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Formulation and evaluation of chlorzoxazone transdermal emulgel by using natural penetration enhancer

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ABSTRACT

Emulgel is one of the recent technologies in NDDS used for dual control release of emulsion and gel for topical use. Gel formulations generally provide faster drug release compared with conventional ointments and creams. Chlorzoxazone is a well-known therapeutic agent that is used mainly for its skeletal muscle relaxants. The aim and objective of the study is to formulate Chlorzoxazone emulgel for topical application. Emulgel of Chlorzoxazone, consist of Carbopol-940 or HPMC K4 as a gelling agents for gel formulation and tween 80, span 20, for emulsion formulation. Emulgel was formulated by emulsion incorporated in gel. Chlorzoxazone loaded emulgel was formulated by using o/w emulsion because of lower solubility in water. Lemon grass oil, Menthol was used as a penetration enhancer in emulgel formulation. Optimized formulation was evaluated for physical examination, swelling index, skin irritation study, extrudability study, drug content determination, spreadability, globule size determination and *invitro* drug release, rheological study. Optimized formulation shown drug release 98.8%. for 12 hrs.

Keywords: Emulgel, Chlorzoxazone, Carbopol 940P, Span 20.

INTRODUCTION

The delivery of drugs across the skin is gaining wide acceptance among patients and termed as Topical drug delivery. It is a viable administration route for potent, low molecular weight therapeutic agents susceptible to first pass metabolism. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. In developing a transdermal delivery system, two criteria are considered: one is achieving adequate flux across

the skin and the other is minimizing the lag time in skin permeation [1].

Emulgel is emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. Emulsified gel is stable one and better vehicle for hydrophobic or poorly water soluble drugs. They have a high patient acceptability since they possess the advantages of both emulsions and gels. Direct (oil-in-water) systems are used to entrap lipophilic drugs, whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. Emulgel allow dual

control of the drug release from the formulation, i.e. emulsion and gel. Emulsions possess a certain degree of elegance and are easily washed off whenever desired [2].

Chlorzoxazone is a centrally acting skeletal muscle relaxant. It inhibits polysynaptic reflex arcs on the spinal cord and sub cortical areas of the brain, thereby reducing skeletal muscle spasm which results increased mobility of the muscle and relief of pain. It also inhibits degranulation of mast cells, subsequently preventing the release of histamine and slow-reacting substance of anaphylaxis (SRS-A), mediators of type-I allergic reactions [3].

MATERIALS

Chlorzoxazone, Lemon grass oil was purchased from Yarrow chemicals (Mumbai), Carbopol 940, HPMCK4, Menthol, Arachis oil, Cetostearyl Alcohol, Propylene Glycol, Tween 80, Span 20, Lemon grass oil, Methyl paraben, Propyl paraben, were purchased from S.D Fine Chemicals Ltd., Mumbai (India) All other chemicals and reagents used were of analytical grade. Deionized distilled water was used throughout the study.

METHOD

Formulation and development of emulgel formulation [4]

Preparation of Emulsion

The emulsion itself consists of oily base and aqueous base. The drug was dissolved in Arachis oil, Span20, Lemon grass oil and cetostearyl alcohol. Then oil phase was prepared. At the same time the propylene glycol, Tween80, Methyl paraben and Propyl paraben were added in water. Then aqueous phase was prepared. Then the oil base was added to aqueous base with continuous stirring at 70°C.

Preparation of gel base

Appropriately weighed amount of viscosity increasing agents dispersed and hydrated in 70% of medium (water + NMP) for 24 H and pH was adjusted to 6-7.4 by using tri ethanolamine.

Mixing of emulsion with gel base

Then mix the both emulsion and gelbase at moderate speed with a mechanical stirrer its form emulgel.

Table 1: Composition of Formulation (g)

	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Chlorzoxazone	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Carbopol 940	0.5	1	1.5	2	2.5	3.0	-	-	-	-		
HPMC K4	-	-	-	-			2	2.5	3	3.5	4.0	4.5
Menthol	1	1	1	1	1	1	1	1	1	1	1	1
Arachis oil	5	5	5	5	5	5	5	5	5	5	5	5
Cetostearyl Alcohol	2	2	2	2	2	2	2	2	2	2	2	2
Propylene Glycol	3	3	3	3	3	3	3	3	3	3	3	3
Tween20	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Span20	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Lemon Grass Oil	3	3	3	3	3	3	3	3	3	3	3	3
Methyl Paraben	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	1	1	1	1	1	1	1	1	1	1	1	1

Propyl Paraben	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1	0.00 1
Distilled Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

EVALUATION OF EMULGEL

Gels were evaluated for their clarity, pH. Viscosity, spread ability, in vitro and by using

standard procedure. All studies were carried out in triplicate and average values along with standard deviation were reported

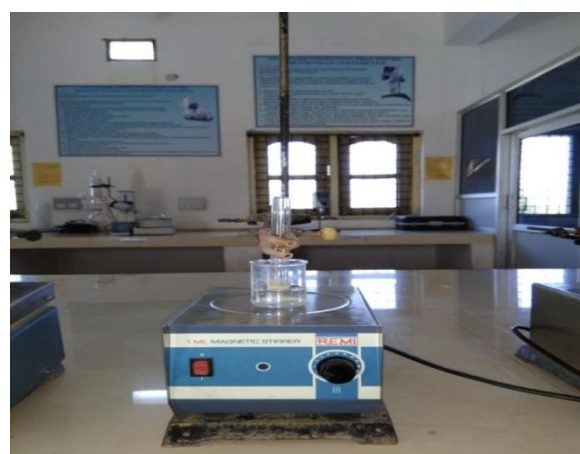


Figure 1: Evaluation of Emulgel (Invitro Diffusion)

Physical appearance

The prepared emulgel formulations are inspected visually for their colour, and phase separation and consistency

Determination of pH

2.5g of gel was accurately weighed and dispersed in 25 mL of distilled water. The pH of dispersion was measured by using digital pH meter (Digital potentiometer 101) [5]

Homogeneity:

All the developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate [6].

Drug content estimation

The Chlorzoxazone gel of 100 mg was dissolved in 50 mL of phosphate buffer pH 7.4. The volumetric this containing gel solution was shaken for 2 h on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at wavelength 280.0 nm. Tests were carried out in triplicate and

mean value of the three observed values was noted along with standard deviation values [7].

Measurement of viscosity

Viscosity of the gels was determined using a Brookfield digital viscometer. It is an instrument used for measuring the viscosity of liquids. The instrument measures the shearing stress on spindle rotating at a definite, constant thixotropic nature speed while immersed in the sample. The degree of spindle lag is indicated on a rotating dial. This reading is multiplied by a conversion factor based on spindle size and rotational speed, gives a value for viscosity in centipoises. By taking measurements at different rotational speeds, an indication of the degree of thixotropy of the sample is obtained [8].

Determination of spreadability

Principle

Spreadability is a term expressed to denote the extent of area to which the gel readily spreads on application to skin. The therapeutic efficiency of a formulation also depends on its spreading value. A special apparatus has been designed to study the

spreadability of formulations. Spreadability is expressed in terms of time in seconds taken by two slides to slip oil" from formulation, placed

between, under the application of a certain load. Lesser the time taken for the separation of the two slides better spreadability [9].

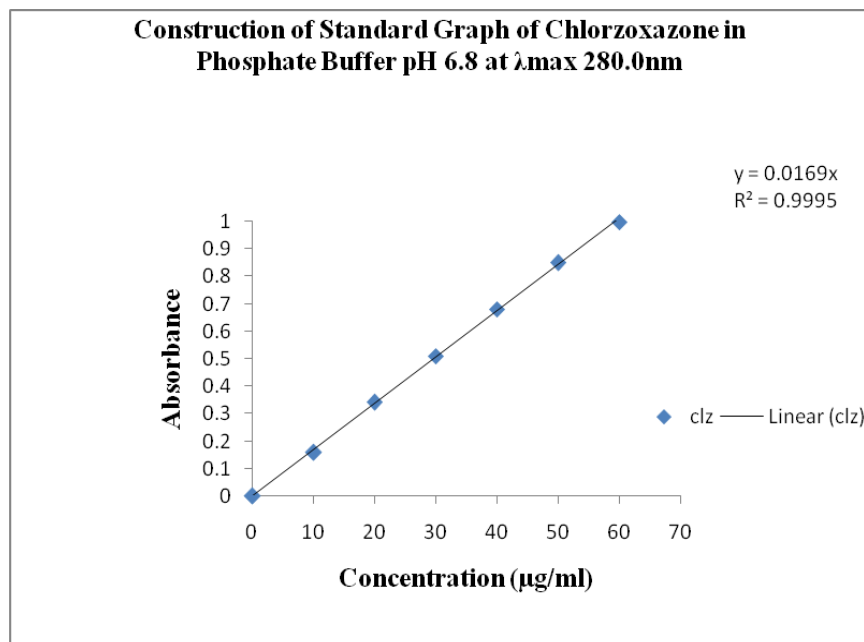


Figure 2: standard graph of Chlorzoxazone in Phosphate Buffer pH 6.8 at λ_{max} 280.0nm

Table 2: Evaluation test of Chlorzoxazone Emulgel

S.No.	Formulation	pH	Viscosity	Spreadability
			(centipoises)	(gm.cm/sec)
1	F1	6.6	8377	33.3
2	F2	6.7	9770	27.4
3	F3	6.7	12288	21.3
4	F4	6.8	13764	17.4
5	F5	6.7	14538	15.8
6	F6	6.7	15478	11.7
7	F7	6.6	3582	31.3
8	F8	6.6	4361	28.9
9	F9	6.5	5012	27.3
10	F10	6.4	5035	26.7
11	F11	6.4	5078	23.9
12	F12	6.3	5098	22.6

DRUG RELEASE STUDY

Invitro Drug release studies

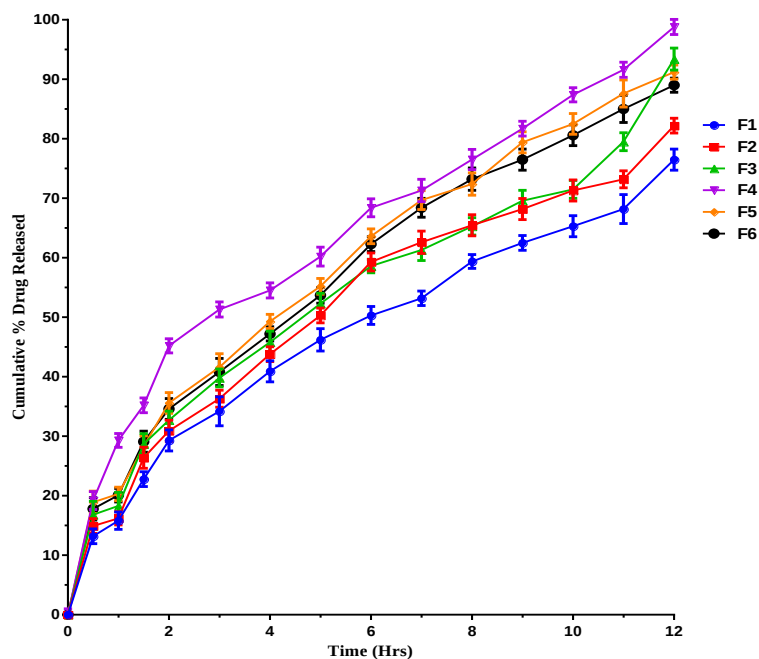


Figure 3: Comparison of *invitro* Drug Release of Chlorzoxazone Emulgel Formulation F1-F6

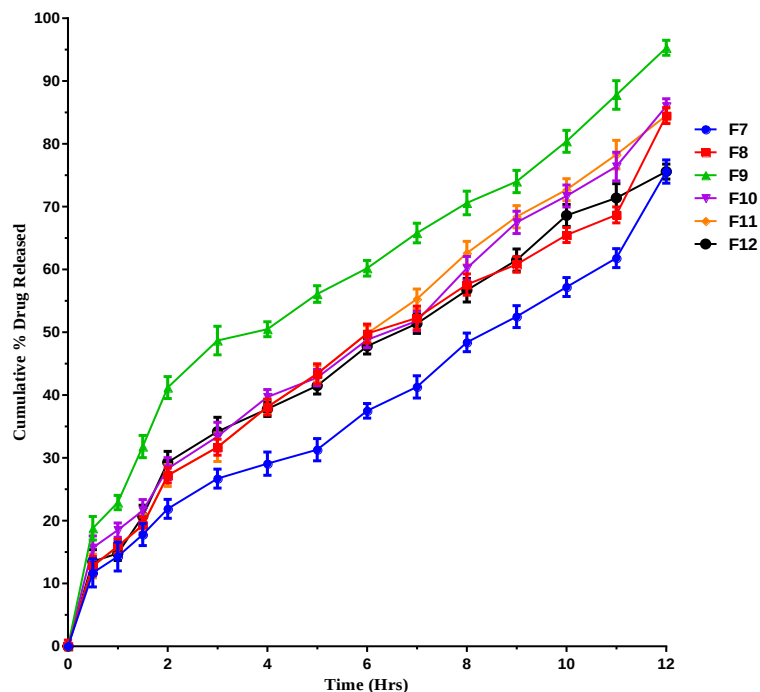


Figure 4: Comparison of *invitro* Drug Release of Chlorzoxazone Emulgel Formulation F7-F12

Discussion of *invitro* drug release studies

The release of the drug from its emulgel formulations can be ranked in the following order :
 F4 > F9 > F3 > F5 > F6 > F10 > F8 > F11 > F2 >

F1 > F12 > F7, where the amounts of the drug released after 12 hours were 98.8%, 95.3%, 93.4%, 91.2%, 89.2%, 84.6%, 84.5%, 82.2%, 76.5%,

75.8%, and 75.6% respectively. Thus, the greatest drug release was observed with formulations F4 according to drug release kinetic data. This finding may be due to presence of liquid paraffin and the emulsifying agent at their high levels respectively, which leads to an increase in the hydrophilicity of the emulgel, which in turn facilitates penetration of the release medium into the emulgel and diffusion of the drug from the emulgel.

CONCLUSION

- Chlorzoxazone emulgel was prepared by emulgel method by using various excipients such as polymers as Carbopol-940 \$ HPMC K4 and cetostearyl alcohol, Arachis oil, Propylene Glycol, Menthol, Glycerol, Tween80, Span20 and with penetration enhancers such as Lemon Grass Oil.

- The prepared emulgel was evaluated for its properties
- Further the analysis of release mechanism was carried out by fitting the drug release data to various kinetic equations like Zero order, First order, Higuchi's and korssemeyer peppas equations and from the values so obtained, the best fit model were arrived at.
- From the above results Formulation F4 was found to be best formulation for the topical release of Chlorzoxazone that complied with all the parameters.
- It releases 98.82 % of drug in 12 h time.
- It follow the Zero order of drug release kinetics.
- It show greater faster released in Ex-vivo release studies, with in one hour 60-70% drug was released.
- It produces greater flux of drug than marketed formulation.

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