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Research Article

Formulation And Evaluation Of Chewable Antidiabetic Gummies From Mangiferin

Sonali A. Wagh[1], Abhishek V. Hole[2]*, Mansi S. Pabale[3]

[1]*Assistant Professor Pune District Education Association's College of Pharmacy, Hadapsar, Pune.*
[2]*Abhinav Education Society's, College of Pharmacy (B.Pharm), Narhe, Pune.*
[3]*All India Shri Shivaji Memorial Society's, College of Pharmacy (B.Pharm), Pune.*

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ABSTRACT

Diabetes is a family of metabolic disorders typified by elevated blood sugar levels brought on by deficiencies in either the production of insulin or the action of insulin on its receptor. The chemical compound known as mangiferin is present in the leaves of the Mangifera indica plant. By blocking the actions of alpha amylase and alpha glucosidase, mangiferin aids in the regulation of postprandial blood glucose levels. Therefore, a formulation with mangiferin might be beneficial for treating individuals with hyperglycemia. Herbal chewable gummies are designed with mannitol as a sweetener that doesn't alter normal blood sugar levels and gelatin as a gelling agent with varying concentrations of 5%, 10%, 15%, 20%, and 25%, respectively, to make the treatment easy to administer and have few adverse effects.

INTRODUCTION

Diabetes mellitus definition and aetiology: Diabetes is a Greek term that meaning "syphon." In the second century A.D., the Greek physician Aretus the Cappadocian named the ailment Diabainin. As if they were a syphon, he described people suffering from polyuria, or the overflow of water. The term "diabetes" was coined after the English adapted the Mediaeval Latin diabetes. Thomas Willis introduced the term diabetes mellitus in 1675, however the illness is most often referred simply as diabetes. Mel's name is derived from the Latin word "honey," which describes the excess glucose present in diabetics' blood. Glucose is so delicious that it makes the diabetes cases of Chinese people look improbable. The phrase "Sweet Urine Disease" was created when it was previously shown that some people's pee would attract ants.(1) A class of metabolic disorders known as diabetes is defined by abnormalities in insulin action, predicted secretion, or both. Hyperglycemia that results in diabetes is another characteristic. The entire population [1. kind 1

***Corresponding Author:** Abhishek V. Hole
Address: *Abhinav Education Society's, College of Pharmacy (B.Pharm), Narhe, Pune.*
Email ✉: abhishekhole2501@gmail.com
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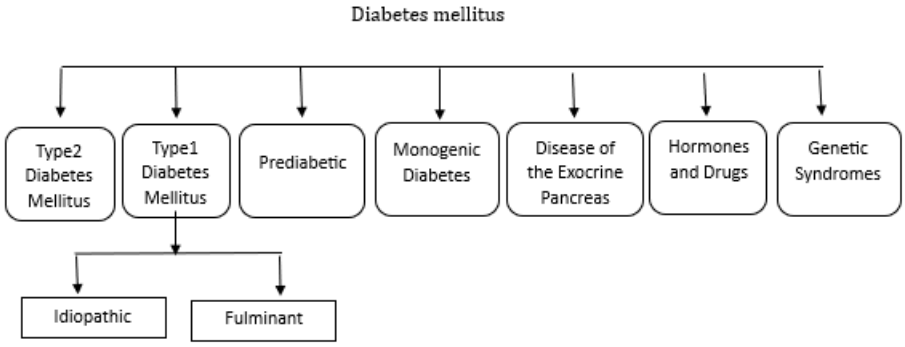
diabetes is the most common kind of diabetes, accounting for 171 million cases in 2000 and 366 million cases in 2030. It is classified into two broad etiopathogenic categories. occurs in categories. People with absolute insulin insufficiency and 5–10% of those with this kind of diabetes are impacted. Type 2 diabetes, which is significantly more common, is primarily caused by a combination of insulin resistance and an insufficient metabolic insulin secretory response in conjunction with hypertension [2].

Obesity, smoking, and control are typically linked to diabetes [3,4]. Some people with diabetes, particularly those with type 2 diabetes, are asymptomatic in the early stages of the disease. Others have significant hyperglycemia and, in particular, polyphagia. Children who have lost all of their weight and have insulin-dependent impaired vision may also experience polyuria, polydipsia, and polyuria. Uncontrolled diabetes can cause nonketotic hyperosmolar syndrome, which is rare but can result in stupor, coma, and death from ketoacidosis if left untrated.[2]

Classification of Diabetes Mellitus



Anti-Diabetic activity of mangiferin

Eight weeks of mangiferin treatment significantly lowered plasma glucose and triglycerides (TG) levels in diabetic mice. It enhanced pancreatic β cell mass and amount of glucose and insulin uptake along with increased the phosphorylation of AMP activated protein kinase (AMPK). Likewise, the oral administration of mangiferin (20 mg/kg) intraperitoneal administration (i.p) for 4 weeks in Streptozocin induced hyperglycemic rats improved insulin sensitivity, modulated lipid profile, and reverted adipokine levels.(10) Mangiferin (10 and 20 mg/kg) administered once daily for 28 days in STZ induced diabetic rats exhibited antidiabetic activity. It significantly reduced plasma low-density lipoprotein cholesterol and TG levels, lowered and cholesterol levels and increased high density lipoproteins (HDL) levels. Furthermore, the anthrogenic index of diabetic rats decreased and mangiferin improved oral-glucose tolerance in normal rats loaded with glucose (10) One of the best effective approaches in the cure of DM is the inhibition of α-amylase and α-glucosidase enzyme, which regulate postprandial glucose absorption. A comparative analysis of mangiferin and mango leaves extract was done to check the efficiency of each extract to inhibit α-glucosidase enzymes. Mangiferin at a concentration of 10, 25, and 50 resulted in 86.85%, 92.35% and 99.11% inhibition of α-glucosidase respectively, It can be concluded that mangiferin is an active ingredient in the inhibition of α-glucosidase enzymes activity and and managing the diabetic conditions. Author reported that mangiferin showed strong inhibition of rat α-glucosidase woth a median inhibitory concentration IC50 of 433.3 µg/ml. Author found that the administration of mangiferin in chemically induced diabetic mice reduced the postprandial glucose level,prevented the surge of glucose in the blood (11)

MATERIALS AND METHODS

MATERIALS

The leaves of Mangifera indica were bought from Pune, Maharashtra, India's local market. The leaves were cleaned with tap water, shade-dried for four to five days at room temperature, and then ground into a powder. The leaf powder was kept in a room temperature environment. Methanol is one of the solvents utilized in this extraction. (5)

Soxhlet Experiment

- Five grams of ground-up leaves were put in a thimble holder and then filled with methanol straight from the distillation flask.
- The thimble-holder solution is extracted by siphoning action and reloaded into the distillation flask when the methanol level overflows.
- This steam contains extracted solutes that have been distillated in a solvent flask to remove the solvent.
- The solvent is sent again for extraction, while the solute stays in the flask. The extraction process took five hours to complete.
- Samples were taken out of the distillation flask and examined to determine the amount of Mangiferin present. (6)

Preparation of Chewable Gummies

Excipients used:

Gelatin:

It has higher blooming capacity, making gelatin a fantastic fit as gelling agent. Hence, act as a gelling agent in thus formula and plays a pivotal role in the formula. (1)

Mannitol: Mannitol is a white, crystalline polyol obtained by hydrogenation of fructose. It is approximately 50% as sweet as sucrose. It is freely soluble in water and it imparts a mild cooling sensation when it is chewed or dissolved in mouth due to negative heat effect.(7)

Citric acid: It is used as an acidulant in this formulation to enhance acceptability of this product.(8)

Neem oil: It is used as an preservative in the formulation and prevents stickiness (9)

Propylene glycol: It is used to increase the elasticity of gummies. (9)

Mango flavour:

It is used as flavouring agent.(9)

The uniform viscous solution of API and excipient was prepared by the following steps and then was moulded into a silicone mold and was chilled at room temperature was the process used to formulate chewable gummies. The following were done to prepare the gummy bases:

1. The distilled water was added to the gelatin, and it was allowed to swell for 30 minutes at room temperature.
2. The mixture of water and gelatin was cooked to 50 degrees Celsius in a water bath until a uniform, viscous liquid formed.
3. Mannitol was then added to the mixture, and then other chemicals like mangiferin, citric acid, neem oil, and propylene glycol etc was added.
4. After being thoroughly mixed, the prepared material was poured into the silicone mold. Room temperature was maintained for the molds for setting gummies.

Table no.1 Formulation of Chewable Gummies.

Ingredients	Composition					Uses
	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5	
Mangiferin	10%	10%	10%	10%	10%	Antidiabetic
Gelatin	5%	10%	15%	20%	25%	Gelling agent

Mannitol	25%	25%	25%	25%	25%	Sweetener And Firming agent
Citric Acid	1.5%	1.5%	1.5%	1.5%	1.5%	Acidulant
Neem Oil	5%	5%	5%	5%	5%	Preservative To prevent the sticking in the mold
Propylene Glycol	4%	4%	4%	4%	4%	Increase the elasticity
Mango flavor	4%	4%	4%	4%	4%	Flavoring agent
Purified water	45.5%	40.5%	35.5%	30.5%	25.5%	Vehicle
Total	100%	100%	100%	100%	100%	_ -

Identification of drug by phytochemical screening

10g of powdered dry mango leaves were extracted by boiling them in water for 15 minutes. Filtered and subjected to normal procedures to determine whether phytochemical substances were present.

Detection of Steroids by Liebermann-Buchard Test

In a test tube, add 1 milliliter of the aqueous extract, 5 milliliters of anhydrous acetic acid, and thoroughly shake. Put four drops of the aforementioned combination into a porcelain dish, followed by one drop of concentrated H2SO4. a shift in hue from rose to green via red, violet, and blue. From compound to compound, the hues differ slightly.

Detection of Cardiac Glycosides (Kellen-Killians Test)

One millilitre of glacial acetic acid with one drop of ferric chloride solution should be added to one milliliter of aqueous extract. Next, add 1 milliliter of strong sulfuric acid to the combination mentioned above, dropping it to create two layers. The presence of cardenolide-specific deoxy sugar was revealed by a brown ring that was obtained at the contact.

Detection of Saponins (Froth Test)

A graduated cylinder containing 1 milliliter of aqueous extract was shaken for 15 seconds after being diluted with 20 milliliters of distilled water. After 15 minutes, the formation of a foam layer suggested the presence of saponins.

Detection of Tannins

A few drops of an alcoholic solution containing 0.1% FeCl3 should be added to 1 milliliter of aqueous extract. Dark blue, greenish black soluble chemicals suggest the presence of tannins.

Detection of Flavonoids

Add a few drops of 10% sodium hydroxide solution to 2 milliliters of aqueous extract. This results in a yellow tint. A shift from yellow to colorless.

Detection of Alkaloids

To one milliliter of aqueous extract, add a few drops of Mayer's reagent. Alkaloid presence is shown by white precipitate. A small amount of Dragondraff's reagent also produces an orange precipitate containing alkaloids.

Table No:- 2 Phytochemical profile of Mangifera indica.L leaves

Phytochemicals	Test	Crude extract
Alkaloids	Dragendroff 's test	+
Flavonoids	Mayer's test	+
Tannins	Alkaline reagent	+
Steroids	Liebermann-Burchard test	+
Saponins	Frothing test	-

Cardiac glycosides	Keller Killians test	+

EVALUATION OF GUMMIES

Determination of UV absorbance maxima of Chewable Gummies

Mangiferin was synthesized by dissolving it in methanol at a concentration of 10 micrograms per milliliter. The isolated chemical was scanned between 200 and 600 nm in wavelength, and the results were compared to the reference standard.

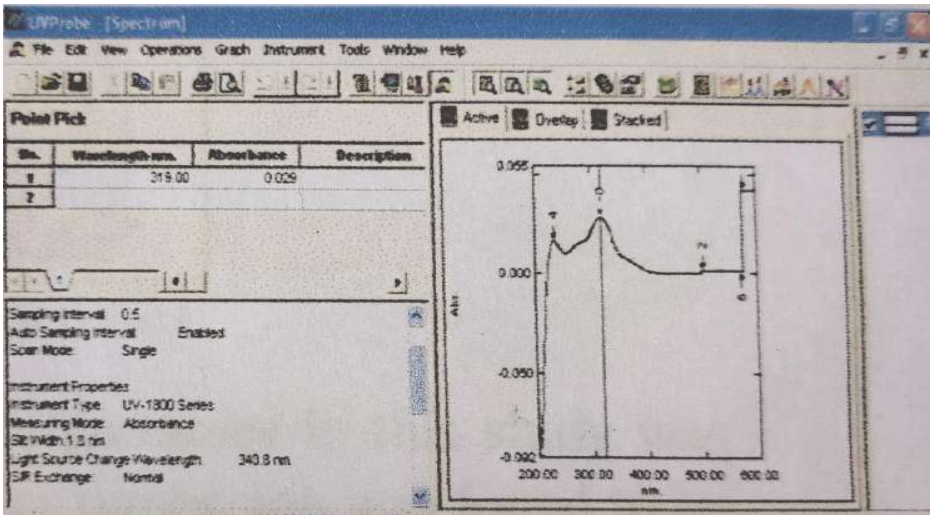


Fig No.1 UV of Mangiferin

Dimention test

The dimention of the gummies was measured to determine the size homogeneity and the necessary dimension of primary packaging to protect the gummies from the environment. For this reason the length, width, and thickness of 10 gummies were measured with vernier calliper. The gummy meet requirement if the standered deviation of its dimension is not higher than 5% (9).

Determination of PH of gummies

A digital pH meter can be used to find the jelly's pH. The pH was measured after 0.5 gm of the weighted formulation was diluted in 50 ml of distilled water. Using a digital pH meter, it was discovered that the chewable gummies had a pH of 6.82.

Normal pH range: 6.74 to 6.98.

Fig No.2 pH of Chewable Gummies

Weight variation test

Weight variation of the gummies was measured to determine the content homogeneity of each gummy. In the initial stage, not less than 20 individual gummies were weighed, and then the average weight was calculated. The gummies are concluded as meeting the predefined requirement if its weight does not deviate moe than 7.5% from the average. If one gummy fall out of this range, the test is carried out to the second stage with an additional set of not less than 20 gummies the test continued to the second stage with an additional set of not less than 20 gummies, in which the tablet is concluded as meeting the requirement if its weight does not deviate more than 10% from average weight (9).

Swelling Ratio

This straight forward technique assesses a gel structure's ability to absorb water. Each formulation's CGT was weighed before being submerged in 100 milliliters of distilled water. Filter paper was used to remove any remaining water from the gummy surface prior to the second weighing. By dividing the weight difference between the gummy's initial weight and its weight after immersion, the swelling ratio was computed.

Dispersion Time Test

A dispersion time test was conducted to estimate how quickly the chewable gummies dissolved in aqueous media to ensure disolution upon contact with saliva. Faster dispersion time indicates faster release of API from a dosage form (9) and a quicker absorption process starting from the point of contact with aqueous media. A previous study described that a pharmaceutically acceptable chewable gummies should disintegrate within 10-30 minutes (1).

Syneresis Test

Syneresis occurs when water drains from a contracting or shrinking structure by extraction or performed at expulsion, potentially reducing the gummies quality. This test was room absorbent paper was temperature (25 ± 5°C) by weighing the samples. First, a of the preparations were attached to the surface of each tablet, then the final weights observed. A final weights significant difference between the initial and indicates syneresis.

Table No: 3 Evaluation test for gummies

Parameter		Formula 3	Formula 4	Formula 5
Organoleptic tests	Colour	Dark brown	Dark brown	Dark brown
	Odour	Pleasant	Pleasant	Pleasant
	Taste	Mango	Mango	Mango
	Shape	Square	Square	Square
	Texture	Smooth, Non sticky, Elastic	Smooth, Non sticky, Hard texture	Smooth, Non sticky, Hard texture
pH		6.82	6.81	6.84
Weight variation test (%)		1.1%	1%	1%
Gummies dimension test	Length (cm)	0.6 cm	0.6 cm	0.6 cm
	Width (cm)	0.6 cm	0.6 cm	0.6 cm
	Thickness (cm)	0.3 cm	0.3 cm	0.3 cm
Dispertion time test (minutes)		15 mins	25 mins	32 mins
Syneresis (%)		0%	0%	0%

Drug content (%)	101%	101%	101%

RESULTS

The determination of Mangiferin using Mangifera indica extract analysis. Leaves was completed using these techniques:

Thin Layer Chromatography (TLC)

Rf value: Distance travelled by solute /Distance travelled by solvent

Rf value: 2.6/5.5

Rf value: 0.47

Rf value of standard Mangiferin: 0.492

UV-visible double-beam spectrophotometer

319 nm was discovered to be the highest absorbance of Mangiferin in Methanolic extract.

Wavelength standard: 319 nm

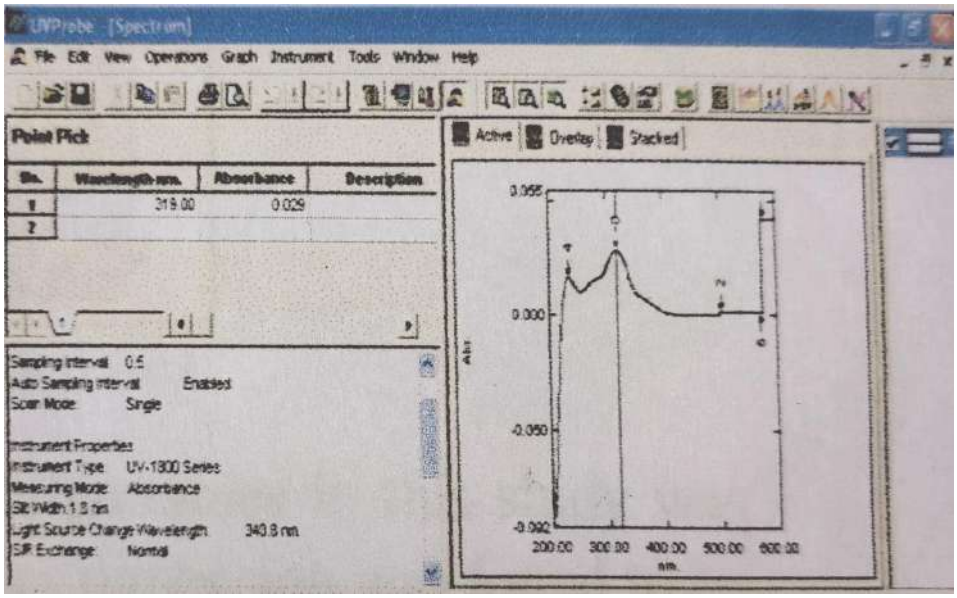


Fig no.4 : UV of Mangiferin

Glucose Bound Test

25 milliliters of a glucose solution with varying concentrations (0.2, 0.8, 2, 4 m mol/L) was mixed with plant extract. The mixture was thoroughly mixed and incubated for six hours at 37 °C in a shaker water bath. After centrifuging for 20 minutes at 4800rpm, the amount of glucose in the supernatant was measured using a UV spectrophotometer.

Table No. 4 : Invitro antidiabetic activity

Sr. No	Concentration Glucose	Absorbance	
		Standard	Mangiferin
1	0.2	0.018	0.012
2	0.4	0.023	0.019
3	0.8	0.045	0.026
4	2	0.168	0.023
5	4	0.249	0.167

CONCLUSION:

The study demonstrates the potential of mangiferin, extracted from Mangifera indica leaves, as an effective agent for managing diabetes mellitus. Mangiferin's ability to inhibit key enzymes, such as α-amylase and α-glucosidase,

highlights its role in regulating postprandial blood glucose levels. The anti-diabetic efficacy was confirmed in animal models, where mangiferin significantly reduced blood glucose, cholesterol, and triglyceride levels, while enhancing insulin sensitivity and improving the lipid profile.

The formulation of chewable gummies using mangiferin offers a convenient and palatable option for diabetic patients. The gummies, developed with varying concentrations of gelatin (5%–25%) and mannitol as a non-glycemic sweetener, were evaluated for organoleptic properties, pH, weight variation, dispersion time, and syneresis. Results indicated that the gummies met the required pharmaceutical standards, demonstrating desirable properties such as a uniform dimension, low weight variation, and optimal dispersion time. Additionally, the UV-Vis spectrophotometry and Thin Layer Chromatography (TLC) results confirmed the presence and concentration of mangiferin, supporting the accuracy of the extraction process.

In conclusion, mangiferin-enriched chewable gummies present a promising approach for diabetes management, combining the therapeutic benefits of a natural compound with ease of administration and patient compliance. Further clinical trials could solidify the formulation's potential as a marketable diabetic treatment.

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