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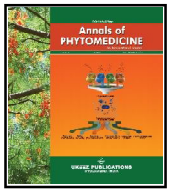

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Formulation and evaluation of capsule of ethanolic extract of *Cnidoscolus chayamansa* Mc Vaugh leaves for the treatment of diabetes

Kulathuran Pillai Kumaraswamy*,◆, Narayanan Nallaperumal, Shaik Karimulla***, Saravanan Devarajan***, Padmavathy Jagannathan****, Venkatachalam Thangavel*****, Ismail Yusuff****** and Bhargavi Boddu*******

**Kamalakshi Pandurangan College of Pharmacy, Ayyampalayam-606603, Thiruvannamalai, Tamil Nadu, India*

***Mohamed Sathak A.J. College of Pharmacy, Medavakkam Road, Sholinganallur-600119, Chennai, Tamil Nadu, India*

****University of Hafr Al Batin, College of Pharmacy, Hafr Al-Batin, Saudi Arabia*

*****Jaya College of Paramedical Sciences, College of Pharmacy, CTH Road, Thiruninravur-602024, Chennai, Tamil Nadu, India*

******Annai JKK Sampoorn Ammal College of Pharmacy, Komarapalayam-638183, Namakkal, Tamil Nadu, India*

*******Crescent School of Pharmacy, B.S. Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India*

********Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram-600117, Chennai, Tamil Nadu, India*

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Abstract

The present study aims in formulating and evaluating the herbal capsules containing the dried ethanol extract of *Cnidoscolus chayamansa* Mc Vaugh. The hot continuous percolation method of powdered plant materials was used in the extraction process using 70% v/v ethanol in the Soxhlet apparatus. The pre-formulation observations (Bulkdensity, Hausnser'sratio, Angleof recline, Tapped density and Compressibility index) of *C. chayamansa* dried ethanolic extract was calculated, followed by the granules formulation necessary for the encapsulation. Three different batches (F1 to F3) of dried ethanolic extract capsules were formulated and moisture content, drug content, disintegration, weight uniformity and dissolution of capsules produced were accomplished. The flow properties of the dried ethanolic extract and its formulated granules were found to be good. Among 3 formulations (F1 to F3), the F3 formulation produced the optimal *in vitro* release (92.75% after 60 min) and uniformity of weight, drug content and disintegration test results were within the Pharmacopoeial standard. The ethanolic extract capsule of *C. chayamansa* leaves were well developed and found to be an utmost common dosage form utilized in the successful control and maintenance of the metabolic condition, diabetes mellitus.

1. Introduction

Cnidoscolus chayamansa Mc Vaugha, a member of Euphorbiaceae family, popularly identified as "Mexican spinach", often called as "Chaya" in Mexico contains high nutritional value such as essential minerals, vitamins, proteins like amino acids and a few fatty acids (Archer *et al*., 2020; Arumugam *et al*., 2013; Aulton and Taylor, 2017). *C. chayamansa* possesses significant medicinal properties, including antidiabetic, antioxidant, hepatoprotective, antitumoral, cardioprotective, antimutagenic, gastroprotective and hypocholesterolemic (Sethumathi *et al*., 2021; García-Rodríguez *et al*., 2014; Pérez-González *et al*., 2016).

Chaya traditionally recommended for the treatment of numerous illnesses like stoutness, renal calculus, acne, piles and problems related to eye. The leaves of Chaya along with the shoots can be used as a water pills, circulation tonic, laxative, in hardening the fingernails, in reviving milk production along with improving digestion (Diaz-Bolio, 1975). Diabetes mellitus (DM) is a deliberate metabolic disorder with heterogenous etiologies (Soumya and Srilatha, 2011; Arumugam *et al*., 2013). A 2019 survey report of International Diabetes Federation (IDF) states that among the age group 20-79 years, 463 million adults have been suffered from diabetes mellitus and by the year 2045, the count is anticipated to outreach 700 million (Wasana *et al*., 2021).

The current treatment regimen for diabetes mellitus includes insulin administration or by prescribing glucose-lowering drugs like sulfonylureas, biguanides, thiazolidinediones and alpha-glucosidase inhibitors. But, this drug produces severe side effects such as disease of liver, hematological effects, coma and kidney, *etc*. (Petchi *et al*., 2014). Plant derived herbal medicines are predominantly considered as less toxic along with less after effects. Hence, this current study was designed to develop and evaluate the herbal capsule containing ethanolic extract of *C. chayamansa* plant for antidiabetic activity.

2. Materials and Methods

2.1 Materials

Silicondioxide was procured from Chemi enterprises LLP, Mumbai; Talc was procured from Astra chemicals, Chennai, Magnesium

Corresponding author: Dr. KK.Pillai

Professor Cum HOD, Department of Pharmaceutics, Kamalakshi Pandurangan College of Pharmacy, Ayyampalayam-606603, Thiruvannamalai, Tamil Nadu, India

E-mail: kkpillai66@gmail.com

Tel.: +91-6383784521

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stearate, croscarmellose sodium, crospovidone, sodium benzoate and microcrystalline cellulose were purchased from Pshkarpharma, Chennai; Starch was purchased from S.P. Associates, Chennai. All additional reagents and alchemical utilized in this investigation were of scientific grade.

2.2 Collection and authentication

The herb planned for the present research, *C.chayamansa*, was assembled from Boothapandy village in district of Kanyakumari, Tamil Nadu in the middle of October-January 2010. The collection process involved the gathering of the entire plant inclusive of the stem, seeds, leaves, flowers and roots. Systematic identification was got from the Botanical Survey of Medicinal Plants, Siddha Unit, Government of India, Palayamkottai and the process of certification was done by Botanist, Mr. Chelladurai with theVoucher Specimen No. (KMCP/KKP/CC-0288).

2.3 Methods

2.3.1. Drying

The leaf parts of the plant were cleansed and dried under cover without sunlight for a period of 15 days to completely remove the dampness from the plant parts. Drying process was followed by weighing the leaves, then by the milling process, after which they are passes though sieve # 40. The air tight container was used for preserving the powder and kept for the further study.

2.3.2 Preparation of ethanolic extract

The milled leaf powder was extracted using ethanol of strength 70%v/v by the process of hot continuous percolation, using the Soxhlet apparatus. Rotary evaporator was used to remove the solvent from the plant extract under reduced pressure. The resulting product is made to undergo freeze drying process in a lyophilizer to get a dry powder. The ethanolic extract of the plant, *C. chayamansa* is then placed in an air tight container and used for further studies (Padmavathy *et al*., 2021; Venkatachalam *et al*., 2021).

2.3.3 Antidiabetic activity

Alloxan induced diabetes in the animal wistar albino rats was the method carried out to evaluate the antidiabetic activity of the *C. chayamansa* ethanol extract as already reported (Kulathuran Pillai *et al*., 2012).

2.3.4 Preparation of granules

Calculated amount of crude extract (EECC), magnesium stearate, carboxy methylcellulose, silicon dioxide, talc, cross povidone, cross-linked carboxymethyl cellulose, starch and sodium benzoate (Table 1) were weighed and correctly mixed and placed for drying. The dried mass is then transferred to sieve no. 36 and placed in air tight containers for further use (Owusu *et al*., 2021).

Table 1: Formulation and development

S.No	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)
1	EECC	250	250	250
2	Silicon dioxide	4.00	4.00	4.00
3	Talc	4.00	4.00	4.00
4	Magnesium stearate	5.00	5.00	5.00
5	CMC	166.5	166.5	166.5
6	Cross linked carboxymethyl cellulose	20	-	-
7	Cross povidone (PVP)	-	-	20
8	Starch	-	20	-
9	Sodium benzoate	0.5	0.5	0.5

2.3.5. Preformulation studies of granules

Preformulation studies of prepared granules were carried out according to the method described by Aulton and Taylor (Aulton and Taylor, 2017).

2.3.6. Formulation of *C. chayamansa* capsules

The encapsulation of the prepared granules was carried out in capsules of size '0'. Fifty capsules were filled simultaneously using the capsule filling machine (Table 1). The formulated capsules were packed and labeled.

2.3.7. Quality assessment of formulated capsules

2.3.7.1 Uniformity of weight

Uniformity of weight of the formulated capsules was carried out by the standard procedure (Pharmacopoeia, 2018; International Pharmacopoeia, 2019).

2.3.7.2 Disintegration test

Disintegration test of the formulated capsules was carried out by the standard procedure (Pharmacopoeia, 2018; International Pharmacopoeia, 2019).

2.3.7.3 Uniformity of drug content test

I. Preparation of stock solution

100 mg of the ethanol extract of *C. chayamansa* leaves was dissolved in small volume of distilled water in a 100 ml standard flask and the volume is made up to 100 ml using distilled water (1000 mg/ml).

II. Determination of absorption maxima

The absorption maxima were determined for the survey scanning of the stock solution from 200-400 nm using Shimadzu UV-1700 Pharma Spec, Japan, UV spectrophotometer.

III. Preparation of calibration curve

The stock solution of the ethanol extract is diluted serially (50, 100, 200, 300, 400 up to 500 mg/ml) in 0.1 M HCl and UV spectro photometer (Shimadzu UV-1700 Pharma Spec, Japan) is used for the measurement of absorbance at 328 nm against the blank. Standard calibration graph (Figure 1) is obtained by plotting the absorbance against their concentrations determining the equation of line (Archer *et al*., 2020).

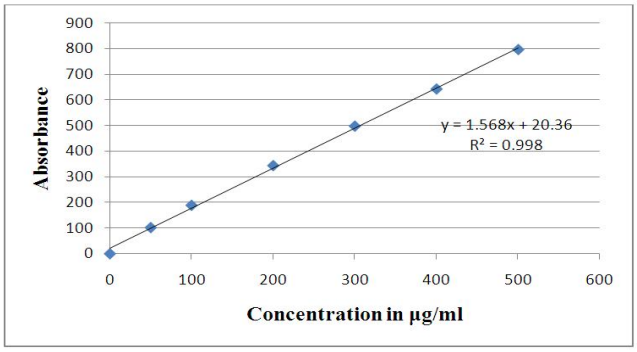

Figure 1: Calibration curve of ethanol extract of *C. chayamansa*.

2.3.7.4 Drug content

Ten capsules were randomly chosen from formulation F1, F2 and F3. The entire capsule from the each batch was drained and squashed. Content was then extracted with 0.1 M HCl in 100 ml standard flask. The quantity of *C. chayamansa* ethanolic extract in each capsule was found by measuring absorbance in UV spectrophotometer at 328 nm. This was done in triplicate.

2.3.7.5 *In vitro* dissolution study of capsules

USP type II paddle apparatus was used for carrying out the dissolution studies that involves the usage of 0.1 M HCl as a release medium at a temperature of 37 ± 0.5^{0}C, and speed of 100 rpm. At 30, 45 and 60 min time interval, 5 ml of dissolution sample medium was taken out and restored using the recently prepared dissolution medium (0.1 M HCl) kept at 37 ± 0.5^{0}C. The samples that were taken out was filtered *via* Whatman filter paper No. 5 and analyzedbythe (Shimadzu UV-1700 Pharma Spec, Japan) UV Spectrophotometer at 328 nm and calculate the amount of drug release from the standard calibration curve of ethanolic extract. The cumulative drug release was calculated and plotted against time.

2.4 Statistical analysis

Graph Pad Prism software is used for statistical analysis and all measurements were carried out in triple and results stated as mean ± standard deviation.

3. Results

3.1 Preformulation and formulation development studies

The formulated granules (F1, F2, and F3) produced the good flow properties with Angle of repose of 30.41 ± 0.01, 29.41 ± 0.03 and 28.01 ± 0.04, Bulk density of 0.71 ± 0.03, 0.76 ± 0.04 and 0.79 ± 0.11, Tapped density of 0.76 ± 0.05, 0.79 ± 0.04 and 0.82 ± 0.02, Hausner's ratios of 6.5 ± 0.7, 6.17 ± 0.3 and 5.95 ± 0.2, Compressibility index of 1.24%, 1.12% and 1.03%, respectively (Table 2).

Table2: Preformulation study of granules

Preformulation factors	F1	F2	F3
Angle of repose	30.41 ± 0.01	29.41 ± 0.03	28.01 ± 0.04
Bulk density	0.71 ± 0.03	0.76 ± 0.04	0.79 ± 0.11
Tapped density	0.76 ± 0.05	0.79 ± 0.04	0.82 ± 0.02
Hausnser's ratio	6.5 ± 0.7	6.17 ± 0.3	5.95 ± 0.2
Compressibility index	1.24	1.12	1.03

Mean ± Standard Deviation (n=3)

3.2 Evaluation test for capsule

The results of the evaluation study such as weight variation, moisture permeation, content uniformity and disintegrat ion test of formulated capsule are shown in Table 3. The results indicate that weight variation, moisture permeation, content uniformity and disintegrat ion test of formulated capsule within the limits as per the Indian Pharmacopoeia standard.

Table 3: Evaluation test for capsule

S.No	Evaluation test	F1	F2	F3
1	Weight variation	448 ± 2.4	447 ± 3.2	448 ± 1.2
2	Moisture permeation	2.6w/w	2.4w/w	2.2w/w
3	Content uniformity	94.5 ± 0.5	96.27 ± 2.2	97.27 ± 2.7
4	Disintegrat ion test	10 min	9 min	7 min

3.3 Dissolution test

Figure 2 and Table 4 exhibit the dissolution profile of the capsules developed. The result indicates that the formulated capsules passed the dissolution test as per the Indian Pharmacopoeia standard.

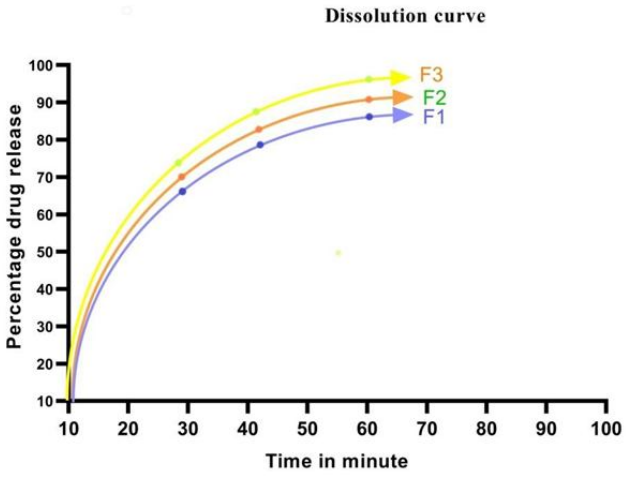

Figure 2: *In vitro* dissolution study curve for F1, F2, and F3.

Table 4: *In vitro* dissolution study

Capsule No	F1			F2			F3		
	30 min	45 min	60 min	30 min	45 min	60 min	30 min	45 min	60 min
1.	59.52	74.28	86.07	61.72	76.07	88.07	63.07	79.07	91.07
2.	58.07	73.07	85.21	62.07	77.12	87.91	64.07	78.01	92.21
3.	57.27	75.07	88.07	68.27	78.27	89.27	69.07	77.29	93.27
4.	58.27	72.21	87.27	61.28	77.29	88.91	68.27	79.27	92.91
5.	59.27	75.12	88.39	62.28	79.27	86.01	69.01	80.27	94.27
Empty capsule	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.006
Average	58.46 ± 0.91	73.95 ± 1.27	87 ± 1.34	62.25 ± 0.60	77.60 ± 1.47	88.03 ± 1.26	66.69 ± 2.89	78.76 ± 1.15	92.75 ± 1.41

4. Discussion

Three formulation trials were done by utilizing various choices of the excipients taking in to account distinct aspect of obstacles related to manufacturing process inclusive of the quality flaws in mind. All the resultant formulations were evaluated for their uniformity of filling, flow property, uniformity of weight, disintegration time and moisture content. The flow properties of trial 3 were within the range of excellent and they were in the specified limits.

According to the IP standard evaluation limit, the individual weight of not more than 2 of the individual weights deviated from the average weight by more than 7.5% and none deviated by more than 15%. Therefore, the formulated capsules passed the uniformity weight test. Moisture content of the empty capsules were found to be 2.62% w/w. As per the Indian Pharmacopoeia standard, the acceptable limit for disintegration time of hard gelatin capsules should be not more than 30 min. No residual mass was observed in the apparatus within 7 min (Table 3). It is found in the limits for disintegration of capsules as per the Indian Pharmacopoeia standard. All the ten capsules have their percentage drug contents as per the Indian Pharmacopoeia standard (Table 3) which indicates that the formulated capsules contained the specified amount of the plant extract (Raphael *et al*., 2011).

The Pharmacopoeia standard for regular dosage forms predicts not lesser than 70% of the drug present should be delivered at 45 min in the medium used for dissolution. Based on the results obtained by the 60th min, 87.00, 88.03 and 98.46% of the drug present was released from the F1, F2 and F3 formulation, respectively. The above statement reveals the capsules produced, get through the dissolution test and it also infers that the drug present can be made to diffuse effectively in physiological solution to release the drug present or extract available for absorption and the necessary pharmacological activity obtained (Jyothi *et al*., 2017).

5. Conclusion

Herbal medicines usage is becoming a new era in the modern treatment of chronic diseases like diabetes mellitus, hypertension, obesity. The formulations using the plant extracts have proven to be the widely used therapy nowadays. Therefore, the present work using the ethanolic extract of *C. chayamansa* leaves as capsules was found to be successful in formulation and the formulated capsules was within pharmacopoeia specification for grade evaluation and is also found as desirable surrogate medicines for controlling and curing diabetes mellitus.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

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References

Archer, M.A.; Kumadoh, D.; Yeboah, G.N.; Kyene, M.O.; Kumatia, E.K.; Antwi, S. and Appiah, A.A. (2020). Formulation and evaluation of capsules containing extracts of *Cassia sieberiana* for improved therapeutic outcome. Sci. Afr., **10**:e00609.

Arumugam, G.; Manjula, P. and Paari, N. (2013). A review: Antidiabetic medicinal plants used for diabetes mellitus. J. Acute Dis., **2**:196-200.

Aulton, M.E. and Taylor, K. (2017). M. Aulton's Pharmaceutics E-Book: The Design and Manufacture of Medicines. Elsevier Health Sciences.

Diaz-Bolio, J. (1975). Chaya (*Cnidoscolus chayamansa*, Euphorbiaceae), a marvelous food (in spanish). Tierra, **30**:407-408.

García-Rodríguez, R.V.; Gutiérrez-Rebolledo, G.A. and Méndez-Bolaina, E. (2014). *Cnidoscolus chayamansa* Mc Vaugh, an important antioxidant, anti-inflammatory and cardioprotective plant used in Mexico. J. Ethnopharmacol., **151(2)**:937-943.

International Pharmacopoeia (2019). WHO, Ninth edition.

Jyothi, D.; Koland, M.; Priya, S. and James, J. P. (2017). Formulation of herbal capsule containing *Trigonella foenum-graecum* seed extract for the treatment of diabetes. J. Young Pharm., **9(3)**:352-356.

Kulathuran Pillai, K.; Chidambaranathan, N.; Mohamed Halith, M.; Jayaprakash, S. and Narayanan, N. (2012). Anti-hyperglycemic effect of alcoholic extracts of *Cnidoscolus chayamansa* in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. Int. J. Res. Pharm. Chem., **2(1)**:179-187.

Owusu, F.W.A.; Asare, C.O.; Enstie, P.; Adi-Dako, O.; Yeboah, G.N.; Kumadoh, D.; Tetteh-Annor, A.; Amenuke, E.M. and Karen, M. (2021). Formulation and

in vitro evaluation of oral capsules and suspension from the ethanolic extract of *Cola nitida* seeds for the treatment of siarrhea. Biomed. Res. Int., pp:1-7.

Padmavathy, J.; Venkatachalam, T.; Sarath Chandiran, I.; Raman, S.G.; Rajkumar, R. and Saravanan, D. (2021). Evaluation of anti-inflammatory and antidiabetic activities of *Actinodaphne madraspatana* Bedd Leaves. Res. J. Pharm. Technol., **14(1)**:47-51.

Pérez-González, M.; Gutiérrez-Rebolledo, G. and Jiménez-Arellanes, M. (2016). Importancia nutricional, farmacológica y química de la chaya (*Cnidoscolus chayamansa*). Temas de Ciencia y Tecnologia, **20(6)**:43-56.

Petchi, R.R.; Vijaya, C. and Parasuraman, S. (2014). Antidiabetic activity of polyherbal formulation in streptozotocin-nicotinamide induced diabetic wistar rats. J. Tradit. Complement Med., **4(2)**:108-17.

Pharmacopoeia (2018). BRITISH and British Pharmacopoeia Commission, Pharmacopeia and it comes as such, The Stationery Office, London.

Raphael, J.; Tunkumgnen, B.M. and Joseph, A. (2011). Formulation and evaluation of *Bridelia ferruginea* and *Canthium glabriflorum* herbal capsules. J. Current Res. Ayurvedic Pharm. Sci., **1(7):**11-18.

Sethumathi, P.P.; Manjuparkavi, K.; Lalitha, V.; Sivakumar, T.; Menaka, M.; Jayanthi, A, and Ashok Kumar, B. (2021). Evaluation of *in vitro* antioxidant and antimicrobial activity of polyherbal formulation of *Thirikadugu chooranam* and *Parangipattai chooranam*. Ann. Phytomed., **10(2)**: 169-174.

Soumya, D. and Srilatha, B. (2011). Late stage complications of diabetes and insulin resistance. J. Diabetes Meta., **2**:1000167.

Venkatachalam, T.; Chitra, M.; Kalaiselvi, P.; Chitra, A.; Sumathi, K.; Suresh Babu, C. M.; Senthilkumar, N. and Sattanathan, K. (2021). Phytochemical screening and antidiabetic potentiality of *Pavetta indica* L. (Angiosperms: Rubiaceae) methanol extract on streptozotocin induced diabetic mice. Ann. Phytomed., **10(2)**:292-297.

Wasana, K.; Attanayake, A.P.; Jayatilaka, K. and Weerarathna, T.P. (2021). Antidiabetic activity of widely used medicinal plants in the Sri Lankan traditional healthcare system: New Insight to Medicinal Flora in Sri Lanka. Evid. Based Complement Alternat. Med., **12**:10.

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