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Development and Evaluation of Herbal Oral Formulation for the Treatment of Diabetes

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ABSTRACT

Herbal remedies have been shown to be truly valuable in the medical field, and parts of medicinal plants have gained popularity as sources for both conventional and modern drugs. Making a herbal formulation of the *Momordica charantia* seed's bioactivities was the aim of this investigation. In a preliminary phytochemical screening, the crude extract of *Momordica charantia* showed a positive (+) response for the presence of alkaloids, polysaccharides, glycosides, saponins, phytosterols, phenols, tannins, flavonoids, proteins, and amino acids. ash values were computed to describe the *Momordica charantia* seed extract. There were found to be 14.5%, 4.5%, 8.5%, and 5.46% of total ash, acid insoluble ash, and water-soluble ash, respectively. The prepared tablets hardness and breakability were both adequate. The formulations were regularly removed from storage afterward and subjected to physical parameter analysis; the results were unchanged. The examined parameters before and after the formulations had been aged in storage did not significantly differ from one another; all were found to be within acceptable limits.

INTRODUCTION

Herbal Formulation

The usage of medicinal herbs and phytochemicals, often known as nutritional supplements, is growing quickly all over the world as more individuals turn to such substances to cure a variety of health issues in various national healthcare systems. [1] Natural treatments have undoubtedly gained enormous popularity over the past ten years, both in developed and emerging nations, as seen by the availability of these herbal cures not only in drugstores but also in food and grocery shops. According to estimates, up to 4 billion people who live in developing nations depend on herbal medicines as their main source of healthcare, and in those communities, traditional medical practices that incorporate the utilization of herbal ingredients are regarded as an essential component of culture. [2,3,4]

Diabetes mellitus

Diabetes mellitus is derived from the Latin term mellitus, which means sweet, and the Greek word diabetes, which means to syphon or flow through. A series of metabolic illnesses known as diabetes mellitus are characterized by persistent hyperglycemia brought on by deficiencies in insulin production, insulin action, or both.

Classification of Diabetes Mellitus

Type 1 Diabetes Mellitus

This kind of diabetes affects 5%–10% of people with diabetes [56] and is brought on by the death of pancreatic beta cells[57]. 80–90% of children and adolescents with diabetes have type 1 diabetes [58]. Due to the high incidence of type 1 diabetes among adolescents and adults above the age of 14, these numbers may not accurately reflect the overall number of type 1 diabetes patients. According to one estimate[60], 3 million Americans had type 1 diabetes in 2010.

This type 1 autoimmune diabetes is more prevalent in children and adolescents and is defined by the lack of insulin secretion.

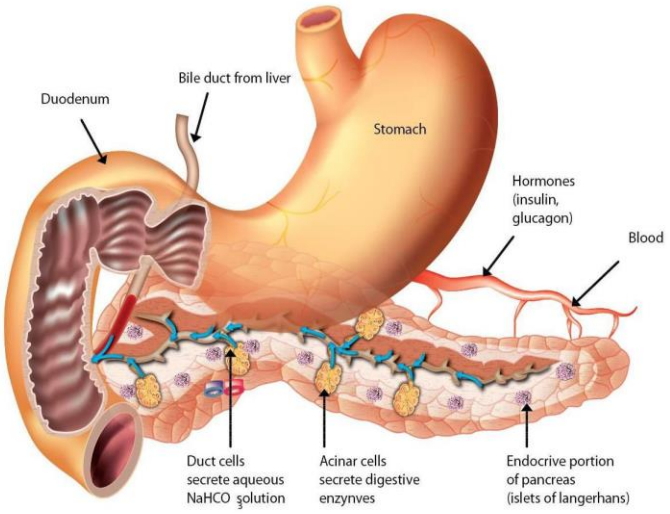

Figure No. 1: Human pancreas

Type 2 Diabetes Mellitus

Over half a billion people worldwide today have diabetes, with 175 million cases going untreated. During pregnancy, 21 million more women receive a hyperglycemia diagnosis.

Insulin demand in insulin-target tissues rises in type 2 diabetes patients with insulin resistance. Along with insulin resistance, the pancreatic cells' dysfunction prevented them from producing enough insulin to meet the increasing demand[68]. Type 2 diabetes is highly connected with the TCF7L2 gene. Type 2 diabetes typically takes years to be diagnosed since the initial symptoms are modest, especially in cultures where routine checkups without symptoms are not common. Given that hyperglycemia is not treated during this undetected time, this delay in diagnosis might lead to an increase in the prevalence of long-term problems in type 2 diabetes patients.

Plant Profile (*Momordica charantia*)

The study offers the required baseline information on the disease's burden and risk profile, allowing them to develop future diabetes reduction strategies and track their progress. Increased diabetes awareness, reduced diabetes risk factors, and improved diabetes diagnosis and treatment are all urgently required programmes and policies. Not only will this reduce the burden of diabetes, but it will also reduce the burden of other diseases linked to it.[175,176]

Figure No. 2 & 3: *Momordica charantia* fruit and seed

Table No. 1: Scientific classification of *Momordica charantia*

Scientific classification	
Kingdom: Plantae	
Clade: Tracheophytes	
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Rosids
Order:	Cucurbitales
Family:	Cucurbitaceae
Genus:	Momordica
Species:	M. charantia
Binomial name	
Momordica charantia	

Description

This herbaceous, tendril-bearing vine may reach a height of 5 metres (16 feet). It has simple, alternating leaves with three to seven firmly divided lobes that are 4–12 cm (1.6–4.7 in) broad. Male and female flowers are produced separately on each plant. Flowering takes place in the Northern Hemisphere from June to July, while fruits takes place from September to November.[177]

Traditional medicinal uses

In Indian traditional medicine, various parts of the plant are employed as purported cures for conditions like cough, respiratory illnesses, skin conditions, wounds, ulcer, gout, and rheumatism in addition to being used as stomachics, laxatives, antibilious, emetic, and anthelmintic agents. Polypeptide-p, an insulin analogue, is one such product.

MATERIAL AND METHODS

The *Momordica charantia* fruit was collected from local market of Lucknow.

Collection of plant material

The fruit *Momordica charantia* was collected from local market, Lucknow, U.P, seeds were dried and authenticated by the Professor of Pharmacognosy of my college.

Preparation of the seeds extract

Extraction was carried out in Soxhlet apparatus not exceeding 60^0C and the extract thus obtained was concentrated below 60^0C.

Soxhlet Extraction

The method of hot continuous percolation was chosen for extraction of *Momordica charantia* following reasons:

- The method is simple and less time consuming.
- Cost effective as the sample is used for the whole extraction.
- End point is easily determined.
- Chances of contamination are less since it is a closed system.
- Removal of marc and menstrum is easy.

Fresh or dried plant material is available. To create more surface area, it has to be crushed using a pestle and mortar. The plant matter should be enough to completely fill the cellulose thimble's pores.

In order to support the extraction equipment, we need to start by constructing a rig out of stands and clamps. The solvent (250 ml of ethanol) is then put to a flask with a circular bottom that is connected to a Soxhlet extractor and condenser that is mounted on an isomantle.

Preliminary Phytochemical Screening

After employing multiple techniques for phytochemical detection, a qualitative chemical test was conducted to provide a basic understanding of the make-up of the peel's contents.

Chemical analyses of the plant's raw extracts were performed in order to identify several active ingredients, as is mentioned below.

Test for alkaloids

a) **Preliminary test:** Diluted hydrochloric acid was used to dissolve a 100gm alcohol extract. Filtration was used to clarify the solution. Using Dragendroff's and Mayer's reagents, the filtrate was examined. We checked for any precipitation in the treated solution.

b) **Confirmatory test:** A 40% calcium hydroxide solution was used to treat five grammes of the alcoholic extract until it was clearly alkaline on litmus paper. The extract was then extracted twice using 10ml parts of chloroform. A mixture of chloroform extracts was concentrated to around 5ml. Then, spots of chloroform extract were placed on thin layer plates. Chromatograms were created using a solvent solution (n-hexane:ethyl acetate, 4:1) and were then sprayed with newly made **Dragendroff's spray** reagent to detect the presence of certain substances. Confirmatory evidence for the presence of alkaloids was orange or black dots on a pale yellow background.

c) Test steroidal compounds

a) 0.5g of the alcoholic extract was dissolved in 2ml of chloroform in a test tube for **Salkowski's test** (optional). To create a lower layer, concentrated sulfuric acid was carefully applied to the test tube's wall. The existence of a steroid ring was revealed by a reddish brown tint at the interface (i.e. the aglycone portion of the glycoside).

b) **Lieberman's test:** After being thoroughly chilled in an ice bath, 0.5g of the alcoholic extract was dissolved in 2ml of acetic anhydride. Then gently added concentrated sulfuric acid. When the hue of

the cardiac glycosides changed from purple to blue to green, it meant that an aglycone part, or steroid nucleus, was present.

c) Test for phenolic compounds

a) To identify phenolic chemicals, 3 drops of a freshly made combination of 1 ml of 1% ferric chloride and 1 ml of potassium ferrocyanide were added to 2 ml of filtered solution of the ethanolic extract of Piper trioicum of the plant material. The development of a bluish-green hue was seen favorably.

b) A 100 mg quantity of dry alcoholic extract was dissolved in water. There were a few ferric sulfate crystals added to the mixture. Phenolic chemicals were present as shown by the development of a dark violet tint.

Flavonoids

a) **Test for free flavonoids,** 0.5g of the extract was dissolved in five milliliters of water. The mixture was mixed, given time to settle, and then examined for the development of a yellow hue in the organic layer, which is seen as a favorable sign for free flavonoids.

b) **Lead acetate test:** 1ml of a 10% lead acetate solution was added to a 0.5g solution of the extract in water. Yellow precipitate production is seen as a sign that flavonoids are present.

Test for saponins

Froth Test: To make a foam, 0.5g of the alcohol extract was mixed with 10ml of distilled water in a test tube. The test tube was violently shook for around 30 seconds while the cork was removed. The test tube was permitted to stand vertically under observation for 30 minutes. After 30 minutes, the liquid should still have a "honey comb" froth on top, indicating the presence of saponins in the sample.

Test for Tannins

a) **Ferric Chloride Test:** The alcoholic extract was partly dissolved in water for the ferric chloride test. The solution was clarified using filtration. 10% ferric chloride solution was added to the clear filtrate. When the color changed to a bluish black, this was evident.

b) **Formaldehyde test:** A solution of around 0.5g of the extract in 5ml water was mixed with three drops of formaldehyde and six drops of diluted hydrochloric acid. After being heated for a minute to boiling, the resulting liquid was cooled. If there was any precipitation, it was washed in this order: hot water, warm alcohol, and warm 5% potassium hydroxide. Phlobatannins were shown to be a significant precipitate that, after washing, left a vibrant residue.

Physicochemical Evaluation

The powdered plant material of …… was evaluated by standard procedure for the determination of following physicochemical parameters.

Loss on drying

Mass loss as a percentage of mass/matter is referred to as loss on drying. A Petri plate containing 5–6g of medication powder is precisely weighed and stored in a hot-air oven with the temperature set at 105°C for 4-5 hours. Each case's weight loss was noted after chilling in a desiccator. Till the consistent weight was achieved, this process was repeated.

Loss on drying (%) = loss in weight X 100/ W W= weight of the drugs in grams.

Determination of Ash Value

Ash value is the methodology of identification of the quality and immaculateness of the unrefined powdered type of medication material. The debris is really the rough material without the natural issue in light of the fact that the natural issue has been burned which reveals to us more huge about the presence of the dynamic constituent inside the unrefined medication.

Total ash value

Take about 2 to 3g, accurately weighed powdered extract in a tarred platinum or silica dish previously ignited and weighed. Scatter the powdered drug on the bottom of the dish. Incinerate by gradually increasing the heat, not exceeding dull red heat until free from carbon, cool and weigh. If a carbon free ash cannot be obtained in this way, exhaust the charred mass with hot water, collect the residue on an ashless filter paper, add the filtrate, evaporate the residue and ignite at low temperature. Firstly, empty silica crucible was taken and put into the muffle furnace

with the help of tong for ignition at 6000C for 30 mins. Took out the silica crucible and weighed it then 2g of powdered drug was added to it. Then placed it in muffle furnace at 500-600^{0}C for 2-3 hours until it become white. Then weighed it. The percentage of total ash with air dried sample was calculated.

$$\text{Total ash value} = (z\text{-}x/y) \times 100$$

Where,

X = weight of the silica crucible Y = weight of the drug powder (g)

Z = weight of the silica crucible with powder ash

Acid-insoluble ash

The insoluble material was removed from the ash after it had been heated for 10 to 15 minutes with around 30 millilitres of diluted hydrochloric acid. It was lit, cleaned with hot water, and weighed. In order to quantify the proportion of acid-insoluble ash, the air-dried medication was used as a reference. To 25 ml of dil HCl, the ash generated by the aforementioned technique was added. For five minutes, boil it. The residue was then collected on filter paper with less ash. Then, it was heated to 5600C for 1 hour in a muffle furnace. With reference to the sample that had been air dried, the percentage of acid-insoluble ash was estimated.

$$\text{Acid insoluble ash value \%} = (a/y) \times 100$$

where,

A = weight of the remaining residue Y = weight of crude powder taken (g)

Water-soluble ash

Boiled the ash obtained from total ash value for 5mins in 25 ml water. The insoluble matter was poured into ash less filter paper. Then it was ignited at low temperature to constant weight. The weight of water soluble ash was determined by subtracting the weight of water insoluble ash from total ash value. The percentage of water soluble ash with reference to air died value was calculated.

Extractive Value

Procedure A medication that had been air dried and ground into a coarse powder was macerated in a closed flask for 24 hours with 100 cc of solvent (chloroform, ethanol, and water), shaking regularly for the first six hours, and then left to stand for the last 18 hours. After that, it was quickly filtered to prevent alcohol loss. A 25 ml sample of the filtrate was dried to dryness in a shallow dish with a flat bottom, dried at 1050°C, and weighed. The proportion of extractive that is soluble in alcohol was estimated using the air-dried medication as a base. The amount of soluble substances needed for extraction in that particular solvent is referred to as the extractive value.

Extractive value was determined using the formula:

$$\text{Extractive value}(\%) = \frac{\textit{weight of residue}}{\textit{weight of dry powder}} \times 100$$

Preparation of herbal tablets

Tableting Procedure:

The 250gm of finely ground seeds was utilized to make tablets. Wet granulation was used to create the tablets, and different concentrations of starch mucilage (5%, 10%, and 12% w/v) were used as the binder and disintegrant. Lubrication was provided by talc. The following steps were used to create tablets using the wet granulation method: milling the drugs and excipients, combining the milled powders, making the binder solution, combining the binder solution with the powder mixture to form a wet mass, drying the moist granules using a 6 to 2 mesh screen, screening the dry granules through a 14 to 20 mesh screen, and combining the dry granules with lubricant. Three different tablet formulations, Fm1, Fm2, and Fm3, were created using a single punch tablet compression machine (Kevin Engineering Pvt. Ltd.). Only one batch of the appropriate number of tablets was created in order to prevent bias in the second batch. As stated in Table 1, the three potential formulations were created using different amounts of starch paste and medications.

Preliminary tests were conducted on each formulation to determine its effectiveness, and each formulation's quality control parameter was thoroughly investigated.

EVALUATION OF TABLETS

Organoleptic properties (color, odor, and taste)

Tablet colour is important for patient acceptability and identification. Particularly with ODT tablets, chewable tablets, and dispersible tablets, taste is crucial for patient acceptability.

Thickness and diameter

For the requisite homogeneity in size and shape, the thickness and diameter of the tablets were precisely measured using a digital Vernier calliper.

Hardness

The strength of a tablet is determined by how hard it is. By measuring the amount of force needed to shatter the tablet throughout its circumference, it is put to the test. The hardness is expressed in kilogrammes (kg), and 4 kg is seen to be a sufficient hardness for uncoated tablets. For this, a Monsanto hardness tester is employed. Six pills were tested for hardness, and the average hardness was determined.

Friability test

The loss of weight of tablets in a container owing to the removal of small particles from their surfaces is known as friability. The friability test evaluates the tablet's resistance to abrasion during handling, packaging, and transportation. The tablet's friability was evaluated using an Electrolab friability tester. Six (6) pills were weighed precisely and put into the device's chamber. The tablets were removed from the device after 100 spins, dusted again, and weighed. The weight loss reveals the pills' brittleness. Tablets can have a maximum friability of 1%, according to the Indian Pharmacopoeia (IP). The formula shown below was used to calculate the percentage of friability:

$$\% \text{ friability} = (W1 - W2 / W1) \times 100$$

Dissolution Testing:

The prepared tablets were evaluated for in-vitro drug release studies using Type-II dissolution apparatus. The dissolution of core tablets is carried out under standard conditions. The results obtained are tabulated and used for selection of best formulation.

Stability studies as per the ICH guidelines

As required by the International Conference on Harmonization (ICH)105, developed SR tablets were placed in High Density Poly Ethylene (HDPE) containers and submitted to stability testing at the following varying temperatures and humidity levels.

25^0C with 60 % RH

40^0C with 75 % RH

RESULT AND DISCUSSION

The use of medicinal plants and their compounds in the treatment of human ailments remains crucial. The idea of using herbs to treat diabetes is not new. Since ancient times, plants and plant extracts have been utilized to cure diabetes. Many traditional treatments make use of medicinal plants, minerals, and organic components. A list of 21,000 medicinal plants used worldwide has been prepared by the World Health Organization (WHO). They utilize 150 species on a large scale economically.

Momordica charantia (*M. charantia*), also known as bitter melon, karela, balsam pear, or bitter gourd, is a well-known plant that has long been used to cure diabetes-related illnesses by native cultures in Asia, South America, India, the Caribbean, and East Africa. Its fruit is known as bitter melon and bitter gourd because of its characteristic bitter flavor, which intensifies as the fruit ripens. The anti-diabetic effects of *M. charantia* have been the subject of extensive biochemical and animal model study. Contrarily, there aren't many badly planned clinical studies using human participants.

Diabetes has been effectively treated at low cost with plant-based medicine all around the globe. In fact, this may be the only therapy choice for diabetics in many areas of the globe, especially in underdeveloped countries.

Table No. 2: Physical Test of Crude Drugs

The physio-chemical characteristics of the plant's powder were assessed, and the results were compared to published literature. the outcomes calculated using the ayurvedic pharmacopoeia of India's published limitations.

Crude drugs	Physical Test			
	Nature	**Colour**	**Odour**	**Taste**
Momordica charantia seed Extract	**Coarse powder**	**Yellowish brown**	**without any specific odor**	**Bitter in taste**

Table No. 3: Extractive Values

The Extractive Values of the plant extract were evaluated for alcoholic and aqueous solutions.

Crude drugs	**Alcohol % w/w**	**Aqueous % w/w**
Momordica charantia seed Extract	**18**	**24**

Table No. 4: Loss on Drying And Foreign Organic Matter

Crude drugs	**Loss on drying (% w/w)***	**Foreign matter (% w/w)***
Momordica charantia seed Extract	**5**	**1.25**

Table 5: Total Ash, Acid Insoluble Ash And Water Soluble Ash Values

Crude drugs	**Total ash value* % w/w**	**Water soluble ash* % w/w**	**Acid insoluble ash value* % w/w**
Momordica charantia seed Extract	**14.5**	**8.5**	**4.5**

The extract from *Momordica charantia* seeds has shown that it contains saponins, tannins, glycosides, and carbohydrates. All of the extracts were determined to be devoid of proteins. According to this research, the extract has more components. The table below lists each extract's preliminary phytochemical screening test outcomes. The early phytochemical screening tests identified flavonoids, tannins, carbohydrates, saponins, tannins, triterpenoids, and proteins in the extract, suggesting that they may be effective in the discovery of bioactive principles. Additionally, the therapeutic actions of the two distinct extracts may be due to the presence of several phytoconstituents.

It is frequently discovered that alkaloids have antibacterial effects. Plant phenolics are a significant class of substances that function as the body's main antioxidants, along with flavonoids and tannins. According to reports, tannins impede the growth of several moulds, yeasts, bacteria, and viruses. The antioxidant properties of *Momordica charantia* seed Extract may be due to the presence of these chemicals, which were discovered in the extracts. *Momordica charantia* seed extract included the secondary metabolites and other chemical components. Considering that entire peel extracts contain a variety of components and have a large number of bioactive substances. Finding chemical components in plant material that might result in their quantitative measurement is made easier with the aid of the preliminary phytochemical tests. Before an extract high in natural antioxidants might be further investigated for future application in health-promoting supplements for the food business, a suitable extraction technique must be devised and enhanced to recover as many antioxidants as feasible.

Table 6: Phytochemical screening for extract of *Momordica charantia* seed Extract

S.No	Chemical Tests	Momordica charantia seed Extract
1.	Tests for Steroids and Triterpenoids:	
	• Liebermann's Burchard Test	+
	• Salkowski Test	+
2.	Test for Saponins:	
	• Foam Test	+
3.	Tests for Alkaloids:	
	• Hager's Test	+
	• Mayer's Test	+
4.	Tests for Glycosides:	
	• Borntrager's Test	-
	• Keller Killiani Test	-
5.	Tests for Tannins and Phenolic compounds:	
	• Gelatin Test	
	• Ferric Chloride Test	+
	• Lead Acetate Test	-
	• Dilute Nitric acid Test	-
6.	Tests for Flavonoids:	
	• Ferric chloride Test	-
	• Alkaline reagent Test	+
	• Lead acetate Test	-
7.	7. Tests for Proteins:	

"+"Found

"-" Not Found

Table 7: Determination of Parameters of drug (post-compression studies)

Post Compressional Studies

Evaluation Parameters	Hardness (%)	Friability (%)	Drug Content(%
Fm 1	4.5	0.35	95.65
Fm2	4.8	0.4	90.16
Fm3	5.7	0.45	91.24

Table No. 8: Measurement of thickness

Evaluation Parameters	Thickness (mm)
Fm 1	3.55
Fm2	3.25
Fm3	3.35

Table No. 9: Dissolution data of optimized batches of tablets in 6.8 pH buffer.

Evaluation Parameters	Time (min) 0	Time (min) 10	Time (min) 20	Time (min)30
Fm 1	0	77.35	81.25	89.45
Fm 2	0	76.36	80.34	88.65
Fm 3	0	75.35	80.77	87.47

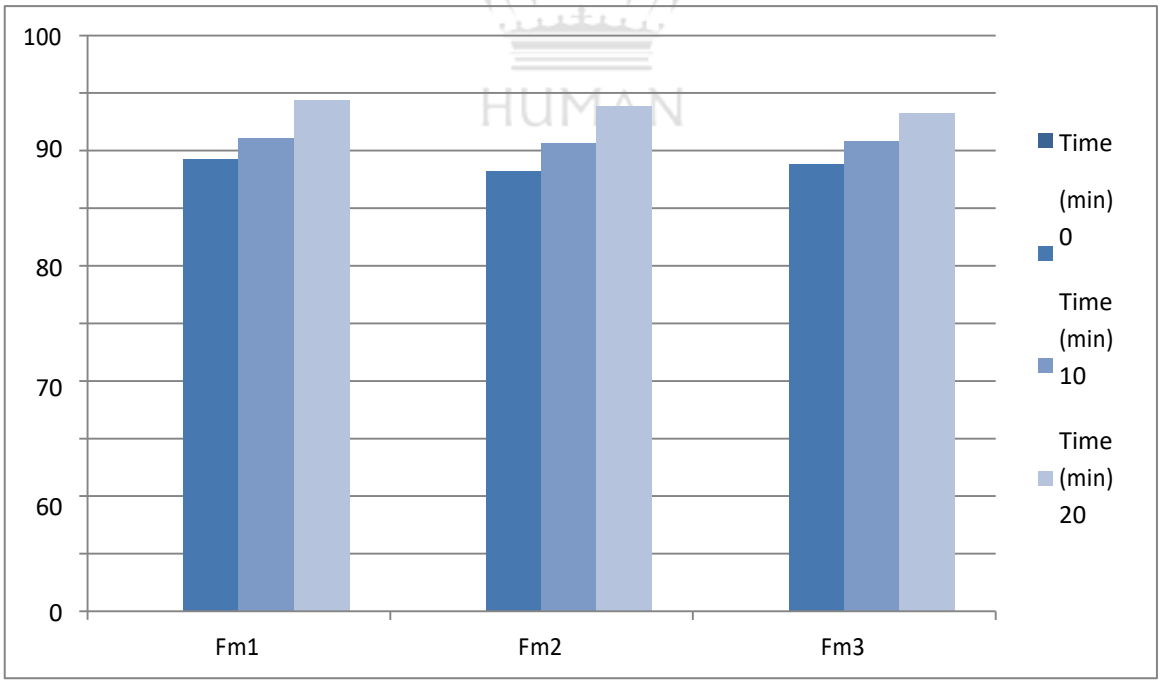

Figure 4: Dissolution data of optimized batches

Table No. 10: Evaluation parameters of batch which was kept for stability study:

Evaluation Parameters	Hardness (%)	Friability (%)
Before stability Storage	6.1	0.25
After 1 month Storage	6.15	0.5
After 2 month storage	6.2	0.35
After 3 month storage	6.3	0.4

CONCLUSION

Herbal remedies have been shown to be truly valuable in the medical field, and parts of medicinal plants have gained popularity as sources for both conventional and modern drugs. Making a herbal formulation of the *Momordica charantia* seed's bioactivities was the aim of this investigation. In a preliminary phytochemical screening, the crude extract of *Momordica charantia* showed a positive (+) response for the presence of alkaloids, polysaccharides, glycosides, saponins, phytosterols, phenols, tannins, flavonoids, proteins, and amino acids.

It was shown to be soluble in hot water, expand to form a gel in the presence of cold water. Additionally, ash values were computed to describe the *Momordica charantia* seed extract. There were found to be 14.5%, 4.5%, 8.5%, and 5.46% of total ash, acid insoluble ash, and water soluble ash, respectively. In the instance of tablets, surface tension affected the polymer's ability to bind.

The prepared tablet’s hardness and breakability were both adequate. The formulations were regularly removed from storage afterward and subjected to physical parameter analysis; the results are shown in the table above. The examined parameters before and after the

formulations had been aged in storage did not significantly differ from one another; all were found to be within acceptable limits.

According to the study, a wide range of metrics were employed to evaluate the assessment of biochemical parameters. The results of the evaluated parameters showed that the herbal formulation derived from may be used as a pharmaceutical adjuvant to create solid oral dosage forms since it had all of the characteristics required to formulate dosage forms, such as hardness and friability. The bulk density, tapped density, and Hausner's ratio values are good enough.

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