



Comparative Pharmaceutical Standardization and Oral Bioavailability Study on *Praval Pishti* and *Praval Bhasma*

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Authors' contributions

This work was carried out in collaboration among all authors. Author MS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author BR managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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Study Protocol

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ABSTRACT

Background: *Praval* (coral) is a very usually occurring calcium form. It is rich source of calcium & minerals. As per text it can be converted into two formulas which are *bhasma* (calcinated ash) and *pishti* (powdered form without *agni*). These forms may have different rate of immersion. This needs to be studied.

Aim: Pharmaceutical Standardization study of *Praval Pishti* & *Praval Bhasma* and comparative evaluation of their relative oral bioavailability.

Materials and methods: The two formulations will be prepared from *Praval* (coral). By triturating with *Gulab jala* *Praval Pishti* will be prepared and by traditional *Putta* method *Praval Bhasma* will be prepared. The prepared formulations will be assessed for *Bhasma Pariksha* mentioned in *Ayurveda*. Organoleptic characters, Physicochemical parameters and Particle size distribution analysis, SEM –EDX (Scanning Electron Microscopy, Energy Dispersive X-Ray Analysis), FTIR (Fourier-transform infrared spectroscopy), XRD (X-Ray Diffraction), and GCMS (Gas

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Chromatography Mass Spectroscopy) will be evaluated. To assess the relative oral bioavailability of *Praval Pishti* & *Praval Bhasma* study will be conducted in healthy volunteers and will be compared with the standard calcium supplement.

Observation and results: The study will be assessed for its relative oral bioavailability in healthy Volunteers by using unpaired “t” Test, One-way ANOVA.

Conclusion: The pharmaceutical study of *Praval Bhasma* and *Praval Pishti* will provide the standard parameters and comparative evaluation with standard will generate evidence for better bioavailability.

Keywords: *Praval pishti; praval bhasma; standardization; bioavailability.*

1. INTRODUCTION

Ayurveda, the science of life is well known age old documented Indian system of Medicine. Rasashastra, commonly known as iatro chemistry a popular branch of an Ayurveda pharmaceuticals, developed during the medieval period. *Rasashastra* deals with ancient pharmaceutical preparation of Ayurveda [1]. Most emphasis is given regarding the therapeutic uses of mercurial, mineral and metallic preparations including calcium containing formulations indicated in various disorders [2]. Modern lifestyle have critical role in developing wide range of diseases and herbomineral formulations have a key role in combating these disorders [3].

Calcium compounds are known in Ayurveda sciences since 2nd Century BC but *Praval* is in use from 8th century. *Praval* is a known calcium compound described under the *Sudha Varga* (group of calcium drugs). It were first named by Yadavji Trikamji Acharya [4].

Praval (Coral) belongs to the phylum coelenterate and found in the form of the calcareous skeleton of the minute marine organism which is a rich source calcium carbonate. The skeleton of coral is supposed to acquire a special affinity for iron which unites with a calcium organic complex to impart color pigments [5].

However the method of preparing calcium compounds in therapeutic dosage form is different according to different *Archaryas*. *Praval Bhasma* is one of such calcium supplement which is chief and abundantly available in nature, few studies showed clinical efficacy of *Praval Bhasma* in calcium deficiency disorder such as osteoarthritis. However considering the different methods of purification and incineration to prepare *Praval Bhasma*, its analytical standardization and oral bioavailability study is still a major gap in

Ayurveda” Sea products having naturally digestible properties and attached with calcium and minerals”.

Some Acharya made *Pishti of Praval* and some are made *Bhasma of Pravala*. All calcium compounds of *Rasashastra* made *Bhasmas* except *Pravala*. *Prava Bhasma* and *Praval Pishti* both drugs included under literally review but only *Pishti* review is available. The efficacy of *Praval Bhasma* is not known today. That’s why the present study is planned to fill the gap. *Praval Bhasma* is indicated in various disorders such as *Timira, Yakshma, Kasa* etc [6].

In *Ayurvedic* system of medicine, the different collection processes, time zones and methods results the same *Bhasma* with dissimilar qualities. In many cases, inferior-quality products are prepared by wrong manufacturing and marketing processes. This ultimately affects the efficacy of products as well as safety parameters. Hence standardization of *Bhasma* and other *Ayurvedic* formulations is essential in order to minimize the variability and to strengthen the quality of *Ayurvedic* formulations [7-9].

1.1 Need of Study

Pishti kalpana is incorporated in Ayurveda from Unani which is used for preparation of amalgamated powders and the *Bhasma kalpana* comes under Ayurveda concepts. For *Praval Pishti* preparation *Bhavana* (wet trituration) of *Gulabjala* (rose water) is mandatory, however *Gulabjala* doesn’t have calcium bioavailability enhancing action. On the other hand for *Praval Bhasma* preparation, *Kumari Swarasa Bhavana* is given, and *Kumari swarasa* have proven to increase bioavailability of calcium. In spite of this, *Praval Pishti* is used in practice and *Praval Bhasma* is not even manufactured. As *Bhasmas* contain Nano particle which is having higher absorption and distribution property [10]. Thus

utilization of *Praval Bhasma* at place of *Praval Pishiti* may increase the effect of drug through few folds. However scientific evidence is needed to be established to know difference in calcium bioavailability between *Praval Pishiti* and *Praval Bhasma* compared to standard compound. Such work is not done before and thus represents need of hour for better drug discovery and development.

2. MATERIALS AND METHODS

2.1 Study Design

Randomized single blind controlled study.

2.2 Sample Size

The sample size calculation for a bioavailability and bioequivalent study is dependent on multiple factors like power, intra subject coefficient of variation, expected geometric mean ratio.

According to C. Bhupati and V.H. Vajjha. (STATISTICA, anno LXXVII, n.1, 2017), power of 85% would be reasonable for bioavailability study to conduct on healthy volunteers. By considering

the values of Lower Bound (LL) =0.80, Upper bound (UL) = 1.25, Alpha=0.05, Geo Mean Ratio (GMR) = 0.947, Coefficient of Variation (CV) = 0.239 as fixed, the sample size can be calculated as shown in table no 1.

2.3 Pharmaceutical Study

Pharmaceutical preparation of *Praval bhasma* & *Praval pishiti* will be prepared. It will be done by following steps.

2.4 Procurement and Authentication of Raw materials

1. *Praval* will be procured from Shri Shaila Agency, Nagpur and will be authenticated by the Department of *Rasashashtra* (MGACH & RC).
2. *Kumari* & *Gulabpushpa* will be collected from medicinal plants garden (MGACH & RC), and primarily authenticated by *Dravyaguna* Department.
3. *Tandulodak* & *Gulabjal* will be prepared in Dattatraya Rasashala which is required for *Shodhan*(purification) of *Praval* & preparation of *Praval bhasma* respectively.

Table 1. The sample size and power

Sample	54	50	47	44	35	30	26	24
Power	97.9	97.0	96.0	95.0	90.0	85.0	80.0	76.6

Preparation of *Tanduliya swarasa* [11]

The fresh *Tanduliya Patra* will be taken in *Khalva Yantra* and make. Into fine paste form.



The paste will be squeezed through clean cotton cloth.



The liquid will be obtained called *Tanduliya Swarasa*.

Extraction of *Kumari Swarasa*

The leaves of *Kumari* will be washed with tap water.



Then the thorny ridges and apex part of *Kumari Patra* will be cut by knife.



After cut into small pieces will be churned in mixer and then strained through Clean cotton cloth.

Shodhana of Pravala [12]

The roughly pounded *Pravala* (coral) will be tide in a *Pottali*.



Subjected for 3 hours of *Swedana* in *Dolayantra* by keeping *Tanduliya Jala* as liquid media.



Later the drug will be washed, dried and stored in airtight container as *SuddhaPraval* for further pharmaceutical use.

Maran (incinration) of praval [13]

Required quantity of *Suddha Pravala* will be taken in clean *Khalva Yantra* and triturated to obtain it in the form of fine powder



This powder will be added with required quantity of *Ghrita kumari Swarasa* (Alovera) and triturated thoroughly to prepare the *Chakrikas* (pellets) of even size and shape



These pellets will be dried under sun, enclosed in *sarava samputa* and subjected for one *Putra* (*Laghu Putra*) all this process is repeated three times to obtained clean bright moon like white *Bhasma of Pravala*.



It will be stored in suitable airtight container for further pharmaceutical as well as therapeutic use

Preparation of Pravala Pishti [14]

Required quantity of *suddha Pravala* will be taken in clean *khalva yantra* and triturated to obtain it in the form of fine powder.



Then it will be again one time triturated in iron *khara*



Shuddha fine praval will be taken in to porcelain *khara* and *Gulab Jal* will be added & triturated for 21days per day 3 hrs to obtain of *Praval Pishti*.



It will be later stored in suitable airtight container for further pharmaceutical as well as therapeutic use.

2.5 Analytical Study

For analytical study organoleptic characters and physicochemical parameters and other sophisticated tests like Particle size distribution analysis, SEM –EDX, FTIR, XRD, and GCMS will be done.

2.6 Bioavailability Study

It will be randomized single blinded study in which 30 healthy Male volunteers in each group will be selected (total 90 volunteers) from *Swastharakshan* OPD, MGACHRC, salod (H), Wardha.

2.7 Eligibility Criteria

Age group from 20 to 40 years of volunteers, after physical examination and complete blood count (CBC), blood sugar, Kidney function test liver function test, lipid profile, blood pressure with normal values will be selected.

2.8 Exclusion Criteria

Patients below 20 and above 40 years of the age, Patients with diabetes / hypertension /IHD/TB/ Nephrolithiasis/ peptic or duodenal ulcer, bowel disease, intestinal resection or mal absorption/ Parathyroid excess or other

endocrine disorder, Patients with other systemic condition such as Gouty arthritis, Rheumatoid arthritis and BMI index less than 18.5 and more than 24.9 and patient with regular medication.

2.9 Interventions

In total 90 volunteers one group with 30 volunteers will be standard group in which standard Calcium supplement will be given 500mg once a day before meal, second group with 30 volunteers *Praval Pishti* will be given 500mg once a day before meal and the third group with 30 volunteers *Praval Bhasma* will be given 500mg once a day before meal. The study will be conducted for 15 days.

2.10 Investigation during Treatment

Complete blood count, Kidney Function test, Liver Function test, Lipid profile, Blood sugar, Urine routine and microscopic, Blood Serum Calcium Level and Bone Density will be done.

2.11 Criteria for Discontinuing or Modifying Allocated Interventions

If patient having any problem related to consumption of medicine or having any sensitivity will be withdraw from study.

2.12 Follow up Period after Treatment

After 24 hours, 3rd day, 7th day, 15th day of drug administration.

2.13 Implementation

Principle investigator will allocate and enroll the patient.

3. OBSERVATION AND RESULTS

Primary outcomes: The relative oral bioavailability of *Praval Pishti* and *Praval Bhasma* in comparison with standard calcium will be observed.

Statistical analysis: Statistical analysis will be done by applying unpaired “t” Test & One-way ANOVA.

4. DISCUSSION

Praval are aquatic animals belong to Anthozoa class of Phylum Coelenterata usually existing in dense colonies of numerous equal individual “polyps”. The group comprises the significant reef builders that dwell in tropical oceans and produce calcium carbonate (CaCO₃) to form solid skeleton. A coral “head” is a colony of myriad genetically identical polyps. Each polyp is a spineless animal with a very small size and shape. A central mouth opening is surrounded by a set of tentacles and near the base an exoskeleton is excreted. Thus number of colonies creates a large skeleton over many generations that is characteristic of the species. Corals can be major contributors to the physical structure of the coral reefs that develop in tropical and subtropical waters. The *Praval* (Coral), which possesses the radiance of deep red color, which is smooth and soft, which has Long and bulky branch, which has no aberrations and which is heavy and strong ; such a sample of *Praval* is Considered fit and selected for therapeutic purposes.

Table 2. Intervention and dose frequency

Sr no	Group	Sample size	Intervention	Dose & frequency	Anupan	Duration
1.	Standard group	30 volunteers	Standard Calcium compound (SDC)	500mg (OD) before meal	Water	15 days
2.	Comparative group	30 volunteers	<i>Praval Pishti</i> (PP)	500mg (OD) before meal	Water	15 days
3.	Comparative group	30 volunteers	<i>Praval Bhasma</i> (PB)	500mg (OD) before meal	Water	15 days

Table 3. Blood collection after administration of drug

Group	Blood collection after administration of drug				
SDC	00	24 hrs	3 rd day	7 th day	15 th day
PP	00	24 hrs	3 rd day	7 th day	15 th day
PB	00	24 hrs	3 rd day	7 th day	15 th day

Ayurvedic medicines are gaining momentum throughout the globe. Growing population, cost effectiveness, no or minimum side effects, all time availability are few notable causes regarding increased emphasis on the utilization of herbs and minerals as source of medicines and health supplements [15]. But for the global acceptance it is the need of the hour to validate the drug scientifically and test its efficacy pre-clinically and clinically [16]. The analytical studies of all Ayurvedic formulations form the basis for standardization. For many formulations pharmacopeia standards are not available hence is the need of the hour to generate various parameters for existing literature and for reproducibility [17]. Few of the studies on standardization of Ayurvedic drugs and bio-availability studies were reviewed [18-21].

The analysis of *Prawal Bhasma* and *Prawal Pishti* will be compared. In both the samples organoleptic characters that is color, odor, taste will be assessed. Particle size will be assessed, which is a major parameter by means of which rate of absorption can be assessed in *Praval Bhasma* and *Prawal Pishti*. From scanning Electron Microscopy Energy Dispersive X-Ray Analyzer (SEM EDX) is elemental identification along with quantitative composition can be finding out in *Praval Bhasma* and *Prawal Pishti*. By Fourier Transform Infrared Spectroscopy (FTIR) chemical bonds will be identified in *Praval Bhasma* and *Prawal Pishti*. With the help of X-Ray Diffraction (XRD) the crystalline structures of the molecule will be recognized in both the samples that is *Praval Bhasma* and *Prawal Pishti*. GC-MS technique will be used to analyze complex organic and biochemical mixtures between *Praval Bhasma* and *Prawal Pishti*. Few studies from modern medicine were reviewed [22,23]. It is protocol paper and study plan is described.

Large number of standard calcium supplements is available in market, but today's necessity is the high solubility calcium content, that could be an efficient source of calcium through dietary intakes. *Bhasma* contain Nano particles which is having higher absorption and distribution property. There is no information available carrying the bioavailability of *Praval Bhasma* and *Prawal Pishti* as calcium form. *Praval Bhasma* is used in many formulations and indicated in many gastrointestinal diseases but oral bioavailability study of *Praval Bhasma* is not conducted till now.

5. CONCLUSION

The conclusion will be drawn from the results obtained and observations which will be observed. The conclusions will content analytical observations between *Praval Bhasma* and *Praval Pishti*. For relative oral bioavailability the maximum concentration of calcium by plotting area under curve (AUC) will be assessed between standard calcium supplement tablet, *Praval Pishti* and *Praval Bhasma*. And the drug with maximum area under curve will be concluded as better relative oral bioavailable. As this is a protocol paper and expected results are predicted here.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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