



# FORMULATION AND EVALUATION OF CHEWABLE TABLET OF POMEGRANATE PEEL EXTRACT

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**Abstract:** Traditional medicine offers a good alternative to synthetic chemical substances. A large number of antibacterial compounds have been isolated from plant species.<sup>5,9</sup> Natural ingredients such as clove oil, aloe vera, turmeric, sesame, cranberry, meswak, sesame, Red clover, are also used for the dental caries treatment. Pomegranate peel extract has been reported to exhibit a high level of antibacterial activity.<sup>12,17</sup> The extract also has other medical activities like antioxidant, anti-diarrheal, antifungal. Chemical constituents present in pomegranate (*punicagranatum L.*) are punicalagin, gallic acid, ellagic acid, Punic acid.<sup>11,20</sup> The objective of this study is to develop an effective formulation containing Pomegranate peel extract and evaluation of in-vitro antibacterial activity of the same, under accelerated storage conditions for 3 months.

**Keywords:** antibacterial, extract, pomegranate, punicalagin, peel.

## INTRODUCTION

The term "dental caries" was first reported in the literature approximately around 1634, and it originates from the Latin word "caries," which stands for decay. The term was initially used to describe holes in the teeth.<sup>1,7</sup> Dental caries is reported to be one of the oldest and most common diseases found in humans. Dental caries is a prevalent chronic infectious disease resulting from tooth-adherent cariogenic bacteria that metabolize sugars to produce acid, which over time demineralizes tooth structure.<sup>3,6</sup>

Dental caries is one of the major oral diseases caused primarily by streptococcus mutans. It is of great concern to dentists as it affects all age groups causing loss of tooth structure, moderate to severe pain, swelling and infection.<sup>4,8</sup> The organism in the presence of fermentable carbohydrate produces acid which induces demineralization of tooth structure. Dental caries have conventional treatments: antibiotics and fluoride, Acetaminophen, Ibuprofen.

## Material And Methods

### Materials:

Fresh fruits of *punicagranatum L.* (pomegranate) were collected from the local market of Ahmednagar, Maharashtra, and transported to the laboratory, authenticated from the Centre for biological survey. The fruits were washed with purified water, rinsed well, and dried at room temperature for about 10 min in open air. The peel from the fruit was removed carefully by knife and allowed to sun-dry. 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 obtain different batches for further Pre-formulation Study. Excipients such as Lactose, Starch, mannitol, sucrose, gum acacia, Talc, obtained from ACS's college of pharmaceutical science and research Ashti, chemical laboratory room.

**Method:****Formulation of Chewable Tablet of Pomegranate Peel Extract:-**

Chewable tablets containing pomegranate peel were formulated as shown in following table No. 1

- 1) The extract was mixed sucrose, mannitol, lactose and the pomegranate powder so obtained was moistened with aqueous solutions of *gum acacia*.
- 2) The material obtained was granulated through sieve number 18 and dried to constant weight at room temperature.
- 3) The dried granules were passed through sieve no 22 and mixed with required quantity of starch and talc.
- 4) The granules were evaluated for angle of repose (funnel method), bulk density, and car's index using method described in literature.
- 5) The tablets were compressed to weight of 450 mg using D tooling on Remake tablets machine (single punch machine) and evaluated for hardness test, friability and uniformity of weight test, disintegration test.

**Table 1: Formula of Chewable Tablets of Pomegranate Peel Extract Tablet**

INGREDIENTS	F1	F2	F3
Pomegranate peel extract	150 mg	150 mg	150 mg
Mannitol	0.05 ml	0.05 ml	0.05 ml
Sucrose	100 mg	90 mg	80 mg/Tab
Lactose	135 mg	145 mg	155 mg
<i>Gum acacia</i>	5 mg	5 mg	5 mg
Talc	4 mg	4 m	4 mg
Water	q.s	q.s	q.s
Total	450 mg	450 mg	450 mg

**Fig. 1: Chewable Tablet of Pomegranate Peel Extract.****Evaluation of Prepared Tablets:**

**General Appearance:** The physical examination is done by visual, colour, odour, size, shape unique identification making etc.

**Thickness:** 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 tablets.

**Weight Variation:** Twenty tablets were taken randomly, weigh individually and average weight was determined. Individual tablet weight was compared with average tablet weight.

**Hardness:** 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 tablets hardness (strength) is the pifzer hardness tester.

Method:- Ten tablets randomly selected and hardness was measured in pifzer hardness tester.

**Friability:** Friability is related to the ability of tablets to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of Roche friability test apparatus. compressed tablets that loose less than 0.5% to 1.0% in weight generally considered as acceptable.

**Method:-** Ten tablets were randomly selected and weighed (initial wt.) and then transfer into friabilator. It was subjected to 100 revolutions in 4 minute The tablets were dedusted and reweighed (final wt.) these two weight ( i.e . initial and final) were applied to calculate the friability.

**Disintegration Test:-** In vitro disintegration time was measured using USP disintegration test apparatus .for DT test randomly one tablets were selected from each batch and test was performed in 900 ml distilled water 37°C temperature and at the rate of 30+ 2 cycle / min.

**Stability Test:** 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)**

25C / 60%RH Long term Testing for 12 months. 30oC / 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.

**Antimicrobial Test:-**

Antimicrobial test perform against Escherichia coli and staphylococcus aureus culture medium.

1. Weigh accurately all the ingredients & prepared nutrient broth and agar medium.
2. Used nutrient brouth for sub culturing of pathogen (freshly prepared bacterial culture.)
3. Take petri plate and test tube wash it properly with tap water and autoclave it (at 121\*c 15 Ib pressure for 15-30 minute.)
4. Prepared aseptc area in aseptc room.
5. Dilute the testing sample in test tube in a range of 10,10, &10 respectively.
6. Transfer the agar medium in petri plate in aseptic condition allowed it cool & solidified.
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 the 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. Calculate the zone of inhibition by comparing with standard.

## EVALUATION PARAMETERS:

### PRE-FORMULATION STUDIES

**Bulk Density:-**

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 and found within the range of 0.50-0.60 g/ml.

**Tapped Density:-**

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. The experiment was performed in triplicate and tapped density was calculated and was found within range of 0.60-0.70 kg/m<sup>3</sup>

### 7.3 Carr's Index:-

The compressibility index and Hauser's ratio was measured and found within the range of 15-20.

### Hausners Ratio:-

Hausners Ratio was calculated and was within the specified limit and found within the range of 1.20-1.30.

### Angle of Repose:-

**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 angle of repose was calculated and found within the range and having good flow property.

## EVALUATION STUDIES FOR PREPARED TABLETS:

### Hardness Test:-

The hardness test off the chewable tablets of pomegranate peel extract was found to be 06 using hardness tester apparatus. The hardness was measured by using Pfizer hardness tester.

### Friability Test :-

Friability can be evaluated by means of Roche friability test apparatus. Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered as acceptable.



**Fig.2: Friability Test Apparatus.**

**Table 2: Weight of Pomegranate Tablets**

Tablets	Weight in mg
01	515
02	495
03	503
04	512
05	498
06	496
07	504
08	510
09	513
10	499
11	502
12	522

13	491
14	489
15	505
16	514
17	504
18	511
19	503
20	507
<b>Total Weight</b>	<b>10093</b>

So friability was found to be **1.07%** which is more than **1.0**. We do not reject the tablets as this test is nonofficial.

### Disintegration Test :-

In vitro disintegration time was measured using disintegration apparatus. The chewable tablet of pomegranate peel extract tablets was dissolve excellent in disintegration time period (15min).



**Fig. 3: Disintegration Test Apparatus.**

The result was identify the chewable tablets of pomegranate peel extract dissolution rate is excellent.

### Thickness Test:-

To determine the uniformity and physical dimension of tablets thickness is measured by Vernier caliper for randomly selected 20 tablets from formulation.

### RESULTS:

#### Preparation of Tablets:-

In preparing chewable tablets from ethanolic extract of pomegranate peel powder, wet granulation method was used.

The ingredients of chewable tablet from pomegranate peel powder extract were indicated in table no.1. Initially formula I & formula II were tried it was observed at granulation stage become sticky, because the sucrose is hygroscopic therefore it was decided to reduce the quantity of sucrose and increase the quantity of lactose in formula F3, therefore formula 3 were used for the chewable tablet formulation.

**Table 3: Pre-Compression Study**

Sr. No.	Test	Observation	Conclusion
01	Angle of repose	46°	Excellent
02	Bulk density	0.53	Excellent
03	Tapped density	0.66	Excellent
04	Carr's index	19	Excellent
05	Hausner ratio	1.24	Excellent

The tablets were evaluated for physical appearance of the tablets were smooth, absence of crack, uniform. The chewable tablets were evaluated for various performance properties. The hardness test was performed to provide a measure of tablets strength by using Monsanto hardness tester. Tablet should be hard enough for packaging and shipping but not so hard as to create difficulty during chewing. The hardness was 6 kg/cm<sup>2</sup>. % Friability of tablets was found to be 1.07%. Results for post compression tests are shown in table no. 4

**Table 4: post compression tests**

Sr. No.	Test	Observation
01	Average weight	450(mg)
02	Friability	1.07%
03	Hardness	06 (kg/cm <sup>2</sup> )

### ANTIMICROBIAL TEST:-

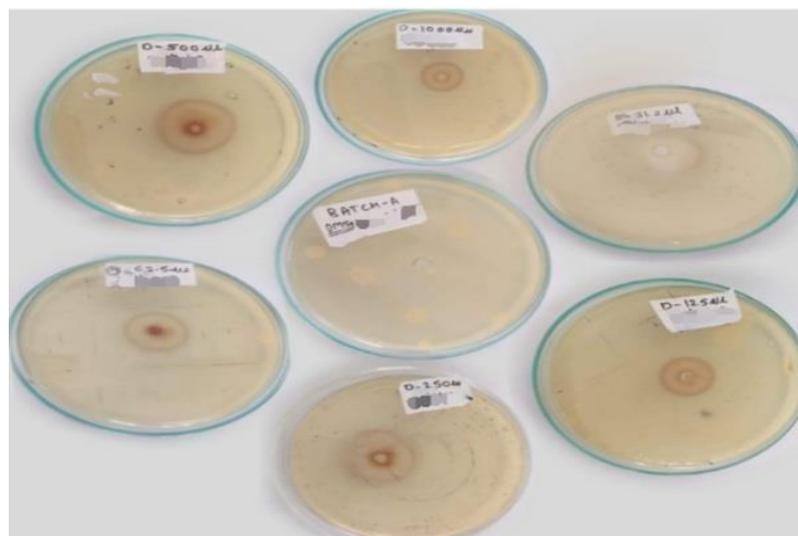
#### In Vitro Antibacterial Activity Against Streptococcus Mutans.

The ethanolic extract of pomegranate peel powder and formulated chewable tablets were tested for antibacterial activity against streptococcus mutans that was carried out by Agar diffusion method. The observed results are as shown in Fig. no .4 and Table no .5

Ethanolic extract of pomegranate peel powder and its chewable tablet showed a significant antibacterial activity against streptococcus mutans. MIC were determined by the cup platye method by CLSI guidelines with Brain heart infusion broth. Based on the observation , It would be concluded that Chewable tablet of pomegranate peel extract contains constituents that are responsible for antibacterial activity .

**Table 5: In Vitro Antibacterial Activity Against Streptococcus Mutans.**

Sr. No	Concentration (ug/ml)	Conc.in well (mg)	Zone of inhibition (mm)
01	1000	25	34
02	500	12.5	28
03	250	6.25	28
04	125	3.12	20
05	62.5	1.56	17
06	31.25	0.8	0
07	DMSO	25	-



**Fig. 4: Study to Determine MIC Of Extract Against Streptococcus Mutans.**

Antibacterial study of ethanolic extract of pomegranate peel powder, chewable tablet of pomegranate peels, DMSO was tested against streptococcus mutans. as shown fig no.10 and table no. 6.

**Table 6: Antibacterial Activity of Chewable Tablet.**

Sr. No.	Sample solution	Concentration In well (mg)	Zone of inhibition(mm)			
			Initial Tablet	First month	Second month	Third month
1.	Ethanolic extract	1.56	17	NA	NA	NA
2.	Pomegranate peel chewable tablet.	11.25(equivalent to 3.75 extract)	30	26	24	22
3.	DMSO	-	-	-	-	-

**CONCLUSION:**

The chewable tablets prepared of the pomegranate peel powder extract can be used as a potential treatment of dental caries. It is seen that prepared chewable tablets can be a good dosage form for the dental carries treatment. The activity was retained even upon exposure of tablets to accelerated storage condition of 40<sup>0</sup>C. Herbs play major role in the treatment than the allopathic medicine because of less side effects, low cost and easy availability. The research work done on that basis and selected plant for the formulation was proved for the use to prevent of dental carries.

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