RESEARCH PAPER

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Formulation and Evaluation of Topical Drug Delivery Systems of Ciprofloxacin

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Eight semisolid formulations belonging to anhydrous, cream (O/W and W/O), water soluble and gel categories were prepared and evaluated for drug release and antibacterial and antifungal activities. Ciprofloxacin release from mono-phasic systems (anhydrous, PEG base and gels) followed zero order kinetics and from biphasic systems (creams) followed $\sqrt{time}$ release order. Overall, PEG and gel formulations gave higher release rate and exhibited higher antibacterial and antifungal activities when compared to cream and anhydrous bases.

CIPROFLOXACIN is a new widely used antibacterial drug. Ciprofloxacin tablets are official in USP XXII, First Supplement[1]. Ciprofloxacin is available as tablets (200, 500 and 750 mg.), i.v. infusion, (200 mg/100 ml or 100 mg/50 ml) eye drops (3 mg/ml) and eye ointment (0.3 and 0.5% w/w). Topical drug delivery systems of ciprofloxacin for skin are not available. As ciprofloxacin is known to possess superior antibacterial activity against a wide range of microorganisms, a topical drug delivery system localizing the drug at skin will be much effective for the treatment of skin infections. In the present work topical drug delivery systems of ciprofloxacin were formulated and evaluated with a view to develop localized drug delivery system of ciprofloxacin for skin. The results are reported here.

EXPERIMENTAL

Materials

Ciprofloxacin hydrochloride, U.S.P., Carbopol 940 (BF Goodrich Company Cleveland, Ohio), sodium alginate (Loba-Chemie), sodium carboxy methyl cellulose (H.V., Loba-Chemie), and stearic acid (S.D. Fine Chemicals). Other materials used in semisolid formulations were of pharmacopoeial grades/superior grade.

*For Correspondence

Preparation of Semisolid Formulations

Eight semisolid formulations were prepared by standard methods as per the formulae given **Table-1**. In the each of these semisolid formulations, ciprofloxacin hydrochloride was incorporated at 1% w/w concentration.

Evaluation of Drug Release

Release of ciprofloxacin hydrochloride from various semisolid formulations was studied employing the permeation apparatus designed as described by Fites **et al**[2]. A glass cylinder with both ends open, 10 cm height, 3.7 cm outer diameter and 3.1 cm inner diameter, was used as permeation cell. A cellophane membrane (soaked in distilled water for 2 hours before use) was fixed to one end of the cylinder with the aid of an adhesive to result in a permeation cell. Three g of medicated semisolid was taken in the cell (donar compartment) and the cell was immersed in beaker (150 ml) containing drug free distilled water (100 ml) as receptor compartment. The

Table - I :Formulae of Semisolid Formulations of Ciprofloxacin Prepared

Ingredient (% w/w)	Semisolid formulation							
	F1	F2	F3	F4	F5	F6	F7	F8
Hard paraffin	3	-	-	-	-	-	-	-
Sodium lauryl sulfate	-	1.0	-	-	-	-	-	-
Stearic acid	-	-	13.0	-	-	-	-	-
Sorbitan mono oleate	-	-	-	8.0	-	-	-	-
Bees wax	2	-	-	12.0	-	-	-	-
Cetostearyl alcohol	5	8.0	2.0	-	-	-	-	-
White soft paraffin	90	15.0	-	24.0	-	-	-	-
Liquid paraffin	-	6.0	-	12.0	-	-	-	-
Sodium CMC	-	-	-	-	-	-	8.0	-
Sodium alginate	-	-	-	-	-	8.0	-	-
Carbopol 940	-	-	-	-	-	-	-	1.25
Potassium hydroxide	-	-	0.9	-	-	-	-	-
Glycerin	-	-	10.0	-	-	7.5	24.0	-
Propylene glycol	-	-	-	-	-	-	-	10.0
Triethanolamine	-	-	-	-	-	-	-	1.5
Ethanol	-	-	-	-	-	-	-	30.0
PEG 1000	-	-	-	-	80.0	-	-	-
PEG 6000	-	-	-	-	20.0	-	-	-
Calcium chloride	-	-	-	-	-	0.6	-	-
Sodium sulphite	-	-	-	-	-	-	-	0.1
Methyl paraben	-	0.2	0.2	0.2	-	0.2	0.2	0.2
Propyl paraben	-	0.1	0.1	0.1	-	0.1	0.1	0.1
Purified water	-	69.7	73.8	43.0	-	83.6	67.7	56.85

cell was immersed to a depth of 1 cm below the surface of water in the receptor compartment. The medium in the receptor compartment was agitated using a magnetic stirrer and a temperature of 37°C ± 1°C was maintained. Samples (5 ml) of the receptor compartment were taken at various intervals of time over a period of 6 h and assayed for ciprofloxacin at 276 nm. The volume withdrawn at each time was replaced with drug free receptor fluid. Amount of ciprofloxacin released to various intervals of time was calculated and plotted against time as shown in Fig.1.

Evaluation of Antimicrobial activity of Ciprofloxacin from semisolid formulations

The antibacterial and antifungal activities of ciprofloxacin from various semisolid formulations

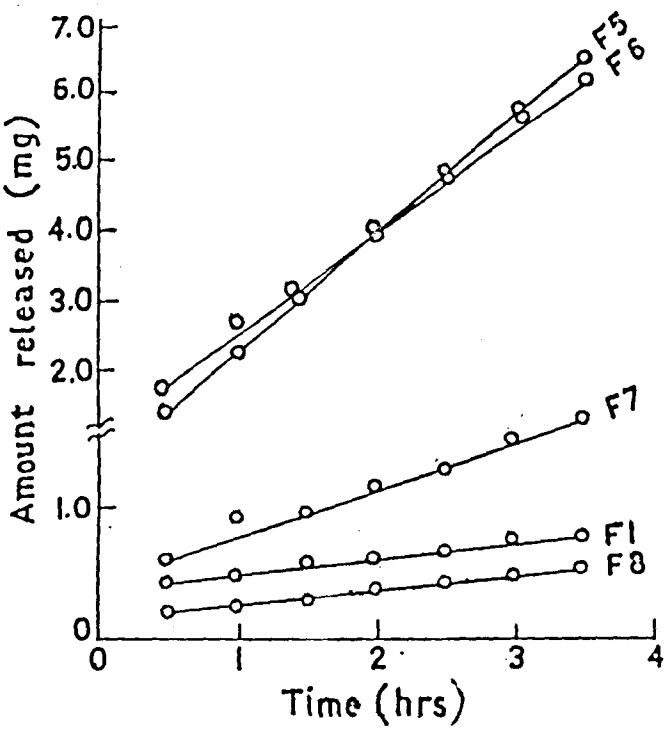

Fig.1: Release profiles of Ciprofloxacin from various semisolid formulations.

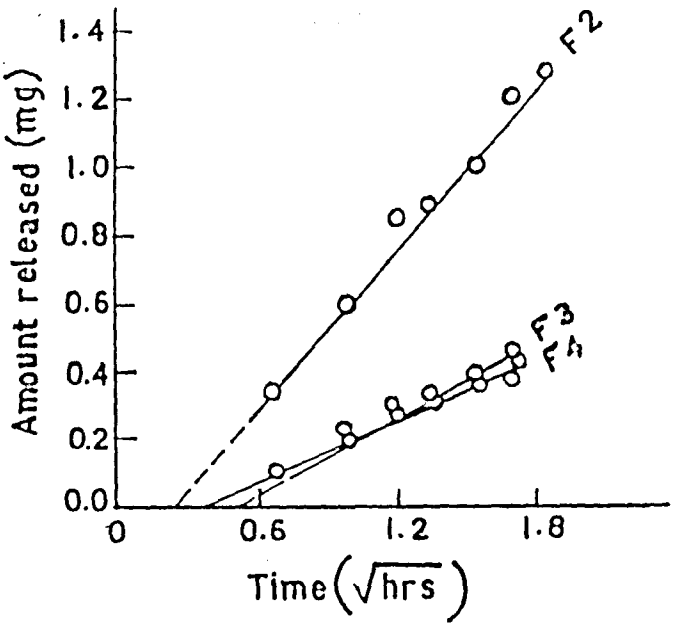

Fig.2: Release profiles of Ciprofloxacin from cream formulations

was evaluated by standard agar cup plate method employing two antibacterial test organisms namely **Staphylococcus aureus** and **Escherichia coli**, and two antifungal organisms namely **Aspergillus niger** and **Trichoderma virioae**. The diameters of the inhibition zones are given in **Table-2.**

RESULTS AND DISCUSSION

Eight semisolid formulations of ciprofloxacin belonging to anhydrous, emulsion (o/w and w/o), water soluble and gel categories, were prepared and evaluated for drug release and antimicrobial activity.

Release of ciprofloxacin from semisolid formulations was found to be slow and extended over longer periods of time. Release from monophasic systems (anhydrous, water soluble and gel bases), formulations E1, F5, F6, F7 and F8, obeyed zero order kinetics (**Fig.1**). The corresponding release rates are given in Table-2. Formulation F6 (sodium alginate gel) gave highest release rate. The order of increasing release rate from various formulations is as follows:

$$F8 < F1 < F7 < F5 < F6$$

Ciprofloxacin release from biphasic systems (creams), formulations F2, F3 and F4, followed $\sqrt{time}$ release order (**Fig.2**). The corresponding release rates ($mg\sqrt{hr}$) are given in Table-2. Among the creams o/w type gave higher release rate than w/o type.

Over all creams gave lower release than gels and PEG base. The low release observed with creams may be due to their biphasic nature and the partitioning of the drug in the two phases. Whereas in the case of gels the drug diffusion is through the fluid phase and hence they offer little resistance to drug diffusion and release. As such sodium alginate and sodium carboxy methyl cellulose gave higher release rates when compared to creams. With car-

Table - 2: Release Rate and Antimicrobial Activity of Ciprofloxacin from Various Semisolid Formulations

Formulations	Release rate*		Antimicrobial activity Inhibition zone diameter (cm)*			
	mg/hr	mg/$\sqrt{hr}$	S.A.	E.C.	A.N.	T.V.
F1	0.133	-	3.80	3.85	-	-
F2	-	0.780	4.00	3.75	1.4	1.7
F3	-	0.428	5.22	4.30	1.1	1.1
F4	-	0.320	3.95	3.90	-	1.0
F5	1.514	-	6.32	5.85	1.9	1.8
F6	1.760	-	4.50	3.95	1.3	1.2
F7	0.373	-	6.00	5.10	1.6	1.4
F8	0.107	-	5.82	5.32	1.5	1.4

* Average of three reading
SA: Staphylococcus aureus E.C. : Escherichia coli
AN : Aspergillus niger T.V. : Trichoderma virioae

bopol gel, the release was found to be very low and at lower rate. This may be due to the presence of solvents, propylene glycol and ethanol in the carbopol gel. The drug, ciprofloxacin may be having high affinity towards these solvents lowering the release rate. PEG base also gave high release rate. As it is a water soluble base, during the release experiments it absorbed water into the donor compartment and liquified, thus offering little resistance and giving high release rate.

The diameter of the inhibition zone (**Table-2**) is taken as a measure of the antimicrobial activity of ciprofloxacin from semisolid formulations. Cream (o/w), PEG base, sodium CMC and carbopol gels gave larger inhibition zones indicating that ciprofloxacin from these formulations exhibited higher antibacterial and antifungal activities when compared to other semisolids. Overall the antimicrobial activity of ciprofloxacin was higher with PEG and gel formulations when compared to cream and anhydrous bases. Ciprofloxacin from all semisolid vehicles exhibited higher antibacterial activity than antifungal activity. However the antifungal activity of ciprofloxacin from these vehicles was comparable to and even higher, in some cases, than that of clotrimazole (candid -B) formulations.

Thus basing on the results of both release study and antimicrobial activity. Cream (o/w), PEG base and gel formulations are considered as suitable topical drug delivery systems of ciprofloxacin for skin.

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