IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND IN VITRO EVALUATION OF HALOBETASOL PROPIONATE LOADED HYDROGEL

[1] MAYUR PARGI, [2] Jaini Patel, [3] Divykant Patel, [2] Priyanka Yadav

[1]Student Pharmaceutics Sharda School of Pharmacy, Gandhinagar, Gujarat. 382610

, [2] Associate Professor, Department of pharmaceutics Sharda School of Pharmacy, Gandhinagar, Gujarat. 382610

[3] Principal, Sharda School of Pharmacy, Gandhinagar, Gujarat. 382610

[1] Department of pharmaceutics

[1]Sharda School of Pharmacy, Gandhinagar, Gujarat. 382610

Abstract: The aim of this research was to develop and evaluate a topical hydrogel Containing Halobetasol. Various gelling agents, including HPMC, Sodium CMC, And Polaxomer, were utilized at different concentrations to formulate the gel. Parameters such as drug release, drug content, pH, physical appearance, and Rheological properties like spreadability and extrudability were examined for the Prepared hydrogel formulations. In vitro drug release from the gels was evaluated Using Franz diffusion cells with cellophane membranes and phosphate buffer pH 6.8 as the receptor medium. Compatibility between drugs and excipients was Investigated using FT-IR analysis, revealing no interaction. Results indicated that All gel compositions met the required criteria and exhibited acceptable Physicochemical and rheological characteristics. Higher polymer concentrations Were associated with reduced drug release, with Polaxomer displaying superior Drug release compared to HPMC and Sodium CMC in all gel formulations. The Most potent antifungal activity was observed in Formulation F4. Factorial design Was employed based on trial batches, with subsequent validation indicatingIndex Terms - Component, formatting, style, styling, insert.Significant model performance. The optimized batch, F12, underwent thorough Analysis and was found to be stable during a 1-month stability study. Therefore, F12 was determined as the optimized batch.

Key Words: Halobetasol, HPMC, Sodium CMC, and Polaxomer, Hydrogel

I. INTRODUCTION

This brief review focuses primarily on hydrogels, which are polymer networks extensively swollen with water. Hydrogels, often referred to as hydrophilic gels, are polymer chains that form colloidal gels in which water Serves as the dispersion medium.Researchers have offered various definitions of hydrogels over the years. The most common definition describes Hydrogels as water-swollen, cross-linked polymeric networks resulting from the reaction of one or more Monomers. Another definition characterizes them as polymeric materials capable of swelling and retaining a Significant fraction of water within their structure without dissolving in water. Hydrogels have garnered Significant attention over the past 50 years due to their wide range of applications and their similarity to natural Tissues in terms of flexibility, owing to their high water content.The ability of hydrogels to absorb water is attributed to hydrophilic functional groups attached to the polymeric Backbone, while their resistance to dissolution stems from cross-links between network chains. Both naturally Occurring and synthetic materials fall under the category of hydrogels.In the last two decades, synthetic hydrogels have gradually replaced natural hydrogels due to their long service Life, high water absorption capacity, and strong gel strength. Synthetic polymers offer well-defined structures That can be tailored to achieve desired degradability and functionality. Hydrogels synthesized from purely Synthetic

components are stable even under sharp temperature fluctuations.Recently, hydrogels have been defined as two or multi-component systems consisting of a three-dimensional
Network of polymer chains and water filling the space between macromolecules. Depending on the properties of The polymers and the nature of network joints, such structures can contain varying amounts of water. Typically, The mass fraction of water in a swollen hydrogel is much higher than themass fraction of polymer. To achieve High degrees of swelling, synthetic polymers that are water-soluble in non-cross-linked form are commonly used.Hydrogels can be synthesized using various chemical methods, including one-step procedures such as Polymerization and parallel cross-linking of multifunctional monomers, as well as multi-step procedures Involving the synthesis of polymer molecules with reactive groups followed by cross-linking. Polymer engineers Design and synthesize polymer networks with precise control over structure, such cross-linking density, and Tailored properties, including biodegradation, mechanStrength, and responsiveness to chemical and biological Stimuli.

MATERIALS AND METHODS

Materials

Halobitasol , HPMC, Poloxamer, Sodium CMC,Propylene glycol, Glycerin ,Methyl Paraben , Propyl Paraben,Methanol

Methods

Organoleptic Characteristics: Colour, Odour of Drug was characterized and recorded using descriptive terminology

1.Bulk density and tapped density :-

A precisely weighed amount of the blend (W) was gently transferred into a 100 ml graduated cylinder, and the initial volume (Vo) was recorded. Subsequently, the graduated cylinder, equipped with a lid, was placed in the density determination Apparatus (Tapped Density Apparatus) set for 100 taps. After tapping, the final volume (Vf), referred to as tapped volume, Was measured. The bulk density and tapped density were then computed using the provided formulas.

Bulk density = W/ Vo Tapped density = W/V……

2.Compressibility index (CI)/Carr's index :-

It was obtained from bulk and tapped densities. It was calculated by using the following formula.

% Carr's index = (Tapped Density – Bulk Density Tapped Density) x 100…(ii)

iii) Hausner's ratio:-Hausner's ratio is a number that is correlated to the flow ability of a powder. It is measured by ratio of tapped density to bulk density.

Hausner's ratio = (Tapped density ÷Bulk Densit)

4.Angle of repose:-

The angle of repose of the powder was assessed utilizing the funnel method. A precise amount of the powder blend was Placed into the funnel. The height of the funnel was adjusted so that its tip barely touched the apex of the powder blend. The powder blend was then allowed to flow freely through the funnel onto the surface below. The diameter of the Resulting powder cone was measured, and the angle of repose was determined using the provided equation.
Tan 0-h/r

Drug-Excipients Compatibility Study By FTIR

The Fourier transform infrared (FTIR) spectra of both the moisture-free powdered drug sample and the final formulation Were obtained using an IR spectrophotometer employing the potassium bromide (KBr) pellet

method. The spectral range Examined was from 600 to 4000 cm-1. Specific peaks corresponding to various functional groups were identified by Comparing them with established standard peaks reported in literature.

Calibration Curve of Halobetasol

Halobetasol was quantified spectrophotometrically at 240 nm using methanolic phosphate buffer. Initially, 10 mg of the Drug was precisely weighed and dissolved in 20 ml of methanol, followed by dilution to a final volume of 100 ml with 7.4 Phosphate buffer. From this stock solution, 1 ml was withdrawn and further diluted with 7.4 phosphate buffer. Subsequently, various dilutions were prepared from this stock solution to achieve a concentration range of 5-25 µg/ml. The absorbance of these solutions was measured at 240 nm, with 10% methanolic phosphate buffer serving as the blank. A calibration curve was constructed by plotting the absorbance values.

Evaluation of Hydrogels

Homogeneity

The gels underwent visual inspection to assess physical attributes such as Color, clarity, and potential phase separation.
Additionally, the presence of Aggregates was investigated during testing.

Grittiness

Presence of any particulate matter in the formulations was observed Microscopically and results were noted down.

pH measurement

The pH of the gel formulations was assessed using a digital pH meter. A Sample weighing 1 gram was dissolved in 100 Ml of distilled water and Allowed to stand for two hours. pH measurements were conducted in Triplicate for each Formulation, and average values were calculated and Recorded.

Spredability

Concentric circles of varying radii were delineated on graph paper, with a Glass plate affixed atop. A quantity of 5 grams Of gel was positioned at the Center of the lower plate. Subsequently, another glass plate weighing 100±5 Grams was Delicately positioned atop the gel, and the spread diameter was Measured after one minute for each increment.

Extrudability

The gel formulations were loaded into collapsible tubes and allowed to set. Subsequently, the extrudability of the gel Formulations was assessed by Measuring the weight in grams needed to extrude a 0.5 cm ribbon of gel Within a 10-second

Drug content

A 1 gram gel was dissolved in 100 milliliters of phosphate buffer with a pH Of 6.8. Dilutions were prepared using th same Phosphate buffer with a pH of 6.8. The absorbance was then measured at the wavelength of maximum Absorption (λmax) Of 240 nanometers using a UV spectrophotometer.

In-vitro drug diffusion study

Drug release studies were conducted in vitro utilizing a Franz diffusion cell Setup. A quantity of 1.0 gram of gel was Administered onto a cellophane Membrane within the donor compartment. Phosphate buffer with a pH of 6.8 Was Introduced into the receptor compartment as the dissolution medium. The entire setup was positioned on a magnetic stirrer With a thermostat set at 37 degrees Celsius. Samples were systematically collected over time Intervals, ensuring Maintenance of sink conditions by replenishing with fresh Buffer solution. The gathered samples were analyzed using a UV Spectrophotometer at a wavelength of maximum absorption (λmax) of 240 Nanometers.

Stability Study

The final formulation was subjected to accelerated stability conditions, Maintained at 45°C and 75% relative humidity (RH). Critical parameters Including appearance, drug content, and diffusion studies will be conducted After one month. Subsequently, the obtained results will be compared to the Initial findings for assessment.

RESULTS & DISCUSSION

Pre-Formulation Studies

Characterization of Drug

Results of API characterization are given in below table**;**

6.1 API Characterization

Sr. No.	Characteristic Properties		Observation/Result
1	Organoleptic Properties	Colour	It is white to off-white crystalline powder
2		Odour	Characteristic odour of API
3	Flow Properties	Bulk density (g /ml)	0.27±0.01
4		Tapped density (g /ml)	0.32±0.02
5		Carr's index (%)	15.6±0.2
6		Hausner's ratio	1.18±0.01
7		Angle of repose (θ°)	41.5±0.3
8	Melting Point	Capillary Method	214°C±1
9	Solubility	Water	Insoluble in water
		Methanol	12.9 mg/ml
		Ethanol	11.4 mg/ml

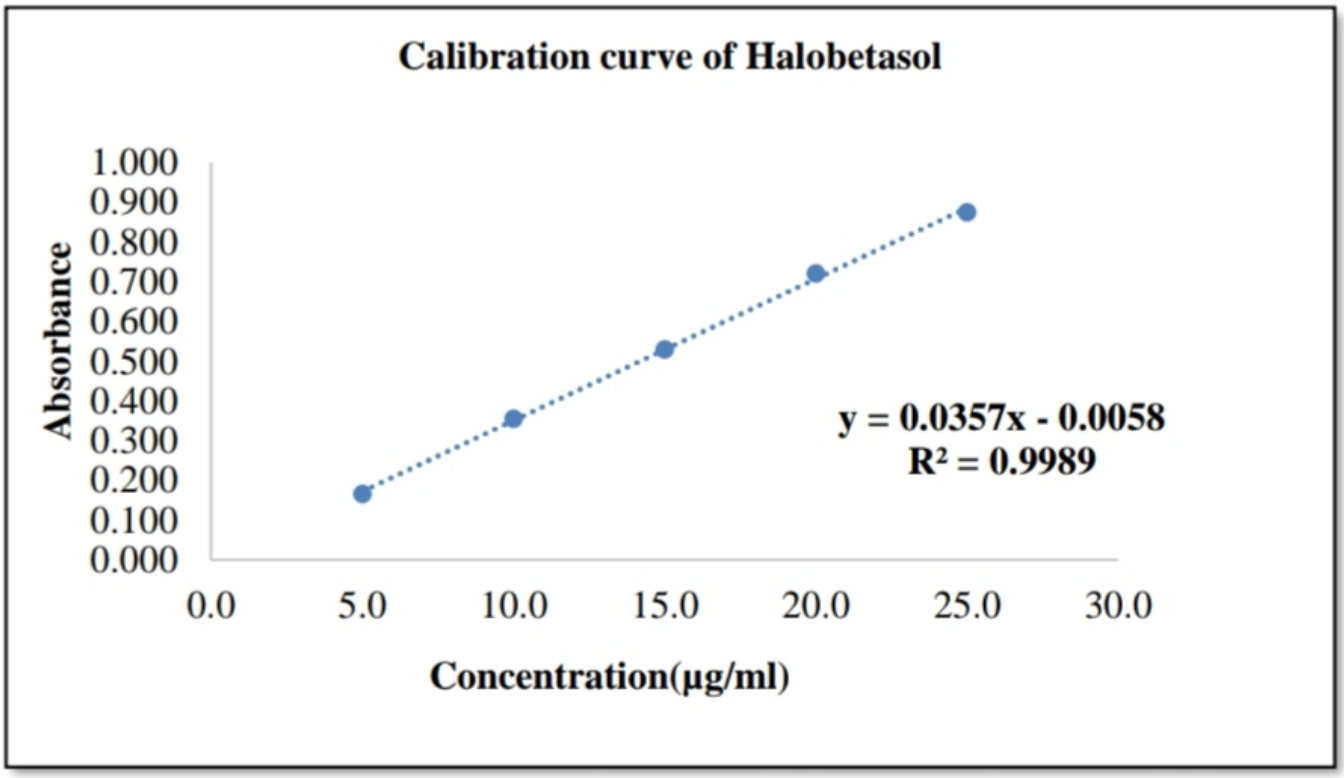
Following the characterization of the active pharmaceutical ingredient (API), It was determined that the API possesses favorable flow properties, making the direct Compression method preferable. However, it is noteworthy that the proposed Formulation, being a liposomal gel, does not necessitate any specific flow properties. Additionally, the melting point of the drug aligns with the reported values.

Calibration Curve:-

The drug shows 240 nm λmax in 10% methanolic Phosphate buffer as solvent**.**

6.2 Standard calibration curve of halobetasol

Sr. No.	Concentration (µg/ml)	Absorbance
1	0.0	0.000±0.000
2	5.0	0.166±0.001
3	10.0	0.355±0.002
4	15.0	0.530±0.004
5	20.0	0.721±0.002
6	25.0	0.875±0.003

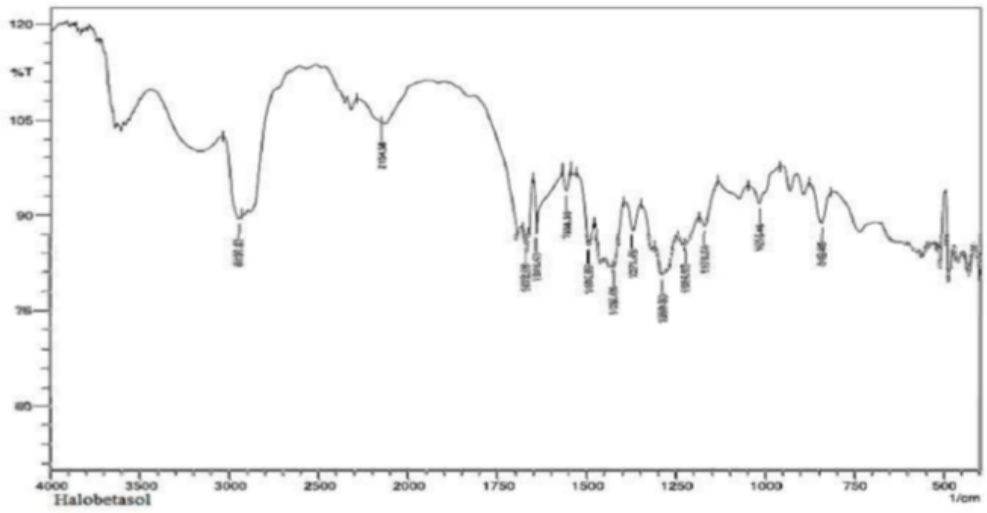


6.1 Standard calibration curve of halobetasol

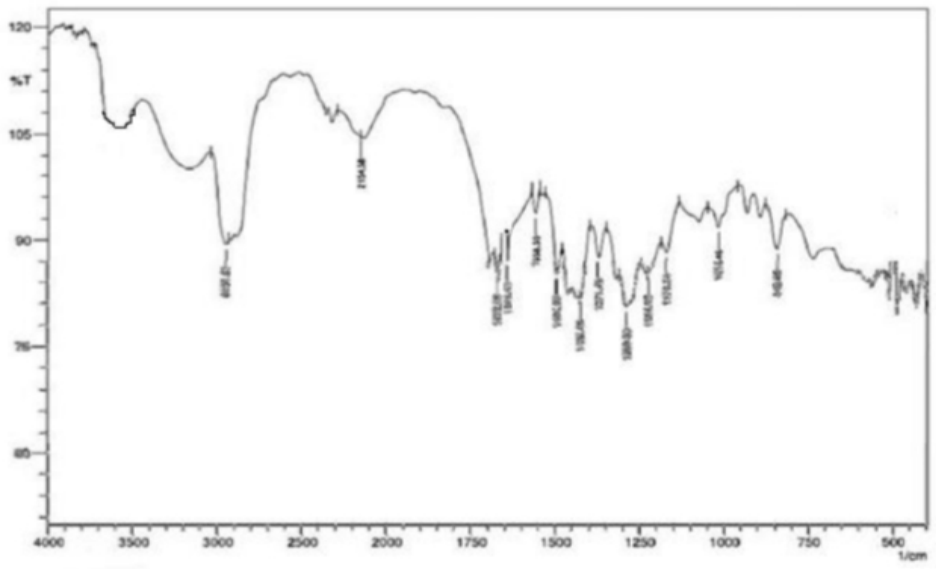
Based on above calibration curve, it was observed that the linearity curve was Achieved and R2 was found 0.9989.

6.2FTIR STUDY

The Fourier-transform infrared (FTIR) study of both the pure drug and the Formulation mixture, as depicted in the figure Below, revealed identical peaks Corresponding to the drug in both spectra. This observation indicates that the proposed Excipients are compatible with the drug



6.2 FTIR spectra of pure drug



6.3 FTIR spectra of formulation mixture

Sr. No.	Assignment	Peak report in Pure Drug (cm^{-1})	Peak report in Physical Mixture (cm^{-1})
1	C-H stretch	1506.9	1505.2
2	C=O stretch	2154.3	2154.3
3	C=C stretch	2935.2	2934.3

EVALUATION OF TRIAL BATCHES

Trial batches T1-T9 was prepared and evaluated for various parameters. Below are The results Observed.

Batch	Physical appearance	Extrudability
T1	White, smooth, homogenous Gel	Excellent
T2	White, smooth, homogenous Gel	Excellent
T3	White, smooth, homogenous Gel	Good
T4	White, smooth, homogenous Gel	Excellent
T5	White, smooth, homogenous Gel	Excellent
T6	White, smooth, homogenous Gel	Excellent
T7	White, smooth, homogenous Gel	Good
T8	White, smooth, homogenous Gel	Good
T9	White, smooth, homogenous Gel	Good

Trial batches T1 to T9 exhibited a uniform, smooth, and white appearance. The Extrudability of the hydrogel Was deemed satisfactory in batches T3, T7, T8, and T9, While the remaining batches demonstrated excellent Extrudability. This suggests that Poloxamer imparts excellent properties to the formulation.

Table 6.4 Evaluation of trial batches of Hydrogel

Batch	pH	Drug Content	Spredability (cm)
T1	6.1±0.3	96.8±0.5	15.9±0.2
T2	6.3±0.1	98.5±0.9	15.7±0.3
T3	6.7±0.4	97.9±0.4	14.6±0.1
T4	6.2±0.2	99.7±0.7	22.6±0.4
T5	6.4±0.1	96.6±0.9	17.1±0.2
T6	6.5±0.2	97.2±0.2	16.5±0.3
T7	6.2±0.1	97.6±0.3	14.8±0.1
T8	6.3±0.2	98.1±0.4	14.2±0.3
T9	6.5±0.3	96.8±0.6	13.9±0.2

Trial batches T1 to T9 underwent evaluation for pH, drug content, and spreadability. All batches met the required drug content specifications, with satisfactory results. The pH of the batches fell within an acceptable range of approximately 6. The spreadability outcomes were primarily determined by the properties of the polymer and the concentration of the humectant. Notably, formulations containing Poloxamer exhibited superior spreadability compared to other batches.

The in-vitro drug release profiles of the topical gels are depicted in the figure below. During the initial hour, drug diffusion ranged from 26% to 11% across all Formulations. Formulations F4 to F6, incorporating Poloxamer, achieved complete Drug release within 6 to 8 hours. Formulations F2 and F7 exhibited drug release Extending up to 9 hours, while formulations F3 and F8 prolonged release up to 10 Hours. Formulation F9 extended drug release up to 11 hours, with the highest and Lowest drug release observed in formulations F4 and F9, respectively. Polymer type And concentration significantly influenced drug release, with higher viscosity leading To a notable decrease in release rate.

IJCRT

Table 6.5 Drug release study of trial batches

Drug Release Study							
Time in Hours							
Batch	**0**	**1**	**2**	**4**	**6**	**8**	**10**
T1	0.0	21.30	37.90	58.20	79.50	96.50	-
T2	0.0	19.50	35.20	55.30	75.90	94.20	99.50
T3	0.0	18.60	32.90	53.60	73.10	92.10	98.90
T4	**0.0**	**26.90**	**45.60**	**74.80**	**99.20**	-	-
T5	0.0	24.80	42.30	71.80	86.90	98.90	-
T6	0.0	22.50	40.90	69.10	84.30	97.50	99.20
T7	0.0	17.20	31.50	52.60	68.90	79.40	89.50
T8	0.0	14.60	28.50	49.10	64.20	75.30	86.90
T9	0.0	11.60	22.30	44.60	61.30	69.50	80.60

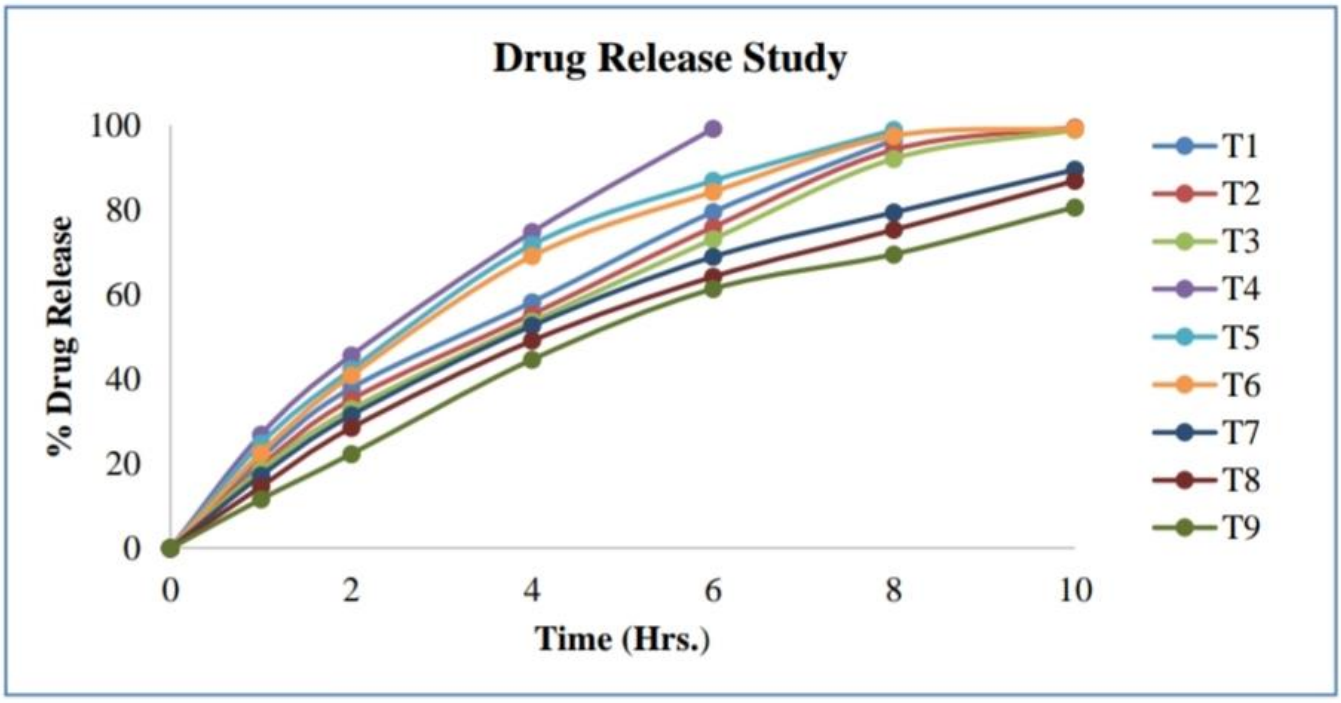


Figure 6:4 Drug release study of trial batches

6.4 EVALUATION OF FACTORIAL BATCHES

Factorial batches of hydrogel formulation, designated as F1 to F9, were prepared and Assessed for various parameters, mirroring those of the trial batches. The results Obtained were comfortably within the acceptable range. Each batch exhibited a white, Smooth structure with homogeneous characteristics. Extrudability was determined to Be excellent across all batches, and pH levels were satisfactory.

Table 6.6 Evaluation of factorial batches of Hydrogel

Batch	Physical appearance	Extrudability
F1	White, smooth, homogenous Gel	Excellent
F2	White, smooth, homogenous Gel	Excellent
F3	White, smooth, homogenous Gel	Excellent
F4	White, smooth, homogenous Gel	Excellent
F5	White, smooth, homogenous Gel	Excellent
F6	White, smooth, homogenous Gel	Excellent
F7	White, smooth, homogenous Gel	Excellent
F8	White, smooth, homogenous Gel	Excellent
F9	White, smooth, homogenous Gel	Excellent

Table 6.7 Evaluation of factorial batches of Hydrogel

Batch	pH	Drug Content	Spredability (cm)
F1	6.3±0.1	99.8±0.4	18.5±0.1
F2	6.2±0.3	98.5±0.5	18.9±0.4
F3	6.4±0.2	97.8±0.7	19.6±0.3
F4	6.1±0.1	99.5±0.5	21.4±0.6
F5	6.3±0.1	99.4±0.4	23.2±0.1
F6	6.4±0.2	99.5±0.5	26.5±0.5
F7	6.2±0.1	99.7±0.6	28.6±0.4
F8	6.1±0.1	98.9±0.5	29.1±0.2
F9	6.3±0.1	99.1±0.3	29.9±0.3

Optimized Batch

Based on Factorial Design data, final optimized batch selected from the Contour plot To achieve desired drug release. Complete analysis of this batch done and recorded Below.

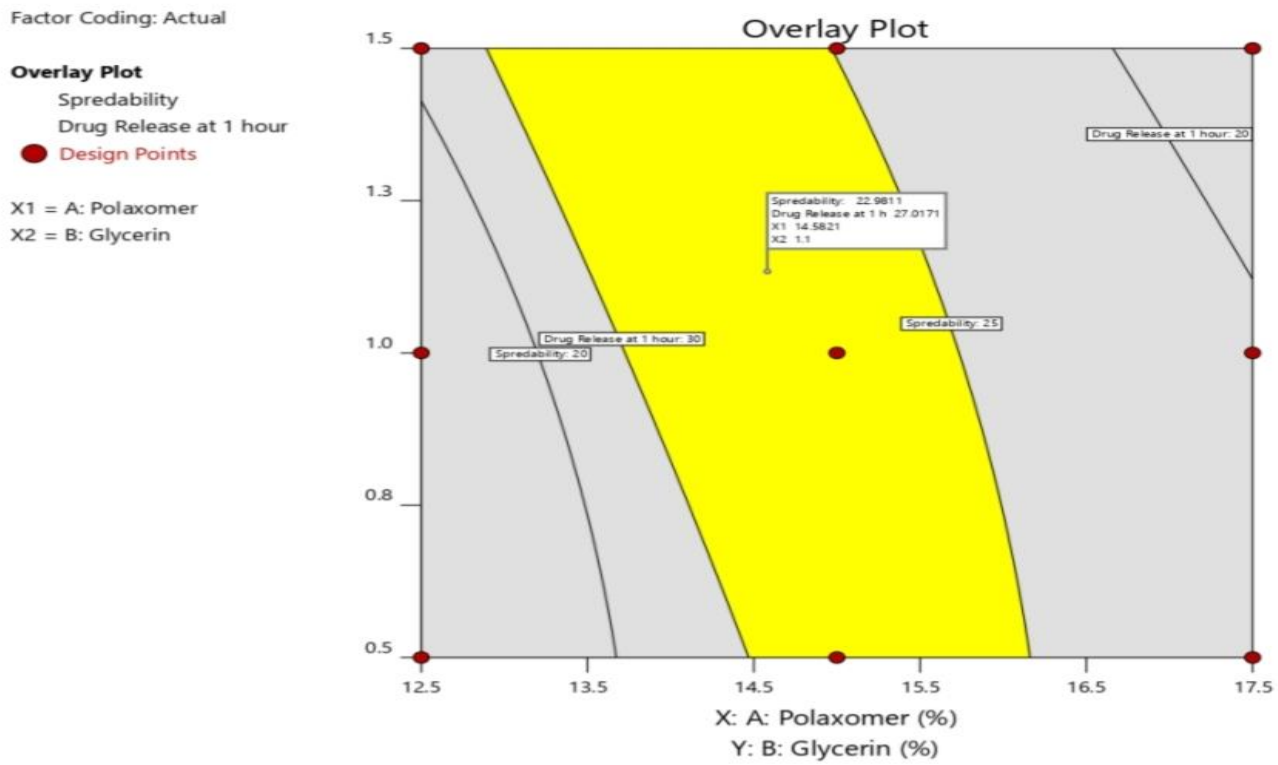


Figure 6:12 Overlay contour plot for optimized batch

Table 6.11 Formula for optimized batch F12

Sr. No.	Ingredients (%)	F12
1	Halobetasol	1.00
2	Polaxomer	14.50
3	Glycerin	1.10
4	Propylene glycol	1.00
5	Methyl paraben	0.030
6	Propyl paraben	0.020
7	Water	Q.S.
8	Methanol	Q.S.

Results of optimized batch:-

Table 6.12 Results of Optimized batch F12

Evaluation Parameters	F12
Physical Appearance	White, smooth, homogenous Gel
Extrudability	Excellent Extrudability
pH	6.4±0.1
Assay (%)	99.1±0.7
Spredability (cm)	23.1±0.2

% Drug Release	
Hours	F12
1	27.1±4.2
2	46.2±2.4
3	62.3±2.1
4	75.1±2.5
6	99.5±1.2

Kinetic Model	Zero Order	First Order	Higuchi	Korsmeyer Peppas	Hixon Crowell
R^2 Value	0.9540	0.8020	0.9970	0.9990	0.6980

Hence, from the above results, the best fitted model for drug release kinetic was found Korsmeyer Peppas model.

Stability Study

The stability study of the final optimized batch, F12, was conducted for a duration of One month at 40°C and 75% relative humidity (RH). Comparison between the initial And one-month results revealed that they were Satisfactory. The batch demonstrated Stability throughout the study period. The recorded results are presented in The table Below

Table 6.13 Stability study of F12 batch

Evaluation Parameters	Initial Results	After 1 Month Results
Appearance	No Change in Appearance	No Change in Appearance
Assay (%)	99.1±0.7	99.0±1.5
% Drug Release after 6 hrs	99.5±1.2	99.1±1.7

CONCLUSION

The aim of this research was to develop and evaluate a topical hydrogel Containing Halobetasol. Various Gelling vbagents, including HPMC, Sodium CMC, And Polaxomer, were utilized at different Concentrations to formulate the gel. Parameters such as drug release, drug content, pH, physical Appearance, and Rheological properties like spreadability and extrudability were examined for the Prepared hydrogel formulations. In vitro drug release from the gels was evaluated Using Franz diffusion Cells with cellophane membranes and phosphate buffer pH 6.8 as the receptor medium. Compatibility Between drugs and excipients was Investigated using FT-IR analysis, revealing no interaction. Results Indicated that All gel compositions met the required criteria and exhibited acceptable Physicochemical And rheological characteristics. Higher polymer concentrations Were associated with reduced drug Release, with Polaxomer displaying superior Drug release compared to HPMC and Sodium CMC in all Gel formulations. The Most potent antifungal activity was observed in Formulation F4. Factorial design Was employed based on trial batches, with subsequent validation indicating Significant model Performance. The optimized batch, F12, underwent thorough Analysis and was found to be stable during A 1-month stability study. Therefore F12 was determined as the optimized batch.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation.

ACKNOWLEDGMENTS:

The authors would like to thank Sharda Pharmacy college staff, non-teaching staff for their kind support

REFRENCE:-

1. David Moreau, Caroline Chauvet, François Etienne, François P. Rannou, Laurent Corte. “Hydrogel films and coatings by swelling-Induced gelation. Proceedings of the National Academy of Sciences of the United States of America,” National Academy of Sciences, 2016, 113 (47), 13295-13300

2. Enas M, “Hydrogel: Preparation, characterization, and applications: A Review,” Journal of Advanced Research, 2015, 6(2), 105-121.

3.Yahia L, Chirani N, Gritsch L, “History and Applications of Hydrogels.” J Biomedical Sci. 2015, 4(2), 1-9.

4.Drug Information, December 2023;

https://pubchem.ncbi.nlm.nih.gov/compound/Halobetasol#section=Literature.

5.Drug Information, December 2023; https://go.drugbank.com/drugs/DB00596.

6.Drug Information, December 2023; https://www.goodrx.com/halobetasol.

7. Drug Information, December 2023; https://www.drugs.com/halobetasol-Topical.html.

8.Drug Information, December 2023; https://medlineplus.gov/druginfo/meds/a601060.html.

9.Praveen K, Chinna M, “Formulation and evaluation of topical hydrogel Containing antifungal drug”, Pharm Pharmacol Int J. 2020, 8(4),249–254