



Research Article

Development and Evaluation of Sustained Release Matrix Tablet of Repaglinide and Miglitol Using Processed Aloe Vera Mucilage as Release Modifier

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The present investigation aims to develop and evaluate sustained release matrix tablets of Repaglinide and Miglitol using processed Aloe vera mucilage as a natural release modifier. Both drugs are widely used in the management of Type 2 diabetes mellitus but suffer from short biological half-lives and require frequent administration. The study explores the potential of Aloe vera mucilage as a hydrophilic matrix-forming agent to prolong drug release. Matrix tablets were formulated using wet granulation technique and evaluated for pre-compression and post-compression parameters. In vitro drug release studies demonstrated sustained drug release up to 12 hours. Release kinetics indicated that drug release followed Higuchi diffusion model with non-Fickian transport mechanism. The results suggest that Aloe vera mucilage is an effective, economical, and biocompatible alternative to synthetic polymers for sustained drug delivery.

Keywords: Repaglinide, Miglitol, Aloevera Mucilage.

INTRODUCTION

Diabetes mellitus is a chronic endocrine disorder characterized by hyperglycemia due to insulin deficiency or resistance. Repaglinide, a short-acting insulin secretagogue, stimulates pancreatic β -cells, while Miglitol, an alpha-glucosidase inhibitor, delays carbohydrate digestion and glucose absorption in the intestine. Despite their effectiveness, both drugs exhibit short elimination half-lives, necessitating multiple daily dosing, which reduces patient compliance. Natural polymers have gained attention due to their biodegradability, safety, and availability. Aloe vera mucilage contains polysaccharides that swell in aqueous environments, forming a gel-like matrix capable of controlling drug diffusion. This property makes it a promising release modifier in SR formulations.

MATERIAL AND METHODS

METHODOLOGY

Drug Study

- Tests such as Drug excipient compatibility were undertaken
- IR spectral studies were conducted on the pure drug and its physical mixes using an FTIR spectrophotometer in the wave number range of 4000 cm^{-1} to 400 cm^{-1} . A comparison of the pure drug spectra and the physical mixes spectra were done.
- Studies for drug stability
- Studies for drug compatibility
- Studies for evaluation of drug
- Drug Content (Assay)
- Kinetic study of dissolution data

Aloe Vera mucilage extraction

- Fresh aloe Vera plant leaves were gathered and cleaned with water for elimination of dirt and debris.
- Cut leaves were placed in water for 5-6 hours prior to cooking for 30 minutes and standing time 1 hour for proper mucilage release.
- Three volumes of acetone were added to the filtrate to precipitate the mucilage after the material was pressed off the cloth to eliminate marc from the solution.
- Mucilage was separated and dried at a temperature of 50 degrees Celsius in an oven.
- No. 80 sieve was used to sieve dried powder and kept in a dessicator for later use.
- Flow characteristics were assessed;
- Bulk density was assessed;
- Compressibility index was assessed

Matrix tablets preparation:

Various tablet formulations will be made with various drugs: 1:1, 1:2, 1:3, 1:4, 1:5 are the polymer ratios. Before compression, the powder blend was examined.

- a) Powder blend evaluation
- b) Tablets' evaluation Thickness
- c) Weight variation test
- d) Friability and hardness
- e) The drug's composition
- f) Characteristics of swelling
- g) Experiments on release in vitro.
- h) Profile of kinetic release
- i) Stability studies at a faster pace

Experimental Studies on Aloe Vera Extraction of mucilage:

A range of procedures were used to extract aloe Vera mucilage. To begin, plant leaves were collected and thoroughly cleaned in clean water to eliminate dirt and debris. For the release of mucilage in water, cutting of leaves and placement in water for 5-6 hours was done. It was then boiled for 30 minutes and left to stand for 1 hour. This causes precipitation of the mucilage, three liters of acetone. No. 80 sieve was used to sieve the powder after drying, before being stored in a desiccator. Before tablet compression, the mucilage was tested for flow characteristics.

PLANT LEAVES COLLECTED AND WASHED



LEAVES CUT AND SOAKED IN WATER FOR 5-6 HRS.



BOILED FOR 30MINS AND ALLOWED TO STAND FOR 1 hr



**FILTERED AND THREE VOLUMES OF ACETONE ADDED FOR
PRECIPITATION**



Fig 24: Procedure of extraction

Mucilage from *A. barbadensis* has physicochemical and microbiological characteristics

Mucilage from *A. barbadensis* has physicochemical and microbiological characteristics. Percentage yield, chemical test, particle size, weight loss on drying,

solubility, viscosity, pH, swelling index, bulk and tapped density, angle of repose, compression characteristics, and microbial load were all investigated in dried mucilage. The $^1\text{H-NMR}$ spectrum in Figure 29 clearly shows that the *A. vera* gel material employed in this work contains the three primary marker components alovera rose, glucose,

and malic acid, allowing it to be positively identified. Low quantities of lactic acid and succinic acid were also found in the findings.

A **chemical test** was performed. Molisch's reagent and ruthenium red were used to treat the dried mucilage powder. Positive staining was seen in both the test which showed presence of mucilage.

Drying causes weight loss. For an acceptable quantity of mucilage, weight loss on drying was assessed at 105 °C for 2 h. 86 For dried mucilage the weight loss was 4.89%.

Size of the particle: The microscopic approach was used to determine the particle size of the dried-powder mucilage, and the investigation was done in triplicate.

The solution's pH: pH metre for evaluation of pH of the 1 percent solution. (0.5-7.0)

Density: Dried mucilage was dissolved in a 0.5 percent weight/volume (w/v) solution and transferred to a density-measurement vial. Weighing an empty bottle of distilled water the dried mucilage's density was determined.

Charring: In a melting-point device, a few milligrammes of dried mucilage were inserted. When the material began to char, the temperature was collected and recorded. (220OC)

Ratio of swelling: A 100-mL stoppered graduated cylinder was used for the experiment. The initial bulk volume of dried mucilage was measured at 1 g. A suitable amount of water was added to produce a uniform dispersion of 100 ML. Remaining amount of swelled mass was noted after 24 hours of storage at room temperature. The swelling ratio was obtained by multiplying the ratio of the swollen with the ratio of the non-swollen.⁹⁰



Fig. 25: Bulk density apparatus

Density in bulk and tapped

The volume of dried mucilage put into a graduated cylinder was measured after it was pre-weighed and sieved. The powder-bed volume was tapped until it reached a minimal value, and the tapped volume was

noted. Determination of the bulk and tapped densities were done.⁹¹

The Hausner ratio and Carr's index- Calculation was done by the bulk and tapped densities.¹⁰⁴⁻¹⁰⁵

Table 7: Significance of Carr's index

S. No.	Carr's Index	Properties
1	5-12	Free flowing
2	13-16	Good
3	18-21	Fair
4	23-35	Poor
5	33-38	Very poor
6	>40	Extremely poor

Viscosity: Various concentrations (0.1–0.5 percent w/v) of dried mucilage were made in distilled water for rheological tests. Measurement of the viscosities were done by an Ostwald viscometer and sodium CMC solutions at the same concentration range was used for comparison.

Hausner's Ratio:

It's estimated by taking measurements of (1) the powder's initial apparent volume, V_0 and (2) the final tapped volume, V_f , after tapping the material till no change in volume is seen.

$$\text{Hausner's Ratio} = \frac{\rho_{\text{tapped}}}{\rho_{\text{bulk}}}$$

Table 8: Significance of Hausener's Ratio

S. No.	Hausner's Ratio	Property
1	0-1.2	Free flowing
2	1.2-1.6	Cohensive powder

The repose angle: By fixed-height funnel method and following equation calculation was done.

Where h = height of the powder heap, and radius of the powder heap = r .

$$\text{Angle of Repose} = \tan^{-1} (12h/D)$$

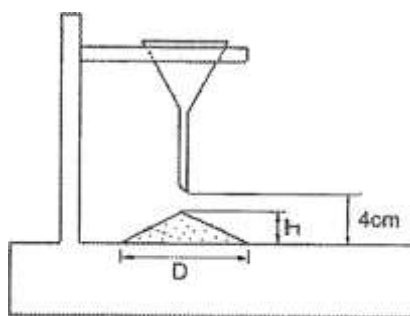


Fig. 26: Funnel method for determination of angle of repose

Table 9: Significance of Angle of Repose

S. No.	Angle of repose	Flow property
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Poor

Count of microbes: Plate count method as mentioned by Indian Pharmacopoeia for total aerobic microbial

count of bacteria and fungus the microbiological count of the dried mucilage was evaluated. 95

Table 10: Aloe vera mucilage flow properties

Parameter	Value
Angle of repose	22.5±0.32
Loose bulk density(g/cm ³)	0.72±0.07
Tapped bulk density(g/cm ³)	0.86±0.06
Carr's index	13.27±0.19
Hausner's ratio	1.191±0.02

• Experimental Analysis

Repaglinide and Miglitol was purchased. Microcrystalline cellulose was received from RSITC

lab. Magnesium stearate were received from RSITC lab. Aloe vera leaves were brought from local areas of Jalgaon, Maharashtra.

Table 11: Preparation of matrix tablets containing varying ratios of PAG

Ingredients	Formulation Code				
	PAG1 (mg)	PAG2 (mg)	PAG3 (mg)	PAG4 (mg)	PAG5 (mg)
Repaglanide	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

Reposing angle

The grains are allowed to flow freely through a funnel on a flat surface to calculate the angle of repose. Measurement of height and diameter of heaped powder and the equation was used for calculation.

$$\tan\theta = h/r$$

Where h and r are the powder cone's height and radius, respectively.

Bulk density

Loose bulk density & Tapped bulk density were determined using the following formulas.

$$\text{Loose Bulk Density} = \frac{\text{Weight of Granules}}{\text{Bulk Volume of Granules}}$$

$$\text{Tapped Bulk Density} = \frac{\text{Weight of Granules}}{\text{Tapped Volume of Granules}}$$

Compressibility index: Formula used for evaluation is:

$$\text{Compressibility Index} = \frac{\text{Tapped Density} - \text{Loose Bulk Density}}{\text{Tapped Density}} \times 100$$

Drug-Excipient Compatibility Studies

FTIR Research: Figures 27 & 28 show the FT-IR spectrum of pure medicine (Repaglinide and Miglitol)

and its physical mixing with various grades of polymers and excipients, demonstrating the excipient-drug compatibility.

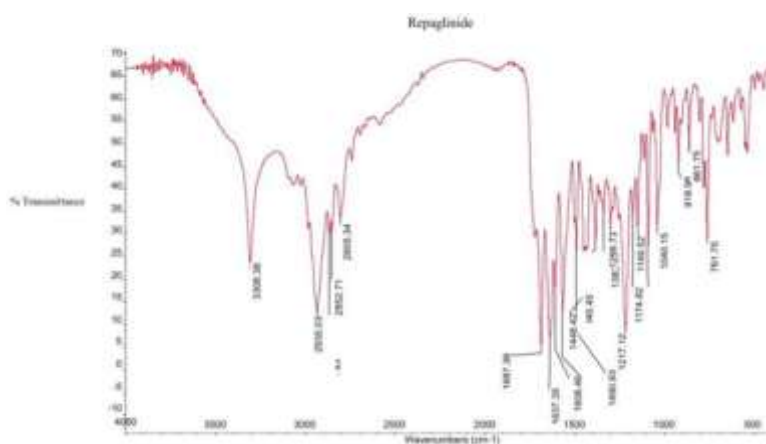


Figure 27: FT-IR spectrum of Repaglinide and Miglitol (pure form)

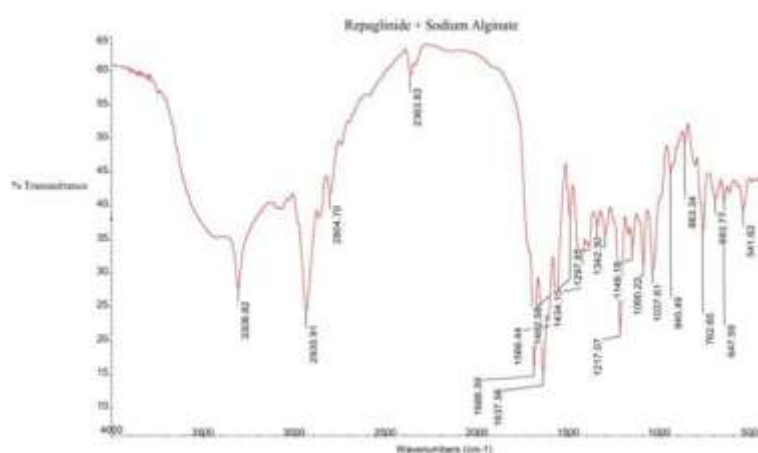


Figure 28: FT IR Spectrum of PAG and Repaglinide and Miglitol

Evaluation of Tablets

The following parameters were evaluated after compression tablets are evaluated.

Dimensions (thickness and diameter)

Vernier calliper was used for the tablet's physical dimensions measurement in millimetres. Each batch included 20 tablets, and the average was computed.

Aesthetics and texture

Visual examination was used to assess the tablets' appearance, colour, shape, and texture.

Hardness

The Monsanto Hardness Tester was used to determine the hardness of the tablets.

A total of 20 tablets were chosen at random. The weight was steadily raised until the tablet shattered when the scale was reset to zero. The load at that location provides a measure of the tablet's hardness. kg/cm² is used for its representation.

Friability

Roche friabilator was used to conduct the test. In the friabilator, 20 pre- weighed tablets were placed, the device was run for around 4 minutes at a speed of 25rpm. The percentage weight reduction was calculated after weighing the tablets again.

Formula used:

$$\% \text{ Weight loss} = \frac{(\text{Weight})_{\text{initial}} - (\text{Weight})_{\text{final}}}{(\text{Weight})_{\text{initial}}} \times 100$$

Variation in weight

20 tablets were chosen at random and weighed single pan balance separately and in combination. The standard deviation and the average weight was computed. If no more than two tablets go outside the % restriction and none of the tablets differ by more than double the percentage limit, the tablet passes the test. According to official techniques, all manufactured matrix tablets were assessed for weight uniformity, hardness, friability, and thickness.

Drug Content Uniformity

$$C_u/C_s = \frac{A_u}{A_s} \times \text{dilution factor}$$

Where C_u denotes the concentration of the unknown sample and C_s denotes the concentration of the standard sample.

A_u Absorbance of an unknown sample
 A_s Absorbance of the reference sample

In Vitro Drug Release Profile

Dissolution experiments were carried out at $37 \pm 0.5^\circ\text{C}$ in a USP Dissolution Test Apparatus II (Paddle technique) at a $37 \pm 0.5^\circ\text{C}$. 50 revolutions per minute was the paddle spinning rate. The dissolution test was carried out by immersion the produced (Repaglinide and Miglitol) tablets in 0.1 N HCl solutions (pH 1.2) for 2 hrs in a dissolving tank and then these tablets were placed in phosphate buffer (pH 7.4) for 2 to 12hrs. At regular intervals 5 ml of sample solution was withdrawn at predetermined time interval and filtered through 0.45 μm filter paper. 5 ml of fresh equivalent media was added to the dissolving flask at each (hour) time of withdrawal. Drug content of each sample was determined by using UV spectrophotometer at 242nm for 0.1NHcl and 278 nm for phosphate buffer.

Details of dissolution test:

Dissolution test apparatus: USP II
 Stirrer: Paddle type
 Speed: 50 rpm
 Volume of medium: 500 ml

Pulverisation of 5 tablets were done and weighed. Powder equal to 100 mg of Repaglinide and Miglitol was weighed and placed in a 250 ml volumetric flask. 150 mL of 0.1N HCL was added, mixed well, and 25-30 mins of sonication was done. With 0.1N HCL, a volume of up to 250 ml was created. The solution was filtered, and 10 mL of the filtrate was placed in a 100 mL volumetric flask with 0.1N HCL to form the volume. The absorbance of the resultant solution was measured spectrophotometrically at the peaks at around 242 nm. The following equation was used to calculate the medication concentration in tablet powder:

Time interval: 2, 3,4,6,8,10 and 12 hours
 Medium used: 0.1N HCl for first 2 hours and the phosphate buffer pH 7.4 from 3 to 12 hours
 Temperature: $37 \pm 0.50^\circ\text{C}$

Kinetic Analysis of Dissolution Data

To analyze the in vitro release data various kinetic models were used to describe the release kinetics.

The zero-order rate Eq. (1) describes the systems where the drug release rate is independent of its concentration (Hadjioannou et al., 1993).

The first order Eq. (2) describes the release from system where release rate is concentration dependent (Bourne, 2002).

Higuchi (1963) described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion Eq. (3).

$$C = K_0 t \text{ (Eq.1)}$$

Where, K_0 is zero-order rate constant expressed in units of concentration/time and t is the time.

$$\text{Log}C = \text{Log}C_0 - K_1 t / 2.303 \text{ (Eq. 2)}$$

Where, C_0 is the initial concentration of drug and K_1 is first order constant.

$$Q = K_H t^{1/2} \text{ (Eq. 3)}$$

Where, KH is the constant reflecting the design variables of the system. The dissolution data were fitted to Koresmeyer equation (Equation 4) which describes the drug release behaviour from polymer system.

$$\text{Log } (M_t/M_\infty) = \log K + n \log t \text{ (Eq. 4)}$$

Where

M_t is the amount of drug release at time “t” M_∞ = amount of drug release after infinite time

K = release constant signifying structural and geometric characteristic of the n = diffusion exponent indicating the mechanism of drug release.

A plot of log cumulative % drug release vs. log time was made. Slope of the line was n . Case-II generally refers to the erosion of the polymeric chain and anomalous transport (Non-Fickian) refers to a combination of both diffusion and erosion controlled-drug release (Peppas, 1985)

Table 12: Diffusion Exponent and Solute Release Mechanism for Cylindrical Shape

Diffusion exponent (n)	Overall solute diffusion mechanism
0.45	Fickian diffusion
$0.45 < n < 0.89$	Anomalous (non-Fickian) diffusion
0.89	Case-II transport
$n > 0.89$	Super case-II transport

Characteristics of swelling

The percentage of the tablet's weight increase was used to calculate the amount of swelling. Swelling behaviour was found in all formulations. In a petridish containing 0.1 NHCL, one tablet from each formulation was preserved. The tablet was extracted after 1 hour, soaked in tissue paper, and weighed. This technique was carried out for a total of 12 hours.

$$S_t = \frac{M_t - M_0}{M_0} \times 100$$

was used to compute the tablet's percentage weight gain.

Where SI stands for swelling index, M_t for tablet weight at time t (h), and M_0 for tablet weight at zero time.

RESULT

Characterization of Polymer Matrix

Table 14 shows the granules' assessed pre-compression parameters.

Table 14: Blend precompressive settings (n = 3)

Formulation code	Loose bulk density (g/ml)	Tapped bulk density (g/ml)	Hausners factor	Angle of repose (°)	Carr's index (%)
PAG1	0.250±0.005	0.285±0.012	1.142±0.14	25.67±01.84	12.28±1.29
PAG2	0.268±0.006	0.304±0.015	1.134±0.12	25.78±1.54	11.84±1.31
PAG3	0.278±0.005	0.309±0.010	1.115±0.21	27.35±1.79	11.15±1.34
PAG4	0.262±0.004	0.292±0.014	1.114±0.14	27.21±1.25	10.27±1.39
PAG5	0.289±0.003	0.317±0.012	1.096±0.22	27.12±1.64	9.779±1.35

Evaluation Of Matrix Tablet

Table 15: Matrix tablet post compressive parameters

Formulation code	Thickness (mm) n = 3	Weight variation (mg) n = 20	Hardness (kg/cm ²) 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

Studies on Dissolution in vitro

Dissolution experiments were carried out at 37°C ± 0.5°C in a USP Dissolution Test Apparatus II (Paddle technique) and 50 revolutions per minute was the paddle spinning rate. The dissolution test was carried out by immersion the produced (Repaglinide and Miglitol) tablets in 0.1 N HCl solutions (pH 1.2) for 2 hrs in a dissolving tank and then these tablets were placed in phosphate buffer (pH 7.4) for 2 to 12 hrs. At

regular intervals 5 ml of sample solution was withdrawn at predetermined time interval and filtered through 0.45µm filter paper .5 ml of fresh equivalent media was added to the dissolving flask at each (hour) time of withdrawal. Drug content of each sample was determined by using UV spectrophotometer at 242nm for 0.1N HCl and 278 nm for phosphate buffer. Figure 37 depicts the dissolving characteristics of several formulations.

Table 16: Dissolution characteristics of PAG 1 - PAG 5 and marketed (MKT) drug

Time	Cumulative Drug Release %					
	MKT	PAG 1	PAG 2	PAG 3	PAG 4	PAG 5
0	0	0	0	0	0	0
0.5	8.42	12.15	10.78	10.22	6.98	6.54
1	50.53	25.67	22.28	21.65	20.67	20.12
2	66.74	50.89	30.83	24.17	22.62	22.56
3	74.56	68.32	42.92	32.43	28.23	25.65
4	80.51	78.71	60.89	38.54	32.98	30.28
5	88.15	89.84	72.65	52.21	42.78	36.69
6	90.15	94.73	84.38	64.66	53.91	46.65
7			90.97	74.43	64.17	56.31
8			96.92	84.98	72.49	64.73
9				89.53	76.72	70.93
10				92.89	85.89	78.91
11					95.29	89.72
12						98.89

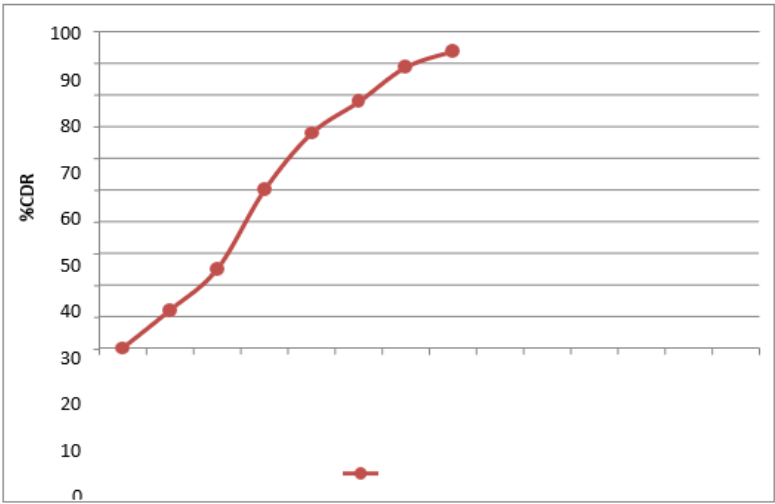


Fig. 31: In-vitro dissolution of PAG 1

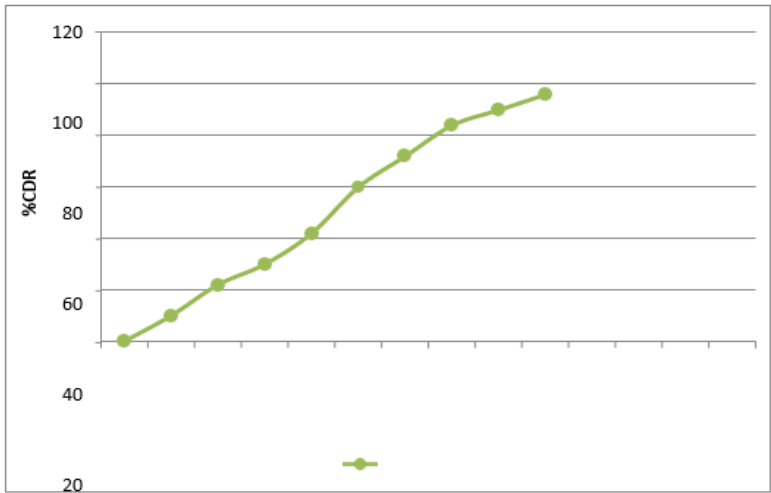


Fig. 32: In-vitro dissolution of PAG 2

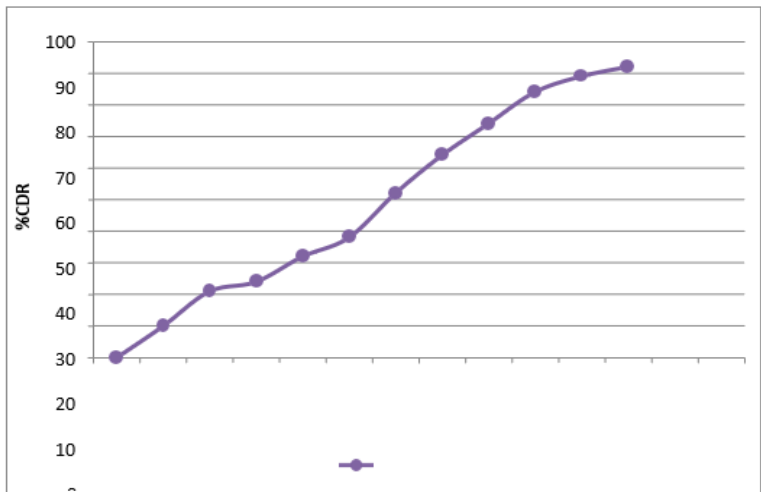


Fig. 33: In-vitro dissolution of PAG 3

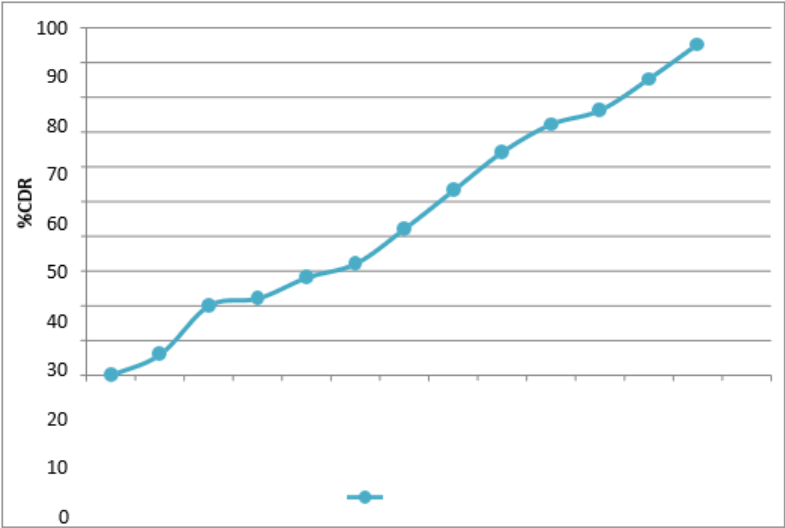


Fig. 34: In-vitro dissolution of PAG 4

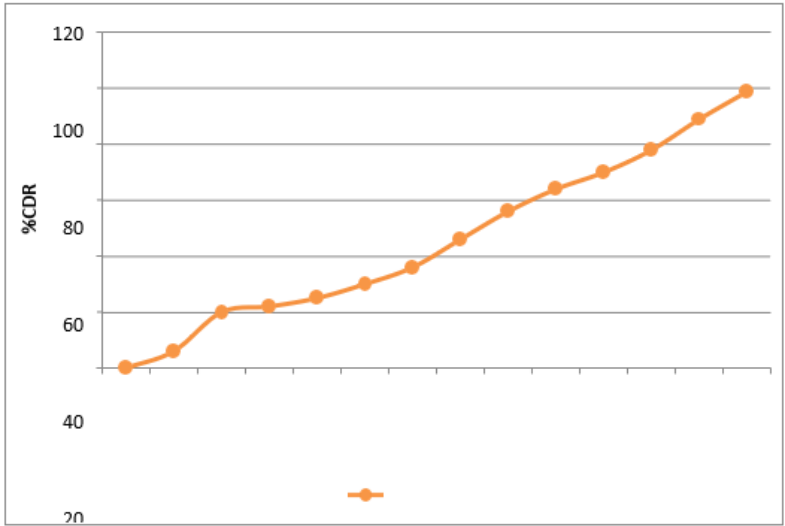


Fig. 35: In-vitro dissolution of PAG 5

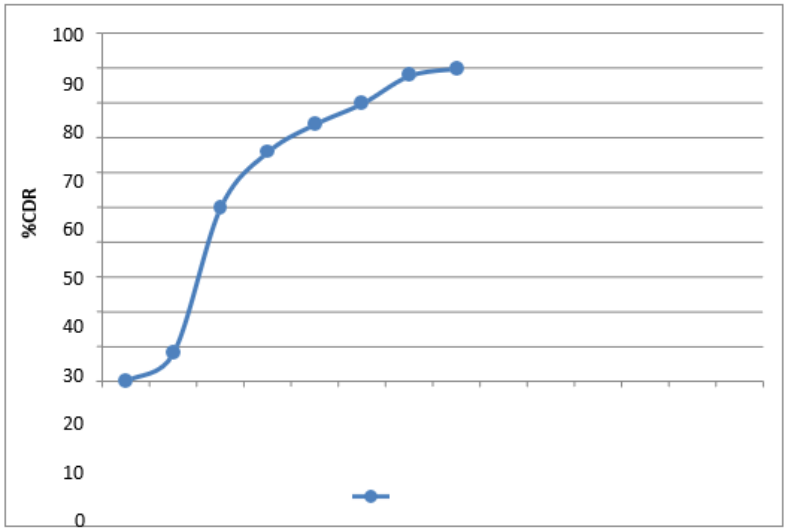


Fig. 36: In-vitro dissolution of MKT (Marketed)

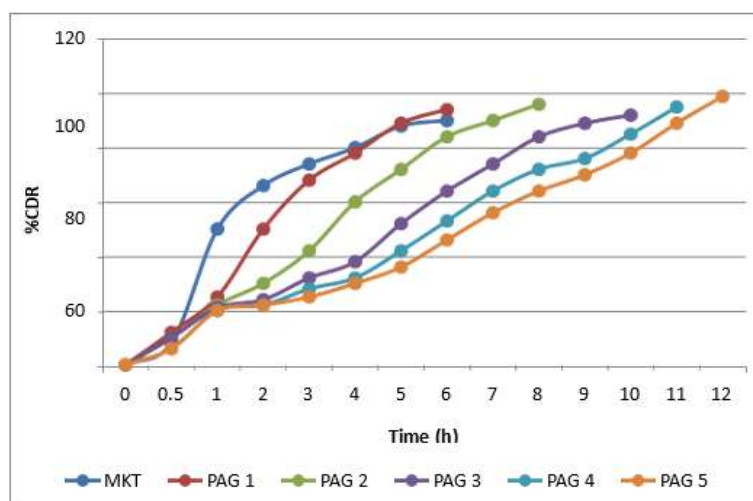


Figure 37: Dissolution characteristics of PAG1 to PAG5 Formulations

It has been shown that increasing the concentration of polymers in the formulations retards drug release from the matrices in all formulations.

• Kinetics of Drug Release

The drug release data from an in-vitro dissolution research was evaluated with multiple kinetic equations to establish the mechanism of drug release from this formulation. Different kinetic equations.

The information was analysed using the following criteria:

- Cumulative percent medication released vs time in a zero order kinetic model.
- Log cumulative percent drug left vs time in a first-order kinetic model.
- Cumulative percent of medication released vs. square root of time is Higuchi's model.
- Log cumulative percent medication released vs log time is Korsmeyer equation / Peppas's model

Table 17: Correlation coefficients according to different kinetic equations

Formulation	Zero order	First order	Higuchi model	Korsmeyer model	
		r ²		N	r ²
PAG1	0.989	-0.863	0.987	0.647	0.936
PAG2	0.987	-0.824	0.984	0.612	0.942
PAG3	0.992	-0.864	0.989	0.564	0.944
PAG4	0.992	-0.849	0.989	0.555	0.959
PAG5	0.994	-0.772	0.991	0.565	0.964
Marketed Preparation	0.962	-0.642	0.982	0.5145	0.934

Drug Release Kinetics

Zero order equation, $C = K_0 t$

First order equation, $\log C = \log C_0 - K_1 t / 2.303$

Higuchi's equation, $Q = K_H t^{1/2}$

Korsmeyer's et al equation, $\log (M_t/M_\infty) = \log K + n \log t$

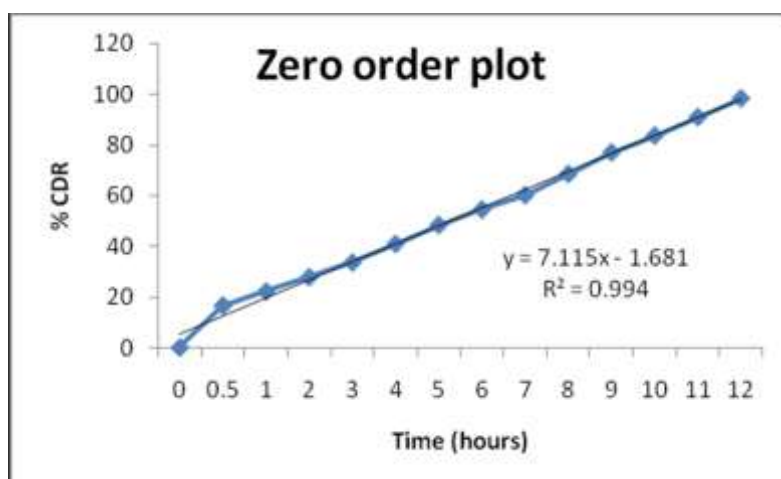


Fig. 38: Zero order release kinetics of optimized formulation PAG 5

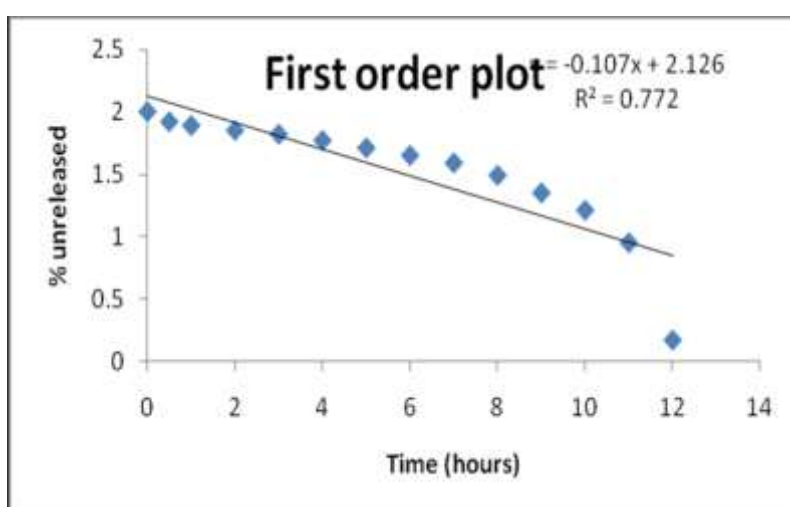


Fig. 39: First order release kinetics of optimized formulation PAG5

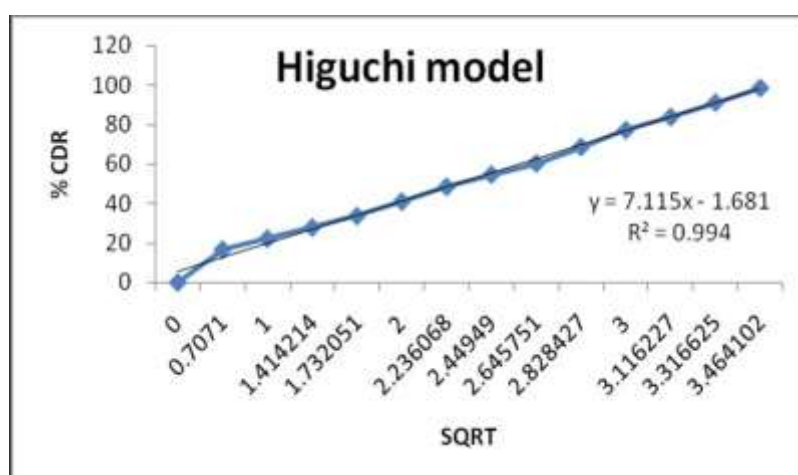


Fig. 40: Higuchi model release kinetics of optimized formulation PAG5

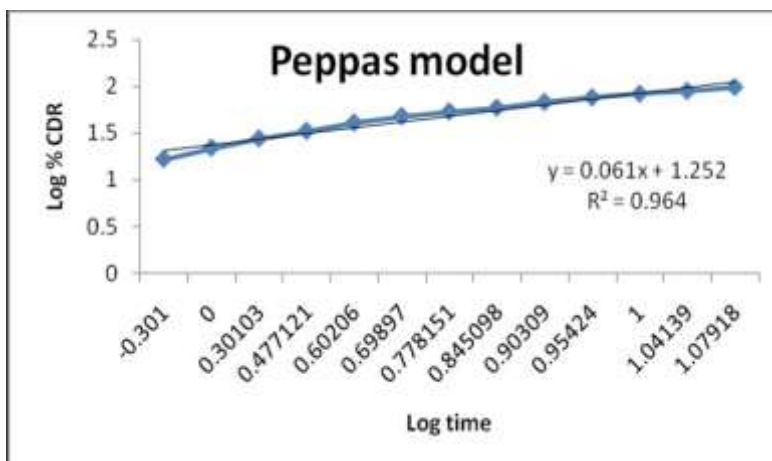


Fig. 41: Korsmeyer and Peppas release kinetics of optimized formulation PAG5

• Characteristics of swelling

The swelling was calculated as a percentage of the tablet's weight increase. Swelling behaviour was found in all formulations. In a petridish containing 0.1N HCL, one tablet from each formulation was preserved. The tablet was extracted after 1 hour,

soaked in tissue paper, and weighed. This technique was carried out for a total of 12 hours. $SI = (M_t - M_o) / M_o \times 100$ was used to compute the tablet's percentage weight gain. Where SI stands for swelling index, M_t for tablet weight at time t (h), and M_o for tablet weight at zero time.

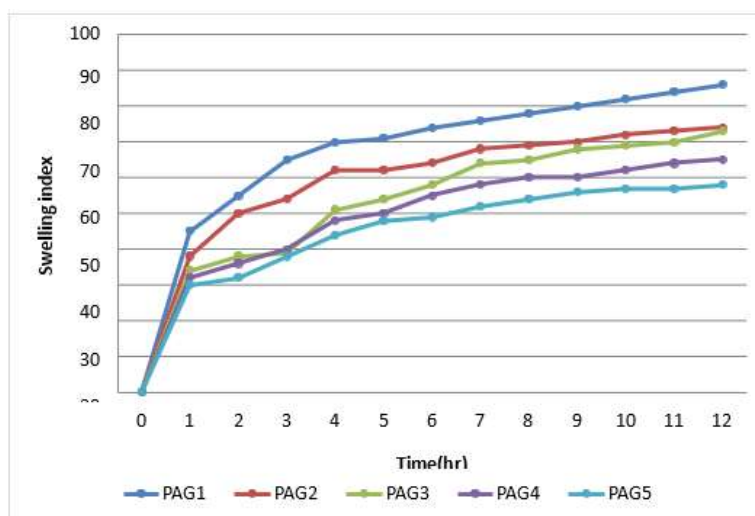


Fig 42: Swelling index of PAG1, PAG2, PAG3, PAG4, PAG5 matrix tablets

• Stability Analysis

Optimized formulation PAG 5 was packed in an air tight high-density polythene bottles and kept at 45°C

with 75% RH for 3 months as per ICH guidelines for stability. Samples were withdrawn at 0, 30, 60 and 90 days of storage and evaluated for appearance, hardness and drug content.

Table 18: Physical and chemical properties of prepared tablets (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

Deviation from the mean

Analysis Statistically

For the data acquired, the following statistical analyses were performed:

ANOVA

The ANOVA Methodology: The ANOVA table separates the components of data variance into treatment variation and error or residual variation. ANOVA tables are produced by statistical computing packages as part of their standard output for ANOVA, and the ANOVA table is set up as follows:

Table 19: The ANOVA table

Source of Variation	Sums of Squares (SS)	Degrees of Freedom (df)	Mean Squares (MS)	F
Between Treatments	$SSB = \sum n_j (\bar{X}_j - \bar{X})^2$	k-1	$MSB = \frac{SSB}{k-1}$	$F = \frac{MSB}{MSE}$
Error (or Residual)	$SSE = \sum \sum (X - \bar{X}_j)^2$	N-k	$MSE = \frac{SSE}{n-k}$	
Total	$SST = \sum \sum (X - \bar{X})^2$	N-1		

where X denotes an individual observation, $\bar{X}_j$ = sample mean of the jth treatment (or group), $\bar{X}$ = overall sample mean, and k denotes the number of treatments or comparison groups. N denotes the total number of observations or sample size.

The ANOVA table calculations.**Summary of data****Table 20: ANOVA table 1**

	Treatments					
	1	2	3	4	5	Total
N	20	20	20	21	20	101
$\sum X$	19.677	19.649	19.695	20.687	19.859	99.568
Mean	0.9839	0.9825	0.9848	0.9851	0.993	0.986
$\sum X^2$	19.3598	19.3047	19.397	20.381	19.719	98.1616
Std. Dev.	0.0057	0.0054	0.011	0.0109	0.0016	0.0085

Result details**Table 21: ANOVA table 2**

Source	SS	df	MS	
Between treatments	0.0014	4	0.0003	$F=5.51729$
Within treatments	0.0059	96	0.0001	
Total	0.0073	100		

The f- ratio value is 5.51729. The p-value is 0.000484. The result is significant at $p < .05$.

DISCUSSION

Determination whether direct compression or alternative granulation procedure is affected by the mixture flowability, assortment of excipient. Aloe barbadensis is a succulent from which mucilage of

aloevera is taken which pertains a yellow color. Matrix tablet preparation was done from it. 30° was the angle of repose of the mucilage which showed satisfactory flow. Flow ability of the powder blend's was inspected. A satisfactory flow was obtained. The tablets were directly compressed. From the dry powdered mucilage following parameters were inspected which were as follows; angle of repose, LBD, TBD, Carr's index, and Hausner's ratio. Carr's index (percent) value seen was 9.779 ± 1.35 to 12.28 ± 1.29 . Angle of repose seen was 25.67 ± 0.184 to 27.35 ± 1.79 . Also 0.250 ± 0.005 to 0.289 ± 0.003 reading was seen in LBD and 0.285 ± 0.012 to 0.317 ± 0.012 TBD respectively. Hausner's factor was 1.096 ± 0.22 to 1.142 ± 0.14 . Flowability was checked for the powder blend's. The results showed excellent flowability. This was further supported by lower Carr's index values. A range till 15% depicts very good flowability. The output product was reviewed for pharmacopoeial standards. Ideal parameters for difference in weight was obtained by the product. A steady breadth of tablet was measured. Shock proofing was obtained by The condition to be hard was $>5 \text{ kg/cm}^2$ and chances of crumpling less than 1%. An ideal amount of Repaglinide and Miglitol seen in the manufactured tablets. Checking of thickness, drug content, friability (crumpling capacity), and hardness for all tablets were done, and all the parameters were found admissible. Results demonstrated. The measured variation of 197 ± 2.24 to 203 ± 2.01 (weight variation) was seen. Difference (%) variation) on an average was unobjectionable (adequate), attributing approval of official weight test by all tablets. Difference in hardness was assessed 5.7 ± 0.2 to $6.6 \pm 0.1 \text{ kg/cm}^2$ for 10 tablets. Crumpling capacity in percentage (friability) for 10 tablets were assessed as 0.077 ± 0.31 to $0.087 \pm 0.13\%$. All of the tablet formulations had a percentage friability of less than 1%. The drug content of several batches of tablets ($n = 20$) was found to be consistent, ranging from 98.10 ± 0.3 to 99.67 ± 0.4 . All of the tablet formulations' swelling indexes were calculated over time. Because the weight obtained by the tablet rose proportionally as the rate of hydration increased up to a specific limit, the swelling index increased as time passed. Later on, as the tablet's outermost gelled coating dissolves into the dissolving media, it steadily shrinks. Swelling index and polymer concentration had a direct connection, with swelling index

increasing as polymer concentration rose. Figure 42 shows the swelling index of the produced tablets. The swelling index was shown to grow with time, but then decrease. In the PAG5 formulation, the proportion of edema was higher. When cumulative percentage of drug release for PAG1, PAG2, PAG3, PAG4, PAG5 were 94.73%, 96.92%, 92.89%, 95.29% and 98.89% respectively at the end of 12 h. Formulation of PAG1 failed to sustain release beyond 6 h. Among all the preparations PAG5 showed 98.89% at the end of 12 h. It was observed that cumulative percentage of drug release decreased with increase in processed aloevera concentration.

Drug release kinetics

The data were fitted to various mathematical models to evaluate the kinetics and mechanism of drug release. The coefficient (regression coefficient) obtained for zero order kinetics were seen higher ($R^2=0.987$ to 0.994), in comparison to first order kinetics ($R^2=0.772$ to 0.864) indicating that for all formulation drug release followed zero order kinetics. In this analysis the in vitro release profile of drug from all these formulations could be best expressed by Higuchi's equation which relates to the drug dissolution of water-soluble drug. This is because this plot showed highest linearity ($R^2=0.984$ to 0.991). In order to relate and confirm the diffusion mechanism the data were fitted to Korsemeyer-Peppas equation. It was observed that all these formulations showed good linearity ($R^2=0.936$ to 0.964) with slope (n) value ranging from 0.55 to 0.647. For the preparation of PAG1 to PAG5, the mechanism of release showed behaviour of anomalous (non-Fickian) diffusion. The ratio of drug and processed aloevera matrix increases it leads to the increase in n value. Coupling of diffusion, erosion mechanism (anomalous non-Fickian diffusion) is indicated by this n value. Therefore, it can be stated that diffusion coupled with erosion might be mechanism for drug release from aloevera matrix sustained release matrix tablets of Repaglinide and Miglitol. To conclude that in order to maintain effective plasma concentration, an ideal drug release with preset kinetics must be maintained for SR tablets. This can be consummated by such tablet fabrication which would release drug in calculable and repeatable way. Frequency of drug release can be calculated by researching the biopharmaceutical and

pharmacokinetic characteristics.⁵⁶ After 2 hours, drug release from the produced tablets was determined to be >20 percent, with zero-order release kinetics. When tablets made with A. Vera gel mucilage were compared to marketed tablets made with A. Vera gel mucilage, the rate of drug release from the marketed preparation was higher, confirming its release retardant qualities. The diffusion process and the de-integration procedure affects drug release. The PAG1 formulation had the greatest medication release rate. Within two hours, 12.15 - 50.89% of the medication had been released. Surface erosion of the matrix tablet prior to the creation of the gel layer surrounding the tablet core has been suggested as a possible reason. When compared to commercially available tablets, PAG5: the tablet with the greatest content of Aloe Vera mucilage displayed sluggish Repaglinide and Miglitol release. The PAG5 formulation released 64.73 percent of the medication in 8 hours, compared to 80 percent in 4 hours for commercially available Repaglinide and Miglitol tablets. A notable thing to be mentioned is that this formulation had more amount of aloe vera mucilage, which inhibited or delayed drug release. Calculation of drug release for 6 hrs depicted PAG1 having 94.73%. Where as when seen for 8 hrs. in PAG2 was 96.92%. PAG 3 being third had 84.98%. PAG 4 had 72.49%. When PAG1, PAG2, PAG3, PAG4 and PAG5 formulations were compared, PAG5 had more A. vera mucilage, which worked as a release retardant. According to the stability experiments, the formulation PAG5 did not alter significantly in terms of physical appearance, hardness, or drug content. As a result, the formulation remained stable under various storage circumstances. The findings clearly show that PAG may be used to modulate medication release by employing it in different ratios. We can eventually infer from the aforementioned experiments that aloevera mucilage can delay drug release. However further in IVIVC (invitro-in vivo correlation) can be established using in vivo animal models to claim the potential use of aloevera extract mucilage as release modifier.

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