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Preparation and characterization of topical Cetirizine hydrochloride hydrogel

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ABSTRACT

Cetirizine HCl is H_1-receptor antagonist antihistaminic commonly used orally and no topical local preparation available. The aim of this study is to prepare semisolid, topical hydrogel, skin preparation of Cetirizine HCl as an antihistaminic drug for the treatment of dermatological allergic diseases. Different hydrogel formulations were prepared using different water-soluble gelling agents at different percentages. Hydroxypropyl methylcellulose (HPMC), Carbapol 934P, and Methylcellulose were used as a gelling agent at percentages of 2 and4%. The prepared hydrogels were evaluated regarding visual examination, pH determination, spreadability, drug content determination, and *in vitro* release studies. The results revealed that all the prepared formulas show good physical properties with acceptable spreadability and pH values. On the other hand, the release profiles show the following descending order of release; HPMC >carbopol >MC2% >MC4%. It was concluded that cetirizine HCl hydrogel that consists of HPMC showed best homogeneity, consistency, stability, and spreadability, and this formula was chosen as the suggested formulations.

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INTRODUCTION

According to USP definition, gels are semisolid systems formed from either suspension of the large organic molecules or small inorganic particles; the dispersing medium movement is restricted by the presence of the interlacing three-dimensional network of particles or the solvated macromolecules into dispersed phase (Ferry, 1980). The polymer gels have interchangeability between the solution and gel state; the fluid could dissolve large molecule. However, some polymer gels are disappearing at reversibility because their chains are covalently bonded (Kwon *et al.,* 2011).The main advantages of gel dosage forms are non-invasive easily washable optimal cutaneous and percutaneous drug delivery, high patient compliance, and can use it on the skin directly for local action (Gregory and Ho, 1981; Nicole and Rouse, 2010). Although gel has wide acceptability there is some limitation such as allergenic reactions (Burn, 1969; Release *et al.,* 2015). Topical antihistamines are applied to skin to provide relief of pruritus and temporary relief of pain and itching associated with multiple insults, including insect bites, minor skin irritations, and contact dermatitis associated with the use of antihistamine compounds in the treatment of allergic dermatoses as the local use of Benadryl shows some antihistamine efficiency (Ba, 1992). Topical doxepin as antihistamine has been demonstrated to reduce pruritus with atopic dermatitis. It has an apparent short-term low risk of major side effects. (Eschler and Klein, 2010; Fallon and Sober, 1994). Cetirizine hydrochloride is an orally active, H_1-receptor antagonist soluble in water and the drug

mostly exists as a zwitterion at pH (3.5–7.5) as (Figure 1) (British National Formulary, 2015; Lee Barnes *et al.,* 1993).

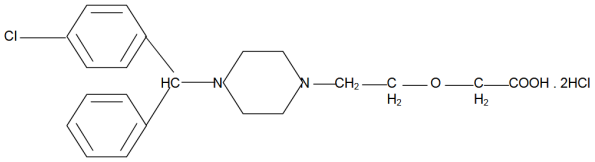

Figure 1: Structure of Cetirizine hydrochloride

Cetirizine hydrochloride is available as tablets, oral solution, and oral drops (Saimalakondaiah *et al.,* 2014). It is an antihistamine used for oro-nasopharyngeal itching, sneezing, itching eyes, rhinorrhea, lacrimation, upper respiratory allergies, allergic rhinitis, and used for the treatment of the chronic Idiopathic Urticaria (Jafilan and James, 2015; Wheatley and Togias, 2015). The more commonly observed untoward events reported during cetirizine administration are a headache, fatigue, dizziness, insomnia, nervousness, dry mouth, and nausea or vomiting (Lockey *et al.,* 1996; Salmun *et al.,* 2000).

The study was aimed for developing topical hydrogel formulations of Cetirizine hydrochloride for local action with low systemic side effects using different gelling agents.

MATERIALS AND METHODS

Materials

Cetirizine hydrochloride was obtained from Aurobindo Pharma, Hyderabad, India. Carbopol 940 was purchased from Goodrich, USA. Methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), methyl and propylparaben were purchased from Shin-Etsu Chemicals Co. Ltd., Japan. All other used chemicals are of high purity and analytical grades

Preparation of cetirizine hydrochloride topical hydrogel

Cetirizine hydrochloride hydrogel was prepared by direct dispersion method and composition shown in table 1. Propylparaben and methylparaben were added to glycerin (Welin-Berger *et al.,* 2001). polymers including methyl Cellulose (MC), hydroxypropylmethylcellulose (HPMC), or Polyacrylic acid polymer (carbopol 940) gels were prepared by dispersing the polymer and warm distilled water (40°C) with continuous mixing by a magnetic stirrer. Then add drug containing mixture. pH adjustment of carbopol gel is done by few drops of TEA until adjusted to pH 6. Finally, the drug was added to the mixture with continuous stirring for hydrogel production. Produced hydrogel kept in a clean glass container and store at the cold and dark place.

Physicochemical Evaluation of Prepared Cetirizine Hydrogel

Calibration curve preparation

Ten mg of cetirizine hydrochloride was dissolved in 100ml of phosphate buffer prepared solution in a volumetric flask. The solution of cetirizine hydrochloride was subsequently diluted with buffer phosphate pH 6.8 to obtain a series of dilutions. The solutions absorbances were measured at 230 nm by using a UV spectrophotometer. The absorbance was plotted against the concentration of cetirizine as shown in Figure 2.

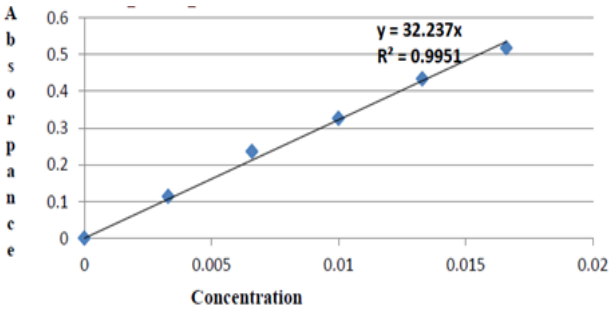

Figure 2: Calibration curve of cetirizine hydrochloride in Buffer Phosphate pH 8.6.

Visual examination

The prepared hydrogel was examined regarding the clarity, color, homogeneity, and syneresis.

pH Determination

pH meter was used for measurement of the pH of diluted hydrogel solutions at 25 °C.

Spreadability

To determine the credibility of cetirizine hydrochloride hydrogel, 0.5 g of gel was placed within a circle of 1 cm diameter pre-marked on a glass plate, over which a second glass plate was placed. A weight of 500 g was allowed to rest on the upper glass plate for 5 min. The increase in the diameter due to gel spreading was noted

Drug Content determination

The study was done by dissolving prepared hydrogel (1g) with phosphate buffer (500ml) at pH (6.8). The hydrogel was shaken for complete dissolving. The solution was filtered byMillipore filter (0.45µm) and then diluted with buffer and drug content was determined by UV- spectrophotometer at λ_{max} 230 nm

In Vitro Release Studies

The release study was done by using dialysis method in (model VK 7010, Varien dissolution tester, and autosampler unit VK 8000, made in the USA). Each formulation (1 gram) was taken and

Table 1: Composition of Cetirizine hydrochloride topical hydrogel

Ingredients (gm)	F1	F2	F3	F4
Cetirizine hydrochloride	1	1	1	1
Carbopol 940	2	–	–	–
HPMC	–	2	–	–
Methyl Cellulose	–	–	2	4
Glycerin	10	10	10	10
Methyl Paraben	0.03	0.03	0.03	0.03
Propyl Paraben	0.01	0.01	0.01	0.01
Purified water to	100	100	100	100

Table 2: Physical appearance of Cetirizine topical hydrogel

Topical hydrogels	Clarity	Color	Homogeneity	syneresis
F1	+	White	fair	-ve
F2	+++	transparent	good	-ve
F3	+	Opaque transparent	good	-ve
F4	+	Opaque transparent	good	-ve

placed on cellophane membrane which is previously immersed before this step for 24 hours in phosphate buffer at pH 6.8 to fill circle diameter (2.5) cm. The loaded membrane (donor compartment) was linked strongly on glass tube (lower open end) of 2.5 cm internal diameter made watertight by a rubber band. Phosphate buffer (900 ml) put in the tube at pH 6.8 which is the release medium (receptor compartment). The system was maintained for 3 hours at (37±0.5)°C in a thermostatic shaking water bath at 50 rpm. Samples of 5ml were withdrawn at intervals of 0.25, 0.5, 0.75, 1, 1.5, 2, and 3 hours with replacement each sample with the same volume of fresh buffer to keep a constant volume. Samples were analyzed for cetirizine content spectrophotometrically at λmax 230nm against blank.

RESULTS AND DISCUSSION

All prepared hydrogel reveals high homogeneity product without lumps and syneresis. The F2 preparation was very transparent and clear as compared to F1**,** F3, and F4 formulation as showed in table 2 and figure (3). When the developed gel applied on rabbit skin, it didn't show any side effect such as irritation for all formulations.

Figure 3: Transparency of prepared Cetirizine hydrochloride topical hydrogel

The pH for prepared gel formulationsF1, F2, F3, and F4 were 5.5, 5.0, 4.4 and 4.4 respectively as shown in the table (3); this is because of the acidic nature of cetirizine (Thakare *et al.,* 2014). Although all prepared hydrogel has acceptable pH formulation F1 contains carbopol has the optimum pH for the skin. The spreadability values showed the hydrogel is easily spreadable by a small amount of shear. Formulated hydrogel spreadability for F1, F2, F3 and F4 was 2.8, 7.8, 7 and 6 g cm/sec respectively as shown in table 3. Hence spreadability of the F2 formulation was good as compared to other formulations, and we note that F1 (Carbopol 940) is the lowest spreadability because of its high micro-viscosity. When the developed gel used on volunteers, it had shown no side effect such as irritation in all formulations. The results showed that the in-vitro permeation of F1, F2, F3, and F4 formulations were compared with each other.

In Vitro Release Studies

HPMC gels showed higher drug release than methylcellulose and Carbopol940 gels. The result shows a low viscosity and a high hydrophilicity of HPMC. Ana Krese *et al*. found that the HPMC molecules are large molecules if compared to water and drug. HPMC, as it is hydrophilic, have a high affinity for water so when the polymer chains being in contact with water, polymer-water replaces the polymer-polymer interactions (Krese *et al.,* 2016).

The percent of cetirizine released from methylcellulose gels was slightly decreased by increasing polymer concentration from (2%) to (4%) w/w due to increase the viscosity. These results may be explained by the controlled release of drug from methylcellulose. There is a negative relationship between cetirizine released, and polymer concentration that is the same as Lauffer's molecular diffusion theory (Welin-Berger *et al.,* 2001). Welin-Berger *et al*. found that an increase in the macro-

Table 3: Physiochemical properties of Cetirizine hydrochloride topical gel

Topical Hydrogel	pH	Spreadability (cm)	Drug content (%)
F1	5.5	2.8	97.3
F2	5.0	7.8	99.2
F3	4.2	7	98.1
F4	4.3	6	95.4

Table 4: Percent of cetirizine released from prepared hydrogel formula

Time (min)	Percent of drug released			
	F1	F2	F3	F4
0	0	0	0	0
10	7.5	13	8.3	6.7
20	9.2	16.7	10	8.3
30	11.7	23.4	12.3	9.2
45	12.7	25.12	14.1	10.8
60	14.3	26.8	18.5	12.5
90	19.2	27.6	21.8	13.2
120	20.9	30.1	24.6	14.7
150	25.12	31.8	26.8	13.6
180	27.6	34.3	29.3	19.2
210	30.1	36	33.5	22.6

viscosity may affect the release rate of the active compound inversely (Welin-Berger *et al.,* 2001).

At three hours, Carbopol gel showed lower drug release than the other polymers except for MC4. This indicates that drug release is affected by the nature of each individual polymer. The Carbopol structure plays a vital role in drug release. The mechanical layer is a factor that works as a barrier for the drug releasing from carbopol polymer gels which are formed from a network of polymer molecules and entraps water. Drug diffusion from gel occurs through this aqueous phase which is present in a high concentration of polymer (more than 0.5% w/w), will result in higher density and tortuosity of the gel through which drug release occurs through the hydrogel network and these results are in good agreement with that obtained by Aksungur *et al.,* (2004).The results are shown in the Table (4) and Figure (4).

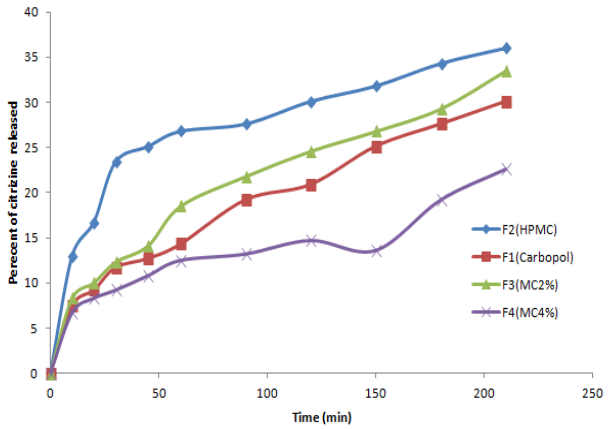

Figure 4: Cetirizine release profile from prepared hydrogel formulas

CONCLUSION

According to the obtained results, it can be concluded that; the HPMC hydrogel of Cetirizine (F2) t produced better spreadability and consistency as compared with the carbopol 934P hydrogel (F1) and Methylcellulose hydrogels (F3 & F4) formulations.

The developed F2 hydrogel revealed no skin irritation, good homogeneity, good stability, water washability and higher *in vitro* release. Therefore, it can be suggested that this formula could be a very promising topical formula for the treatment of dermatological disease.

REFERENCES

Aksungur, P., Sungur, A., Ünal, S., Iskit, A.B., Squier, C.A., Şenel, S., 2004. Chitosan delivery systems for the treatment of oral mucositis: In vitro and in vivo studies. J. Control. Release 98, 269–279.

Ba, J., 1992. Some indications for the gynecological use of budesonide (Apulein). Ther Hung 40, 90–92.

British National Formulary, 2015. British National Formulary [WWW Document]. BMJ Gr. Pharm. Press. URL www.medicinescomplete.com

Burn, J.H., 1969. Essential Pharmacology. Annu. Rev. Pharmacol. 9, 1–21.

Eschler, D.C., Klein, P.A., 2010. An evidence-based review of the efficacy of topical antihistamines in the relief of pruritus. J. Drugs Dermatol. 9, 992–7.

Fallon, J.D., Sober, A., 1994. Relief of pruritus in patients with atopic dermatitis after treatment

with topical doxepin cream. J. Am. Acad. Dermatol. 31, 613–616.

Ferry, J.D., 1980. Viscoelastic properties of polymers, Viscoelastic properties of polymers.

Gregory, G.K.E., Ho, D.S.S., 1981. Pharmaceutical Dosage Form Packages. United States Pat. 2–7.

Jafilan, L., James, C., 2015. Urticaria and Allergy-Mediated Conditions. Prim. Care - Clin. Off. Pract.

Krese, A., Kovačič, N.N., Kapele, T., Mrhar, A., Bogataj, M., 2016. Influence of ionic strength and HPMC viscosity grade on drug release and swelling behavior of HPMC matrix tablets. J. Appl. Polym. Sci. 133.

Kwon, G.H., Jeong, G.S., Park, J.Y., Moon, J.H., Lee, S.H., 2011. A low-energy-consumption electroactive valveless hydrogel micropump for long-term biomedical applications. Lab Chip 11, 2910–2915.

Lee Barnes, C., Mckenzie, C.A., Webster, K.D., Poinsett-Holmes, K., 1993. Cetirizine: A New, Nonsedating Antihistamine. Ann. Pharmacother. 27, 464–470.

Lockey, R.F., Widlitz, M.D., Mitchell, D.Q., Lumry, W., Dockhorn, R., Woehler, T., Grossman, J., 1996. Comparative study of cetirizine and terfenadine versus placebo in the symptomatic management of seasonal allergic rhinitis. Ann. Allergy, Asthma Immunol. 76, 448–454.

Nicole, P., Rouse, M.J., 2010. Scope of contemporary pharmacy practice: Roles, responsibilities, and functions of pharmacists and pharmacy technicians Executive summary. Am. J. Heal. Pharm.

Release, C., Forms, D., Compliance, P., 2015. Controlled Drug Delivery, Time.

Saimalakondaiah, D., Kumar, V.R., Rama, T., Reddy, M., Ajitha, A., Uma, V., Rao, M., 2014. Stability indicating HPLC method development and validation. Int. J. Pharma Res. Rev. 3, 46–57.

Salmun, L.M., Gates, D., Scharf, M., Greiding, L., Ramon, F., Heithoff, K., 2000. Loratadine versus cetirizine: Assessment of somnolence and motivation during the workday. Clin. Ther. 22, 573–582.

Thakare, V.M., Tekade, B.W., Patil, B.R., 2014. Formulation and characterization of ketoprofen topical gel. international J. Curr. Pharm. Clin. Res. 4, 35–42.

Welin-Berger, K., Neelissen, J.A.M., Bergenståhl, B., 2001. The effect of rheological behavior of a topical anesthetic formulation on the release and permeation rates of the active compound. Eur. J. Pharm. Sci. 13, 309–318.

Wheatley, L.M., Togias, A., 2015. Clinical practice. Allergic rhinitis. N. Engl. J. Med. 372, 456–63.