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Research Article

Formulation and evaluation of Thiocolchicoside Topical Gel by using different method

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Abstract

Thiocolchicoside used for the effective treatment of muscle spasm, cramps, musculoskeletal and neuromuscular disorders. It is available in market in the form of capsules and injection. The major problem associated with thiocolchicoside is it's bioavailability which is very low i.e. 25-30% only so in order to minimize drug loss due to first pass metabolism, and overcome problem associated with low bioavailability of drug there is a need to formulate semisolid preparation in the form of gel so we try to formulate and evaluate thiocolchicoside gel using different polymer and comparative study of their drug release.

In vitro release of thiocolchicoside gel from three different polymers i.e. carbapol, HPMC, and Na CMC to an aqueous receptor phase through goat skin was monitored spectrophotometrically at a wavelength of 259nm. This study was conducted to develop gel formulation of thiocolchicoside using three types of gelling agent i.e. carbopol, HPMC, Na CMC. Effect of penetration enhancer (propylene glycol) on the release has been studied. The gels were evaluated for physical appearance, rheological behaviour, drug release, and stability. Drug release from all gelling agent through goat skin was evaluated using keshary-chien diffusion cell.

All gels show acceptable physical properties concerning colour, homogenity, consistancy spredability and pH value. Among all gel formulation carbapol showed superior drug release then followed by Na CMC and HPMC. Drug release decreased with increased in the polymer concentration. Drug release was not linearly proportional with the conc. of penetration enhancer or co-solvent stability studies showed that the physical appearance, rheological properties and drug release remained unchanged upon storage for two month at ambient condition.

Keywords: Thiocolchicoside topical gel; carbopol; HPMC; Na CMC; penetration enhancer

1. Introduction

Delivery of drugs to the skin is an effective and targeted therapy for local dermatological disorders. This route of drug delivery has gained popularity because it avoids first pass effects, gastrointestinal irritation, and metabolic degradation associated with oral administration [1]. Due to the first past effect only 25- 45% of the orally administered dose reaches the blood circulation. In order to bypass these disadvantages the gel formulations have been proposed as topical application [2].

Gel base formulation makes the drug molecules more easily removable from the system than cream and ointment [3][4]. Gels for dermatological use have several favourable properties such as being thixotropic, greaseless,

easily spreadable, easily removable, emollient, nonstaining compatible with several excipients and water-soluble or miscible [5].

TDDS avoid the first pass metabolic effect of the liver ensure compliance provide steady state sustained released and reduce pill burden. There is a lack of literature related to the formulation and evaluation of Thiocolchicoside gel. Hence in the present work, it is planned to prepare and evaluate Thiocolchicoside gel for topical application.

2. Material and Methods:

Thiocolchicoside, carbopol, HPMC, Na CMC, Propylene Glycol, Methyl Paraben, Potassium Di Hydrogen Ortho Phosphate.

2.1 Instruments: UV-Visible spectrophotometer, Brookfield LVPV Viscometer, Franz diffusion cell

2.2 Preparation of Gels:

Appropriate quantity of carbopol 934was soaked in water for a period of 2 hours. carbopol was then neutralized with triethanolamine (TEA) with stirring. Then specified amount of drug was dissolved in appropriate and preweighed amounts of propylene glycol and alcohol. Solvent blend was transferred to carbopol container and agitated for additional 20 min. The dispersion was then allowed to hydrate and swell for 60 min. finally adjusted the pH with 98% TEA until the desired pH value was approximately reached (7- 7.4). During pH adjustment, the mixture was stirred gently with a spatula until homogeneous gel was formed.[6-10]

2.3 Physical Examination:

The prepared thiocolchicoside gels were inspected visually for their colour, homogeneity, consistency, spread ability and phase separation. The pH was measured in each gel, using a pH meter which was calibrated before each use with standard buffer solutions at pH 4, 7, 9. [11] The electrode was inserted in to the sample 10 min priors to taking the reading at room temperature.

3. Result

3.1 Evaluation of drug release

Release of thiocolchicoside from various gel formulations were studied using a modified Keshary-Chien diffusion cell. A goat skin was fixed between donor and receptor compartment with the help of adhesive. One gram of gel was taken in the cell (donor compartment) and receptor compartment was filled with drug free phosphate buffer pH 7.4 (15 ml). The buffer solution was agitated using a magnetic stirrer and a temperature of 32^0C ± 1oC was maintained externally.

Sample (1 ml) of the receptor compartment was taken at various interval of time (60, 120,180, 240, 300, 360 min) over a period of 6 hours and assayed for thiocolchicoside at 259 nm. The volume withdrawn at each time was replaced with drug free phosphate buffer. Amount of thiocolchicoside released at various intervals of time was calculated and plotted against time.

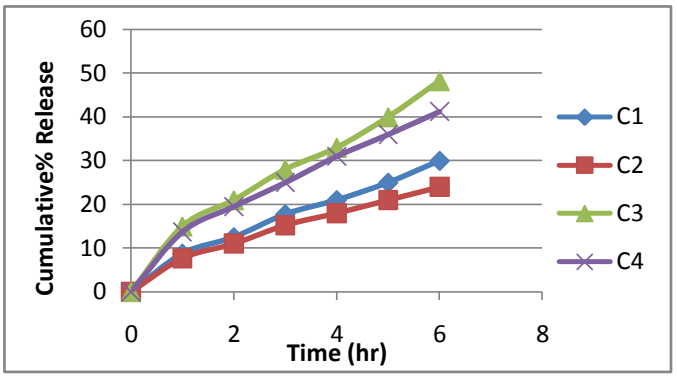
Table I: Formulation thiocolchicoside gels using different gelling agent

Ingredients	C1	C2	C3	C4	H1	H2	H3	N1	N2	N3
Thiocolchicoside	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Polymer	0.25	0.50	0.25	0.25	300	300	300	1.25	1.25	1.25
Propylene glycol	----	-----	1.25	2.50	----	1.25	2.50	----	1.25	1.25
Triethanolamine	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s
Methyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Propyl paraben	0.080	0.080	0.080	0.080	0.080	0.08	0.08	0.08	0.08	0.08
Dist. water	24	24	23	22	23.5	22.5	21.5	23.5	22.3	21.3

Table II: Viscosity, steady state flux, permeability and spreadability parameters of carbopol gels

Formulation	Viscocity (cps)	Flux (mcg/cmh) Sd n=3	Permeability (cm/h) sd n=3	Spreadability Gm cm/sec	Drug content (%) sd n=3	Ph sd n=3
Carbopol 1	155	53.54±0.765	0.013	32.00	99.65±0.87	6.8±0.877
Carbopol 2	450	45.67±0.665	0.011	21.05	98.78±0.56	6.7±0.876
Carbopol 3	153	88.29±0.567	O.22	26.60	99.07±0.67	6.9±098
Carbopol 4	235	78.64±0.876	0.019	22.22	98.87±87	6.8±0.56

Figure I: Graph Showing Dissolution profile of carbopol gel containing thiocolchicoside

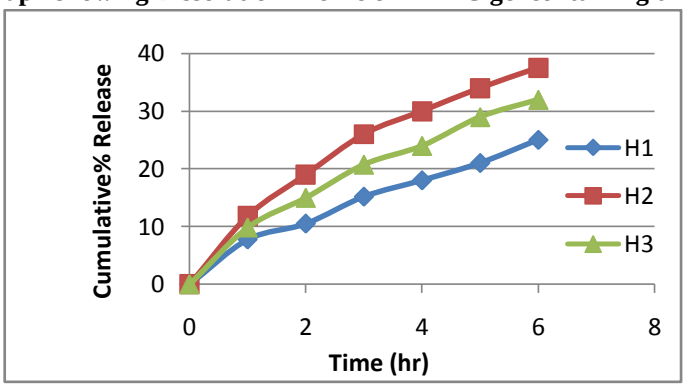


Key: (♦) C1; (■) C2; (▲) C3; (x) C

Table III: Viscosity, steady state flux, permeability and spreadability parameters of hydroxypropylmethyl cellulose gels

Formulation	Viscosity cPs×10^3	Flux (mcg/cm^2) n=3	Permeability (cm/h)	Spreadability (gm*cm/sec)	Drug content (%) n=3	pH n=3
HPMC 1	160	46.08±0.76	0.11±0.065	16.00	99.65±0.78	6.7±0.86
HPMC 2	225	72.09±0.87	0.18±0.098	15.09	98.56±0.98	6.6±0.87
HPMC 3	290	60.22±0.76	0.015±0.089	13.55	99.09±0.65	6.8±0.76

Figure II: Graph showing Dissolution Profile of HPMC gel containing thiocolchicoside

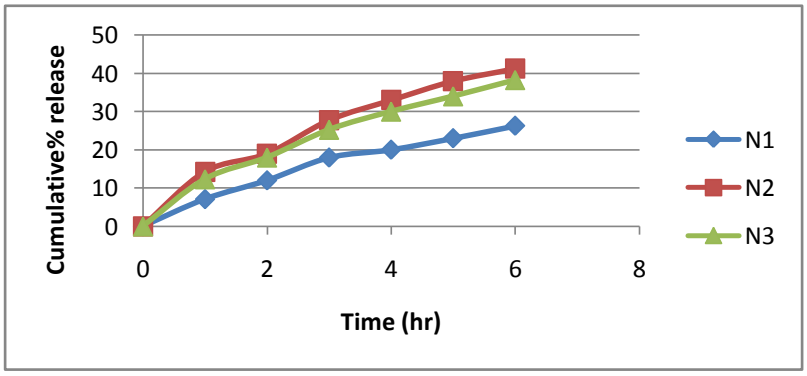


Key: (♦) H1 ;(■) H2 ;(▲) H3

Table IV: Viscosity, steady state flux, permeability spreadability parameters of Carboxymethylcellulose sodium

Formulation	Viscosity cPs x 10^3	Flux (mcg/cm^2/h) n=3	Permeability (cm/h) n=3	Spreadability (gm x cm/sec)	Drug content (%) n=3	pH ± n=3
Na CMC 1	325	47.5±0.768	0.011±0.001	20.51	99.67±0.78	6.0±0.9
Na CMC 2	505	82.63±0.876	0.020±0.003	19.09	98.86±0.56	5.9±1.2
Na CMC 3	550	73.78±0.654	0.018±0.007	17.06	98.99±0.54	5.9±0.7

Figure III: Graph showing Dissolution Profile of NaCMC gel containing thiocolchicoside



4. Conclusion

Among all gel formulations, carbopol gels shows superior drug release after that Na CMC, HPMC shows decreasing order of drug release. In carbopol gel formulations, the drug release was decrease with increase in carbopol concentration. Viscosity is negatively related to the release of active substance (Thiocolchicoside) from formulations. The formulations containing penetration enhancer (propylene glycol) were used at different concentrations (5 to 10%), among them formulations containing 5% propylene glycol showed higher flux (permeability and drug release) values. Therefore 5% propylene glycol shows maximum release and 10% shows comparative less release. In HPMC gel formulations, penetration enhancer (propylene glycol) were used at different concentrations (5 to 10%) among them formulations containing 5% propylene glycol showed higher flux (permeability and drug release) values. In, Na CMC and sodium alginate gel formulations found same results as compared to carbopol or HPMC with propylene glycol (penetration enhancer).Stability studies in all gel formulations showed that, the physical appearance, drug content, pH, rheological properties, drug release in all gel formulations remain unchanged upon storage for two months.

Conflict of interest:

Authors declare no conflict of interest.

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