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COMMUNICATION

PHYSIOLOGIC SURFACTANTS AFFECTING PERMEATION AND BSL LOWERING IN RABBIT FROM GLIBENCLAMIDE TABLETS

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ABSTRACT

The physiologic surfactants (e.g. sodium taurocholate and sodium tauroglycocholate) were included in the tablet formulations to increase the solubility, permeability and absorption of gliben-clamide. Sodium tauroglycocholate was found to increase the permeation, AUC, C_{maxl} and % F_{rel} with its increasing concentrations in tablets. Sodium taurocholate, at submicellar level, had increased the permeation, AUC, C_{maxl} and % F_{rel} and decreased the above parameters beyond critical micelle concentration.

INTRODUCTION

Glibenclamide, a potent hypoglycaemic agent, is almost insoluble in water and only 45% of the oral dose is absorbed

through the gastrointestinal tract[1]. In our previous studies, the surfactants have enhanced drug permeation through jejunal sac[2,3] and bioavailability in animals and human volunteers[4,5]. In the study, therefore, physiologic surfactants e.g. sodium taurocholate (ST) and sodium tauroglycocholate (STG) have been included in tablet formulations to investigate their effects on the in-vitro permeation through jejunal sac and in-vivo bioavailability in terms of the rate and extent of BSL lowering in rabbits.

MATERIALS

Glibenclamide B.P. was obtained from Hoechst, Bombay. Sodium taurocholate and sodium tauroglycocholate were received from Ward, Blenkinsop & Co. Ltd., England.

METHODS

Preparation of Tablets - Each tablet contained glibenclamide (5 mg), dicalcium phosphate (90 mg), 10% w/v aqueous solution of PVP as a binder (equivalent to 2 mg PVP), nymcel ZSB-16 as a disintegrant (5 mg), talc (2 mg), magnesium stearate (1 mg) and the surfactant. Each batch consisted of 200 tablets. Tablets were prepared by wet granulation by the method of Singh and Jayaswal[2].

In-Vitro Permeation - The in-vitro permeation of the drug through rabbit jejunal sac was studied by the method of Singh and Jayaswal[2]. Seven tablets from each batch were subjected to in-vitro permeation.

Bioavailability in Rabbit White male albino rabbits of about 2 kg weight were selected for studying the hypoglycaemic effect of drug from tablet formulations. Rabbits were divided into control and treated groups and each group was consisted of seven rabbits. Placebo was fed to each rabbit of the control group and glybenclamide tablet/solution to each of the treated group. BSL lowering at different intervals was calculated by substracting the BSL of treated group from the control group. Maximum mg% reduction in BSL (C_{maxl}), time to achieve the maximum mg% reduction in BSL (t_{maxl}), area under the lowering in BSL-time curve (AUC), % bioavailability ($\%F_{rel}$) in terms of therapeutic effect and statistical analysis were performed by the method of Singh[5].

RESULTS AND DISCUSSION

Sodium taurocholate was found to increase the permeation, AUC, C_{maxl} and $\%F_{rel}$ from the batches ST-1 to ST-2 (Table 1 & 2). Further, the increasing concentration of the surfactant had lowered the above values due to miceller solubilization of the drug beyond critical micelle concentration of the surfactant. But, the sodium tauroglycocholate was found to increase the permeation, AUC, C_{maxl} and $\%F_{rel}$ values with the increasing concentrations (Table 1 and 2). Thus, tablets of the batch STG-4 exhibited the highest

TABLE 1

Batch Specification and In-Vitro Permeation of Glibenclamide from Tablets Through Rabbit Jejunal Sac

Batch	Surfactant Solution % w/v ml/batch	Cumulative % Permeation (Mean ± S.D.)			
		0.5 hr	1 hr	2 hr	3 hr
ST-1	6	27.33± 1.45	34.17± 2.11	42.71± 2.53	47.83± 3.11
ST-2	8	27.72± 2.13	34.35± 2.33	40.76± 2.50	65.50± 3.50
ST-3	10	19.99± 2.45	30.17± 3.20	45.71± 2.31	47.00± 3.85
ST-4	20	18.26± 1.35	27.39± 1.85	40.17± 2.81	45.65± 3.75
STG-1	6	12.53± 1.85	26.86± 1.95	44.77± 2.51	62.68± 3.01
STG-2	8	24.46± 5.05	27.72± 5.13	48.92± 4.95	65.22± 5.75
STG-3	10	41.69± 2.05	52.11± 2.51	83.38± 2.31	88.81± 3.11
STG-4	20	45.35± 1.89	61.82± 2.50	86.00± 2.33	93.11± 2.51

TABLE 2

Bioavailability in Terms of Therapeutic Effect in Rabbit

Batch	AUC (mg%-hr)	C_{maxl} (mg%)	t_{maxl} (hr)	$\%F_{rel}$
Solution	797.42±63.33	45.90± 3.69	3.00± 0.001	100.00± 7.94
ST-1	757.30±62.60	40.44± 3.82 P < 0.05	3.99± 0.05	90.14± 7.19 P > 0.05
ST-2	904.23±100.22	48.28± 5.65 P > 0.05	4.00± 0.002	98.37±10.90 P > 0.05
ST-3	779.75±83.12	43.49± 5.74 P > 0.05	3.99± 0.001	72.40± 7.71 P < 0.01
ST-4	692.13±78.65	39.50± 8.26 P > 0.05	4.00± 0.002	73.20±11.76 P < 0.01
STG-1	668.47±134.85	37.34± 5.66 P < 0.05	4.00± 0.01	83.40± 9.80 P < 0.05
STG-2	779.29±82.12	40.75± 6.04 P > 0.05	4.00± 0.001	82.55±15.31 P < 0.05
STG-3	972.97±70.13	50.67± 6.57 P > 0.05	4.00± 0.002	139.70±10.07 P < 0.01
STG-4	1046.06±54.92	51.50± 3.80 P > 0.05	4.00± 0.002	151.93± 7.97 P < 0.01

in-vitro permeation through jejunal sac, rate and extent of BSL lowering in rabbits. However, there was no significant difference ($P > 0.05$) in the rate but, the extent of BSL lowering was significantly higher ($P < 0.01$) from tablets of the batch STG-4 than the solution of the drug.

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