



INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF *PUNICAGRANATUM* PEEL

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ABSTRACT

The present study was aimed to formulate & evaluate the antidiabetic tablet of *Punicagranatum* peels waste. Hyperglycemia is the most common metabolic endocrine disorder. It is the chronic condition in which blood glucose level is elevated than normal due to the improper insulin production in body or due to insulin resistance, high blood glucose level and low blood glucose level leads to diabetic condition. Allopathic treatment for diabetes mellitus is too costly so focus on herbal medicines is necessary. Pomegranate peels or rind are considered as an waste material these peels consists of numerous important active chemical constituents such as flavonoids, vitamins and minerals. The main principle active chemical constituents including punicalagin, punicalin, β -sitosterol and valoneic acid dilactone (VAD) from pomegranate peels powder shows potent antidiabetic activity *Punicagranatum* peels extract have stability problem than other dosage form by converting it into tablet dosage form. We enhance its acceptability, elegance and patient compliance. Manufacturing of tablets was done by using wet granulation method on lab level tablet press (CEMACH) by wet granulation method. Evaluations tests performed on tablets such as Hardness, Weight variation, friability, disintegration test etc

KEY WORDS

punicagranatum, antidiabetic, valoneic acid dilactone (VAD), herbal medicine

1. INTRODUCTION:

Diabetes mellitus is a metabolic disorder identified as increased in blood glucose level than normal. This is happened due to either insufficient insulin production or insulin resistance. High amount of lipids, free fatty acid and glucose in our body affects the B-cells function by various mechanisms such as generation of various reactive oxygen species (ROS). Generally, there are three types of Diabetes occurs one is the Insulin Dependence Diabetes Mellitus (IDDM) second is the (NIDDM) that is Non-Insulin Dependence Diabetes Mellitus and third one is the Gestational Diabetes.

1.1 Biological Sources: ^[17-20]

- a) Botanical Name: *Punicagranatum*
- b) Family Name: Puniaceae
- c) Common Name: Pomegranate, Anar
- d) Part Used: Seeds, flowers, peels, roots etc.

1.2 Common Name: ^[17-20]

- i. Hindi: Anar
- ii. English: Pomegranate
- iii. Latin: *Punicagranatum*
- iv. Sanskrit: Dadimah
- v. Marathi: Dalimba

2. MATERIALS:

Fresh Fruits of *punicagranatum* was collected from local market of Buldana, Maharashtra and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra. This authentication is done by Prof. Dr. S.V. Ambekar Sir. The fruits were washed with purified water, rinsed well and dried at room temperature for about 10min in open air. The peel from the fruit was removed carefully by knife and allowed to sun-drying. The dried material was

properly ground into powder. This powder material was separated according to particle size with the help of sieves no; #44, #60, #80, #85 to obtained different batches for further Preformulation Study.

Excipients: - Lactose, Starch & Amaranth obtained from Research Lab Akola.

Method: -

3. Preformulation study: -

3.1 Bulk Density: [22-39]

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity of tablet blend was transferred into 100ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was calculated by using formula

$$\text{Bulk Density} = \frac{m}{V_i}$$

Where, m = mass of the blend, V_i = Bulk volume

3.2 Tapped density: [22-39] Weighed accurate quantity of powder sample was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 & 300 taps in tap density apparatus.

Tapped density was calculated.

$$\text{Tapped Density} = \frac{m}{V_t}$$

Where, m = mass of the blend, V_t = tapped volume

3.3 Carr's Index (Compressibility): [22-39] 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 formula:

$$\text{Carr's index} = \frac{TD - BD}{TD} \times 100$$

3.4 Hausner's Ratio: [22-39] It is measurement of frictional resistance of tablet blend. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density.

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

3.5 Angle of Repose (θ): [22-39] 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;

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

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

Procedure: Weighed quantity of the powder sample was passed through a funnel kept at a height 2cm from the base. The **powder** was passed till it forms a heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated by using above formula.

3.6 Flow Rate [22-39]: -

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

$$\text{Flow Rate} = \frac{\text{Weight powder}}{\text{Time required to flow}}$$

3.7 Water Soluble Extractive: [19-21]:

Useful for the evaluation of a crude drug. Give idea about the nature of the chemical constituents present in a crude drug.

1. Weigh about 5gm of the coarsely powdered drug and transfer it to a dry 250ml conical flask.
2. Fill a 100 ml graduated flask with water and transfer into conical flask.
3. Cork the flask and set aside for 24 hours, shaking frequently. (Maceration).
4. Filter into a 50 ml cylinder. When sufficient filtrate has collected, transfer 25ml of the filtrate to a weigh thin porcelain dish.
5. Evaporate to dryness on a water- bath and complete the drying in an oven at 105°C for 6 hours.
6. Cool and weigh immediately.
7. Calculate the percentage w/w of extractive with reference to the air-dried drug.

Calculation:

- a) Weight of empty porcelain dish =(X).....gm
- b) Weight of porcelain dish with residue =(Y).....gm
- c) Weight of residue =(X - Y).....gm

$$\text{W.S.E. (\%)} = \frac{\text{Weight of residue} \times 100 \times 100}{\text{Weight of drug taken} \times \text{Volume of filtrate (25 ml)}}$$

3.8 Alcohol Soluble Extractive: ^[19-21] Same as water soluble extractives only water is replacing with alcohol.

3.9 Moisture contents: ^[19-21] Weigh 1.5g of sample in a porcelain dish containing 6-8 cm diameter and 2-4 cm depth in it. Dry the sample in an oven at 105°C. cool & weigh. Calculate the moisture contents by using formula.

Moisture Contents(%)=Final weight-Initial weight×100

3.10 Total Ash Value: ^[19-21] Used to determine quality and purity of crude drug and to establish the identity of it.

Procedure:

1. Weigh 2gm of powder drug into the crucible
2. Ignite sample on burner (flame) until all the carbon is burned off.
3. Cool it and weigh the ash.
4. Calculate the percentage of total ash with references to the air-dried sample of crude drug.

Calculation:

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

$$\text{Total ash} = \frac{100(Z-X)}{Y}$$

3.11 Antimicrobial test: Antimicrobial test Perform against *Escherichia coli* & *Staphylococcus aureus* culture medium.

3.13 Formulation Designing:

Table 1 Formulation Designing

Sr.no	Ingredients in (mg)	F1	F2	F3	F4	F5	F6
01	Pomegranate powder	20	40	60	80	100	120
02	Lactose	100	100	80	80	50	60
03	Starch	130	110	110	90	100	70
04	Amaranth	q.s	q.s	q.s	q.s	q.s	q.s
Total		250mg	250mg	250mg	250mg	250mg	250mg

3.14 Wet Granulation Method: ^[33-36]

1. Starch was weighed and made into an emulsion and cooked well on a water bath until translucent semisolid mass was formed.
2. The Amaranth solution was prepared by using required quantity of water separately.
3. The weighed quantities of excipients were mixed thoroughly with powder drug, the cooked starch and Amaranth solution were

1. Weigh accurately all the ingredients & prepared nutrient broth and agar medium.
2. Used nutrient brouth for sub-culturing of phathogen (freshly prepared bacterial culture).
3. Take petri plate and test tube wash it properly with tap water & autoclave it (at 121°C 15 lb pressure for 15-30 minute).
4. Prepared aseptc area in aseptc room.
5. Dilute the testing sample in test tube in a range of 10⁻¹, 10⁻², & 10⁻³ respectively.
6. Transfer the agar medium in Petri plate in aseptc condition allowed it cool & solidify.
7. Then transfer the microbial culture which is required (*E. coli* & *S.aureus*) with the help of sterile disposable syringe.
8. Shake it properly 2-3 times for proper mixing.
9. Then transfer the sample which is diluted with the help of disc or bohr plate technique.
10. Then incubate the plate for 24-48 hours in Incubator.
11. Calculate the zone of inhibition by comparing with standard.

3.12 Drug Excipient Compatibility study: ^[33-38]

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combining it with the excipients. The samples were taken for FT-IR study

added slowly till the powder became a damp mass.

4. This damp mass was passed through sieve number 22# and dried in an oven at a temperature of 105°C, until granules were dried properly.
5. Then the dried granules subjected to compression.

6. Finally, the tablets were compressed with 8 mm punches by using multiple punch Tablet press machine (CEMACH).

4. Evaluation of prepared tablets:

4.1 General appearance: ^[22-39] Physical examination is done by visual inspection, Color, Odor Size, Shape Unique Identification Marking etc.

4.2 Thickness: ^[22-39] Ten Tablets were selected randomly from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement. The average of 3 readings was taken as thickness of the tablet.

4.3 Weight variation: ^[22-39] Twenty tablets were taken randomly, weigh individually and average weight was determined. The individual tablet weight was compared with average tablet weight.

4.4 Hardness: ^[22-39] Tablets require certain amount of strength or hardness, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (strength) is the pfizer hardness tester.

Method: Ten tablets were randomly selected and hardness was measured in Pfizer hardness tester. The average of 3 readings was taken as hardness of the tablet.

4.5 Friability: ^[22-39] **Friability** is related to the ability of tablet to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus friabilator. Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered as acceptable.

Method: Ten tablets were randomly select and weighed (initial wt.) and then transfer into friabilator. It was

subjected to 100 revolutions in 4 minutes. The tablets were dedusted and reweighed (final wt). These two weights (i.e. initial and final) were applied to calculate the friability.

$$\% \text{Friability} = \frac{(\text{Initial Weight} - \text{final weight})}{(\text{Initial weight})} \times 100$$

4.6 Disintegration test: ^[22-39] In vitro disintegration time was measured using USP disintegration test apparatus. For DT test randomly one tablet were selected from each batch and test was performed in 900 ml distilled water at 37 ± 0.5 °C temperature and at the rate of 30 ± 2 cycles/min.

4.7 Stability Study: ^[33&37] The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. The International Conference on Harmonization (ICH) Guidelines titled "Stability Testing of New Drug substance and Products" (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

Stability conditions: (ICH guidelines)

25°C / 60%RH Long term Testing for 12 months

30°C / 65% RH Intermediate condition if significant change occurs due to accelerated testing

40 °C / 75% RH Accelerated testing for 06 month

Method:

The selected formulation was exposed to different storage condition. As per ICH guidelines for 3 months and evaluated.

5. RESULTS & CONCLUSION:

Table no 2: Preformulation Study of Powder Sample

Sr.no:	Parameters	Sieve no: #44	Sieve no: #60	Sieve no: #80	Sieve no: #85
01	Colour	Light Brown	Light Brown	Light Brown	Light Brown
01	Bulk Density (gm/ml)	0.645	0.56	0.476	0.454
02	Tapped Density (gm/ml)	0.772	0.64	0.638	0.556
03	Carr's Index (%)	16.45	12.29	17.39	18.34
04	Hausner's ratio	1.19	1.14	1.24	1.22
05	Porosity (%)	25	16.66	23.80	19.047
06	Angle of Repose (θ)	33° 42"	29° 98"	26° 56"	31° 29"

07	Moisture contents (%)	10	09	10	20
08	Flow Rate (gm/sec)	0.78	0.66	0.44	0.33
09	Ash value (NMT4%)	0.32	0.32	0.32	0.32
10	Water Soluble Extractive (%)	45.6	45.6	45.6	45.6
11	Alcohol Soluble Extractive (%)	49.6	49.6	49.6	49.6
12	Antimicrobial Test (<i>E. coli</i> & <i>S. aureus</i>)	+ve	+ve	+ve	+ve

From above preformulation data powder from Sieve no: #60 shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, Moisture contents. The batch shows good data as compared with other batches. Therefore, it was concluded that the Powder from Sieve no: #60 consider as an optimized batch.

Table No 3: Antimicrobial test

Sr. no	Name of Pathogens	Zone of Inhibition in mm diameter			
		Dilutions	Sample A	Sample B	Std. Ciprofloxacin
01	<i>Escherichia coli</i>	10 ⁻¹	17	16	15
		10 ⁻²	14	12	12
		10 ⁻³	12	11	10
		10 ⁻¹	15	14	14
02	<i>Staphylococcus aureus</i>	10 ⁻²	13	12	12
		10 ⁻³	10	11	10

Sample A = Pomegranate peel powder, Sample B = Pomegranate Tablet

From the above evaluation details it can be concluded that *punicagranatun* peel powder shows +ve antimicrobial activity against *E.coli* & *S.aureus*, shows more potency than that of Standard Ciprofloxacin.

❖ Drug Excipient Compatibility study

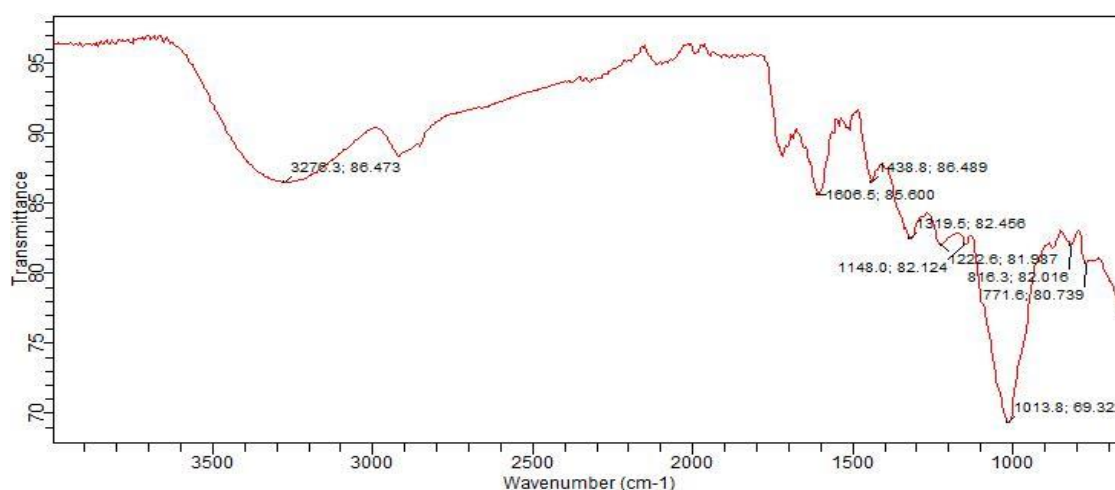


Figure 1: FTIR Spectra of pomegranate peel powder

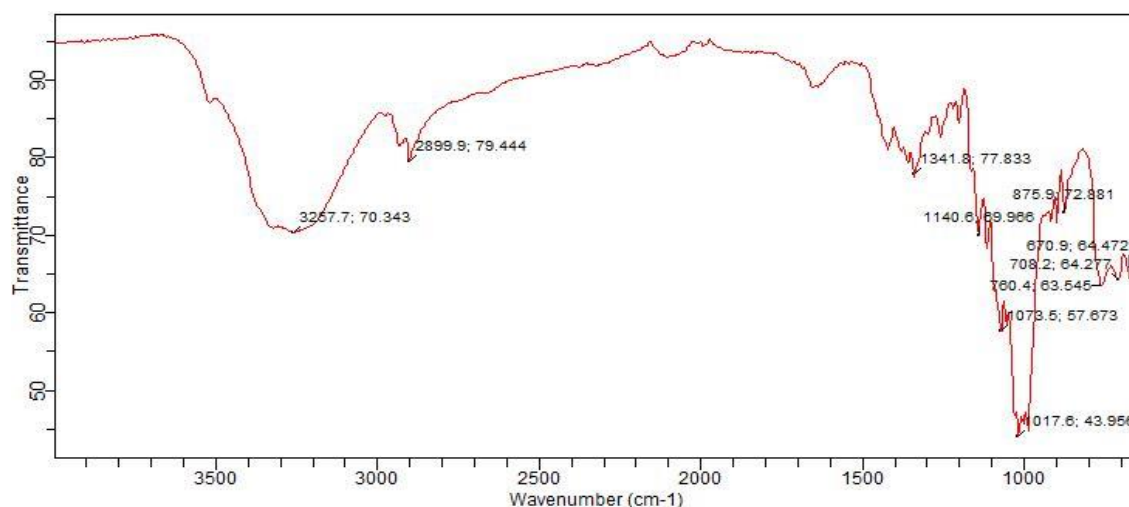


Figure 2: FTIR Spectra of pomegranate peel tablet

Table No 4: Preformulation Study of Granules

Sr.No:	Parameters	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
01	Bulk Density (gm/ml)	0.645	0.640	0.540	0.769	0.689	0.740
02	Tapped Density (gm/ml)	0.952	0.740	0.689	0.833	0.740	0.866
03	Carr's Index (%)	33.24	13.51	21.62	7.68	6.89	14.54
04	Hausner's ratio	1.475	1.156	1.275	1.083	1.074	1.170
05	Porosity (%)	10	32.25	9.37	13.33	25	6.896
06	Angle of Repose (°)	35°52"	36°02"	34°59"	33°69"	34°13"	33°69"
07	Moisture contents (%)	07	09	08	06	09	08
08	Flow Rate (gm/sec)	0.77	0.44	0.66	0.33	0.85	0.75

From above preformulation study of granules, F₄ and F₅ batch shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, and Moisture contents.

Table No 5: Evaluation of Formulation

Sr.No:	Parameters	Formulation Batch					
		F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
01	a) Colour	Pink	Pink	Pink	Pink	Pink	Pink
	b) Odour	None	None	None	None	None	None
	c) Taste	None	None	None	None	None	None
	d) Size (Diameter)	1.7mm	1.8mm	1.7mm	1.8mm	1.7mm	1.7mm
	e) Shape	Round	Round	Round	Round	Round	Round
02	Hardness (kg/cm ²)	3.5	5	3.5	3	3.5	4
03	Thickness (mm)	3	3.2	3	3	3	3.5
04	Friability (%)	0.79	0.85	0.50	0.70	0.85	0.16
05	Weight variation test	Pass	Pass	Pass	Pass	Pass	Pass
06	Dis. time (sec.)	20	25	20	15	30	25
07	Antimicrobial Test	+ve	+ve	+ve	+ve	+ve	+ve
08	Moisture content (%)	7	8	6	9	8	9

From the above evaluation parameter like thickness, average weight, hardness, friability, disintegration time etc. It can be concluded that the F₁ and F₄ batch show all parameter within acceptable limit, as compared to other batches therefore it is considered as a good formulation.

Table No 6: Comparative Study

Sr.no	Parameters	Batch		
	General appearance	F1	F4	MF
01	a) Color	Pink	Pink	White
	b) Odor	None	None	None
	c) Taste	None	None	Bitter
	d) Size (Diameter)	1.7mm	1.8mm	1.5mm
	e) Shape	Round	Round	Round
02	Hardness (kg/cm ²)	3.5	3	3.5
03	Thickness (mm)	3	3	3
04	Friability (%)	0.79	0.70	0.49
05	Weight variation test	Pass	Pass	Pass
06	Dis. time(sec.)	20	15	280
07	Antimicrobial Test	+ve	+ve	+ve
08	Moisture content (%)	7	9	8

Stability Study of optimized batch: -

The effects of temperature and humidity, on the physical characteristics of the tablets, were evaluated for assessing the stability ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ / $75\% \pm 5\% \text{RH}$) of the prepared formulation.

Table No 7: Stability Study of Optimized Formulation

Duration (Months)	General Appearance	Hardness (kg/cm ²)	Weight Variation	Friability (%)	Disintegration Time (sec)
1 Month	No change	3.5	249	0.70	20
2 Months	No change	3	248	0.60	15
3 Months	No change	3	250	0.79	25

Stability study of the tablets at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ / $75\% \pm 5\% \text{RH}$ for 3 months showed no significant changes in the mechanical strength or in disintegration time of the tablets.


Figure 3 Pomegranate Fruit

Figure 4 Pomegranate Peel



Figure 5 Pomegranate peel powder



Figure 6 Pomegranate Tablet

7. DISCUSSION AND CONCLUSION:

Herbs plays major role in the treatment than the allopathic medicines because of less side effects, low cost and easy availability. The research work done on that basis and the selected plant for the formulation was proved for the use of antidiabetic purpose. The *Punicagranatum* peel powder were used to formulate tablets and evaluated for physical parameters and standardize as per pharmacopoeial standards. Preformulation study and Physical Parameter revealed that all the values were within acceptable limit shown in table no 5. The herbal formulation showed significant antidiabetic activity and the tablet standardize as per Pharmacopoeial standards. From the above evaluation parameters, it can be concluded that overall batches the F1 & F4 batch show all parameter in acceptable limit. Therefore, it is considered as a good Formulation.

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8. REFERENCE:

1. 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" Pharmacognocny Journal 2017,9 (5);689-695.

2. Kartik J. Salwe, Devender Sachdev, Yogesh Bahurupi, "Evaluation of antidiabetic, hypolipidemic, extract of leaves and fruit peel of *punicagranatum* in male wistar albino rats," Journal of natural science, & medicine 2017; volume 6, Issue 1; 56-62.
3. 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.
4. Mona Mohamed AbdEl Mageid, Nadia Abdel Rahman Salama, Mahmoud Abd-Allah Mouhamed Saleh, Hossam Mahmoud Abo-Taleb "Evaluation of Antidiabetic, Hypocholesterolemic of Pomegranate (*punicagranatum*L) Juice Powder & Peel Powder Extract in male albino rats," IOSR Journal of pharmacy & biological science volume 11, Issue 6 Ver2 2016 pp 53-64.
5. 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, volume 6 issue no.4, 2016, page no:3329-3332.
6. Imad Hadi Hameed, Ghaidaa Jihadi Mohammed, Mohammed J.Al- Jassani "Antibacterial, Antifungal and Chemical analysis of *punicagranatum* (pomegranate peel) using GC-MS and FTIR Spectroscopy" International Journal of Pharmacognosy and Phytochemical Research 2016; 8(3); 480-494.
7. Syed Ayaz Ali, Shaik Asma Afreen, Mohammed Mukhtar Khan "Antidiabetic effects of *punicagranatum* peel extract, *Spilanthus paniculata* flower extract & selenium in streptozotocin Induced Diabetes" International Journal of pharmaceutical Research & Allied sciences 2015, volume 4 Issue (2);112-118.

8. Sangeetha R. and Jayaprakash A. Research Article "phytochemical screening of *punicagranatum* linn. Peel extracts" Journal of Academia and Industrial Research volume 4, octomber 2015,160-162.
9. Entsar A Saad, Mohamed M. Hassanien, Maha A. El-Hagrasy, Kholoud H. Radwan, "Antidiabetic, Hypolipidemic & Antioxidant activities and protective effects of *punicagranatum* peels powder against pancreatic and Hepatic tissue injuries in Streptozotocin induced IDDM in Rats" International. Journal of pharmacy & pharmaceutical sciences 2015; volume 7, issue 7, 397-402
10. Nizamul Haque, Gulamuddin Sofi, Waris Ali¹, Mohd Rashid, Malik Itrat "A comprehensive review of phytochemical and pharmacological profile of Anar (*Punicagranatum* Linn) A heaven's fruit" Journal of Ayurvedic and Herbal Medicine 2015; 1(1): 22-26.
11. Sachin A Nitave, Vishin Ashish Patil Study of "Antibacterial & Antifungal activity of *punicagranatum* peel and its phytochemicals screening", World Journal Of Pharmaceutical Research, Volume3, Issue10,2014;505-512.
12. Amani Al-Rawahi, Amani S. Al-Rawahi¹, Giles Edwards, Mohammed Al-Sibani, Ghanim Al-Thani, Ahmed S. Al-Harrasi and Mohammed Shafiur Rahman "Phenolic Constituents of pomegranate peels (*punicagranatum* L) Cultivated in European" Journal of Medicinal plants 2013; 315-331.
13. Manodeep Chakrabroty, Jagdish Kamath, & Dipak Garachh "Phytochemical & Pharmacological Profile of *Punicagranatum*" International Research Journal of Pharmacy 2012 page no; 65-68.
14. Vishal Jain, G. L. Viswanatha, D.Manohar, and H. N. Shivaprasad "Isolation of Antidiabetic Principle from Fruit Rinds of *Punicagranatum*" Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine Volume 2012, 1-11.
15. 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 vol,3-page no.2222 to 2245.
16. S. Radhika, K.H. Smila and R. Muthezhilan "Antidiabetic and Hypolipidemic Activity of *Punicagranatum* Linn on Alloxan Induced Rats" World Journal of Medical Sciences 6 (4): 178-182, 2011
17. Debjit Bhowmik, Harish Gopinath, B. Pragati Kumar, S.Duraivel, Aravind. G, K. P. Sampath Kumar "Medicinal uses of *punicagranatum* and its health benefit" Journal of pharmacognocny & phytochemistry, no.8192 volume - 1 Issue 5, 2013; 28-35.
18. Abhay Jayprakash Gandhi, Jayanta Kumar Maji, Dr. Vinay J Shukla "Ayurvedic And Allopathic Formulations For Diabetes Mellitus : A Pharmaco Economic Study" World Journal of Pharmaceutical Science & Technology Apr-May – 2017 Issue I page no; 49-68.
19. Vinod D. Rangari "Pharmacognocny and Phytochemistry" volume IInd second edition Career publication page no: 265-267.
20. "The Ayurvedic Pharmacopoeia of India" first edition part-I volume-II-page no; 31to 33.
21. K. R. Khandelwal and Vrunda Sethi "Practical Pharmacognosy Techniques and Experiments" Nirali Prakashan Page no;23.1-23.11.
22. Maninder Kaur, Vandana Valecha, Diabetes and Antidiabetic Herbal Formulations: An alternative to Allopathy EJM, Vol. 6, No. 4, pp. 226-240, 2014 pp.227-231.
23. Lachman L, Lieberman A, Kanig J L, 2008. The Theory and Practice of Industries Pharmacy, 3rd edition, Varghese publishing house:171-196, 293-344.
24. Anoop Agnihotri & Vijender Singh "Formulation development and evaluation of antidiabetic polyherbal tablet" The Pharma Innovation Journal 2014; 3(6): 01-03.
25. Indian Pharmacopoeia, Edn 6, Vol. 1, Govt. of India, Ministry of Health and family Welfare, 2010, A-185.
26. K. Sirisha, & J. Shivani "Antihyperglycemic and Antihyperlipidemic Activities of New Polyherbal Formulations" IJAPBC – Vol. 3(1), Jan - Mar, 2014;189-198.
27. Ashok Kumar Pal, Upendra Nagaich, Charu Bharti, Neha Gulati, "Formulation and Evaluation Of Nutraceutical Tablet Using Herbal Drugs By Direct Compression Method" Journal of Drug Delivery & Therapeutics; 2014, 4(2), 47-51.
28. Harpreet S, Sudhanshu A, Munish M, Kamal KM and Phool C. Development of multicomponent formulation of herbal drugs for evaluation of Antidiabetic activity. Der Pharmacia Lettre, 2014; 6(1): 219-223.
29. Rane Rajashree, Gangolli Divya, Panigrahy Smita, Sarkar Saptashree and Kundalwal Sachin "Mouth Dissolving Tablets and Candies prepared from popularly Known Spices" Research Journal of Chemical Sciences May (2013) Vol. 3(5), 57-62.
30. Parul Namdev, Rajinder K Gupta "Herbal green tea formulation using *Withania somnifera* stems, *Terminalia arjuna* bark, Cinnamon bark and *Tinospora cordifolia* stems and nutritional & phytochemical analysis" Journal of Pharmacognosy and Phytochemistry 2015; 4(2): 282-291.
31. Margret Chandra and B. Jaykar "Formulation and Evaluation of herbal tablet containing, *Ipomoea Digitata* Linn extract" International Journal of pharmaceutical sciences Review & Research volume 3 July- August 2010 page no; 101-110.
32. Farah Yousef, Rim Salame, & Tamim Hammad "Formulation and Evaluation of Herbal tablet and Hard

- capsule Containing *Urticadioica* soft extract” International Journal of pharmaceutical sciences Review & Research, 32 (2) May- June 2015 98-102.
33. Sanjay Kumar kushwaha, & Mohan Lalkori “Development & Evaluation of Polyherbal Tablet from Some Hepatoprotective Herbs” Scholar Academic Journal of Pharmacy 2014; 321-336.
34. N. Himaja, Ashok Kumar Appapurapu and Bharat Kumar B “Formulation and Evaluation Of Poly Herbal Anti Diabetic Tablets” World Journal of Pharmacy and Pharmaceutical Sciences Vol.5, Issue 1, 2016; 1353-1362.
35. Maninder Kaur, Vandana Valecha, “Diabetes and Antidiabetic Herbal Formulations An alternative to Allopathy” EJM, Vol. 6, No. 4, pp. 226-240, 2014 pp.227-231.
36. 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-page no; 1-15
37. V. S. Kashikar & Pooja Patkar “Formulation & Evaluation of Taste Masked Chewable Herbal Tablet for cough Remedy” International Journal of Research in Ayurveda & Pharmacy, 2 (3) 2011 830-833.
38. Hammad Yousaf, Muhammad jamshaid, Irfan bashir, Yasir Mehmood “Formulation development of Glipizide matrix tablet using different proportion of natural and semi synthetic polymers” Pharm Methods, 2017; 8(1): 45-53
39. Deepak Khobragade, Richa Gupta, K. Ravalika, P. Vasukumar, Arun kotha “Formulation and Development of Oro- Dispersible Tablet of Ayurvedic powder Formulation Efficient Use” International Research Journal of Pharmacy 2016, 7 (6); 48-50.

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