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Formulation and Evaluation of Topical Bigel Containing Mometasone Furoate

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ABSTRACT
The objective of this present study is to overcome the disadvantages of hydrogel and organogel by preparing Mometasone furoate loaded bigel. Mometasone furoate is a glucocorticoid or corticosteroid used topically to reduce inflammation of the skin or in the airways. Mometasone furoate loaded bigel was prepared by combining organogel in hydrogel in different ratio. The hydrogel was prepared by using different ratio of HPMCK100M, carbopol 934 and carbopol 940 as polymer. The organogel was prepared by using different oils like cottonseed oil, sesame oil and different ratio of stearic acid, stearyl alcohol and bees wax as thickening agent. Organogel and hydrogel were evaluated on the basis of appearance, viscosity and spreadability. The optimum parameters were selected for the preparation of bigel. The prepared bigel was evaluated for pH, viscosity, spread ability, drug content and in vitro drug release. All formulations of bigel showed extended release out of which formulation BG3 showed higher % drug release and it was found to be 88.45% upto 8 hrs.

I. INTRODUCTION

Topical drug delivery system is the favourable route for localized drug delivery due to its convenience and economic. The specific challenges of therapeutics system are to achieve an optimum concentration of a certain drugs at site of action for specific duration[1]. Topical drug delivery is generally used where the systems minimal effect of drugs or in the local skin infections[2]. Topical drug delivery system can be defined as direct effects of dosage form or drug containing medication to the skin to get local effect of drug or directly cure cutaneous diseases. Topical drug delivery system has several benefits such as ability to deliver drug more selectively to a specific site, avoidance of gastro-intestinal incompatibility and metabolic degradation associated with oral administration.[3]

Bigels have advanced as one of the capable formulations with the improved mechanical and controlled release drug delivery. Bigels is defined as topical formulation prepared by the mixing two gels hydrogels are polar and organogels are a polar[4].It is biphasic system in which both phases are in semisolid form. The immobilization of the external phase arrests the motion of the internal phase thus, the chances of a coagulation of the internal phase is fully abolished and the internal phase is also immobilized so, the chances of the leaching of the internal phase are diminished[5]. When mixing of hydrogel and organogel some important parameters are absorbed mixing temperature, mixing speed and the storage of bigels. The preparation of bigels by mixing individual systems at reasonably higher temperature while room temperature is also use to mix both phases with continuous stirring. Bigels produced by storage of the individual systems (hydrogel and organogel) at a particular temperature and for a specified time period followed by mixing of both systems. Bigels systems also prepare by the mixing the both gels and store as the final system[6]. Mometasone furoate is a synthetic non-fluorinated topical corticosteroid. is indicated for the relief of inflammatory and pruritic manifestations of corticosteroid responsive dermatoses, including psoriasis.

II. MATERIALS AND METHODS

Mometasone furoate received as gift sample from Envee Drugs pvt Ltd Nadiad. All other chemicals were used of analytical grade.

Screening of hydrophilic polymer for hydrogel

HPMC K100M, carbopol 934 and carbopol 940, were separately soaked in distilled water at different concentrations (1%, 1.5% and 2%) for 24 hrs. The Screening of hydrogel was

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done by visual inspection, spreadability and viscosity measurement.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
HPMC K 100 M (%)	1	1.5	2	-	-	-	-	-	-
Carbopol 934 (%)	-	-	-	1	1.5	2	-	-	-
Carbopol 940 (%)		-	-	-	-	-	1	1.5	2
Benzalkonium Chloride (g)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Distilled water (q.s) ml	100	100	100	100	100	100	100	100	100

Table No. 1: Composition of hydrogels

Screening of oils for organogel

Various oils were screened on the basis of solubility of drug in oils. Solubility of drug was checked in cotton seed oil, sunflower oil and sesame oil. The selection was based on solubility of Mometasone furoate in oil. The method used was carried out in triplicates. Excess amounts of Mometasone furoate was added to each capped glass vail containing 5ml of oils, on a mechanical shaker for 72 hrs. The resulting dispersion was centrifuged for 10 min at 15000 rpm. Filtrates were diluted appropriately using methanol and analyzed. The absorbance of solutions was measured at 249 nm on a double beam UV spectrophotometer using the respective medium as the blank[9].

Screening of thickening agent for organogel

Thickening agent was screened from appearance, viscosity and spreadability of the organogel. Organogels were prepared using different of Bees wax, stearyl alcohol, stearic acid and at different concentration (5%, 10%, 15%) with Sesame oil.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bees wax (%)	5	10	15	-	-	-	-	-	-
Stearic acid (%)	-	-	-	5	10	15	-	-	-
Stearyl alcohol (%)	-	-	-	-	-	-	5	10	15
Butylated hydroxyl anisole (g)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Sesame oil (q.s) ml	100	100	100	100	100	100	100	100	100

Table No. 2: Composition of organogel

Screening of ratio of organogel and hydrogel for the preparation of bigel

The screening ratio of Hydrogel (2 %w/w of carbopol 940): organogel (10 %w/w of bees wax) was based on the appearance, viscosity, spreadability. The bigel was prepared using different ratio (50:50, 60:40, 70:30, 90:10) of hydrogel and organogel. The drug (%) was dispersed in organogel[7, 8].

Contents	B1	B2	B3	B4	B5
Mometasone furoate (%)	0.1	0.1	0.1	0.1	0.1
Hydrogel (g)	50	60	70	80	90
Organogel (g)	50	40	30	20	10
Triethanolamine q.s (ml)	q. s	q. s	q. s	q. s	q. s

Table No. 3: Composition of bigels

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EVALUATION STUDIES

- **Solubility determination**

Solubility studies in different solvent medium (oils, water and 5.5 phosphate buffer) were carried out by adding an excess amount of drug in the respective medium and keeping the screw capped tubes containing the solutions, on a mechanical shaker for 24 hrs. After 24 hrs the solutions were transferred into other test tubes and centrifuged at about 2000 rpm for 30 min at room temperature. One ml of supernatant liquid from each test tube was placed into 100 ml volumetric flasks and suitably diluted with the respective medium and finally filtered through Whatman filter paper. The absorbance of solutions was measured at 249 nm on a double beam UV spectrophotometer using the respective medium as the blank. The amount of drug dissolved was quantified from the calibration curve. The average solubility from three such experiments was determined[9].

Evaluation of bigel

- **Viscosity:**

Viscosity of the formulated bigel was determined by using Brookfield viscometer by using spindle no 63. The procedure was repeated three times for each bigel[11].

- **Spreadability:**

For the determination of spreadability excess of bigel was applied in between 2 glass slide and compressed to uniform thickness by placing weight (in grams) for 5 minutes. Weight (in gram) was added to pan. Time required separating the two slides that was the time in which the upper glass slide move over the lower plate can be taken as measure of spreadability. The procedure was repeated three times for each bigel[12].

$S = (m \times l)/t$

S= Spreadability
m=Weight tied to upper slide.
l=Length moved on upper glass slide
t=Time taken

- **pH of bigel:**

The pH was measured by dispersing the accurately weighed bigel into 10 ml of distilled water and then pH value of the dispersion is measured by a digital pH meter at room temperature. The procedure was repeated three times for each bigel[13,14].

- **Drug content:**

About 1g of the bigel was dissolved in 25 ml of phosphate buffer pH 5.5 appropriate dilutions were made with the same buffer solution, filtered was measured at 249 nm using UV visible double beam spectrophotometer. The procedure was repeated three times for each gel[15,16].

- **In vitro drug release:**

The drug release of the Mometasone furoate bigel was measured by using Franz diffusion cell. Diffusion membrane was immersed in receptor compartment having phosphate buffer pH 5.5 as diffusion medium, maintained at 32±0.5°C for 8 hrs for equilibrium. Diffusion cell was assembled on magnetic stirrer along with diffusion membrane, which separates donor and receptor compartments. Bigel (2g) was kept on membrane in donor compartment. The contents were stirred using magnetic stirrer at 50 rpm and 1 ml aliquots of sample 1 ml were withdrawn from the release medium at time intervals of 0, 0.5, 1, 2, 3, 4,5, 6, 7, 8 hours. Withdrawn samples were replaced by equal volumes of same fresh medium. Absorbance of these samples was measured spectrophotometrically at 249nm by UV-Visible double beam spectrophotometer.[15]

III. RESULTS AND DISCUSSION

Tests	Parameters	Observation (±S.D.) n=3
Physico-chemical properties	**Melting point**	219-223°C
Solubility (mg/ml)	**Distilled water**	0.0052±0.001
	Phosphate buffer pH 5.5	0.763±0.002
	Cotton seed oil	15.63±0.39
	Sunflower oil	29.38±0.001
	Sesame oil	150.64±4.71

Table No. 4: Physical Properties of Mometasone Furoate

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❖ **Evaluation of hydrogel**

Formulations	Appearance	Viscosity (cps) (±S.D.)	Spreadability gm.cm/sec (±S.D.)
HG1	Transparent	1091±1	5.5±0.5
HG2	Transparent	1240±1.5	5.7±0.6
HG3	Transparent	1564±1.11	8.9±0.5
HG4	Transparent	1566±5.5	7.7±0.5
HG5	Transparent	4511±9.5	9.7±0.2
HG6	Transparent	6923±4.9	16.7±0.4
HG7	Transparent	1772±3.05	9.2±0.6
HG8	Transparent	2494±3.7	11.8±0.8
HG9	Transparent	3024±4.16	13.48±0.4

***Each observation values are expressed as mean ±S.D. of n=3**

Table No. 5: Evaluation parameters of Preliminary batches HG1-HG9

❖ **Evaluation of organogel**

Formulations	Appearance	Viscosity (cps) (±S.D.)	Spreadability gm.cm/sec (±S.D.)
OG1	Yellow	3338±1.52	7.2±0.3
OG2	Yellow	4846±6.08	11.8±0.2
OG3	Yellow	6823±3	16.73±0.8
OG4	Off-White	9047.33±4.2	19.3±0.1
OG5	Off-White	1180±1.5	22±0.5
OG6	Off-White	22190±4	29.6±0.3
OG7	Off-White	5369±3	13.46±0.3
OG8	Off-White	8580±1.15	18.53±0.1
OG9	Off-White	9087±1.52	22.84±0.02

***Each observation values are expressed as mean ±S.D. of n=3**

Table No. 6: Evaluation parameters of Preliminary batches OG1-OG9

❖ **Evaluation parameters of topical Bigel containing Mometasone furoate.**

Formulations	Appearance	Viscosity (cps) (±S.D.)	Spreadability gm.cm/sec (±S.D.)	PH (±S.D.)	Drug content %(±S.D.)
BG1	Off-White	12545±4.5	18.39±0.4	5.3±0.1	98.39±0.09
BG2	Off-White	7654±2.08	11.73±0.3	5.4±0.13	98.64±1.6
BG3	Off-White	6524±4.58	11.54±0.02	5.3±0.16	99.70±0.3
BG4	Off-White	8924±2.6	17.24±0.02	5.3±0.01	98.97±0.2
BG5	Off-White	10486±3	22.12±0.3	5.3±0.14	96.39±0.15

***Each observation values are expressed as mean ±S.D. of n=3**

Table No. 7: Evaluation parameters of Preliminary batches BG1-BG5

In vitro drug release study of formulate on (BG1 to BG5)

All the formulations were evaluated for drug release study. The data and curve obtained from in vitro drug release test are as fallows.

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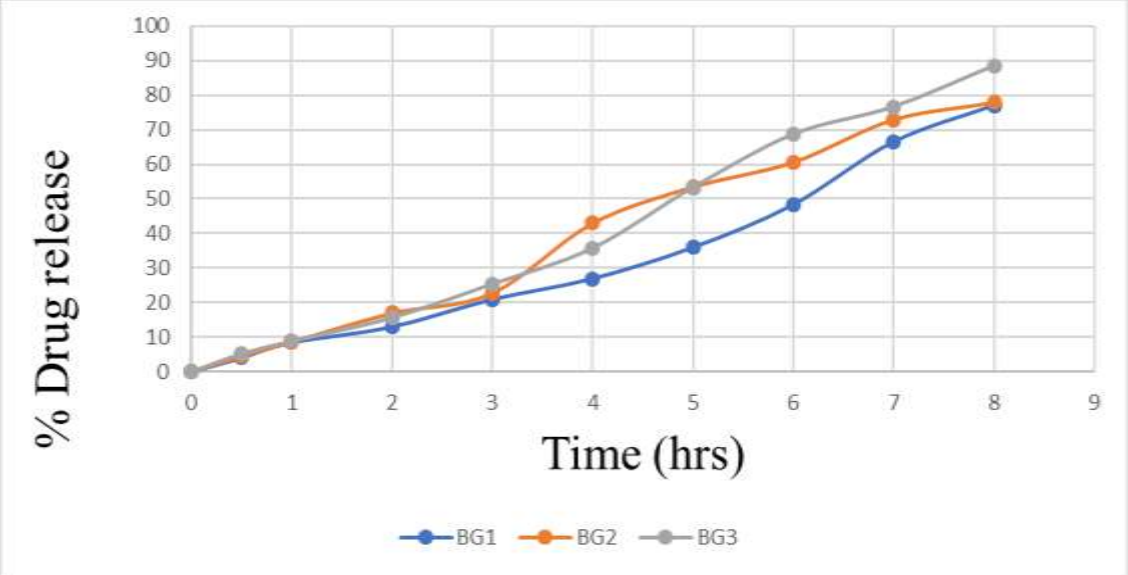

Figure No.1: In vitro drug release of BG1-BG3

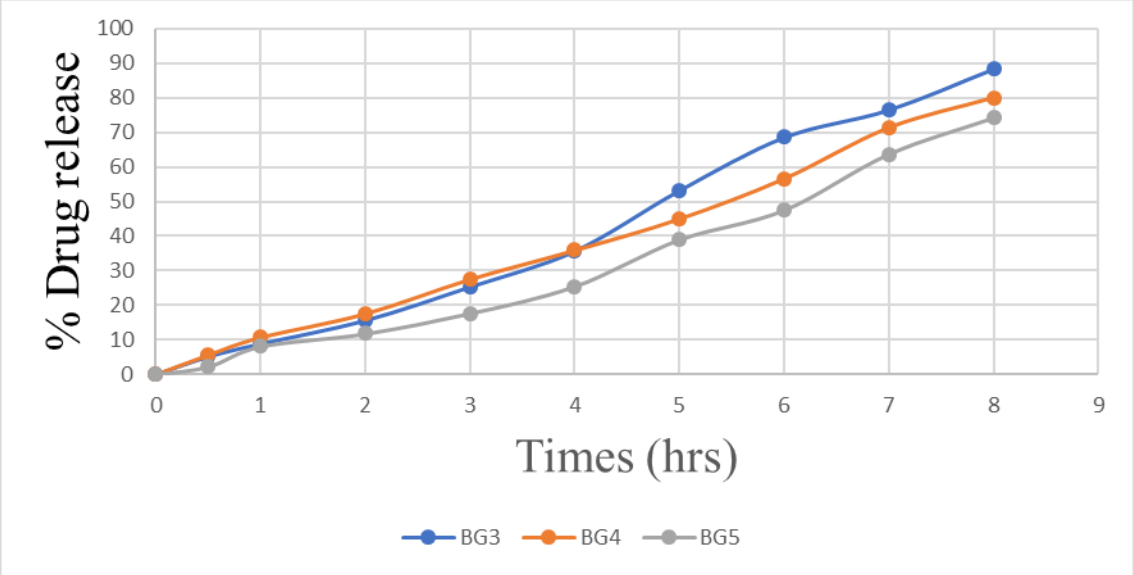

Figure No.2: In vitro drug release of BG3-BG5

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