Research Article

Formulation and Evaluation of Topical Hydrogel of Mometasone Furoate using Different Polymers

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ABSTRACT

A gel can be described as the cross-linked material that retains a large amount of solvent inside its medium and if the solvent retained is water, such material is known as hydrogel. Drug therapy of the inflammation of skin is mainly topical. This necessitates the treatment of symptoms, since in most cases causal treatment is impossible due to unknown etiology. Topical corticosteroids are the most commonly used drugs in these skin conditions. Although there are many dosage forms available for the treatment of skin disorders, only lotions have shown to be suitable for hairy areas. Mometasone furoate (MOF) is a potent corticosteroid which presents an improved risk/benefit ratio. The aim of this work was to prepare a hydrogel formulation using various polymers like Carbopol-940, HPC, MC, Poloxamer-407, Sodium alginate, and HPMC with 0.1% (w/w) Mometasone furoate for scalp dermatitis. The formulated gel was evaluated for drug content, pH, viscosity, spreadability and in vitro drug release. Comparison of data obtained from successful gel formulation with marketed product. Spreadability of Carbopol gel containing Mometasone furoate (C1) was 26.76g.cm/sec as compared to 21.61g.cm/sec of marketed gel, indicating good spreadability of the prepared gel (C1). The percent drug release was 74.58 and 73.50 from C1 and marketed gel respectively. Stability studies under room temperature showed satisfactory results. It can be concluded that Carbopol gel containing Mometasone furoate showed good homogeneity, drug content, spreadability and stability and has wider prospect for topical preparations.

Keywords: Mometasone furoate, Topical, Hydrogel, HPMC, HPC, MC, Sodium alginate, Carbomer.

INTRODUCTION

Gels are semisolid systems in which a liquid phase is constrained within a three-dimensional polymeric matrix (consisting of natural or synthetic gums) in which a high degree of physical (or sometimes chemical) cross-linking has been introduced. The clarity range from clear to a whitish translucent. Gels are usually clear transparent semisolid containing the solubilised active substances.[1] The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three dimensional “house of cards” structure. Gels consist of two-phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains. When solvent used as continuous phases is water, the gel formed is called hydrogel.[3] Various topical application dosage forms like creams, ointments, liniments, lotions, gels and jellies have been in use for many decades. The extensive studies on release properties of gels have revealed that the active ingredients in gel based formulations are better percutaneous absorbed than from creams and ointment bases.[1] Thus facts have clearly indicated that a formulation and development of a gel based topical dosage form for dermatitis will be proved to be worthwhile. Hence a study on formulation and evaluation of hydrogel of “Mometasone furoate” was selected as the principle object of this project work.

Psoriasis is a chronic, non-contagious autoimmune disease which affects the skin and joints. It commonly causes red scaly patches to appear on the skin. The scaly patches caused by psoriasis, called psoriatic plaques, are areas of inflammation and excessive skin

production. Both solutions and moisturizers help soothe affected skin and reduce the dryness which accompanies the build-up of skin on psoriatic plaques. Medicated creams and ointments applied directly to psoriatic plaques can help reduce inflammation, remove built-up scale, reduce skin turn over, and clear affected skin of plaques.[2]

Topical application of gels overcome the problems to be associates with other dosage forms are: Avoidance of first pass metabolism. Convenient and easy to apply. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time etc. Achievement of efficacy with lower total daily dosage of drug by continuous drug input. Avoids fluctuation in drug levels, inter- and intra-patient variations. Ability to easily terminate the medications, when needed. A relatively large area of application in comparison with buccal or nasal cavity Ability to deliver drug more selectively to a specific site. Avoidance of gastro-intestinal incompatibility. Providing utilization of drugs with short biological half-life, narrow therapeutic window. Improving physiological and pharmacological response. Improve patient compliance. Provide suitability for self-medication.[1]

Mometasone furoate (MOF) is a medium-potency topical corticosteroid which presents an improved risk/benefit ratio. It is therefore of great value for inflammatory skin diseases, showing a strong anti - inflammatory action, rapid onset of action and low systemic bioavailability after topical application. It depresses formation, release, and activity of endogenous mediators of inflammation, including prostaglandins, kinins, histamine, liposomal enzymes, and complements system; modifies body's immune response. Its C_{max} ranged from about 1 to 2.5hr and V_d is 152L. The in vitro protein binding was 98% to 99%. It is metabolized in the liver by the CYP3A4 isozyme to multiple metabolites. Its $t_{1/2}$ is about 5hr. Excretion upto 7 days is primarily in the feces (74%) and, to a lesser amount, in the urine (8%).[2]

MATERIALS AND METHOD

Mometasone furoate was received as a gift samples from Swisschem (P) Ltd., H.P., India. Pluronic F-127 was generous gift from Sigma-Life Science. Carbopol 934, HPMC, MC, Sodium alginate, HPC were procured from C.D.H, Mumbai (India). Ethanol was procured from Qualigens Fine Chemicals, Mumbai (India). Other materials used in the study were of analytical grade. Double-distilled water was used throughout the study. The commercial product MESON®gel (Articon) was sponsored by Articon labs, Gurgaon. The product is a semi-solid gel containing Mometasone furoate 0.1% (w/w) as active substance.

METHODS

Preformulation studies of MOF

Preformulation studies are the first step in the rational development of dosage form of a drug substance. Preformulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients.[2] Preformulation investigations are designed to identify those physicochemical properties and excipients that may influence the formulation design, method of manufacture and pharmacokinetic-biopharmaceutical properties of the resulting product.[4]

Organoleptic Characteristics

The colour, nature and odor of the drug were characterized and recorded using descriptive terminology.

Identification

a) By I.R. absorption spectroscopy

Infra-red absorption spectroscopy (I.R.) measurements were performed using Perkin Elmer, FT-IR spectrophotometer using the KBr disc method from IICB, Kolkata.

b) By U.V.-Visible spectrophotometeric studies

MOF was scanned in U.V. range from 200-400nm in methanol using Shimadzu U.V. Spectrophotometer (Model 1700). λ_{max} of MOF was recorded.

c) Melting point

Melting point of the drug was determined by taking a small amount of the drug in a capillary tube closed at one end. It was placed in melting point determination apparatus and the melting point was noted.

d) By TLC

TLC of MOF powder was performed using Chloroform:Ethylacetate (3:1 v/v) as solvent system and 10mg/ml sample solution in dichloromethane was used. TLC plates were examined in UV chamber and R_f value was calculated. This then compared with standard value.

Solubility

Saturation solubility of MOF was determined in pH 7.4 Phosphate buffer, Ethanol:Water(1:1), Methanol and Dichloromethane. Excess amount of drug was added to known volume of solvent, solution was shaked in 'wrist action shaker' for 48 hr, to dissolve the drug. The content was then filtered through Whatmann filter paper. Filtrate was suitably diluted with solvent and analyzed spectrophotometrically.[5,6]

Partition coefficient

A known concentration of MOF (50mg) in 25 ml of n-octanol was shaken for 2hr with an equal volume of water in a separating funnel and allows standing for 24hr. The aqueous phase and organic phase were collected separately. After suitable dilution, the concentration of MOF in n-octanol was analyzed spectrophotometrically at 249nm against blank. The concentration of the drug in aqueous phase was calculated from the difference between the initial and final concentrations in the n-octanol phase. Partition coefficient was calculated by taking the ratio of the concentration of drug in oily and in aqueous phase.[5,6]

A dispersion of MOF powder in glycerin was taken on a glass slide and mounted under optical microscope at 10x magnification particle size analysis was carried out by Photomicroscope RXT-5T.

Compatibility studies of drug and polymers

Drug and excipients in 1:1 ratios were mixed and stored in glass vials at room temperature. The samples were analyzed for compatibility by I.R. and TLC after 4 weeks.[5]

Preparation of Hydrogels

For Formulation C1, C2, C3 specified amount of MOF was weighed and dissolved in a specified quantity of suitable solvent (solution A). Weighed quantity of Carbopol was dispersed in distilled water with continuous agitation using magnetic stirrer till complete dispersion of polymers and left overnight in dark (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted. The formed gel was then neutralized by adding sufficient quantity of NaOH (1%) solution.

For Formulation P1, P2, P3 specified amount of MOF was weighed and dissolved in a specified quantity of suitable solvent (solution A). Weighed quantity of Pluronic F-127 was dispersed in distilled water using magnetic stirrer till complete dispersion of polymers and left in a refrigerator overnight (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted.

For Formulation S1, S2, S3, specified amount of MOF was weighed and dissolved in a specified quantity of suitable solvent (solution A). Weighed quantity of SA was dispersed in distilled water using magnetic stirrer till complete dispersion of polymers and left overnight in dark (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted.

For Formulation H1, H2, H3, specified amount of MOF was weighed and dissolved in a specified quantity of suitable solvent (solution A). Weighed quantity of HPMC was dispersed in distilled water using magnetic stirrer till complete dispersion of polymers and left overnight in dark (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted.

For Formulation M1, M2, M3, specified amount of MOF was weighed and dissolved in a specified quantity of

suitable solvent (solution A). Weighed quantity of MC was dispersed in distilled water using magnetic stirrer till complete dispersion of polymers and left overnight in dark (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted.

For Formulation h1, h2, h3, specified amount of MOF was weighed and dissolved in a specified quantity of suitable solvent (solution A). Weighed quantity of HPC was dispersed in distilled water using magnetic stirrer till complete dispersion of polymers and left overnight in dark (solution B). Solution A and B were mixed thoroughly and the final weight was adjusted. (Table 1 & 2).

Table 1: Formulation of Mometasone furoate gels using different gelling agents

S. No.	Ingredients	C1	C2	C3	P1	P2	P3	S1	S2	S3
1	MOF	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
2	Ethanol	3	3	3	3	3	3	3	3	3
3	Propylene glycol	5	10	15	5	10	15	5	10	15
4	NaOH (1%)	Q.S	Q.S	Q.S	-	-	-	-	-	-
5	Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
6	Propyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
7	Water upto	100	100	100	100	100	100	100	100	100
8	Carbopol 934	0.5	1.0	1.5						
9	Pluronic-407				15	20	25			
10	Sodium alginate							4	6	8

Table 2: Formulation of Mometasone furoate gels using different gelling agents

S. No.	Ingredients	H1	H2	H3	M1	M2	M3	h1	h2	h3
1	MOF	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
2	Ethanol	3	3	3	3	3	3	3	3	3
3	Propylene glycol	5	10	15	5	10	15	5	10	15
4	Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
5	Propyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
6	Water upto	100	100	100	100	100	100	100	100	100
7	HPMC	3.5	4	4.5						
8	MC				3.5	4	4.5			
9	HPC							3.5	4	4.5

Evaluation of formulated gel

Appearance

The prepared gel formulations were inspected for visual (color, homogeneity, consistency), olfactory (smell), tactile (texture, feel upon application such as grittiness, greasiness, stickiness, smoothness, stiffness and tackiness) characteristics.

Homogeneity[7]

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate.

Spreadability[8]

It was determined by wooden block and glass slide apparatus. A ground glass slide was fixed on the block and an excess of formulated gel (2 g) was placed on it. Gel was sandwiched by using another glass slide which was provided with hook. Weight (100 g) was placed upon the upper slide for 5 minutes to remove entrapped air and to form a uniform thin gel layer between slides. The weight was removed and the excess gel from the edges was scrapped off. The two slides in positioned were fixed to a stand without slightest disturbance and in such a way that only the upper slide to slip off freely by the force of weight tied to it.

A 20 g weight was tied to upper slide carefully. The time taken for the upper slide (movable) to travel the distance of 6 cm and separate away from the lower slide (fixed) under the direction of weight was noted. The determinations were carried out in triplicate and the average of three reading was recorded.

Spreadability was calculated by using the formula:

$$S = \frac{ML}{T}$$

where,
S = Spreadability
M = Weight tide to upper slide
L = Length moved on the glass slide
T = Time taken to separate the slide completely from each other

Extrudability[1]

It is a useful empirical test to the measure the force required to extrude the material from a tube. Since the packing of gels have gained a considerable importance in delivery of desired quantity of gel from jar or extrusion of gel from collapsible tube, therefore measurement of extrudability becomes an important criteria for gels.

The extrudability test was carried out by using Pfizer hardness tester. A 15gm of gel was filled in aluminium tube. The plunger was adjusted to hold the tube properly. The pressure of 1kg/cm2 was applied for 30 sec. The quantity of gel extruded was weighed. The % of gel extruded was calculated; and grades were allotted (+ + + Excelent, + + Good, + fair). The procedure was repeated at three equidistance places of the tube. Test was carried out in triplicates.

Viscosity

The viscosity of formulated gel bases was determined at room temperature. The viscosity determinations were carried out on Brook-field viscometer using spindle number S-06 and the determinations were carried out in triplicate and the average of three reading is recorded.[1]

Drug content

Gel formulations (100 mg) was dissolved in methanol and filtered and the volume was made to 100 ml with methanol. The resultant solution was suitably diluted with methanol and absorbance was measured at 249 nm using Shimadzu –1700 UV Visible spectrophotometer. Drug content was determined from calibration curve for MOF.

Drug content uniformity

To determine the drug content uniformity, the sample has taken from top, middle, and bottom from the container. And further assay is done to determine uniformity in label claim.[1]

pH

The pH of each gel, was measured, using a pH meter, which was calibrated before each use with standard buffer solutions at pH 4, 7, 9. The electrode was inserted into the sample 10 min prior to taking the reading at room temperature. The pH of gel was determined after diluting and dispersing it in distilled water (10% w/v). The determinations were carried out in triplicate and the average of three reading is recorded.[9]

***In-vitro* drug diffusion study**

Drug diffusion rate from different gel formulations were studied by Franz diffusion cell using cellophane membrane as a barrier. Diffusion membrane was immersed in receptor compartment having Ethanol:Water (1:1) as diffusion medium, maintained at 37±2^{o}C for 24hr for equilibrium. Diffusion cell was assembled on magnetic stirrer along with diffusion membrane, which separates donor and receptor compartments. Gel (2g) was kept on membrane in donor compartment. The contents were stirred using magnetic stirrer at 50 rpm and aliquots each of 5 ml were withdrawn from the release medium at time intervals of 10, 20, 30, 60, 90, 120, 180, 240, 300, 360, 420 and 480 minutes. Withdrawn samples were replaced by equal volumes of same fresh medium. Absorbance of these samples was measured spectrophotometrically at 250nm by UV-Visible double beam spectrophotometer. Cumulative release (%) of MOF from different gel formulations was calculated. The data obtained from the *in vitro* release experiments were analyzed using linear regression method according to zero order ($C_t = C_0 – kt$), and first order ($\ln C_t = \ln C_0 – kt$).

Comparison with marketed products

Selected formulations (C1, S1, and H1) were compared with marketed gels (Meson), for different tests like

appearance, pH, viscosity, spreadability, extrudability, and in-vitro diffusion study.

Stability studies

Based on the results obtained from the previous studies, formulations were maintained at an ambient condition over a period of two months. The physical appearance, pH value, and drug content were analyzed periodically after the 1st and 2nd month of topical gel preparation.

RESULTS AND DISCUSSION

Preformulation studies of MOF

Table 3: Data obtained from preformulation studies of Mometasone furoate

Parameter	Observation and Results	Conclusion
Organoleptic parameters	a) Colour-white to off white b) Nature-crystalline powder c) Odour-none	Complies with IP 2010 monograph
Identification of drug substance	a) By I.R. spectroscopy	Complies with IP 2010 monograph
	b) By thin layer chromatography R_f value-0.986	Matches with reported value (USPC, 2010)
	c) By melting point method Melting point - 219-223°C	
Preparation of calibration curve of Mometasone furoate	a) By U.V.-Visible spectroscopy $(\lambda_{max})_{methanol}$- 249.0nm $(\lambda_{max})_{ethanol:water}$-250.0nm	Solvent specific (λ_{max}) Beer's-Lambert law followed Good linearity with R^2=0.99
Physicochemical parameters	a) Solubility • pH 7.4 Phosphate buffer-0.068mg/ml • Methanol- 10.04mg/ml • Dichloromethane- 59.36mg/ml • Ethanol:Water(1:1)-0.292mg/ml b) Partition coefficient logP- 2.09 c) Particle size and size distribution Average particle size was 6.026µm	Drug is practically insoluble in water and slightly soluble in ethanol. Drug is lipophilic. Max. particles present between 0-5µm.
Compatibility study	Compatibility test for semisolid dosage form No changes were observed in major peaks or R_f values of the drug, in 4 weeks.	Excipients were compatible i.e. no drug-excipient interaction was seen.

Identification

U.V.-Visible spectrophotometeric studies

The MOF was identified by the light absorption in the U.V. range of 200-400nm. The absorbance of drug solution was 0.528 at λ_{max} 249nm. The results are shown in Table 3.

Melting point

There is a linear correlation between log flux and reciprocal of melting point, indicating that the lower the melting point, the better the penetration. The melting point of MOF is in the range of 219°C to 223°C. Values of preformulation parameters are tabulated in Table 3.

Solubility

The solubility of neutral form of MOF in water is 0.85µg/ml at 25°C exemplifying the fact that the drug is practically insoluble in water. Further the drug was found to be slightly soluble in ethanol, and soluble in methylene chloride, acetone etc.

It was found that by using ethanol:water (1:1) mixture has the capacity to solubilize the drug, a solubility of 0.292 mg/ml of MOF was achieved.

Hence Ethanol:Water (1:1) was used as a solvent for establishing the standard calibration curve of MOF & as a receptor medium for in vitro release studies.

Partition coefficient

The octanol-water partition coefficient (log P) value of 2.09 indicates high lipophilicity character of MOF and the drug may possess high permeability.

Compatibility studies of drug and polymers

The drug–polymer interaction was ruled out as there were no major shifts in the absorption bands and R_f value of drug in presence of polymer.

Formulation Design

Eighteen formulations of gel containing Mometasone furoate were prepared using various polymers viz HPMC, Carbopol, MC, Pluronic F-127, sodium alginate and HPC in different ratios (Table 1 and 2) until a suitable gel was formed. Propylene glycol was used as humectant and methyl paraben, propyl paraben were used as preservative.

Evaluation of formulated gel

Physical evaluation

Gel formulations were found to be translucent in nature with ethanolic odour, smooth feel on application and homogenous.

Table 4: Physical appearance and feel on application of different MOF gels

Formulations	Physical Appearance	Feel on Application
C1	Whitish translucent	Smooth
C2	Whitish translucent	Smooth
C3	Whitish translucent	Smooth
P1	Transparent	Smooth
P2	Transparent	Smooth
S1	Opaque	Smooth
S2	Opaque	Smooth
H1	Whitish translucent	Smooth
H2	Whitish translucent	Smooth
H3	Whitish translucent	Smooth
M1	Whitish translucent	Smooth
M2	Whitish translucent	Smooth
M3	Whitish translucent	Smooth
h1	Whitish translucent	Smooth
h2	Whitish translucent	Smooth
h3	Whitish translucent	Smooth
M*	Whitish translucent	Smooth

Spreadibility

Results of the spreadability testing are shown in table 5. All the prepared gels using different polymers in different concentrations were spreadable on the skin surface. The addition of propylene glycol to all the prepared formulae improved the physical characteristics concerning spreadability, consistency and skin feel. Also, its addition helped the dissolution of the drug and prevented its precipitation upon storage.

In general, it is obvious from table 5 that all the polymers used gave gels of acceptable spreadability. Data in table 5 revealed that increasing the concentration of any of the gelling agents was always associated with a decrease in the spreadability.

Viscosity

The data represent that with increase in the concentration of polymer viscosity was increased.

Table 5: Spreadability, Viscosity, Homogeneity and Extrudability of different MOF gels

Formulations	Spreadability (g.cm/sec) (mean ± SD)	Viscosity (CPs)	Homogeneity	Extrudability
C1	26.76 ± 0.014	16600	Good	+ + +
C2	19.15 ± 0.023	31500	Very good	+ +
C3	16.03 ± 0.016	44140	Good	++
P1	15.51 ± 0.101	54100	Very good	+++
P2	14.04 ± 0.027	66800	Very good	++
P3	11.23 ± 0.131	82400	Good	+
S1	23.10 ± 0.011	22000	Good	+ + +
S2	20.91 ± 0.032	30610	Good	+ +
S3	17.83 ± 0.045	36480	Good	++
H1	25.09 ± 0.104	19920	Very good	++
H2	22.55 ± 0.031	25200	Good	++
H3	17.02 ± 0.027	33290	Good	+
M1	15.18 ± 0.013	63400	Good	+ + +
M2	12.30 ± 0.015	78430	Very good	+ +
M3	11.49 ± 0.076	84370	Good	+
h1	13.79 ± 0.041	68500	Good	+ + +
h2	13.55 ± 0.145	76000	Good	+ +
h3	12.49 ± 0.096	80120	Good	+
M*	21.61 ± 0.144	16700	Very good	+ + +

Drug content and Drug content uniformity

The content of MOF in all the gels was found to be within permissible limits (> 97%). This indicates that the drug was uniformly distributed throughout the formulations as evident from the low standard deviation value.

pH

The pH of the developed formulations was in accordance with that of human skin pH enduring them more acceptable to avoid the risk of irritation upon application.

Table 6: Results of pH and drug content of different formulations

Formulation	pH (mean ± SD)	Drug content (%)
C1	6.57 ± 0.607	99.83 ± 0.205
C2	6.49 ± 0.311	98.18 ± 0.014
C3	6.73 ± 0.425	99.71 ± 0.172
P1	6.68 ± 0.23	97.18 ± 0.106
P2	6.62 ± 0.58	98.36 ± 0.031
P3	6.42 ± 0.41	99.42 ± 0.104
S1	7.14 ± 0.32	96.55 ± 0.015
S2	7.02 ± 0.74	98.82 ± 0.130
S3	6.42 ± 0.32	95.63 ± 0.145
H1	6.31 ± 0.25	99.27 ± 0.023
H2	6.42 ± 0.41	97.31 ± 0.067
H3	6.34 ± 0.52	99.36 ± 0.110
M1	6.81 ± 0.86	96.00 ± 0.051
M2	6.33 ± 0.92	97.91 ± 0.102
M3	6.35 ± 0.73	94.64 ± 0.108
h1	6.68 ± 0.81	97.45 ± 0.035
h2	6.53 ± 0.64	95.18 ± 0.054
h3	6.74 ± 0.37	97.45 ± 0.082
M*	6.71 ± 0.45	99.78 ± 0.014

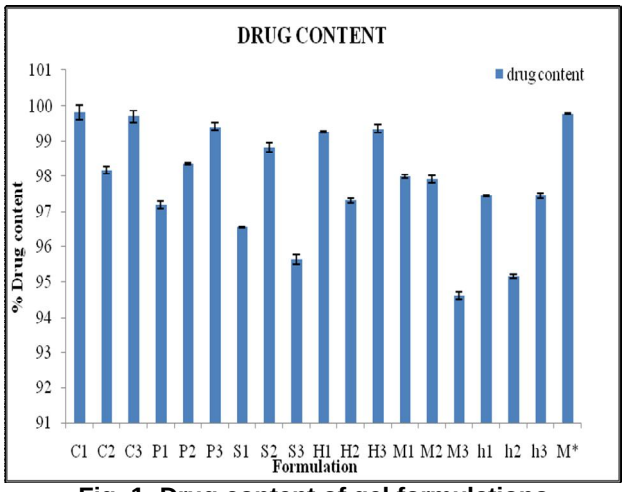

Fig. 1: Drug content of gel formulations

Table 7: Percentage drug content uniformity of formulations

Formulations	Top (mean ± SD)	Middle (mean ± SD)	Bottom (mean ± SD)
C1	99.43 ± 0.247	99.21 ± 0.51	99.07 ± 0.64
C2	98.21 ± 0.056	97.93 ± 0.417	99.91 ± 0.315
C3	97.37 ± 0.143	98.54 ± 0.328	97.68 ± 0.052
P1	99.56 ± 0.062	97.36 ± 0.416	98.07 ± 0.123
P2	98.38 ± 0.401	98.46 ± 0.054	98.73 ± 0.072
P3	96.72 ± 0.130	97.56 ± 0.067	99.61 ± 0.15
S1	97.32 ± 0.074	99.74 ± 0.281	98.38 ± 0.314
S2	98.85 ± 0.223	98.73 ± 0.117	98.21 ± 0.109
S3	99.23 ± 0.135	99.67 ± 0.241	97.68 ± 0.128
H1	99.16 ± 0.171	99.42 ± 0.064	99.57 ± 0.230
H2	99.14 ± 0.052	99.27 ± 0.249	99.35 ± 0.186
H3	99.27 ± 0.248	99.38 ± 0.036	99.31 ± 0.402
M1	98.79 ± 0.127	97.36 ± 0.215	98.48 ± 0.163
M2	97.71 ± 0.071	97.94 ± 0.137	97.83 ± 0.046
M3	98.72 ± 0.503	99.63 ± 0.406	99.28 ± 0.718
h1	97.31 ± 0.148	97.56 ± 0.65	97.62 ± 0.091
h2	97.23 ± 0.211	96.07 ± 0.82	96.14 ± 0.317
h3	97.34 ± 0.537	97.62 ± 0.41	97.57 ± 0.062
M*	99.81 ± 0.137	99.93 ± 0.117	99.95 ± 0.128

In-vitro drug diffusion study

These gels were subjected to in-vitro release studies across cellulose membrane. Release profiles of MOF from various gel formulations depicted that drug release decrease with increase in concentration of the gelling agent. It was found that gel prepared using Carbopol, Sodium alginate and HPMC gave CPR of 74.58%, 74.17%, 73.42% respectively after 6 hrs and that of Marketed gel gave a CPR of 73.50% after 6hrs. Thus, gel prepared using Carbopol 934, Sodium alginate revealed better release profile when compared to Marketed gel.

Table 8: Cumulative percentage drug release of formulations

TIME	C1	C2	C3	P1	S1	S2
0	0.00	0.00	0.00	0.00	0.00	0.00
30	9.62	11.33	10.53	11.42	7.46	7.96
60	11.96	14.10	14.30	14.20	11.53	12.32
90	14.07	19.40	19.10	21.15	17.30	16.26
120	22.85	24.48	23.91	28.40	24.53	21.83
150	32.26	32.81	34.32	34.97	31.22	25.36
180	37.50	39.55	37.41	42.15	38.83	32.56
210	42.75	43.75	42.99	45.85	44.19	37.21
240	54.49	51.82	47.95	51.11	51.91	44.16
300	64.59	58.72	55.45	56.56	60.28	52.20
360	69.20	67.00	60.16	60.06	68.35	66.54
420	73.76	69.31	65.20	65.53	73.99	69.48
480	74.58	69.66	67.73	66.40	74.17	71.69

Table 9: Cumulative percentage drug release of formulations

TIME	S3	H1	H2	H3	M*
0	0.00	0.00	0.0	0.00	0.00
30	7.24	9.04	10.1	5.08	10.10
60	13.60	13.36	13.1	7.81	12.25
90	21.63	21.09	19.2	12.52	13.82
120	25.66	28.21	25.4	17.01	23.81
150	31.73	34.58	30.6	21.74	33.91
180	38.78	42.30	37.2	29.46	36.28
210	43.28	51.62	44.7	33.59	44.44
240	55.63	56.35	51.1	42.31	55.40
300	59.78	61.70	58.1	47.65	66.78
360	65.03	68.25	64.7	53.83	69.01
420	67.37	72.70	68.9	67.61	72.70
480	69.25	73.42	69.7	68.28	73.50

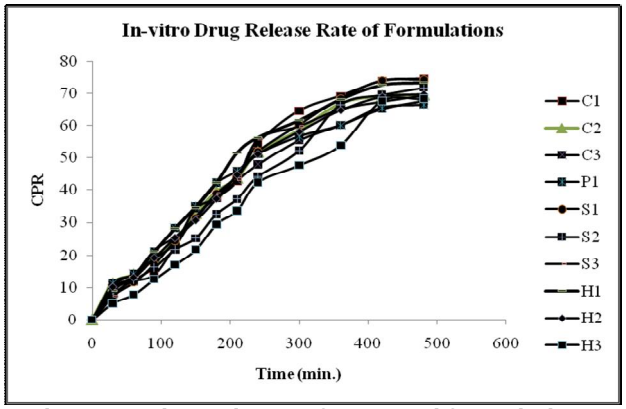

Fig. 2 : In-vitro release of prepared formulations

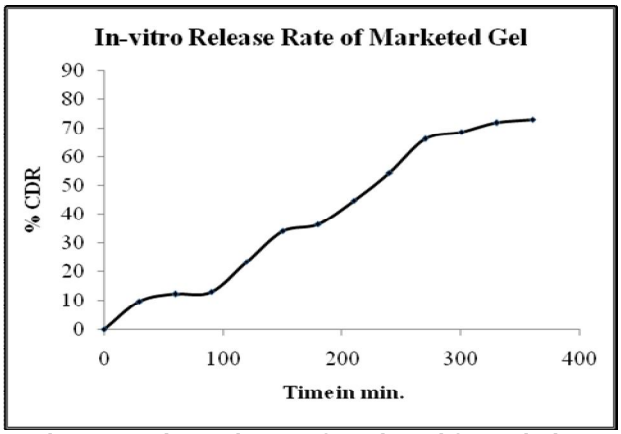

Fig. 3 : In-vitro release of Marketed formulation

Table 10: Kinetic values of formulations in Ethanol:Water (1:1)

Formulation code	Zero order R^2	First order R^2
C1	0.9922	0.9926
C2	0.9981	0.9936
C3	0.9824	0.9745
P1	0.9934	0.9877
S1	0.9837	0.9724
S2	0.9824	0.9708
S3	0.9974	0.9831
H1	0.9937	0.9876
H2	0.9838	0.9787
H3	0.9867	0.9772
M*	0.9989	0.9839

Stability studies

The Carbopol gels showed good physical stability, as the Appearance and pH remained same as that of gels before stability study. The assay values did not show much variation before and after the stability studies.

Table 11: Stability parameters for formulations

S. No	Batches	Months	Appearance	pH	Drug content (%)
1.	C1	0	Clear	6.57	99.83
		1	Clear	6.54	99.81
		2	Clear	6.53	99.80
		3	Clear	6.51	99.78
2.	S1	0	Clear	7.14	96.55
		1	Clear	7.13	96.53
		2	Small lumps	7.11	96.52
		3	Lumps	7.06	96.50
3.	H1	0	Clear	5.21	99.27
		1	Clear	5.20	99.24
		2	Lumps	5.18	99.23
		3	Lumps	5.17	99.21
4.	M*	0	Clear	6.71	99.78
		1	Clear	6.70	99.77
		2	Clear	6.68	99.76
		3	Clear	6.67	99.74

CONCLUSION

From above results, it can be concluded that Preformulation studies on MOF corroborate with the reported literature limits. FT-IR studies of gels indicated no chemical interaction. Hydrogels of Mometasone furoate with hydrophilic polymers viz., MC, HPMC, Poloxamer

407, Sodium alginate, Carbopol 934, and HPC were successfully prepared. The gel formulation was optimized on the basis of different physical parameters and mainly with the comparison of formulations on the basis of in-vitro diffusion study. The adopted method yielded translucent, smooth and viscous hydrogels. The viscosity, spreadability, pH and drug content of gels were uniform and reproducible. Decrease in viscosity was observed with subsequent increase in the concentration of polymers. The drug content of formulations was found to be within the limits. From the in-vitro release it can be concluded that gel prepared using Carbopol 934 would be a better gelling agent in terms of release property. As among all gel formulations, carbopol gels shows superior drug release after that HPMC and sodium alginate shows decreasing order of drug release. The mechanism of drug release was found to be tending towards zero order release kinetics. From the results of all the physical and in-vitro diffusion data it was found that formulation C1, S1 and H1 were most promising formulation. Stability studies showed that C1 formulation was stable with respect to physical appearance, drug content, and pH for three months when stored at room temperature.

ACKNOWLEDGEMENT

The authors are thankful to Dr. Laxman Prasad, Director of R.K.G.I.T, College of Pharmaceutical Sciences, Ghaziabad, U.P. for providing necessary facilities and to Swisschem (P) Ltd (H.P., India) for providing gift sample of pure drug.

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