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FORMULATION AND EVALUATION OF GEL CONTAING AMLEXANOX FOR MOUTH ULCER

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Abstract: Objective: To formulate and evaluate mouth gel of amlexanox using an admixture of gelling agent i.e. carbopol p940 and penetration enhancer i.e. propylene glycol. Experimental work: Gel containing amlexanox was prepared by taking carbopol p934 and propylene glycol as penetration enhancer in different ratio. The concentrations of carbopol p934 and propylene glycol were optimized using 3^2 full factorial designs. The parameters determined were pH, drug content, viscosity, spradability, extrudability, in vitro drug release. Results: The pH values of gels were between 6.0 to 7.0. Drug content values were between 89% to 98%. Drug release was dependent on the concentration of carbopol and concentration of propylene glycol. The *in vitro* drug release time was 3 hr. Drug release from the gels increased with increase in the concentration of propylene glycol up to 10%. However, drug release decreased with further increase in the concentration of the propylene glycol to 20%. Conclusion: Formulation F6 with concentration of carbopol (1%) and concentration of propylene glycol (7%) showing maximum drug release upto 3 hr. was selected as the optimized formulation

Keywords: Mouth Gel, Gelling Agent, Penetration Enhancer

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INTRODUCTION

Topical liver and increase the bioavailability of the drug. Topical preparations give its action directly at the site of action delivery is an attractive route for local and systemic treatment. The delivery of drugs onto the skin is recognized as an effective means of therapy for local dermatologic diseases. It can penetrate deeper into skin and hence give better absorption. Topical application has many advantages over the conventional dosage forms[1]. In general, they are deemed more effective less toxic than conventional formulations due to the bilayer composition and structure. In the formulation of topical dosage forms, attempts are being made to utilize drug carriers that ensure adequate localization or penetration of the drug within or through the skin in order to enhance the local and minimize the systemic effects, or to ensure adequate percutaneous absorption. Topical preparation avoids the GI-irritation, prevent the metabolism of drug in the[2].

A gel is a two-component, cross linked three-dimensional network consisting of structural materials interspersed by an adequate but proportionally large amount of liquid to form an infinite rigid network structure which immobilizes the liquid continuous phase within. The structural materials that form the gel network can be composed of inorganic particles or organic macromolecules, primarily polymers. Cross links can be formed via chemical or physical interactions.[3] This leads to gel classification into chemical and physical gel systems, respectively. Chemical gels are associated with permanent covalent bonding while physical gels result from relatively weaker and reversible secondary intermolecular forces such as hydrogen bonding, electrostatic interactions, dipole dipole interactions, Vander Waals forces and hydrophobic interactions The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid.[4] Gels consist of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains.[5]

The term ‘Gel’ was introduced in the late 1800 to name some semisolid material according to their physiological characteristics rather than molecular composition. Gels are semisolid systems in which a liquid phase is constrained within a three dimensional polymeric matrix of natural or synthetic gums in which a high degree of physical or chemical cross linking has been established.[6] The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three-dimensional house of cards structure. Gels consist of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains. These chains are entangled with each other and

shown as a single phase. The interaction between the colloidal phase, (inorganic or organic) set up the 'structural viscosity.[7]

Most topical gels are prepared with organic polymers, such as carbomers, that impart an aesthetically pleasing, clear, sparkling appearance to the products and are easily washed off from the skin with water. The type of base used in formulating a topical dermatological product greatly influences its effectiveness. Bases containing large amounts of oleaginous substances provide an emollient effect to dry irritated skin. More importantly, bases made up of non-volatile oleaginous substances (e.g. hydrocarbon bases) can form an occlusive barrier on the skin that prevents escape of moisture from the skin into the environment.[8]

MATERIAL AND METHOD

Amlexanox obtained from Emcure Pharmaceutical, Gandhinagar, India, carbopol and aspate obtained from Corel Pharma. Benzalkonium Chloride obtained from S. D. fine chemical Ltd

PREPARATION OF AMLEXANOX GEL BY FUSION METHOD

Amlexanox gel formulations were prepared using carbopol 930 as gelling agents and Propylene Glycol as penetration enhancer. The carbopol P940 was mixed with Propylene Glycol in a beaker heated at 70 ^{0}c and Amlexanox in a suitable solvent (ethanol) was added to the is dispersion. The preservative sodium benzoate was dissolved in water using heat the solution was left to cool and then warmed to about 70 ^{o}c with vigorously stirring using an electric stirrer. Resulting solution added to above solution with stirring until a clear gel was formed.

Optimization Using Factorial Design:

In this study, a 3^2 factorial plan was used to determine the effects of formulation variables. In this design two factors are evaluated, each at three levels, and experimental trials are performed at all eight possible combinations. The concentration of carbopol P934 *(X1*) and concentration of Propylene Glycol(*X*2) was selected as independent variables. The % drug diffusion and viscosity at 12 RPM (physiological condition) were selected as dependent variables. The two factors and three levels are shown in Table 1.

The results obtained are shown in Table 4. For the % drug diffusion all two factors were found to be statistically significant (P<0.05): level of carbopol P934 & Propylene Glycol. For t90% level of one factors was found to be statistically significant (P<0.05): level of Carbopol 940.

EVALUATION PARAMETERS [9,10]

Measurement of pH

The pH of various gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values are calculated. The results obtained are as shown in table 4.

Drug content

1 g of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of different concentration were prepared by suitable dilutions after filtering the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve. The results obtained are as shown in table 4.

Viscosity study

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gels were rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding dial reading was noted. The viscosity of the gel was obtained by multiplication of the dial reading with factor given in the Brookefield Viscometer catalogues. The results obtained are as shown in table 4.

Spreadability

It indicates the extent of area to which gel readily spreads on application to skin or affected part. The therapeutic potency of a formulation also depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel which is placed in between the slides under the direction of certain load. Lesser the time taken for the separation of two slides, better the spreadability. It is calculated by using the formula: S = M. L / T where, M = wt. tied to upper slide L = length of glass slides

T = time taken to separate the slides

Extrudability study

After the gels were set in the container, the formulations were filled in the collapsible tubes. The extrudability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 second. The results obtained are as shown in table 4.

***In vitro* Diffusion studies**

The diffusion studies of the prepared gels can be carrying out using modified USP XXIII dissolution apparatus for studying the dissolution release of gels through a cellophane membrane. Gel sample (0.5g) was taken in cellophane membrane and the diffusion studies were carried out at 37 ± 1° using 250 ml of phosphate buffer (pH 7.4) as the dissolution medium. Five milliliters of each sample was withdrawn periodically and each sample was replaced with equal volume of fresh dissolution medium. Then the samples were analyzed for the drug content by using phosphate buffer as blank. The results obtained are as shown in figure5.

RESULTS AND DISCUSSION

pH, drug content , Spradability, Extrudability

The pH was within acceptable range and hence would not cause any irritation upon administration of the formulation. Table 5 shows the result of percent drug content for all the formulations. The drug content was found to be in acceptable range for all the formulations. Percent drug content in all four formulation were in the range 89-98 % indicating uniform distribution of drug. viscosity of formulation were found to be satisfactory.

All formulation were easily spreadable and extrudable.

Table 4: pH, %drug contents, viscosity, Spredability and Extrudebility of F1 to F9

In vitro diffusion

In vitro diffusion of factorial batches F1 to F9 are sow in figure1.

Release kinetic profile

To gain a better insight into the mechanisms underlying the release of amlexanox from gel. The release kinetics of amlexanox was investigated. Dissolutuion data was given zero order, first order, Higuchi and Korsmeyer kinetic treatment for optimized the formulations (table 6). These different kinetic equations were applied to interpret the release rate from all the formulations. The best with higher correlation coefficient (R2 = 0.9849) was found with Zero Order.

Table 5: Release kinetic data of optimized formulation

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Table 1: Full factorial design layout for 3^2

Batch No.	X1	X2
F1	-1	-1
F2	-1	0
F3	-1	+1
F4	0	-1
F5	0	0
F6	0	+1
F7	+1	-1
F8	+1	0
F9	+1	+1

X1 =Concentration of carbopol p940

X2 =Concentration of Propylene Glycol

Table 2: Coded value for Carbopol 940 and Propylene Glycol

Independent variables	Variables level		
	Low(-1)	Medium(0)	High(+1)
Concentration of carbopol (%)	0.5	1	1.5
Concentration of Propylene Glycol (%)	5	6	7

Table 3: COMPOSITION OF FACTORIAL DESIGN FORMULATIONS

Formulation code no.	Drug (mg)	Carb5opol p 940(mg)	Propylene Glycol (%)	Aspartame (mg)	Pippermint oil(ml)	Water (ml)
F1	2	0.5	5	100	1	50
F2	5	0.5	6	100	1	50
F3	5	0.5	7	100	1	50
F4	5	1	5	100	1	50
F5	5	1	6	100	1	50
F6	5	1	7	100	1	50
F7	5	1.5	5	100	1	50

F8	5	1.5	6	100	1	50
F9	5	1.5	7	100	1	50

Table 4: pH, %drug contents, viscosity, Spredability and Extrudebility of F1 to F9

Formulation	pH	%drug contents	viscosity	Spredability	Extrudebility
F1	7.8	93.8	11200	17.33	*
F2	7.1	89.4	12100	19.44	*
F3	7.2	89.6	13600	24.65	**
F4	7.3	89.3	13880	28.40	**
F5	7.4	94.3	13520	27.39	***
F6	7.4	98.4	14100	32.15	***
F7	7.4	96.7	14800	35.92	***
F8	7.4	91.3	15000	32.61	***
F9	7.5	90.8	18000	36.95	***

Note:

*** *** Excellent***

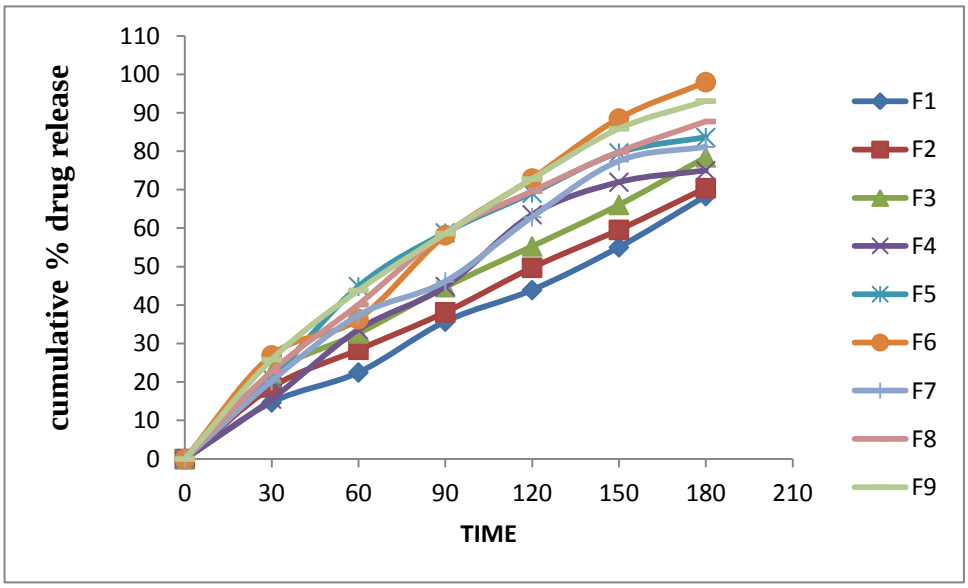
** ***Good,***

* ***Satisfactory***

Table 5: Release kinetic data of optimized formulation

Batch	Parameter	Model				
		Zero order	First order	Higuchi	Hixon-crowell	Korsmyer-Peppas
F6	R^2	0.9849	0.952	0.979	0.9846	0.972
	Slope	47.43	12.25	0.097	0.642	0.780
	Intercept	-33.24	8.30	1.31	-0.97	1.29

Figure 1 invitro drug release of F1 TO F9



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