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Fast Dissolving Tablet: A Novel Approach for Delivery of Glibenclamide.

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Research Article

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ABSTRACT

Glibenclamide is a poorly water-soluble orally active hypoglycemic agent, with problems of variable bioavailability and bio-bioequivalence releated to its poor-water solubility. This work investigated the possibility of developing Glibenclamide tablets, allowing fast, reproducible and complete drug dissolution by using Suerdisintegrants in different concentrations, FT-IR were carried out to confirm that drug is not interacting with polymer under experimental conditions and shelf-life. The tablets were prepared by direct compression technique. The prepared tablets were evaluated for thickness, uniformity of weight, content uniformity, Hardness, friability, wetting time, in vitro disintegration time and in vitro drug release. The tablets apart from fulfilling all officials and other specifications, the Glibenclamide dissolution profile from the formulated tablets was clearly better than those from various conventional tablets at the same drug dosage.

INTRODUCTION

Tablets and hard gelatin capsules constitute a major portion of the drug delivery systems that are currently available. However, many patient groups such as elderly, children, and patients mentally retarded, uncooperative, nauseated, or on reduced liquid intake diets have difficulty in swallowing these dosage forms. Many elderly persons face difficulties in administering conventional oral dosage forms because of hand tremors and dysphagia. Swallowing problem is common in children because of their underdeveloped muscular and nervous systems. In some cases like motion sickness, sudden episodes of allergic attack or coughing, and during unavailability of water, swallowing conventional tablets is difficult. To fulfill these medical needs, formulators have devoted considerable efforts for developing a novel type of dosage form for oral administration known as Fast dissolving tablets (FDT). This is an innovative technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient. Glibenclamide, a sulphonylurea, is an orally active hypoglycemic agent. It also has a mild diuretic action, increasing free water clearance from the body, in addition to its blood glucose lowering effect. Its elimination half-life is approximately two hours after intravenous administration and two to five hours after oral dosage and it is 84±9% absorbed from GIT, but its bioavailability is low indicating extensive fist pass metabolism in liver. In view of substantial first pass effect and its shorter elimination half-life, therefore is an ideal drug candidate for rapid release drug delivery system [1,2].

MATERIALS AND METHODS

Materials

Glibenclamide was obtained as gift sample from Ind Swift. Pharmaceuticals Ltd. (Panchkula) Ac-Di-Sol, Sodium starch glycolate and Crospovidone were obtained as gift samples from Signet Chemicals (Mumbai).

Methods

Preparation and Evaluation of Tablet

Tablets were prepared by direct compression method using single punch tablet machine (Cadmach). All the ingredients (shown in Table 01) were passed through sieve no. 60 and co- grounded in a glass pestle motor. The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. The mixed blend of excipients was compressed using a single punch tablet machine to produce flat faced tablets weighing 80 mg each with ≈3.2 mm thickness and 5 mm in diameter. The tablets were evaluated for physical organoleptic characteristics like color, odor, taste, Uniformity of weight, diameter, thickness, Hardness, Friability, and, Disintegration time, wetting time, Content uniformity [3,4].

RESULTS AND DISCUSSIONS

Table 1: Formulation of Fast dissolving tablets of Glibenclamide

Ingredients	FDT1	FDT2	FDT3
Glibenclamide	10	10	10
Ac-Di-Sol	3.2	-	-
Sodium starch glycolate	-	3.2	-
Crospovidone	-	-	4
Aspartame	19.4	19.4	19
Saccharin sodium	19.4	19.4	19
Avicel PH 101	24	24	24
Talc	2.4	2.4	2.4
Magnesium Stereate	1.6	1.6	1.6

Table 2: Drug Content in the Fast Dissolving Tablet of Glibenclamide

Parameters Formulations	Drug Content (mg per Tablet)	Drug Content %
FDT1	9.83±0.25	97.2
FDT2	9.87±0.35	98.7
FDT3	9.80±0.30	96.7

Table 3: Characterization of Blend of Glibenclamide Tablet

Parameters Formulations	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausner's Ratio	Compressibility Index (%)	Angle of Repose (º)
FDT1	0.391	0.405	1.035	3.456	25.32
FDT2	0.376	0.399	1.061	5.764	26.43
FDT3	0.398	0.407	1.022	2.211	25.54

Table 4: Characterization of Glibenclamide Fast Dissolving Tablet

Parameter Formulation	Diameter (mm)	Thickess (mm)	Weight (mg)	Hardness (kg/cm²)	Friability (%)	Disintegration Time (s)	Swelling Time (s)
FDT1	5.014	3.11	81.33 ±1.53	2.2±0.1	0.54 ±0.10	32±2	18±4
FDT2	5.014	3.11	79.67 ±1.56	2.3±0.2	0.71 ±0.09	48±5	21±3
FDT3	5.014	3.11	80 ±4.36	2.6±0.1	0.62 ±0.13	46±4	24±2

The drug content of all formulations was determined spectrophotometrically at 300 nm. It varied from 9.80±0.30 to 9.87±0.35 mg per tablet. The correlation of variation was found to be less than 0.35 %, indicating uniformity of the drug content in the prepared tablets. The uniformity of drug content was also shown the uniformity of tablet punching process. The results of the content uniformity were shown in Table 02.

IR Spectra of physical mixtures of polymers and drug was done to observe for any interaction between drug and polymer. The IR Spectra of the various mixtures revel all the peak of the drug. No significant shifts in the peaks corresponding to the drug were observed on the mixing. The drug is distributed uniformly and there is no interaction between drug and polymers used. Both the drug and polymers were compatible with each other. Hence the drug and polymers can be successfully incorporated in the design of Fast Dissolving Tablets. The IR Spectra of Pure drug (A), Sample of Glibenclamide (B) and polymers with mixture of drug were shown in Fig. 01 (A and B)-04.

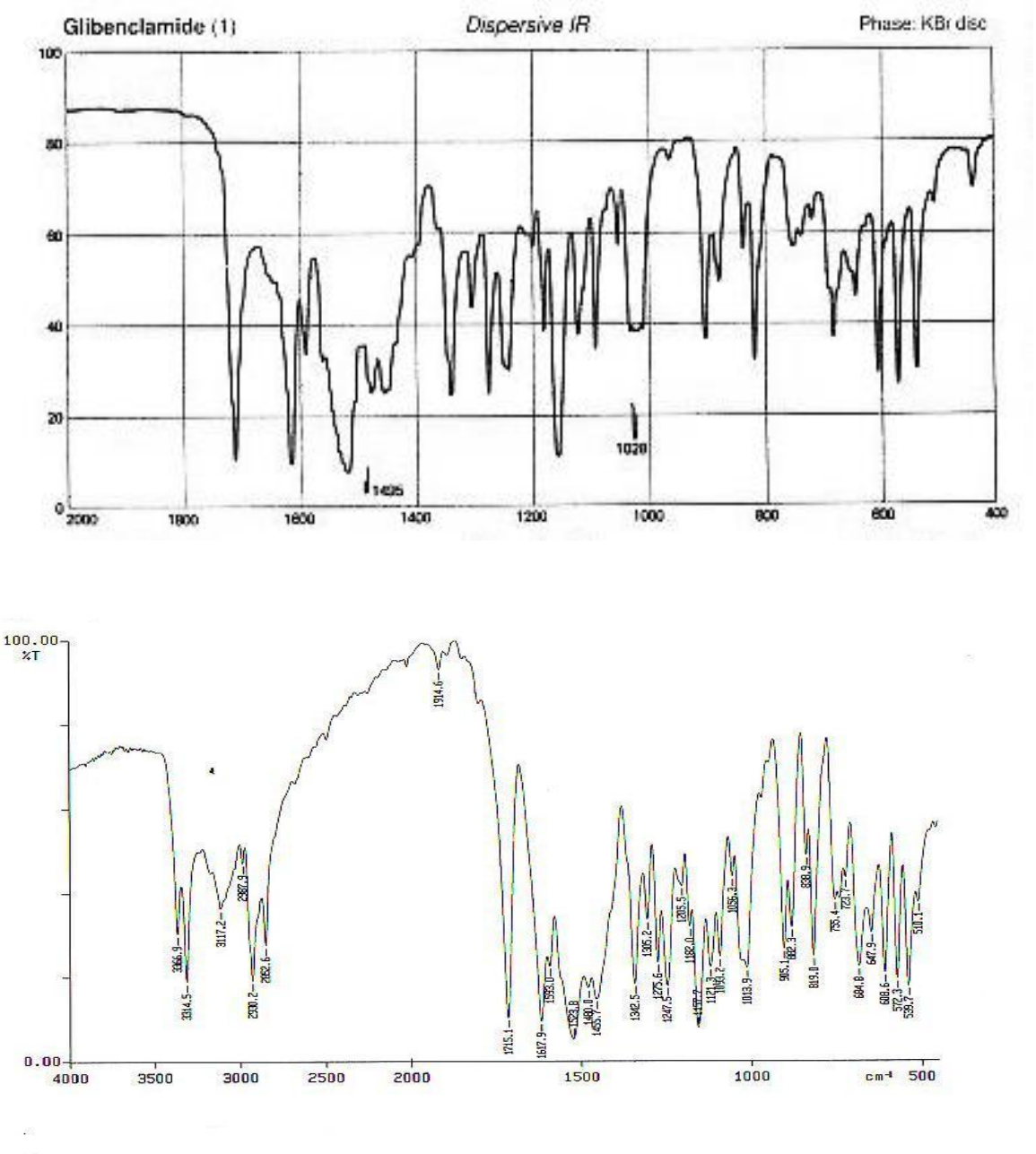

Figure 1: FT-IR Spectra

(A) Glibenclamide Pure Drug (B) Sample of Glibenclamide

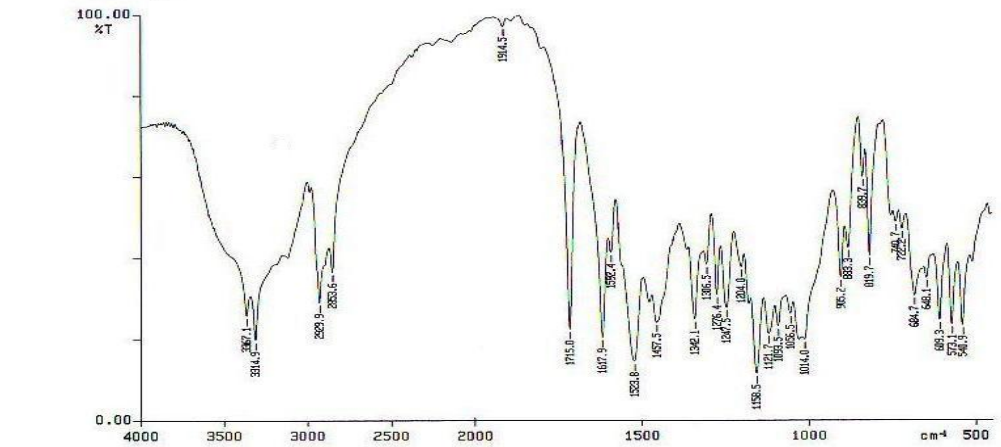

Figure 2: FT-IR Spectra of Mixture of Drug and Ac-Di-Sol

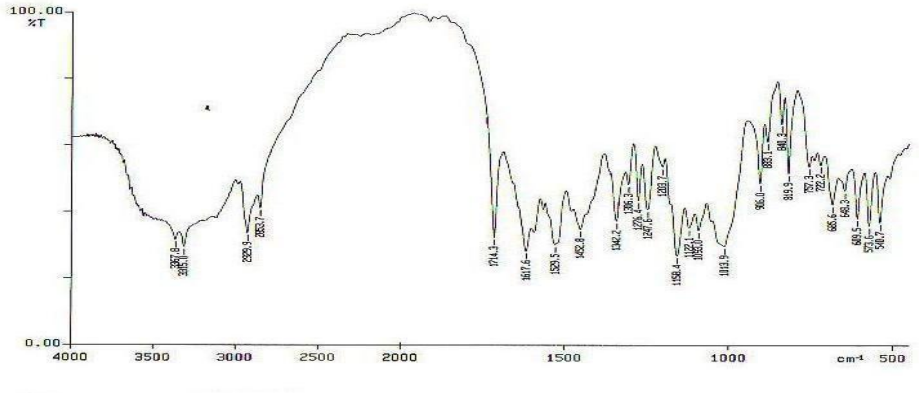

Figure 3: FT- IR Spectra of Mixture of Drug and Sodium Starch Glycolate

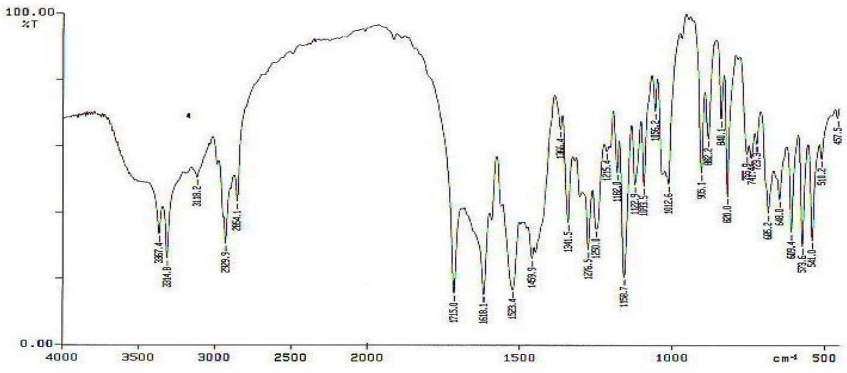

Figure 4: FT-IR Spectra of Mixture of Drug and Crospovidone

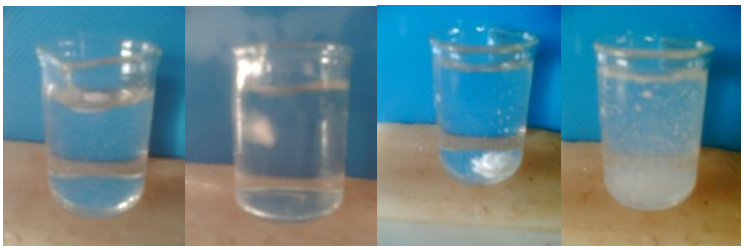

Figure 5: *In Vitro* Disintegration Property

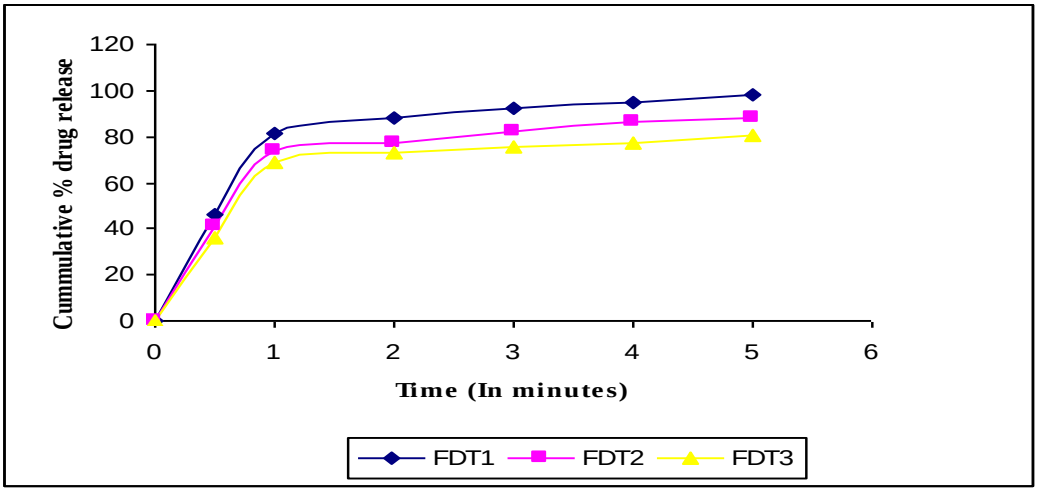

Figure 6: *In vitro* release curve of Glibenclamide tablet-Zero Order Release

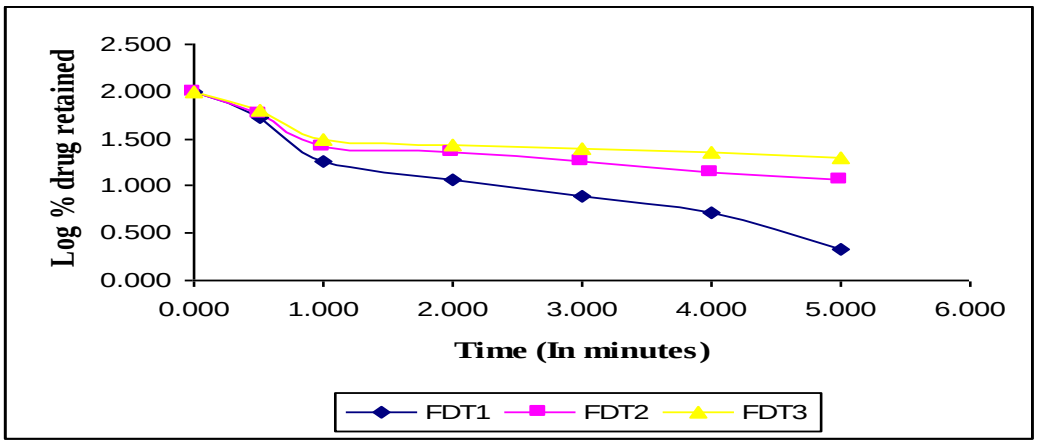

Figure 7: *In vitro* release curve of Glibenclamide tablet-First Order Release

All the formulations were white in color, odorless, flat in shape with smooth surface without any defects. The prepared tablets were elegant and having lot to lot tablet uniformity and also free from any surface texture problems. The average weight of the prepared tablets was found 79.67 to 81.33. The thickness and diameter of the tablet was found 3.11 mm, 5.014 mm respectively. The Hardness of the prepared tablet varied from 2.2 to 2.6 kg/cm^2. The friability of all the formulation was found to be less than 1.0 %. The results indicate resistance to loss of weight and ability to withstand abrasion in handling, packaging and shipment. A disintegrant was found in most of the formulations to facilitate a breakup or disintegration of the tablet when it contacts with water or saliva in mouth. Disintegrants drawing the water into the tablet causes swelling and burst apart. In the formulation of fast dissolving tablet the three superdisintegrants were used in different concentrations. The disintegration time of these tablets was varied from 32±2 to 48±5 s. The in vitro swelling time of all the formulations were varied between 18±4 to 24±2 s. The tablets with Ac-Di-Sol may disintegrate faster then the tablets with the Sodium Starch Glycolate and Crospovidone.

For the in-vitro drug release profile it was evident that the kinetics of drug release from prepared FDT was followed first order kinetics. For all the prepared fast dissolving tablets as the plot between Log percent drug retained versus Time showed the good linearility than on other kinetic treatments. The value 'n' obtained from Korsmeyer curves was near to one, which indicates Super Case-II transport mechanism. The good relationship was

also evidenced in the Hixon-Crowell's Cube Root Law, which signifies that drug is assumed to dissolve out from the tablet matrix or from the surface of the device. As the drug is released the distance for diffusion becomes increasing greater.

CONCLUSION

Fast dissolving tablet of Glibenclamide would be an effective alternative approach for management of Type II diabetes. The prepared tablets were maintained rapid and constant drug level in the blood and avoid excess drug loading into the body. This forms it more patient compliance and compatible to prescription.

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