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Exploring the Potential of *Momordica charantia* Fruits Mucilage as a Novel Pharmaceutical Excipient

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The discovery and developments of new drug formulations are inspired by medicinal plants. Polysaccharides, such as mucilage or gum from medicinal plants, have a variety of physicochemical properties and are commonly used in pharmaceutical applications.
Objectives: The current study's objectives are to construct and assess Metformin HCl tablets employing *Momordica charantia* (MC) natural mucilage as a binder and release modifier.
Methods: The mucilage was isolated from the fruits of MC. The tablet was made using a wet granulation process, and the formulation included several mucilage ratios (1%, 2.5%, 5%, and 10%).
Results: It was found that the granules and tablets had good flow qualities based on results of the pre- and post-compression parameters. The release kinetic study showed that F4 showed the first order release kinetics and F8 showed the zero and the higuchi's release kinetics. In low

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concentration of mucilage tablets showed good binding properties with immediate release properties. As the concentration was increased, tablets showed good binding properties with sustained release properties.
Conclusion: The isolated mucilage from Momordica charantias has the potential to be used as a tablet binder and as an intermediary in the development of a sustained-release drug

Keywords: Momordica charantia; mucilage; binder; metformin HCl; sustained release.

1. INTRODUCTION

Mucilage is a thick, sticky substance produced by almost all plants and some microorganisms [1]. It is a polymeric polysaccharide complex and water-soluble adhesive material that contains glycoprotein and a variety of bioactive components present in different parts of plants, such as seeds, leaves, and fruits [2]. Because of the bio-incompatibility, toxicity, and carcinogenic activity of synthetic polymers, plant-based, naturally generated biopolymers such as mucilage have received more attention as crucial constituents in the creation of sustainable, eco-friendly, and cost-effective goods [3,4]. Mucilage is used as tablet binders and disintegrates, as well as, suspending, emulsifying [5], thickening, gelling, stabilizing, and sustaining agents in tablets [1]. Nowadays, natural mucilage may be changed into synthetic or artificial excipients to satisfy the necessities of drug delivery systems [6]. In the manufacturing of tablets, binders, often referred to as adhesives and pharmaceutical excipients, are utilized. Improving the flow characteristics of granules by aggregating the powder of other ingredients in a tablet. The disintegration time increases in direct proportion to the binder concentration in a tablet. Binder is widely used in the wet granulation process [7]. The Cucurbitaceae family includes *Momordica charantia* (MC), often known as the bitter melon, bitter guard, karela, etc. Throughout the world, *Momordica charantia* fruits, seeds, and other parts have been used to treat both normal and diabetic individuals for diabetes[8]. By enhancing glucose absorption and glycogen synthesis in the liver, muscles, and fat cells, oral treatment with the fruit juice or seed of M. charantia decreases fasting blood glucose and improves glucose tolerance [9]. Metformin hydrochloride is an anti-diabetic drug that is taken orally, is derived from the biguanide family, and is widely used in the treatment of type II diabetes [10]. Metformin has a 50–60% bioavailability and a 1.5–4.5 h plasma half-life, which are both relatively short. Therefore, the requirement for administration 2-3 times a day when higher dosages are required can reduce patient compliance [11].

The objective of the current study was to manufacture oral sustained-release tablets of Metformin hydrochloride (HCl) using a wet granulation process, mucilage from *Momordica charantia* fruits, starch, and other ingredients with various concentration ratios and to evaluate the effects of polymer concentration on the duration of drug release.

2. MATERIALS AND METHODS

2.1 Plant Materials

The fruits of *Momordica charantia* were collected from Local Market at Chittagong division in Bangladesh and authenticated by Md. Boktear Uddin, Professor, Department of Botany, University of Chittagong, Bangladesh. A voucher specimen was deposited (Accession No.TA-03122022-6443) at the herbarium in the Department of Botany, University of Chittagong, Bangladesh.

2.2 Drug and Chemicals

Metformin HCl was obtained from Ibne Sina Pharmaceutical Limited, Barisal, Bangladesh as gift sample. All the other materials, such as Potato Starch, Lactose, Microcrystalline Cellulose (MCC), Talc and Magnesium stearate were of pharmaceutical grade and were purchased from Taj Chemical Store, Chittagong, Bangladesh.

2.3 Separation of Mucilage Fruits

For the purpose of isolating mucilage from the fruits of *Momordica charantia*, an established procedure previously reported by Barua et al., [12] was used with a few slight modifications, as will be explained below.

Step 1: Extraction of Mucilage

Momordica charantia fruits were collected, washed of any adhering dirt, and then dried in the sun. The dried fruits were mashed using a mechanical grinder. To release the mucilage into the water, the powdered fruits (150 g) was macerated in 400 mL of warm (50 °C) distilled water for 8 hours, boiled for 2 hours, and then left to stand for an additional 2 hours. The macerate was poured into a muslin bag, and 100 mL of the filtrate was obtained after filtering.

Step 2: Isolation of Mucilage

Acetone (450 mL) was added to the filtrate (150 mL) that was collected in the previous step. Due to the insolubility of mucilage in acetone, the mucilage was precipitated from the solution. Then the mucilage was washed into distilled water and precipitated by filter paper. The precipitated mucilage was filtered and dried in an oven at 40 °C. The dried mucilage was grounded and passed through an 80-mesh sieve. The sieved mucilage (11.85 g) was stored in desiccators until further use.

2.4 Physicochemical Identifications of Isolated Mucilage

2.4.1 Chemical characterization

An aqueous solution of the isolated mucilage was used for chemical characterization. Carbohydrates, proteins, mucilage, gums, alkaloids, fats, and tannins were tested according to standard procedure [13].

Solubility test: Solubility of the dried fruits mucilage of *Momordica charantia* was determined by dissolving in different solvents like acetone, methanol, ethanol, etc [13]

2.4.2 Organoleptic properties

The isolated mucilage was taken for organoleptic properties like color, odor, taste, and texture[13].

2.5 Swelling Index

About 1g of the mucilage powder with a tapped volume in a 25 ml glass-stoppered measuring cylinder was dispersed with 25 ml of distilled water and cylinder and shaken thoroughly every 10 minutes for 1 h. Then it was allowed to stand for 3 hours at room temperature. The increased volume of water that was occupied by the swollen mucilage was measured. The procedure was repeated twice more, and the swelling index was calculated [13].

2.6 Evaluation and preparation of Metformin Tablets with Mucilage

2.6.1 Preparation of granules

Wet granulation technique was used to uniform distribution of drug as well as improve flow property. So, this approach was carried forward for the formulation development of new metformin tablets. Metformin HCl was used as a model drug to formulate the granules. Microcrystalline cellulose was used as disintegrate, and lactose was used as a diluent in the composition. Tablets were prepared by using mucilage at 2.0%, 2.5%, 5.0%, and 10.0% w/v with 10.0% starch in concentrations [14].

2.6.2 Preparation of tablets compression

The granules were prepared by a wet granulation process with a single punch machine for tablet manufacturing. In vitro drug release, hardness

Table 1. Formulation of *Momordica charantia* tablets (mg)

	Formulations (mg)								
Ingradients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Metformin HCl	500	500	500	500	500	500	500	500	500
Mucilage	1%	2.5%	5%	10%	1%	2.5%	5%	10%	-
Maige starch	-	-	-	-	10%	10%	10%	10%	10%
Povidone	9.6	9.6	9.6	9.6	9.6	9.6	9.6	9.6	9.6
Mcc	88	88	88	88	88	88	88	88	88
Mg stearate	4	4	4	4	4	4	4	4	4
Talc	8	8	8	8	8	8	8	8	8
Lactose	182.4	170.4	150.4	110.4	102.4	90.4	70.4	30.4	110.4
Water	qs	qs	qs	qs	qs	qs	qs	qs	qs
Total	800	800	800	800	800	800	800	800	800

(by Monsanto hardness tester), friability (Roche Friabilator), disintegration time, and average weight variation were just some of the parameters that the produced tablets were analyzed for [14].

3. RESULTS

3.1 Physicochemical Characterization

The results of Molisch's Test, which produced a purple color on powdered particles, and the Ruthenium Red Test, which produced a pink color on powdered particles, respectively, indicated the presence of carbohydrates and mucilage. The phytochemical analysis of natural mucilage showed the presence of polysaccharides in nature (Table 3). Mucilage's physical, chemical, and organoleptic characteristics were established. The results of the morphological and physical evaluation examinations showed a brownish powder that was odorless and tasted distinctive (Table 2).The mucilage was completely soluble in warm water, whereas all of the chemical solvents used to dissolve it were essentially insoluble (Table 4). The mucilage's pH was discovered to be 6.1, which is extremely close to neutral, with a swelling index of 13.6 and a yield of 5.33 %.

Table 2. Organoleptic properties of isolate mucilage

Parameters	Results
Colour	Brownish
Odour	Odourless
Taste	Characteristic
Yield	5.33%
pH	6.1
Swelling Index	13.6

Table 3. Phytochemical properties of isolated mucilage

Phytochemicals	Result
Carbohydrates	+
Tannins	-
Alkaloids	-
Glycosides	-
Flavonoids	-
Reducing sugar	-
Protein	-
Mucilage	+

Note: '+' sign indicates Present and '–' sign indicates absent

Table 4. Solubility profile of isolated mucilage

Solvent	Solubility
Water	Soluble (Colloidal solution)
Hot water	Soluble (Thicky solution)
Methanol	Insoluble
Ethanol	Insoluble
Acetone	Insoluble
n-Hexan	Insoluble

3.2 Pre-compression Evaluation of Granules

Granules were established to have an acceptable appearance. The formulation of the granules was done, and their bulk density (BD), tapped density (TD), Carr's index, Hausner's ratio, and angle of repose were all analyzed. With the funnel method, the angle of repose was calculated. By applying the cylinder method, the bulk density and the tapped density were calculated, and the Carr's index (CI) was then calculated by this formula: (TBD-BD)/100. Powder flow properties could be predicted using Hausner's ratio, which was connected to interparticulate friction [15]. The bulk density and tapped density for all formulations were found in the range of 0.31±0.01 F (1) to 0.33±0.03F (9) g/cm3 and 0.33±0.03F (1) to 0.37±0.01F (9) g/cm3, respectively. Hausner's values ranged from 1.06±0.01F (1) to 1.12±0.01F (9) (<1.25) indicating good flow properties. The value of the angle of repose the range of 22.78± 0.02F (1) to 23.75± 0.01F (9) (<40º) which indicates a good flow property of the powder. It was observed that the granules showed good to excellent flow properties based on the values of angle of repose, bulk density, tap density, compressibility index, and Hausner's ratio as per Table 5.

3.3 Post-Compression Evaluations of Tablets

The physical appearance of the tablets was found to be satisfactory. The compressed tablet and reference standard were tested for hardness, thickness, percentage friability, weight variation, disintegration time, and dissolution. The hardness of the tablets was tested using a hardness tester. The thickness of the tablets was measured by a digital vernier caliper. Friability of the tablets was determined in a Roche friabilator (Electrolab). A weight variation test was performed according to the laboratory method [16]. The average weight of twenty tablets was calculated for each batch, which varied from

796.8±1.46 (F1) to 798.29±1.38F (9) mg. Hardness was found to be from 2.17±0.29 (F1) to 4.00±0.87 (F9). The friability values of the prepared tablets ranged from 0.61±0.01 (F1) to 0.35±0.13 (F9). All formulations showed less than 1% (w/w) friability, which was within the prescribed limits. Disintegration time for all formulations ranges from 2.00±0.45F (1) to 4.99±0.59 (F9) in minutes. The present study shows that among all the formulations of tablets, batches F4 and F8 have good disintegration properties (Table 6).

3.4 *In vitro* Drug Release Study

The mucilage of MC was used to prepare nine batches of tablets containing four different concentrations of the drug (1, 2.5, 5, 10% w/w). In in-vitro dissolution profile analysis, formulations F-4 to F-8 were composed of 10% of mucilage along or with 10% starch, released the 40.8% and 31.63 % of drug in 60 minutes respectively. It was found that varied ratios of mucilage were used in the release of drugs from tablets; as mucilage concentration increased, so increased the extent of the drug release. Sustain released formulation were developed by using mucilage with starch (10%) and release were prolonged by increasing concentration of mucilage (Table 7).

3.5 Drug Release Kinetics

Release kinetics is crucial for new drug formulation as it directly impacts therapeutic efficacy, pharmacokinetics, patient compliance, safety, and intellectual property. To describe the kinetics of drug release from tablets, release data was analyzed according to different kinetics, e.g., zero order, first order, and Higuchi plots are shown in Figs 1, 2 and 3, respectively. The regression coefficient (R^2) value obtained from the first order, zero order and Higuchi plot were examined to find out the release mechanism [17,18]. In the release kinetic study (Table 8) showed that F4 showed the first order release kinetics and F8 showed the zero and the Higuchi,s release kinetics as sustained release dosage form.

Table 5. Pre-compression evaluation of Metformin HCl granules

Formulations	Bulk density(g/cm^3)	Tapped density(g/cm^3)	Hausner's Ratio	Carr's Index (%)	Angle of repose (°)
F1	0.31± 0.01	0.33± 0.01	1.06± 0.01	6.14± 0.01	22.78± 0.02
F2	0.34± 0.01	0.38± 0.01	1.12± 0.02	10.41± 0.01	23.73± 0.08
F3	0.35± 0.04	0.41± 0.02	1.13± 0.01	16.74± 0.77	23.32± 0.03
F4	0.42± 0.02	0.52±0.02	1.19± 0.01	16.63± 0.74	24.35± 0.02
F5	0.37± 0.03	0.43± 0.02	1.16± 0.01	13.87± 0.06	24.23± 0.02
F6	0.40± 0.01	0.47± 0.01	1.19± 0.01	15.99± 0.06	22.57± 0.03
F7	0.41± 0.01	0.52± 0.03	1.23± 0.06	16.85± 0.06	23.76± 0.03
F8	0.44± 0.03	0.51±0.01	1.14± 0.01	12.79± 0.07	22.22± 0.02
F9	0.33± 0.03	0.37± 0.01	1.12± 0.01	13.73± 0.03	23.75± 0.01

Note: All data represent as Mean ± SD

Table 6. Post-compression evaluation of Metformin HCl tablets

Formulations	% of mucilage	Average weight(mg)	Hardness (kg/cm^2)	Friability (%)	DT(min)
F1	1	796.86 ± 1.46	2.17± 0.29	0.61± 0.01	2.00± 0.45
F2	2.5	797.57± 1.81	3.33± 0.29	0.52± 0.01	3.06± 0.46
F3	5	797.71 ± 1.11	3.83± 0.29	0.46± 0.01	4.26± 0.18
F4	10	797.86 ± 1.35	5.17± 0.29	0.38± 0.01	5.03± 0.40
F5	1	796.86 ± 1.86	3.83± 0.29	0.52± 0.01	4.17± 0.15
F6	2.5	797.29 ± 1.11	5.00± 0.50	0.42± 0.01	5.55± 0.44
F7	5	797.43 ± 1.51	6.50± 0.50	0.30± 0.01	6.31± 0.87
F8	10	797.57± 1.62	7.83± 0.29	0.21± 0.01	8.23± 0.79
F9	-	796.14 ± 1.07	4.00± 0.87	0.35± 0.13	4.99± 0.59

Note: All data represent as Mean ± SD

Table 7. *In vitro* percentage of drug release study

Time(min)	Percent of Drug Release	
	F4	F8
5	8.96	5.21
15	15.33	10.48
30	23.96	19.33
45	28.83	26.96
60	40.8	31.63

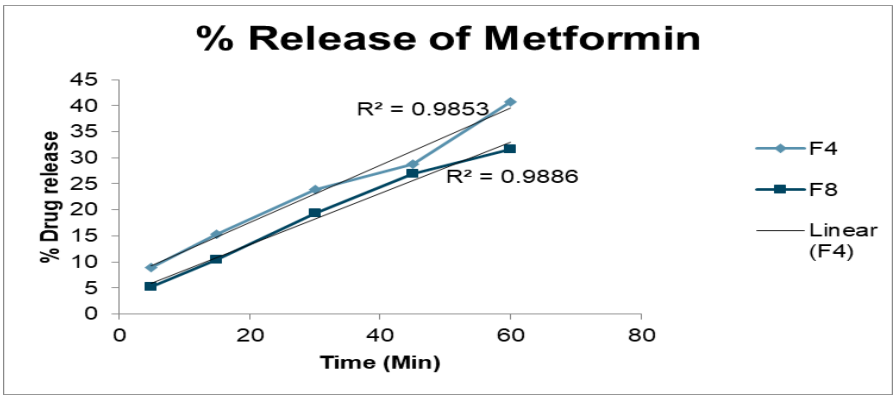

Fig. 1. Zero order release kinetics of formulation F4 and F8

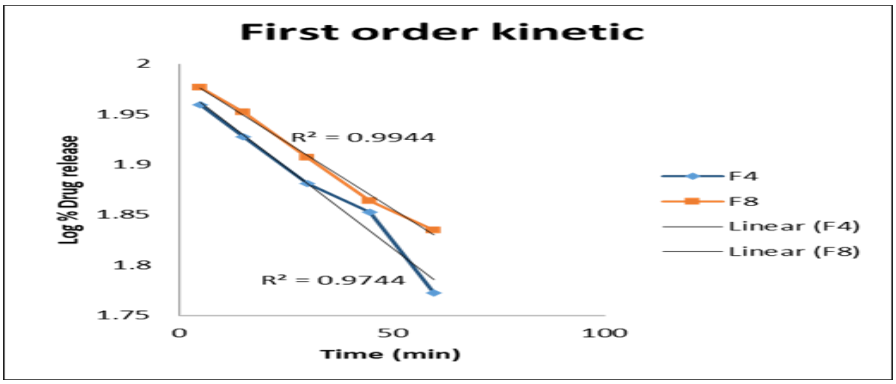

Fig. 2. First order release kinetics of formulation F4 and F8

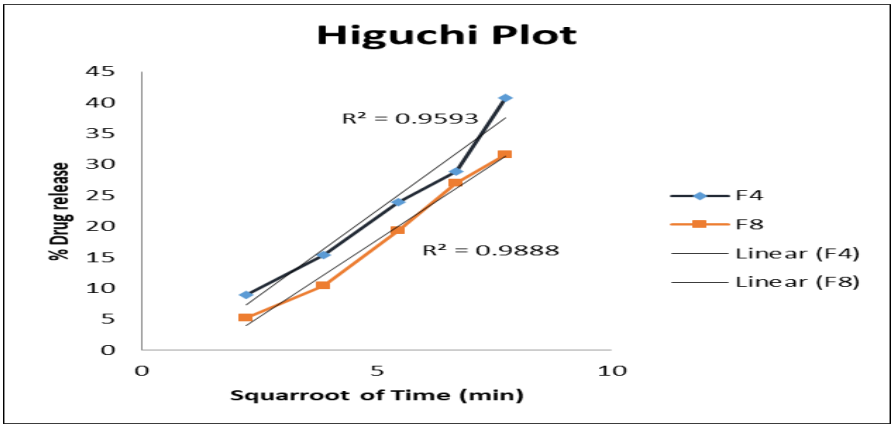

Fig. 3. Higuchi release kinetics of formulation F4 and F8

Table 8. Regression coefficient(R) of drug release kinetics of different formulation

Formulations	Zero order	First order	Higuchi's
F4	0.985	0.994	0.959
F8	0.988	0.974	0.988

4. CONCLUSION

In conclusion, natural mucilage can be easily isolated from *Momordica charantia* fruit with good yield. Metformin tablets containing a various concentrations of isolated mucilage alone and in combination with starch demonstrated promising outcomes as binder and release modifier. Formulations F4 and F8 exhibited commendable binding capabilities, while F4 showing excellent immediate release kinetics and F8 displaying sustained release characteristics. This research concludes that the mucilage extracted from *Momordica charantia* possesses noteworthy binding and drug release properties. Consequently, it has the potential to serve as a binder and/or release modifier in pharmaceutical formulations.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Amiri M, Mohammadzadeh V, Yazdi M, Barani M, Rahdar A, Kyzas G. Plant-Based Gums and Mucilages Applications in Pharmacology and Nanomedicine: A Review; 2021. Available:https://doi.org/10.3390/molecules 26061770
2. Manjunath MR. Pharmaceutical applications of natural gums, Mucilages and Pectins - A Review. International Journal of Pharmaceutical and Chemical Sciences. 2013;2(3).
3. Bhosale, Rohit, Osmani, Riyaz, Moin, Afrasim. Natural gums and mucilages: A review on multifaceted excipients in pharmaceutical science and research. International Journal of Pharmacognosy and Phytochemical Research. 2014;6: 2014-15.
4. Gouranga Nandi, Chowdhury S. (2015). An Overview of Natural Polysaccharides and Their Chemical Modifications: Application in Drug Delivery. Asia Journal of Drug Delivery (Asio-Jdd). 2015;1(1).37-43. DOI:12.2015-38368922
5. Nokhodchi A, Nazemiyeh H, Khodaparast A, Sorkh-Shahan T, Valizadeh H, Ford JL. An *In vitro* evaluation of fenugreek mucilage as a potential excipient for oral controlled-release matrix tablet. Drug Development and Industrial Pharmacy. 2015;34(3):323-9. DOI: 10.1080/03639040701662594. PMID: 18363148.
6. Malviya RP. Applications of mucilages in drug delivery-a review. Advances in Biological Research. 2011;5.1.
7. Ashwini S. Jadhav AK. Evaluation of Aloe vera and Hibiscus rosa-sinensis mucilage as a binder in different Tablet Formulations. Asian Journal of Pharmaceutical Technology ; 2020. DOI:10.5958/2231-5713.2020.00007.0
8. Grover JK, SY. Pharmacological actions and potential uses of *Momordica charantia*: a review. Journal of Ethnopharmacology; 2004.
9. Zhuo Liu JG. The Effect of *Momordica charantia* in the treatment of diabetes mellitus: A Review. Evid Based Complement Alternat Med; 2021. DOI:10.1155/2021/3796265.
10. Klepser TB. Metformin hydrochloride: An antihyperglycemic agent. American Journal of Health-System Pharmacy. 1997;54.8.

11. Defang OSN. *In vitro* and *In vivo* evaluation of two extended release preparations of combination metformin and glipizide. Drug Development and Industrial Pharmacy; 2005. DOI:10.1080/03639040500216410
12. Barua A, HM. Isolation and characterization of mucilage from *Tinospora cordifolia* as Tablet Binder and Release Modifier. Tropical Journal of Natural Product Research. 2019;3(1) :1-5.
13. PK L. Practical pharmacognosy. Calcutta, India. Lina Guha Publication. 1981;35-153.
14. Gilbert GB. Modern Pharmaceutics (4th ed. Ed.). New York: Marcel Dekker Inc; 2002.
15. Remington. The Science and Practice of Pharmacy (21st Edn ed.). India: Wolter Kluwer Health. 2006;1:939-964
16. Chandraprakash Dwivedi. S. Formulation and characterization of metformin hydrochloride sustained release matrix tablet containing *Cassia tora* Mucilage. Journal of Drug Delivery and Therapeutics. 2017;7(6):66-75.
17. Diwedi RA. Preparation and in vitro evaluation of sustained release tablet formulations of metformin HCl. Asian Journal of Pharmaceutical and Clinical Research. 2012;5(1):45-48.
18. Wadher KJ, Kakde RB, Umekar MJ. Study on sustained-release metformin hydrochloride from matrix tablet: Influence of hydrophilic polymers and *In vitro* evaluation. International Journal of Pharmaceutical Investigation. 2011;1(3): 157–163.
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