"FORMULATION AND EVALUATION OF CURCUMIN LOADED TOPICAL GEL"

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ABSTRACT

The present study was aimed to develop topical gel of Curcumin which enhances the bioavailability & permeation with the help of combination of polymers which will be useful in further drug delivery. Polymers play a major role in various characterization parameters of topical gel such as in vitro release and rheological properties.

KEYWORDS: CURCUMIN, TOPICAL GEL, CARBAPOL, CARCINOGENIC ACTIVITY

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INTRODUCTION

Neoplasm/tumour is defined as growth/mass of abnormal tissue formed due to excess and uncoordinated cell proliferation. Characteristic abnormal uncontrolled cell division, dedifferentiation and loss of function, ability to spread to other parts of the body, metastasis. There have been concerns related to the conventional topical dosage forms such as lotions, creams, ointments and powder in terms of drug diffusion or release from the vehicle and delivery through the skin. Creams and Lotions often provide poor bioavailability of the drug because they are rapidly cleared from the skin and poorly release the drug from base. Non hydrophilic ointments are oleaginous, greasy and are non convenient to patients and also medicated powders for topical application have short residence time on the skin. Gels are semisolid systems in which the movement of the dispersion medium is restricted by interlacing three dimensional network of particles or solvated macromolecules of dispersed phase. The increased viscosity caused by interlacing and consequently internal friction is responsible for the semisolid state. Also a gel may consist of twisted matted strands often tied together by stronger types of Vander Waals Forces to form crystalline and amorphous regions throughout the system.1

The use of gel as a delivery system can increase the residence time of drugs on the skin and consequently enhance
bioavailability. Gel delivery systems have several advantages such as the ease of administration, non greasy, patient compliance, high residence time on the skin and better drug release. Curcumin (CUR) a constituent of Curcuma longa (Family – Zingeberaceae) chemically known as diferuloul methane has been reported to possess antioxidant, anti-inflammatory ant carcinogenic and hypocholesterolemic properties. Curcumin has also been shown to counter inflammatory responses similarly to the action of steroids, but without side effects. Following oral administration (up to 8g per day) it is poorly absorbed and only the traces of compound appear in blood. It undergoes extensive first pass metabolism and hence is a suitable candidate for topical gel formulation.

Among polymers used for formulation of gel base is combination of CRB and HPMC, combination of CRB and Sodium Alginate, alone CRB to describe physical properties, rheological behavior and to determine the amount of drug diffused better. These polymers have several attributes as a gelling agent like high viscosity at low concentration and give pleasant texture, do not support bacterial or fungal growth and are non irritating. A ideal penetration enhancer should have no pharmacological activity in body, should work rapidly, nontoxic, nonirritating, no allergic, should be suitable for formulation into topical formulation and should be compatible with drug excipient.

MATERIALS
Curcumin, carbopol-934, propylene glycol, triethanolamine, propylparaben, sodium hydroxide, ethanol used were analytical grade.

METHODS
Preparation of gels: Carbopol 934 gels were formulated by first preparing a stock solution of the Carbopol in distilled water and propylene glycol. Separately curcumin (1%w/w) was dissolved in pre weighted amounts of propylene glycol and ethanol. 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 neutral pH by sodium hydroxide solution with stirring. All the samples were allowed to equilibrate for at least 24 hours at room temperature prior to performing rheological measurements.

Other gel formulations were prepared by dispersing carbapol in water by continuous stirring. curcumin was dissolved in propylene glycol or ethanol and the solution was added gently carbapol dispersion under continuous stirring. The mixture was stirred gently with a spatula until homogeneous gel was formed. All the samples were allowed to equilibrate for at least 24 h at room temperature prior to performing rheological measurements.

Characterization of Formulations
The prepared curcumin gels were inspected visually for their homogeneity, grittiness, viscosity, Spreadability, pH, drug content, skin irritancy, in vitro drug release, stability studies.

Homogeneity
All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container.
They were tested for their appearance and presence of any aggregates.

**Grittiness**
All the formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation.

**Viscosity**
The measurement of viscosity of the prepared gel was done with a Brookfield viscometer. The gels were rotated at 20 and 30 rpm using spindle no. 64. At each speed, the corresponding dial reading was noted.

**Spreadability**
Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load, lesser the time taken for separation of two slides, better the spreadability. It is calculated by using the formula: 

\[ S = \frac{M \times L}{T} \]

Where 
- \( M \) = weight tied to upper slide 
- \( L \) = length of glass slides 
- \( T \) = time taken to separate the slides

**pH**
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. The electrode was inserted in to the sample 10 min priors to taking the reading at room temperature.

**Drug content**
To ensure uniform formulation of the gel, it was sampled from the different locations in the mixer and assayed for the drug content. Drug content of the gels was determined by dissolving an accurately weighed quantity of gel (about 1 gm) in about 100 ml of pH 6.8 phosphate buffer.

These solutions were quantitatively transferred to volumetric flasks and appropriate dilutions were made with the same buffer solution. The resulting solutions were then filtered 0.45 mm membrane filters before subjecting the solution to spectrophotometric analysis for curcumin at 276 nm. Drug content was determined from the standard curve of curcumin.

**Skin irritation**
The albino mice of either sex weighing 20-22gms were used for this test. The intact skin was used. The hair was removed from the mice 3 days before the experiment. The animals were divided into two batches and each batch was again divided into two groups. The gel containing drug was used on test animal. A piece of cotton wool soaked in saturated drug solution was placed on the back of albino mice taken as control. The animals were treated daily up to seven days and finally the treated skin was examined visually for erythema and edema.

**In Vitro Release**
The in vitro release experiments were carried out by using Franz-diffusion cells apparatus from different formulations. An exact amount of formulations (1.0 g) was spread out on membrane positioned between the donor and receptor chambers with an available diffusion area. The receptor compartment was filled with phosphate buffer pH 6.8 and continuously stirred with a small magnetic bar at a speed of 50 rpm during the experiments to ensure homogeneity and maintained at 37.2±0.5 °C. The samples were withdrawn at various time intervals and replaced with the same volume of PBS. Sink conditions were met.
in all cases. The samples were analyzed spectrophotometrically at 276 nm (Shimadzu UV-Visible-1800).

**Stability study**

For the evaluation of stability study, maintaining the formulations at an ambient condition over a period of two months. The physical appearance, pH value, drug content, rheological properties, drug release studies were determined periodically after the 1st and 2nd month after topical gel preparations.⁸

**RESULTS AND DISCUSSION**

**Characterization of Formulations**

The prepared formulations shared a smooth and homogeneous appearance. The Carbopol curcumin gels were transparent were dark yellow gummy with smooth and homogeneous appearance. All preparations were easily spreadable, with acceptable bioadhesion and fair mechanical properties. The pH values ranged from 5.71 to 6.82, which are considered acceptable to avoid the risk of irritation after skin application. Viscosity is an important physical property of topical formulations, which affects the rate of drug release; in general, an increase of the viscosity vehicles would cause a more rigid structure with a consequent decrease of the rate of drug release. Viscosity increased from 3245.31 cPs to 4208.35 cPs, as polymer concentration increased. Increased consistency was ascribed to enhanced polymeric entanglements, thereby increasing the resistance to deformation. For all formulations the viscosity was found to be lower from 2.3 to 4.1 times as the rotational speed increased. In fact, when the speed increases, the normally disarranged molecules of the vehicle are caused to align their long axes in the direction of flow. Such orientation reduces the internal resistance of the material and hence decreases the viscosity. The result of stability studies are shown that there were no significant changes in the viscosity, drug content and physical appearance of the gel, after storing at different temperature conditions for three months. These results indicate that drug remain stable after stability studies.

**In Vitro Release Results**

In vitro dissolution profile of curcumin gels containing different concentration of carbopol are shown in table 3 and fig. 1. Release profiles of curcumin from various gel formulations across the cellulose membrane depicted that drug release decrease with increase in concentration of the gelling agent. The drug release values were also found lower for the formulation in which polymer concentration was kept high (Table 3). In addition, viscosity increased from 3245 cPs to 4208 cPs, as polymer concentration increased. Viscosity is negatively related to the release of active substance from formulations and its penetration through the diffusion barriers. The decrease in the release could be attributed to increased microviscosity of the gel by increasing polymer concentration. Thus, both high concentration of polymer and high viscosity compete each other in decreasing the release of active substance from the formulation. In our study, the finding that higher polymer concentration resulted in lower drug release from the vehicles is in agreement with Lauffer's molecular diffusion theory of polymer gels, which states that the diffusion
The coefficient of a solute is inversely proportional to the volume fraction occupied by the gel-forming agent.

Figure 1: Cumulative %Drug release from Curcumin gel formulations at different time intervals

CONCLUSION
Curcumin is a anticancer drug to possess antioxidant, anti-inflammatory ant carcinogetic and hypocholesterolemic activities. To overcome the side effects associated with Curcumin therapy and to have the benefits associated with topical therapy; Curcumin topical gels are prepared in this study. Studies showed that drug release was decrease with increase in gelling agent concentration because polymer concentration increases, viscosity increases. Drug was absorbed from site of application as long as it remains in higher concentration gelling agent in solution form. So with an intention to keep the Curcumin in solution form, and thus prolonging the time of absorption, gel formulations were prepared.

Table-1 formulations

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<th>Sl. No.</th>
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Table 2: Physicochemical characteristics of Curcumin gels formulations

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<th>Formulation</th>
<th>Homogeneity</th>
<th>Grittiness</th>
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<th>pH</th>
<th>Viscosity</th>
<th>Drug Content</th>
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Table 3: Cumulative % Drug release from gel formulations at different time intervals

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REFERENCES