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"Enhancing Dissolution Rate of Glipizide Immediate Release Tablets with Sodium Starch Glycolate as a Superdisintegrant: Formulation and Assessment"

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ABSTRACT:

The main goal is to develop, assess, and optimize the wet granulation method for the Glipizide quick release tablet. Glipizide is a medication used to treat diabetes. Nine distinct formulas were created in an effort to get the optimum results. Various lubricants, disintegrants, and binders are used as variables. Pre-compression metrics such as angle of repose, bulk density, and true density demonstrate that all of the formulations exhibit favorable flow characteristics. After the granules are compressed, the weight variation, hardness, friability, disintegration, and dissolving properties of the tablets are assessed. Of all the formulations, F9 exhibits a release profile that is comparable to that of the innovator. Stability tests were conducted on the compressed pills at 400C and 75% RH, 250C and 60% RH, and packaged in blisters. Samples underwent routine analysis. As stated in the stability protocol, tons. In comparison to traditional formulations, it can be inferred that Glipizide tablets manufactured as immediate release formulations are superior.

Keywords: Glipizide, weight variation, Hardness, Friability, Disintegration and Dissolution.

I. INTRODUCTION:

The largest and most established section of the drug delivery industry is oral delivery, which is also the fastest and most favoured method of medication administration. There are many different kinds of drug delivery systems available to improve the therapeutic activity of the medicine; however, immediate release drug delivery systems are becoming more and more important due to their many advantages over other types, including convenience, non-invasiveness, and ease of administration. In 1922, glipizide was discovered. In the 1950s, French physician Jean Sterne started studying humans. In 1995, it made its debut in the US after first appearing in France in 1957.It is one of the most vital drugs required in a basic healthcare system, according to the World Health Organization's List of Essential Medicines. It is thought that the most commonly prescribed oral medication for diabetes is called glipizide (2).An oral hypoglycaemic medication called Glipizide (MH) has been used to treat non-insulin-dependent diabetic mellitus. It is administered as 500- and 850-milligram tablets, with limited and inadequate absorption by the digestive system; the recommended daily dosage is 2 grams, and the highest amount is 3 grams.

IMMEDIATE RELEASE DRUG DELIVERY SYSTEM

Dosage types known as immediate release tablets dissolve and quickly disintegrate to release the medication and start working right away. Within a short while, it ought to dissolve or break down in the stomach. It should be less sensitive to temperature and humidity in the surrounding air. be produced at a minimal cost utilizing standard processing and packaging machinery. When used orally, it shouldn't leave much, if any, residue in the mouth. It causes the medication to dissolve and absorb quickly, which could result in a quick start of effect. The provision of immediate release can be achieved by the use of suitable pharmaceutically acceptable diluents or carriers that do not significantly slow down the rate of drug release and/or absorption.

This definition does not cover formulations designed for controlled, sustained, prolonged, extended, or delayed release of drugs. In the case of immediate-release tablets, the disintegration of the tablet plays a crucial role in ensuring that the tablet matrix breaks down upon contact with stomach fluid. This breakdown allows the active component to be released and become

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available, either entirely or partially, for absorption from the gastrointestinal tract.

ANTIDIABETICS[2, 16, 13, 14]

Drugs used in diabetes deal with diabetes mellitus by means of lowering glucose tiers in the blood. With the exceptions of insulin, eventide, liraglutide and pramlintide, all the administered orally and are accordingly also known as oral hypoglycemic sellers or oral anti hyperglycemic marketers. There are unique instructions of anti-diabetic pills, and there are unique instructions of anti-diabetic drugs, and their selection depends on the character of the diabetes, age and conditions of the character, in addition to other elements. The Diabetes Mellitus describes a metabolic disorder of multiple etiology. The impact of Diabetes Mellitus includes dysfunction, failure and long-term damage of various organs. In most excessive form of DM nonketotic hyperosmolar country might also expand.

Diabetes mellitus type1

It is a disorder resulting from the lack of insulin .It comes approximately because of the lack of pancreatic characteristic. The lack of pancreatic characteristic may be due to disease or harm to the pancreas which in the long run ends in lack of most advantageous glycaemia control. Thus, insulin needs to be injected subcutaneously two times daily to compensate for the needs of the body (also referred as insulin-structured-diabetes mellitus, and juvenile diabetes).

Diabetes mellitus type2

There is a decrease inside the frame's secretion and sensitivity to insulin, which typically caused by weight problems. It is a ailment of insulin resistance by cells. Type 2 diabetes mellitus is the maximum common type of diabetes. Treatments include

1) Agents that growth the amount of insulin secreted through the pancreas.
2) Agents that boom the sensitivity of goal organs to insulin.
3) Agents that decrease the rate at which glucose is absorbed from the gastrointestinal tract.

II. MATERIALS & METHODS:

List of materials for preparation of Glipizide

S.NO	Name of materials used	Specifications	Use
1	Glipizide	IP	Activeingredient
2	Starch	IP	Diluent
3	SFP	IP	Thickening agent
4	Gelatin	IP	Thickening agent
5	Methylparaben	IP	Preservative
6	Propylparaben	IP	Preservative
7	Talc	IP	Lubricant
8	Sodiumstarch glycolate	USP	Superdisintegrant

Steps involved in Formulation of Glipizide granules Preparation of Raw materials:

The raw materials and active pharmaceutical ingredients are weighed and sieving through the 22#mesh and check the weight of the raw materials. And they are collected in suitable baskets.

Dry mixing:

Check weight of the materials and sift pregelatinized starch through 40#mesh load in to mixer come granulation. Dry mix for 15min at low speed.

Wet granulation:

Add binder solution to above powder which mixing for 5-15 min in mixer at slow speed. Change mixer speed to fast and mix for 5-15 min till requiredend point achieved. If required add additional wet mass through mixer come granulator hole. Switch granulator at fast speed and mix for next 15 minute. And then pass through the cad mill to get required type of granules. And unload in to Fluidized bed dryer bowl, scrap material from cad mill bowl to Fluidized bed dryer bowl at end of batch.

Drying:

Dry the wet milled granules in Fluidized bed dryer for 30 minute and check for loss on drying for 30minute and rake again. Dry till loss on drying at not more than o.5%.Check loss on drying at 90^0C.

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Pulverization:

Pass the dried granules in to the cad mill. And add additional quantity of ingredients then, collect the good fractions of granules passing through the #14/150 mesh through metal detector loads the granules and get uniform sized granules.

Lubrication:

All ingredients are lubricated by using the double cone blender and blend for 10minute at 6rpm.

COMPARATIVE DATA OF NINE FORMULATIONS OF GLIPIZIDE(n=9)

Comparative data of nine formulations of Glipizide

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
Glipizide	500	500	500	500	500	500	500	500	500
Starch	80	85	90	-	-	-	80	85	90
Sodium starch glycolate	-	-	-	6.20	6.25	6.20	6.25	6.20	6.25
Talc	66.18	61.18	56.18	139.98	130.93	139.88	59.98	54.93	50.18
Methylparaben	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16
Propylparaben	0.66	0.66	0.66	0.66	0.66	0.66	0.66	0.66	0.66
Gelatin	2	2	2	2	2	2	2	2	2
SFP	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total	650	650	650	650	650	650	650	650	650

COMPRESION OF TABLETS

Compression parameters:

The compression is carried out by using using CADMACH 45 station compression gadget in particular designed for the compression of pills having specific hoppers for the float of granules. Two punches are putting within the compression gadget for the compression of the drugs. The strain adjustment devises are used to regulate the pressure in the gadget. It facilitates to adjust the burden of the pill. The granules are passed thru the two hoppers, and are stuffed within the die hollow space and the final compression takes area with favored weight and the hardness being set. Due to the strain at the top and the lower punch the granules are compressed to get the tablet.

Weight and the content uniformity of pill are tested.

Punch specification:

Upperpunch:6mmplainroundwithbiweledgesand kgembossedupperpunch Lower punch: 6mm plain round with biweled edges lower punch

Temperature and relative humidity record:

Temperature: 25-26^{0}C RelativeHumidity:46-47%

Compression parameter

Descriptionoftablet–

Whitecolored,round,biweledgesandkgembossed.

Weight of tablet - 650±5%

Hardness – 8mm Friability–NMT0.8%

Disintegration time–NMT 15min.

III. RESULTS AND DISCUSSION:

Physiochemical Parameters

DESCRIPTION:

Color: White

Odor: Odorless

Taste: Tasteless

Solubility: It is freely soluble in water and 95% alcohol and is practically insoluble in acetone, ether and chloroform. It also freely soluble as HCl salt.

pH: 6.68

Melting Point: 222^{o}C to 226^{o}C.

Nature: Hygroscopicity.

Losson Drying: Not more than 0.5% determined on 1.0g by drying in an oven at 105^0

SieveAnalysis:100%passthroughthe20#mesh.

Flow Property Measurement: 33.69- Good Flow Nature.

Density:

Bulk Density: 0.714.

TappedDensity: 0.909

Compressibility Index: 21.45-Passable

Hausner Ratio: 1.27-Passable

Drug Content: It contains not less than 98.5%andnotmore than 101.0% of $C_4H_{11}N_5.HCl$

COMPATIBILITY STUDIES

Compatibility study of Glipizide with excipients

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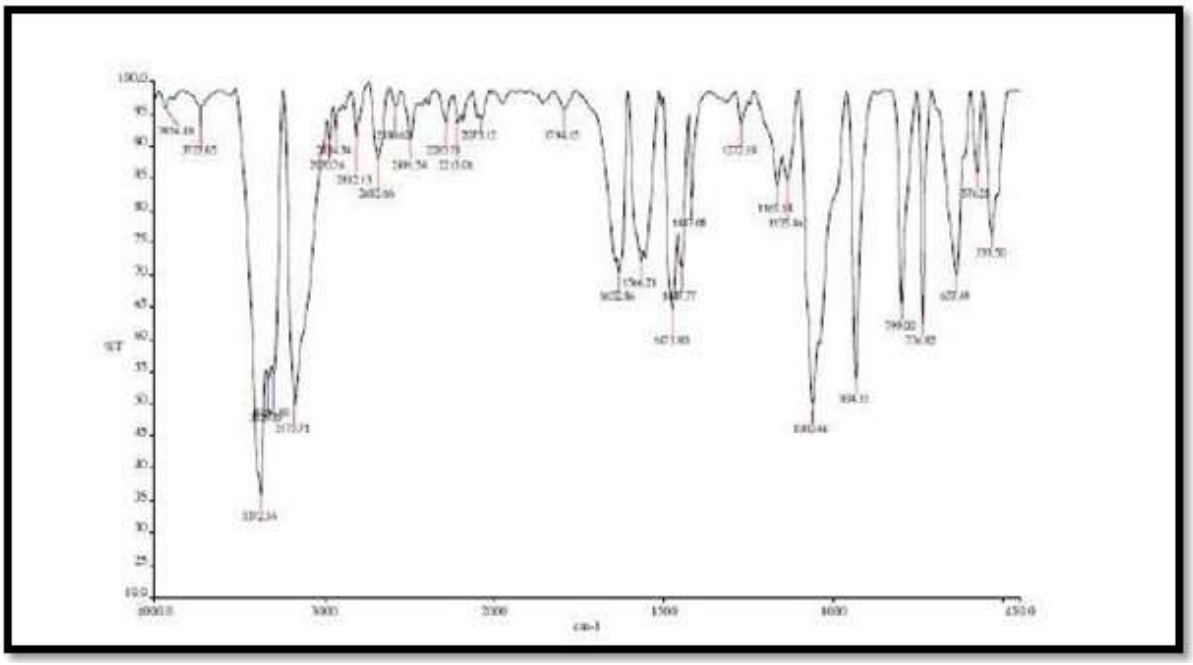
Drug	Excipients	1st day 40^{0}C&75% RH	1st week 40^{0}C&75% RH	2nd week 40^{0}C&75% RH	3rd week 40^{0}C&75% RH
M	Starch	ND	ND	ND	ND
M	Gelatin	ND	ND	ND	ND
M	Methyl Paraben	ND	ND	ND	ND
M	Propyl Paraben	ND	ND	ND	ND
M	Sfp	ND	ND	ND	ND
M	Talc	ND	ND	ND	ND
M	Sodium Starch Glycolate	ND	ND	ND	ND

Where,
M=Glipizide RH=Relative humidity ND=Change not detectable



FTIR spectrum of optimized formulation

PRECOMPRESSION PARAMETERS OF GLIPIZIDE TABLETS

Precompression parameter of Glipizide granulestrials:

Formulations	Bulk density (gm/cm^2)	Tapped density (gm/cm^2)	C.I(%)	Angle of repose(^{0})	H.R	Moisture content
F1	0.72	0.90	20.0	35^0.41'	1.25	0.0213
F2	0.702	0.93	23.22	37^0.95'	1.32	0.0235
F3	0.714	0.95	24.84	42^0.23'	1.2	0.026
F4	0.710	0.83	14.45	45^0.72'	1.16	0.0231
F5	0.68	0.79	13.92	38^0.95'	1.16	0.0245
F6	0.57	0.67	14.92	43^0.55	1.17	0.022
F7	0.59	0.68	13.23	31^0.63'	0.09	0.219
F8	0.710	0.82	13.41	32^0.23'	1.15	0.274
F9	0.8	0.912	12.28	33^0.69	1.14	0.274

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Inference: Formulations F1 to F3 has showing the vast waft property, attitude of repose and Hauser's ratio due to the absence of sodium starch glycolate and inclusion of starch and in case of F4-F6 has indicating the excessive attitude of repose because of the negative waft assets inside the absence of starch.F7-f9 shown appropriate flow as indicating the less attitude of repose due to boom in awareness of lubricant Sodium starch glycolate and starch additionally.POST COMPRESSION PARAMETER OF GLIPIZIDE TABLETS

Postcompression parameter of Glipizide tablets

Formulations	Weight variations (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time(min)	Friability (%)
F1	630-684	8	3.64	7	0.05
F2	625-691	7	3.93	9	0.06
F3	609-674	8	4.82	8	0.07
F4	622-688	5	4.56	9	0.08
F5	623-689	9	3.52	8	0.06
F6	610-674	12	3.29	7	0.07
F7	612-676	14	4.86	7	0.05
F8	626-691	9	3.46	8	0.07
F9	621-687	8	4.56	8	0.06
Innovator	550-600	11	3	9	0.04

DRUG CONTENT

Drug Content Values of Glipizide

FORMULATION	GLIPIZIDE
F6	88.53
F7	95.43
F8	96.64
F9	96.44

DRUG RELEASE

INNOVATOR DRUG RELEASE PROFILE

Innovator drug release profile

Time	Glipizide(Innovator)
0	0
5	68.05
10	79.45
15	85.87
30	96.57
45	99.89

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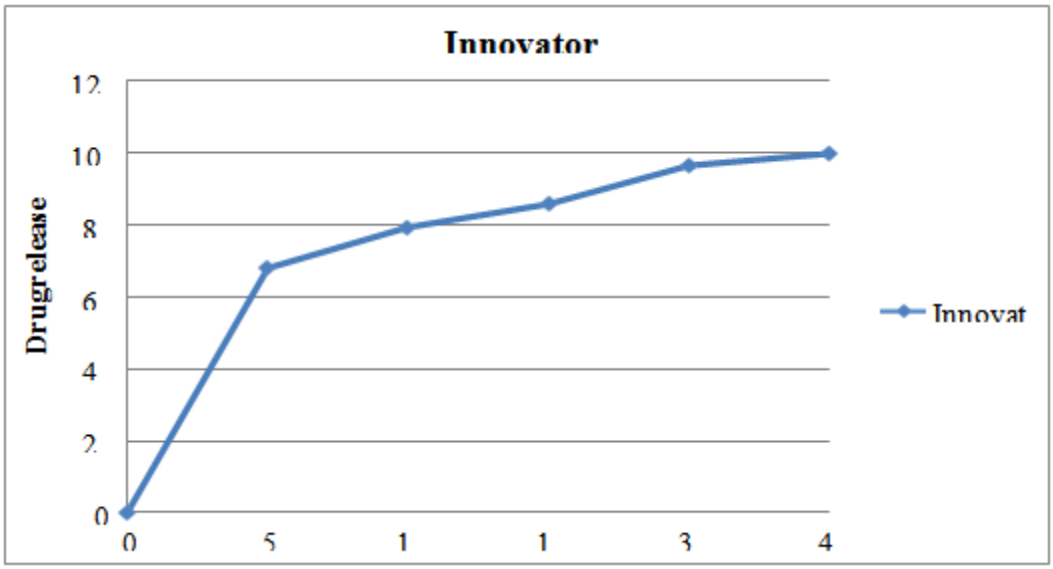

Release profile of innovator

DRUG RELEASE VALUE OF GLIPIZIDE

Percentage Drug release value of Glipizide

FORMULATIONS	%Drug release of Glipizide at 45minutes
F1	78.42%
F2	84.76%
F3	82.96%
F4	89.43%
F5	83.07%
F6	95.42%
F7	93.09%
F8	96.68%
F9	98.85%

COMPARISON OF DISSOLUTION PROFILE OF FORMULATIONS WITH INNOVATOR

Comparison of dissolution profile of Glipizide formulations with innovator

Time (min)	Innovator	% DrugRelease			
		F6	F7	F8	F9
5	68.05	58.93	65.45	66.53	65.54
10	79.45	72.63	75.43	77.82	80.57
15	85.87	84.32	87.54	85.42	84.32
30	96.57	89.95	90.42	92.53	93.05
45	99.89	95.42	93.09	96.68	98.85

COMPARITIVE RELEASE PROFILE OF GLIPIZIDE INVARIOUS FORMULATIONS WITH INNOVATOR

Comparative release profile of Glipizide in various formulations with innovator

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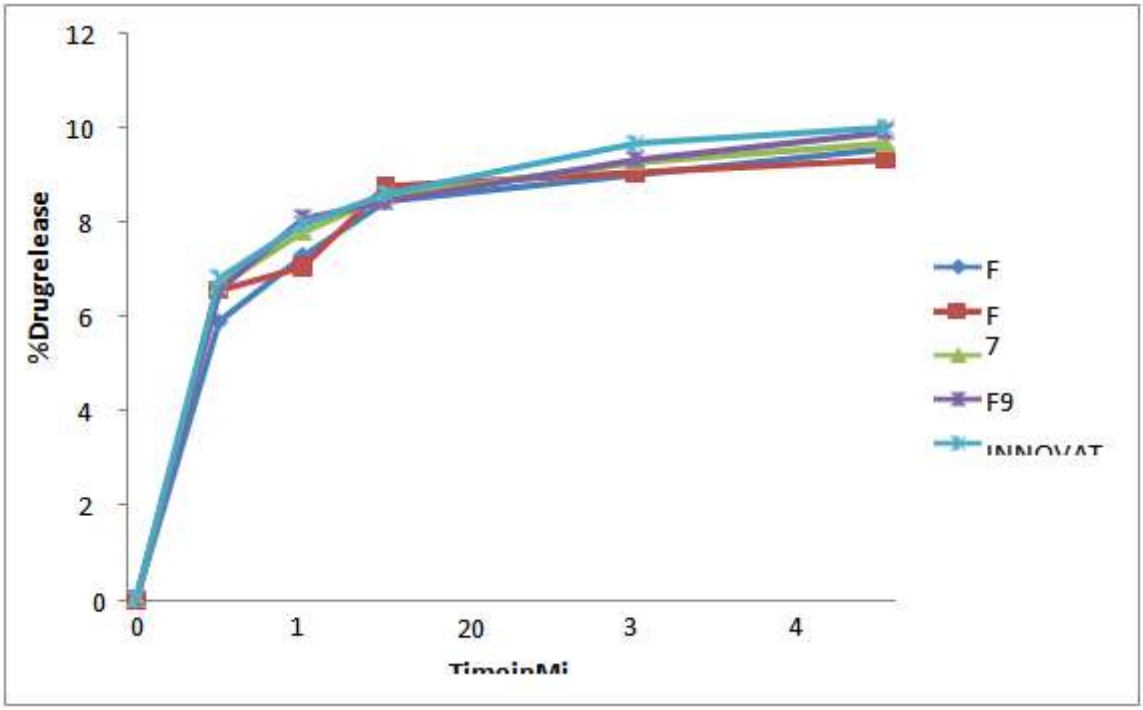

Inference: Comparative release profile of Glipizide from various formulations showing the release from the F9 matching with the innovator.

Stability studies of Glipizide Drug release at 25^0C & 60% RH

DRUG	%Drug release		
	Initial	30 days	45 days
Glipizide	99.88	99.88	99.87

Inference: The drug release was not significantly reduced at the end of 30 days and 45 days storage at 25^0c & 60% RH indicating stability of the formulation. All parameters are within the specified limits at the end of the storage.

IV. SUMMARY AND CONCLUSION

The gift take a look at was aimed at growing, evaluating and optimization of the oral hypoglycemic drug Glipizide Totally nine formulations are organized by way of using specific ratios of Glipizide ,Starch ,Gelatin ,Talc, Methyl paraben sodium, Propyl paraben sodium and Sodium starch glycolate. Each 9 formulations comprise the twenty capsules. The granules are organized one by one in a Max mixer. Pre compression parameters like Bulk density, True density, Angle of repose imply all of the formulations are showing drift homes. The tablets are compressed with the aid of double rotary compression gadget and pills are evaluated for submit compression parameters like weight variation, Hardness, Friability, Disintegration and Dissolution parameters. Formulations F1-F3 sodium starch glycolate isn't always used, in that formulations starch is utilized in exact proportions. F4-F6 sodium starch glycolate is used and the starch is not use in those formulations. Sodium starch glycolate and starch utilized in case of F7-F9. These formulations may be compared to innovator. In the formula of F9 is more matched to the innovator (Glipizide) consistent with the drug release profile. A exact result is getting by using using each sodium starch glycolate and starch. The F9 formula carries Glipizide- 500mg, starch- 90mg, Sodium Starch Glycolte-6.25mg, Talc-50.18, Methyl Paraben-1.Sixteen, Propyl Paraben-zero.66mg, Gelatin-2mg. The compressed capsules are subjected to stability research at 400C and seventy five%RH, 250C and 60p.CRH. Samples have been analyzed at normal intervals as cited in stability protocol. From the examine, it is able to be concluded that system F9 (it consists of both

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sodium starch glycolate and starch in suitable proportions) may be prepared as instant release components compared to traditional components.

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