RESEARCH PAPER

Received 4th February, 1997.
Accepted 26th July, 1997
Indian J. Pharm. Sci., 1997, 59(5) pp. 232-235

In-Vitro studies on Buccal strips of Glibenclamide using Chitosan

R. ILANGO*, S. KAVIMANI, A. R. MULLAICHARAM AND B. JAYAKAR.
Dept. of Pharmaceutics, Periyar College of Pharmaceutical Sciences for Girls, Trichy, Tamil Nadu - 620 021.

As glibenclamide is metabolised completely in the liver, the principal metabolite being only very weakly active, buccal strip glibenclamide may be very useful for the treatment of diabetes more efficiently. The objective of this work is to investigate the possibility of obtaining a slow release, relatively constant effective levels of glibenclamide from buccal strips using chitosan. Here attempts were made to develop suitable chitosan- based buccal strips and to characterise it using different *in vitro* methods. Chitosan-based strips of glibenclamide showed suitability over Eudragit-based glibenclamide buccal strips for controlled release behaviour.

GLIBENCLAMIDE is a Sulphonylurea group of drug, used in the treatment of maturity onset diabetes as an oral hypoglycaemic[1-2], Glibenclamide, chemically is 1-(p-(2-(5-chloro-O-anisamido), ethyl), phenyl), sulfonyl)-3-cyclohexyl urea. The plasma half life is about 5-10 h. In the present work an attempt has been made to develop a buccal mucodhesive dosage form[3-7] of glibenclamide for improving and enhancing bioavailability. It may also be possible to bypass the hepatic first pass effect by administering it through the buccal mucosa, which is richly perfused with blood vessel and offers greater permeability than the skin[4]. The required therapeutic plasma concentration of glibenclamide can possibly be achieved more rapidly by using such buccal dosage forms. Chitosan is (1-4)-2-amino-dexoy-βD-glucan. It has similar structural characteristics as that of glycosamino glycans. It is tough, biodegradable and non- toxic[8-9].

METHODS

Glibenclamide (I.P), chitosan, Eudragit L 100, Eudragit S 100, Polyvinylpyrrolidone (Kollidone), propyleneglycol, acetic acid were the chemicals used.

*For correspondence

Polyvinylpyrrolidone was used as a mucoadhesive polymer. Propylene glycol (5% v/v) was used as a plasticizer and penetration enhancer. One percent w/v of chitosan was prepared in 5% v/v of acetic acid. Glibenclamide in concentration of 1% and 2% were used. The chitosan buccal strips were prepared by casting technique[10]. Mixed quantity of chitosan that was required to produce 1% w/v of its solution with 5% v/v of acetic acid. Allowed to stand for one and half weeks with moderate stirring for the first 3-4 days. The solution was then filtered through a muslin cloth to remove debris and suspended particles. Polyvinylpyrrolidone was accurately weighed and dissolved in ethanol alongwith accurately weighed quantity of chitosan solution and propylene glycol (5% v/v) were added to obtain a viscous solution. The drug was then dispersed uniformly in the viscous solution with continous stirring. The resulting mass was then poured into glass moulds lined with Aluminium foil. The solvent was evaporated at room temperature for about 24 hours. The dried strip thus obtained was cut into required size consisting of required amount of the drug and stored in a dessicator. Strips having an oval form of 4 cm length and 3 cm width, 40 micron thickness and density 1.2031±0.5 were used for the studies.

Table 1: Composition of glibenclamide buccal strips

Ingredients	Chitosan strip		Eudragit strip		
	1% Drug	2% Drug	1% Drug	2% Drug	Control
Glibenclamide	1%	2%	1%	2%	2%
Chitosan	1%	1%	--	--	--
Eudragit	--	--	1%	1%	--
Acetic Acid	5%	5%	--	--	--
Ethanol	--	--	5%	5%	5%
Poly vinyl pyrrolidone	500 mg	500 mg	500 mg	500 mg	500 mg
Propylene Glycol	5%	5%	5%	5%	5%

Table 2 : Swelling studies of buccal strips* (in CM)

Time in minutes	Chitosan buccal strip		Eudragit buccal strip	
	1% Drug	2% Drug	1% Drug	2% Drug
0	3.0	3.0	3.0	3.0
5	3.2 + 0.002	3.3 + 0.002	3.05 + 0.002	3.04 + 0.002
10	3.8 + 0.05	3.6 + 0.04	3.09 + 0.006	3.08 + 0.004
30	4.2 + 0.03	4.0 + 0.1	3.15 + 0.005	3.15 + 0.07
60	4.3 + 0.2	4.2 + 0.4	3.2 + 0.001	3.18 + 0.06

* Average of Three Trials with Standard deviation

For Eudragit buccal strip preparation (1:1) ratio of Eudragit L 100 and Eudragit S 100 were used instead of chitosan solution. Ethanol was used as solvent for Eudragit buccal strips. Drug free strips were prepared for comparison.

Evaluation of Buccal strips

Buccal strips of 4 cm length and 3 cm width were placed petridishes, 50 ml water was added and surface diameter was measured at 0, 5, 10, 30 and 60 minutes intervales. Four replications of each test were carried out. Buccal strips of equal density (1.203) were weighed accurately and kept immersed in 50 ml of water. Strips were taken out carefully at 5, 10, 30 and 60 minutes intervals blotted with filter paper to remove the water present on their surface and weighed accurately. The percent swelling was calculated using the following formula[11].

$$\text{Percentage Swelling} = \frac{\text{Wet Weight-Dry Weight}}{\text{Wet weight}} \times 100$$

Density Determination of the strips was made employing the film thickness and by using the relation D=m/v

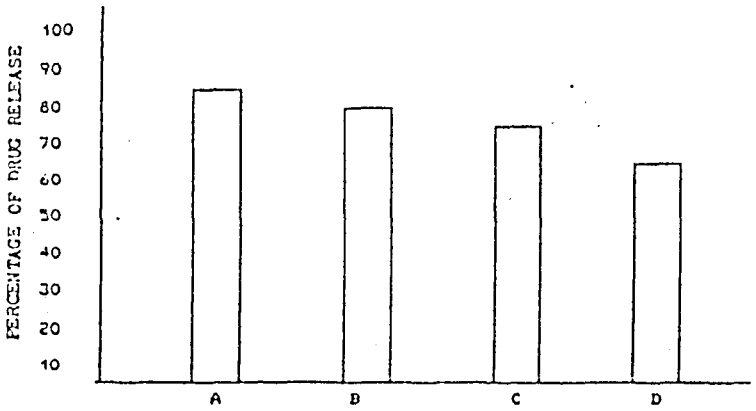
Where D = Density of free strips
M = Wt of strip samples in grams
and V = Volume of strip sample $(cm)^3$

Table 3 : Percentage swelling of chitosan buccal* strips

Time In Minutes	Chitosan strips 1% Drug	Chitosan strips 2 % Drug
5	24 ± 0.02	20 ± 0.02
10	27 ± 0.05	26 ± 0.02
15	29 ± 2.3	28.5 ± 2.5
30	31 ± 3.2	30 ± 1.6
60	32 ± 2.21	31.5 ± 0.06

* Values expressed as the mean of four readings with S.D.

Effect of concentration on drug release



A – Chitosan Strip (1% Drug)
B – Eudragit Strip (1% Drug)
C – Chitosan Strip (2% Drug)
D – Eudragit Strip (2% Drug)

The thickness of each film was measured in the centre and around the periphery with a horizontal metroscope. All thickness and weight measurements were made after residual moisture has been removed from the samples by storing in a dessicator for 1 week.

In Vitro release study

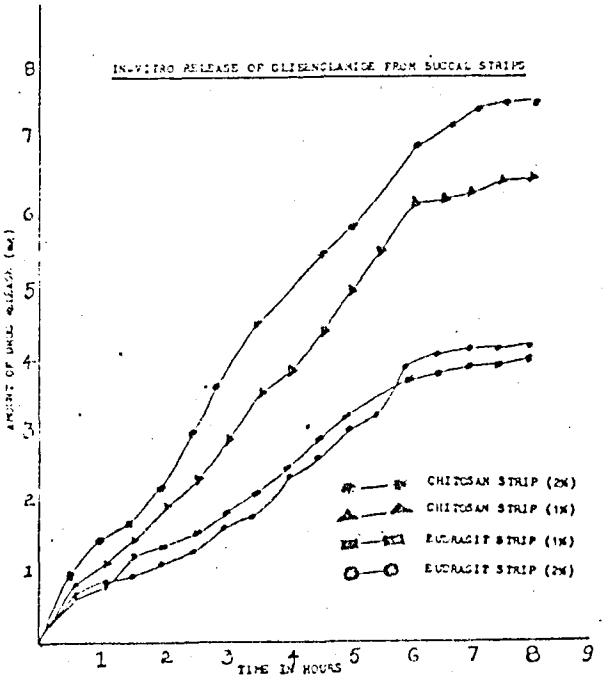
The strip was carefully pressed on to a microscopic slide. The slide was placed at an angle of 45° in a 250 ml beaker containing 200 ml of pH 7.4 buffer preheated to 37°. The beaker was kept in 37° waterbath. A non agitated system was selected to eliminate any effect of turbulence on the release rate as to assure that no disruption of the strip occured. Periodic assay samples were obtained by removing the slide, stirring the solution and pipetting a 5 ml sample with a graduated pipette, whose tip was covered with a piece of muslin cloth. The slide was quickly reinserted, making sure that the strip remained completely immersed throughout the release study. The beaker was kept covered through-out the run to prevent evaporation. All samples were analysed using an UV spectrophotometer at 226 nm.

RESULTS AND DISCUSSION

There is no interaction between chitosan and glibenclamide which was confirmed by Infrared spectrum of physical mixture of chitosan and glibenclamide.

Chitosan buccal strips with 1% and 2% drug and Eudragit buccal strips with 1% and 2% drug were prepared and evaluated. The content uniformity of glibenclamide in the prepared buccal film was found to be satisfactory and was within 5% variation. Polyvinylpyrrolidone was used as the mucoadhesive polymer which have a molecular weight of 49,000. This is water soluble hydrocolloid, mucoadhesive by the dissolution kinetics of the polymeric carrier. Thus the polymer dissolution was the rate controlling step in drug release. When a swellable polymeric matrix was made by incorporating chitosan or Eudragit with the polymer solution, delay in the dissolution of polymer due to swelling of the incorporated substances occurs. This leads to controlled release of drug from mucodhesive strips.

Chitosan swells more than Eudragit, which may lead to controlled release of drug in case of buccal strips prepared with chitosan. The Eudragit polymer solution consisting of equal proportion of (1:1) Eudragit S 100 and Eudragit L 100. Eudragit S 100 has swelling property whereas Eudragit L 100 has no swelling property.



Graph I: *In Vitro* studies of Glibenclamide in various concentrations in the Chitosan and Eudragit Strip system

In vitro studies of glibenclamide in various concentrations in the chitosan matrix showed that the percent release was maximum at 1% drug concentration (80.5%) when the drug content was increased to 2%, the rate of drug release was decreased. The controlled release of drug may be by diffusion through the chitosan matrix.

With Eudragit buccal strips also, *in vitro* studies showed that the percent release was maximum with 1% drug concentration (78%). Here also when the drug content was increased to 2%, the rate of drug release was decreased. However when the results of study was compared with those obtained with chitosan matrix, maximum percent release of drug as well as the controlled rate of drug release was shown only in chitosan matrix. The greater swelling nature of chitosan may perhaps be responsible for the promising diffusion controlled drug release than the Eudragit- based system.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the receipt of gift sample of glibenclamide from Hoechst Marion Roussel Limited., chitosan from Central Institute of Fisheries Technology (Cochin), Eudragit from Rohm pharma, Germany. They are also thankful to K. Veeramani, President, Periyar Maniammai Educational and charitable society for his encouragement and the college authorities for the facilities.

REFERENCES

1. Martindale, In, Reynolds, E.R. and Parfitt, K., Eds, The Extra Pharmacopoeia, 29th Ed, The Pharmaceutical Press, London, 1989, 389.
2. Ilango, R., Vetrichelvan, T., Kavimani, S., Jayakar, B and Mullaicharam, A.R., **Indian Drugs**, 1995, 12, 578.
3. Reinhold, A. and Merkee, H.P., **Int. J. Pharmaceutics.** 1989, 49, 231.
4. Marvola, M., Vanhervue, K., Soyhman, A and Marttilla, E., **J. Pharm. Sci.,** 1982, 71, 1975.
5. Gandhi, R. B., **Ind. J. Pharm. Sci.,** 1988, 50, 145.
6. Illum, L., Farrag, N and Davis, S.S., **Int. J. Pharmaceutics,** 1988, 46, 261.
7. Garren, K.W. and Repta, A.J., **J. Pharm. Sci.** 1989, 78, 60.
8. Kineemaki, K., Fujita, T and Bull, T., **Reg. Fis. Res. Lab,** 1968, 56, 89.
9. Lands, P.R., Bough, W.A. and Bull, T., **Environ contam Toxical,** 1976, 15, 555.
10. Thimma Shetty, J., Suresh Babu, C and Udupa, N., **Pharmag.** 1996, 2, 8.
11. Garacia, G and Kellaway, N., **Int. J. Pharmaceutics,** 1993, 100, 65.