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Formulation and Evaluation of Anti-Inflammatory and Analgesic Herbal Ointment of Pomegranate Peels Extract

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Abstract: The current study intended to produce a formulation for the anti-inflammatory and analgesic activities of Punicagranatum peel waste. Nonsteroidal anti-inflammatory medicines (NSAIDs) are associated with excessive side effects and adverse drug reactions. Constant usage of NSAIDs causes gastrointestinal discomfort and other negative effects on body organs such as the liver and kidneys. Punicagranatum peel extract has previously been shown to have anti-inflammatory and analgesic effects in many animal conditions. Pomegranate peels are typically a waste product from many pomegranate processing enterprises. These peels contain polyphenols, flavonoids, and β-sitosterol, which help with inflammation. Inflammation is associated with discomfort, redness, and swelling. Flavonoids exhibit antioxidant action and indirectly reduce inflammatory indicators such as tumor necrosis factor alpha. Punicagranatum peels have analgesic properties and can help control discomfort. The ointment formulation of Punicagranatum peel performs well in all evaluation test parameters, including general appearance, consistency, pH, spreadability, extrudability, diffusion study, non-irritancy test, and stability study.

Keywords: Anti-inflammatory, Pomegranate, Herbal ointment, Analgesic.

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Introduction:

Herbal medicines are increasingly popular in both developing and developed countries due to their natural origin and minimal adverse effects. Herbal medications can help prevent unpleasant drug reactions. Punicagranatum, or pomegranate, belongs to the Punicaceae family. Punica granatum, a tiny tree ranging from 5 to 8 meters tall, is commonly found in Iran, the Himalayas, northern India, China, and the Mediterranean region.The juicy arils of fruit are eaten fresh, and the juice is the source of grenadine syrup, used in flavorings and liqueurs. Pomegranate is high in dietary fiber, folic acid, vitamin c, and vitamin k. in western diets, meat and meat products are one of the main source are one of main sources of high-biological value proteins, in addition to containing micronutrients such as a minerals (iron, magnesium, potassium, selenium and sodium) and vitamins (a, b12, folic acid, amongs others) that are highly bio-available. Despite these excellent nutritional properties, the intake of meat and meat products is related with a higher incidence of cardiovascular diseases and obesity, increasing the negative perception attach to consumer of these food product in recent years. Fruit season extends from October to February in the northern hemisphere and March to May in the southern hemisphere. Currently, the genus Punica has two species: Punica protopunica and the one under study. Pomegranates are among the earliest known edible fruits. Punicagranatum has a long history of usage as a medicinal medication for inflammatory illnesses. Punicagranatum aqueous ethanolic extract from fruit, flower, and leaves exhibits anti-inflammatory, analgesic, antibacterial, and antioxidant activities. Although pomegranate peel is often discarded, it contains active chemicals including tannins and beta sitosterol, which have anti-inflammatory properties. Pomegranate peel is typically a waste product from the processing industry. These peels are rich in polyphenols, flavonoids, beta-sitosterol, and tannins, which can help with inflammation and pain relief. Inflammation is

associated with discomfort, redness, and swelling. Punicagranatum peels have analgesic properties that make them effective for pain management. It contains numerous medicinal characteristics and activities. People are well familiar with acute inflammation. Injuries can cause redness, warmth, swelling, and discomfort in the surrounding tissues and joints. The inflammation is prevented by regular exercise, every day, avoid hungry, spice things of, take a break from alcohol, etc. the analgesic drug used to prevent or reduce the pain. An ointment is a smooth substance that you put on sore of skin injury to help it to get better. They are easier applied as compared to the liquid dosage forms & gives rapid results.

Drug Profile:

Biological Sources:

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

Chemical constituents: Pomegranate contains a high concentration of flavonoids (0.2% to 1.0% of the fruit). Pomegranate peels provide roughly 30% of the antioxidants found in the fruit. The seeds include isoflavones (genistein, diadzein, genistin, and diadzin) and estron, a metabolic derivative of estradiol. Pomegranate stems and roots include alkaloids such as isopelletierine, pseudopelletierine, n-methlyiso pelleteirine, anthocyanin's, pelagronidine, ellagotannin, Gallic acid, and ellagic acid.

Material and Methods:

Material: Fresh fruits of Punicagranatum were collected from a local market in kopargaon, Maharashtra, and transferred to a laboratory, where they were certified by the Center for Biodiversity SSGM College, Kopargaon.
1) The fruits were washed with tap water, rinsed thoroughly, and dried at room temperature in the open air for about 10 minutes.
2) The peel from the fruit was carefully removed using a knife and sun dried.
3) The dried material was suitably ground to powder.
4) This powder material was separated by particle size using sieves #44, #60, and #80.
5) To collect various batches for further reformulation research.

Excipients: Cholesterol, Petroleum Jelly, Cetyl alcohol, White soft paraffin etc.

Method:

A)Preformulation study:

a) **General Appearance:** Physical examination like Colour, Odor, Taste is done by visual Inspection.

b) Bulk density: It refers to the packing of particles in a powder sample. Bulk density is used to calculate the amount of powder sample in a volume in grams per milliliter. A weighed quantity of powder sample was placed into a 100ml measuring cylinder. The volume of powder material was measured. Bulk density was calculated by using formula,

$$\text{Bulk Density} = \frac{\text{mass of powder}}{\text{Bulk Volume of powder}}$$

c)Tapped density: An accurately weighed powder sample was transferred to a graduated measurement cylinder. The volume occupied by the powder was observed. The cylinder was then exposed to 100–300 taps in a tap density instrument. Tapped density was calculated by using formula,

$$\text{Tapped Density} = \frac{\text{mass of powder}}{\text{Tapped Volume}}$$

d)Cars index: The compressibility index and Hausner's ratio were used to measure the properties of the powder to be compressed. The packing ability of powder material was tested using the change in volume caused by packing rearrangement during tapping. Cars index was calculated by using formula,

e) Hausner's ratio: It measures the frictional resistance of powder. The optimal range is 1.2–1.5. It was determined by the ratio of tapped density to bulk density.

$$\text{Carr's index} = \frac{[\text{Tapped density} - \text{Bulk density}]}{\text{Tapped density}} \text{ X } 100$$

$$\text{Hausner Ratio (HR)} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

f) Angle of repose: The maximum angle which is formed between the surface of pile of powder and horizontal surface is called the angle of repose.

g) flow rate: precisely measured the amount of powder sample. Put a cotton plug in the neck of a 1- to 2.5-cm stem-diameter funnel that has been cleaned and dried. Put a sample of powder into the funnel. Take off the neck plug and note how long it took for all of the powder to flow. Determine the flow rate using the formula.

h) Water soluble extractive: Useful for evaluating a crude medication. Give an insight of the nature of

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

the chemical ingredients found in crude drugs. Weigh around 5g of coarsely powdered medication and transfer it to a dry 250ml conical flask. Fill a 100mL graduated flask with water and transfer to a conical flask. Cork the flask and leave it for 24 hours, shaking frequently. Filter into a 50mL cylinder. When enough filtrate has been collected, transfer 25ml to a thin porcelain dish for weighing. Evaporate to dryness in a water bath, then finish drying in an oven at 1050C for 6 hours. Cool and weigh immediately. Calculate the percentage w/w of extractive in relation to the air-dried medication.

I) Alcohol soluble extractive: Same as water soluble extractives only water is replace with alcohol

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

j) moisture content: Weigh the sample 1.5 grams in a porcelain dish that is 6 to 8 cm in diameter and 2-4 cm deep. Samples are dried in an oven set at 1050 C. and weigh. Utilize the formula to determine the moisture contents.

$$\text{Moisture Contents}(\%) = \text{Final weight} - \text{Initial weight} \times 100$$

k) Total ash value: used to ascertain the identify and assess the quality and purity of crude medication. Put two grams of the drug's powder into the crucible. Sample should be ignited on a burner or flame until all of the carbon is gone. After cooling, weigh the ash. Determine the percentage of total ash by using the air-dried crude drug sample as a reference.
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)

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

l)Antimicrobial test: Antimicrobial test Perform against Escherichia coli and Staphylococcus aureus culture media. Weigh all of the components precisely, and produce the nutrition broth and agar medium. Nutrient broth was used to subculture pathogen. Take a petri dish and a test tube, wash them thoroughly with tap water, and autoclave them. Prepared the aseptic area in the aseptic room. Dilute the testing sample in test tubes to 10-1, 10-2, and 10-3, respectively. Transfer the agar medium to a Petri plate under aseptic conditions, allowing it to cool and harden. Then, using a sterile disposable syringe, transfer the needed microbiological culture (E.coli and S. aureus). Shake it properly 2-3 times to ensure adequate mixing.

Preparation Of Ointment Base: By Using Fusion Method
1) Weigh An Accurate Gm Of All Excipients Such As Cholesterol (1 gm) , Petroleum Jelly (1 gm), Cetyl Alcohol (1 gm) , White Soft Paraffin (17 gm).
2) For Small Scale : Porcelain Dish Is Place On Water Bath.
For Large Scale : Carried Out In Large Steam Jack.

Procedure: A) The ingredients and base are melted and properly mixed to produce a uniform product. B) Melt the ingredients with the highest melting point first, then add the remaining ingredients in decreasing order.
C) Remove the mixture from the water bath and stir until it cools.

Preparation of ointment:
1) All ingredients were combined and gently heated while stirring, then cooled. 2) The extract of Punicagranatum Peel was added to 40 gm of base.
3) Clove oil is then added as a penetration enhancer to 40 grams of base.
4) Mix it properly with an ointment slab.
5) Transfer it to a suitable container.

Extraction method:

A) Maceration method:

1) This process involves placing solid ingredients in a stoppered container with solvent and agitating frequently for at least 3 days until soluble matter dissolves.
2) The mixture is then strained, the mare pressed, and the combined liquid clarified or decanted after standing.
3) Weigh 20 gm of crude powder and add 100 ml of ethanol. Shake continuously with a magnetic stirrer for 4 hours, then filter.
4) For Filtrate Preparation, add 1 mL of residue, followed by 25 mL of ethanol, and shake continuously for four hours.
5) To Prepare Filtrate 2, Add Residue and 25 mL Ethanol and let overnight.
6) For Filtrate Preparation, Add 25 Ml Ethanol Residue and Allow to Stand Overnight.
7) To prepare the filtrate, add 25 ml of ethanol and pool the filtrates for evaporation. The extract was then obtained.

B) Soxhlet extraction method:

1) This is a continuous process of extraction using a hot organic solvent.
2) A powder (crude drug) is placed in the thimble, which is then placed in the soxhlet extractor.
3) The extractor, which has a siphoning system, is mounted on top of the round bottom flask.
4) A condenser is installed at the extractor.
5) Pour a sufficient amount of the extracting solvent into the flask and place it on a heating metal.
6) Heat the solvent vapour, which rises to the condenser, condenses, and drains back into the extractor, containing the crude drug material.
7) When the extractor becomes full of hot solvent. The solvent and extracted constituents are siphoned into the flask.

Formulation designing:

1) Formulation of herbal ointment:

SR.NO.	Ingredients	Quantity Taken
1	Pomegranate peel extract	2 gm
2	Clove Oil	2 gm
3	Base material	q.s
	Total	10 gm

2)Formulation of ointment base

SR. NO.	Ingredients	Quantity Taken
1	Cholesterol	2 gm
2	Petroleum jelly	2 gm
3	Cetyl alcohol	2 gm
4	White soft paraffin	34 gm
5	Total	40 gm

Evaluation of herbal ointment:

Prepared Punicagranatum ointment were evaluated for the following evaluation parameters.

1)Colour & Odour: Visual inspection was used to assess colour and odour.

2) Consistency: The transition is smooth, with no greetiness.

3. pH: The pH of the herbal ointment was measured using a digital pH meter. The ointment solution was made with 100 cc of distilled water and allowed to sit for 2 hours before being tested for pH.

4) Spreadability: The spreadability was measured by inserting the sample between two glass slides and compressing them to a uniform thickness with a specific weight over a specific time period. Spreadability was calculated using the time it took to separate the two slides. Less time taken to separate two slides shows superior spreadability measured using the formula.

5. Extrudability: The ointment was stored in a collapsible tube. The extrudability was measured by the weight of ointment required to extrude a 0.5 cm ribbon in 10 seconds.

6)Diffusion Study: Using the Boher method, an agar nutrient medium was prepared for the diffusion study. An open mouth ampoule is used to make a hole in the agar medium, and ointment is added. It was noticed how long the ointment took to diffuse.(sixty minutes later).

7) L.O.D. : The formulation was placed in a china dish and dried at 105 degrees to determine the LOD.

8)Solubility: Miscible with ether and alcohol, soluble in boiling water.

9)Washability: After applying ointment to the skin, the skin's water-washability was assessed.

10)Non-Irritancy: A prepared formulation was applied to a human's skin, and the results were monitored.

11)Stability study: For three months, the manufactured herbal ointment was physically stable at a range of temperatures, including 2˚C, 25˚C, and 37˚C.

Result and discussion:

Preformulation study of powder sample :

SR NO	PARAMETERS	Sieve no #44	Sieve no #60
1	Colour	Brown	Brown
2	Bulk density	0.640	0.560
3	Tapped density	0.772	0.645
4	Car's index	16.3	12.4
5	Hausner's ratio	1.14	1.18
6	Porosity	25	16.66
7	Angle of repose	33	29
8	Moisture content	10	9
9	Flow rate	0.78	0.66
10	Ash value	0.32	0.32
11	Water soluble extractive	45.6	45.6
12	Alcohol soluble extractive	49.6	49.6
13	Antimicrobial test	+ ve	+ ve

The above preformulation data powder from Sieve #60 indicates an adequate angle of repose, bulk density, tapered density, Carr's index and Hausner's ratio, flow rate, and moisture content. When compared to previous batches, the data from this batch is good. As a result, it was determined that the powder from Sieve #60 should be considered an optimized batch.

Evaluation of formulation:

SR.NO.	Parameters	F1	F2
1)	Colour	Yellowish Brown	Yellowish Brown
2)	Odour	Characteristic	Characteristic
3)	Consistency	Smooth	Smooth
4)	pH	6.4	5.5
5)	Spreadability	8	7
6)	Extrudability (gm)	0.4	0.5
7)	Diffusion study (after 60 min)	0.7	0.9
8)	Loss on drying	25%	30%
9)	Washability	Good	Good
10)	Non Irritancy	Non irritant	Non irritant
11)	Stability study	Stable	Stable

Conclusion:

Punicagranatum peel powder was used to make an anti-inflammatory and analgesic herbal ointment, which was then tested for physical properties. The preformulation research and physical parameter showed that all of the results were within acceptable ranges. The herbal ointment has anti-inflammatory and pain-relieving properties.

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