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Research Article

# Studies on Inorganic Materials Based Antiulcer Pharmaceutical Gel for Oral Cavity: Formulation and Evaluation

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## Abstract

The objective of the present investigations was to formulate and evaluate inorganic gel for mouth ulcer treatment containing inorganic materials like Tankan bhasma and Gairik bhasma.

The present investigations were based on the objective of formulating and evaluating an inorganic gel for mouth ulcer treatment using Tankan bhasma and Gairik bhasma. This inorganic gel was prepared by using different concentrations of Tankan bhasma and Gairik bhasma and Carpobol 394, Propylene glycol as a gel base.

Formulations were evaluated for various parameters like pre-compression parameters, infrared spectroscopy, and post-compression parameters invitro antifungal study, invitro dissolution study, and also evaluation of the stability batch.

By infrared analysis it was revealed that there was no interaction between drugs and polymer. Excellent efficacy against *Aspergillus aureus, Candida albicans* was shown by the anti-fungal studies done for this formulation. This gel prepared was transparent, homogenous and the pH ranges from 7 to 7.5. This formulation showed the properties of applicable spreadability and excludability with the acceptable rheological behavior. Percent drug content of the inorganic gel formulations were found to be in the range of 90 ± 0.52% to 93 ± 0.55%. Optimized inorganic gel formulation shows good drug release of 40.83 ± 0.50, 39.216 ± 0.47 and 71.405 ± 0.07 at the end of 4 hours. The result of stability study indicated that formulation was stable at room temperature.

Developed formulation was stable, safe and effective for treatment of mouth ulcer

**Keywords:** Tankan Bhasma; Gairik Bhasma; Gel

## Introduction

A mouth ulcer is a breach of break in the mucous membrane which lines the inside of the mouth. It usually looks like a depression in the mucous membrane and usually has yellow or white colour [1]. Semi-solid formulations include gel having a liquid phase which are then thickened by other components. Topical gels are intended for the application on skin or to certain mucosal surfaces for local action or percutaneous penetration of medicament preparations [2].

Synthetic and semi-synthetic active agents have several disadvantages like staining on the teeth, irritation and burning sensation. These disadvantages are due the presence of high degree of alcohol content and some organic compounds. Such active agents are included in the commercially available gel. The use of combination of inorganic compounds such as Tankan bhasma and Gairik bhasma in the treatment of mouth ulcer in pharmaceutical gel was involved in this present investigation.

Among the most global oral health problems oral diseases are major health problems with oral cancer, dental caries and periodontal diseases. Oral diseases and the cavities of microbial species that form part of the micro biota of the oral cavity forms a well-established link between them. The global need for alternative prevention and treatment options and products for oral diseases that are safe, effective and economical comes from the rise in disease incidence particularly in developing countries, increased resistance by pathogenic bacteria to currently used antibiotics and chemotherapeutics, opportunistic infections in immunocom-

promised individuals and financial considerations in developing countries. Also, for a developing country like India allopathic medicine is too expensive and capital intensive. Only limited success had achieved in the periodontal disease and treatment of a variety of oral disease. Hence, this leads to the search of alternative products and the use of plant extracts in traditional medicines are considered as good alternatives to western medicines [3].

Oral hygiene is an integral part of health of a person. Oral health when neglected, results in different types of oral ailments like dental caries and periodontal diseases. Oral disorders can significantly affect the general well-being of a person by causing considerable pain and discomfort, thus affecting their quality of life. Dental caries and periodontal diseases are the two common threats to oral health and because of their prevalence, there is an impact on individuals and society, and the expense of their treatment. Oral diseases are caused due to bacterial infections, food habits and life style. Most of these herbs have alkalinity property along with antibacterial activity. Hence acid-alkaline balance of the saliva is maintained by these herbs. Also these herbs decrease plaque formation and are less prone to periodontal diseases. Antibacterial plant extracts produced no allergy in the gingival and other soft tissue in the oral cavity [4]. Dental biofilm formation develops oral infectious diseases such as periodontal inflammation, caries, and gingivitis. Other serious health problems can be caused by these kind of dental problems and, this is the reason why the study in the development of referred pathologies has been a theme of growing interest [5].

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In oral diseases mouth ulcer is also one of them which are treating by the inorganic compound containing products like tankan bhasma and Gairik bhasma. A mouth ulcer is a breach or break in the mucous membrane which lines the inside of the mouth. It usually looks like a depression in the mucous membrane and usually has yellow or white colour. The size may vary from a millimeter or less in diameter to several centimeters. It is often painful.

Commonly known as Tankan bhasma is Borax, Boron and for Gairik bhasma is Iron Oxide. One of the most important transition metal oxides is Iron oxides. Iron oxides that are known to date are oxides, hydroxides or oxy-hydroxides are known to date. Iron oxide is $Fe_2O_3$ this is structurally known [6].

Synonym of Tankan in Sanskrit- Tankan, Hindi- Sohaga, English- Borax, Panjabi- Tinkal, and Telgu- Velligarm is known in various regions. Tankan structurally known as ($Na_2B_4O_7$ $10H_2O$) is composed of boric acid and soda [7]. In the treatment of mouth ulcer a pharmaceutical gel deals with inorganic compounds such as tankan bhasma and Gairik bhasma in the present investigation.

## Material and Methods

Inorganic drug Tankan bhasma and Gairik bhasma were collected from Dr Malekar (M.D. Ayurveda) Karad, Satara district. All other analytical grade ingredients are purchased from LobaChemie Mumbai.

### Preparation of Gel

In the required amount of distilled water specified amount of Carbopol 934 was dispersed with the continuous stirring. Required quantity of methyl paraben and propyl paraben were dissolved in 5 ml of distilled water by heating it on eater bath and then propylene glycol was added after cooling. Further to the above mixture varying concentration of Tankan and Gairik bhasma was mixed and with distilled water volume was made up to 20 ml. With continuous stirring finally to the Carbopol 934 gel full mixed ingredients were mixed and then to adjust the required pH (6.8 - 7) triethanolamine was added dropwise to the formulation [8].

The composition of gel prepared from the inorganic drugs coded as F1 to F7 is tabulated in table 1

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| Gairik | 1% | - | 0.5% | - | 1% | 0.5% | 1% |
| Tankan | - | 1% | - | 0.5% | 1% | 1% | 0.5% |
| Carbopol 934 | 2% | 2% | 2% | 2% | 2% | 2% | 2% |
| Methyl Paraben | 0.0015% | 0.0015% | 0.0015% | 0.0015% | 0.0015% | 0.0015% | 0.0015% |
| Propyl Paraben | 0.01% | 0.01% | 0.01% | 0.01% | 0.01% | 0.01% | 0.01% |
| Triethanolamine | q.s + pH 6.5-7 | q.s + pH 6.5-7 | q.s + pH 6.5-7 | q.s + pH 6.5-7 | q.s + pH 6.5-7 | q.s + pH 6.5-7 | q.s + pH 6.5-7 |
| Distilled water | Up to 20 ml | Up to 20 ml | Up to 20 ml | Up to 20 ml | Up to 20 ml | Up to 20 ml | Up to 20 ml |

**Table 1:** Composition of various gel formulations containing inorganic compound.

## Evaluation of Gel

### Antifungal activity

The comparison of the formulated herbal gel was done with the marketed antifungal formulation (Zolef Cream) by carrying out the antifungal activity pf all developed batches and blank formulation by Cup-plate method. *Aspergillus aureus* and *Candida albicans* were the two different bacteria cultures used.

Using agar the antifungal test was performed. Petri plates with well diffusion prepared nutrients was kept for drying and cooling. With the help of micro wire loop each bacterial culture was spread. To drill holes of 4 mm a sterile cork borer of 6 mm diameter was used. In to these holes then 0.5g of gel was added form each batch. Incubation of plates were then done at 270C for 48 hr. If any zone of inhibition develops (diameter in mm) it was then measured for the particular compound with each fungal strength [9]. Table 4 reported antifungal studies.

After antifungal test then batch optimization was done. Then further evaluation was done with optimized batch as follow.

### Physical Appearance

Color and appearance being physical parameters were checked for this herbal topical gel.

### Measurement of pH

Digital pH meter was used to determine the pH of gel formulation. Gel weighing accurately I gm in quantity is dispersed in 10 ml of distilled water and stored for two hours. pH measurement of formulation was carried out in triplicate representing the average values [10]. Table 2 reports the pH of gel formulation.

### Homogeneity

By visual inspection all developed gels are tested for homogeneity after setting the gels in container. Testing was done for their appearance and presence of any aggregates [11]. Table 2 reports homogeneity of gel formulation.

### Spreadability

Wooden block and glass slide apparatus were used to determine the spreadability. 20 gm weights were added to the pan and noting the time for upper slide i.e. movable to separate completely from the fixed slide [12].

2 gm excess gel on this ground slide was placed under study. Sandwiching of gel was done between this slide and another glass slide having fixed ground slide and provided with the hook. Weight of 1 kg was placed on the top of the two slides for 5 minutes to expel air which helps to provide a uniform film of the gel between the slides. From the edges excess of the gel was scrapped off. With the help of string attached to the hook the top plate was subjected to pull and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. Better spreadability is indicated by the shorter interval. Following formula is used to calculate Spreadibility [13]. Table 2 reports the spreadability of gel.

$S = M \times L / T$

Where, S = Spreadibility,

M = Weight in the pan (tied to the upper slide),

L = Length moved by the glass slide and

T = Time (in sec.) taken to separate the slide completely each other.

### Viscosity

Using Brookfield viscometer (DV-III programmable Rheometer) the gels were tested for their rheological characteristics at 250C. Over the whole range of speed settings from 10 rpm to 100 rpm with 30 seconds between 2 successive speeds and then in a descending orders [14] the measurement was done.

### Extrudability

Standard capped collapsible aluminum tubes were used to fill in the gel formulations and the tubes were sealed by crimping to the end. By pressing of the thumb then the extrudability was determined.

### Gel strength

Penetration of weight to 0.5 cm in the gel determines the strength of the gel. Sample of each of 5 gm of the optimize batches was taken and 3.5 gm weight was placed on the gel surface. 0.5 cm area of the gel was penetrated by the weight in time in seconds. Table 3 reports the strength the gel.

### Bioadhesive Strength

By using wooden block and glass slide apparatus by measuring the force required to detach the formulation from cellophane membrane bioadhesive strength was determined. On glass slide with the help of the cellophane membrane 1 gm of gel was taken. By placing the movable glass slide on fixed slide intimate contact was provided. To ensure intimate contact between membrane and formulation two minute contact time was given. The weight was added in the pan until slides got detached. By the formula the bioadhesive force, expressed as the detachment stress in dyne/cm2 was determined [15]. Table 3 reports the Bioadhesive strength.

Detachment stress = m·g/A

Where,

m = Weight required to detach two glass slides from each other (gm).

g = Acceleration due to gravity (980 $cm/s^2$).

A = Area of membrane exposed ($cm^2$).

### Uniformity

Gel was weighed 1 gm accurately and the same was transferred to 100 ml volumetric flask containing simulated salivary fluid. The sample solution was filtered using filter paper. From the filtrate 1 ml of quantity was pipetted out and was suitably diluted with simulated salivary fluid up to 10 ml. Then the sample was estimated spectrophotometrically by using respective $\lambda_{max.}$

### *In vitro* diffusion study

Egg membrane was used for this study. In donor compartment of cell, 1 gm of gel was placed in modified Franz diffusion cell. The entire surface of membrane was in contact with the receptor compartment used simulated salivary fluid. At normal body temperature i.e. 37 ± 10C, the receptor compartment was continuously stirred (100 rpm) using a magnetic stirrer with temperature maintained. At predetermined time interval the sample was withdrawn and same volume was replaced with fresh simulated salivary fluid. After suitable dilution at respective $\lambda_{max}$ to estimate drug concentration the absorbance of withdrawn sample was measured [16].

### Stability Study

Open and close container was used to perform stability studies, here, by for 1 month by subjecting the product to room temperature [9,17]. Table 3 reports stability studies.

## Results and Discussion

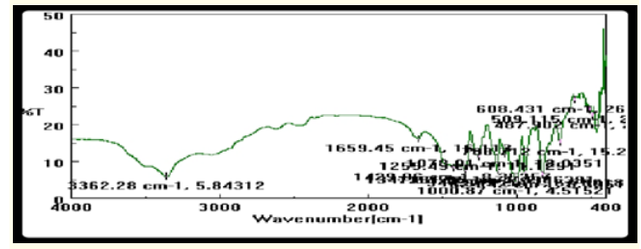


**Figure 1:** IR Spectra of Tankan bhasma.

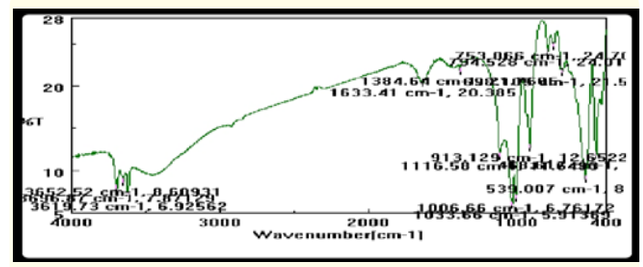


**Figure 2:** IR Spectra of Gairik bhasma.


**Figure 3:** IR spectra of Physical mixture of Tankan, Gairik and Polymer.

| Formulation | Antifungal Study | |
|---|---|---|
| **Fungal Strength** | ***Aspergillus aureus* (mm)** | ***Candida albicans* (mm)** |
| Blank | 12 | 15 |
| F1 | 17 ± 0.8 | 18 ± 0.8 |
| F2 | 20 ± 0.8 | 18 ± 0.4 |
| F3 | 19 ± 0.8 | 17 ± 0.4 |
| F4 | 19 ± 0.8 | 17 ± 0.9 |
| F5 | 20 ± 0.8 | 17 ± 0.4 |
| F6 | 13 ± 1.8 | 13 ± 0.4 |
| F7 | 21 ± 0.8 | 17 ± 0.8 |
| Marketed Formulation | 26 ± 0.2 | 28 ± 0.4 |

**Table 2:** In vitro anti-fungal study.

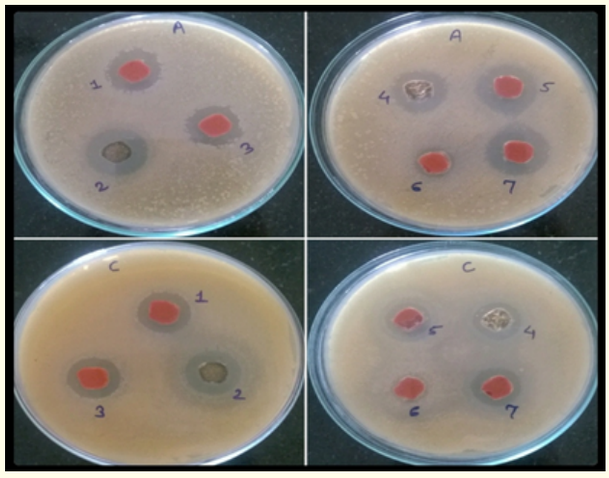


**Figure 4:** Antifungal Activity of developed inorganic gel formulation.

A: Aspergillus aureus, C: Candida Albicans

1-7 = F1-F7

From above study batch optimization was done. Batches were selected as F1, F2, F5 respectively. Further evaluation was done with optimized batch.

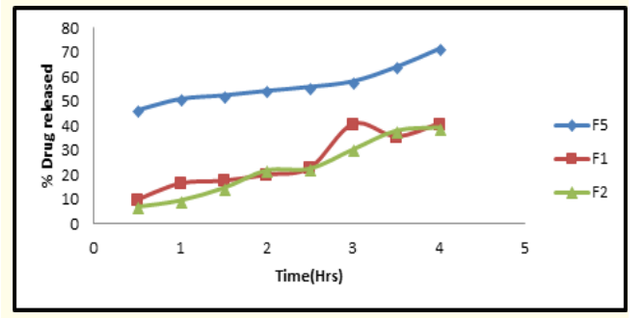


**Figure 5:** Graphical representation of drug diffusion studies of gel.

| Sr. No | Batch | | Drug Content (%) |
|---|---|---|---|
| 3 | F1 | | 90 ± 0.52 |
| 4 | F2 | | 93 ± 0.55 |
| 5 | F5 | Tankan | 90 ± 0.66 |
| | | Gairik | 91 ± 0.29 |

**Table 5:** % Drug contains uniformity.

| Formulation | Physical Appearance | pH | Homogeneity | Spreadability (gm.cm/sec) | Viscosity (Pa·S) | Extrudability |
|---|---|---|---|---|---|---|
| F1 | Transparent | 7.2 ± 0.08 | Good | 6.23 ± 0.055 | 2.302 ± 0.012 | Good |
| F2 | Transparent | 6.7 ± 0.04 | Good | 6.31 ± 0.020 | 2.152 ± 0.021 | Good |
| F5 | Transparent | 7.1 ± 0.08 | Good | 5.35 ± 0.030 | 3.251 ± 0.172 | Good |

**Table 3:** *In vitro* evaluation parameters.

| Formulation | Bioadhesive strength (dyne/cm$^2$) | Gelling Strength (Sec) | Stability study for 1 Month | |
|---|---|---|---|---|
| | | | Open Container | Closed Container |
| F1 | 3012.13 ± 14.09 | 27 ± 0.01 | Not Stable | Stable |
| F2 | 3142.02 ± 0.07 | 26 ± 0.42 | | |
| F5 | 4321.22 ± 84.18 | 40 ± 1.03 | | |

**Table 4:** *In vitro* evaluation parameters.

| Sr. No | Time (h) | % CDR | | |
|---|---|---|---|---|
| | | F1 | F2 | F5 |
| 1 | 30 min | 9.825 ± 0.04 | 6.825 ± 0.05 | 46.25 ± 0.40 |
| 2 | 1 | 16.513 ± 0.44 | 9.451 ± 0.47 | 50.86 ± 0.12 |
| 3 | 1:30 | 17.598 ± 0.47 | 14.471 ± 0.46 | 52.325 ± 0.53 |
| 4 | 2 | 19.997 ± 0.47 | 21.681 ± 0.47 | 54.20 ± 0.04 |
| 5 | 2:30 | 22.844 ± 0.47 | 22.419 ± 0.46 | 55.83 ± 0.04 |
| 6 | 3 | 40.63 ± 0.02 | 30.237 ± 0.47 | 58.10 ± 0.16 |
| 7 | 3:30 | 35.59 ± 0.08 | 37.843 ± 0.47 | 63.905 ± 0.07 |
| 8 | 4 | 40.83 ± 0.50 | 39.216 ± 0.47 | 71.405 ± 0.07 |

**Table 6:** *In-vitro* drug diffusion study of prepared gel formulation.

It is clearly evident from the results that all the gel formulations showed good gelling property and homogeneity [11]. The pH of all the formulations was in the range compatible with normal pH range of the skin [10]. The rheological behavior was studied with rheometer ranging between 2.302 ± 0.012 to 3.251 ± 0.172 Pa.S. Which is indicated that formulated gel was neither too thick and nor too thin [14]. The study of spreadability shows that with increasing the viscosity of formulation spreadability decreases and vice versa [12]. Extrudability study was done by pressing thumb and it's easily extendable. The gel strength and bioadhesive strength of all the three batches was found in the suitable range [16]. 1 Month stability study was done with open and close container and it's showed that open container containing gel was not stable and close container gel was stable. Formulated gel containing open container when expose to ambient room temperature then syneresis was observed it means liquid exudates separating [17]. Syneresis takes place when the interaction between the dispersed phase particles becomes so great that on standing in that, dispersing medium is squeezed out in droplets forms and shrinking of the gel occurs. Syneresis it means the form of instability in aqueous gels. In syneresis system separation of a solvent phase is occur only because of the elastic contraction of the polymer means polymeric molecules [9]. $\lambda_{max}$ of tankan bhasma was found to be 227 nm and for Gairik bhasma was found to be 562 nm. Good uniformity of drug content among the gels was observed with optimized inorganic gel batches and ranged from 90 ± 0.52% to 93 ± 0.55%. *In vitro* drug release studies were carried out. Percentage of drug release at the end of 4 hr. The *in vitro* drug diffusion study for gel showed good result for % CDR at 40.83 ± 0.50, 39.216 ± 0.47, 71.405 ± 0.07 respectively [16].

Infrared spectra of gel formulations did not show the presence of any additional peaks solvent. No interaction was revealed between drugs and polymer by infrared spectroscopy. Infrared spectra shown groups 3362.28- OH, 1659.45- CO2, 1633.41- $COO^-$, 1006.66- C-O-C, 1116.58- Feroxyhyte.

The major peaks of the drug remained unchanged in the mixture were observed in Infrared spectra. All the three batches of developed formulation showed excellent antifungal activity compares to all other batches against as *Aspergillus aureus* and *Candida albicans* this are main microorganism responsible for mouth ulcer and formulation it can also use to treat mouth ulcer infection [16].

## Conclusion

The data present in this study and on the basis of data collected from evaluation and result, it was demonstrated that the developed gel formulation possess significant, therapeutically efficacious, suitable vehicle for drug delivery in low cost but definitely with high potential. Developed new gel formulation is suitable for mouth ulcer treatment.

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**Volume 2 Issue 7 July 2018**