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FORMULATION DEVELOPMENT, CHARACTERIZATION AND IN-VITRO EVALUATION OF NADIFLOXACIN AND CLOBETASOL PROPIONATE HYDROGEL

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ABSTRACT The aim of this work was to prepare and evaluate the topical hydrogel for the treatment of atopic dermatitis. Nadifloxacin and Clobetasol Propionate based hydrogel was prepared using the Carbopol 940 gelling agent, the drug concentration was kept constant at 10 mg and 500 mcg respectively. The concentration of propyl paraben and methyl paraben was kept constant at 1:10 ratio. The hydrogel formulation was evaluated for various physicochemical parameters like percentage drug content, spreadability and drug release. Formulation F3 was highest drug content 93.50%, 91.5% and hydrogel released 89.03%, 91.72% of the Nadifloxacin and Clobetasol Propionate in 8 hr. The drug release data was fitted in various kinetic model and short term stability studies revealed that there is no significant change in the drug content and drug release. Developed hydrogel formulation can be better effect to treat atopic dermatitis due to high drug retention and permeation in skin layers.

KEYWORDS : Nadifloxacin, Clobetasol Propionate, Hydrogel, Drug Delivery, Atopic Dermatitis, Psoriasis

INTRODUCTION

A hydrogel is a unique type of soft biomaterial having a hydrophilic polymer network and have been the center of attraction for biomaterials scientists for many years. As we know, hydrogels available for clinical use are under continuous change due to their own limitations. Actually, each hydrogel system prepared by using selective preparation technique shows its own merits and demerits in terms of applications particularly regenerative medicines, being employed *in-vitro* and *in-vivo*. Hydrogels are water-swollen three-dimensional crosslinked polymer network, consisting of hydrophilic polymers and can be swollen with water up to 99% w/w of their dry weights [1].

Hydrogels can be categorized in two ways, as permanent (chemically crosslinked or irreversible) and non-permanent (physically crosslinked or reversible) [2].

Atopic dermatitis (AD) is a chronic inflammatory skin disease that typically manifests in early childhood and may precede the development of other atopic disorders, including asthma, allergic rhinitis, and food allergies [3].

The onset of AD most commonly occurs between 3 and 6 months of age, with approximately 60% of children with AD presenting symptoms in the first 12 months. Consensus guidelines indicate that AD is characterized by essential features such as pruritus and eczema (acute, subacute, or chronic), with eczema lesions displaying typical morphology or age-specific patterns and having a chronic or relapsing history.

Nadifloxacin contains a class of antibiotics known as fluoroquinolones, primarily used to treat topical infections caused by the bacteria, including skin infections and acne vulgaris. Clobetasol Propionate may be used to treat moderate-to-severe eczema, plaque psoriasis, and some other skin conditions, such as lichen sclerosis [4]. This study is aimed to formulate and evaluate hydrogel of nadifloxacin and clobetasol propionate for the treatment of acute dermatitis.

MATERIALS

Nadifloxacin and Clobetasol Propionate Hydrogel was prepared using Clobetasol propionate (SGS Formulations), Nadifloxacin (SGS Formulations), Carbopol 940 (Tristar formulations), Methyl paraben (Lab chemicals), Propyl paraben (Lab chemicals) and Tri ethanol amine (Lab chemicals).

METHOD

Hydrogels were fabricated using different concentrations of polymeric dispersions. Different concentrations of Carbopol 940 colloidal dispersions were prepared with distilled water by using magnetic stirrer (500rpm). After complete dispersion, the polymer solutions were kept in dark for 24 h for complete swelling. Aqueous drug solution was added to the polymeric dispersion. Methyl paraben and propyl paraben were added. Finally, the remaining distilled water was added to obtain a homogeneous dispersion of gel under magnetic stirring [5]. Different formulation trials were made using different concentrations of hydrophilic and hydrophobic polymers along with sodium bicarbonate summarized in the **Table 1**.

Table 1: Formulation Of Nadifloxacin With Clobetasol Propionate Hydrogel

Ingredients	Formulation code				
	F1	F2	F3	F4	F5
Nadifloxacin	10 mg	10 mg	10 mg	10 mg	10 mg
Clobetasol Propionate	500 mcg	500 mcg	500 mcg	500 mcg	500 mcg
Carbopol 940	0.5 gm	1.0 gm	1.5 gm	2.0 gm	2.5 gm
Methyl Paraben	0.1 gm	0.1 gm	0.1 gm	0.1 gm	0.1 gm
Propyl Paraben	0.01 gm	0.01 gm	0.01 gm	0.01 gm	0.01 gm
Purified Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Characterization of Nadifloxacin and Clobetasol Propionate Hydrogel

Evaluation parameters like pH, Swelling index, Spreadability, Viscosity and Drug content were performed [6-9].

In-Vitro Drug Diffusion Study

The *in vitro* drug release studies were performed by using diffusion cell with cellophane paper. The water jacketed recipient compartment had total capacity of 20 ml. The donor compartment was placed in such a way that it just touches the diffusion medium in receptor compartment. The receptor compartment contained phosphate buffer saline (PBS) that was maintained at 37°C ± 1°C. The membrane was equilibrated before application of the hydrogel onto the donor side. Samples were periodically withdrawn from the receptor compartment, replacing with the same amount of fresh PBS solution, and assayed by using a spectrophotometer at 237 and 240 nm for Nadifloxacin and Clobetasol Propionate respectively [10].

Kinetic Modeling Of Drug Release

To analyze the mechanism of drug release from the hydrogel the *in*

vitro diffusion data was fitted to zero order, first order, Hixson-Crowel model, Higuchi's release model and Korsmeyer – Peppas model [11].

Stability Studies

Stability studies were carried out as per ICH guidelines. The Hydrogel were kept at 40±2ºC and relative humidity 75±5% for period of 45 days in stability chambers. After 30 and 45 days, samples were taken out and analyzed for their physical appearance and drug content [12].

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RESULTS AND DISCUSSIONS

All the formulations were evaluated for their various parameters like pH, Swelling index, Spreadability, Viscosity and Drug content (**Table 2 & 3**).

Table 2: pH, Swelling Index, Spreadabilty, And Viscosity Of Nadifloxacin And Clobetasol Propionate Hydrogel

Formulation Code	pH	Swelling Index (%)	Spread ability (cm)	Viscosity (cps)
F1	7.02	19.4	5.32	1432
F2	6.90	22.8	5.13	1523
F3	6.89	25.5	5.35	1493
F4	6.98	21.8	5.53	1502
F5	7.07	24.3	5.24	1482

Table 3: Percentage Drug Content

Formulation Code	Nadifloxacin	Clobetasol Propionate
F1	75.6	86.7
F2	82.6	87.6
F3	93.5	91.5
F4	80.2	89.4
F5	72.1	82.3

In-Vitro Drug Diffusion Study

The *in-vitro* drug profile of nadifloxacin and clobetasol propionate from different formulations was carried and the results are depicted in **Table 4 & 5.** The highest drug release was found in the formulation F3 i.e. 91.72% (Clobetasol Propionate) and 89.03% (Nadifloxacin) within 8 hrs. F3 was found to be optimized formulation based on the dissolution and other evaluation parameters.

Table 4: *In-Vitro* Drug Release of Clobetasol propionate

Time (hours)	Cumulative percentage drug release				
	F1	**F2**	**F3**	**F4**	**F5**
1	7.02	8.80	7.98	8.50	5.02
2	17.97	10.40	16.77	17.23	13.23
3	23.67	25.73	25.44	28.60	23.34
4	41.43	40.60	39.60	38.97	38.64
5	50.68	53.56	53.64	44.80	46.23
6	57.45	59.44	68.12	54.76	54.89
7	65.82	67.90	77.87	68.90	62.23
8	70.90	75.00	91.72	77.03	67.40

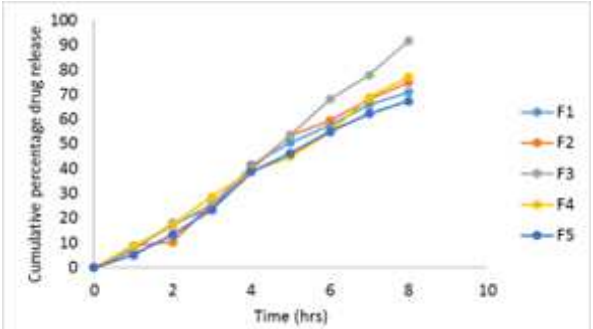

Figure 1: *In-Vitro* drug release of Clobetasol propionate

Table 5: *In-Vitro* Drug Release of Nadifloxacin

Time (hours)	Cumulative percentage drug release				
	F1	**F2**	**F3**	**F4**	**F5**
1	4.70	6.50	8.43	8.90	5.07
2	10.45	11.72	16.93	18.38	12.48
3	26.34	23.87	27.51	29.8	20.54
4	36.78	38.23	37.97	40.75	37.53
5	42.63	48.98	44.61	45.74	45.72
6	52.87	53.68	59.32	54.78	54.31
7	64.78	63.89	71.89	69.78	60.34
8	68.0	68.20	89.03	78.50	62.0

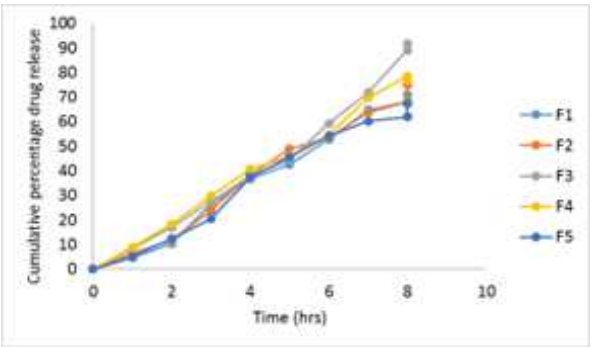

Figure 2: In-Vitro drug release of Nadifloxacin Kinetic modeling of drug release

Table 6: Release Order Kinetics Of Optimized Hydrogel

Kinetic Models	Clobetasol Propionate (R^2)	Nadifloxacin (R^2)
Zero order	0.9921	0.9920
First order	0.9454	0.9389
Higuchi	0.8839	0.8911
Korsmeyer and Peppas	0.9575	0.9599
Hixson Crowell	0.9820	0.9762

From the above results it is apparent that the regression coefficient value closer to unity in case of zero order plot indicates that the drug release follows a zero order mechanism (**Table 6**). Further the 'n' value obtained from the Korsemeyer-Peppas plots i.e. 1.0238 suggest that the drug release from hydrogel was super case II transport.

Stability Studies

Optimized formulation F3 was selected for stability studies on the basis of high cum ulative % drug release. Short term stability studies were conducted according to ICH guidelines. From the results it was concluded that, There is no significant changes in physical appearance, drug content and drug release at the storage conditions of 4ºC±2ºC / 75±5%RH, 40ºC±2ºC and at room temperature after the end of 30 days.

CONCLUSIONS

Aim of this research was to prepare of Nadifloxacin and Clobetasol Propionate loaded Hydrogel for the treatment of atopic dermatitis and psoriasis and overcome the disadvantages faced in semisolid formulations. The cumulative % drug release for the Nadifloxacin and Clobetasol propionate loaded hydrogel was 89.03 % and 91.72% at 8 hrs. The slope of the Korsmeyer Peppas plot (n = 1.0238) was found to be more than 0.89 indicating the diffusion was super case II transport. F3 was stable and retained their original properties with minor differences.

REFERENCES:

1. Kumar, Anuj & Han, Sung Soo. (2016). PVA-Based Hydrogels for Tissue Engineering: A Review. International Journal of Polymeric Materials and Polymeric Biomaterials. 66. 159 182.
2. Malpure PS et al., A Review on Hydrogel. American Journal of PharmTech Research 2018.
3. Berke R, Singh A, Guralnick M. Atopic dermatitis: an overview. American family physician. 2012 Jul 1;86(1):35-42.
4. Frazier W, Bhardwaj N. Atopic dermatitis: diagnosis and treatment. American family physician. 2020 May 15;101(10):590-8.
5. Gulrez SKH, Assaf S, Phillips G. Hydrogels: Methods of Preparation, Characterization and Applications. Glyn O Phillips Hydrocolloids Research Centre Glyndwr University, Wrexham United Kingdom.
6. Kumari K, Sara UVS, Sachdeva M. Formulation and Evaluation of Topical Hydrogel of Mometasone Furoate using different polymers. International Journal of Pharmaceutical and chemical sciences. 2013; 2(1).
7. Khapare SS, Bhandare MG, Talele SG, Jadhav A. An Emphasis on Hydrogels for Pharmaceutical Applications. American Journal of Pharmatech Research. 2016; 6(3).
8. Bindu SM, Ashok V, Chatterjee A. As a Review on Hydrogels as Drug Delivery in the Pharmaceutical Field. International Journal of Pharmaceutical and Chemical Science. 2012; 1(2).
9. Chaturvedi K, Ganguly K, Nadagouda MN, Aminabhavi TM. Polymeric hydrogels for oral insulin delivery. J Control Release. 2013 Jan 28;165(2):129-38.doi: 0.1016/j.jconrel.2012.11.005.
10. Bettini R, Colombo P, Massimo G, Catellani PL, Vitali T. Swelling and drug release in hydrogel matrices: polymer viscosity and matrix porosity effects. Eur J Pharm Sci. 1994;2(3):213-9.
11. Askarizadeh M, Esfandiari N, Honarvar B, Sajadian SA, Azdarpour A. Kinetic modeling to explain the release of medicine from drug delivery systems. ChemBioEng Reviews. 2023 Dec; 10(6):1006-49.
12. ICH. International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use Ich Harmonised Tripartite Guideline Stability Testing Of New Drug Substances And Products Q1A (R2) [Internet]. 2003 Feb. Available from: https://database.ich.org/sites/default/files/Q1A%28R2%29%20Guideline.pdf