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Formulation and Evaluation of Anti-Hyperglycemic Solid Herbal Product of *Plicosepalus curviflorus* Flowers Extract

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ABSTRACT

Plicosepalus curviflorus plant widely distributed in Yemen, traditionally used to treat tonsilitis and otitis media. Also, it has various types of biological activities such as antihepatotoxic, anti-diabetic especially against colon and liver cancers, antimicrobial, antioxidant and cytotoxic activities, Increases Lactation Cows, camels and goat liver troubles. Flowers extract of *P. curviflorus was* evaluated for its Anti-hyperglycemic activity using 36 healthy rats (males) average weight has 191g distributed into six groups, giving them different doses of the extract. The study followed by measuring the change in their blood sugar level after inducing hyperglycemia by Alloxan. The glucose level of 100mg of *P. curviflorus* extract was decreased from 456 mg/dI to 289 mg/dI, while when the dose was 200mg, decreased from 544 mg/dI to 110 mg/dl as compared with Glibenclamide which decrease the blood glucose level from 446 mg/dI to 264 mg/dI. *P. curviflorus was f*ormulated as capsules and evaluated for organoleptic properties of methanolic extract of *P. curviflorus*. The results show that the extract was sparingly soluble, particle size was very fine, tapped density was m/V 1250, in g per ml, flowability of extract powder was excellent, moisture content was 2% and microbial limit test of extract. While weight variation was 704mg, dissolution was 99.51% after 60 min., and stability under various storage condition were also performed.

INTRODUCTION

There has been a great interest in the last few decades in using plants to cure diseases in general, and to consider it as a main source in Alternative Medicine to cure the chronic diseases in particular.**[1]**Prescriptions that contain compounds refer to chemical groups produced by plants are called Botanical Products.

According to the World Health Organization (WHO), "Herbal Preparations" contain plant parts or plant material in the crude or processed state as active ingredients and may contain excipients (foreign substances. **[2]** Combinations with chemically defined active substances or isolated constituents are not considered herbal preparations. **[3]**

Plant medicines are generally considered to be safer and less damaging to the human body than synthetic drugs. Furthermore, there is a current upsurge of interest in plants that is further supported by the fact that many important drugs in use today were derived from plants or starting molecules of plant origin: digoxin/Digitoxin, vinca alkaloids, reserpine and tubocurarine are some important examples. **[4]**

Plicosepalus curviflorus plant widely distributed in Southern-East of Egypt, Northern-west of *Saudi Arabia: Hejaz, Southern-West of Saudi Arabia: Yemen*, and we can found it's in *Sudan, Ethiopia, Eritrea, Somalia, South Sudan, Uganda, Kenya, Tanzania*. **[5]**

Plants belonging to this family have been traditionally used to treat different diseases like smallpox, diarrhea and hookworm's infections. Furthermore, they treat tonsillitis and otitis media. **[6]**

Earlier investigations on genus Plicosepalus reported various types of biological activities such as antihepatotoxic, anti-diabetic, especially against colon and liver cancers. **[7],** antimicrobial, antioxidant and cytotoxic activities**[8] [7]**, colon and liver cancers**. [6]**, Increases Lactation Cows, camels and goat**[9]**, liver troubles. **[10]**

Prior to the development of dosage forms, it is essential that certain fundamental physical and chemical properties of the drug molecule and other derived properties of the drug powder are determined. This first learning phase is known as pre-formulation. **[11]** Pre-formulation is an important step in the development of a new drug. It influences the safety, effectiveness, controllability, stability and compliance of the drug**. [12]**

The capsule is the unit dosage form considered as oldest and used by ancient Egyptians. **[13]** The term capsule is derived from a Latin word 'capsula' meaning a "small box".**[14]** To cover the unpleasant taste of pure Turpentine, in the year 1730 a pharmacist de Pauli from Vienna produced oval-shaped capsules. In terms of frequency of use, capsules have become a popular dosage form and occupy a position only second to tablets **[14].**

In this study, *P. curviflorus freeze* -dried extract powder was prepared and analyzed in the pre-formulation study. In total eight assessments were performed in the pre-formulation study and they are described below.

MATERIALS

The flower methanolic extract of *Plicosepalus curviflorus* with the following concentration were prepared: 100, 1000, 2500, 4000, and 5000 mg/kg.

Glibenclamide, distilled water, Freeze -dried extract of *P. curviflorus*, hard gelatin capsules (Size 0; Color: Red body. Black Cap); Microcrystalline Cellulose 10%, Crospovidone, Sodium starch glycolate, Magnesium Stearate, Talc; hydrochloric acid (HCl) were obtained from Sigma Aldrich. All chemicals used were all of analytical grade.

Equipment

Includes Advice to measure blood glucose level, Oven (Giffin & Geong L-TD) (Metler-Made in Germany); Disintegrator (Erweka- Germany); Dissolution apparatus (SCIENTIFIC Model-DA.60) (Metler- Germany); Balance (Sortorius BP310S NO:91206635- Germany); Balance2 (DENVER Instrument APX-100 - Germany); Hot Plate (Vision Scientific Co. LTD); Freezer (KELON-Model- KDR-20W); Freeze -Dryer (LABONCO Freeze Drier System/LYPH Lock 4.5); Light Microscope; Sieves; Water Bath (CFL 1083 - Germany), UV Spectrophotometer (SHIMADZU Model-UV-1601PC); Capsule filling machine, PH meter (Sartorius PB-11); Chamber 40C" (LAB TECH-LHI-0250E); Chamber 30C" (LAB TECH-LBI-300M).

METHODOLOGY

Experimental animals

The experiment was conducted on Young Swiss-albino rats aged 45 weeks, average weight 200-300 gm were the experiment used 36 healthy rats (males) average weight has 191g. The

rats were distributed into six groups, the rats were randomly selected, marked to permit individual identification and kept in their cages for at least 5 days prior to dosing for acclimatization to laboratory conditions. All rats were maintained on a 12-h light/dark cycle and located at room temperature approximately 23 °C with constant humidity. **[15]**

The dose concentration level given 100, 1000, 2500, 4000 and 5000mg/kg body weight. Body weight of the rats was determined and the dose was calculated in reference to the body weight. **[15], [16], [17]**

Table [1]: **Generalappearanceandbehavioralobservationsforcontrolandtreatedgroups**

Observation			Skin and fur	Behavioral patterns	Salivation	Lethargy	Sleep	Diarrhea	Coma	Tremors
Control group	6 hrs.		+	+	+	+	+	+	No	No
	24 hrs.		+	+	+	+	+	+	No	No
	72hrs.		+	+	+	+	+	+	No	No
Test group	G1	6 hrs.	+	+	+	+	+	+	No	No
		24 hrs.	+	+	+	+	+	+	No	No
		72hrs.	+	+	+	+	+	+	No	No
	G2	6 hrs.	+	+	+	+	+	+	No	No
		24 hrs.	+	+	+	+	+	+	No	No
		72hrs.	+	+	+	+	+	+	No	No
	G3	6 hrs.	+	+	+	+	+	+	No	No
		24 hrs.	+	+	+	+	+	+	No	No
		72hrs.	+	+	+	+	+	+	No	No
	G4	6 hrs.	+	+	+	+	+	+	No	No
		24 hrs.	+	+	+	+	+	+	No	No
		72hrs.	+	+	+	+	+	+	No	No
	G5	6 hrs.	+	+	+	+	+	+	No	No
		24 hrs.	+	+	+	+	+	+	No	No
		72hrs.	+	+	+	+	+	+	No	No

Key: + = Normal

Freeze -Drying *of P. curviflorus* extract powder

The extract frozen in freezer and then freeze - dried under vacuum over 3 days using (LABCONCO freeze dry system/LYPH LOCK 4.5). Once the material dried, it was collected and placed in a moisture-free package and kept in a desiccator until use.

Determination of the organoleptic properties of the plant extract powder

The following **organoleptic properties of** *P. curviflorus* **materials** such as physical appearance, odor and taste were inspected and assessed using the natural senses (e.g. eyes, nose, mouth).

Determination of the solubility of the plant extract powder:

Solubility is an important factor for drug absorption. It is described by the Noyes- Whitney equation: **[18]**

The equilibrium solubility of the freeze -dried extract of ***P.*** *curviflorus* determined as follows: A saturated solution obtained by stirring excess extract powder solute with distilled water for 3 hours at the required temperature (25°C, 37°C) by using water bath until equilibrium has been attained. Samples are withdrawn every 30 minutes and filters. Absorbance of the sample was measured at (280 nm for ***P.*** *curviflorus)* using UV Spectrophotometer. The absorbance reading should increase until one gets to a maximum when equilibrium is reached. This indicates the time required for equilibration.

The solubility was obtained by the following equation:

Solubility = (weight of initial powder - weight of dried residue) / volume of solvent x100%. **[18]**

Particle size determination of the extract powder

One of the most fundamental and easy methods for determining particle size is a sieving method. This method involves passing the material being sized through openings of a particular standard size in sieves. **[19]** So the degree of fineness of powders is determined by sieving. The sieve receiver and the sieves of number 2.4, 2, 1.6, 0.125, 0.1 were arranged in a descending order on the sieve shaker, then 10g of *P. curviflorus was* poured in the top sieve. The process of shaking took 30 minutes. Thereafter the powder collected on each of the sieves was weighed and the percentage(w/w) of each fraction determined.

Determination of the density of the extract powder:

A simple test has been developed to evaluate the flowability of a powder by comparing the poured density (bulk density) and taped density of a powder and the rate at which it packed

down. A useful empirical guide is given by Carr's compressibility index equation: ('compressibility' is a misnomer, as compression is not involved). **[11]**

Carr's index (%) = (Tapped density - Poured density) / Tapped density

In study, the density of *P. curviflorus* extract powder was determined as follows:*P. curviflorus* extract powder was poured into the tared cylinder on apparatus up to a volume between 8-10ml before compacting. The cylinder was then weighed and the weight of extract recorded. Thereafter the cylinder was secured in its holder and the reading of unsettled apparent volume, V0, was taken to the nearest milliliter. The machine was switched on, the powder in the cylinder tapped for approximately 1250 times and the final volume V1250, again taken to the nearest milliliter. The bulk and tapped densities were then calculated using the following equations.

Bulk density (poured density): m /V0, in g per ml

Bulk density = weight of the powder/bulk volume

Tapped density: m /V1250, in g per ml.

Tapped density = weight of the powder / tapped volume

Determination of flowability of the plant extract powder:

The angle of repose (0) is another important parameter that can be used to describe the flowability of a powder (Wells, 2002). In the present study, a special apparatus was used for the test. The apparatus consisted of a glass cylinder kept in the center of the plate, a plate with scale and a ruler for measuring the height of powder mound. To determine the angle of repose, the glass cylinder was filled with 4 g of plant extract, the cylinder smoothly lifted allowing the powder to flow out at the bottom unto the plate leaving a conical mound. The height and radius of the mound was measured and angle of repose then calculated using the following equation: $\tan \theta = h / r$

θ: Angle of repose, h: height of the conical mound, r: radius of the conical mound

Determination of the moisture content of extract powder:

About 0.50 g of the *P. curviflorus* powdered extract was finely powdered and rapidly weighed in a flat-bottomed dish. The extract was then dried in an oven at 100- 105ºC for 3 hours, allowed to cool (approximately 10 minutes) in a desiccator over anhydrous silica gel, weighed and the weight recorded. The moisture content as determined by this gravimetric method was then calculated using the following equations:

Moisture weight = Initial weight (before drying) - Final weight (after drying)

Moisture content = (Moisture weight / Initial weight) 100%

Determination of the microbial limit tests of extract powder:

There are tests for estimation of the number of viable aerobic microorganisms and fungi present and for freedom from designated microbial species; Yeast & Mold, *Escherichia coli, and Salmonella*, *Enterobacteriaceae in* pharmaceutical article of all kinds, from raw materials to the finished forms. The samples are plated out on to Mackonky and Cled, Chocolate, Blood environments at 37ºC for 24 hours.

Determination of the dose of freeze -dried extract per capsule

Formulated capsules of *P. curviflorus* that contain an amount of active ingredient equal to that approved in the effectiveness in treatment of diabetic rate, the amount of freeze -dried extract to be used in the *P. curviflorus* capsules was decided as 200mg/kg which reported in Anti-hyperglycemic activity study. Then we converted rate dose to human dose as below:

Animal dose according to **[20]** in table **[2].**

Table [2]: Dose conversion

Species	Cat 2kg	Monkey 4kg	Dog 12kg	Man 70kg
Mouse 20g	29.231	61.53846	123.0769	384.6154
Rat 200g	4.2222	8.888889	17.77778	55.55556
Guinea pig 400g	1.4902	3.137255	6.27451	19.60784
Rabbet 1.5kg	1.0857	2.285714	4.571429	14.28571
Cat 2Kg	1	2.105263	4.210526	13.15789
Monkey 4kg	0.475	1	2	6.25
Dog 12kg	0.2375	0.5	1	3.125
Man 70kg	0.076	0.16	0.32	10

Formulation and manufacture of the *P. curviflorus* capsules

The selection of the capsule size, the filling machine, the filling method and the excipients where carried out in which 475mg of this drug mixed with excipients in table [3], place manually in a separate size "0" capsules, then taken four capsule daily to provide the desired dose.

Table [3]: Formulation Batches

Ingredient mg / capsule	Amount/ Unite
Extract	475 mg
Microcrystalline Cellulose	96 mg
Crospovidone	12 mg
Sodium starch glucolate	12 mg
Magnesium Stearate	3 mg
Talc	6 mg
Capsule shell weight	100 mg
Total Weight of capsules	704mg

Evaluation of the Manufactured *P. curviflorus* capsules:

Determination of uniformity of weight and the amount of material in the capsules

For the determination of the uniformity of weight, the British Pharmacopoeia method was used **[21].** In which twenty of the *P. curviflorus* capsules prepared as described above were taken at random, their contents individually weighed and the average weight (mass) of the content determined. Not more than two of the individual weights (masses) had to deviate from the average weight (mass) by more than 7.5% and none of the deviates by more than twice that percentage. The amount of powder actually filled into the capsules was also compared with the desired quantity and the difference (in percentage) between the desired and actual quantity calculated. According to the formulation, 468mg of *P. curviflorus* extract was to be filled in one capsule each. Twenty capsules were thus randomly chosen, their contents weighed, the percentage difference between this and the desired weight calculated and averaged for the 20 capsules to assess the accuracy of the filling process.

Determination of moisture content of *P. curviflorus* capsules

For this study, the shell of the capsules was removed and the moisture level of the contents of the capsules determined by using the moisture content analyzer.

Determination of the dissolution profile of *P. curviflorus* capsules.

In this study, the paddle method was used. Further, the quantitation of the amount of plant material dissolved was measured based on UV absorbance measured at 280nm, the wavelengths for maximum UV absorption of solutions of the *P. curviflorus* extract determined by using a UV- Vis Spectrophotometer.

Determination of stability of *p. curviflorus* capsules [22]

In which the capsules were stored in a glass bottle container under two conditions by using a climate chamber.

Table [4]: The storage conditions for the stability study

Batch	Temperature ºC	Relative humidity (RH)	Container
1	30±2 ºC	70%±5% (RH)	Glass container
2	45±2 ºC	70%±5% (RH)	Glass container

The manufactured *P. curviflorus* capsules were stored under the afore-mentioned conditions and every 2 weeks,6 weeks,10 weeks and 12 weeks' samples of capsules were taken from each site and assessed for organoleptic properties (*i.e.* gross physical nature, color and odor of the powder content and overall size, shape and appearance of the capsule).

At 6 weeks and at the end of 12 weeks, the moisture content of the capsules was determined. The organoleptic properties and the moisture level of the content of the test capsules were compared with that of the content of *P. curviflorus* capsules before storage.

RESULTS AND DISCUSSIONS

For Toxicity Study. Acute toxicity testing showed that the methanolic extract of *Plicosepalus curviflorus* at a single oral dose of 100, 1000, 2500, 4000, or 5000 mg/kg BW did not cause mortality or clinical symptoms in rats. The toxic effect of methanolic flower

extract of *Plicosepalus curviflorus* on the appearance and the general behavioral pattern of rats are shown in Table [1].

No toxic symptoms or mortality were observed in any animals after the administration of methanol flower extract at single dose level of 5000 mg/kg body weight. The behavioral patterns of animals were observed first 6 h, 24 h and followed by 72h after the administration of extract and the rats were normal and did not display significant changes in behavior, skin effects, breathing, impairment in food intake and water consumption, postural abnormalities and hair loss.**[23]**

Yield of freeze -dried extract *of P. curviflorus*

The yields of freeze dried extract obtained from *P. curviflorus* using the method are summarized in table [5]. On percentage yield, 85.5 % of extract was obtained from *P. curviflorus crude* flowers. **[24]**

Table [5]: Yield of freeze -dried extract of *P. curviflorus*

Weight of the dry flowers (g)	**Yield of freeze- dried Extract**	
	G	%
83	**71**	**85.5**

The organoleptic properties of the freeze -dried extract *of P. curviflorus*

Figure 1 and table [6], show the freeze -dried extract and a summary of the organoleptic properties.

Figure [1]: Freeze -dried extract of *P. curviflorus*

Table [6]: The organoleptic properties of extract of *P. curviflorus*

Properties	***P. curviflorus***
Physical Appearance	Brittle, free-flowing, small particulate powder
Color	Brown, darker than ground leave powder
Odor	Unpleasant odor
Taste	Bitter

The bitter taste and unpleasant odors normally result in poor patient acceptance of dosage forms. Hopefully, these negative characteristics still present in the extract can be masked when incorporated in capsule form.

The solubility of the freeze -dried extract *of P. curviflorus*

For oral solid dosage forms, aqueous solubility is a crucial factor influencing the bioavailability of drugs. The results obtained in the solubility testing of the freeze dried extract of *P. curviflorus* show that the extract is being sparingly soluble in water. **[25]**

The size of particles the freeze -dried extract of *P. curviflorus*

Particle size and shape are crucial parameter. They are important for the manufacture of the dosage forms, influence dissolution and bioavailability. Particles can be classified under 4 different classes as shown in Table [7].

Table [7]: British Pharmacopoeia 2013 Appendix XVII A. Particle Size of Powders.

Coarse powder	Not less than 95% by weight passes through a number 1400 sieve and not more than 40% by weight passes through a number 355sieve.
Moderately fine Powder	Not less than 95% by weight passes a number 355 sieve and not more than 40% by weight passes through a number 180 sieve.
Fine powder	Not less than 95% by weight passes a number 180 sieve and not more than 40% by weight passes through a number 125 sieve.
Very fine powder	Not less than 95% of the powder by weight passes a number 125 sieve and not more than 40% by weight passes through a number 90 sieve.

The above terms are used in the description of powders and the results of the particle size study are given in Table [8].

Table [8]: Particle size of *P. curviflorus freeze* -dried extract powders

European Sieve No.	ISO Sieve No. (mm)	Wt. retained
2800	2.5	0
2000	2	0
1400	1.6	0
125	0.125	0.09g
90	0.1	2.3g

According to the above results, the *P. curviflorus freeze* -dried extract powders were very fine powders based on the British Pharmacopoeia (BP 2013) standard.

The densities of the freeze - dried extract powders According to Carr's

Bulk of density = Wt. of powder/bulk volume= 0.67 g/ml

Tapped density = 0.76g/ml

Carr>s index % = (Tappdens. -pour density) / Tappdens. = 11.8%

The Carr's index of Compressibility for *P. curviflorus extract* is 11.8 %.

The density study researches show that the extract of *P.curviflorus* freeze -dried extract powders can all be categorized as having excellent flow properties.

The flowability of the freeze -dried extract powder.

The *P. curviflorus* freeze-dried extract powders had angles of repose of 19. Therefore had excellent flow properties.**[24]** This implicated that the *P. curviflorus* freeze-dried extract powders possessed appropriate flowability for the manufacture of capsule dosage form.

The moisture content of the extract. The results of moisture content were 2 %.

The microbial quality of the extract. The microbial contamination testing results on the extract were all within the limitation.

Table [9]: The summary of pre-formulation testing results on *P. curviflorus*.

Testing	*P. curviflorus*
The solubility of extracts	sparingly soluble
Particle size	very fine
Carr's index (%)	11.8%
Angle of repose (°)	19
The moisture content (%)	2%

The amount of the dose of freeze-dried extract per capsule.

The dose which gave the effectiveness as anti-hyperglycemic in rat which reported was 200 mg/kg. Then we converted rat dose to human dose according to Pager and Barenes (1964) as follows:

Mouse dose: 200mg/kg, so 40mg/200g* Average Wt. of rate dose was 200g.So, 40 mg/Rat

Human dose: Adult dose: 40 mg/Rat X **55.556** mg/man **= 2222.24 mg/Man (70kg) =2.222g/Man**)

According to density of powder 0.85 g/ml the total dose will be 1900mg, in which this amount is too large to be filled in one capsule. So; we have divided the total dose into small doses which will be suitable to be filled in capsule, the chosen capsule size was (0) and we will need for 4 capsule each one will be contain 475mg of *P. curviflorus* freeze dried.

Uniformity of weight and content of the capsules.

The results of the uniformity of weight and content of the *P. curviflorus* capsules are given in table (10). The average deviation in weight from average for *P. curviflorus* capsules were 0.75% and amount of content of capsule was *100.61%*, respectively. According to the British Pharmacopoeia (British Pharmacopoeia, 2013), the limit on the acceptable deviation in weight from average for capsules is ± 7.5% and the limits on the amount of content in the capsules 99% to 102%. The afore-mentioned results thus indicated that the *P. curviflorus* capsules met the British Pharmacopoeia specifications.

Table [10]: The Content uniformity test results *for P.* curviflorus capsules.

Sample	Weight of Empty capsule (g)	Weight of filled capsule (g)	Weight of extract (g)	Deviation in Weight from Average (%)	Amount of Content of Capsule(%)
1	0.101	0.707	0.606	0.165%	100..33%
2	0.102	0.704	0.602	0.821%	99.67%
3	0.099	0.702	0.603	0.659%	99.834%
4	0.100	0.709	0.609	0.329%	100.83%
5	0.101	0.715	0.614	1.153%	101.66%
6	0.102	0.708	0.606	0.165%	101.33%
7	0.103	0.707	0.604	0.988%	100.00%
8	0.103	0.707	0.604	0.988%	100.00%
9	0.098	0.714	0.616	1.480%	101.99%
10	0.103	0.710	0.607	0.000%	100.05%
Average	0.1012	0.7083	**0.607**	**0.75%**	100.61%

** Deviation = [Weight of extract (g) - Average weight of extract (g)] / Average * 100%

** % = Weight of extract (g) / 0.604 (g) * 100%

Moisture level of the content of *P.* curviflorus capsules

After the capsules were filled the moisture level of its contents were again tested just to ascertain if there had been changes in moisture level during the manufacturing procedure. The results of these tests are given and indicated that the moisture level of the contents of the *P. curviflorus* capsules were 2.2 % and when analyzed in the pre-formulation study, the moisture content for the *P*. curviflorus extract were however 2%. Thus appeared to have a slight increase in the moisture level of the *P*. curviflorus material after encapsulation. This suggested that this extract absorbed some moisture during the filling procedure, presumably because it was hygroscopic.

Dissolution profile of *P.* curviflorus capsules

The results of the dissolution studies on the *P*. curviflorus capsules are summarized in Table 11 and showed that >70% of the *P. curviflorus* capsule contents dissolved in the dissolution

medium within 45 minutes. These results are within the specification set in the British Pharmacopoeia and indicated that the *P. curviflorus* capsules were immediate release solid oral dosage forms with good *in vitro* bioavailability.

Table [11]: Dissolution profiles of *P. curviflorus* capsule

Time (min)	%amount
15	75.78%
30	83.37%
45	96.61%
60	99.51%

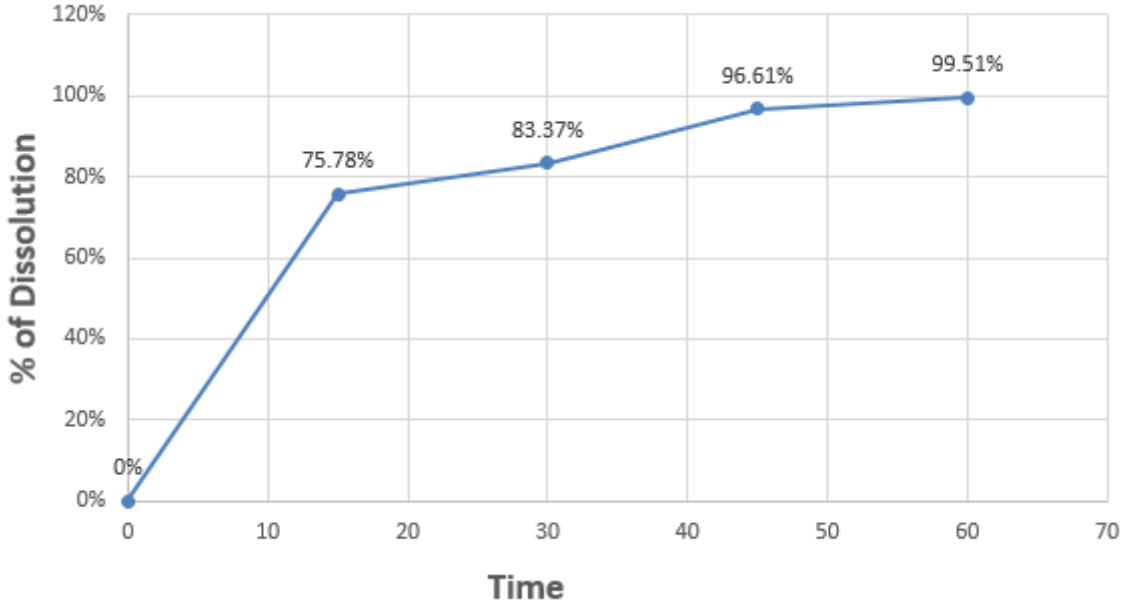

Figure [2]: Dissolution profile of *P.* curviflorus capsules.

Stability of *P. curviflorus* capsules

For the study of stability, two batches of capsules were stored under different conditions. And the results of the organoleptic properties, weight variation, moisture content tested during stability study are given below.

The organoleptic properties of the *P. curviflorus* capsules

When *P. curviflorus* capsules were stored in the glass container, whether at 30±2℃ / 70%±5% RH and 45±2℃ / 75%±5% RH, the organoleptic properties of the plant material

remained relatively unchanged during the 12 weeks' storage. And the results were shown in Table [12].

Table [12]: Organoleptic properties *P. curviflorus* capsules during storage.

No Week	Size, shape of capsule	Gross nature of powder in capsule	Color of powder	Odor of powder
0	Regular '0' size & shape	Powder	Brown	No change
2	No change	Powder	Brown	No change
6	No change	Powder	Brown	No change
10	No change	Powder	Brown	No change
12	No change	Powder	Brown	No change

The Moisture content of *P.* curviflorus capsules

The moisture levels of the *P.* curviflorus capsules contents at 6 weeks and at the end of 12 weeks were determined, Tab. [13]. The results were compared with that of the content of *P.* curviflorus capsules before storage

Table [13]: The moisture levels of the *P. curviflorus* capsules

Time	Percentage of moisture%
Before storage	2.2%
After 6 weeks at 30± ℃/ 70%±5%(RH)	2.4%
After 6 weeks at 45± ℃/ 75%±5%(RH)	2.6%
After 12 weeks at 30±℃/ 70%±5%(RH)	2.4%
After 12 weeks at 45±℃/ 75%±5%(RH)	2.7%

From the results above there was no large change in the moisture levels of the *P. curviflorus* capsules stored in the glass bottle containers under high temperature 45±2℃ / 75%±5% (RH) and 30 ± 2℃ / 70% ± 5% (RH) during storage, and it is strongly suggested that storage in glass bottle containers protect *P. curviflorus* capsules against moisture.

CONCLUSIONS

From the results obtained, we can be concluding the following:

1. Freeze -dried extract powders of *P. curviflorus* have excellent flowability, irregular particle size and shape, is sparingly soluble with high wet ability, on average contained 2.2 % moisture for *P. curviflorus* respectively, had microbial contamination counts well within the specifications and were suitable plant raw materials for incorporation in hard capsule dosage form.

• Elegant capsules that were uniform in content and weight, respectively, Moreover, the manufactured capsules met the British Pharmacopoeia dissolution specification for immediate release solid oral dosage forms and had good *in vitro* bioavailability.

• Because the freeze-dried extract *P. curviflorus* absorbed some moisture during the capsule filling procedure, presumably because it was hygroscopic and since the moisture absorbed may speed up degradation, the humidity conditions during the manufacture of the capsules could be a crucial factor and these capsules should preferably be manufactured under more tightly controlled humidity conditions *i.e.*in conditions of < 40% relative humidity (RH).

Collectively, the results showed that the extract *P. curviflorus* was suitable as raw materials of the plants as far as manufacture of capsules were concerned, but that the stability of these extract containing capsules was acceptable.

The study has achieved its objectives in the flowers extract provide that the extract has high anti-hyperglycemic activity. The study indicated that the presence of the flavonoid as a major active constituent for treatment of diabetes.

In addition, the study provide that the lethal dose is above 5g/kg which consider as safe extract. Also, the study suggest that the freeze-dried of extract and make it as a powder to enhance density, solubility, flowability to became suitable to formulated as capsules dosage form.

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