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FORMULATION OPTIMIZATION AND EVALUATION OF RAPID DISINTEGRATING TABLET OF GLIBENCLAMIDE BY USING NATURAL SUPERDISINTEGRANT

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ABSTRACT

The present study focuses on formulation, optimization, and evaluation of Rapid Disintegrating Tablets (RDTs) using a micronized drug, Glibenclamide, through the direct compression method, incorporating natural superdisintegrants. Glibenclamide, known for its hepatic metabolism and modest absorption rate of 40–45%, prompted the exploration of RDTs to enhance its bioavailability. Three concentrations (2%, 3.5%, and 5%) of natural superdisintegrants were employed to achieve the optimal formulation, balancing disintegration time and drug release. Formulation B5, comprising guar gum and microcrystalline cellulose, emerged as the preferred independent variable based on preliminary screening batches, exhibiting minimal disintegration time and maximal drug release. A 3^2-center composite design was implemented, with guar gum (GG) and microcrystalline cellulose (MCC) concentrations significantly influencing disintegration time (DT) and percentage drug release (%DR). The optimized formulation, GLB6, featuring GG (3.5%) and MCC (40%), demonstrated rapid disintegration (13.18 seconds) and increased drug release (92.72%) within 10 minutes. Comprehensive pre-compression and post-compression studies were conducted, ensuring adherence to pharmacopoeial standards. The outcomes affirm that GG and MCC possess excellent disintegration properties, as evidenced by GLB6's superior disintegration and dissolution profiles. In conclusion, GLB6, comprising (3.5%) GG and (40%) MCC, stands out for its enhanced disintegration and dissolution profiles, emphasizing its potential as a promising formulation for Glibenclamide RDTs.

KEYWORDS: Rapid Disintegrating Tablet, Natural Superdisintegrant, Micronized Drug, Direct Compression, DOE, Glibenclamide.

1. INTRODUCTION

1.1 Rapid disintegrating tablet

The novel technology of fast disintegrating dosage forms is known as fast dissolve, rapid dissolve, rapid melt, and quick disintegrating tablets. Still, all these dose forms have a similar principle and purpose. Oral route has been one of all the most popular routes of drug delivery due to its ease and self-administration, patient acceptance, least sterility constraints, and flexible design of dosage forms with a high rate of aqueous solubility and quick dissolution; the slowest rate of drug permeation or crossing of cell membrane limiting step.[1]

For teenagers and the elderly who have trouble swallowing traditional pills and capsules, oral disintegrating tablets offer a benefit. Additionally, pediatric patients may suffer from ingestion problems because of underdeveloped muscular and nervous control. Furthermore, the usefulness of typical pills or capsules taken orally is limited for patients who are traveling with limited or no access to water. Mouth dissolving tablets result in quick dissolution and rapid absorption which supplies rapid onset of action. Additionally, medication candidates that are formulated as mouth dissolving tablets and undergo pregastric absorption may have higher oral bioavailability. It supplies good stability, exact dosing, and easy manufacturing.[2]

1.2 Micronization

Micronization exhibits a high energy particle size reduction technique which is used for increasing the solubility of BCS class II drugs.[3] It is well-known to be a straightforward process where the coarse drug powder will be transferred into an ultrafine powder, which resembles a mean particle range of 2-5 micrometer as well as only a little part of the particles will lie below 1 micrometer size range.[4] As a result, the equilibrium solubility of the drug itself will not be increased but the dissolution rate will be enhanced due to the increase in the surface area to volume ratio. Micronization results in uniform dosage form that has uniform, narrow particle size distribution. Not to mention that micronization is not considered as an approach for drug substances having high dose number since it does not change the saturation solubility of the drug.[3]

The resulting micronized drug substance properties, for instance particle size, size distribution, shape, agglomeration, surface properties behavior and powder flow influenced

by the type of micronization technique used. The following techniques are the most utilized techniques for production of micronized drug particles involving micronization: Mechanical communication such as ball milling and jet milling. For each drug, micronization improved their digestive absorption, and so their bioavailability and clinical efficacy. Micronization Glibenclamide exhibited more than 10-fold (1.3% to 20%) increase in dissolution in at 30 minutes bio relevant media.

Ball Milling: A ball mill usually constitutes of a cylinder crushing device that grinds the pharmaceutical powders by rotating them around a horizontal axis. (4)

Fig. 1.4: Ball Mill (All-purpose Equipment).

1.3 Definitions

1. According to EP: These MDTs should dissolve/disintegrate very quickly in the mouth without the need of water.[5]
2. As per WHO, "MDT intended to be dispersed within few seconds in water before administration, giving a homogenous dispersion".[6]

- Glibenclamide is an oral hypoglycemic agent Glibenclamide used in the treatment of Non-Insulin Dependent Diabetes. To lower blood sugar levels, glibenclamide is taken in combination with a healthy diet and exercise routine. Glibenclamide also known as Glyburide belongs to Sulphonyl urea.
- The mechanism of action is an inhibition of the ATP Sensitive K+ Channels which leads to depolarization of the cells and insulin secretion.
- Glibenclamide is readily absorbed from the gastrointestinal track. By producing a smaller particle size, micronization increases bioavailability.

2. MATERIALS AND METHOD

2.1 Material

Glibenclamide was obtained from SSJIPER college of pharmacy Jamner. MCC, SSG, were received as gift samples from Medley Pharma Ltd. Andheri. Other excipients & chemicals used were of AR grade.

2.2 Experimental design

Central composite design (CCD) was used for Experimental Design containing two independent variables Guar Gum (X1) & MCC PH 102 (X2) were investigated at Three Levels as Low, Medium, High given in Table 1. While putting the values nine batches were generated using DOE software (version 13). In that independent variables were investigated in the response i.e. percentage drug of release (Y1), Disintegration time (Y2). Using the Design Expert Software (Version 13), the analysis of variance (ANOVA) test was used to assess the statistical experimental design.

A two-independent variable experimental design was conducted using central composite design (CCD). Guar Gum (X1) & MCC PH 102 (X2) and were examined at three different levels, as indicated by Table 1. (Low, Medium, and High). Using DOE software (version 13), nine batches were created while entering the values. In this case, the response's independent variables, Drug Release percentage (Y1) and disintegration time (Y2)—were examined. Using the Design Expert Software (Version 13), the analysis of variance (ANOVA) test was used to assess the statistical experimental design.

Table 1: Independent Variables and Their levels of central composite design.

Independent Variable	Unit	Levels				
		-α̃	Low	Medium	High	+α̃
Guar Gum	%	1.3786	2	3.5	5	5.6213
MCC-PH-102	%	32.9289	35	40	45	47.0711

2.3 Preformulation study[14,15]

Preformulation studies are a vital part of the drug development process because they give important information on the physicochemical characteristics of novel therapeutic compounds before formulation development begins. Preformulation studies were conducted to verify the integrity and appropriateness of the drug and excipient for formulating a rapidly disintegrating tablet. These studies included physical appearance, solubility, melting point, hygroscopicity, and drug excipient compatibility.

2.3.1 Pre-compression parameter

1) Bulk density

In the arena of pharmaceutical research, bulk density is the mass of a unit volume of a granular or powdered material. It is an important parameter because it regulates how materials in formulations are handled and processed. The mass of the powder is divided by its volume to determine its bulk density. When a material has a low bulk density, it may be less dense and more difficult to compress; on the other hand, a high bulk density indicates more compressibility. This can be determined with the help of the graduate cylinder in which weight powder (passed through standard sieve #20) is poured into the cylinder and initial weight was noted.

$$\text{Bulk density} = \frac{\text{Mass of powder in gm}}{\text{Bulk volume of powder in ml}}$$

2) Tapped density

A tapped density tester, that utilizes procedures like predetermined mass or fixed volume measurements, is used to measure the tapped density. For industries to improve manufacturing, design, and quality standards, this measurement is critical. For example, understanding the tapped density in pharmaceutical research helps to enhance powder flowability for crushing tablets and filling capsules. Then the bulk density can be measured by the following formula.

$$\text{Tapped Density} = \frac{\text{Weight of powder in gm}}{\text{Tapped volume of powder in ml}}$$

3) Compressibility index

An important factor in evaluating a powder's flow ability is the compressibility index. A percentage is used to denote it. can be measured by the following formula.

$$CI = \frac{(pb - pt)}{pt} \times 100$$

Where, Pb. is tapped density.

Pt. is bulk density.

4) Hausner's ratio

It is an indirect index to measure the flow property of the powder and granules. Hausner's ratio can be calculated by the given formula.

$$Hausner, s\ Ratio = \frac{pb}{pt}$$

Where pt. is tapped density. Pb is bulk density.

Lower Hausner's ratio (<1.25) indicate better flow properties.

5) Angle of repose

The angle of repose is one of the evaluation parameters for studying the flow properties of powder. This analysis can be done by using the funnel method in which funnel is used and kept vertically at 6.3 cm height. Then the powder is poured by the upper side and closing the end of funnel with the help of thumb until is powder filled in the funnel. After pouring powder completely, the pile was formed by which radius of the heap can be measured and then the angle of repose was calculated by the following formula.

$\theta = \tan^{-1}(h/r)$

Where, θ is angle of repose.

h is the height of pile.

R is the Radius

2.3.2 Determination of uv spectrum

Phosphate buffer pH 6.8 was used to create a Glibenclamide solution in the concentration range of 10 ug/ml. The spectra for this solution were obtained in the 200–400 nm wavelength range using a double-beam UV visible spectrophotometer (Shimadzu-1800).

2.3.3 Preparation of calibration curve of glibenclamide

10mg of Glibenclamide were dissolved in phosphate buffer (pH 6.8) to create the stock solution, which had a final volume of 100ml. The solutions were created by appropriately diluting the stock solution to concentration ranges of 5–30 µg/ml. Using spectrophotometry, the absorbance of these solutions was determined at ʎmax = 299 nm. Plotted the Glibenclamide absorbance vs concentration graph in the Excel spreadsheet and found the intercept and slope.

2.3.4 Fourier transform infrared spectroscopy (FTIR)

FTIR Spectroscopy was used to assess the compatibility of Glibenclamide with the excipients. In FTIR Spectroscopy Methodologies Significant alterations in the location and form of the absorbance bends are examined. In addition, examine the functional group that is present and whether it interacts with each other.

2.3.5 Differential scanning calorimetry (DSC)

DSC analysis was used to find the melting temperature and to search for possible drug-excipient interactions during the formulation of RDT tablets.

2.4 Preparation of rapid disintegrating tablet

Glibenclamide micronization by an organoleptic approach employing direct compression as a common technology resulted in the preparation of rapid disintegrating tablets. Several superdisintegrants were applied during direct compression, including guar gum and (Table 2).

1) Weighed all the ingredients properly.
2) Glibenclamide, MCC PH 102, Pearlitol SD 200, were passed through sieve # 30. Mixed in a poly bag.
3) Aspartame, magnesium stearate, Aerosil and superdisintegrants were passed through sieve # 60. Mixed it in a polybag.
4) Peppermint Flavour passed through sieve # 100.
5) The final lubricant blend was passed through sieve # 60.
6) The lubricated blend was compressed onto 200 mg weight of tablet by using 8 mm FFBE punch Hydraulic Press (Model-15).

Table 2: Formulation table of optimized batches of glibenclamide.

Ingredient (mg/tablet)	Batches								
	GLB1	GLB2	GLB3	GLB4	GLB 5	GLB 6	GLB 7	GLB 8	GLB 9
Glibenclamide	20	20	20	20	20	20	20	20	20
MCC PH 102	70	90	90	80	94	80	65.84	70	80
Pearlitol SD 200	94	72	78	88	72	84	100	90	80
Aspartame	2	2	2	2	2	2	2	2	2
Guar Gum	4	10	4	2.74	7	7	7	10	11.24
Mint Flavor	3	3	3	2.26	2	2	1	3	1.8
Magnesium Stearate	6	2	2	4	2	4	4	4	4
Aerosil	1	1	1	1	1	1	1	1	1
Avg.Wt.(mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

2.5 Post-compression parameter of rapid disintegrating tablet of glibenclamide[15,16]

Following pharmacopeial standards, the compressed tablets were tested for weight variation, thickness, hardness, friability, wetting time, water absorption ratio, drug content, in vitro dissolution studies, disintegration test, uniformity of dispersion, and stability studies.

1) Weight variation test

- To perform the weight variation test, 20 tablets were weighed separately using a Shimadzu digital scale. The average weight of each tablet was then determined, and the weights of each tablet were compared to the average.
- After calculating the % weight deviation, the results were compared to the USP requirements.

2) Thickness

The Vernier calliper, which provides an accurate measurement of thickness, is used to measure the thickness of individual tablets. It gives details on how the thickness of the tablet's changes. Usually, mm is used as the measurement unit for thickness. Every tablet has a maximum thickness deviation of 5%.

3) Hardness

A tablet's hardness level shows how well it can tolerate handling-related mechanical shock. Crushing strength, often known as hardness, can be measured. The Monsantro hardness tester's unit of measurement is kg/cm2. The FDT hardness limit is typically maintained at a lower value to promote early breakdown in the mouth. Three readings of the test were taken.

4) Friability

The mechanical strength of tablets can be measured using this measurement method. The friability is tested using the Roche friabilator. It can be difficult for a formulator to achieve a % friability within the range of 0.1% to 0.9% because every process used in the manufacturing of RDT enhances the percentage of friability values. A total of 100 times, or 20 pre-weighed tablets, revolved at a speed of 25 rpm for four minutes, dropping one tablet every six inches. The tablets were then reweighed, and the formula was used to determine the percentage of weight loss.

$$\%\ Friability\ (F) = \frac{W0}{W} \times 100$$

Were,

W0 and W are the weight of the tablets before and after the test respectively. The limit for percentage of friability is between 0.5-1% w/w.

5) Wetting time

The dosage form's wetting time and contact angle are connected. A shorter wetting time means the tablet will dissolve faster. 10 cm of round tissue paper was placed in a 10cm Petri dish containing 6 ml of artificial saliva (pH 6.8). A water-soluble dye named Methylene Red is added to the petri dish. The tissue paper's surface is gently touched with a tablet. Wetting time is defined as the amount of time needed for water to reach the tablet's upper surface. When compression forces increase or porosity decreases, the pores get smaller and the wetting time increases. Wetting time and disintegration time have a linear relationship. Wetting is therefore an essential step in the disintegration process.

6) Water absorption ratio

Before being stored in a Petri dish, the tablet's weight was recorded (Wb). From the Petri plate, a thoroughly wet tablet was removed and weighed again (Wa). The following formula can be used to calculate the water absorption ratio R.

$$Water\ Absorption\ Ratio = \frac{Wa - Wb}{Wa} \times 100$$

Were,

Wa represents the tablet weight prior to the test, and

Wb represents the tablet weight following water absorption.

7) Drug content

The assay method was used to determine the drug content of the Glibenclamide rapid disintegrating tablet. The manufactured tablet was first broken up and put into 10 ml of pH 6.8 phosphate buffer. Following a half-hour, the mixture was passed through Whatmann filter paper 42. Out of a ten-milliliter batch, two ml were taken out and diluted with phosphate buffer pH 6.8 (10 µg/ml). The drug content was measured using a UV spectrophotometer at ʎmax 229 nm compared with a blank.

$$Drug\ Content(\%) = \frac{Test\ Absorbance}{Standard\ Absorbance} \times 100$$

8) In vitro dissolution studies

The release rate of Glibenclamide Rapid Disintegrating tablets was determined using United States Pharmacopoeia (USP) dissolution testing apparatus type 2 (paddle method). The dissolution test was performed using 900 ml of Phosphate buffer pH 6.8, at 37 ± 0.5^{o}C and 50 rpm. In specified time intervals (0, 2, 4, 6, 8, 10 min) an aliquot of 5 ml samples of the solution was withdrawn from the dissolution apparatus and with replacement of fresh fluid to dissolution medium. The samples were filtered through Whatmann filter paper of 42 µm. Absorbance of these solutions were measured at ʎmax 229 nm using a UV/Visible Spectrophotometer (shimadzu-1800). The drug release was plotted against time to determine the release profile of various batches.

$$\%\ DR = \frac{Sample\ Absorbace}{Standard\ Absorbance} \times Standard\ dilution \times Test\ dilution \times \frac{Purity}{Label\ Claim}$$

9) Disintegration test

This evaluation of the metric system is used to calculate how long it takes to break a tablet in the mouth to determine how effective a medication is. By inserting the six tablets into each of the apparatus's six tubes, the disintegration time may be recorded. This device uses distilled water that is at a temperature of 370C±20C as the disintegration medium. The drug's activity was then determined by timing the tablet's disintegration.

10) Stability study

A stability study's objective is to offer confirmation about a drug's or product's quality, which changes over time under the influence of multiple factors. Like environmental factors such as temperature, humidity, and light. The formulation was subjected to accelerated stability studies as per ICH (The International Conference of Harmonization) guidelines. The packed tablets were placed in stability chambers maintained at 30 ± 2ºC, 65 ± 5% RH and at 40 ± 2ºC, 75 ± 5% RH for 3 months. In a stability chamber. Tablets were periodically removed and evaluated for physical characteristics, drug content, invitro drug release etc.

3. RESULT AND DISCUSSION

3.1 Preformulation study

1. Organoleptic properties of glibenclamide

Table 3: Organoleptic Properties of Glibenclamide.

Sr. No.	Properties	Observation	Standard	Conclusion
1.	Colour	White	White	Complies With Standard
2.	Odour	Odourless	Odourless	Complies With Standard
3.	Taste	Practically without Taste	Practically without Taste	Complies With Standard

2. Melting point

The melting point of the Glibenclamide was found in the ranges of 168 ^{0}C to 170 ^{0}C by capillary method.

3. Pre-compression parameter

Precompression parameters such as bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose show that the powder mixtures flow freely, and Table 4 presents the results.

Table 4: Evaluation of Precompression Parameters of Glibenclamide RDT.

Precompression parameter	Batches								
	GLB1	GLB2	GLB3	GLB4	GLB5	GLB6	GLB7	GLB8	GLB9
Bulk Density (gm/ml)	0.416 ±0.02	0.355± 0.05	0.335 ±0.06	0.395± 0.08	0.535± 0.01	0.515± 0.02	0.300 ±0.04	0.378± 0.068	0.323± 0.05
Tapped Density (gm/ml)	0.485 ±0.06	0.392± 0.07	0.389 ±0.03	0.395± 0.07	0.626± 0.07	0.564± 0.03	0.341 ±0.03	0.418± 0.01	0.345± 0.04
Compressibility Index (%)	14.09 ±3.9	9.42±. 0.73	13.85 ±1.21	17.63± 0.80	14.57± 1.04	8.72± 1.49	11.82 ±0.72	9.54± 1.03	6.45± 0.18
Hausner's Ratio	1.16± 0.05	1.1± 0.01	1.15± 0.10	1.21±0. 01	1.16±0. 02	1.09± 0.08	1.13± 0.11	1.1± 0.42	1.06± 0.1
Angle of Repose (0)	34.52 ±1.42	29.95. 8±1.44	34.87 ±1.78	38.28± 1.61	33.99± 2.07	28.25± 3.07	31.15 ±0.87	28.83± 1.43	26.38± 0.05
Flow Ability	Good	Excellent	Good	Fair	Good	Excellent	Good	Excellent	Excellent

4. Determination of UV Spectrum and Calibration Curve of Glibenclamide

UV Spectrum of Glibenclamide was presented in fig.1. and the calibration curve shows the straight-line equation given in fig.2.

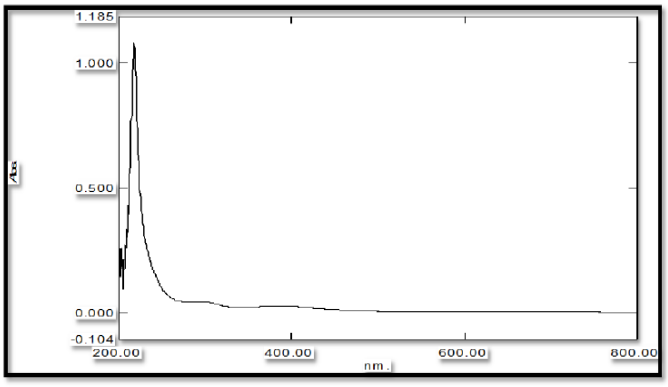

Fig. 1: Wavelength Maxima of Glibenclamide in phosphate buffer pH. 6.8.

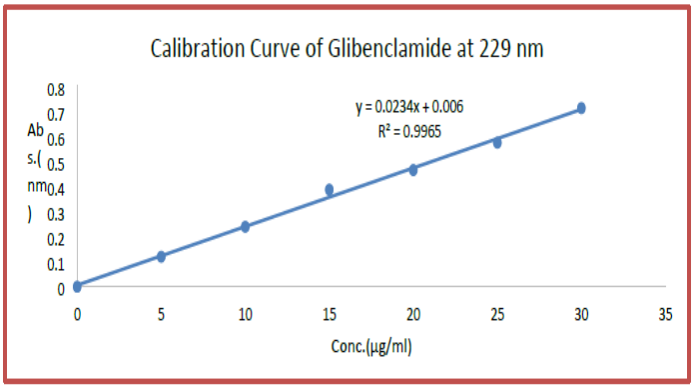

Fig. 2: Calibration curve of Glibenclamide in phosphate buffer pH 6.8.

5. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR results show when the IR Spectrum of the drug (Glibenclamide) and Guar Gum were compared with that of the mixture of drug and excipients to analyze the drug and excipients interaction. Fig.3,4,5

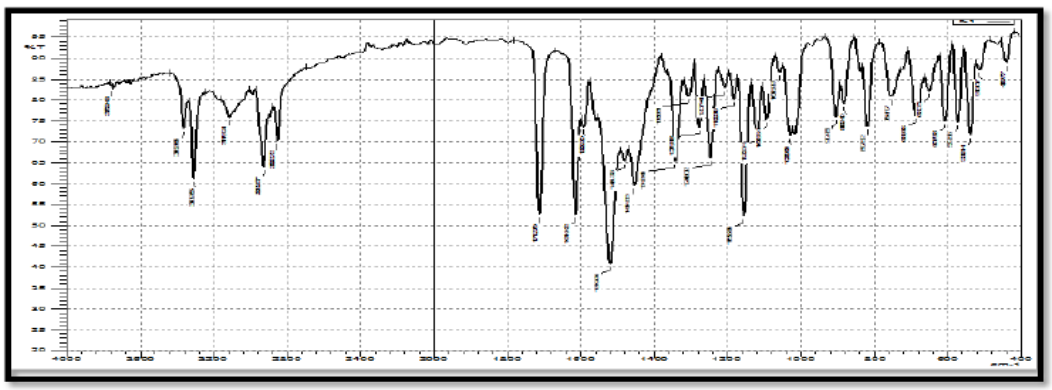

Fig. 3: FTIR Spectra of Glibenclamide.

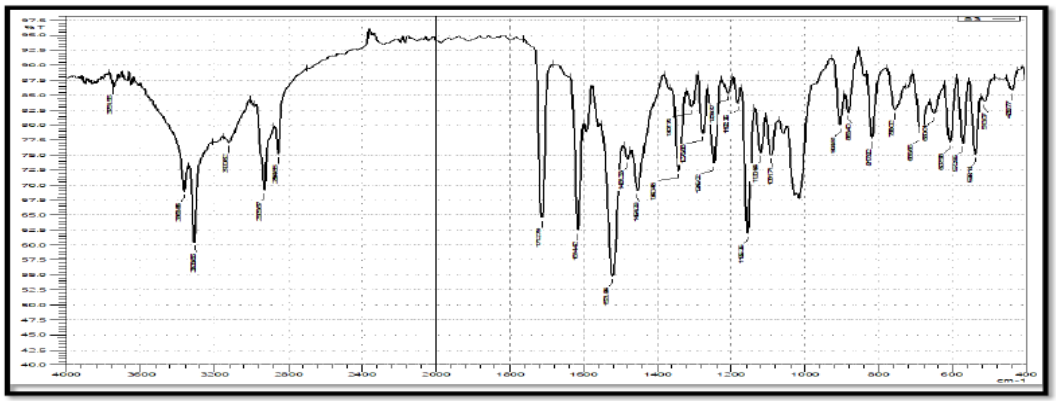

Fig. 4: FTIR Spectra of Guar Gum.

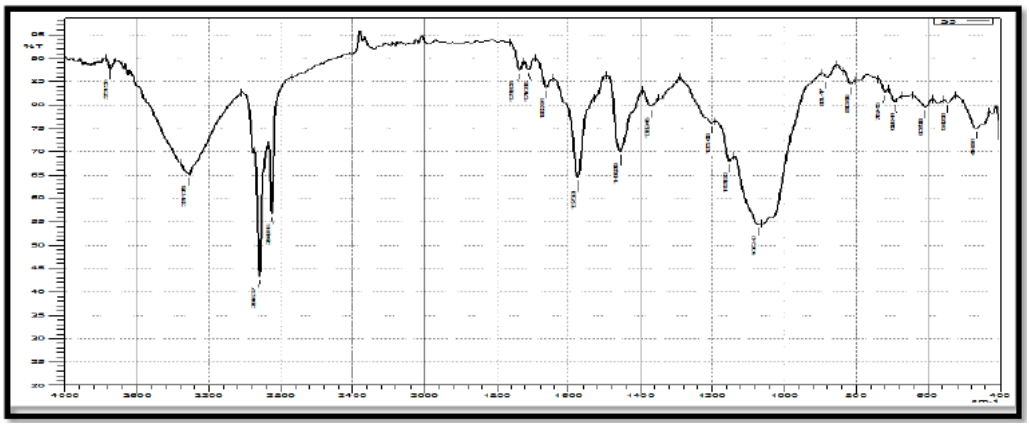

Fig. 5: Overlay spectra of glibenclamide, guar gum.

6) Differential Scanning Calorimetry (DSC)

The drug excipient mixture's melting point was 129 °C, according to the DSC thermograph, while the pure drug's melting point was 174 °C, there were very minor variations in the melting points, which suggests that the medication and excipients don't interact. Was given in Fig.6,7.

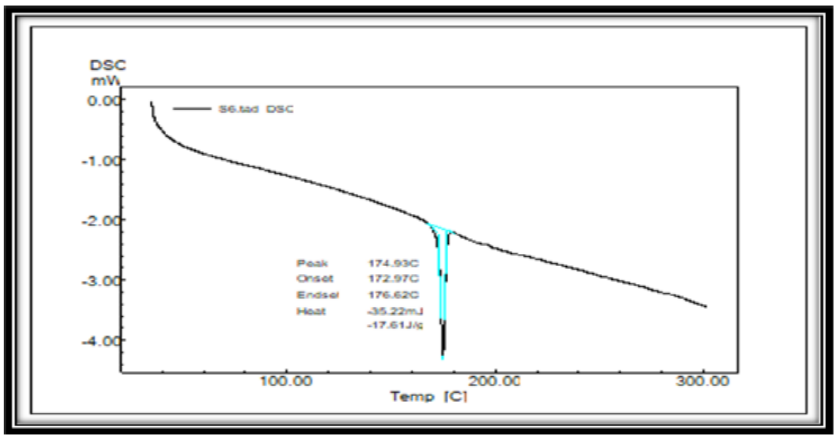

Fig. 6: DSC Thermogram of Glibenclamide.

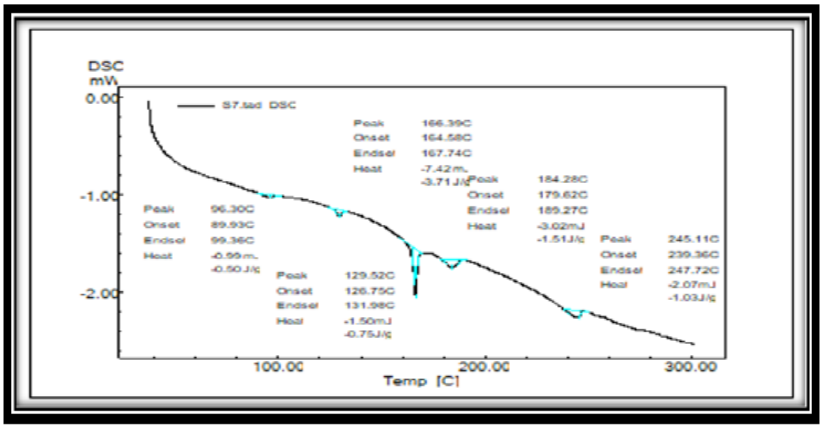

Fig. 7: DSC Thermogram of Glibenclamide and Excipient.

3.2 Optimization and Data analysis of optimized RDT of glibenclamide

Nine batches of Rapid Disintegrating tablets were made using the CCD method, each with a different concentration of independent factors generated using DOE software. The tablets were analyzed using a variety of statistics, such as the percentage of drug release and the disintegration time. (Table 5)

Table 5: Central composite design with dependent variables.

Batches	Variable Level in Coded Form		Dependent variable (Y)	
	X1	X2	% Drug Release (%)	Disintegration Time (Sec)
GLB1	-1	-1	85.15	14.9
GLB2	+1	+1	100.47	12.41
GLB3	-1	+1	84.85	15.23
GLB4	-α	0	81.64	16.01
GLB5	0	+α	92.68	13.17
GLB6	0	0	92.72	13.08
GLB7	0	-α	94.05	13.84
GLB8	+1	-1	99.08	12.02
GLB9	+ α	0	102.2	11.05

Effect of independent variables on % drug release

Impact of Independent Variables on Drug Release Percentage: Rapid Disintegrating tablet drug release in vitro was carried out in Phosphate Buffer pH 6.8 using a USP type II-paddle dissolution testing apparatus to maintain a temperature of 37 ± 1 °C. The drug release percentage is shown in Fig. 8. and Table 5.

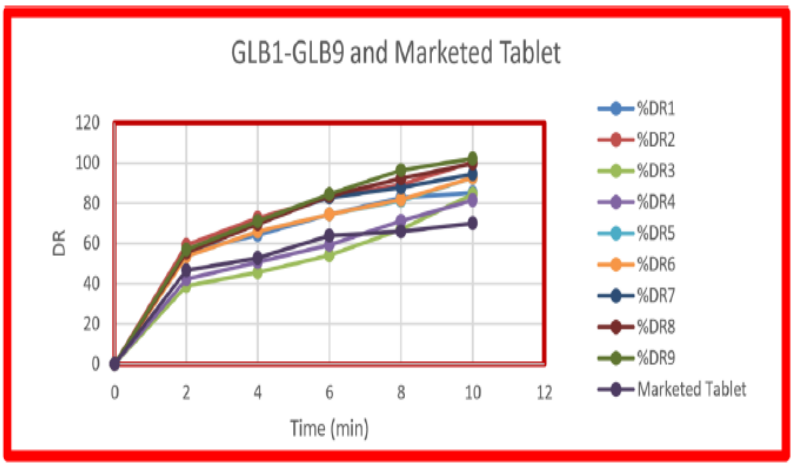

Fig. 8: In-Vitro Drug Released Study of Optimized Batches of Glibenclamide RDT Generated by (GLB1-GLB9 and Marketed Tablet).

On applying CCD, it produces an equation in terms of coded form for % drug release.

Final equation in terms of coded form

% DR=76.87593+4.94552A-0.039187B

Concerning dissolution, the results of multiple linear regression analysis showed that the coefficients A bear positive sign and B bear a negative sign. It revealed that % drug release increases with increases in Guar Gum and while % drug release minor increases with increase in MCC PH 102. A smaller amount of Guar Gum was expected to increase the % drug release due to faster disintegration of tablet. To determine the significant effect, an ANOVA was used. The result was found to be significant at that level of probability ($p<0.0001$). given in fig.9 & Fig.10.

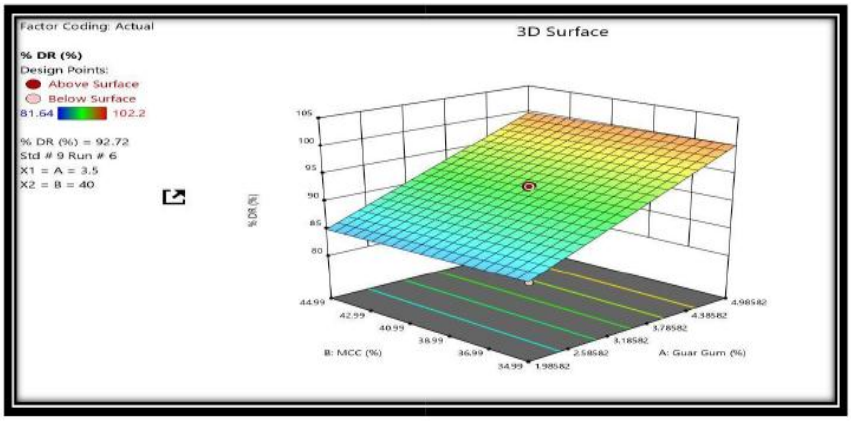

Fig. 9: 3D Response Surface Graph Showing the Influence of Guar Gum and MCC PH 102 on %

Drug Release (Y1)

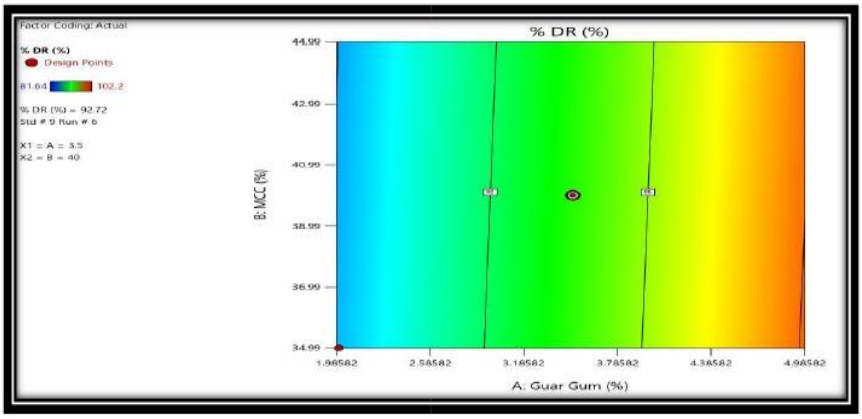

Fig. 10: Response Surface Contour Graph Showing the Influence of Guar Gum (X1) and MCC PH 102 on % Drug Release (Y)

Effect of independent variables on disintegration time

The disintegration time of nine batches of highly dispersible tablets varied according to the various independent variable values that were determined using the disintegration apparatus. On applying CCD, it generates an equation in terms of coded form for disintegration time.

Disintegration time

Final equation in terms of coded form-

DT=16.90762-1.00212A+0.0008550B

Concerning disintegration time, the results of multiple linear regression analysis showed that the coefficients A bear negative sign and B bear a positive sign. It revealed that disintegration time increase with increase in Guar Gum and while disintegration time Minor increase with increase in MCC PH 102. Guar Gum 3.5% w/w and MCC PH 102 40% w/w were selected as optimum concentration that showed the minimum disintegration time of 11 seconds. It was observed that further increase in concentration of superdisintegrant led to the increases in disintegration time. To determine the significant effect, an ANOVA was used. Obtained value of F is larger than critical F-value, the result was found to be significant at that level of probability ($p<0.0001$). given in Fig.11. & Fig12.

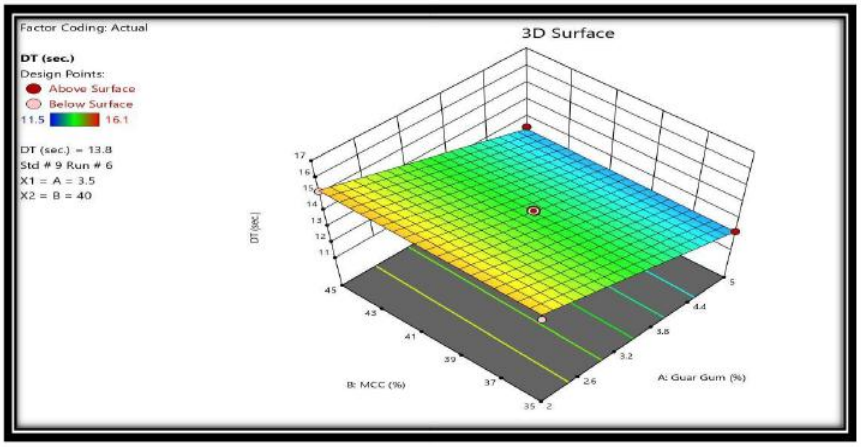

Fig. 11: 3D Response Surface Graph Showing the Influence of Guar Gum (X1) and MCC PH 102 on the Disintegration Time (Y2).

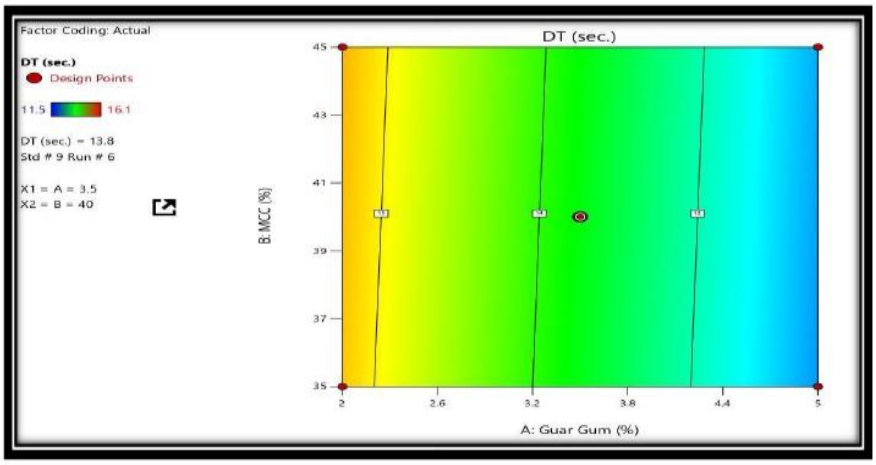

Fig. 12: Response Surface Contour Graph Showing the Influence of Guar Gum (X1) and MCC PH 102 on the Disintegration Time (Y2).

Table 6: Evaluation of Post-Compression Parameters of Optimized Batches of Glibenclamide RDT Generated by CCD.

Post Compression Parameter	Batches								
	GLB1	GLB2	GLB3	GLB4	GLB5	GLB6	GLB7	GLB8	GLB9
Weight Variation (mg)	196.95± 0.68	197.9± 1	193.9± 1.13	194.7± 0.71	192.35± 1.19	199.1± 0.71	198.7± 0.89	197.2± 0.98	195.15± 1.18
Thickness (mm)	3.01± 0.01	3.70± 0.02	3.70± 0.025	3.76± 0.04	3.55± 0.07	3.59± 0.03	3.77± 0.02	3.55± 0.4	3.75± 0.04
Diameter	8.0± 0.5	8.0± 0.05	8.0± 0.1	8.0± 0.05	8.0± 0.05	8.0± 0.11	8.0± 0.5	8.0± 0.1	8.0± 0.1
Hardness (Kg/Cm^2)	1.6± 0.1	1.7± 0.1	1.6± 0.17	1.5± 0.4	1.4± 0.1	1.8± 0.1	1.5± 0.2	2±0. 02	1.9±0. 1
Friability (%)	0.9±	0.85±	0.4±	0.80±	0.72±	0.5±	0.60±	0.45±	0.7±

	0.1	0.07	0.02	0.08	0.01	0.02	0.08	0.09	0.01
Wetting Time (Sec)	18	13	21	22	12	11	13	16	10
D. T. (Sec)	14.9	12.41	15.23	16.1	13.17	13.18	13.84	12.2	11.5
Water Absorption Ratio	72.16	69.89	72.82	74.24	81.34	86.93	97.96	95.47	86.66
Drug Content (%)	94.73	100.75	93.98	90.60	97.74	98.49	99.24	99.62	102.25

3.3 Post-compression parameters

1) Weight variation test

Table 6 displays the results of the optimized RDT weight variation test, which range between the range of 192.15±1.8 to 199.1±0.7 mg.

2) Thickness (mm) test

Using a vernier calliper the thickness of RDT was measured; the findings are displayed in Table 6 and vary from 3.01±0.01 to 3.7±0.02 mm.

3) Hardness test

The strength of RDT observed in the range of 1.4±0.1 to 2.1±0.2 Kg/Cm2 shown in table 6 was examined using a Monsanto hardness tester.

4) Friability

Table 6 presents the results of the determination of the tablets' friability using the Roche friabilator.

5) Water absorption ratio

Table 6 shows the water absorption ratio for the rapidly disintegrating tablet, which ranges from 69.89 to 97.96.

6) Drug content

A UV spectrophotometer was used to weigh and dissolve a 20 mg powdered Glibenclamide tablet in 100 milliliters of phosphate buffer pH 6.8. This allowed for the determination of the drug concentration in the formulation. Table 6 displayed the drug content results.

7) Dissolution test of marketed formulation

Brand name: Glifort 10 mg

Strength: Each Uncoated Tablet Contains

Colour: White Colour

Manufacturer: John lee Pharmaceutical Pvt Ltd

Table 7: Comparison of Percentage Drug Released of Optimized Formulation (GLB6) Of RDT of Glibenclamide and Marketed Tablet (Uncoated tablet).

Sr. No.	Time (min.)	% DR. GLB6	Time (min)	% DR. Marketed Tablet (Glifort 10 mg)
1	0	0	0	0
2	2	53.44	2	46.68
3	4	65.96	4	52.77
4	6	74.41	6	63.93
5	8	81.86	8	65.96
6	10	92.72	10	70.02

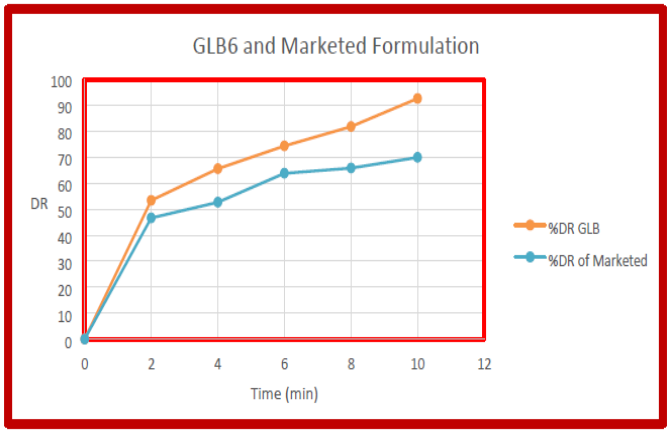

Fig. 13: Comparison of Optimized Batch (GLB6) with Marketed Uncoated Tablet of Glibenclamide.

8) Stability study

I) Accelerated stability study

Table 8: Accelerated Stability Data for GLB6 Optimized Batch of Glibenclamide RDT.

Parameters		Condition 40±2^{0}C/75% ± 5 RH		
		Initial	1 Month	2 Month
Physical	Average Weight (mg)	200	199	198
	Thickness (mm)	3.59	3.59	3.57
	Hardness (Kg/Cm^2)	1.8	1.7	1.6
	Friability (%)	0.51	0.52	0.51
	DT. Sec.	13.18	14.2	15
Chemical	% Drug Release (%)	92.72	91.36	90.86
	Drug Content (%)	98.49	98.95	99.25

II) Long term stability study

Table 9: Long term Stability Data for GLB6 Optimized Batch of Glibenclamide RDT Product.

Name: - Rapid Disintegrating Tablet of Glibenclamide

Parameters		**Condition 30 ± 2^{0}C/65% ± 5 RH**		
		Initial	**1 Month**	**2 Month**
Physical	Average Weight (mg)	200	199	198
	Thickness (mm)	3.59	3.59	3.57
	Hardness (Kg/Cm^2)	1.8	1.7	1.6
	Friability (%)	0.51	0.52	0.51
	DT. Sec.	13.18	14.2	15
Chemical	% Drug Release (%)	92.72	91.36	90.86
	Drug Content (%)	98.49	98.95	99.25

III) Long Term Stability Study (Store in refrigerator)

Table No. 6.10.3: Long Term (Stored in Refrigerator) Stability Data for GLB6 Optimized Batch of Glibenclamide RDT.

Product Name: - Rapid Disintegrating Tablet of Glibenclamide

Parameters		**Condition 5±3^{0}C**		
		Initial	**1 Month**	**2 Month**
Physical	Average Weight (mg)	200	199	198
	Thickness (mm)	3.59	3.59	3.57
	Hardness (Kg/Cm^2)	1.8	1.7	1.6
	Friability (%)	0.51	0.52	0.51
	DT. Sec.	13.18	14.2	15
Chemical	% Drug Release (%)	92.72	91.36	90.86
	Drug Content (%)	98.49	98.95	99.25

4. CONCLUSION

Since creating an oral quick disintegrating tablet involves several requirements that must be met, it is best to research every facet of the formulation. When considering physiochemical characteristics and efficacy, super disintegrating is one of the most crucial parts of RDT formulation. RDT of Glibenclamide has been prepared by direct compression method by using micronized drug and guar gum as superdisintegrant have significant impact on responses of the RDT such as post compression parameters like hardness, friability, wetting time, DT, and %DR at 10 Min. However, the %DR of Glibenclamide Rapid Disintegrating Tablet at 10 min. was significantly influenced with an increase of concentration of superdisintegrant. CCD of RSM was employed to find an optimum formulation with acceptable hardness, friability, wetting time, DT, enhanced %Drug release.

The desired optimum condition was obtained at 7 mg Guar Gum and 80 mg MCC102 with their optimum conditions, the experimental results of hardness, friability, wetting time, Disintegration time, % Drug release at 10 min. 1.8. ±0.1, 0.5±0.02, 11sec, 13.18sec, and 92.72respectively.

The experimental response was found to be in close agreement with the predicted value. Validity of the optimized formulation was confirmed by less the 5%. Prediction errors comparison of drug release between the optimized RDT & uncoated marketed tablet Glifort (10mg). Showed drug release from RDT was higher than Glifort (10mg.)

The results showed that GLB RDT was having adequate crushing strength and exhibiting faster Disintegration and enhanced Dissolution rate can be successfully prepared by using a combination of a superdisintegrant and binder through the application of CCD in Optimizing formulation Variables.

The obtained FTIR spectrum was compared with standard, the peak of functional group found in the obtained spectrum matches with peak in standard FTIR spectrum. It indicates the drug was pure and confirmed as Glibenclamide.

The DSC study showed the melting point of Glibenclamide is 174℃ and sharpness of peak indicates the purity of Glibenclamide.

Drug-excipients compatibility study was performed by using FTIR & DSC. All the major peaks of Glibenclamide were found in overly FTIR spectra, and in DSC study the melting point of Glibenclamide does not change in overly thermogram. Hence it was concluded there were no drug-excipient interaction, drug-excipient compatible with each other.

The stability study was carried out for optimized batch (GLB6). The result indicates that there were no significant changes in physical and chemical parameters up to 2 months.

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