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Design and Evaluation of bioadhesive tablets of Glimepiride

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ABSTRACT

Different types of bioadhesive polymers, intended for buccal tablet formulation, were investigated for their comparative bioadhesive force, swelling behavior, residence time and surface pH. The selected polymers were HPMC3 cps, HPMC5cps, HPMC K4M, and HPMC K15M along with Carbopol 940 as bioadhesive polymers showed the highest bioadhesion force, prolonged residence time and high surface acidity. Different polymer combinations as well as formulations were evaluated to improve the bioadhesive performance of the tablet. The formulation F7 containing hydroxypropyl methylcellulose K4M, K15M, Carbopol940, and mannitol was found to be promising, which shows an invitro drug release of 99.85% in 12 h along with satisfactory results. Formulation of bioadhesive buccal tablets of Glimepiride can be prepared by using different proportion & combination of excipients and we selected F7 as best formulation based on dissolution profile and physical characteristics. Formulation (F7) showed total drug release in 12hr and showed fair flow properties when compared to other formulations. The formulations F7, followed first order kinetics.

Keywords: Glimepiride, Bioadhesive Drug delivery system, Direct compression method

INTRODUCTION

Buccal drug delivery system

Bioadhesion

Longer and Robinson defined the term "bioadhesion" as the attachment of a synthetic or natural macromolecule to mucus and/or an epithelial surface. The general definition of adherence of a polymeric material to biological surfaces (bioadhesive) or to the mucosal tissue (mucoadhesive) still holds. A bioadhesive has been defined as a synthetic or biological material which is capable of adhering to a biological substrate or tissue and when the biological substrate is mucus the term was known as mucoadhesive [1].

Factors affecting mucoadhesion [2, 3]

The mucoadhesion of a drug carrier system to the mucous membrane depends on the below mentioned factors**.**

Polymer based factors

- Molecular weight of the polymer
- Concentration of polymer used
- Flexibility of polymer chains

- Swelling factor
- Stereochemistry of polymer

Environment related factors

- pH at polymer substrate interface
- Applied strength
- Contact time

Physiological factors

- Mucin turnover rate
- Diseased state

Method of Preparation of Mucoadhesive Buccal Tablets [4, 5]

The design of mucoadhesive was mainly do ne by three processes namely wet granulation process, dry granulation process and direct compression process. From this the wet granulation process was the most widely used and most general method of tablet preparation. Its popularity is due to the greater probability that the granulation will meet all physical requirements for the compression of good tablets. The dry granulation process explained as when the tablet ingredients are sensitive to moisture and are unable to withstand elevated temperatures during drying and when the tablet ingredients have sufficient inherent binding or cohesive properties, slugging may be used to form granules.

This method is known as dry granulation or pre-compression method or the double compression method. Finally, the third method was direct compression method in this method of tablet manufacturing the all ingredients such as drug, diluents, binders, lubricants and other required excipients and chemicals are weighed individually then mixed and blended together for some time period and then directly compressed into a compact mass. This process was the most preferred method of tablet manufacturing because of it is the cheapest and fastest direct method of tablet production.

MATERIALS AND METHODS

Table No 1: Materials and Equipements

S.NO	NAME OF THE MATERIALS	NAME OF EQUIPMENTS
1	Glimepiride	Electronic balance
2	HPMC 3cps	USP dissolution apparatus
3	HPMC 5cps	UV spectrophotometer
4	HPMC K4M	Tablet compression machine
5	HPMC K15M	Hardness tester
6	Mannitol	Friability test apparatus
7	Carbopol 940	P^H meter
8	Magnesium stearate	Thickness tester
9	Talc	Tap Density Tester USP
10	Ethyl cellulose	Bulk Density apparatus
11	Sodium hydroxide	Sieves
12	Potassium di hydrogen phosphate	Stability Chamber
13	Cyanoacrylate	Melting Point apparatus

RESULTS

Table No 2: Results of identification tests of drug

S.no	Parameter	Drug
1	Colour	White
2	Odour	Characteristic
3	Taste	Bitter
4	Appearance	Crystalline powder

Standard Calibration Graph of Glimepiride

Standard graph of Glimepiride was prepared by taking 25mg of drug in 25ml of Methanol solution to get (1000µg/ml stock solution) from the above stock solution suitable dilutions were made to get 5,10,15,20,25 µg/ml solution and the absorbance was measured at 231nm in UV spectrophotometer. A graph was drawn by taking concentration on X axis and absorbance on Y axis. From the graph, the regression was found to be 0.9996. It obeys Beers law.

Table No 3: Calibration Graph

S.No	Concentration µg/ml	UV Absorbance at 226 nm
1	0	0.00
2	5	0.183±0.02
3	10	0.358±0.02
4	15	0.536±0.02
5	20	0.710±0.02
6	25	0.891±0.02

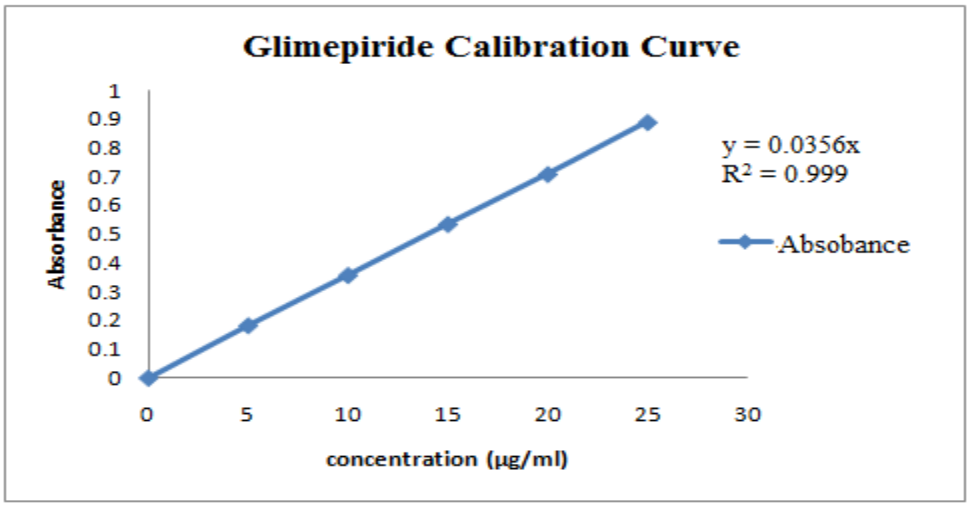

Fig No 1: Standard Calibration Curve of Glimepiride

FTIR Studies

- Drug polymer interactions were studied by FTIR spectroscopy. One to 2mg of Glimepiride, polymer and physical mixtures of samples were weighed and mixed properly with Potassium bromide to a uniform mixture.
- A small quantity of the powder was compressed into a thin semitransparent pellet by applying pressure.
- The IR spectrum of the pellet from 450-4000cm^{1} was recorded taking air as the reference and compared to study any interference.

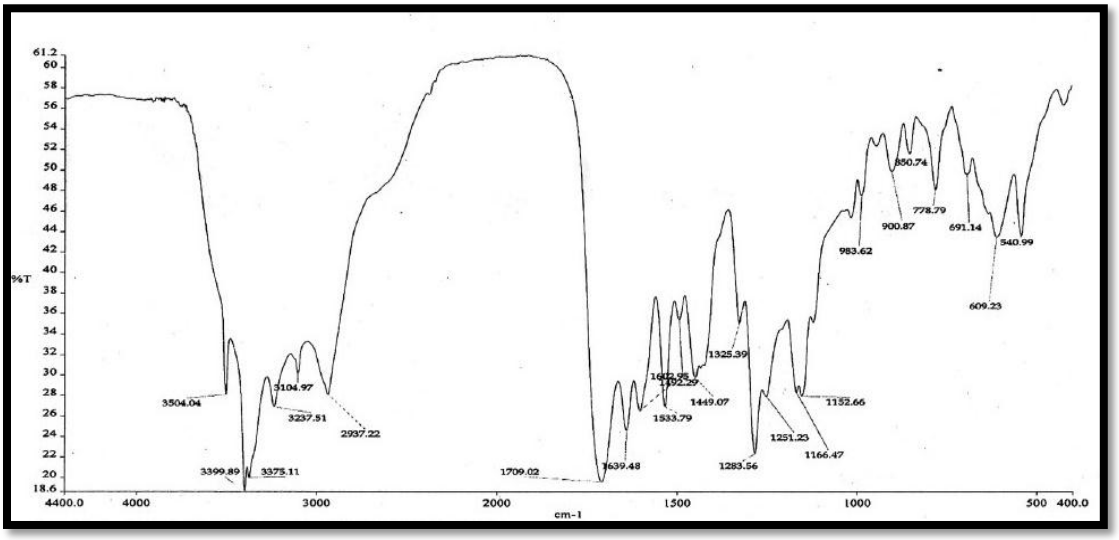

Fig No 2: FTIR Spectrum of Optimized Formulation

Evaluation of pre-compression parameters

Table No 4: Evaluation of Pre-Compression parameters

S.no	Formulations	Angle of repose (0)	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility index	Hausner's ratio
1	F-1	38.86	0.325±0.03	0.452±0.05	22.64±0.06	1.12±0.02
2	F-2	42.92	0.330±0.05	0.445±0.08	25.74±0.05	1.09±0.06
3	F-3	41.86	0.445±0.09	0.553±0.06	19.25±0.02	1.36±0.03
4	F-4	39.09	0.390±0.02	0.446±0.01	21.25±0.09	1.19±0.01
5	F-5	37.26	0.495±0.01	0.407±0.04	18.33±0.01	1.15±0.04
6	F-6	40.59	0.313±0.10	0.405±0.08	27.62±0.05	1.25±0.09
7	F-7	28.65	0.376±0.11	0.632±0.05	17.25±0.07	1.21±0.08
8	F-8	36.58	0.374±0.10	0.529±0.04	26.75±0.06	1.14±0.15
9	F-9	34.24	0.321±0.07	0.474±0.03	22.33±0.04	1.17±0.06
10	F-10	36.89	0.389±0.02	0.538±0.07	23.56±0.08	1.25±0.08

All the values are expressed as mean ± S.D; No. of trails (n) =6

Evaluation of post compression parameters

Table No 5: Evaluation of Post Compression Parameters

S.no	Formulations	Thickness (mm)	Weight Variation (mg)	Friability (%)	Hardness (kg/cm2)	Surface PH	Swelling Index
1	F-1	2.93±0.06	148.7±0.95	0.56±0.02	3.93±0.12	6.56±0.95	42.55±0.56
2	F-2	2.93±0.06	150.5±0.95	0.52±0.87	4.23±0.06	5.23±0.95	57.83±0.99
3	F-3	2.90±0.00	150.2±0.97	0.56±0.67	4.47±0.06	5.77±0.97	78.04±0.98
4	F-4	2.99±0.01	149.6±0.78	0.78±0.01	3.00±1.22	7.08±0.74	27.11±0.01
5	F-5	2.99±0.03	150.1±0.22	0.70±0.00	3.50±0.20	6.94±0.12	38.02±0.24
6	F-6	3.00±1.00	149.0±1.99	0.59±0.12	4.00±0.33	5.00±0.88	45.90±0.41
7	F-7	2.97±0.06	148.6±0.84	0.72±0.98	3.83±0.23	7.43±0.08	40.90±0.89
8	F-8	3.10±0.35	150.2±0.72	0.57±0.43	4.20±0.12	5.12±0.45	60.43±0.22
9	F-9	3.00±0.03	148.8±0.22	0.55±0.33	4.40±0.56	5.08±0.34	81.23±0.45
10	F-10	2.87±0.06	150.7±1.06	0.87±0.03	3.47±0.10	6.87±0.12	29.54±0.09

Dissolution profiles of glimepiride bioadhesive tablets trial batches

Table No 6: Dissolution profiles of Glimepiride Bioadhesive tablets trial batches

Time(hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
1	12.34	13.43	9.68	14.21	8.12	8.9	20.85	17.96	7.5	9.84
2	22.43	28.9	17.84	30.31	17.5	18.59	43.75	35.31	15.93	20
4	36.54	55.93	38.59	58.12	35.62	36.09	67.34	60.15	30.93	38.75
8	60.92	72.78	57.03	63.24	52.65	54.53	86.79	75.15	51.09	40.32
10	80.56	80.87	60.43	82.96	83.12	85.46	94.68	85.15	60.82	57.34
12	86.34	100.46	94.59	100.62	97.56	95.35	99.85	100.78	81.93	98.12

Dissolution profiles of F1-F10 formulations

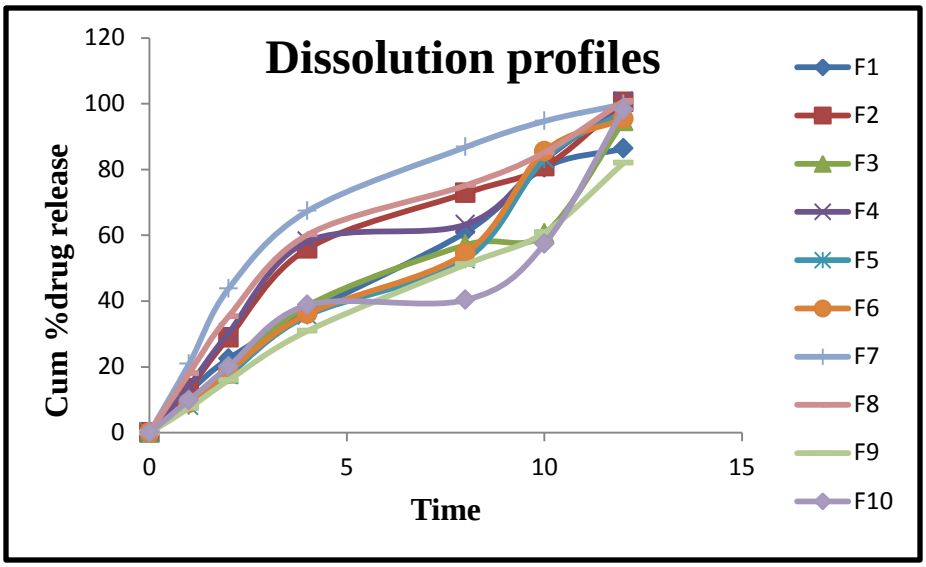

Fig No 3: Dissolution profiles of F1-F10formulations

Dissolution profile of optimised batch (F-7)

Table No 7: Dissolution profile of optimized batch

Time(hr)	F-7
0	0
1	20.85
2	43.75
4	67.34
8	86.79
10	94.68
12	99.85

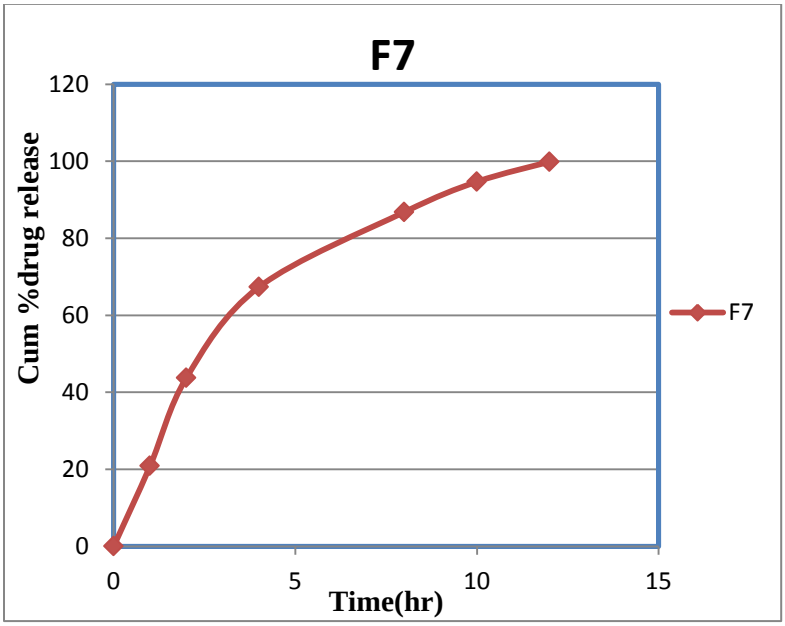

Fig No 4: Dissolution profile of optimized batch

Determination of release kinetics

Table No 8: kinetic studies of Glimepiride Tablet

Release kinetics	R^2	Intercept	Slope
Zero order	0.934	10.49	3.29
First order	0.953	4.964	-0.14
Higuchi	0.934	11.0	25.61
Korsmeyer peppas	0.991	0.66	0.74

Table No 9: Stability dissolution profile of F-7 for 1st, 2nd & 3rd months

S.NO	Time(hr)	F-7 1M	F-7 2M	F-7 3M
1	0	0	0	0
2	1	20.75	20.72	20.68
3	2	43.65	43.62	43.59
4	4	67.24	67.21	67.18
5	8	86.69	86.63	86.59
6	10	94.58	94.54	94.50
7	12	99.73	99.63	99.48

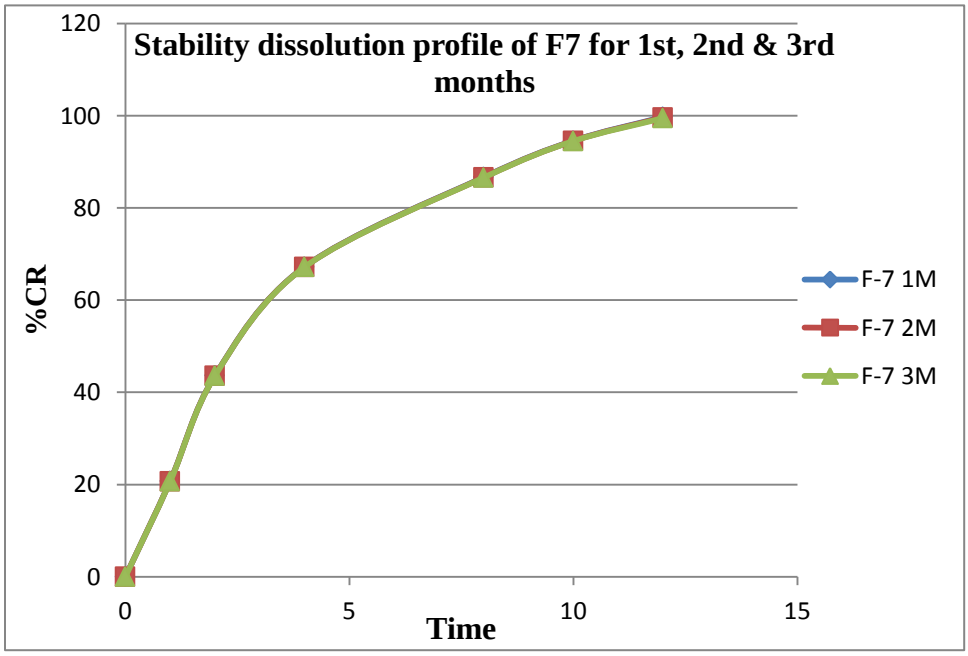

Fig No 5: Stability dissolution profile

SUMMARY AND CONCLUSION

The present study was mainly based upon the "design and evaluation of Bioadhesive tablets of Glimepiride" by direct compression method. The blends were also evaluated for various recompression parameters. These blends displayed angle of repose values of about 350; bulk density, tapped density and Carr's index values were found approximately to the 0.35 g/cc, 0.41 g/cc and 14.63 % respectively. The surface pH of all the tablets was within a range of 6.8 to 7.4, which was close to

neutral pH. Hence it is assumed that these formulations cause no irritation in the oral cavity. The calibration curve was constructed having regression value of 0.999. Compatibility studies were performed and it was observed that all the ingredients used were compatible with the drug. Formulation F7 results showed within limits and 99.8% drug release was found in 12hr. So, formulation (F7) was taken as optimized formulation. Accelerated stability studies were performed for this batch.

In vitro Drug Release

From dissolution data, it is evident that the designed formulations have displayed more than 50% drug release in 8 h. The formulation F7 containing HPMC K4M, HPMC K15M, Carbopol 940 and mannitol was found to be promising, which showed 99.85% drug within 12 h.

CONCLUSION

From the above experimental results it can be concluded that bioadhesive buccal tablets of Glimepiride can be prepared by using different proportion and combination of excipients and we selected F7 as best formulation based on dissolution profile and physical characteristics. Formulation (F7) showed total drug release in 12hr and showed fair flow properties when compared to other formulations. The formulations F7, followed first order kinetics.

REFERENCES

[1]. Jain NK. Controlled and novel drug delivery. 1st ed. New Delhi: CBS Publishers & Distributors; 1997, 52-81.

[2]. Shojaei HA. *Buccal mucosa as a route for systemic drug delivery*: A Review. J Pharm Sci. 1(1), 1998, 15-30.

[3]. 5.Tor-Tora Gorahowski. *Principles of anatomy and physiology*. Edited by Gerad J. Tor- Tora and Sandro Reynolds Gorahowski: Harpet Collins College Publishers; 7, 1992, 770-774.

[4]. Ross & Wilson. *Anatomy & physiology in health and illness*. Edited by Anne Waugh and Allison Goraw: Churchill Livingstone Edinburgh Publishers; 7, 2001, 289-293.

[5]. Robinson JR, Yang X. *Absorption enhancers*. In: J. Swarbrick, JC. Encyclopedia of pharmaceutical technology. New York: Marcel Dekker Inc; 18, 2001, 1-27.