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Research Article

Assessment of Targeted Millet Therapy for Oral Aphthous

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ABSTRACT

Recurrent aphthous stomatitis (RAS), commonly called "canker sores," is a perplexing oral condition characterized by the recurrent development of painful aphthous ulcers on non-keratinized oral mucous membranes. This condition poses a significant challenge to patients and healthcare professionals due to its uncertain etiology. The study aims to evaluate the efficacy of millets in the management oral ulcers (aphthous). Millets are formulated in the form of an oral gel as gels are low cost and easily administered. Three types of millets are used for the study- pearl millet, foxtail millet and finger millet. Millets are evaluated for antimicrobial and anti-inflammatory activity due to their rich content of essential vitamins, minerals, and antioxidants. The antimicrobial activity of the millets and the standard drug, amoxicillin were observed and the zone of inhibition was calculated at 100, 300 and 500 mg/mL concentrations. The anti-inflammatory activity was assessed by calculating the % inhibition of protein denaturation using the absorbance value. Millets showed significant activities when compared with the standard drug. All these properties of millets and the chemical constituents heal mouth ulcers providing efficient drug delivery. Thus, these millets can be incorporated in the form of gel for the treatment of mouth ulcer.

Introduction

A mouth ulcer (aphtha) manifests as a lesion on the mucous membrane within the oral depression, resulting in the loss of peripheral tissue and the decomposition and necrosis of epithelial tissue.[1] The blisters develop on any of the mouth's delicate spots, such as lingua, cheeks, oral gingival membranes, lips, bottom, and roof of the mouth.[2] Oral ulcers, which are common painful lesions, are related to multitudinous conditions that occur during oral depression.[3] The majority of ulcers are benign and heal on their own, but there is a slim possibility that they won't.[4] Regional trauma is one of the most frequent causes of mouth ulcers. The most common causes are dental work, braces, jagged or broken teeth, tongue piercings, impertinence, and eating hot or harsh meals. Usually, ten days after the cause is eliminated, these ulcers begin to heal.[5] In around 60% of instances, oral ulcers coexist with intestinal symptoms in patients with Crohn's disease.[6]

There are essentially three different kinds of aphthous ulcers: the minor, major, and herpetiform forms. About 70 to 80% of cases involve minor aphthous ulcers. It usually appears on non-keratinized surfaces, especially the mouth's mucosa, lips, and bottom of the mouth. Major aphthous ulcer affects about 10% of cases. These ulcers generally appear on the lips, cheeks, lingua, palate, and pharynx. Herpetiform aphthous ulcer affects about 1 to 10% of cases. Multiple intermittent picks of minor, expansive, painful ulcers categorized it.[7]

The etiology of aphthous ulcers includes a cell-intervened immunological response and an inheritable predilection. The oral epithelium is infiltrated by lymphocytes (mononuclear cells), which also cause edema and, vacuolization and vasculitis in keratinocytes (oral epithelial cells). This leads to localized edema and, eventually, epithelial ulceration. Before the epithelium heals and regenerates, neutrophils, lymphocytes, and

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plasma cells infiltrate the area.[8] The purpose of treatment of ulcers is to palliate symptoms, drop the inflexibility of the ulcers (number and size), promote mending, and protract complaint-free ages.[9] To prevent further bacterial infection, milder cases are typically treated with NSAIDs and topical corticosteroids, such as mouthwash containing benzylamine and mouthwash containing chlorhexidine. These have been shown to shorten the duration and reduce the rigidity of aphthous ulcers.[10] The most essential medication for treating aphids is topical steroids, such as triamcinolone and prednisolone; nevertheless, these medications have a number of side effects, including immunological suppression, adrenal repression, osteoporosis, gastrointestinal problems, and elevated blood sugar.[11] Commercially available gels containing synthetic and semi-synthetic active substances have several disadvantages, such as tooth staining, vexation, and burning sensation, caused by their high alcohol content and organic composites.[12] A stable oral gel that can be used as an essential treatment for aphthous ulcers is produced considering these adverse effects and based on primary investigations on millets and their efficacy on aphthous ulcers. Gels can absorb swiftly in seconds when placed on the lingua or in oral mucosa of a patient and release the medicine for oro mucosal or intragastric assimilation.

Millet species have been used for centuries in many folk remedies. Millets are abundant in essential amino acids, micronutrients (carotenoids and tocopherols), vitamins and minerals (magnesium, manganese and phosphorus). Millets retain phenolic acids, flavonoids, tannins, xylo oligosaccharides, fibers, carotenoids and vitamin E. In addition to minerals and vitamins, the consumable portion of millet is composed of proteins (7–11%), fat (1.5–5%) and carbohydrates (60–70%). According to the study's findings, pearl millet, foxtail millet, and finger millet all contain high portions of phytochemical exertion.[13] Foxtail millet (*Setaria italica*) is a periodic lawn grown for immortal food. It is the second species of millet that is cultivated most widely. Pearl millet (*Cenchrus americanus*) is the most extensively grown type of millet. Finger millet (*Eleusine coracana*) is a periodic herbaceous factory extensively grown as a cereal crop.[14] The millets are shown in Fig. 1, foxtail millet 2 pearl millet 3 finger millet.

Fig. 1: Foxtail millet

Fig. 2: Pearl millet

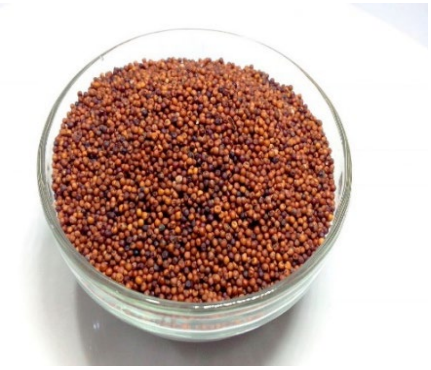

Fig. 3: Finger millet

MATERIALS AND METHODS

Preparation of Medicine

High-quality millet grains were chosen. The millet grains were placed in a large coliseum and irrigated entirely under running water to remove any dirt or contaminations. The millets were dried at room temperature and ground into fine dust using a sieve.

Phytochemical Screening

Phytochemical screening was carried out to check the existence of carbohydrates, alkaloids, phenolic composites, saponins, and tannins.

Antimicrobial Exertion

Well, the diffusion method determined the antibacterial exertion of the sample on a nutrient medium. The media was sterilized, then put into sterile petri dishes and allowed to solidify for an hour. After the medium had been set, the inoculums were added to the solid plates using a sterile swab saturated with the bacterial solution. Wells were made with the help of a cork borer. Petri plates were loaded

with three different concentrations of sample (100, 300, and 500 mg/mL) and separate wells containing 500 mg/mL of amoxicillin. The microbial growth on these plates was measured by calculating the periphery of the zone of inhibition, and they were incubated for 24 hours at 37°C.

Anti-inflammatory Exertion

In 2.8 mL of phosphate saline buffer (PBS, pH 6.4), 0.2 mL of fresh hen's egg albumin, and 2 mL of various sample dosages (100, 300, and 500 mg/mL) made up the reaction mixture (5 mL). As a control, double-distilled water was utilized. Additionally, the solutions had been heated to 70°C for five minutes and incubated for 15 minutes at 37 ± 2°C in a BOD incubator. Following cooling, their viscosity was ascertained with an Ostwald viscometer, and their absorbance was calculated by applying a blank vehicle at 660 nm. As a reference medication, diclofenac sodium at a final dose of 500 mg/mL was also utilized to measure absorbance and viscosity. The percentage inhibition of protein denaturation was calculated using the procedure below.

$$\frac{\text{Absorbance of control} - \text{Absorbance of treated}}{\text{Absorbance of control}} \times 100$$

Preparation of Oral Gel

In 2.5 g of carbopol was measured and mixed with 6 mL of distilled water using a magnetic stirrer. Another mixture containing varying amounts of propylene glycol, methylparaben, propylparaben, and powders of millet had been mixed. Carbopol 934 was put in addition, exactly, and continuously stirred. To acquire the required thickness of the gel, 20 mL of distilled water was added, and triethanolamine was added to maintain the pH level.

Evaluation of Gel

Physical appearance

Physical characteristics like color and appearance were examined.

Homogeneity

After the gels had been positioned inside the vessel, the gel preparations were examined visually. They underwent testing to determine whether any lumps were there or not.

pH determination

To measure the pH of produced gel formulations, digital pH testing equipment was appllid. After dissolving 1 g of gel in 100 mL of distilled water, it was left out for two hours. Triplets were used to determine the pH, and average values were computed.

Spreadability

The time it takes for a pair of slides to separate themselves from the gel placed between them while a particular weight is applied is expressed in seconds. Improved spreadability results from a shorter time needed to split the slide. Spreadability was determined by applying the following formula

$$S = M \times L / T$$

Where,
M = weight tied to upper slide, L = length of glass slide, T = time taken to separate the slides

Gel strength

The amount of time in seconds required for the weight to enter the gel was used to calculate the strength of the gel. Five grams of gel were obtained as a sample, and 3.5 g of weight were added to the gel's surface. The weight-related time in seconds required to reach 0.5 cm in the gel.

Results And Discussion

The phytochemical evaluation of the chosen millets was performed, and the results have shown the existence of carbohydrates, tannins, phenolic composites as well as saponins in, foxtail millet, pearl millet and finger millet and the presence of alkaloids in only finger millet along with pearl millet as shown in Table 1. Due to the presence of these chemical entities in the millets, they were named for the management of mouth ulcers, which shows good anti-inflammatory exertion and antimicrobial exertion.
The antimicrobial exertion of the millets and the standard medicine amoxicillin were observed using gram-negative as well as gram-positive bacteria, and the zone of inhibition was calculated in centimetres. The results are shown in Tables 2 & 3. For gram-negative bacteria, the zone of inhibition at 100, 300 and 500 mg/mL for Foxtail millet were seen to be 1.3, 2.5 and 3 cm; for finger millet, it was seen to be 1, 2.8 and 3.2 cm; for pearl millet it was seen to be 1.8, 2.8 and 3.5 cm, respectively. For the standard medicine, the zone of inhibition was seen to be 3.5 cm, as mentioned in Table 2.
For gram-positive bacteria, the zone of inhibition at 100, 300 and 500 mg/mL for foxtail millet were set up to be 0.5, 1 and 1.8 cm; for finger millet it was seen to be 0.8, 1.5 and 2 cm, for Pearl millet it was seen to be 0.5, 1.2 and 2 cm, respectively. For the standard medicine, the zone of inhibition was seen to be 2.8 cm, as mentioned in Table 3. The $p < 0.0001$, the distinction is indicated to be highly statistically significant for all the three millets when compared with standard medicine, when the t-test was applied. The zone of inhibition of the three chosen millets seemed to show significant antimicrobial exertion compared with the standard medicine.
The absorbance of foxtail millet, finger millet and pearl millet for 3 samples each were recorded using calorimeter at 660 nm; absorbance of the chosen millets and standard medicine (Diclofenac) were recorded described in Table 4 to compute the percentage inhibition of protein denaturation.

Table 1: Phytochemical evaluation of millets

S. No	*Constituents*	*Test*	*Foxtail millet*	*Finger millet*	*Pearl millet*
1	Alkaloids	Mayers test	-	+	+
2	Carbohydrates	Benedict's test	+	+	+
3	Saponins	Foam test	+	+	+
4	Phenolic compounds	Ferric chloride test	+	+	+
5	Tannins	Ferric chloride test	+	+	+

Table 2: Antimicrobial exertion of millets for gram-negative bacteria (*E. coli*)

S. No	*Concentration mg/mL*	*Foxtail millet*	*Finger millet*	*Pearl millet*	*Standard 300 mg/mL*
1	100	1.3 ± 05	1 ± 0.08	1.8 ± 0.05	
2	300	2.5 ± 0.05	2.8 ± 0.11	2.8 ± 0.05	3.5 ± 0.05
3	500	3 ± 0.05	3.2 ± 0.05	3.5 ± 0.11	

The Mean SEM (n =3) value is expressed in cm. $p<0.0001$, which indicates that the difference is highly statistically significant.

Table 3: Antimicrobial exertion of millets for gram-positive bacteria *(Bacillus Subtilis)*

S. No	*Concentration (mg/mL)*	*Foxtail millet*	*Finger millet*	*Pearl millet*	*Standard 300 mg/mL*
1	100	0.5 ± 05	0.8 ± 0.08	0.5 ± 0.05	
2	300	1 ± 0.05	1.5 ± 0.11	1.2 ± 0.05	2.8 ± 0.05
3	500	1.8 ± 0.05	2 ± 0.05	2 ± 0.11	

The Mean SEM (n = 3)Value is expressed in cm. $p < 0.0001$, which indicates that the difference is highly statistically significant.

Table 4: Absorbance of millets at 660 nm

S. No	*Concentration (mg/mL)*	*Foxtail millet*	*Finger millet*	*Pearl millet*	*Standard 300 mg/mL*
1	100	2.1 ± 0.05	2.38 ± 0.11	2.0± 0.05	
2	300	0.8 ± 0.05	0.7 ± 0.08	0.8± 0.05	± 0.2
3	500	0.4 ± 0.05	0.4 ± 0.05	0.3 ± 0.11	

Value is expressed as Mean SEM (n = 3). $p< 0.0001$, the distinction is indicated to be highly statistically significant.

The percentage inhibition of protein denaturation had been measured with the help of absorbance value. The percentage inhibition at 100, 300, and 500 mg/mL for foxtail millet was seen to be 73.4, 89.8 and 94.9%; for finger millet, it was seen to be 70.8, 91.1 and 94.9%; for pearl millet it was seen to be 74.6, 89.8 and 96.2%, respectively. The percentage inhibition of protein denaturation of standard medicine had been seen to be 97.4%, as mentioned in Table 5.

The %inhibition displayed by chosen millets has shown significant exertion when compared with the standard medicine, is relatively analogous and hence can be used in the treatment of mouth ulcers.

The millets have shown significant anti-inflammatory exertion and antimicrobial exertion in comparison to the standard medicine. So, these herbal medicines can be recommended mainly for the treatment of mouth ulcers.

The gel was formulated after the evidence of antimicrobial exertion and anti-inflammatory exertion. The gel was subordinated to the evaluation test. The color of the gel was transparent, the odor was characteristic, the homogeneity was good, the spreadability was seen to be 4, and the pH was set up to be 6.8, as shown in Table 6. The gel fulfills all the conditions to be used in the orally.

Table 5: Protein denaturation of millets

S. No	*Concentration (mg/mL)*	*Foxtail millet*	*Finger millet*	*Pearl millet*	*Standard 300 mg/mL*
1	100	73.4%	70.8%	74.6%	
2	300	89.8%	91.1%	89.8%	97.4%
3	500	94.9%	94.9%	96.2%	

Value is expressed as Mean SEM (n = 3)

Table 6: Evaluation tests of gel

S. No	*Evaluation tests*	*Results*
1	Color	Transparent
2	Odour	Characteristic
3	Homogeneity	Good
4	Spreadability	4 ± 0.1
5	pH	6.8 ± 0.5

Conclusion

A mouth ulcer happens on the oral cavity's mucus membrane. Mouth ulcers are prevalent and associated with numerous conditions, but generally, there's no serious underpinning cause. Topical gels containing anesthetics like benzocaine and lidocaine are used to give relief from pain. The use of conventional medicines has numerous bad signs associated with mouth vexation, teeth staining, and dry mouth. Oral gels are formulated for treating mouth ulcers using three kinds of millets such as pearl millet, foxtail millet along with finger millet. According to the findings of studies, all three millets retain an advanced position of antioxidant exertion, antimicrobial properties and anti-inflammatory properties. Millets are abundant in essential amino acids, micronutrients, vitamins and minerals. Therefore, this study validates the use of millet for the treatment of mouth ulcers.

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