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ORIGINAL ARTICLE **OPEN ACCESS**

Aloe Vera Mucilage Based Sustained Release Matrix Tablets of Repaglinide: Formulation and Evaluation

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ABSTRACT

This study aims to investigate the usefulness of mucilage from Aloe barbadensis Miller leaves as an excipient in pharmaceutical sustained-release tablet formulations, as well as examine and create Repaglinide sustained-release matrix tablets using the mucilage from these leaves. After being isolated from Aloe barbadensis Miller leaves, dried powdered mucilage was put through a series of tests to investigate its physicochemical properties. In order to maintain the effective plasma concentration, a long-acting tablet needs to deliver the necessary amount of drug with a kinetic profile that has been defined in advance. This can be accomplished by making the drug release in a preset and repeating manner. Direct compression is used to compress these matrix tablets. Each tablet's structure was created using a distinct material: polymer ratio, such as 1: 1, 1: 2, 1: 3, 1: 4, and 1: 5. A resting angle, LBD, TBD, Carr index, and Hausner scale were used to assess dry powder mucilage derived from Aloe vera leaves. Pharmacopoeial standards were used to test the tablets that had been prepared. The current study clearly illustrates how ground aloe vera (PAG) can be used to adjust medication release at various dosages. PAG as mucilage in modified matrix tablets has the potential to provide a mechanism for continuous matrix tablets to be released.

Keywords: Repaglinide, sustained release matrix tablets, natural polymers, synthetic polymers, PAG

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INTRODUCTION

Diabetes mellitus is a long-term metabolic condition defined by high blood glucose levels brought on by insulin insufficiency and/or resistance [1]. (+) 2-ethoxy Repaglinide The amino group of -4 (2 (methyl-1 ((2-piperidinyl) phenyl) - - butyl). An anti-hyperglycemic drug, benzoic acid is an oral agent. for the treatment of people with diabetes who are not on insulin (NIDDM). Is part of a class of short-acting insulin secretagogues called meglitinides, which attach to pancreatic beta cells and stimulate insulin production. Many people have done extensive study on RPGN, and the medicine is expected to be released in the near future. it has been found to be composed of Repaglinide (RPGN) matrix tablets containing Aloe vera as a release modifier [2]. In the present study, an attempt was made to make Repaglinide matrix pills released using aloe vera fiber as a release agent. Aloe vera mucilage has been well studied for its use in mammals. On the line the fraction of polysaccharide present in the extraction of Aloe vera finds new information in drug delivery technology. Aloe vera has a history of its use in traditional skin treatments and other diseases that go back thousands of years. Many scientific reports have established beneficial effects on the inner leaf gel and the weight of the high polysaccharides associated with the effects. Possible use of PAG to correct drug withdrawal using different dosages. So it's safe to deduce from all of this that the modified matrix tablets with PAG mucilage can be utilised as an impediment to subsequent releases of matrix tablets [3].

A number of researchers believe that the polysaccharides in Aloe vera gel have therapeutic capabilities such as immunological stimulation and wound healing; encouragement of radiation damage repair [4]; promotion of hematopoiesis[5]; anti-oxidant effects[6]; Hepatoprotective activities, Antimicrobial activities [7], Intestinal drug absorption enhancement [8], and Skin penetration enhancement [9].

For oral medication delivery, the oral route remains the most desirable and preferred route even after optimal in vivo patterns of drug release. These physiological aspects include gastrointestinal transit and

GRT, the latter of which has a significant impact on the overall transit of dose forms. The GRT of an oral controlled release method is always 12 hours or less. Drug delivery systems that remain in the stomach for a long period of time can be developed because to these qualities. Hence Gastric medication retention has garnered a great deal of attention in recent decades [10].
GRDF stands for dosage forms that remain in the stomach after ingestion. There have been various GRDFs designed to extend gastric residence duration over the past two decades [11].

MATERIAL AND METHODS

Materials:

Repaglinide, Hydroxypropyl Methylcellulose K4M and Hydroxypropyl Methylcellulose, Polyvinil Povidone, Magnesium stearate (MS), Talc and Lactose was obtained.

- Drug excipient compatibility investigations were studied.
- The active pharmaceutical medication and its physical mixes were submitted to infrared spectrum investigations using FTIR spectrophotometer in the wave number region from 4000 cm-1 to 400 cm-1. The spectra obtained for active medicinal medication and the physical mixes were compared.
- Evaluation investigation.
- Drug Content analysis (Assay).
- Dissolution research kinetic analysis.
- Stability studies.
- Compatibility studies [12]

Aloevera mucilage extraction: Aloe vera mucilage extraction was done.

- Aloevera fresh plant leaves were collected, dirt and debris were removed by washing with water.
- To extract mucilage from leaves, make incisions in the leaves, soak them in water for 5-6 hours, boil them for 30 minutes, and leave them to cool for an hour.
- Once the marc had been removed, a cloth was used to extract the substance.
- The mucilage was precipitated by adding three volumes of acetone to the filtrate.
- Oven drying at a temperature of about 50 degrees Celsius separated the mucous membranes.
- As a result of the sieving process, the dried powder was kept in a desiccator for future use. Before compressing the tablets, the mucilage was tested for flow characteristics.
- Evaluations of flow characteristics were made
- The density of the bulk was evaluated.
- As a measure of compressibility [13],
  Flow properties of Aloe vera mucilage:

Table 1 Precompressive parameters of blend (n = 3)

Loose bulk density (g/ml	Tapped bulk density (g/ml)	Hausners factor	Angle of repose (°)	Carr's index (%)
0.46±0.05	0.59±0.02	1.282±0.14	23.35±0.01	13.34±1.80
0.45±0.05	0.57±0.03	1.268±0.12	20.48±0.02	12.41±1.40
0.43±0.04	0.55±0.05	1.279±0.21	24.44±0.02	15.99±1.56
0.41±0.04	0.54±0.01	1.317±0.14	22.36±0.06	12.32±0.88
0.41±0.03	0.54±0.04	1.317±0.22	21.91±0.03	14.54±1.48

There are a number of alternative ways to make matrix tablets, ranging from 1:1 to 1:5, depending on the ratio of medication to polymer.

Table 2 Preparation of matrix tablets containing varying ratios of PAG

Ingredients	Formulation Code				
	Processed aloevera gel 1 (mg)	Processed aloevera gel 2 (mg)	Processed aloevera gel 3 (mg)	Processed aloevera gel 4 (mg)	Processed aloevera gel 5 (mg)
Repaglinide	10	10	10	10	10
PAG	15	30	45	60	75
Microcrystalline cellulose	171	156	141	126	111
Magnesium stearate	4	4	4	4	4
Isopropyl alcohol	Q.S	Q.S	Q.S	Q.S	Q.S

1. Powder blend evaluation.
2. Tablets Thickness evaluation.
3. Weight variation.

4. Hardness.
5. Friability.
6. Drug content.
7. Swelling characteristics.
8. In vitro release studies.
9. Kinetic release profile.
10. Accelerated stability investigation

RESULTS

FTIR Studies: Excipient compatibility can be shown in the FT-IR spectra of pure medication (Repaglinide) and its physical mixing with different grades of polymers and excipients as depicted in figure 1 and 2 [14].

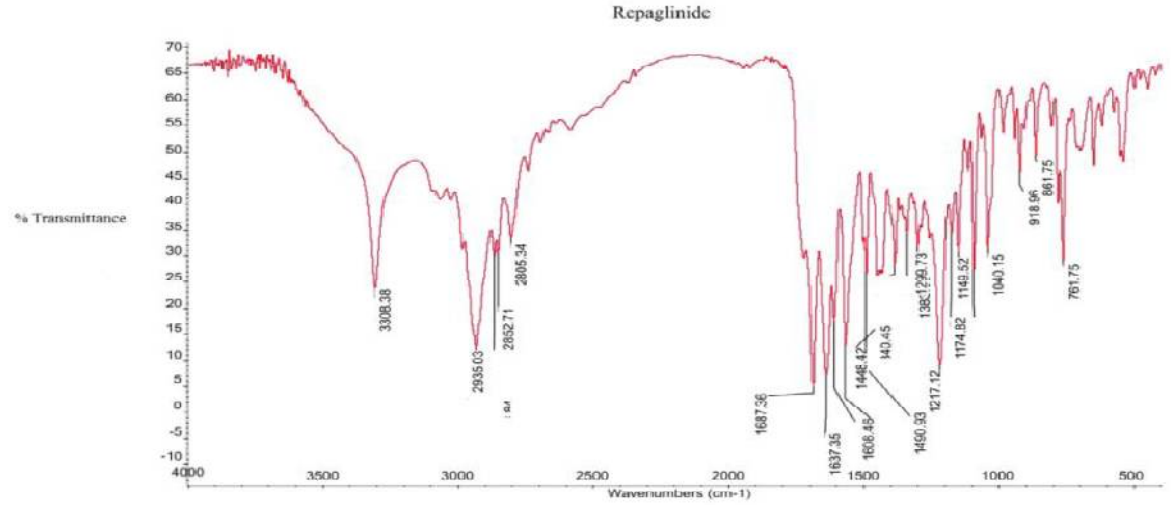

Figure 1: FT-IR spectrum of Pure Repaglinide.

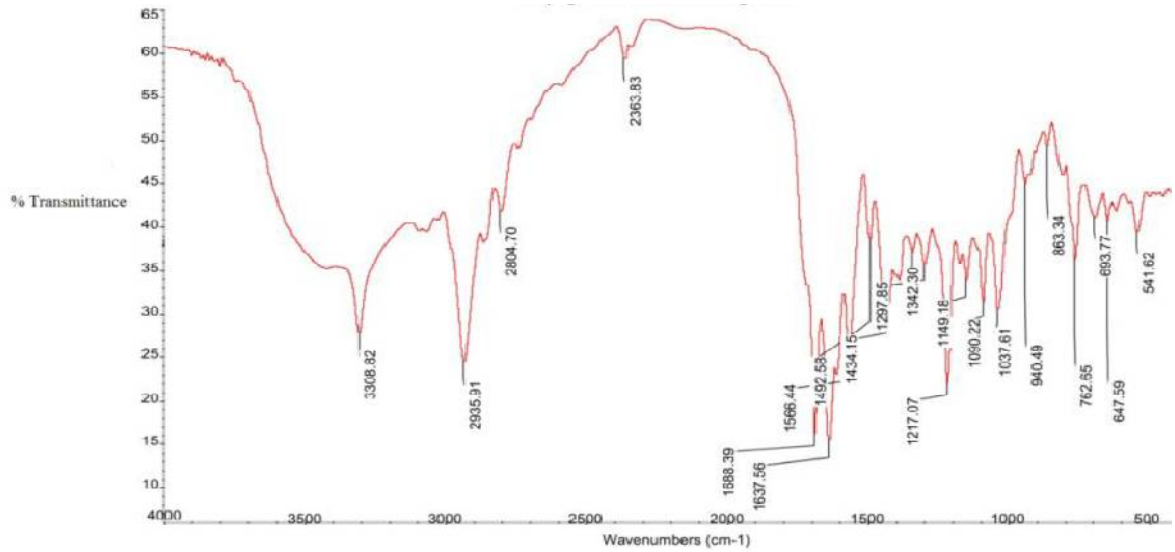

Figure 2: FT IR Spectrum of Repaglinide + PAG

In-vitro Dissolution Research

A USP Dissolution Test Apparatus II (Paddle technique) was used to conduct the dissolvability experiments at 37±0.5°C. They were spun at a rate of 50 revolutions per minute. (Repaglinide) tablets were placed in a disintegration tank (pH 1.2) for two hours with the pre-arranged tablets. Disintegration was then carried out in a phosphate cushion with a pH of 7.4. Sifted through 0.45 m channel paper and the content of Repaglinide was resolved using spectrophotometry at 242 nm for the first 2 hours and 278

nm for the second 2 hours. Crisp comparison medium was added to the disintegration carafe every (hour) season of withdrawal. As the most efficient strategy, discharge focuses on the definition that provided the desired once-daily arrival of Repaglinide. Various plans' disintegration curves are shown in the image [15].

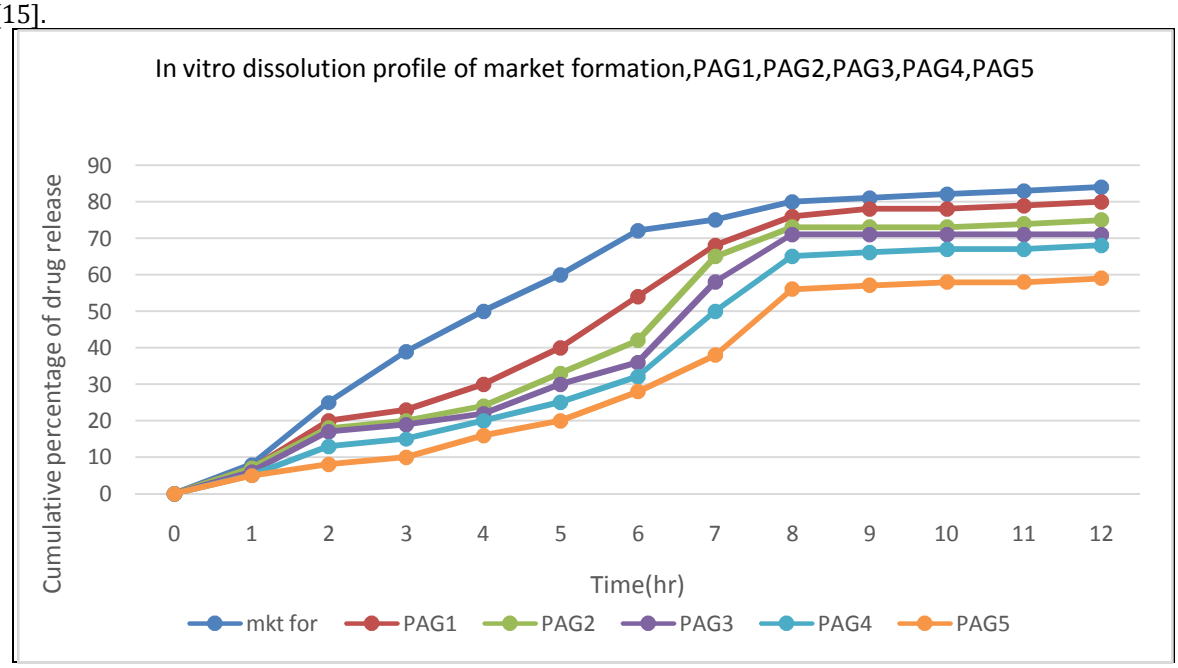

Fig 3 In Vitro Dissolution Profile of PAG1 to PAG5 Formulations

The drug release from the formulations were sustained in the following manner F1 > F2> F5. In all the formulations, t has been seen that by increment the grouping of polymers in the plans there by individually impede the medication discharge structure the networks [16].

Table 3 Postcompressive parameters of matrix tablets

Formulation Code	Thickness (mm) n = 3	Weight variation (mg) n = 20	Hardness (kg/cm2) n = 10	Friability(%) n = 10	Drug content (%) n = 20
PAG1	3.6±0.1	203±2.01	6.6±0.1	0.077±0.31	99.12±0.1
PAG2	3.5±0.2	200±2.31	5.7±0.2	0.083±0.30	99.67±0.4
PAG3	3.3±0.3	202±3.11	6.2±0.1	0.085±0.35	98.96±0.3
PAG4	3.2±0.3	198±2.15	6.1±0.2	0.087±0.13	98.22±0.2
PAG5	3.2±0.1	197±2.24	6.4±0.2	0.081±0.32	98.10±0.3

Kinetics of Drug Absorption

Various kinetic equations were used to analyse in vitro dissolution data in order to identify the drug release mechanism from this formulation. According to the following guidelines, the data were analysed:
Cumulative percent of medication released over time in a zero-order kinetic model.
Log cumulative percent drug remaining over time in the first-order kinetic model.
Higuchi's model - The square root of the cumulative percentage of medication released.
Calculate the log cumulative percent medication released against the log time using the Korsmeyer equation/ Peppa's model.

Table 4 Correlation coefficients according to different kinetic equations

Formulation	Zero Order	First order	Higuchi model	Korsmeyer model	
		r2		N	r2
PAG1	0.9858	−0.8953	0.9834	0.7249	0.9892
PAG2	0.9756	−0.9025	0.9712	0.7015	0.9846
PAG3	0.9865	−0.9154	0.9674	0.6852	0.9817
PAG4	0.9884	−0.9461	0.9617	0.6741	0.9784
PAG5	0.9944	−0.8257	0.9488	0.6580	0.9688
Marketed preparation	0.9648	−0.7046	0.9983	0.5145	0.9942

Study of Stability

Over the course of 90 days, the optimised formulation was tested for stability at temperatures ranging from 25°C to 20°C and at relative humidity levels of 60 percent to 5 percent at each of these temperatures. Physical features and medication release profiles were assessed on a monthly basis on tablet samples.

Table 5 Physical and chemical parameters of formulated tablets stored at 45°C (n = 10)

Formulation	Time	Appearance	Hardness	Drug content
PAG5	Initial	Pale white	6.0±0.12	99.84±0.43
	30 days	Pale white	5.4±0.16	99.84±0.32
	60 days	Pale white	5.4±0.16	99.84±0.02
	90 days	Pale white	5.4±0.16	98.52±0.21

PAG – Processed *Aloe vera* gel

DISCUSSION AND CONCLUSION

Chronic infection: Diabetes mellitus occurs when the pancreas does not create enough insulin, or when the body is unable to use the insulin it produces. Insulin is a hormone that regulates blood glucose levels. The long-term consequences of untreated diabetes, including nerve and vascular damage, are exacerbated by hyperglycemia, or hyperglycemia.

Other short insulin secretagogues known as Glinides work directly on pancreatic beta cells to speed up insulin production. In the treatment of type 2 diabetes, repaglinide is the most used oral meglitinide. Repaglinide has various advantages, including the ability to use one of only a few great oral specialists for renal failure. The greatest burden of Repaglinide is that it has an exceptionally short life expectancy (60 minutes) which is the reason it is a test in fostering an oral prophylactic that upholds the arrival of the medication as well as broadens the presence of interior portion from digestive system until all the medication is totally eliminated at the ideal time [17].

Aloevera is known for its numerous medical advantages including wound recuperating, antifungal action, hypoglycemic impacts or antidiabetic mitigating, anticancer, immunomodulatory and gastro-defensive properties. It was as of late found that both Aloevera gel and entire leaf can possibly work on the bioavailability of nutrients given in mix in human investigations. The reason for this study is hence to create and assess network pills for constant arrival of repaglinide utilizing aloe Vera adhesive processed as a delivery cure [18].

The construction of the various tablets was arranged utilizing an alternate material: polymer proportion i.e., 1: 1, 1: 2, 1: 3, 1: 4, 1: 5. dry powdered adhesive removed from A leaves. vera tried for resting point, LBD, TBD, Carr marker, and Hausner rating. The stream designs of the powder blend still up in the air. The resting point results (<30) demonstrate the fine stream attributes of the granules. Compressibility list values in our outcome show fantastic stream qualities. Tablets with various form codes under various test conditions, like strength, solidness, toughness, and comparative medication content. All shapes showed a similar thickness (CV <0.5%), a similar load with the smallest contrast in esteem (P> 0.1) saw with various organization code. The level of unfaithfulness of all tablet designs was under 1%. Drug content was viewed as comparable between various gatherings. It was noticed that the frequency of irritation expanded over the long haul however later diminished. The energy information got from the review show that the creation follows the zero-discharge request energy and that the medication discharge rate is free of fixation [19].

Our outcomes obviously show the conceivable utilization of PAG to address drug withdrawal utilizing various doses. From the above examinations, we can at last reason that the adjusted grid tablets that utilization PAG as adhesive can be utilized as an obstruction to the arrival of framework tablets for additional delivery.

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