of mometasone furoate.

INTRODUCTION

Psoriasis is chronic inflammatory skin disarray that may drastically affect the feature of life of an affected person.¹ Various treatments are presented for psoriasis and with this topical therapy are most generally used in majority of patients. Psoriasis has genetic and life manner triggers; the treatment guidelines involve continuous monitoring and lifelong care for the patients. Knowledge of the disease trigger factors and their part in precipitating the psoriasis is quiet significant in the disease management. Care should be taken to avoid these psoriasis triggers.² In recent years, new biological therapies have been introduced and numerous existing treatments have been superior giving new anticipate to people with psoriasis. Superiority of life in a disease whether it's pre-treatment or post-treatment speak a lot about its all round impact on patients. Psoriasis has depressingly effects on quality of life. ³ Psoriasis is a lifelong, chronic, and recurrent disease. In a patient surveys conducted by the National Psoriasis Foundation between 2001 and 2008 in the USA, 33% of patients with soft disease and 60% of patients with moderate-to- severe psoriasis accounted that their disease extensively affect their everyday life. Psoriasis can be as devastating as many other severe medical or psychiatric conditions. The physical, psychological and social dimensions of life are negatively precious by the psoriasis and can be greater than those consequential from life threatening illnesses such as myocardial infarction. Different treatment options are available to control and eliminate the indication of psoriasis. Nevertheless, most of them cannot be observed as an ideal drug molecule⁴

Drug profile

Mometasone furoate

Mometasone is a medium-potency synthetic corticosteroid with anti-inflammatory, antipruritic, and vasoconstrictive properties. Studies in asthmatic patients have demonstrated that mometasone provides a favorable ratio of topical to systemic activity due to its primary local effect along with the extensive hepatic metabolism and the lack of active metabolites.⁵ Though effective for the treatment of asthma, glucocorticoids do not affect asthma symptoms immediately. Maximum improvement in symptoms following inhaled administration of mometasone furoate may not be achieved for 1 to 2 weeks or longer after starting treatment. The anti- inflammatory actions of corticosteroids are thought to involve phospholipase A2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes.⁶



Figure no.1: Structure of Mometasone Furoate

Excipient Profile

Polyethyleneglycol, Carbopol, Carbomers are white-colored, 'fluffy', acidic, hygroscopic powders with a characteristic slight odor. A granular carbomer is also available (Carbopol 71G). Nonproprietary names BP: Carbomers PhEur: Carbomers USP-NF: Carbomer Synonyms: Carbopol; carboxy polymethylene; polyacrylic acid; carboxyvinyl polymer; Pemulen; Tego Carbomer. Chemical Name: Carbomer. Hypromellose, short for hydroxylpropyl methylcellulose (HPMC), is a semisynthetic, dormant, viscoelastic polymer utilized as an ophthalmic oil, and additionally an excipient and controlled-conveyance segment in oral medicaments, found in an assortment of business items. As a nourishment added substance, hypromellose is an emulsifier, thickening and suspending operator, and an other option to creature gelatin. Its Codex Alimentarius code (E number) is E464. It is by and large perceived as sheltered by the FDA.⁷

PREFORMULATION STUDY

Material Used in Investigation

Materials which are used in the investigation are listed in Table 6.1.

| Sr. No. | Chemicals | Supplier | |
|---------|---|--------------------------------------|--|
| 1. | Mometasone furoate | Euphoria Healthcare Pvt. Ltd. Mumbai | |
| 2. | Disodium Hydrogen Phosphate | S. D. Fine Chem. Ltd., Mumbai | |
| 3. | Di potassium Hydrogen Orthophosphate | S. D. Fine Chem. Ltd., Mumbai | |

| Table no. 1: Materials used for formulation dev | velopment of Emulgel |
|---|----------------------|
|---|----------------------|

| 4. | Sodium Chloride | S. D. Fine Chem. Ltd., Mumbai | |
|-----|------------------|----------------------------------|--|
| 5. | Methanol | Qualigens Fine Chemicals, Mumbai | |
| 6. | Ethanol | Qualigens Fine Chemicals, Mumbai | |
| 7. | Chloroform | Qualigens Fine Chemicals, Mumbai | |
| 8. | Carbopol 934p | S. D. Fine Chem. Ltd., Mumbai | |
| 9. | Methyl Paraben | S. D. Fine Chem. Ltd., Mumbai | |
| 10. | Propyl Paraben | S. D. Fine Chem. Ltd., Mumbai | |
| 11. | Propylene Glycol | S. D. Fine Chem. Ltd., Mumbai | |

Instruments Used in Investigation

Instruments which are used in the investigation are listed in Table .

| Table no.2: Instruments used for the preparation and evaluation of Emulge |
|---|
|---|

| Sr. No. | Instruments | Supplier | |
|---------|---|---|--|
| 1. | UV -Visible Spectrophotometer | Labindia 3000+ | |
| 2. | Fourier Transform Infra Red Spectroscopy | Brucker, Germany | |
| 3. | Mechanical Stirrer | Bionics Scientifics, Delhi | |
| 4. | Optical Microscope | Lyzer, Ambala | |
| 5. | Micro Centrifuge | REMI laboratory, Mumbai | |
| 6. | Franz Diffusion Cell | Electro Lab, Mumbai | |
| 7. | pH Meter | Accumax India, New Delhi | |
| 8. | Electronic Balance | Contech Instruments Ltd. , Mumbai | |
| 9. | Melting Point Apparatus | Contech Instruments Ltd. , Mumbai | |
| 10. | Hot Air Oven | Oracle Equipments, New Delhi | |
| 11. | Vortex Apparatus | Ambros Lab Equipments, Ambala | |
| 12. | Brook Field Viscometer | Precision Electro Instrumentation India Private Limited, Thane | |

Preformulation

Preliminary stability studies

Characterization of drug:

Physiochemical Properties of Mometasone furoate

A) Physical evaluation

It refers to the evaluation by sensory characters-taste, appearance, odor, feel of thedrug, etc.

Table no.3: List of Sensory characters

| S. No. Sensory characters | | Result | |
|---------------------------|------------|--------------------|--|
| 1. | Taste | Tasteless | |
| 2. | Appearance | White to Off-White | |
| 3. | Odor | Odorless | |
| 4. | Texture | Crystalline | |

B) Solubility: Solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, Chloroform and 7.4 pH buffer) Shake vigorously and kept for some time. Note the solubility of the drug in various solvents (at room temperature).⁸

| S. No. | Solvent | Solubility | |
|--------|---------------|-----------------------|--|
| 1. | Water | Slightly Soluble (+) | |
| 2. | Ethanol | Freely soluble (++) | |
| 3. | Methanol | Freely soluble (++) | |
| 4. | 0.1N HCL | Insoluble (+) | |
| 5. | 0.1N NaOH | Sparingly Soluble (+) | |
| 6. | Chloroform | Poorly soluble (-) | |
| 7. | 7.4 pH buffer | Soluble | |

 Table no. 4: Solubility of mometasone furoate

B) Melting point:

It is one of the parameters to judge the purity of drugs. In case of pure chemicals, melting points are very sharp and constant. Since the drugs contain the mixed chemicals, they are described with certain range of melting point.⁹

Procedure for determine melting point:

A small quantity of powder was placed into a fusion tube. That tube was placed in the melting point determining apparatus (Chemline) containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all thepowder gets melted.¹⁰

Table no.5: Melting point of the mometasone furoate

| S. No. | Melting Point of Mometasone | Average Melting Point of | |
|--------|-----------------------------|--------------------------|--|
| | furoate | Mometasone furoate | |
| 1. | 218-219° C | | |
| 2. | 216-220° C | 218-220° C | |
| 3. | 218-220° C | | |

D.Partition coefficient: It is a measurement of a drug's lipophilicity and an indication of its ability to cross cell membrane is the oil/water partition coefficient in system such as octanol/water and chloroform/water. The partition coefficient is defined as the ratio of unionized drug distributed between the organic and aqueous phases at equilibrium. It does provide a mean of characterizing the lipophilic/hydrophilic nature of the drug.

Procedure:

Taken well cleaned and dried separating funnel, then transferred the octanol/water system (50:50 20 ml) as sufficient quantity in separating funnel and added the 1 gm drug in it. Shaked the funnel continuously until the drug was distributed in both phases. Then placed the funnel on stand for settle both phases. After that taken both phases in beaker separately and calculated the drug amount present in both phases.

 Table no.6: Partition coefficient of the Mometasone furoate

| S. No. | Amount of drug in | Amount of drug in water | Partition coefficient | rage partition coefficient |
|--------|----------------------|----------------------------|-----------------------------|-------------------------------|
| | octanol | | (P ₀ /w) | |
| 1. | 370.08 | 440.47 | 0.84 | |
| 2. | 375.50 | 447.02 | 0.84 | 0.84 |
| 3. | 365.25 | 440.06 | 0.83 | |

C) Determination of pH (1% w/v solution in water):

Procedure:

About 100mg of the Powder was taken and dissolved in 100ml of distilled water with sonication and filtered. The pH of the filtrate was checked with standard glass electrode.

Table no.7: pH of the Mometasone furoate

| S. No. | pH of the solution | Average pH of the solution |
|--------|--------------------|----------------------------|
|--------|--------------------|----------------------------|

| 1. | 7.4 | |
|----|-----|-----|
| 2. | 7.5 | 7.5 |
| 3. | 7.5 | |

D) Identification test using FTIR Spectroscopy

Infra- red spectrum is an important record which gives sufficient informationabout the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. The region from 0.8μ to 2.5μ is called Near Infra-red and that from 15μ to 200μ is called Far infra-red region.

Identification of Mometasone furoate was done by FTIR Spectroscopy with respect to marker compound. Mometasone furoate was obtained as White or almost white crystalline powder. It was identified from the result of IR spectrum as per specification.

Sample of pure Mometasone furoate

The IR spectrum of sample drug shows the peak values which are characteristics of the drug and the graph were shown in figure no. 6.1



Figure no.7: FT-IR Spectrum of Pure Drug (Mometasone furoate)IR

Spectrum of Mometasone furoate + All EXCIPIENTS





Loss on drying: The moisture in a solid can be expressed on a wet weight or drywet basis. On a wet weight basis, the water content of a material is calculated as a percentage of the weight of the weight solid. The term loss on drying is an expression of moisture content on a wet weight basis.

Procedure:

Loss on drying is directly measured by IR moisture balance. Firstly calibrated the instrument by knob then taken 5.000 gm sample (powder) and set the temp at 100°C to 105°C for 15 minutes and constant reading set the knob and check % moisture.

| S. No. | Initial weight | Final weight after | % loss of drying | Avg. % loss |
|--------|----------------|--------------------|------------------|-------------|
| | | 15 minutes | | of drying |
| 1. | 5gm | 4.92 gm | 1.67 % | |
| 2. | 5gm5gm | gm | 1.82 % | 1.672 % |
| 3. | | gm | 1.67 % | |

Table no. 8: Loss of drying of drug sample

E) Determination of λ max of mometasone furoate:

The λ_{max} of mometasone furoate was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer.

Procedure:

Accurately weighed 10 mg of drug was dissolved in 10 ml of 7.4 pH buffer solution in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from thissolution 1 ml pipette

out and transfer into 10 ml volumetric flask and volume make up with 7.4 pH buffer solution prepare suitable dilution to make it to a concentration range of 5-25 μ g/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). The spectrum peak point graph of absorbance of mometasone furoate versus wave length was shown in figure 6.3.:



Figure no.9: Standard calibration curve of mometasone furoate

F) Calibration curve of Mometasone furoate at λ max

242nmObservation table:

Table no. 10: Calibration curve of Mometasone furoate

| S. No. | Conc. (µg/ml) | Absorbance (λ max at 242nm) | | | | | | |
|--------|----------------|-----------------------------|-------|-------|---------|--|--|--|
| | | Ι | II | III | Average | | | |
| 1 | 5 | 0.121 | 0.121 | 0.123 | 0.122 | | | |
| 2 | 10 | 0.241 | 0.214 | 0.216 | 0.224 | | | |
| 3 | 15 | 0.358 | 0.359 | 0.358 | 0.358 | | | |
| 4 | 20 | 0.481 | 0.482 | 0.481 | 0.485 | | | |
| 5 | 25 | 0.601 | 0.602 | 0.602 | 0.602 | | | |



Figure no.10 : The linear regression analysis for standard curve

The linear regression analysis was done on Absorbance data points. The results are as follow for standard curve

| Slope | = | 0.024 |
|---------------------------------------|---|-------|
| The intercept | = | 0.004 |
| The correlation coefficient $(r^2) =$ | | 0.999 |

Compatibility studies of drug and excipients

In the compatibility testing program, blends of drug and excipients are prepared by triturating the drug with Individual excipients.

Procedure: Taken 50 mg accurately weigh of mometasone furoate dry powder and 50 mg of excipients and mix the blend of drug and excipients and binary/tertiary blends of extract and excipients were prepared and transferred to inert glass vials. The mouths of the vials were covered with rubber closures followed by the aluminum seal caps. Binary/tertiary blends of extract and excipients, Mometasone furoate neat and excipients were stored at 4°C (refrigerator) as control and at 40°C/75%RH for accelerated stability studies for 4 weeks. The visual observations (color, flow, & sticking) were recorded for initial and at the end of the first, second, third and fourth week.



Figure no.11: U.V. Graph of standard Mometasone furoate



Figure no.12: U.V. Graph of standard mometasone furoate + all excipients

PREPARATION AND CHARACTERIZATION

Formulation development

Preparation of carbopol

Fifty grams of the carbopol gel was prepared by dispersing one gram of carbopol powder in 50 ml purified water with aid of moderate speed stirrer (50 rpm), and then the pH was adjusted to 6-6.5 using 0.5 N sodium hydroxide.

Preparation of emulsion

Different formulations F1, F2, F3, and F4, were prepared using Carbopol 934 as gelling agent whereas formulations F5, F6, F7 and F8 were prepared by dispersing HPMC in heated distilled water (80°C), and the dispersion was cooled and left overnight. The pH of all the formulations was adjusted to 6-6.5 using tri ethanol amine (TEA). The oil phase of the emulsion was prepared by dissolving Span 20 in light liquid paraffin, while the aqueous phase was prepared by dissolving Tween 20 and ethanol in purified water. Methylparaben was dissolved in propylene glycol and mixed with aqueous phase. Drug was dissolved in oil phase. Permeation enhancers were dissolved in the oily phase. Both the oily and aqueous phases were separately heated to 70° to 80°C, then the oily phase was added to the aqueous phase with continuous stirring until it got cooled to room temperature. The obtained emulsion was mixed with the gel in 1:1 ratio along with the addition of a few drops of glutaraldehyde followed by gentle stirring to obtain the Emulgel.

| Formulation | Mometasone | Carbomer | arbomer HPMC | | Span | Tween | ropylene |
|-------------|------------|----------|--------------|----------|------|-------|----------|
| | furoate | 941 | (g) | Paraffin | 20 | | glycol |
| | (g) | (g) | | (g) | (g) | | |
| F1 | 500 | 1 | - | 5 | 1 | 0.5 | 5 |
| F2 | 500 | 1 | - | 5 | 1 | 0.5 | 5 |
| F3 | 500 | 1 | - | 5 | 1 | 0.5 | 5 |
| F4 | 500 | 1 | - | 5 | 1 | 0.5 | 5 |
| F5 | 500 | - | 1 | 10 | 2 | 1 | 5 |
| F6 | 500 | - | 1 | 10 | 2 | 1 | 5 |
| F7 | 500 | - | 1 | 10 | 2 | 1 | 5 |
| F8 | 500 | - | 1 | 10 | 2 | 1 | 5 |

Table no.11 : Different formulas of Mometasone furoate emulgel (% w/w)

Evaluation of emulgel

Physical Characteristic

The Physical Characteristic was checked for emulgel formulations (colour, clogging, homogeneity and texture) and observations were shown in Table 8.1.

Determination of pH

The pH of the emulgel was determined by digital pH meter. One gram of gel was dissolved in 25 ml of distilled water and the electrode was then dipped in to gel formulation for 30 min until constant reading obtained. And constant reading was noted. The measurements of pH of each formulation were replicated two times.

Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually and observations were shown in Table 8.1.

Extrudability study

The emulgel formulations were filled into collapsible metal tubes or aluminium collapsible tubes. The tubes were pressed to extrude the material and the extrudability of the formulation was checked.

Spreadability

Method:

Two glass slides of standard dimensions (6×2) were selected. The emulgel formulation whose spreadability had to be determined was placed over one of the slides. The second slide was placed over the slide in such a way that the formulation was sandwiched between them across a length of 6 cms along the slide. 100 gramsof weight was placed up on the upper slide so that the emulgel formulation between the two slides was traced uniformly to form a thin layer.

The weight was removed and the excess of the emulgel formulation adhering to the slides was scrapped off. The lower slide was fixed on the board of the apparatus and one end of the upper slide was tied to a string to which 20 gram load could be applied 50with the help of a simple pulley. The time taken for the upper slide to travel the distance of 6 cms and separate away from lower slide under the direction of the weight was noted. The experiment was repeated and the average of 6 such determinations was calculated for each emulgel formulation Ahmad (2008).



Where, S=Spreadability (gcm/sec)

m = weight tied to the upper slide (20 grams)l= length of

glass slide (6cms).

t = time taken is seconds.

Viscosity

The measurement of viscosity of the prepared gel was done using Brookfield digital Viscometer. The viscosity was measured using spindle no. 6 at 10 rpm and 25° C. The sufficient quantity of gel was filled in appropriate wide mouth container. The gel was filled in the wide mouth container in such way that it should sufficiently allow to dip the spindle of the Viscometer. Samples of the gels were allowed to settle over 30 min at the constant temperature ($25\pm/1^{\circ}$ C) before the measurements.

In-vitro drug release studies using the prehydrated cellophane membrane

1. Preparation of cellophane membrane for the diffusion studies:

The cellophane membrane approximately 25 cm x 2cm was taken and washed in the running water. It was then soaked in distilled water for 24 hours, before used for diffusion studies to remove glycerin present on it and was mounted on the diffusion cell for further studies.

2. Diffusion Studies:

The *in-vitro* diffusion of drug from the different gel preparations were studied using the classical standard cylindrical tube fabricated in the laboratory; a simple modification of the cell is a glass tube of 15mm internal diameter and 100mm height. The diffusion cell membrane was applied with one gram of the formulation and was tied securely to one end of the tube, the other end kept open to ambient conditions which acted as donor compartment. The cell was inverted and immersed slightly in 250 ml of beaker containing neutralizing phthalate buffer, freshly prepared (pH 5.4) as a receptor base and the system was maintained for 2 hrs at $37\pm 0.5^{\circ}$ C. The media was stirred using magnetic stirrer. Aliquots, each of 5 ml volume were withdrawn periodically at predetermined time interval of up to 12 hrs and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium and analyzed by UV-Vis spectrophotometer at 260.0 nm using neutralizing phthalate buffer as blank.

RESULTS AND DISCUSSION

Characterization of emulgel

Gels were evaluated for their clarity, pH, viscosity, spreadability, skin irritation test, in vitro diffusion studies using standard procedure. All studies were carried out in triplicate and average values were reported.

Results of psychorheological characteristic

The Psychorheological Characteristic was checked for emulgel formulations (colour, clogging, homogeneity and texture) and observations were shown in Table.

Results of Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually and observations were shown in Table.

| Formulation | Washability | observation |
|-------------|-------------|-------------|
| F1 | +++ | white cream |
| F2 | +++ | white cream |
| F3 | +++ | white cream |
| F4 | +++ | white cream |
| F5 | ++ | white cream |
| F6 | ++ | white cream |
| F7 | ++ | white cream |
| F8 | ++ | white cream |

Table no.12: Psychorheological Characteristic

Washability - Excellent: +++, Good: ++, Average: +, Poor: -

Results of extrudability study

The emulgel formulations were filled into collapsible metal tubes or aluminium collapsible tubes. The tubes were pressed to extrude the material and the extrudability of the formulation was checked.

Results of Spreadability

| Formulation | Extrudability | Spreadability (gcm/sec) |
|-------------|---------------|-------------------------|
| F1 | ++ | 11.11±1.23 |
| F2 | +++ | 10.23±0.89 |
| F3 | +++ | 11.56±0.87 |
| F4 | +++ | 12.32±0.58 |
| F5 | ++ | 9.85±0.45 |
| F6 | ++ | 8.65±0.65 |
| F7 | +++ | 9.12±0.12 |
| F8 | ++ | 7.98±0.32 |

Table no.12: Extrudability and Spreadability study

Excellent: +++, Good: ++, Average: +, Poor: -



Figure no.13: Graph of Spreadability study

Results of Viscosity

The measurement of viscosity of the prepared gel was done using Brookfield digital Viscometer. The viscosity was measured using spindle no. 6 at 10 rpm and 25°C. The sufficient quantity of gel was filled in appropriate wide mouth container. The gel was filled in the wide mouth container in such way that it should sufficiently allow to dip the spindle of the Viscometer. Samples of the gels were allowed to settle over 30 min at the constant temperature $(25\pm/1^{\circ}C)$ before the measurements.

Determination of pH

| Formulation | Viscosity (cps) | рН |
|-------------|-----------------|-----|
| F1 | 2569 | 6.5 |
| F2 | 2365 | 6.8 |
| F3 | 2789 | 6.5 |
| F4 | 2654 | 6.6 |
| F5 | 1984 | 6.8 |
| F6 | 1950 | 6.5 |
| F7 | 1898 | 6.7 |
| F8 | 1812 | 6.8 |

Table no.13 : Viscosity and pH







Figure no15 : Graph of pH

In-vitro drug release studies using the prehydrated cellophane membrane

Release of drug from Mometasone furoate emulgel was significantly slower, which confirmed that slight prolonged drug release rate. Incorporation of carbomer affected the release rate of the drug. By increasing the amount of carbomer, the release rate of the drug decreased, which could be related to the increased rigidity of the formulation, followed by its de-creased permeability for the drug.*In-vitro* drug release studies of formulation F1-F8

| S. | Time (min) | % Cum. drug release | | | | | | | |
|------|---------------|---------------------|-------|-------|-------|-------|-------|-------|-------|
| 110. | (11111) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 15 | 15.65 | 18.98 | 23.36 | 25.65 | 11.23 | 16.65 | 15.65 | 11.23 |
| 3 | 30 | 28.65 | 32.25 | 36.65 | 40.23 | 18.98 | 22.36 | 23.36 | 20.14 |
| 4 | 45 | 36.56 | 46.65 | 40.12 | 46.65 | 25.65 | 28.98 | 34.56 | 31.56 |
| 5 | 60 | 46.56 | 58.98 | 58.98 | 55.65 | 33.36 | 36.65 | 40.25 | 39.98 |
| 6 | 120 | 55.65 | 72.25 | 78.98 | 88.98 | 48.98 | 50.14 | 55.65 | 45.65 |
| 7 | 240 | 78.98 | 87.98 | 95.56 | 98.89 | 56.69 | 62.12 | 69.98 | 52.12 |

Table no.14: % Cum. drug release of formulation F1-F8



Figure no.16: Graph of % Cum. drug release of formulation F1-F8 Table no.15 : *In Vitro* Drug Release Data for optimized formulation F4

| S. No. | Time (min) | Square Root of Time | Log Time | Cumulative * Percentage Drug Release ± SD | Log Cumulative Percentage Drug Release | Cumulative Percent Drug Remaining | Log cumulative Percent Drug Remaining |
|-----------|---------------|---------------------------|-------------|---|--|--|---|
| 1 | 15 | 3.873 | 1.176 | 25.65 | 1.409087369 | 74.35 | 1.871280973 |
| | | | | | | | |
| 2 | 30 | 5.477 | 1.477 | 40.23 | 1.604550033 | 59.77 | 1.776483256 |
| 3 | 45 | 6.708 | 1.653 | 46.65 | 1.668851648 | 53.35 | 1.727134424 |

| 4 | 60 | 7.746 | 1.778 | 55.65 | 1.745465169 | 44.35 | 1.646893624 |
|---|-----|--------|-------|-------|-------------|-------|-------------|
| 5 | 120 | 10.954 | 2.079 | 88.98 | 1.949292401 | 11.02 | 1.042181595 |
| 6 | 240 | 15.492 | 2.38 | 98.89 | 1.995152377 | 1.11 | 0.045322979 |

* Average of three determinations

Zero order release Kinetics of Optimized formulation F4



Figure no.17: Graph of Zero order release Kinetics of Optimized formulation

F4First order release Kinetics of Optimized formulation F4



Figure no.18 : Graph of First order release Kinetics of Optimized formulation F4 *In vitro* drug release from the semisolid preparation of Mometasone furoate emulgel optimized formulation F4 shows significantly improved in drug release rate as compare to marketed preparation. It was concluded that developed formulations deliver the drug for the treatment of fungal disease. Hence it could be concluded thatthe carbomer based semisolid preparation would providing local onset of action without need of any device for their application on skin. The preparation of emulgel has potential advantages over marketed preparation as they improved patient compliance rapid local onset of action for longer period with cost effectiveness. The pediatric and geriatric populations are the primary ones whose problems are easily targeted.

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