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Formulation and Evaluation of Antidiabetic Tablet from Custard Apple Leaves

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ABSTRACT

Custard apple leaves having a antidiabetic and antimicrobial properties, enhance the brain activity, Improve heart function, improve eye health. In this study we have used the Annona Squamosa Leaves family Annonaceae to investigate its anti-diabetic activity. Custard apple Leaves found in local area mainly in village place. These Leaves were dried for 3-4 day under sun light and size is reduced and passed through sieve no # 44, 60,80,100 The powder sample was analysed for different physicochemical & flow properties. The powder sample of sieve no #80 and various excipient were used for preparing tablets. Tablets were analysed for various evaluation parameters like hardness, thickness, friability, weigh variation. The Tablets found to be stable after evaluation. Annona Squamosa showed Antimicrobial activity against gram positive organism staphylococcus aureus and Bacillus Subtilis but did not show any activity against E.coli.

Keywords: *Custard apple, antioxidant, antidiabetic, antimicrobial, Annona squamosa L.*

INTRODUCTION

Custard apple is important dry land horticultural crop of Maharashtra. Pune district stands first in the state with respect to area and production. custard apple leaves help in the regulation of sugar in the body due to presence of fibers and antioxidant custard apple leaves source is *Annona squamosa* family *Annonaceae*.in which content flavonoids, alkaloid work as a antidiabetic agent. Leaves having a properties like control diabetes symptoms, enhances brain activity, improve heart function, improve eye health, treat skin infection, boost immune system, antimicrobial activity. Besides these nutritional properties, custard apple has some unique ethnomedicinal properties. Leaves and bark of the Custard apple plant is reported to contain flavonoids, glycosides, tannins, phenolic compounds, etc. Likewise, phytochemical characterization of fruits, seeds and other parts of custard apple revealed the presence of alkaloids, flavonoids, and acetogenins which exhibit lipid peroxidation, antidiabetic, antioxidative activity against various ROS, hypoglycaemic.

Biological Sources

1) Botanical Name: *Annona squamosa*
2) Family Name: A*nnonacea*e
3) Common Name: *custard apple leaves*
4) Part Used: Leaves

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Common Name

1) Hindi: Sitafal leaves
2) English: Custard apple leaves
3) Marathi: Sitafal leaves

MATERIALS AND METHODS

Plant Material Collection and Preparations

Custard apple leaves are collected from the rural area of the Loha city. In this area these plants are mainly found in the farms, leaves of custard apple are collected in winter season for the presentation of antidiabetic custard apple leaves tablets. after properly collection of the leaves wash the leaves properly with clean water then dry under morning sunlight, then crush the leaves and prepare powder.

Method

A) Preformulation Study

a) General Appearance Physical examination like Colour, Odor, Taste is done by organoleptic inspection.

b) Bulk Density: It refer to packing of particles in powder sample. Bulk density is used to determine the amount of powder sample that occupies the volume in g/ml. Weighed quantity of powder sample was transferred into 100ml measuring cylinder. The volume occupied by powder material was measured. Bulk density was calculated by using formula;

$$Bulk\ density = \frac{mass\ of\ powder}{bulk\ volume\ of\ powder}$$

c) Tapped density: Weighed accurate quantity of powder sample was transfer into a graduated measuring cylinder. Volume occupied by the powder was noted down. Then cylinder was subjected to 100-300 taps in tap density apparatus. Tapped density was calculated by using formula;

$$Tapped\ Density = \frac{mass\ of\ powder}{Tapped\ volume}$$

d) Carr's Index (Compressibility): The compressibility index and Hausner's ratio was measures the property of powder to be compressed. The packing ability of powder material was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated by following

$$Carr's\ Index = \frac{(Tapped\ density\ -\ Bulk\ density)}{Tapped\ density} \times 100$$

e) Hausner s' Ratio: It is measurement of frictional resistance of powder. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density.

$$Hausner's\ Ratio = Tapped\ density / Bulk\ density$$

f) Angle of Repose (θ): It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is determined by the equation;

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$$\textbf{Angle of repose}\ (\theta) = tan^{-1}(h/r)$$

Where, θ = Angle of repose. h = Height of powder heap. r = Radius of the powder cone.

g) Flow Rate: Weighed accurate quantity of powder sample. Place a cotton plug at the neck of a clean and dry funnel of stem diameter 1-2.5cm. Place powder sample in the funnel. Remove plug from the neck & record the total time required for all the powder to flow. Calculate flow rate by using formula.

$$\textbf{Flow rate} = \frac{\textbf{Weight of powder}}{\textbf{Time Required to flow}}$$

h) Total Ash Value: Used to determine quality and purity of crude drug and to establish the identity of it. Weigh 2gm of powder drug into the crucible. Ignite sample on burner (flame) until all the carbon is burned off. Cool it and weigh the ash. Calculate the percentage of total ash with references to the air-dried sample of crude drug.

- Weight of the empty dish = x
- Weight of the drug taken = y
- Weight of the dish with ash = z
- Weight of the ash = (z - x)

$$\textbf{Total ash} = \frac{100(Z - X)}{y}$$

Tablet Formulation: In direct compression process powdered material is directly compressed into tablets without modifying physical properties. This is a cost-effective way to develop tablets, and it's a common solution for producing generic products in the pharmaceutical industry. Direct compression also avoids a wide range of wet and dry granulation problems.

Here are the steps for a successful direct compression tablet manufacturing process:

1) Mill therapeutic agents and excipients.
2) Mix the milled powders (active ingredient) starch, lactose, sufficient quantity colouring agent, talc.
3) Compress the tablets.

i) Antimicrobial Test: Antimicrobial test has to be performed against *Escherichia coli* & *Staphylococcus aureus* in proper culture medium. Weigh accurately all the ingredients & prepare nutrient broth and agar medium, which will be used for sub-culturing of pathogen (freshly prepared bacterial culture). Take petri plate and test tube wash it properly with tap water & autoclave it (at 121^0 C 15lb pressure for 15-30minute). In aseptic room, dilute the testing sample in test tube in a range of 10:1, 10:2, & 10:3 respectively. Transfer the agar medium in petri plate in aseptic condition allowed it cool & solidify. Then transfer the microbial culture which is required (*E.coli & S.aureus*) with the help of sterile disposable syringe. Shake it properly 2-3 times for proper mixing. Then transfer the sample which is diluted with the help of disc or boher plate technique. Then, incubate the plate for 24-48hrs in incubator. Calculate the zone of inhibition by comparing with standard.

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Fig.1: Antimicrobial Activity against staphylococcus aureus

Fig.2: Antimicrobial Activity against Bacillus subtilis

Fig.3: Antimicrobial Activity against E.coli

j) Hardness test: This test is also known as "Crushing Strength Test". Tablets require a certain amount of strength, or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping. Tablet hardness has been defined as the force required to break a tablet in a diametric compression test. The hardness is measured in Kg/cm^2. Official standards for Hardness is 5-8 kg/cm^2 for standard compressed tablet except Effervescent tablet, Dispersible tablet, Orodispersible tablet, Chewable tablet etc. More than 8-12 kg/cm^2 for Sustain released tablet and controlled release tablet.

k) Thickness test: Tablet thickness is determined by the diameter of the tablet. Micrometer and vernier caliper are used for checking tablet thickness. Thickness should be controlled within ± 5% variation of a standard value. Thickness must be controlled for consumer acceptance of the product, and to facilitate packaging.

Note: As per official standard, tablet thickness variation alloted upto (+ or -) 5% of standard.

l) Friability test: "FRIABILITY is the phenomenon where the surface of the tablet is damage or shown a site of damage due to mechanical shock." The purpose of friability test is to

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evaluate the ability of the tablets to withstand the breakage during the transportation and handling. Friability testing is a method, which is employed to determine physical strength of uncoated tablets upon exposure to mechanical shock and attrition. In simple words, friability test tells how much mechanical stress tablets are able to withstand during their manufacturing, distribution and handling by the customer. It means Surface Erosion by certain mechanical shock and loss of material.

m) Disintegration test: Disintegration is a process in which tablets are break up into granules or smaller particles. The time it takes a tablet to disintegrate is measured in a device described in the USP/NF. So, disintegration test is a measure of the time required for a group of tablets to break up into particles under a given set of conditions. This test is essential for tablets intended for administration by mouth, except those intended to be chewed before being swallowed or those that should dissolve slowly in the mouth, e.g., lozenges, glyceryl trinitrate, or effervescent tablets. Also, disintegration does not apply to some types of sustained- release tablets

RESULT

Table 1: Pre-formulation Study

Sr.No.	Test	Sample[A]	Sample[B]	Sample[C]	Sample[D]
1	Color	green	green	**green**	green
2	Oduor	Little like vanilla	Little like vanilla	**Little like vanilla**	Little like vanilla
3	Taste	sweet	sweet	**sweet**	sweet
4	Bulk density (gm/ml)	0.27	0.31	**0.31**	0.28
5	Tapped density (gm/ml)	0.41	0.38	**0.32**	0.31
6	Carr's index (%)	34%	18%	**3%**	9%
7	Hausners ratio	1.51	1.22	**1.03**	1.10
8	Angle of repose	36.129	24.227	**24.702**	18.778
9	Ash value	15%	11%	**18%**	15%

Table no 2: Solubility Test

Test	*Sample [A]*	*Sample[B]*	*Sample[C]*	*Sample[D]*
Water	*Sparingly soluble*	*Slightly soluble*	*Insoluble*	*Insoluble*
0.1N NaOH	*Slightly soluble*	*Soluble*	*Insoluble*	*Insoluble*
0.1N HCl	*Soluble*	*Sparingly soluble*	*Insoluble*	*Insoluble*

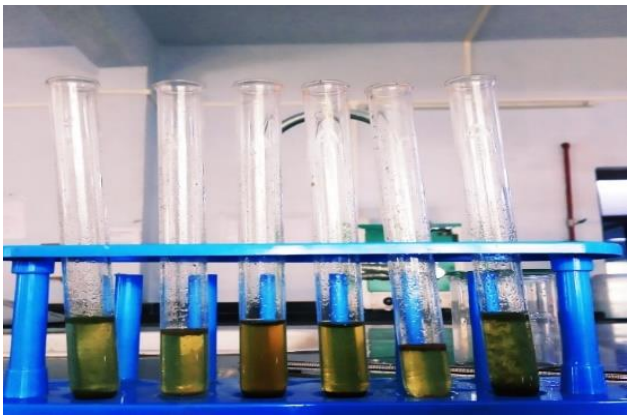

Fig. 4: Solubility Test

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Fig.5: Powdered drug from seive no #44,60,80,100

Antidiabetic tablets are formulated and evaluated from custard apple leaves.

Fig.6: Prepared Tablet

3.Formulation Table

Sr. No.	Name of Ingredient	Batch f1	Batch f2	Batch f3	Batch f4
1	API (mg)	100	150	200	250
2	Starch (mg)	40	40	40	40
3	Lactose (mg)	350	300	250	200
4	Coloring agent (q. s)	10	10	10	10
	TOTAL	500	500	500	500

Table No 4. Evaluation of Tablets

Test	Standard value	Result
Hardness	5-8 kg/cm^2	4.23kg/cm^2
Thickness	4 mm	3.057mm
Friability	0.5 to 1%	1.080%
Disintegration	5 to 3 min	3 min

Table No 5. Weight Variation Test

Average weight of tablets	Percentage deviation
509 mg	-1.7 to 4.12

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CONCLUSION

As we know that, custard apple leaves have good antidiabetic activity. In current research study it has been observed that, our batch C (sieve no # 80) Passes all the preformulation parameter. We utilized this batch for preparation tablets having codes like F1(100%), F2(150%), F3(200%), F4(250%) at last we come to the conclusion that batch F1(100%) passes all the quality control test. After that the antimicrobial profile of custard apple leaves zone of inhibition against gram+ve *staphylococcus aureus* and *bacillus subtills* but did not show any activity against *E.coli.*

REFERENCES

1) Vijay K and Sriram S, "Antioxidant activity of seed extracts of Annona reticulata and Carica papaya". Nutrition and Food Science. 2010; 40 (4): 403-408
2) Alali, Liu, X and McLaughlin, J. L. "Annonaceousacetogenins: recent progress". Journal of Natural. Products. 1999; 62: 504-540.
3) Kalidindi N., Thimmaiah N.V., Jagadeesh N.V., Nandeep R., Swetha S., Kalidindi B. "Antifungal and antioxidant activities of organic and aqueous extracts of Annona squamosa Linn." leaves. J. Food Drug Anal. 2015;23:795-802.
4) 1. Singh Y, Bhatnagar P, Thakur N. "A review on insight of immense nutraceutical and medicinal potential of custard apple" (Annona squamosa Linn.). Int J Chem Sci [Internet]. 2019 Apr 1 [cited 2022 June 1];7(2):1237-45.
5) Bansal V.S., Bhatnagar P.K. Antihyperglycemic effect of "Annona squamosa hexane extract in type 2 diabetes animal model": PTPIB inhibition, a possible mechanism of action. Indian J. Pharmacol. 2012;44:326-332. doi: 10.4103/0253-7613.96304.
6) Bhattacharya A, Chakraverty R. The "pharmacological properties of Annona squamosa Linn": A Review.IJPE.2016;4(2):692-699.
7) Mazahery, A. R. F., Dator, R. P., Concepcion, G. P. & Jacinto, S. D. Murihexocin C from the "Leaves of Annona squamosa Linn. Induces Apoptosis in Human Colon Carcinoma" Col 2 Cell Line. Philipp Agric Sci 92, 122–132 (2009).
8) Mazahery, A. R. F., Dator, R. P., Concepcion, G. P. & Jacinto, S. D. Murihexocin C from the "Leaves of Annona squamosa Linn. Induces Apoptosis in Human Colon Carcinoma" Col 2 Cell Line. Philipp Agric Sci 92, 122–132 (2009).
9) Kotkar, H. M. et al. "Antimicrobial and pesticidal activity of partially purified flavonoids of Annona squamosa". Pest management science 58, 33–37
10) Dr K. R. Khandelwal and Dr. Vrunda Sethi "Practical Pharmacognosy Techniques and Experiments" Nirali Prakashan Printed by Yogiraj Printers Page no; 23.1-23.11.
11) 5 Ahmed Abdul Sabour and Ahmed Bader "Study of Anti-inflammatory & Analgesic Activities of Pomegranate seed Arils Extract on Different Experimental Models of Acute Inflamation" International Journal of Experimental Pharmacology 2017; 21-27.
12) Shubhangi E. Sawant, Monali D. Tajane "Formulation and evaluation of herbal ointment containing Neem and Turmeric extract" Journal of Scientific and Innovative Research, 2016; 5(4): 149-151
13) Nitin Nema, et.al; "In Vivo Topical Wound Healing Activity of Punica Granatum Peel Extract on Rats" American Journal of Phytomedicine and Clinical Therapeutics, 2013; 195-200.
14) Nalla Arvinda and Chinnala Krishna Mohan "Formulation and Evaluation of Herbal Ointment For Antimicrobial Activity" World Journal of Pharmaceutical and Medical Research, 2017; 3(7): 113-117.
15) Sekar Mahendran & Nurashikin Abdul Rashid "Formulation, Evaluation and Antibacterial Properties of Herbal Ointment Containing Methanolic Extract of Clinacanthus nutans

Leaves" International Journal of Pharmaceutical and Clinical Research, 2016; 8(8): 1170-1174.
16) Narendra Naik D, Bastipati Suresh, Mohana Priyanka P, Geethanjali B, Karanam Yamini, Ramesh Malothu "Formulation and Evaluation of Herbal Ointment Consisting Sida Spinosa Leaves Extract" Journal of pharmaceutical biology, 2012; 2(2): 40-42.
17) Anathnarayan R, panikar CK, Textbook of Microbiology, orient Longman pvt. Ltd, Chennai, 1993; 114-681.
18) Lachman L, Lieberman A, Kanig J L, The Theory and Practice of Industries Pharmacy, 3rd edition, Varghese publishing house, 2008; 171-196, 293-344.
19) Anoop Agnihotri & Vijender Singh "Formulation development and evaluation of antidiabetic polyherbal tablet" The Pharma Innovation Journal, 2014; 3(6): 01-03.
20) Himaja N, Ashok Kumar Appapurapu and Bharat Kumar B "Formulation and Evaluation of Poly Herbal Anti Diabetic Tablets" World Journal of Pharmacy and Pharmaceutical Sciences, 2016; 5(1): 1353-1362. www.wjpps.com Vol 8, Issue 8, 2019. 1316 Ghodke et al. World Journal of Pharmacy and Pharmaceutical Sciences.
21) Uma Shankar Mishra, P.N.Murthy, Gourishyam Passa, & Debananda Mishra Formulation, Development & Evaluation of Herbal Tablet containing methanolic extract of Butea frondosa" International Journal of Institutional Pharmacy & Life Sciences, 2011; 1-15.
22) Arshad Husain Rahmani, Mohamed Ali Alsahli, Saleh Abdulrahman Almatroodi "Active constituents of Pomegranates (punicagranatum) as a potential Candidates in the Management of Health through Modulation of Biological Activities" Pharmacognocy Journal, 2017; 9(5): 689-695.
23) Richa Saxena, Richa Sharma, Bankim Chandra Nandy, "Chromatographic determination of phenolic profile from punicagranatum fruit peel" International Research Journal of pharmacy, 2017; 8(1): 61-65.
24) K. Subashini Research Artical "Review of Phytochemical Screening for Pomegranate peel extract using crude, aqueous, ethanol and chloroform" International Journal of Engineering Science and computing, 2016; 6(4): 3329-3332.
25) Sangeetha R. and Jayaprakash A. Research Article "phytochemical screening of punicagranatum linn. Peel extracts" Journal of Academia and Industrial Research, October, 2015; 4: 160-162.
26) Sachin A Nitave, Vishin Ashish Patil Study of "Antibacterial & Antifungal activity of punicagranatum peel and its phytochemicals screening", World Journal Of Pharmaceutical Research, 2014; 3(10): 505-512.
27) Sharmin Soni, Vijay Lambole, Dikshit Modi, Biren Shah "A Review on Phytopharmacology of Punicagranatum Linn" Pharma Science Monitor an International Journal of Pharmaceutical Sciences, July-2012; 3: 2222 to 2245.
28) Deepali C. Mahajan, Usha S. Satyapal, Pratima A. Tatke, Vikram A. Naharwar "Evaluation Of Punicagranatum Fruit Peels Extracts For Its Free Radical Scavenging And Anti-Inflammatory Activity" International Journal of Pharmacy & Pharmaceutical Sciences, 2015; 7(7): 222-225. www.wjpps.com Vol 8, Issue 8, 2019.
29) Atique, A., Iqbal, M. & Ghouse, A. Use of Annona squamosa and Piper nigrum against diabetes. Fitoterapia 56, 190–192 (1985).
30) Lakshmi Kalyani, R.; Chandra, VS; Vijaykumar P.PN.; Pammi, S.V.N., Rajkumar, M.; Swamy P.V; Murthy, K. V.K. Biosynthesis of silver nanoparticles using Annona squamosa leaf extract with synergistic antibacterial activity. Indian J. Pharm, Sci. 2019, 81, 1036-1044.