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Evaluation of Polyherabal Antidiaebtic Syrup.

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia and altered metabolism of carbohydrates, lipids and proteins. It is a condition that impairs the body's ability to process blood glucose as result of this increased blood glucose level occurs inour body, which causes a diabetes mellitus. The present study reveals to develop a Polyherbalanti-diabetic herbal syrup by using an extract of a leaves of Gymnemasylvestre and dried seedsof Syzygium cumini. Three formulation of herbal syrup were formulated (F1, F2, F3) Herbals plants used in the formulations shows a potent anti-diabetic action over synthetic ones.F1, F2,F3 formulation were prepared and evaluated. Evaluation parameters of these formulation was found to be within the standard limits and in vitro studies were performed for detection of anti-diabetic activity

Key words **– Polyherbal syrup, Diabetes mellitus, Gymnemasylvestre ,Syzygiumcumini**

AIM AND OBJECTIVES: -

Aim :- The aim of the present work is to develop a polyherbal anti- diabetic syrup from the selected plant material and evaluate the same..

Objectives*:* -

1. To perform the raw material analysis.
2. To extract the plant material by continuous Hot Percolation method using ethanol as solvent.
3. To formulate and evaluate polyherbal syrup.
4. To evaluate the antidiabetic activity by In vitro and In vivo models

INTRODUCTION:

Diabetes mellitus is a group of chronic metabolic disorder caused due to high blood sugar levels over a prolonged period. Diabetes caused by either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. Diabetes mellitus is a growing health problem in the world that causes severe morbidity and mortality. The prevalence of diabetes was rising day by day. The facts about the diabetes mellitus, its prevalence, morbidity, and mortality were published in many statistical reports. Diabetes mellitus (DM), or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced.

This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Conventionally, diabetes has been divided into three types namely: Type 1 DM or insulin-dependent diabetes mellitus (IDDM) in which body fails to produce insulin, and presently requires the person to inject insulin or wear an insulin pump. This is also termed as "juvenile diabetes". Type 2 DM or non- insulin-dependent diabetes mellitus (NIDDM), results from insulin resistance, a condition in which cells fail to use insulin properly, with or without an absolute insulin deficiency.

HISTORY OF THE DIABETES

Diabetes mellitus is a growing health problem in the world that causes severe morbidity and mortality. The prevalence of diabetes was rising day by day. The facts about the diabetes mellitus, its prevalence, morbidity, and mortality were published in many statistical reports. Diabetes mellitus (DM) is one of the very oldest diseases and was mentioned three thousand years ago in Egyptian literature. Around 1500 B.C the physicians in India noticed the sweetness of urine of the diabetic people and called it as “Madhumeha”. Ebers papyrus, the oldest literature was written around the same time by Egyptians and it was also the first document that describes a condition of frequent emptying of urine.

Around 5th and 6th century the ancient Indian physician Susruta and Sharuka described first time about the extreme thirst, foul breath and polyuric state associated with sweet taste substance in the urine. They were the first identified the difference between the type I and type II DM. Aretaeus of cappodocia a Greek physician, he was the first person coined the term diabetes by observing the clinical condition that increased frequency of urine in diabetic individuals. He was also the first to distinguish diabetes mellitus and diabetes insipidus. Later on, Thomas Willis in 1670 was added the term mellitus (honey sweet) after rediscovering the sweetness of urine in the patient was due to the high blood glucose level. In 1776, Matthew Dobson, a British physiologist first confirmed that the sweetness of urine is due to the presence of excess glucose in blood and urine. Around 30 BC- 50AD, the Aulus Cornelius Celsus has given the complete clinical description for diabetes mellitus in Latin and entitled De medicina. Effective treatment was not created until the early part of the twentieth century, when Canadians Frederick Banting and Charles Herbert Best separated and sanitized insulin in 1921 and 1922. This was trailed by the improvement of the long-acting insulin NPH in the 1940s.

GLUCOSE HOMEOSTASIS AND DIABETES MELLITUS

Glucose is a chief fuel in biology. Glucose is metabolized in the mitochondria to release the ATP which provides energy to the cell. This energy is utilized for cell movement, nerve conduction, hormone production and to nourish the genetic machinery of the cell (DNA). Glucose in the body is maintained within the narrow range by two main hormones- Insulin and Glucagon- which acting antagonistically to increase or decrease blood glucose level in the blood. Both these hormones are released by the pancreas. High blood sugar level stimulates the release of insulin which is secreted by Beta cells of Islets of Langerhans in the pancreas that increases the uptake of glucose by cells. Moreover, in the cell, the glucose is used as energy, converted to glycogen and stored mainly in the liver and muscles or used in the synthesis of fats. In some abnormal conditions, the cell resists insulin which leads to considerable reduction in the glucose uptake, glycogen synthase activity, glycogen synthesis and storage in peripheral tissue. While there is a lack of insulin secretion or cell resists insulin, which leads to diabetes mellitus.

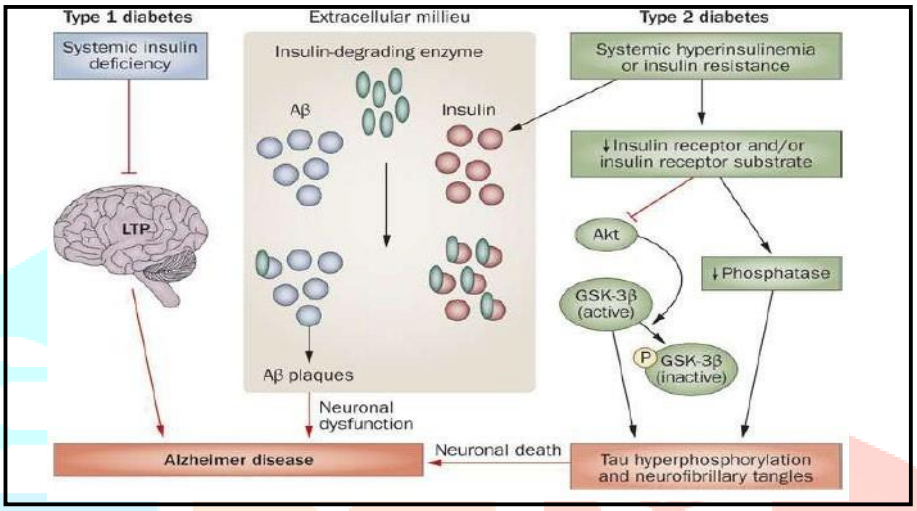
Blood glucose level:

Fasting blood glucose level: 90 – 130 mg/dl

Blood glucose level after 2 hours of meal greater than or equal to 150 mg/dl

SIGNS AND SYMPTOMS:

1. Weight loss
2. Polyuria (Increased urination)
3. Polydipsia (Increased thirst)
4. Polyphagia (Increased hunger)
5. Loss of vision
6. Slow healing of wounds
7. Itchy skin
8. Fatigue



Pathophysiology of Type I and Type II diabetes. Abbreviations: Aβ- Amyloid- β, GSK-3β-glycogen synthase kinase 3β, LTP- long term potentiation, P- Phosphate

CLASSIFICATION OF DIABETES

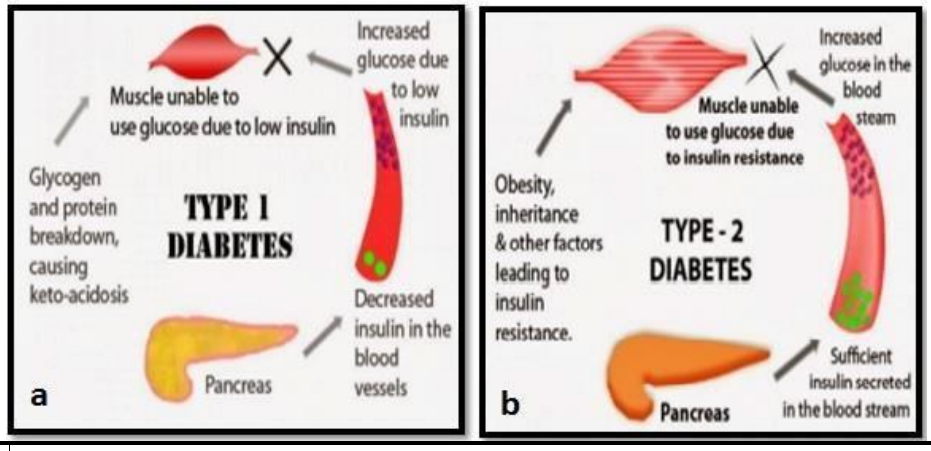
TYPES:

Type 1- Insulin Dependent Diabetes mellitus
Type 2 - Non- Insulin Dependent Diabetes mellitus Type 3 – Gestational Diabetes mellitus

Type 1: Insulin Dependent Diabetes mellitus [IDDM] is an autoimmune disorder, in which antibodies destroy the beta cells of the islets of Langerhans in pancreas causes an insulin deficiency. In other words, pancreas fails to produce an enough insulin.

Type 2: Non-insulin Dependent Diabetes mellitus [NIDDM] is an adult onset diabetes, Most of the patients are obese. There is a reduced sensitivity of tissues to insulin and impairs an insulin secretion.

Type 3: Gestational Diabetes mellitus, which occurs around 20-24 weeks of pregnancy during which placental hormones are raising and responsible for insulin resistance



(a) Type 1 diabetes mellitus and (b) Type 2 diabetes mellitus

Gestational diabetes.

PATHOPHYSIOLOGY:

Insulin is a principal hormone that regulates the uptake of glucose from blood in to cells of the body, it plays an important role in balancing glucose levels in the body.

Insulin is released into the blood by beta cells of islets of Langerhans present in the pancreas. Decreased insulin release from the beta cells results in breakdown of glycogen to glucose. Due to insulin insufficiency glucose will not absorbed properly by body cells, which results in poor protein synthesis, high blood glucose level. Increased osmotic pressure of the urine causes an increased fluid loss, due to the fluid bless other body compartments leads to dehydration (polydipsia).

SYRUP:

Syrup is viscous, concentrated or nearly saturated aqueous solution of sucrose containing 66.7 % w/w of sugar. Medicated syrup: Medicated syrups are nearly saturated solution of sugar in water in which medicaments and drugs are dissolved. It is intended for oral use.

Herbal syrup: An herbal syrup is prepared by mixing a concentrated decoction with either honey or sugar or alcohol. It is intended for oral use. Herbal syrups shows more potent action then other types of syrup.

Advantages:

1. Good patient compliance.
2. They are more palatable.
3. Disguised the bad taste of medication.

Disadvantages:

1. During storage it causes a crystallization of the sugar within the screw cap.
2. Not suitable in emergency and unconscious patients.
3. Delayed onset of action because absorption takes time.

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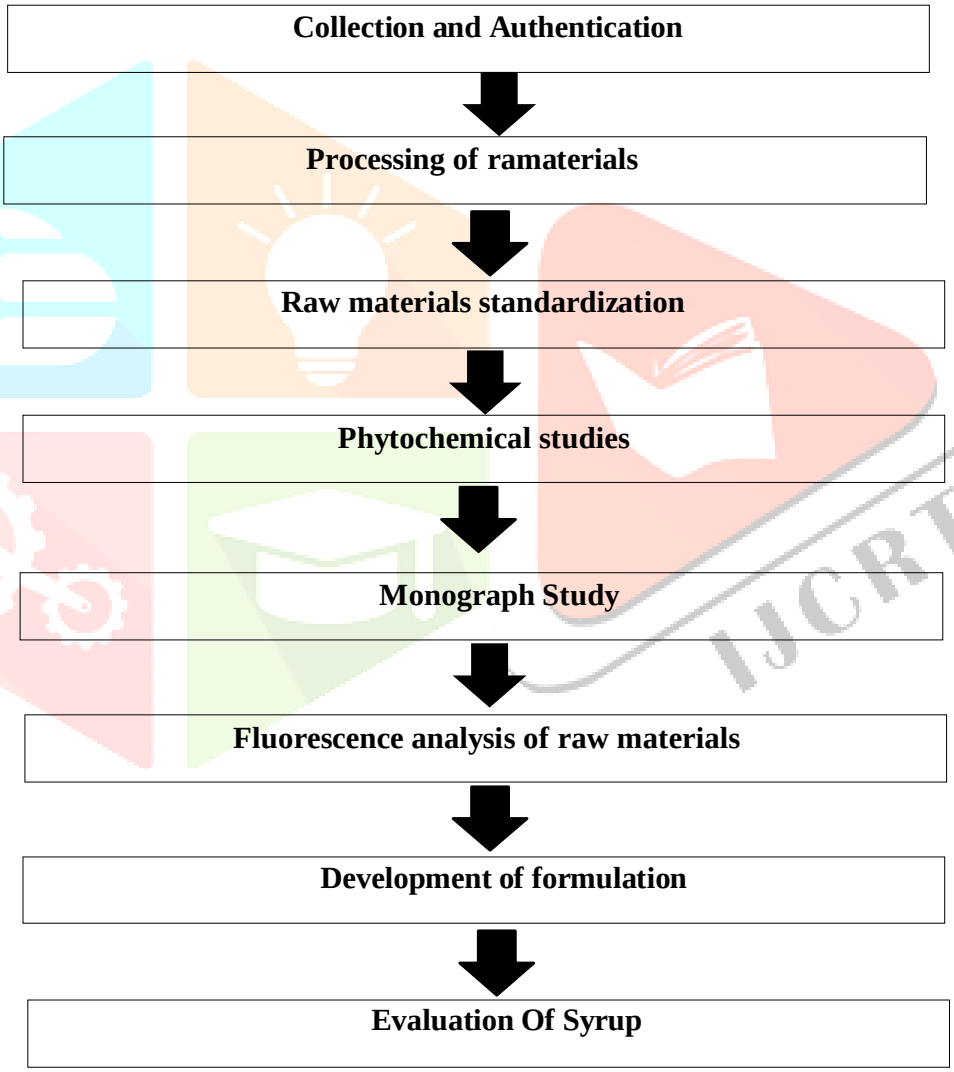
Plan Of work: -



MATERIALS AND METHODS

INGREDIENTS USED IN HERBAL SYRUP

Following ingredients are used in Polyherbal antidiuretic syrup are listed below;

GYMNEMA SYLVESTRE: [Meshashringi]

Leaves of Meshashringi have a potent hypoglycemic effect on diabetic patient. Consumption of these leaves improves insulin level and glucose metabolism. The active components of Meshashringi leaves is Gymnemicacid , which helps to control blood glucose level. It also blocks the sugar receptors on our taste buds. It can be used in the treatment of both type 1 and type 2 diabetes.

SYZYGIUM CUMINI: [Indian Black Jamun]

Dried Black Jamun seeds are used to treat diabetes. Active ingredient present in jamun seeds are jamboline and jambosine that slows down the rate of sugar released into the blood and increases the insulin level.

PROPYLENE GLYCOL: [Stabilizer]

It is viscous, colorless liquid, odorless and has faintly sweet taste. It is commonly used as food additive and drug stabilizer, it helps to preserve moisture in the formulation. Used in medications and cosmetic products.

METHYLPARABEN: [Preservative]

It is commonly used as "Preservative" in topical, oral medication, it prevents the germ growth, used as food preservative and antifungal preservative in food and pharmaceutical industries.

PIPPERMENT OIL: [Flavoring agent]

It is an essential oil extracted from the leaves of peppermint plant belongs to mint family, It has sharp odour and refreshing properties and produce coolness feel in our mouth, it is commonly used as flavoring agents in pharmaceutical medications. Concentrated form of peppermint oil can be used for aromatherapy.

ERYTHROSINE: [Coloring agent]

It is a pink dye which is primarily used for food coloring made from coal tar. It is an organic compound containing iodine and sodium. It is used in pharmaceutical industries.

SACCHARIN SODIUM: [sweetener]

Saccharin sodium is an artificial sweetener. It is 500 times sweeter than sugar but no caloric value and be used as a dilute 1% solution. It is stable and nontoxic, it is used in preparations for diabetes and in slimming diets.

MATERIALS:

Plant materials:

Gymnemasylvestre (Meshashringi) Syzygiumcumini (Indian black Jamun)

Excipients:

1. Propylene glycol
2. Methyl paraben
3. Peppermint oil
4. Erythrosine
5. Saccharin sodium
6. Purified water

PLANT PROFILE

Table 1: Plant Profile of Polyherbal anti-diabetic syrup

Sr. No.	Plants	Biological sources	Chemical Constituents	Uses
1	Meshashringi	Gymnemasylvestre	• Gymnemic acid , Lupeol, • Anthraquinone, Flavones, • Stigmasterol, Dammarene, • Pentatriacontane, • Hentriacontane, • 5- Deoxyinositol	• Used to treat diabetes, metabolic syndrome, Cough, malarial fever. • Used to reduce weight loss, Antidote for snake bite , It acts as an digestive, stimulant, laxative, appetite suppressant and diuretic

2	Indian Black Jamun	Syzygiumcumini	• Ellagic acid, • Gallic acid, • Myricetin, • kaempferol, • Oleanolicacid • ,Petunidin, • Beta – sitosterol, Delphinidin.	• Used to treat type 2 diabetes mellitus, worm infection, asthma, diarrhea, cough and Cold. • It is an anthelmintic, and also used to treat ulcers, dysentery, Bronchitis. • It purifies blood.

EXCIPIENT PROFILE:

Table 2: Excipient profile of Polyherbal anti-diabetic syrup

Sr. No.	Excipients	Uses
1	Propylene glycol	• Food additive • Drug stabilizer • Preservative
2	Methyl paraben	• Preservative • Antifungal preservative • Prevents germ growth
3.	Peppermint oil	• Flavoring agent • Topical analagesic • Anti-pruritic
4	Erythrosine	• Coloring agent • Biological stain • Printing ink
5	Saccharin sodium	• Artificial sweetener • Low calorie value

METHODOLOGY

Collection of Herbal plant materials: Meshashringi leaves and Indian black jamun seeds were collected from our locality, Thiruvallur, it is native to Asia, Africa, and Australia.Leaves of Meshashring were dried about a period of one week to remove moisture, jamun seeds were also dired in a sun shade for 3 days Then the dired leaves and dried seeds were crushed by using a mortor and pistle and it is finely grinded. The finely powdered praticles were sieved by using a sieve no 2.

Preparation of Polyherbal anti-diabetic herbal syrup: Formulation of Polyherbal syrup (50 ml)

Table 3: formulation of herbal syrup

Sr. No.	INGREDIENTS	QUANTITY
1	Meshashringi Leaf Powder	10gm
2	Propylene Glycol	2.5ml
3	Methyl paraben	2.5gm
4	Peppermint Oil	1.5ml
5	Erythrosine	0.1ml
6	Saccharin Sodium	3.3gm
7	Purified Water	Upto 50ml

Formula 2:

Table 4: formulation of herbal syrup

Sr. No.	INGREDIENTS	QUANTITY
1	Indian Black Jamun Seed Powder	10gm
2	Propylene Glycol	2.5ml
3	Methyl paraben	2.5gm
4	Peppermint Oil	1.5ml
5	Erythrosine	0.1ml
6	Saccharin Sodium	3.3gm
7	Purified Water	Upto 50ml

Formula 3

Table 5: formulation of herbal syrup

Sr. No.	INGREDIENTS	QUANTITY
1	Meshashringi Leaf Powder	5gm
2	Indian Black Jamun Seed Powder	5gm
3	Propylene Glycol	2.5ml
4	Methyl paraben	2.5gm
5	Peppermint Oil	1.5ml
6	Erythrosine	0.1ml
7	Saccharin Sodium	3.3gm
8	Purified Water	Upto 50ml

MANUFACTURING PROCESS

Step 1: Preparation of Decoction:
Take 5gm of meshashringi leaf powder and 5gm of Indian black jamun seed powder, then mix it with a 500ml of purified water. Boil the mixture until the volume becomes ¼ of initial volume and then cool the decoction and filter it by using a filter paper. Filtrate obtained from the boiled mixture is used to prepare a final Polyherbal syrup.

Step 2: Preparation of flavor solution:
1.5 ml of peppermint oil in 2.5 ml of propylene glycol was prepared separately.

Step 3: Preparation of simple syrup with sodium saccharin:
Mix 3.3gm of sodium saccharin with 10 ml of distilled water to prepare an concentrated solution, and added to mixing vessel.

Step 4: Preparation of poly herbal syrup:
Filtrate was taken and added to mixing vessel containing simple syrup, and stir it thoroughly and the add excipients like methyl paraben (2.5gm), and add the flavor solution to the mixing vessel and finally add an coloring agent erythrosine (0.1)ml, and then finally make up the value upto 50 ml with purified water

EVALUATION PARAMETERS

Colour:

5 ml of final syrup was taken in a watch glasses and placed under light , and colour is observed by naked eye.
Odour:
2 ml of final syrup was smelled individually and then the odour can be detected.

Taste:
A pinch of final syrup was placed on the taste bud of tongue to identify the taste.

Determination of pH:

Take 5 ml of final syrup in the volumetric flask and make the volume up to 50ml with purified water.
The pH can be determined by using digital pH meter.

Determination of viscosity:

Viscosity of herbal syrup can be determined by using an Ostwald viscometer.
Ostwald viscometer is thoroughly cleaned with chromic acid or acetone. Viscometer should be placed in a vertical position in a suitable stand. Fill the water upto the mark in dried viscometer. Now note the time required for water to flow from mark A to mark B. Repeat the process for 3 times, to obtain accurate reading. Now wash the viscometer and fill it with herbal syrup, and then note the time required for syrup to flow from mark A to mark B.

Determination of density:
The density of syrup can be determined by using a pyncometer. Clean the pyncometer (Specific gravity bottle) with chromic acid and nitric acid, and rinse with purified water. Note the weight of empty dry bottle (w1). Fill the pyncometer with 10 ml of water and weigh it (w2). Finally note the weight of bottle with 10 ml of syrup (w3).

Formula for density
w1 - Weight of empty specific gravity bottle
w2 - Weight of empty specific gravity bottle + 10 ml of water. w3 – Weight of empty specific gravity bottle + 10 ml of syrup.

$$\text{Density of syrup} = \frac{w3 - w1}{w2 - w1} \times \text{Density of water}$$

Determination of specific gravity:
Formula for specific gravity

$$\text{Specific gravity} = \frac{w3}{w2}$$

In vitro evaluation for anti-diabetic syrup:
Glucose bound test:
Plant extract was added to 25 ml of glucose solution of increasing concentration (5, 10, 20, 50, 100 m mol/ L).The mixture was stirred well incubated in shaker water bath at 37 °C in shaker water bath for 6 hours . Centrifuge at 4800rpm for 20 min and the glucose content in the supernatant was determined by using UV spectrophotometer.

RESULTS AND DISCUSSION

Evaluation parameters of herbal syrup and comparison of test and standard syrup:

Table 5: Evaluation Parameters of herbal syrup

Sr. No.	Evaluation Parameters	Formulation 1	Formulation 2	Formulation 3
1	Color	Reddish brown	Reddish brown	Reddish brown
2	Odour	Aromatic	Aromatic	Aromatic
3	Taste	Intensity bitter	Lightly bitter	Lightly bitter
4	pH	6.3	6.3	6.2
5	Viscosity	1.05	1.20	1.23
6	Density	1.21	1.16	1.14
7	Specific gravity	1.01	1.05	1.06

In vitro evaluation for anti-diabetic Polyherbal syrup;

Glucose bound test:

Table 6: In vitro anti-diabetic activity

Sr. No.	**Concentration of glucose**	**Absorbance**			
		Standard	F1	F2	F3
1	5	0.172	0.175	0.179	0.163
2	10	0.163	0.165	0.163	0.153
3	20	0.154	0.163	0.155	0.145
4	50	0.145	0.142	0.143	0.138
5	100	0.135	0.135	0.132	0.122

Conflict of interest: There is no conflict of interest.

CONCLUSION

Herbal medicines are used by 50% of world population, because of their better acceptability, better compatibility with humans. It has lesser side effects than synthetic ones. In this study we prepared a Polyherbal anti-diabetic syrup using a leaf extract of Meshashringi and seed extract of Indian Black jamun, these two herbals possess a potent anti-diabetic effect as referred from the literature study. The prepared syrup undergo various evaluation parameters and it possess the value within the standard limits. In vitro studies for anti-diabetic activity has been done with prepared Polyherbal syrup, it shows a potent anti-diabetic action. Nowadays, increasing demand for herbal medicine has been increased. People may like to accept the herbal medicine due their lesser side effects.

Based on the results of the syrup pre formulation study and the standardization parameter of the formulated syrup, it is concluded that all of the parameters evaluated were within the acceptable range. Physical testing revealed that the formulation had acceptable hardness, friability, and disintegration time. In conclusion, it can be stated that the formulated tablet necessitates additional research to fully investigate the underlying mechanism of action, as well as long-term toxicity studies.

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