

RESEARCH PAPER

Formulation Design and Evaluation of Sustained-Release Tablets of *Luffa cylindrica* for Anti Diabetic activity

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ABSTRACT

The objective of the present work is to develop a sustained release tablets from the hydro-alcoholic extract of fruits of *Luffa cylindrica* (LCHA) for anti-diabetic activity. Nine formulations (F1-F9) were developed by direct compression method on the basis of varying ratios of polymers HPMC K 100 M and ethyl cellulose. The pre-compression properties of powder blend and post compression parameter of developed SR tablets were determined. From the micromeritics (Flow properties) study it was found that all batch formulations exhibited the good flow properties of the powder blend. Prepared tablets were evaluated for thickness, diameter, weight variation, hardness, friability, Drug content, swelling behavior and drug release rate. The *In-vitro* dissolution studies was carried out in Phosphate buffer (pH 6.8) by using paddle over disc method. Among all the formulations, F9 formulation was comparatively releases maximum percentage of drug over 24 hrs. From the release kinetics study, it was concluded that optimized sustained release formulation F9 follows zero order drug release kinetics. Under the Stability study, no appreciable differences in the appearance, drug content, or in-vitro release of drug at 24 hours were seen. F9 exhibited significant antidiabetic activity.

Keywords: *Luffa cylindrica*, Antidiabetic, Sustained release, Direct compression, Pre- compression, Post-compression.

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INTRODUCTION

A person with diabetes mellitus has excessive blood sugar levels, which can be caused by either insufficient insulin production by the body or improper cell response to the insulin that is generated. The pancreas produces the hormone insulin, which allows body cells to absorb glucose and convert it into energy. If the glucose is not absorbed by the body's cells, it builds up in the blood and causes problems with the nerves, arteries, and other systems (Atulkathriya, 2012). Non-insulin dependent diabetes mellitus (NIDDM), a diverse group that encompasses milder types of the illness that mostly affect adults, accounts for the majority of patients with diabetes (Bhujbal et al., 2011). Despite their effectiveness in reducing blood glucose levels, insulin and synthetic oral anti-diabetic drugs, which are currently used to treat diabetic complications, have a number of side effects and cannot manage diabetic complications (Grover et al., 2002). Traditional medicinal plants are used to treat a range of diabetes issues all around the world. Numerous herbal remedies and minerals are used to cure diabetes mellitus, according to older traditional literature. Herbal medicines are believed to be less harmful and safer than synthetic manufactured drugs (Hayat et al., 2013). Examining the hypoglycemic potential of medicinal plants is essential to provide humanity with a safer alternative to herbal medications.

Predictable and repeatable release rates, longer half-life of short-acting medications, reduced toxicity, lower dosage

requirements, improved therapy, and increased patient compliance are all possible with sustained release delivery systems (Gilbert, 2002).

The synonym for *Luffa cylindrica* (L.) is *Luffa aegyptiaca*. Mill, sometimes called sponge gourd, loofa, vegetable sponge, bath sponge, or dish cloth gourd, is a member of the Cucurbitaceae family. It is a monoecious plant. It climbs on other solid surfaces to produce its large, cylindrical, green fruit, called a gourd (Oboh and Aluyor, 2009). *L. Cylindrica's* fruits, leaves, and flowers are frequently used medicinally (Chakravarty, 1990; Khare, 2007). *Luffa cylindrica's* potent antidiabetic properties were demonstrated by earlier research published by several researchers (Sahai & Kumar, 2023; Saliu et al., 2019; Sola et al., 2021; Hazra et al., 2011; Shukla et al., 2015; Akther et al., 2014). Therefore, the goal of the current study is to create sustained-release tablets containing a hydroalcoholic extract of *Luffa cylindrica* fruits in order to improve diabetes management, reduce the negative effects of synthetic oral medications, increase patient compliance, and stop the body's therapeutic concentration of the drug from fluctuating.

MATERIALS AND METHODS

Chemicals and reagents

In the present experimental work, all the reagents used were of analytical grade.

Collection and Authentication of Plant Material

The fresh immature fruit of *Luffa cylindrica* was collected and get authenticated by Department of Botany, University of Rajasthan, Jaipur Herbarium (RUBL). The submitted herbarium of plant is authenticated for future reference. Plant authentication numbers is RUBL21762.

Procurement and selection of animals

IEC School of Pharmacy, IEC University, Solan Himachal Pradesh provided Wistar albino rats of either sex weighing 150–200 gm. The animals were stabilized for a week before being housed in regular room temperature circumstances with a usual light-dark series. They were fed a standard pellet feed and provided unrestricted water during the study. The animals were handled carefully to reduce stress, which might result in an increase in adrenal production. The Institutional Animals Ethics Committee (IAEC) of the IEC School of Pharmacy approved all animal experimentation. The Reference number is IECU/SOP/IAEC/14/05/512.

Preparation of Extracts

The immature edible fruits of *L. cylindrica* were cleaned with water, chopped into small pieces, dried under shade for several days and then dried in an oven at reduced temperature (not more than 38.0 °C) to make it suitable for

grinding purpose. After grinding into coarse powder and sieved through Sieve no.40 it was were stored in an air-tight container. For the preparation of the extracts, a Soxhlet extraction procedure was carried out using Hydroalcoholic solvent (ethanol and water in the ratio of 70:30). For the preparation of extract, 500 g of powder and 1 L of solvent were placed in a Soxhlet extractor at 60-65 °C for 24 h. After completion of extraction, the solvent was removed by distillation, and the concentrated extract obtained was dried under reduced pressure using a rotatory evaporator at a temperature at 45°C under reduced pressure (97.3 kPa) (Brglez Mojzer et al., 2016) (Zhang et al., 2023). Extract was labelled as LCHA and stored in an airtight sterile container for further research.

Preparation of Sustained release matrix tablet of LCHA

A direct compression method was used to produce sustained release matrix tablets that contained 400 mg of *Luffa cylindrica* hydroalcoholic extract (LCHA). With the exception of talc and magnesium stearate, all materials were thoroughly combined in a polybag for a few minutes after passing through 60 mesh. After breaking up the clumps with a 100-mesh screen, talc and magnesium stearate were added to the mixture in a polybag and left for no more than five minutes. After that, the mixture is compressed at a steady compression force using a station rotary tablet press.

Table 1. Composition of different SR formulations (F1-F9) of LCHA

Ingredients(mg)	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
LCHA	400	400	400	400	400	400	400	400	400
HPMC K 100 M	100	120	140	140	140	140	150	160	170
Ethyl Cellulose (EC)	10	10	10	20	30	40	40	40	40
MCC	120	120	120	100	100	100	100	100	100
Magnesium stearate	10	10	10	10	10	10	10	10	10
Talc(mg)	20	20	20	20	20	20	20	20	20
Total weight	660	680	700	690	700	710	720	730	740

MCC= Microcrystalline cellulose

Pre-compression parameters

Using the static funnel method, the angle of repose (α) was estimated using the formula $\tan \theta = h/r$ (Krishnarajan et al., 2013; Pawan & Kumar, 2013; Patidar et al., 2011).

By adding five grams of the material to the measuring cylinder, the bulk density (BD) was determined. The unsettled apparent volume, V_0 , was read to the closest graded unit after the powder was leveled without compacting. Following formula was used to get the bulk density in grams per milliliter.

$$\text{Bulk Density} = m / V_0, \text{ (Krishnarajan et al., 2013)}$$

The powder's fill weight (5gm) was divided by its new reduced volume following 100 taps using a tap density device to determine the tap density (TD). By adding 5 grams of powder to the measuring cylinder, recording its initial volume, then subjecting the cylinder to 100 drops, the taped density was ascertained. The sample's ultimate volume in the measuring cylinder was noted and computed in relation to the powder's weight. The tapped density is calculated by using formula

$$\text{Tapped Density} = m / V_p$$

Where m – weight of the powder,

V_p - Tapped volume (Mahajan, et.al., 2011).

A powder's tendency to compress is gauged by the Compressibility Index, often known as Carr's Index. The bulk and tapped densities are used to calculate it. Compressibility Index is calculated using the following formula:

$$\text{Carr's Index} = [(tap - b) / tap] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Hausner's Ratio is a number that is correlated to the flow ability of a powder. Hausner's ratio is an indirect index of ease of powder flow.

$$\text{Hausner's Ratio} = \text{Tapped Density} / \text{Bulk Density}$$

Results of pre-compression parameters of Powder blend of all formulations are reported in table no.3.

Post compressional parameters

Physical appearance

The general appearance of all tablets like colour and size is determined. Size and shape of formulated tablets were evaluated. The diameter and thickness of the tablets were measured using Vernier caliper (Kasahikar & Patkar, 2011) and results are reported in table 4.

Weight variation

Twenty tablets of each formulation were chosen at random in order to calculate their average weight and examine the weight variation. According to Rathore et al. (2013), no individual weight shall differ from the average weight by more than twice the percentage, and no two weights may differ from the average weight by more than the percentage deviation. Table 4 reports the weight variation test results.

Hardness test

Hardness was measured using Monsanto harness tester. Unit of hardness is Kg/cm². 10 tablets were chosen randomly from each batch. Hardness of each tablet was noted (Patidar et.al., 2011; Rathore et.al., 2013; Kushwaha & Kori, 2014; Deepu et.al., 2014). Average hardness was determined and reported in 4.

Friability

A Roche friabilator was used to test the tablets' friability. From each batch, twenty tablets were chosen, and a soft brush was used to remove any remaining dust. After being weighed (W), the tablets were put into the friabilator. The tablets were taken out of the drum after it had been spinning at 25 rpm for four minutes. The tablets were weighed once again after any remaining dust was eliminated (W_F). The percentage friability was then calculated by,

$$\% F = W - W_F / W \times 100$$

Where,

% F = Friability in percentage

W = Initial weight of tablets

W_F = Weight of tablets after revolution (Radhika et al., 2015)

The results of % Friability is reported in table 4.

Drug content

Five tablets were selected at random from each batch. Each tablet was ground into a powder. Three separate 100ml volumetric flasks were filled with powder equal to the average weight of each tablet. The pH 6.8 phosphate buffer was added to each volumetric flask. The powder was completely dissolved in the pH 6.8 phosphate buffer. A sufficient amount of pH 6.8 phosphate buffer was poured to fill the volume. Solution was kept for 1hr. Wattman filter paper was used to filter the solution. At 274 nm, the filtrate's absorbance was measured with a double beam UV spectrophotometer (Systronics, India). (Krishnarajan et. al., 2013; Patidar et.al., 2011; Mahajan et.al., 2011). Results for Drug content are depicted in table 4

Swelling index

It is conducted to assess the degree of media penetration into the tablet. The swelling index was calculated using the equilibrium weight growth approach. A single tablet was

selected at random from each formulation batch. They were submerged in a beaker filled with medium (pH 6.8). Tablets were taken out, wiped with tissue paper, and weighed at regular intervals. This process was repeated for up to 24 hrs (Singh et al., 2010). SI was calculated using equation:

$$SI = W_t - W_0 / W_0 \times 100$$

Where: SI = Swelling Index

W₀ = weight of tablet at time zero

W_t = weight of tablet at time t

Swelling for formulation F1-F9 is shown in figure 1.

In-vitro Dissolution studies

Using a 500 mL phosphate buffer pH 6.8 and the paddle over disc method, a drug release study of sustained release tablets was performed. 500 cc of dissolution medium were utilized, and the paddle over disc apparatus was employed and run at a speed of 50 rpm with dissolution media at 32°C ± 0.5°C. Every time, a UV-visible spectrophotometer was used to study 5 ml aliquots for up to 24 hours, and evaluated spectroscopically (Reddy, 2010; Cherukuri et al, 2017). Withdrawn samples were analyzed using double-beam UV-Visible spectrophotometer (Systronics) at determined wavelength of 274 nm. A plot of cumulative % drug release v/s time was plotted. The results of In vitro dissolution study of formulation F1-F9 is shown in figure 2.

Drug Release Kinetics

Numerous mathematical models, including the Zero-order, first-order, Higuchi matrix, the Korsmeyer-Peppas models and the Hixson Crowell kinetic models, were used to study the drug release kinetics. The gathered information on drug dissolving in vitro was integrated into these graphical models in order to investigate the mechanism for releasing and release rate kinetics of the dosage form (Costa & Lobo, 2001; Gangurde, 2011). The best-fit model in this case was chosen by contrasting the obtained r² values.

Stability Study

Using a stability chamber, a stability analysis of the optimized and chosen SR formulation was carried out in accordance with ICH requirements at 75± 5% relative humidity (RH) and 40 ±2 °C temperature. The optimized formulation was maintained under observation for six months, during which time it was evaluated for its physical parameters, drug content, and drug dissolution to determine its physicochemical stability (Parhi & Padilam, 2018). Results of stability study of Optimized formulation F9 are reported in table 6.40.

In-vivo Antidiabetic Activity of Optimized sustained release tablets (F9)

Wistar albino rats of either sex weighing 150-200gm are taken for the study. There are six rats in each group. Fasted animals were deprived of food for at least 16 hrs., but allowed free access to water. Water was given to the first group, which served as the control. A single dosage of STZ (60 mg/kg b.wt) dissolved in citrate buffer was administered to the second group, which was then split into three subgroups following a week of diabetes establishment. The

first subgroup was maintained as a diabetic control group, and for a period of 12 weeks, the second and third subgroups had daily gastric intubation to receive the standard medicine (Glibenclamide, 5 mg/kg) and F9 (400 mg/kg b.wt) respectively (Swathi et al., 2017). Groups and treatment are shown in table 2.

Table 2. Treatment of animal groups

Groups	Treatment
I: Normal Control	0.5 % w/v sodium CMC in distilled water
II: Diabetic Control	STZ +0.5 % w/v sodium CMC in distilled water
III: Standard control	STZ + Glibenclamide, (5 mg/kg body weight)
IV: F9 SR Tablets	STZ + F9 (400 mg/kg body weight) suspended in 0.5 percent w/v sodium CMC

EXPERIMENTAL PROCEDURE

A blood sample was taken from the tail vein 24 hours post-injection, and the Accu-Chek Glucometer was used to determine the blood glucose level using the glucose oxidase method both before and 72 hours post-STZ injection. Animals with blood glucose levels greater than 250 mg/dl were chosen for additional anti-diabetic treatment. On the first, seventh, fourteen, and twenty-first days of the treatment, blood samples were drawn by pricking the rats' tail veins. The blood samples were then used right away to measure blood glucose using the Accu-Chek glucometer (Gajdosik et al., 1999). And results are reported in table 6.41 and figure 6.39.

STATISTICAL ANALYSIS

All the data expressed as mean \pm SEM were evaluated by one-way analysis of variance (ANOVA), followed by Dunnett's test using prism Graph pad version 5.0 and values of $P < 0.05$ were considered as statistically significant.

RESULT AND DISCUSSION

Several micromeritic parameters were used to estimate the powder blend's flow property. It is commonly recognized that flowability is influenced by particle shape and size. Larger, denser particles tend to flow freely, while finer particles (less than 100 μ m) tend to be more cohesive and less free-flowing. The angle of repose will increase with the particles' surface roughness and irregularity (Fu et al., 2020).

Table 3. Pre-compression parameters of powder blend for F1-F9

Formulation Code	Angle of Repose (Degree \pm SD)	Bulk density (g/ml \pm SD)	Tapped density (g/ml \pm SD)	Compressibility index (%)	Hausner's ratio
F1	26.03 \pm 0.20	0.489 \pm 0.00	0.572 \pm 0.05	14.51 \pm 0.12	1.16 \pm 0.011
F2	25.20 \pm 0.14	0.479 \pm 0.03	0.560 \pm 0.06	14.46 \pm 0.09	1.16 \pm 0.012
F3	25.09 \pm 0.16	0.472 \pm 0.02	0.548 \pm 0.12	13.86 \pm 0.13	1.16 \pm 0.011
F4	25.12 \pm 0.15	0.473 \pm 0.11	0.552 \pm 0.21	14.31 \pm 0.11	1.16 \pm 0.013
F5	26.71 \pm 0.27	0.481 \pm 0.10	0.563 \pm 0.16	14.56 \pm 0.07	1.17 \pm 0.015
F6	24.21 \pm 0.42	0.474 \pm 0.05	0.544 \pm 0.15	12.86 \pm 0.05	1.14 \pm 0.012
F7	24.28 \pm 0.18	0.476 \pm 0.01	0.549 \pm 0.12	13.29 \pm 0.02	1.15 \pm 0.011
F8	24.27 \pm 0.22	0.478 \pm 0.07	0.552 \pm 0.16	13.40 \pm 0.08	1.15 \pm 0.011
F9	24.11 \pm 0.23	0.475 \pm 0.06	0.543 \pm 0.07	12.52 \pm 0.04	1.14 \pm 0.010

*All the values are expressed as mean \pm SD, n=3.

Table 3 displayed the results of the powder blend's micromeritic characteristics. For every batch of powder blend, the angle of repose ranges between 20 and 30, indicating good flow characteristics. The homogeneous particle size range and reproducibility of the drug are confirmed by the small variances between the bulk density and the tapped density, which show that the change volume is much less even after 100 tappings (Ding et al., 2020). The flowability of the powder blend was further calculated using Hausner's ratio and the compressibility index. Table 3 shows that all batch powder blends had excellent to good flow qualities, with the percentage compressibility index value falling between 12.52 \pm 0.04 and 14.56 \pm 0.07 (%). The Hausner ratio for every batch powder blend was less than 1.25, indicating that all batches' powder blends had excellent flow characteristics. It was discovered that the

granules' Hausner's ratio ranged from 1.14 \pm 0.010 to 1.17 \pm 0.015. As a result, the micromeritics investigation revealed that every batch composition had good powder blend flow characteristics.

Post compressional parameters

All nine batches were discovered to be Bi-convex in shape. The color of the SR tablet was found to be Brown for all batches. The SR tablet's surface was smooth. As a result, it was determined that the preparation had no undissolved particles and that all of the excipients had been correctly dissolved. Thickness and diameters are determined and reported in Table 4. Tablet diameter and thickness were found to be in the range 10.00 \pm 0.01 to 10.07 \pm 0.07 mm \pm SD and 4.01 \pm 0.02 to 4.06 \pm 0.03 mm \pm SD respectively for all nine batches (Table 4).

According to IP, the limit of standard deviation should be ± 5 for the tablets weighing more than 250 mg. The weight of 20 tablets from each batch comes under the lower and upper limits. All the batches (20 tablets / batch) passed the weight variation test as per the upper and lower limits.

Table 4. Post compression Parameters of SR Tablets F1-F9

Formulation Code	Diameter (in mm) \pm SD	Thickness (in mm) \pm SD	Weight variation	Hardness (in kg/cm ²) \pm SD	% Friability	Drug content (%)
F1	10.02 \pm 0.01	4.02 \pm 0.04	Pass	4.59 \pm 0.28	0.26	95.1 \pm 0.43
F2	10.06 \pm 0.04	4.05 \pm 0.01	Pass	4.79 \pm 0.51	0.30	95.4 \pm 0.31
F3	10.07 \pm 0.07	4.01 \pm 0.02	Pass	4.86 \pm 0.37	0.27	93.1 \pm 0.72
F4	10.07 \pm 0.02	4.02 \pm 0.03	Pass	4.38 \pm 0.11	0.31	93.7 \pm 0.42
F5	10.04 \pm 0.04	4.06 \pm 0.03	Pass	4.42 \pm 0.18	0.27	94.1 \pm 0.50
F6	10.06 \pm 0.06	4.04 \pm 0.02	Pass	4.52 \pm 0.72	0.28	94.7 \pm 0.48
F7	10.03 \pm 0.02	4.02 \pm 0.02	Pass	4.46 \pm 0.32	0.30	95.3 \pm 0.25
F8	10.00 \pm 0.01	4.03 \pm 0.03	Pass	4.66 \pm 0.51	0.27	95.2 \pm 0.31
F9	10.00 \pm 0.03	4.02 \pm 0.03	Pass	4.72 \pm 0.63	0.28	95.6 \pm 0.26

*All the values are expressed as mean \pm SD, n=3.

To be able to endure and resist the stresses of mechanical shock and avoid breaking easily, tablets need to possess a specific amount of strength. Additionally, they ought to be resilient to moderate friction and abrasion. For tablets to be accepted by consumers, they must be sufficiently firm, resistant to powdering, and friable. It might also have an impact on the pace of breakdown and disintegration. As indicated in Table 4, the tablet hardness for each of the nine batches ranged from 4.38 \pm 0.11 to 4.86 \pm 0.37 kg/cm² \pm SD. According to table 4, the friability of each batch ranged from 0.26 to 0.31 percent, falling within the advised range of less than 1 percent. The comparatively high concentration of the binder utilized as matrix forming, however, might have been the source of this.

The drug content results of F1-F9 formulations were recorded in the table 4. All the batches were noted to have drug content within the limit. The prepared SR tablets showed drug content in the range of 93.1 \pm 0.72 to 95.6 \pm 0.26 %, which indicated the proper and even distribution of drug. Out of all the formulations, F9 showed best result in drug content study. All the results are depicted in table 4. Swelling is also an essential factor to confirm the drug dissolution of the matrix tablet. The percentage water

uptake of the formulations (F1-F9) was calculated and shown in Figure 1. The results show that an increase in polymer concentration and time duration results in an improvement in the swelling index. The swelling index rose as the concentration of polymers increased. According to a swelling index study, swelling grows with time as a result of the polymer's hydrophilic nature, which causes it to progressively absorb water. The hydrophilic polymer on the outside hydrates, swells, and forms a gel barrier on the outside. The integrity of the dosage form is maintained as the hydration swelling release process continues towards newly exposed surfaces as the gelatinous layer gradually dissolves and/or disperses. In the current investigation, tablets of batch F9 containing 170 mg of HPMC K 100 M (High viscosity polymer) had the highest swelling index. High viscosity grade polymers were discovered to have a greater swelling index. Thus, the swelling process, matrix integrity, and sustained release capability were all significantly impacted by the polymer's viscosity. Based on the aforementioned findings, it can be said that there is a linear relationship between the swelling process and the concentration of high viscous polymer.

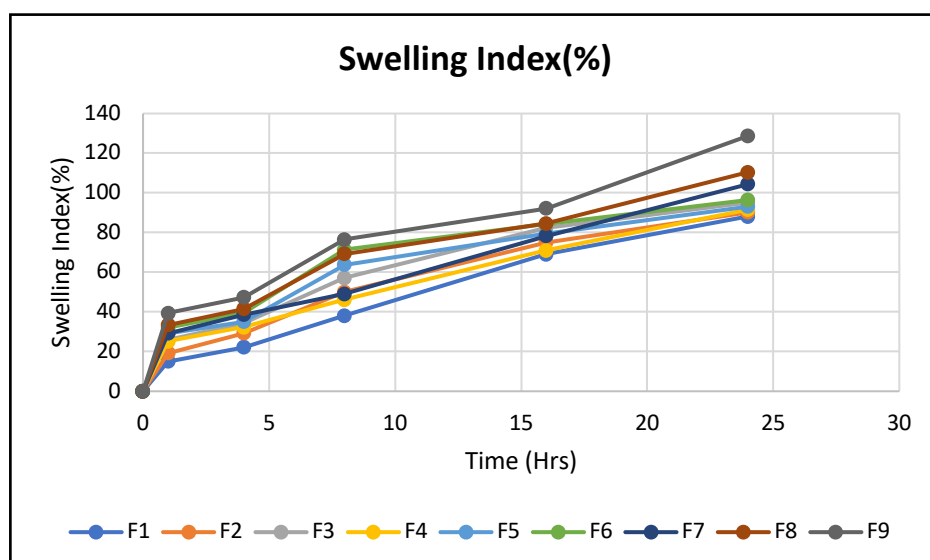


Figure 1. Swelling Index (%) of SR Tablets F1-F9

In Vitro Drug Release

As indicated in Figure 2, formulations F1, F2, and F3 demonstrated bursts of LCHA release ($52.12 \pm 0.11\%$, $49.16 \pm 0.21\%$, and $45.14 \pm 0.29\%$ during a 2-hour period). This is explained by the time it took HPMC K 100 M to produce the fully hydrated gel; during this period, drug release was not controlled, even if ethyl cellulose was present but appeared to be insufficiently concentrated. MCC, which also possesses disintegrating properties because to its capillary structure, appeared to increase this impact. The initial burst of drug release was caused by water dissolving the medication more quickly through these

capillary pores of MCC. There was minimal improvement in regulating the initial burst of drug release even after raising the HPMC K 100 M concentration in F2 and F3 to 120 mg and 140 mg, respectively. The drug release slowed once the hydrated matrix of HPMC K 100 M was established, however it was still comparatively quick ($89.66 \pm 0.47\%$, $86.05 \pm 0.15\%$, and $79.12 \pm 0.24\%$ within 8 hours). For the F2 and F3 formulations, cumulative drug release at the end of 10 and 12 hours was 91.71 ± 0.70 and 92.13 ± 0.14 percent, respectively.

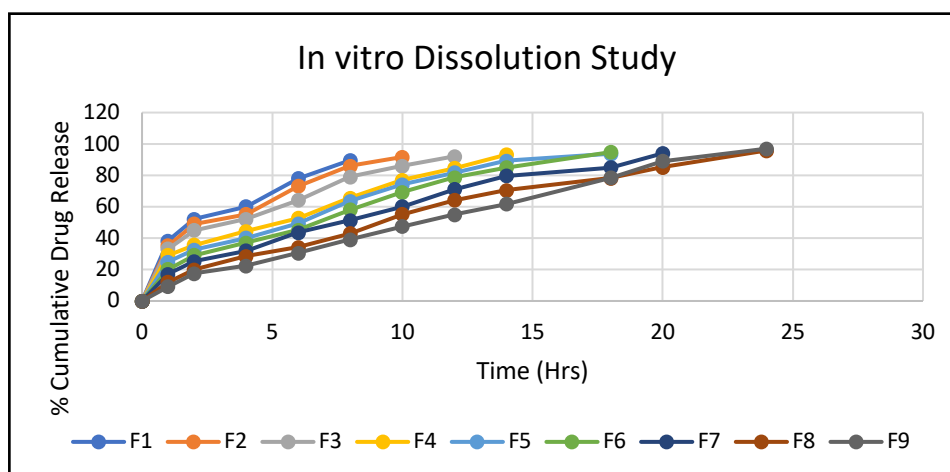


Figure 2. In Vitro Drug Release of SR Tablets F4-F6

Based on these findings, the concentration of HPMC K 100 M was maintained at 140 mg for the next three batches, and MCC was decreased to lessen the impacts of disintegration. To regulate the initial drug release till the development of the fully hydrated HPMC K 100 M matrix, the concentration of ethyl cellulose was raised. Following these modifications, as indicated in figure 2, F4, F5, and F6 displayed comparatively smaller initial bursts of drug

release ($29.10 \pm 0.05\%$, $24.86 \pm 0.22\%$, and $20.18 \pm 0.33\%$, respectively after one hour); this could be because ethyl cellulose was added. Because EC is hydrophobic, solvent molecules were unable to enter the tablet core, which decreased the drug's diffusion from the matrix. When 40 mg of EC was added to F6, this impact was greatest. Drug release was comparatively faster but more uniform once the HPMC K 100 M matrix was created. After 14 hours, the

cumulative drug release for the F4 formulation was $93.20 \pm 0.32\%$. After 18 hours, the cumulative drug release for the F5 and F6 formulations was 93.77 ± 0.49 and 94.80 ± 0.36 percent, respectively.

Therefore, in the next three batches finest concentration of EC was taken as 40 mg and was kept constant while concentration of HPMC K 100 M was increased to get more uniform drug release.

Following these modifications After an hour, the initial burst of drug release was comparatively lower in F7, F8, and F9 ($17.12 \pm 0.25\%$, $12.05 \pm 0.19\%$, and $9.22 \pm 0.14\%$, respectively). Lastly, F7, F8, and F9 displayed remarkably consistent drug release. After a 24-hour period, the cumulative drug release in formulations F8 and F9 was 95.89 ± 0.19 and $97.02 \pm 0.54\%$, respectively. The current study demonstrated that drug release from the matrix core

becomes more regulated as HPMC K100 M concentration rises. By absorbing water, HPMC K 100 M swells and creates a swelled layer barrier that allows drugs to diffuse through. The diffusion barrier layer gets thicker as the percentage of HPMC K 100 M in the tablet rises.

Drug Release Kinetics

The data of drug release of Optimized formulation F9 was fitted into various kinetic models, including Zero-order, First-order, Higuchi equation, Korsmeyer-Peppas, and Hixson-Crowell equation. The graphs were plotted for all the models as including Zero-order (Figure 3), First-order (Figure 4), Higuchi equation (Figure 5), Korsmeyer-Peppas (Figure 6), and Hixson-Crowell (Figure 7) and results are illustrated in table 5.

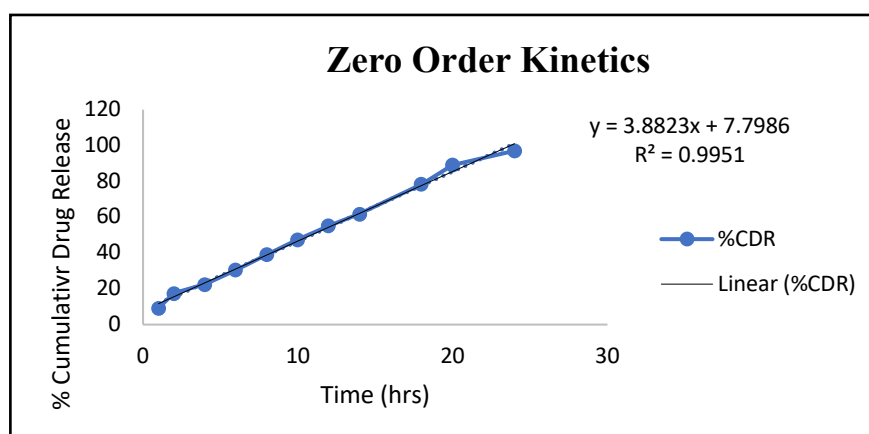


Figure 3. Zero order kinetic plot of F9

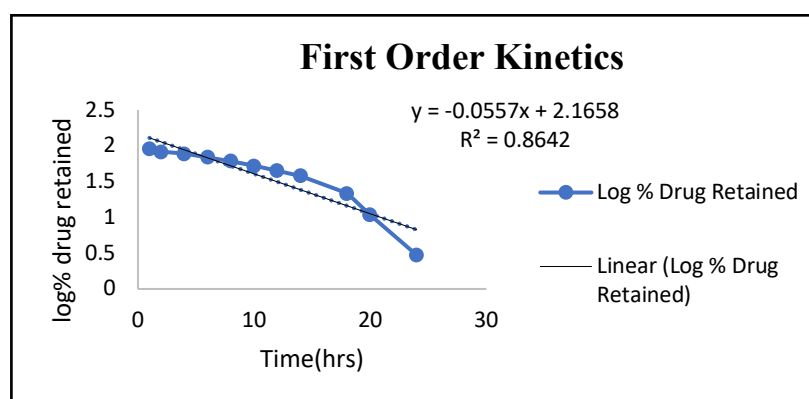


Figure 4. First order kinetics plot of F9

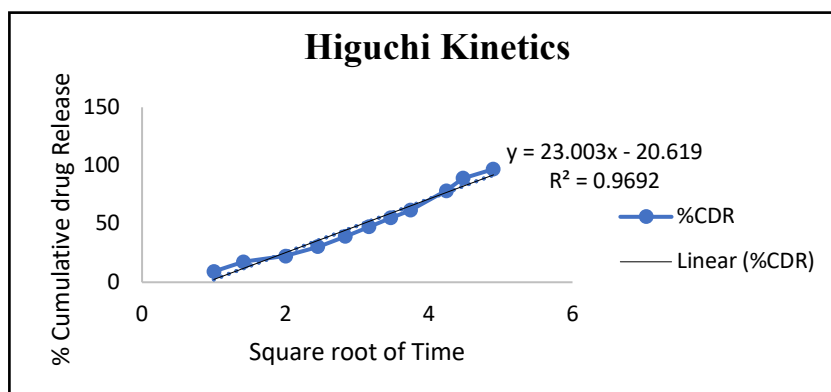


Figure 5. Higuchi plot of F9

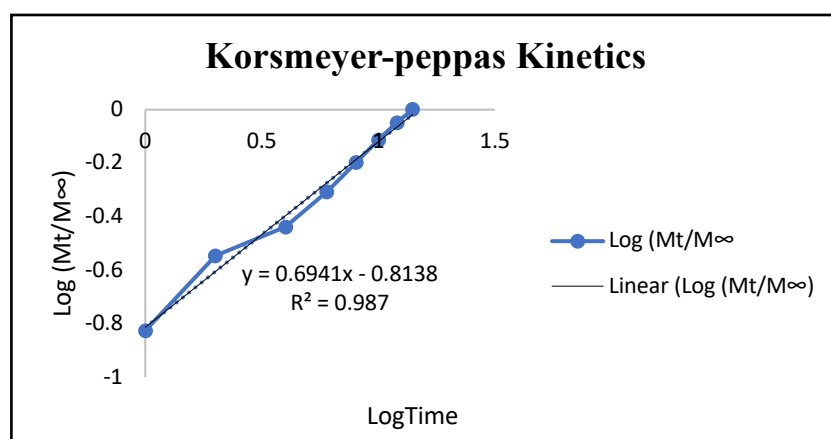


Figure 6. Korsmeyer peppas plot of F9

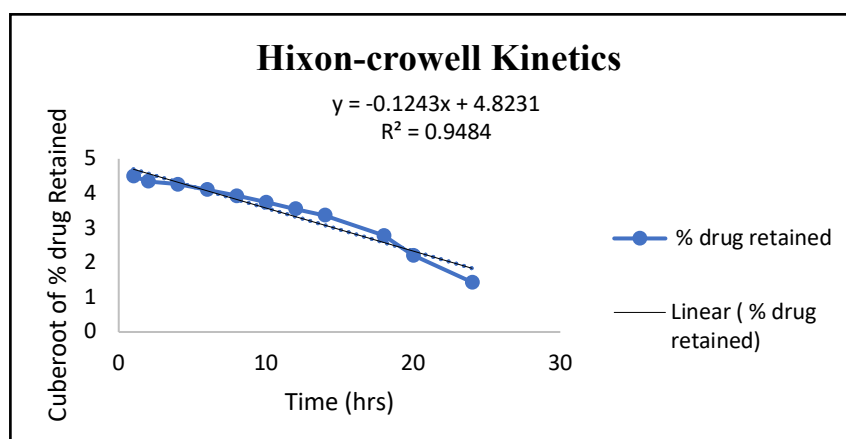


Figure 7. Hixon plot of F9

Table 5. *In-vitro* Release Kinetics of Optimized Formulation F9

Formulation Code	Correlation coefficient (R ²)					Diffusion Exponent 'n'
	Zero order	First order	Higuchi	Hixson	Korsmeyer Peppas	
F9	0.9951	0.8642	0.9692	0.9484	0.987	0.69

The curve fitting for several models was found done and the n value was found to be 0.69. In Zero order, graph was plotted between cumulative percentage drug released versus time and was observed to be linear with the higher regression coefficient value of was $r^2 = 0.995$. From the above data, it was concluded that optimized sustained release formulation F9 follows zero order drug release

kinetics.

The primary mechanism of drug release from hydrophilic matrices involves polymer swelling on contact with the aqueous medium and forming a gel layer and the drug releasing by dissolution, diffusion and/or erosion; hence facilitating zero order release (Colombo, 1993; Ishikawa et al., 2000; Tiwari and Rajabi-Siahboomi, 2008).The exact

mechanism of was confirmed by fitting the data in Korsmeyer-Peppas model, where the regression coefficient was found to be 0.987 with release exponent $n = 0.69$ which is more than 0.45 but less than 1. Hence, it was ascertained that the drug is releasing through anomalous non-Fickian diffusion.

Stability Study

F9 was chosen as the best sustained release tablet from the drug release results and was employed in additional research. By choosing F9 sustained release tablet, the stability study was carried out for six months. The tablets

physical characteristics, drug content, and in-vitro drug release were examined. This study's findings showed that formulation held up well under accelerated settings for 180 days. Under the aforementioned settings, no appreciable differences in the appearance, drug content, or in-vitro release of medicines at 24 hours were seen. Statistical test of data obtained with drug content and drug release study also confirmed the absence of significant difference ($P < 0.05$) among stored and fresh SR tablets, indicating the sufficient stability. Results of stability study are shown in Table 6.

Table 6. Stability Study of F9 Stored at 40°C/75% RH

Tested After Days	Physical Appearance	Drug Content (%)	In-vitro Drug Release
0	Brown Color and smooth	95.6 ± 0.26	97.16±1.2
30	Brown Color and smooth	95.6± 0.26	97.11±1.8
60	Brown Color and smooth	95.6± 0.24	97.02±0.07
90	Brown Color and smooth	94.4± 0.6	96.93±0.03
180	Brown Color and smooth	94.1 ± 0.4	96.51±0.5

Effect of Optimized sustained release tablets (F9) on blood glucose level

Optimized Sustained release tablet (F9) of *Luffa cylindrica* hydroalcoholic extract was subjected to anti-diabetic activity in rats where STZ (60 mg/kg b.wt) used as the diabetogenic agent. A marked rise in fasting blood glucose level was observed in diabetic control rats as compared to normal control rats. After 21 days of treatment, glucose

levels were significantly lowered in Glibenclamide (III Group) and F9 (IV Group) treated groups. F9 significantly ($P < 0.01$) lowered the elevated serum blood glucose level on 7th day post treatment. Glibenclamide produced a significant reduction ($P < 0.001$) in blood glucose as compare to diabetic control on 21st day. F9 Showed significant lowering ($P < 0.001$) in blood glucose level from the 14th day as shown in figure 8.

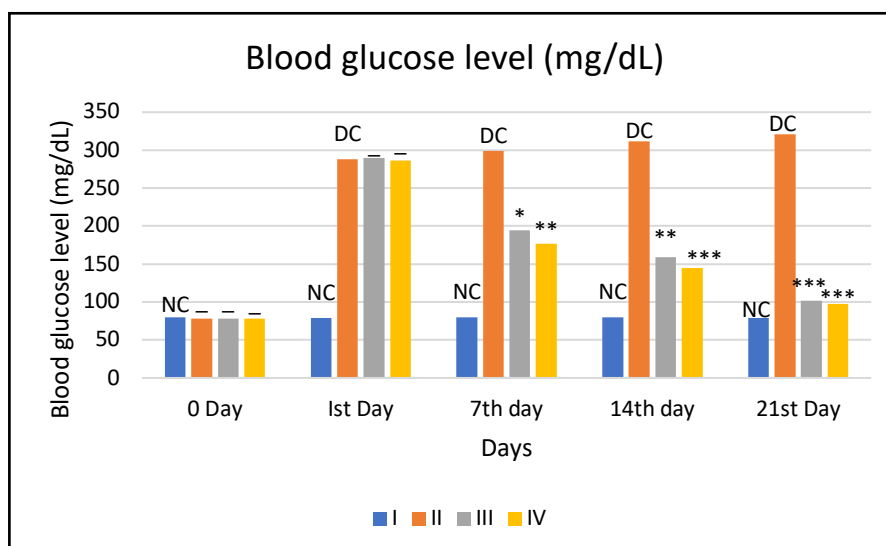


Figure 8. Antihyperglycemic activity of Optimized SR Tablets F9 on STZ-induced diabetic rat. Data were expressed as Mean ± SEM (n=6) * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ Vs Diabetic Control. DC=Diabetic Control, NC= Normal Control.

F9 Sustained-release (SR) tablets show more consistent and potentially more effective blood glucose reduction compared to Glibenclamide due to a more stable and prolonged release of the medication. This controlled release leads to more consistent blood sugar levels.

CONCLUSION

In the present study Sustained release tablets of hydroalcoholic extract of *Luffa cylindrica* fruits are prepared by direct compression method using a combination of HPMC K 100 M and Ethyl cellulose polymers. The optimized formulation F9 showed good post compression properties like thickness, Diameter, weight variation,

hardness, friability, Drug content, swelling behavior and release rate. The *in vitro* drug release is more controlled in SR tablet F9 because of the increased concentration of HPMC K100 M. HPMC K 100 M swells by absorbing water and forms a swollen barrier layer for drug to diffuse through this layer. As proportion of HPMC K 100 M in tablet is increased, thickness of the diffusion barrier layer increases. Formulation F9 exhibited significant anti-diabetic activity. Further extraction and purification of bioactive phytoconstituents from *Luffa cylindrica* fruits might ensure the existence of a strong innovative anti-diabetic drug, also the molecule contrivance overdue their satisfying activity.

Conflict of Interest: The authors declare no conflict of interest.

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