Formulation and Standardizationof Antidiabetic Herbal Tablets.

Nidhi N Chauhan*[1], Rujuta Mistry[1], Parul Vasava[1], Drasti Mandale[1]

[1]Department of Pharmacognosy, Laxminarayan Dev College of Pharmacy, Gujarat, India.

Abstract

Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time. Traditional medicine and herbal formulations have been used by mankind for the cure and treatment of various diseases and disorders. Since time unmemorable natural sources have been used as medicines by the humans. As per Indian System of medicine, Ayurveda, Siddha, Unani plants are formulated in various types of dosage forms like churna, gutika, asavas, aristas, avlehas etc. Mamejva herb, roots of ativis, rhizomes of kutki and fruits of pippli are used in preparation of antidiabetic Herbal Tablets. Here in our studies we have formulated the traditional formulation. Considering the significance of patient compliance and market competition with modern dosage forms, it was observed that, formulation was passing quality control tests. The present studies also deals with the evaluation of Morphological and Microscopical studies, phytochemical evaluations and also evaluation parameters of formulated tablets such as weight variation, friability, and hardness and disintegration time.

Keywords: Diabetes, herbs, medicinal plants, hyperglycaemia.

Accepted on 04 December, 2022

Introduction

Diabetes is one of the major crippling diseases in the world. The persons suffering from this metabolic disease is considered to 'die-a-bit' and hence 'die-a-bit-is' (diabetes). Diabetes mellitus is a chronic disorder with interrelated metabolic and vascular components. A relative or absolute deficiency of insulin secretion and activity is associated with hyperglycaemia and altered lipid and protein metabolism. Studies conducted in India in last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in urban population. It is calculated that there are approximately 33 million adults with diabetes in India this number is likely to increase to 57.2 million by the year 2025. Diabetes mellitus also known as simply diabetes is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. This high blood sugar produces the symptoms of frequent urination, increased thirst, and increased hunger. Untreated, diabetes can cause many complications. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers and damage to the eyes. Globally, as of 2013, an estimated 382 million people have diabetes worldwide, with type 2 diabetes making up about 90% of the cases. This is equal to 8.3% of the adult's population, with equal rates in both women and men. Worldwide in 2012 and 2013 diabetes resulted in 1.5 to 5.1 million deaths per year, making it the 8th leading cause of death. Diabetes overall at least doubles the risk of death. The number of people with diabetes is expected to rise to 592 million by 2035. The economic costs of diabetes globally were estimated in 2013 at $548 billion and in the United States in 2012 $245 billion. Journal of Metabolic Syndrome publishes the articles related to diabetes. In Ayurveda diabetes is known as 'madhumeha' and several herbs are mentioned for its cure. One of the formulations in "Bhaisajya Samhita" is mamejva ghanvati which is used in diabetes. It is an Ayurvedic anti-diabetic formulation. It is well documented in Ayurvedic text for sugar lowering potential and used traditionally since ages for mild to moderate hyperglycaemia. Several market formulations are also available (1-3).

Experimental Section

Collection and Authentication of plant materials

The entire materials mamejva herb, roots of ativis, rhizomes of kutki and fruits of pippli were procured and authentified by the Ayurvedic drug supplier named M/S Lallubhai Vrajlal Gandhi (LVG), Ahmedabad.

Morphological and Microscopically study of plant materials

The morphology of all the plant materials obtained from the market was studied and compared with the standard literature. Powder study of Enicostemma littorale, Aconitum heterophyllum, Picrorhiza kurroa and Piper longum was done.

Formulation of antidiabetic herbal tablets 4-6

Initially 25.60 gm leaf powder of of Enicostemma littorale was taken and water was added and it was kept for 6 hours with constant stirring. It was then filtered with a cloth and heated until ghan (solid extract) prepared. Then 0.4 gm powders of Aconitum heterophyllum, Picrorhiza kurroa and Piper longum were added in their respective quantities. The ingredients were passed through sieve number 60 and the granulation was done by wet granulation technique. 5% starch paste was added as a

binding and disintegrating agent. All the ingredients were mixed properly and the resulting solid mixture was used to prepare granules with the help of sieve no. 10. The granules were sun dried and then passed through sieve no. 22 and 44. Granules was collected on sieve no. 44 and were stored in air tight pot bottle and used for preparation of tablets in the tablet machine. The die and punches used for making tablets were of 7 mm. The tablet machine used was RSB-4 Minipress, Rimek India, Single head Rotary tablet compression machine. Weight of each tablet was of 270 mg. A batch size of 100 tablets was prepared (Table 1).

Table 1. *Composition of Formulation of Herbal Tablets.*

Sr no	Ingridents	Quantity
1	Enicostemma littorale	256 mg
2	Aconitum heterophyllum	4 mg
3	Picrorhiza kurroa	4 mg
4	Piper longum	4 mg
5	Starch	2 mg

Evaluation of Quality Control Parameters for Herbal Tablets 7-13:

Organoleptic parameters:

All the four formulations were evaluated for their appearance, colour and odour. Its results were noted down in Table 2.

Table 2. *Appearance, Colour and Odour of Formulation.*

Sr.no	sample	appearance	colour	odour
1.	Antidiabetic Herbal Tablets	Uncoated	Greenish brown	Characteristic

Physicochemical parameter:

1. Determination of ash values

Total ash: 2 to 3g of the air dried drug was weighed accurately in a silica dish and incinerated at a temperature not exceeding 450^{o}C until free from carbon, cooled and weighed. The percentage of ash on dried drug basis was calculated.

Acid insoluble ash: The ash obtained in (a) was boiled with 25 ml of 2 M hydrochloric acid for 5 minutes, the insoluble matter was collected on an ashless filter paper, washed with hot water, ignited, cooled in desiccators and weighed. The percentage of acid insoluble ash on the dried drug basis was calculated.

Water soluble ash: The ash obtained in (a) was boiled for 5 minutes with 25 ml of water, the insoluble matter was collected on an ashless filter paper, washed with hot water and ignited for fifteen minutes at a temperature not exceeding 450^{o}C. The weight of the insoluble matter was subtracted from the weight of the ash; the difference in weight represented the water soluble ash. The percentage of water soluble ash on dried basis was calculated.

2. Determination of moisture content

2 gm of powdered formulation was taken in previously dried petridish. Then drying was carried out in an oven at 60^{o}C till constant weight was obtained. The difference in the weight before and after drying was calculated. Difference in weight was content of moisture in sample.

3. Determination of extractive values

a. Water soluble extractive value and Alcohol soluble extractive value: 5 g of air dried of all formulations; coarsely powdered was macerated with 100 ml of water in a closed flask for 24 hours, with frequent shaking during the first 6 hours and allowed to stand for 18 hours. Thereafter this was filtered rapidly taking precaution against loss of water, 25 ml of filtrate was evaporated to dryness in a tared flat bottom shallow dish and dried at 105^{o} C and weighed. The percentage of water soluble extractive was calculated with reference to air dried drug. Similar procedure is carried for alcohol soluble extractive value using ethanol instead of water.

4. Determination of disintegration time

Place 5 tablets in a tube of disintegration apparatus and the apparatus were started for up and down movement of the tube in such a manner that the complete up and down movement was repeated 30 times a minute. The tablets were disintegrated when no particle remain above the gauge which would not readily pass through it. The time required for the five tablets to disintegrate in the manner described should be not more than 30 minutes.

5. Uniformity of weight of tablets

The average weight was determined by weighing 20 tablets. The tablets were also weighed singly. The deviation from the average weight in each case were also calculated and expressed as percentage. It was necessary that not more than two tablets of all tablets deviates from the average weight by a greater percentage than the limits and no tablet deviates by more than double that percentage.

6. Determination of hardness of tablets

Tablet was placed between the plungers of the Monsanto hardness tester as mentioned above and then upper plunger was forced against the spring by turning threaded bolt until the tablet fractures. When tablet fractured, reading on the scale of hardness tester was noted.

7. Determination of friability of tablets

For determination of friability of tablets, 20 tablets were preweighed and then tablets were placed in plastic chamber of Roche friabilator and apparatus was started to revolve for 4 minutes at the 25 rpm. After 4 minutes tablets were unloaded from the chamber, dusted and again reweighed. The difference in the weight was calculated.

Results and Discussion

The current Morphological and Microscopical study of plant materials used in formulation

Morphology of plant material used in formulation:

Enicostemma littorale plant

Figure 1. *of Enicostemma littorale plant.*

Aconitum hetrophyllum root

Figure 2. *of Aconitum hetrophyllum root.*

Picrorhiza kurroa rhizome

Figure 3. *of Picrorhiza kurroa rhizome.*

Piper longum fruit

Figure 4. *of Piper longum fruit.*

Powder study of plant material used in formulation:

a) Enicostemma littorale plant

I. Xylem vessels

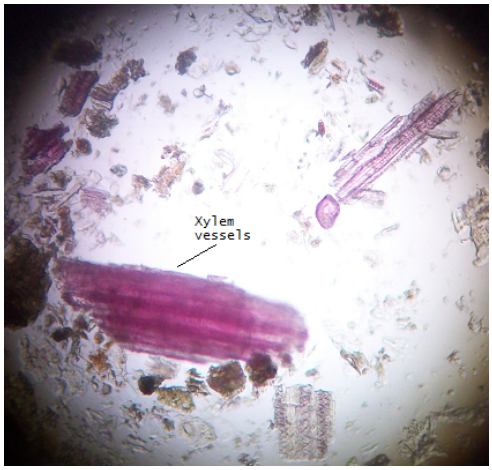

Figure 5. *Xylem vessels.*

II. Seed coat and bordered pitted xylem vessels

Figure 6. *Seed coat and bordered pitted xylem vessels.*

III. Crystals and trichome

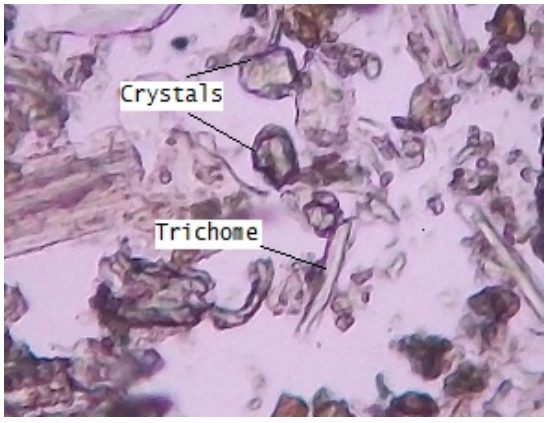

Figure 7. *Crystals and trichrome.*

IV. Epidermal cells

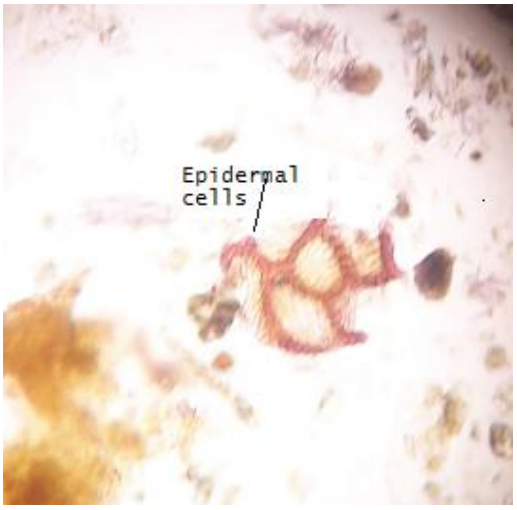

Figure 8. *Epidermal cells.*

V. Anisocytic stomata in leaf surface preparation

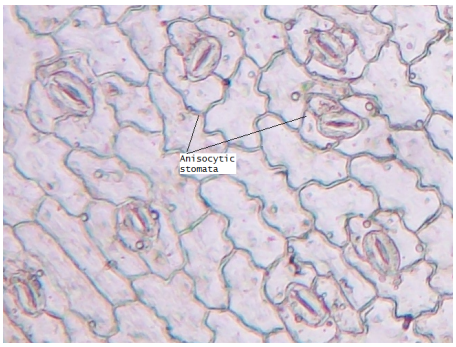

Figure 9. *Anisocytic stomata in leaf surface preparation.*

b) Aconitum hetrophyllum root

I. Starch cells

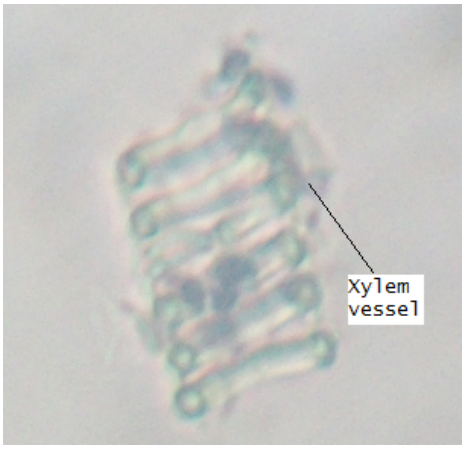

Figure 10. *Starch cells.*

II. Xylem vessel

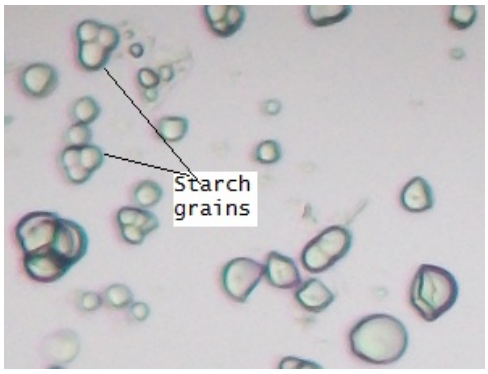

Figure 11. *Xylem vessel.*

III. Cortical tissue (Figure 12)

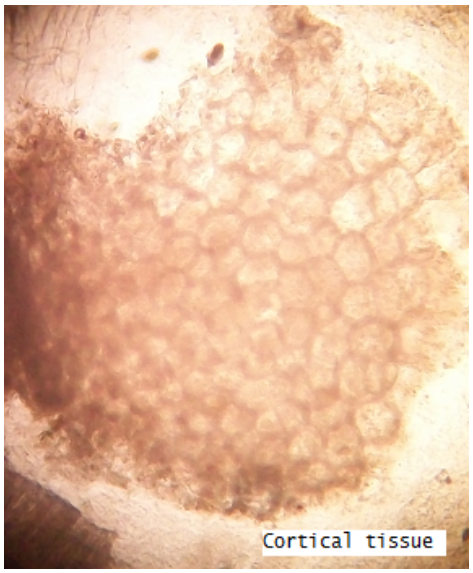

Figure 12. *Cortical tissue.*

IV. Cork cells

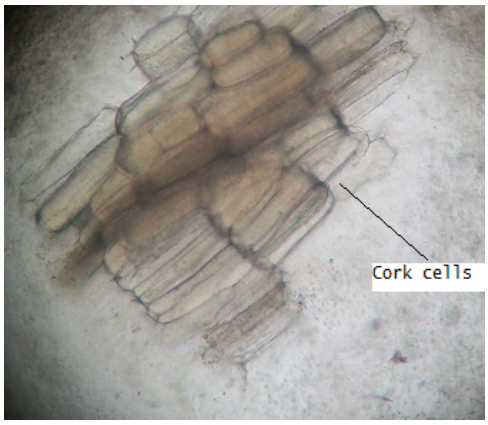

Figure 13. *Cork cells.*

c) Picrorhiza kurroa rhizome

I. Xylem vessels

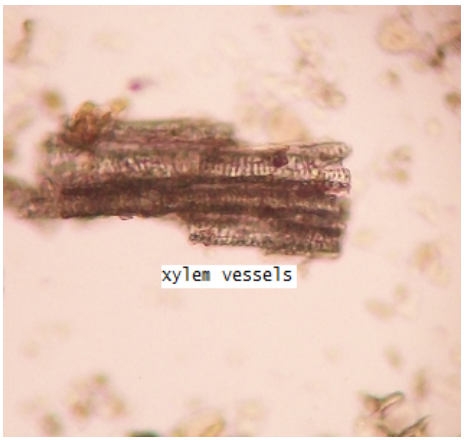

Figure 14 . *Xylem vessels.*

II. Pith cells and Cork cells

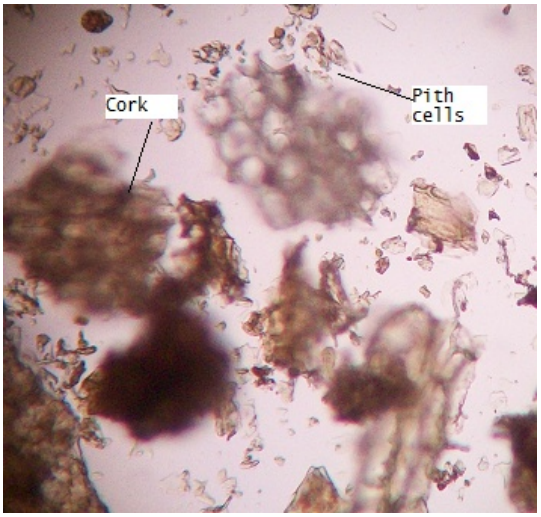

Figure 15. *Pith cells and Cork cells.*

III. Tracheids and pitted xylem vessel

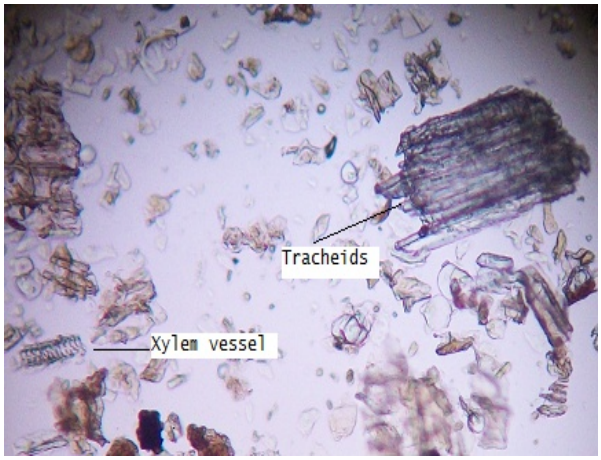

Figure 16 *Tracheids and pitted xylem vessel.*

d) Piper longum fruit (Figure 8)

I. Stone cells

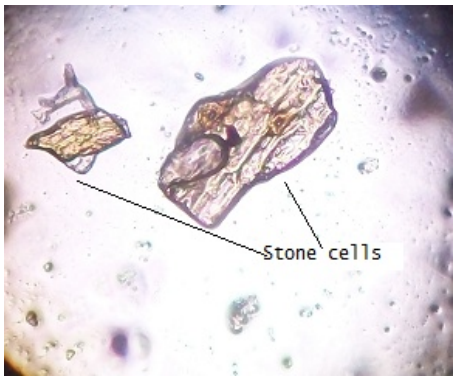

Figure 17 *Stone cells.*

II. Starch cells and crystals

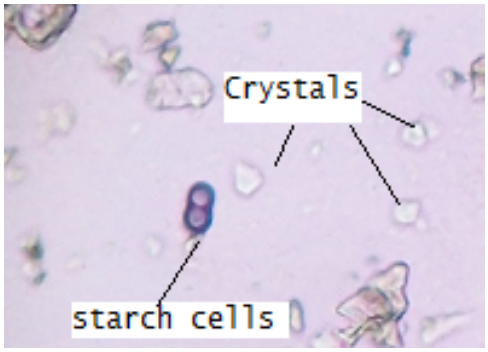

Figure 18. *Starch cells and crystals.*

III. Endocarp

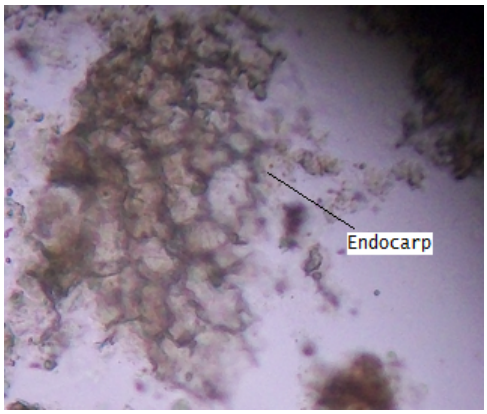

Figure 19. *Endocarp.*

IV. Oil globules

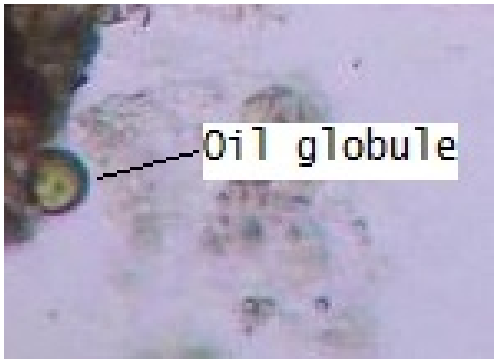

Figure 20.*Oil globules.*

Physicochemical parameter

1. Determination of ash values

Higher ash values indicate contamination due to extraneous material which contains carbonates, phosphates, silicates and silica. High acid insoluble ash is due to present of greater amount of silica especially sand and siliceous earth. Total ash , Acid insoluble ash and water soluble ash of herbal tablets was 6.254%W/W, 2.205%W/W and 2.205 %W/W respectively.

Table 3. *Ash values of formulation.*

Sr.no	Parameter	Ash value Antidiabetic herbal tablets (%w/w)
1.	Total ash	6.254
2.	Acid insoluble ash	2.205
3.	Water soluble ash	4.384

2. Moisture content of formulation

Low moisture content of the formulation is needed to prevent it from microbial spoilage and degradation of active constituents. The moisture content of the Antidiabetic Herbal Tablets formulations was 4.8%.

Table 4. *Moisture content of formulation.*

Sr. No.	Sample	Moisture content
	Antidiabetic Herbal Tablets	4.8%

3. Determination of extractive values

Water extractive value denotes the amount of polar substances present in the formulation. The result shows that laboratory formulation consisted of higher amount of water soluble substances like carbohydrates. Alcohol extractive value denotes the amount of alcohol soluble constituents present in the formulation. Water as well as Alcohol extractive value of Herbal tables was 28.14%W/V and 20.08%W/V respectively.

Table 5. *Water Soluble Extractive Value of Formulation.*

Sr. No.	Sample	Water Extractive value (%w/w)	Alcohol extractive value (%w/w)
1.	Antidiabetic Herbal Tablets	28.14	20.08

4. Determination of disintegration time

It was found from the results that laboratory formulation was within the limit as it was prepared with starch paste (5%w/v) as a binding and disintegrating agent. Disintegration of tablet is very crucial as if the tablet does not disintegrate in time; it remains in the body without any effect as there would be no absorption of the phytochemical constituents. Disintegration time of Herbal tablet was found to be 3 min which is good as per the standards of tablets.

Table 6. *Disintegration time of formulation.*

Sr. No.	Sample	Disintegration time
1.	Antidiabetic Herbal Tablets	3 min

5. Uniformity of weight of tablets

Higher weight variation leads to unequal dose delivery and that would ultimately result in less/more therapeutic effect or adverse effect. The permitted percentage in weight of tablet is 7.5% for tablets of weight 130 mg -324 mg. Weight of 20 tablets was found to be 5.35 gm. Average weight of tablets (20) was found to be 0.267 and Weight Variation (%) of herbal tablets was found to be 0.5%-2.7%.

Table 7. *Weight variation of formulation.*

Sr. No.	Sample	Weight of 20 tablets (gm)	Average weight (gm)	Weight variation (%)
1.	Antidiabetic Herbal Tablets	5.35	0.267	0.5%-2.7%

6. Determination of hardness of tablets

The limit of hardness is 3 -5 kg/cm^2. The laboratory formulation was found to have proper hardness within pharmaceutical limits. Appropriate hardness is required for proper handling during manufacture and storage of formulation.

Table 8. *Hardness of tablets of formulation.*

Sr. No.	Sample	Hardness (kg/cm^2)
1.	Antidiabetic Herbal Tablets	3

7. Determination of friability of tablets

Friability of laboratory formulation was found to be highest. Lower friability is needed for proper production, transportation and storage. The formulation was found to be within the limits of friability which is 1%. Friability of Herbal tablets was 3%.

Table 9. *Friability of tablets of formulation.*

Sr. No.	Sample	Friability (%)
1.	Antidiabetic Herbal Tablets	0.38%

References

1. Singh N, Ayurveda The medicine of the future (part I), in: Pharmacognosy, India. Probe a journal of crude drugs. 1986; 25(2): 121-124.

2. Singh N, Sharma Rakesh K, Arora Rajesh, Ayurvedo-Herbal medicines The Need of the time, Herbal Drugs, A Twenty first Century Perspective, Jaypee Brothers Medical Publishers, New Delhi, 2006;535-547.
3. Agarwal A, Critical issues in Quality Control of Herbal Products, Pharma Times. 2005;37(6):09-11.
4. Sane RT, Standardization, Quality Control and GMP for Herbal drugs, Indian Drugs. 2002; 39(3):184-190.
5. Dixit P P, Londhe J S, Ghaskabdi S, et al. Antidiabetic and related properties of Indian Medicinal Plants, Herbal Drugs, 1st edition ,A Twenty first Century Perspective, Jaypee Brothers Medical Publishers, New Delhi. 2006;377-386.
6. Agarwal S S, Paridhavi M, Herbal Drug Technology, University Press Pvt. Ltd, Hyderabad. 2007; 669-671
7. Ansari S H, Essentials of Pharmacognosy, Birla publications Pvt. Ltd, Delhi. 2008;367-369.
8. Mukherjee Pulok K, Quality Control of Herbal Drugs An Approach to Evaluation of Botanicals, Business Horizons, and New Delhi. 2002;255-349.
9. Anonymous, Quality Standards of Indian Medicinal Plants, 1st edition, Published by Indian Council of Medical Research, New Delhi, 2003, Vol III, p. 386.
10. Vishwakarma L, Rajani M, Bagul et al. A rapid method for isolation of swertiamarin from Enicostemma littorale, Pharmaceutical Biology. 2004; 42(6):400-403.
11. Shah Biren, Seth A K, Textbook of Pharmacognosy and Phytochemistry, 1st edition, Elsevier Publications, New Delhi. 2010;28.

*Correspondence to:

Dr. Nidhi N Chauhan

Department of Pharmacognosy

Laxminarayan Dev College of Pharmacy

Gujarat

India

E-mail: nidhi.berawala11687@gmail.com