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FORMULATION AND EVALUATION OF ORAL HYPOGLYCEMIC TABLETS UTILIZING MUCILAGE EXTRACTED FROM PLANTS REPORTEDLY HAVING ANTI DIABETIC ACTIVITY

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Abstract:

Diabetes is a metabolic disorder that characterized by hyperglycemia, glycomeia and hyperlipidemia. The aim of this study was to investigate the oral hypoglycemic tablets using natural mucilage extracted from okra pod. Natural polymers are economic, easily available and found useful as tablet binder. They also contain anti-nutrient content which help in controlling blood sugar level. The aqueous extract of okra pod was precipitated using ethanol. The precipitate was dried and stored in desiccators for further phytochemicals screening. Glipizide is a first third generation sulphonylurea agent for the treatment of type 2 diabetes mellitus. The binder concentrations used in the formulation were 0.5, 1.0, 1.5, 2 & 2.5 % w/w. The granules were evaluated for bulk density, tapped density, angle of repose. The tablets were subjected to physicochemical studies thickness, friability, weight variation, hardness, in vitro dissolution study. Diabetes was induced by single intra peritoneal injection of freshly prepared solution of streptozotocin (45 mg/kg) and blood glucose level was monitored for 28 days. The optimized formulation reduces blood sugar significantly in STZ induced diabetic rats in comparison to standard drug (Glipizide).This study has demonstrated that mucilage of okra pod can be used for formulation of glipizide tablets.

Keywords: *Okra pod, mucilage, Glipizide, tablets, antidiabetic activity*

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INTRODUCTION:

Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Diabetes is a life-threatening condition affecting millions of people. Diabetes is a major threat to global public health that is rapidly getting worse, and the biggest impact is on adults of working age in developing countries. Diabetes is a common condition and its frequency is dramatically rising all over the world. Although diabetes is sometimes considered a condition of developed nations, the loss of life from premature death among persons with diabetes is greatest in developing countries [1]. Diabetes mellitus defines a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It is one of the most common metabolic syndrome since there are 200 million diabetic individuals in the world this creates a need to understand the etiology of the disease and the factors influencing its onset. Several pathogenic processes are involved in the development of diabetes these range from autoimmune destruction of the cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Deficient action of insulin on target tissues and hyperglycemia are the basis of the abnormalities in carbohydrate, fat, and protein metabolism, causing diabetes characteristic clinical features, micro and macro vascular complications and increased risk of cardiovascular disease [2].

Oral hypoglycemic agents have been used for the treatment of type 2 diabetes (noninsulin-dependent diabetes mellitus) for decades. Although these drugs have proven very effective in combating the hypoglycemia associated with diabetes, they also have potentially serious side effects; predictably, the most common and crucial of these is hypoglycemia, which essentially amount to an extreme form of "over-treatment". Hypoglycemia is characterized by a variety of symptoms, such as lethargy, confusion, dizziness, nausea, sweating and hunger. By definition, the glycemic threshold is the serum glucose value below which symptoms of hypoglycemia occur [3]. Sulfonylureas had been introduced in the 1950's and have played an important role in the management of type 2 diabetes since its introduction to the market. They work by binding to sulfonylurea receptor (SUR) on beta cells of the pancreas thus enhancing insulin secretion from the pancreas blocking hepatic glucose production when being transported through the portal vein [4]. Glipizide is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patient with type 2 diabetes mellitus it belongs to sulphonylurea drug class [5].

Mucilage is polysaccharide macro molecules that dissolve more or less upon contact with water and form colloidal solutions [6]. Mucilage is most commonly used excipient in pharmaceutical preparations. Mucilage is widely used in pharmaceutical industries as thickeners, water retention agents, suspending agents, binders and film formers. Apart from its use in finished medicines, newer uses have been found in the preparation of cosmetics, textiles and paint paper [7]. Vast application of plant mucilage's and gums in various industries is because of low cost, ready availability and important properties which they confer on products. So screening of gums and mucilage's has become a vital pharmaceutical interest [8].

The present study involved with formulation of Oral hypoglycemic tablets of Glipizide. However, many of the oral hypoglycemic tablets of Glipizide are available in the market. In this work we will use mucilage of okra pod in place of any other polymer or binder.

MATERIALS AND METHODS:

Glipizide was obtained as a gift sample from Zim laboratories, Nagpur. Okra pod was collected from local market. All other ingredients were of analytical grade was purchased from Loba Chemical and SD Fine Chem Ltd. Mumbai.

Isolation of mucilage

Okra pod was collected from local market. It was cut into small pieces and soaked in water for 5-6 hours, boiled for 30 minutes and left to stand for 1hr to allow complete release of the mucilage into the water. The viscous mucilage solution was filtered using a multi layer muslin cloth bag to remove the marc from the solution. Ethanol was added (3 times the volume of filtrate) to precipitate the mucilage. The mucilage was separated, dried in an oven at a temperature of less than 50°C, collected, ground, passed through sieve no. 80, weighed to calculate the yield and stored in desiccator till use [5]

Physicochemical properties of dried mucilage

The physicochemical properties of okra pod mucilage such as solubility, swelling index, pH, percentage yield, loss on drying were determined according to pharmacopoeia [9 – 11]

Drug excipient compatibility studies

Compatibility of excipients with Glipizide was studied by Fourier Transform Infrared (FTIR) Spectroscopy. The FT-IR spectra of all combinations containing drug and polymer also show the characteristic peaks same as that of the pure drug. The FT-IR spectrum of all the combinations containing drug and polymer shows same or slightly shift in peak values when compared with the characteristic peak value of pure drug [12]

Table: 1 Formulation chart of Glipizide.

INGREDIENTS	QUANTITY (mg)				
	F1	**F2**	**F3**	**F4**	**F5**
Glipizide	40	40	40	40	40
Mucilage	40	60	80	100	120
Micro crystalline cellulose (MCC)	166	146	126	106	86
Talc	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2
Total	250	250	250	250	250

Preparation of Glipizide tablet by wet granulation method

Preparation of granules

Granules of glipizide were prepared by wet granulation method. All the corresponding powders mentioned in formulation table (Glipizide, Mucilage and MCC) were weighed individually. Then the powder was added in ascending order and grinded to fineness in a mortar and pestle. The powder was kneaded a clean and dry pestle using distilled water as granulating fluid. The wet mass was then passed through a sieve no.22. The prepared granules were allowed to dry for 15-20 minute in an oven at 55℃ then passed through a sieve no.44. Talc and Magnesium Stearate were added and mixed uniformly. These granules were then stored in an air tight container till further processing [13 – 15]

Evaluation of pre-compression parameter

Granules prepared by wet granulation technology were evaluated for various rheological properties like bulk density, tapped density, carr's index, hausner's ratio and angle of repose by using standard procedure. All these properties were carried out in triplicate (n=3) and average values were reported [15].

Angle of repose

Angle of repose is defined as, "the maximum angle possible between the surface of pile of powder and horizontal plane". The angle of repose for granules of each formulation was determined by fixed funnel method. A funnel was kept vertically in a stand at 2cm above a graph paper placed on a horizontal surface. The funnel bottom is closed and 10 gm of granules is filled in funnel. Then funnel was opened to release the granules on the paper to form a smooth conical heap, is found by measuring in different direction. The height of the heap was measured with the help of scale. The value of angle of repose is calculated by using the following formula:

$$\theta = tan^{-1}\frac{h}{r}$$

Where, h- height of the heap, r- radius of the heap

Bulk density

A known quantity of granules blend was poured into the measuring cylinder level the powder without compacting and the total volume was noted. The weight of granules bed is determined by using digital weighing balance. Bulk density is calculated by using the following formula.

$$Bulk\ density = \frac{m}{v_0}$$

Where m- total weight of granules V0- total volume of granule

Tapped density

Tapped density was determined by placing the dried granules in measuring cylinder and measures the volume of granules after 100 tappings. Tapped density was calculated by using the following formula.

$$Tapped\ density = \frac{Vb}{Vf}$$

Where Vb - total weight of granules, Vf - tapped volume of granules.

Compressibility index

It is fast, simple and popular method of predicting powder flow characteristics. It is calculated by using measured values for bulk density and tapped density as following formula:

$$\text{Compressibility index} = \frac{Vt-Vb}{Vt} \times 100$$

Where Vt – tapped density, Vb – bulk density

Hausner's ratio

It is an index which shows the ease of powder flow. The hausner's ratio was calculated by using measured values for bulk and tapped density as follows:

$$\text{Hausner's ratio} = \frac{Dt}{Do} \times 100$$

Where Dt – tapped density, Do – bulk density

Compression of granules into tablets

After adding Anti-adherent (Talc) and Lubricant(Magnesium Stearate) to the dry granules bed and subsequent blending of granules were compressed into tablets on a tablet rotatary

compression machine using 10mm diameter, flat faced punches respectively.

Evaluation of tablets [16 – 18]

Thickness and diameter

Thickness and diameter of tablet was determined by using Vernier Caliper. Five tablets from each batch were used, and average values were calculated and the results were tabulated.

Hardness of tablet

The hardness of a tablet is an indication of its strength, "the force required breaking a tablet in a diametric compression". The hardness of six tablets was determined using Monsanto hardness taster. The tablet was placed in "Monsanto hardness taster" vertically and the force was applied with the help of screw the end point was measured by breaking the tablet.

Weight variation test

In weight variation test twenty tablets were randomly selected and weighed to determine the average weight and compared with individual table weight. The percentage weight variation was calculated as per Indian Pharmacopoeial Specification. Tablets with an average weight more than 250 mg should not be deviate more than ±5 %. According to this all tablet should be in uniform weight. Test was performed using digital weighing balance. From the one batch 20 tablets were selected randomly as sample and their individual weight was determined and average weight was determined. Finally percentage deviation was calculated by using following formula:

$$Percentage\ deviation = \frac{(Individual\ weight - Average\ weight)}{Average\ weight} \times 100$$

Friability test

The friability of the tablets was measured in a Roche friabilator. Twenty tablets from each batch were selected randomly from the batch and initial weight was determined. The entire tablet were placed in a friabilator and rotated for 100 revolutions at 25 RPM. After that final weight was determined. According to standard the weight loss should not be more than 1%. The percentage friability was calculated by following formula.

$$Percentage\ Friability = \frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}} \times 100$$

Determination of drug content

The drug content of Glipizide was determined with the help of pH 7.8 phosphate buffer solution. Tablets were placed in 100 ml of pH 7.8 phosphate buffer solution individually. It was kept for 24 hours in room temperature and filtered. 1ml solution was withdrawn and diluted up to 10 ml with the help of pH 7.8 phosphate buffer solution and absorbance was recorded by uv-visible spectrophotometer at 229 nm. The drug content was determined by using calibration curve [19].

In vitro dissolutation study

Dissolution study of Glipizide tablet was performed all the formulations combinations in triplicate, employing USP - II paddle method and 900ml of pH 7.8 phosphate buffer as the dissolution medium. The medium was allowed to equilibrate to temperature of 37°C±0.5°c. Tablet was placed in the vessel and the vessel was covered. The apparatus was operated in pH 7.8 phosphate buffer at 50 rpm. At definite time intervals, 5 ml of sample was withdrawn and the same volume was replaced to maintain the shrink condition. The sample solution was diluted up to 10 ml and absorbance of these solution measured at 229 nm using the equation obtained from a standard calibration curve. Finally graph was plotted between time in *x* axis and cumulative percentage drug release in y axis [20]

Drug release kinetics [21 – 22]

The dissolution data obtained were fitted into following kinetic model. This was to determine the mechanism of drug release.

Zero Order Kinetics

Zero order as cumulative amount of drug released verses time. A zero-order release would be predicted by the following equation.

$$\mathbf{At = A_0 - K_0 t}$$

Where At is drug release at time t, A_0 is initial drug concentration, K_0 is zero-order rate constant (hr^{-1}). A graph of concentration verses time would yield a straight line with slop equal to K_0 and intercept the origin of the axis.

First Order Kinetics

The application of this model of drug dissolution studies used to describe absorption or elimination of drugs. To study the first order release rate kinetics the release rate data were fitted to the following equation.

$$\log C = \log C_0 \frac{Kt}{2.303}$$

Where C is Amount of drug remained at time t, C_0 is Initial amount of drug, K is first-order rate constant (hr^{-1}) When the data was plotted as log cumulative percent drug remaining versus time, yield a straight line indicating the release follow first-order kinetics.

The constant K can be obtained by multiplying 2.303 with slope values.

Higuchi Model

Higuchi model developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolid and/or solid mass. Drug release by diffusion has been described by following Hinguchi's classical diffusion equation.

$$Q = \left[\frac{D\varepsilon}{\tau(2A-\varepsilon C_S)C_{st}}\right]^{1/2}$$

Where Q is amount of drug released at time t, D is diffusion coefficient of the drug, A is Total amount of drug, C_S is solubility of drug in the diffusion medium, ε is Porosity τ is Tortuosity

t is time (min) at which 'Q' amount of drug released.

Equation may be simplified if one assumes that D, C_S and A are constant. Then equation become

$$\mathbf{Q = Kt^{1/2}}$$

When the data was plotted according to new equation i.e., cumulative drug released versus square root of time, yield a straight line, indicating that the drug was released by diffusion mechanism. The slop is equal to 'K'

Korsmeyer and Peppas Model

The release rates from controlled release polymeric matrices can be described by the equation proposed by Korsmeyer and Peppas model

$$\mathbf{Mt / M_{\infty} = K \cdot t^{n}}$$

Where Mt represents amount of the released drug at time t, M is the overall amount of the drug (Whole dose). K is kinetic constant incorporating structural and geometric characteristics of tablets and 'n' are the diffusional exponent indicative of the release mechanism. The value of n

Indicates the drug release mechanism related to the geometrical shape of the delivery system, if the exponent n = 0.5, then the drug release mechanism is Fickanian diffusion. If n < 0.5 the mechanism is quasi-Fickanian diffusion, and 0.5 < n < 0.5, then it is non- Fickanian or anamolous diffusion and when n = 1.0 mechanism is non-Fickanian case II diffusion, n > 1.0 mechanism is non- Fickanian super case II.

***In-vivo* animal study** [23 – 25]

Induction of diabetes in rats

Diabetes was induced by single intra peritoneal injection of freshly prepared solution of STZ at the dose of 45mg/kg in normal saline (pH 4.5) to the overnight fasted rats. After 3 days of STZ induction, the animals having blood glucose levels between 250–300 mg/dl were selected for the study. Normal healthy Albino Wister rats weighing 180-200 gm each ware used for the *in-vivo* studies. All the animals were housed in polypropylene cages. The Institutional Animal Ethics Committee's approval was obtained before the commencement of the study. The study conducted as per standard institutional guidelines. Five groups of rats with 6 in each were fasted 12h before the study. Before the administration of drug, a blood sample was taken from the tail vein of each rat (control). The blood glucose level of the collected samples was determined using the glucometer method. Pure Glipizide and tablets Glipizide was administered orally to each group. A dose of 0.180 mg/kg of Glipizide was administered in a form of suspension for each rat. Blood sample was collected at a regular intervals of time and analyzed for blood glucose levels with glucometer

Data and statistical analysis

Data was expressed as Mean ± Standard Error Mean (SEM). This test provides a technique to test the goodness of fit and compare a number of frequency distribution. It also used to find out association and relationship between attributes.

RESULT:

Preformulation studies for Mucilage

The dried mucilage was evaluated for its colour and odour.

Table: 2 Physicochemical characterization of Okra pod mucilage

Sr. No.	Tests	Observations
1.	Description	Brownish white powder
2.	Odour	Characteristic.
3.	Appearance	Lustrous
4.	Solubility	Slightly soluble in cold water, soluble in hot water, insoluble in ethanol, acetone and chloroform
5.	Swelling index %	50.0±0.20
6.	Percentage yield	11.92%
7.	pH	5.8±0.07
8.	Loss on drying	10.06 %

Table: 3 Physicochemical characterization of *dried* mucilage

Sr. No.	Properties	Result	Type of flow
1	Angle of repose (ɵ)	28.20°±1.6	Good flow
2	Bulk density (gm/ml)	0.592±0.043	Good flow
3	Tapped density (gm/ml)	0.645±0.026	Good flow
4	Compressibility index (%)	8.68±3.81	Good flow

Preformulation studies for Drug

The drug sample was evaluated for its colour and odor.

Table: 4 Identification of Drug

S. No.	Parameter	Observation
1	Color	White
2	Ordour	Odourless
3	Test	Tasteless
4	Appearance	Crystalline powder

Solubility study

The solubility of the Glipizide was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined.

Table: 5 Solubility of Glipizide

S. No.	Solvent	Solubility
1	Water	Sparingly soluble
2	Methanol	Very slightly soluble
3	Ethanol	Sparingly soluble
4	Phosphate buffer pH(7.8)	Soluble

FTIR Spectrum of Glipizide

The identification of pure drug was performed by FTIR spectroscopy. The spectra were obtained from the FTIR spectrometer at the wavelength from 4000 to 400 cm^{-1}.

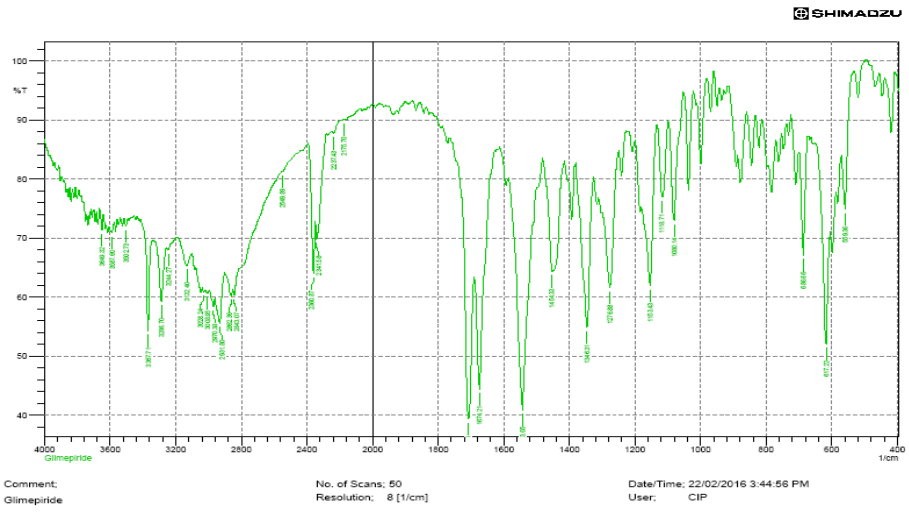

Fig: 1 FTIR Spectra of Pure Drug sample of Glipizide

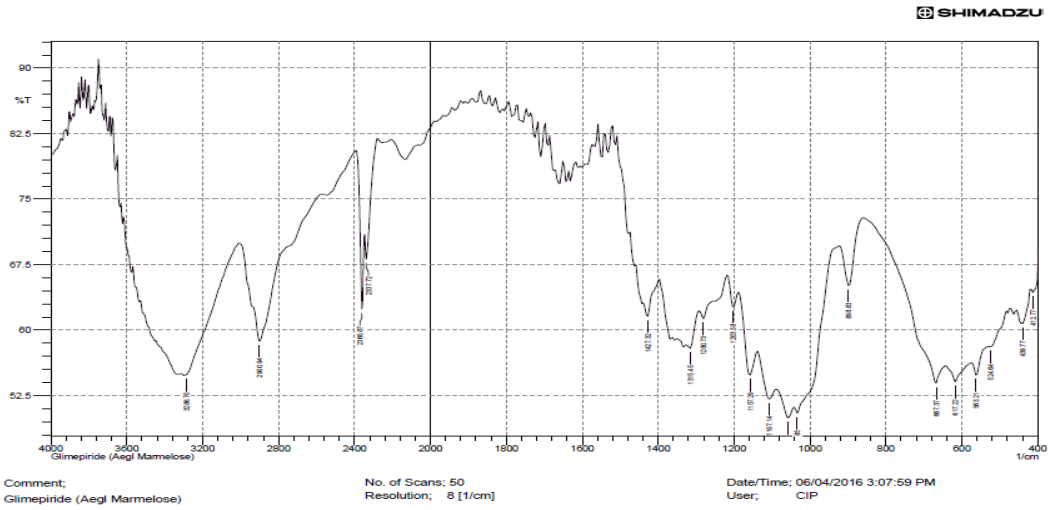

Fig: 2 FTIR Spectra of okra pod mucilage and Glipizide

Evaluation Table

Table: 6 Pre-compression Parameter of Glipizide granules

S.No.	Formulation No.	Bulk Density (gm/ml)±SD	Tapped Density (gm/ml)±SD	Carr's Index (%)±SD	Hausner's Ratio±SD	Angle of repose (ɵ)±SD
1	F1	0.592±0.048	0.645±0.023	8.16±2.46	1.08±0.04	27.5±2.6
2	F2	0.533±0.047	0.6±0.015	11.07±3.39	1.12±0.11	26.4±4.1
3	F3	0.474±0.006	0.561±0.019	15.34±2.62	1.18±0.13	31.5±3.2
4	F4	0.496±0.093	0.576±0.012	13.68±3.22	1.16±0.05	28.9±3.3
5	F5	0.593±0.025	0.677±0.047	12.25±4.26	1.14±0.12	25.6±0.68

Table: 7 Evaluation of Glipizide Tablet

Formulation No.	Thickness (Avg±SD) (mm)	Hardness (Kg/cm^2±SD)	Friability (%)	Drug Content (%)	Disintegration time (sec.)	Average Weight mg±SD	Weight variation
F1	3.7±0.27	6.78±0.116	0.122	93.6	122	249.6±4.44	pass
F2	4.0±0	5.0±0.141	0.100	88.5	172	251±2.32	pass
F3	3.6±0.60	5.48±0.222	0.298	94.5	167	254±2.38	pass
F4	3.9±0.20	6.3±0.147	0.35	95.2	152	252±2.63	pass
F5	4.0±0.66	5±0.170	0.434	94.8	216	255±1.43	pass

Dissolution Study of Prepared Tablet of Glipizide

In vitro drug release of different formulation are shown in figure no. 04

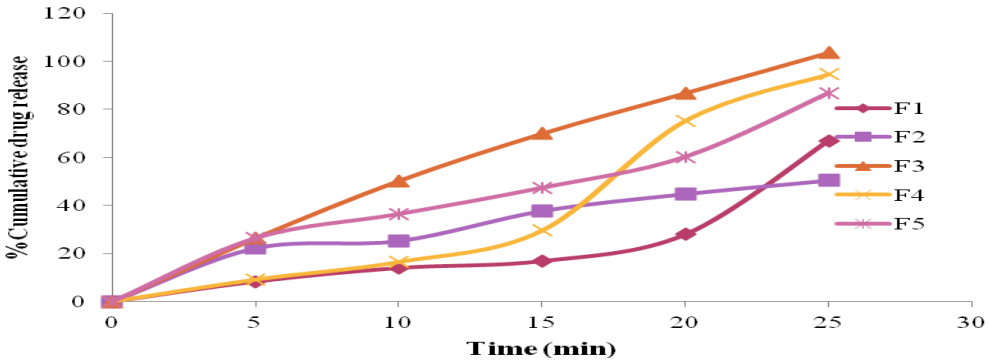

Fig: 3 Drug release kinetics of different formulation

Table: 8 Drug release kinetics of formulations

Formulation No.	Zero order		First order		Higuchi model		Korsmeyer Peppas model	
	K_0 (min^{-1})	R^2	K_1 (min^{-1})	R^2	K_H ($min^{1/2}$)	R^2	n	R^2
F1	2.265	0.796	0.0921	0.694	18.00	0.692	1.138	0.840
F2	1.520	0.939	0.0690	0.974	10.94	0.952	0.542	0.928
F3	3.820	0.994	0.122	0.970	27.82	0.998	0.847	0.997
F4	4.595	0.923	0.0575	0.864	32.31	0.865	1.507	0.937
F5	2.889	0.994	0.0368	0.812	20.41	0.900	0.697	0.941

***In vivo* Animal Study**

Table: 9 Anti-diabetic activity of prepared Glipizide tablets.

Groups	Blood glucose level in mg/dl (Mean ± SEM)				
	1 Day	7 Day	14 Day	21 Day	28 Day
Normal control	93.3 ± 2.06	95.32 ±1.74	94±1.4	93.33 ±1.34	105±5.44
Diabetic control	212.16±3.25	216±4.16	221±4.17	229.55±4.14	230±2.71
Glipizide	207.83±2.85	179.16±3.61	158.66±2.23	123±1.56	121±2.44
Test 1 (F3)	180.83±4.3	169.82±4.09	144.66±4.7	116±4.16	114.33±3.70
Test 2 (F4)	195.16±4.09	175±4.26	140.66±3.38	120.83±2.79	117.33±3.6

SEM: Standard error mean, Values are mean ± SEM, (n = 6 in each group)

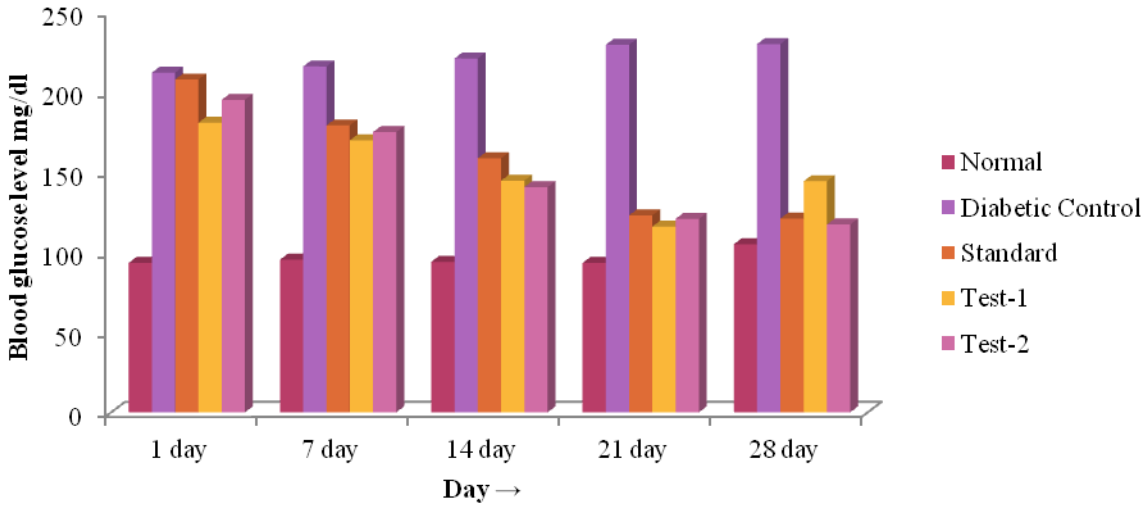

Fig: 4 Hypoglycemic effect of Glipizide of glucose levels was estimated using glucometer

DISCUSSION:

This research work was carried out with an objective of developing Oral hypoglycemic tablet using mucilage. For the fulfillment of this objective various methodologies and materials were used which are discussed further. Materials includes, mucilage extracted from okra pod, MCC, Talc, Magnesium Stearate contains hydrophilic properties which gets swell in dissolution medium helps to drug release. Tablets were prepared with mucilage extracted from okra pod and evaluated for tablet characteristics. Wet granulation technique was used for the preparation of granules. The binder concentrations used in the formulation were 0.5, 1.0, 1.5, 2 & 2.5 % w/w. Tablets were compressed to hardness at about 5 to 6.7 kg/cm^2. The evaluation of tablet showed 0.12% to 0.43 % friability, 2 to 3.6 min disintegration time. The extracted mucilage was found to be useful for the preparation of uncoated tablet. Tablet at concentration of 1.5% w/w can be used as binding agent for preparation of conventional tablet as the hardness, disintegration time, drug content and dissolution profile were as per the prescribed limits of Indian pharmacopeia. Talc and magnesium

stearate were used as glidant and lubricant respectively. In order to determine the mechanism of drug release form the formulations, the in-vitro dissolution data was fitted to Zero order, First order, Higuchi and Korsemeyer Peppas models. Plot was drawn for optimized formula and interpretation of release exponent value (n) was calculated. The results of F3 for zero and first order were obtained R^2 0.994 and 0.970 respectively. Based on the formula we have confirmed that the optimized formulation followed first order release. Higuchi's model was applied to the in-*vitro* release data, linearity was obtained with high 'r^2' value indicating that drug release from the Glipizide tablets through diffusion. The *in-vitro* release data was further fitted to Krosmeyer-Peppas model which is generally used to analyze the release mechanism when more than one type of release phenomenon is operational. Good linearity was observed with high 'r^2' values. The value of release exponent 'n' is an indicative of release mechanism. The value of 'n' obtained for the optimized formulation F-3 was found to be 0.847. Result of all formulation, pre compression and after compression data were satisfactory. The outcomes exhibited that F3 significantly decreases the blood glucose level of diabetic rats as compared to T4. From results it has been observed that the Test1 (F3) showed best anti-diabetic activity. After complete study of the formulation, batch no. F3 was found to be the best and satisfactory among all batches.

CONCLUSION:

Oral hypoglycemic tablets of Glipizide were successfully prepared using okra pod mucilage. The physical properties of tablet and its release kinetics indicate that wet granulation method is an acceptable method for designing of oral hypoglycemic tablets of Glipizide. Tablets containing okra pod mucilage at concentration of 1.5% w/w can be used as binding agent for preparation of conventional tablet as the hardness, disintegration time, drug content and dissolution profile were as per the prescribed limits of Indian pharmacopeia. The rate of release of drug from the tablet was observed to different proportion of binder. It was found that the *in vitro* release of F3 was best, following zero and first order were obtained R^2 = 0.994 and 0.970 respectively. After the oral administration of F3 and F4 in diabetic control rats, a significant reduction in blood glucose level was observed when compared with diabetic control rats it has been observed that the F3 showed best anti-diabetic activity.

REFERENCES:

1.http://www.who.int/diabetes/facts/en/
2.Malecki MT, Klupa T. Type 2 diabetes mellitus: from genes to disease. Pharmacol Rep. 2005 Jan 1;57(Suppl):20-32.
3.Bosse GM, Goldfrank L. 2002. Antidiabetic and hypoglycemic Agents. Goldfrank's Toxicologic New York.
4.Bolen S, Feldman L, Vassy J, Wilson L, Yeh HC, Marinopoulos S, Wiley C, Selvin E, Wilson R, Bass EB, Brancati FL. Systematic review: comparative effectiveness and safety of oral medications for type 2 diabetes mellitus. Annals of Internal Medicine, 2007; 147(6): 386 – 399
5.Fatima GX, Joan VR, Rahul RS, Shanmuganathan S. Formulation and evaluation of sustained release tablet using a natural polymer. Adv J Pharm Sci Res, 2015; 3 (1): 2 – 9
6.Bruneton J. 1999. Pharmacognosy, phytochemistry, medicinal plants. Lavoisier publishing.
7.Monif T, Malhotra AK, Kapoor VP. *Cassia fistula* seed galactomannan: Potential binding agent for pharmaceutical formulation. Indian Journal of Pharmaceutical Sciences 1992; 54: 234
8.Anroop B, Ghosh B, Parcha V, Vasanti S. Studies on Ocimum gratissimum seed mucilage: evaluation of binding properties. International Journal of Pharmaceutics 2006; 325 (1): 191 – 193
9.Malviya R. Extraction characterization and evaluation of selected mucilage as pharmaceutical excipient. Polimery W Medycynie. 2011; 41(3) : 39 – 44.
10.Kumar P, Kulkarni GT. Characterization of Mucilage from Grewia optiva as Pharmaceutical Excipient. Journal of Chronotherapy and Drug Delivery 2012; 3(2): 55-67
11.Gupta MM, Joshi Vishalkumar H, AmiparaLalji PV. MahidaMayur. Development and evaluation of Diclofenac solid dispersion by mixed hydrotropic technique. Int J of Pharm Res and Development. 2011; 3(8): 90 – 96
12.Kannan S, Manivannan R, Ganesan K, Nishad PK, Kumar NS. Formulation and evaluation of sustained release tablets of aceclofenac using hydrophilic matrix system. Int J PharmTech Res. 2010; 2(3): 1775 – 1780
13.Carter SJ. 2002. Powder flow and compaction. Cooper and Gunn's Tutorial Pharmacy, 6th edition, CBS publishers and distributors, New Delhi.
14.Bahadur S, Roy A, Chanda R, Baghel P. Formulation of glipizide tablets using fenugreek seed mucilage: optimization by factorial design. Asian Journal of Pharmaceutics 2016; 10 (4) suppl: S662 – S668
15.Shah RB, Tawakkul MA, Khan MA. Comparative evaluation of flow for pharmaceutical powders and

granules. AAPS PharmSciTech. 2008; 9 (1): 250 – 258
16.Prajapati GB, Patel RK. Design and in vitro evaluation of novel nicorandil sustained release matrix tablets based on combination of hydrophillic and hydrophobic matrix systems. International Journal of Pharmaceutical Sciences Review and Research. 2010; 1: 33-5.
17.Londhe S, Gattani S, Surana S. Development of floating drug delivery system with biphasic release for verapamil hydrochloride: *in vitro* and *in vivo* evaluation. Journal of Pharmaceutical Science and Technology 2010; 2 (11): 361 – 367
18.Hadi MA, Babu VL, Pal N. Formulation and evaluation of sustained release matrix tablets of glimepiride based on combinationof hydrophilic and hydrophobic polymers. Journal of Applied Pharmaceutical Science 2012; 2 (6): 11
19.Harris SM, Jaweria T, Hamid MA, Rabia IY. Evaluation of drug release kinetics from ibuprofen matrix tablets using HPMC. Pak J Pharm. Sci. 2006;19 (2):119-124
20.Sekhar CY, Venu V, Jaganathan k, Senthil Selvi R, Perumal P. Formulation and *in-vitro* evaluation of sustained release matrix tablets of glimepiride by using natural gums as release modifiers. J Global Trends in Pharm Sci. 2011; 2 (4): 394 – 403
21.Setti MV, Ratna JV. Preparation and evaluation of controlled release tablets of carvedilol. Asian J Pharm. 2014; 3 (3): 252 – 256
22.Shoaib MH, Tazeen J, Merchant HA, Yousuf RI. Evaluation of drug release kinetics from ibuprofen matrix tablets using HPMC. Pakistan Journal of Pharmaceutical Sciences 2006; 19 (2): 119 – 1124
23.Guidance, F. D. A. "Estimating the maximum safe starting dose in initial clinical trials for therapeutics in adult healthy volunteers." Rockville, MD, USA (2005).
24.Murthy TE, Mayuren C, Krishna M, Reddy T. Study of interaction between amlodipine besylate and gliclazide in healthy rats. Int J Pharm Biol Sci. 2008; 2 (1): 139 – 142
25.Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium Sativum L.*) in normal and streptozotocin-induced diabetic rats. Phytomedicine 2006; 13: 624-629