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Formulation and Evaluation of Fast Dissolving Tablets of Gliclazide

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ABSTRACT

The objective of this research was to formulate fast dissolving tablet of gliclazide for rapid action. Direct compression method was adapted to prepare the fast dissolving tablets. All formulations are evaluated for post-compression parameters like hardness, disintegration time, weight variation, friability, wetting time, water absorption ratio and mouth feel. The mouth feel was done by taking human volunteers in a panel scale method. Different formulations were prepared using the superdisintegrants in three individual concentrations i.e. (3%, 5%, and 10%). The formulations for different concentrations were selected based on disintegration time, hardness and wetting time and were subjected to in-vitro dissolution studies. The results obtained showed that at 10% concentration superdisintegrants showed less d.t and good hardness. This might be due to high wicking and capillary action along with secondary burst effect of crosspovidone, and more gelling tendency and slow water uptake of tablet containing sodium starch glycolate and crosscarmellose sodium than crosspovidone. For formulation at 10% concentration the hardness was found to be 5 kg/cm^2, 5.14 kg/cm^2 and 4.2 kg/cm^2 and disintegration was found to be about 6 seconds, 11.5 seconds and 8.9seconds. From these datas the formulation sd9 containing crospovidone at 10% was selected to be the best formulation.

KEYWORDS: Fast dissolving tablet, crosspovidone, sodium starch glycolate, crosscarmellose sodium, superdisintegrant.

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INTRODUCTION

The concept of Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. Fast Dissolving Tablet disintegrates and/or dissolves rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few s, and are true fast-dissolving tablets [1-5]. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Fast Dissolving Tablet, as a novel dosage form, has several characteristics to distinguish them from the more traditional dosage forms. As tablet disintegrates in mouth this could enhance the clinical effect of the drug through pre-gastric absorption from the mouth, pharynx and esophagus. This leads to an increase in bioavailability by avoiding first pass metabolism.

DESIRED CRITERIA FOR FAST DISSOLVING TABLET

Mouth Dissolving Tablet should-

- Not require water to swallow, but it should dissolve or disintegrate in the mouth within matter of s.
- Be compatible with taste masking
- Be portable without fragility concern.
- Have a pleasing mouth feel.

SALIENT FEATURES OF FAST DISSOLVING TABLET [6]

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.

- Good mouth feel property helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.

EVALUATION OF FAST DISSOLVING TABLET [7-10]

Weight variation

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. The total weight of 20 tablets from each formulation was determined and the average was calculated. The individual weights of the tablets were also determined accurately and the weight variation was calculated.

Hardness

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm^2 is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation was determined by Monsanto hardness tester.

Friability test

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator was employed for finding the friability of the tablets. 20 tablets from each formulation were weighed and placed in Roche friabilator that rotated at 25 rpm for 4 minutes. The tablets were dedusted and weighed again. The percentage of weight loss was calculated again. The percentage of weight loss was calculated using the formula

$$\% \text{ Friability} = [(W_1-W_2)100]/W_1$$

Where,

W_1= Weight of tablet before test

W_2 = Weight of tablet after test

Disintegration test

The USP device to rest disintegration was six glass tubes that are "3 long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is poisoned in 1 liter beaker of distilled water at 37± 2 ^{o}C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

Uniformity of dispersion

Two tablets were kept in 100ml water and gently stirred for 2 minutes. The dispersion was passed through 22 meshes. The tablets were considered to pass the test if no residue remained on the screen.

Wetting time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10cm diameter were placed in a petridish containing 0.2% w/v methylene blue solution (3ml). A tablet was carefully placed on the surface of the tissue paper. The time required for develop blue color on the upper surface of the tablets was noted as the wetting time.

Water absorption ratio

A small piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then reweighed. Water absorption ratio, R was determined by using following formula were given

$$R= 100 \times W_a-W_b / W_b$$

W_b is the weight of tablet before water absorption

W_a is the weight of tablet after water absorption

Taste/ Mouth sensation

Mouth-feel is critical, and patients should receive a product that feels pleasant. One tablet from each batch was tested for the sensation by placing the tablet on the tongue. The healthy human volunteers were used for evaluation of mouth feel. Volunteer's opinion for the taste were rated by giving different score values i.e .0 = good, 1 = tasteless, 2 = slightly bitter, 3 = bitter, 4 = awful.

IN VITRO DRUG RELEASE STUDIES [11-14]

The Gliclazide fast dissolving tablets were subjected to in vitro drug release studies in pH 6.8 phosphate buffer for 30 minutes to access the ability of the formulation for providing immediate drug delivery. Drug release studies were carried out in eight stage dissolution test apparatus (DISSO 2000, Lab India) using 900ml ml of dissolution medium (pH 6.8 phosphate buffer) maintained at 37±1^{0}C. The tablets were kept in the cylindrical basket and rotated at 100 rpm.

MATERIALS AND METHODS

Gliclazide was received as a gift sample from Sun Pharma, Baroda India. Ac-Di-Sol, crosspovidone, sodium starch glycolate was obtained as gift sample from Signet Chemicals Mumbai. All other materials like Aerosil, Magnesium Stearate, Sodium Saccharin, Tartaric acid used was of analytical grade and procured from commercial sources.

FORMULATION AND EVALUATION OF GLICLAZIDE FAST DISSOLVING TABLET

Table 1: Formula of Gliclazide Fast dissolving tablet using superdisintegrants individually at 3% concentration

Ingredients (mg)	SD1 3%	SD2 3%	SD3 3%
Drug in solid dispersion (GLZ:L-HPC)	80	80	80
MCC	59.5	59.5	59.5
CPV	4.5	-	-
CCM	-	4.5	-
SSG	-	-	4.5
Other excipients	6	6	6

Other excipients = Aerosil, Magnesium Stearate, Sodium Saccharin, Tartaric acid = 1.5 mg each

Table 2: Evaluation of Gliclazide Fast dissolving tablet using superdisintegrants individually at 3% concentration

Evaluation	SD1 3%	SD2 3%	SD3 3%
Hardness (kg/cm^2)	04.3	5	04.78
D.T (secs)	013.5	20	39
Wetting time(secs)	011.5	16	33
Friability (%)	0.27	0.98	0.22
Water abs. Ratio	072.72	057.14	072.22
Weight Variation (%)	01.3	01.3	0.6
Mouth Feel	0	1	1

Table 3: Formula of Gliclazide Fast dissolving tablet using superdisintegrants individually at 5% concentration

Ingredients (mg)	SD4 5%	SD5 5%	SD6 5%
Drug in solid dispersion (GLZ:L-HPC)	80	80	80
MCC	56.5	56.5	56.5
CPV	7.5	-	-
CCM	-	7.5	-
SSG	-	-	7.5
Other excipients	6	6	6

Other excipients = Aerosil, Magnesium Stearate, Sodium Saccharin, Tartaric acid = 1.5 mg each

Table 4: Evaluation of Gliclazide Fast dissolving tablet using superdisintegrants individually at 5% concentration

Evaluation	SD4 5%	SD4 5%	SD5 5%
Hardness (kg/cm^2)	04.2	03.9	04.2
D.T (secs)	9	15	10
Wetting time(secs)	4	012.5	09.5
Friability (%)	0.11	0.13	0.46
Water abs. Ratio	048.27	047.36	051.6
Weight Variation (%)	0	0	0
Mouth Feel	0	0	0

Table 5: Formula of Gliclazide Fast dissolving tablet using superdisintegrants individually at 10% concentration

Ingredients (mg)	SD7 10%	SD8 10%	SD9 10%
Drug in solid dispersion (GLZ:L-HPC)	80	80	80
MCC	49	49	49
CPV	15	-	-
CCM	-	15	-
SSG	-	-	15
Other excipients	6	6	6

Other excipients = Aerosil, Magnesium Stearate, Sodium Saccharin, Tartaric acid = 1.5 mg each

Table 6: Evaluation of Gliclazide Fast dissolving tablet using superdisintegrants individually at 10% concentration

Evaluation	SD7 10%	SD8 10%	SD9 10%
Hardness (kg/cm^2)	5	5.14	4.2
D.T (secs)	6	011.5	08.9
Wetting time (secs)	04.1	09.8	07.5
Friability (%)	0.6	0.17	0.2
Water abs. Ratio	033.33	054.54	049.15
Weight Variation (%)	0	0.61	0.61
Mouth Feel	0	1	2

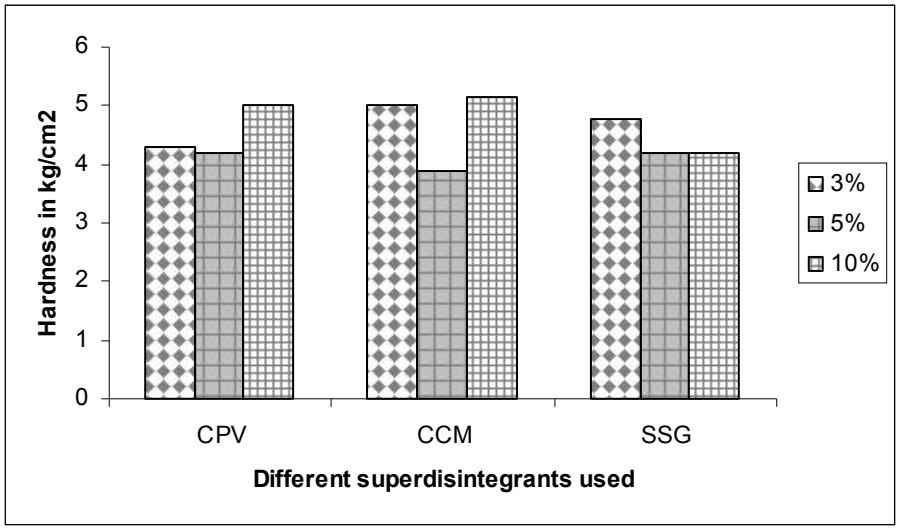

Figure 1: Comparison of hardness for Gliclazide fast dissolving tablets of different superdisintegrants at different concentrations

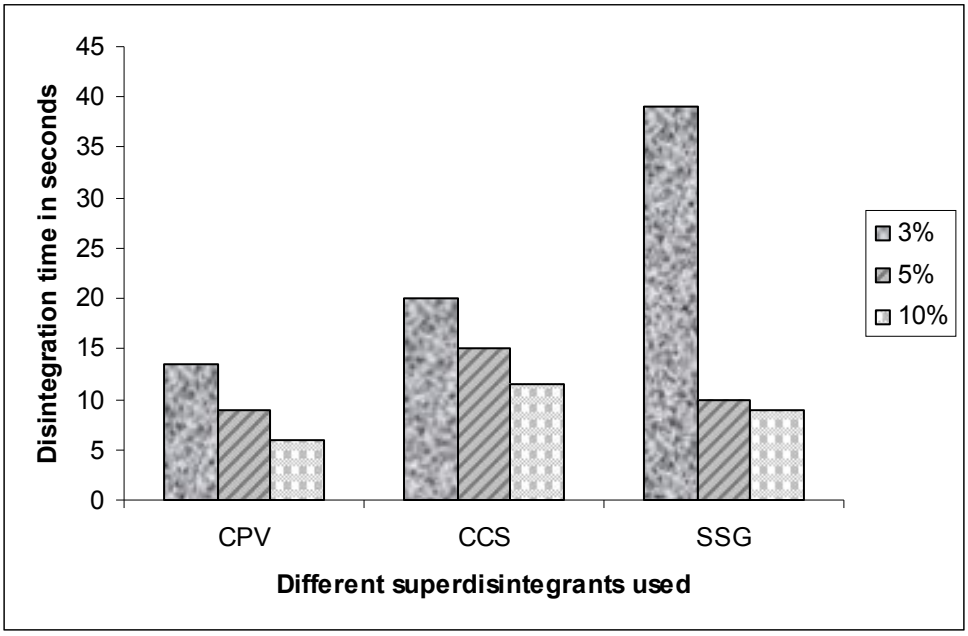

Figure 2: Comparison of Disintegration Time for Gliclazide fast dissolving tablets of different superdisintegrants at different concentrations

RESULTS AND DISCUSSION

In the present study Gliclazide fast dissolving tablets were prepared by using crosscarmellose, crosspovidone and Sodium starch glycolate as a disintegrants at different concentrations (3, 5, and 10%) as shown in Table 1, 3, 5 respectively. Total numbers of nine formulations were prepared by direct compression technique. The data obtained of post-compression parameters such as hardness, friability, weight variation, amount of drug content; in-vitro wetting time and in-vitro disintegration time are done as shown in Table 2, 4, 6 respectively. The hardness was found to be in the range of 3.9 to 5.14 kg/cm^2 for all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations the friability values are less than 1% and meet the IP limits. All the tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits. The weight of all the tablets was found to be uniform with low standard deviation values indicating efficient mixing of drug, disintegrants and excipients. The results of in-vitro wetting time and in-vitro disintegration time of all the tablets were found to be within the prescribe limits and satisfy the criteria of fast dissolving tablets. The in-vitro wetting time was found to be in the range of 4 to 33 s while the in-vitro disintegration time was founds in the range of 6 to 39 s respectively. Among all the concentrations at 10% concentration results were better as CPV, SD7 (10%), minimum DT was found to be 6 s. Formulation containing SSG, SD9

(10%), minimum D.T. was found to be 8.9 s, formulation containing CCM, SD8 (10%), minimum DT was found to be 11.5 s. So it was found that at 10% concentration superdisintegrants showed less D.T and good hardness. This might be due to high wicking and capillary action along with secondary burst effect of CPV, and more gelling tendency and slow water uptake of tablet containing SSG and CCM than CPV. The faster disintegration of super disintegrant can be attributed to the increase rate & extent of water uptake and consequent swelling & increased hydrodynamic pressure to induce complete disintegration.

CONCLUSION

The Fast dissolving tablets of Gliclazide are developed by using the superdisintegrants. The mixture prepared in the ratio of drug to crosspovidone in 10% concentration by direct compression possessed ideal and reproducible characteristics of disintegration time of 6 s.

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