

# Apitherapy: A Holistic Agent in Canker Sore

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## Abstract:

**Background:** The term apitherapy is a branch of alternative medicine used to denote a form of medicine (honey) that falls in the main stream of western countries. The various allopathic and traditional remedies have been tried in aphthous ulcer. In this open label trial study, the aim was to observe the effectiveness of a novel topical agent honey on recurrent aphthous stomatitis.

**Material and method:** The present study was conducted on 400 patients diagnosed to have recurrent minor aphthous ulcers. The baseline parameters which were recorded on the first visit include number of ulcers, size, pain, erythema, exudation and recurrence. Patients with increased frequency of stomatitis were advised to use 100% natural honey for three to four times daily till ulcer heals. The changes in parameters were observed and recorded on each visit of the patient. The efficacy and safety evaluations were made on the 2<sup>nd</sup> and 3<sup>rd</sup> Visit (3<sup>rd</sup> and 6<sup>th</sup> day). Patients were followed for a period of 1 year and the number of ulcers per month was recorded to evaluate for recurrence rate.

**Results:** The erythema, exudates and pain in the ulcer started to reduce in 2-3 days. The size of ulcer started to reduce in almost 2<sup>nd</sup> visit (3rd day) and complete resolution seen on 3<sup>rd</sup> visit (6<sup>th</sup> day). There was no recurrence in any case till 1 year of treatment.

**Conclusions:** Honey showed complete resolution of recurrent aphthous stomatitis due to antimicrobial, antibacterial, anti-inflammatory and antioxidant effect.

**Keywords:** Recurrent Aphthous Ulcer, Honey, Aphthous Minor.

## Introduction:

Apitherapy is the use of honey and honey bee products in the field of medicine. In ancient medicine system, Ayurveda defines honey and its products like pollen, bee bread, propolis, royal jelly and bee venom as the nectar of life and suggest its use in the treatment of various ailments such as diarrhea, ulcers, etc. The father of modern medicine Hippocrates said that “Let your food be your medicine”. Honey has been mentioned in the Holy Quran (1400 years ago) and said that Bee (Al Nahl) and part of it says “And thy LORD taught the bee to build its cells in hills, on trees and in men’s habitations, wherein healing for men.” In recent time, honey is known as natural sweetener but it is nature’s gift to Mankind.<sup>1,2,3</sup>

In oral mucosa different diseases can present as ulcer, among all lesion aphthous is the most common of oral ulcerative diseases. Every human in their lifetime is atleast once affected by ulcers of oral mucous membrane and it is estimated that 15-20% of the population worldwide is affected by (RAU). Recurrent aphthous ulcers (RAU) are characterized by the development of painful, recurring solitary or multiple necrotizing ulcerations of the non-

keratinized oral mucosa. Historically, the wide range of possible etiology can be local and systemic factors that encompassed microbial agents, hematologic and hormonal disturbances, physical injury, emotional stress and other influences. RAS is the least understood oral diseases and is among the most troublesome problems faced by affected patients and clinicians. Clinically, the RAS can be classified as aphthous minor, aphthous major and Herpetiform ulcers. The 80-95% of aphthous ulcers are minor whereas the least common is Herpetiform ulcer. Aphthous minor present as white ulcerative lesions that may be single or multiple and round or oval. The ulcer may remain for 7 to 14 days and then resolve without scars. Whereas aphthous major account for 10-15% and Herpetiform ulcer account for 5-10%, both are differentiated by larger lesions. The RAU major and minor appear on non-keratinized area whereas the Herpetiform appear on both non-keratinized and keratinized mucosa. The various measures have been taken for treating and preventing RAU like elimination of predisposing factors (if any) Stress, food, topical and systemic therapy and physical therapies. Although the exact etiology of RAS remains doubtful, this has considerably inclined towards the traditional and contemporary approaches en route for its management.<sup>4,5</sup> Here in this research the holistic topical agent honey has been used to treat minor recurrent aphthous ulcer. The investigator tried this agent as till date, this holistic and novel agent is still in infancy stage.

## Materials and Methods:

### Study design:

The study was designed and included 400 patients diagnosed to have recurrent minor aphthous ulcers. They were randomly selected from the out-patients attending the Department of Oral Medicine and Radiology. The selection was done on the basis of inclusion and exclusion criteria as mentioned in Table 1.

Inclusion criteria	Exclusion criteria
Patients with age range from 18 to 60 years.	A known history of hypersensitivity or anaphylactic reaction.
Patients with known history of recurrence of ulcer.	Patients suffering from any systemic disorders.
Patients with single or multiple aphthous ulcers with size less than 5 mm in diameter.	Patients who were on any kind of medications.
	Subjects who were pregnant and breast feeding.

**Table 1: Selection criteria**

**Material:**

The study agent used was local honey provided by forever company. Honey consist of several biologically active constituents such as flavonoids and phenolic compounds, vitamins, trace elements, amino acids and proteins as well as certain enzymes including glucose oxidase, invertase and catalase. Some of the flavonoids and phenolic compounds that have been identified in honeyinclude chrysin, kaempferol, quercetin, pinobanksin, pinocembrin, luteolin, apigenin, genistein,naringenin, hesperetin, p-coumaric acid, gallic acid, ellagic acid, ferulic acid, syringic acid, caffeic acid and vanillic acid.

**Subjects:**

Patients reporting with single or multiple minor aphthous ulcers visiting the out-patient department were selected. The commonest site of occurrence and gender affected was recorded and noted. The baseline parameters (number of ulcers, ulcer size, pain, erythema and exudation, recurrence) were recorded on the first visit before the honey application. The first application of the agent was supervised and provided the subject with written instructions on how to apply the drug. The patients were advised to apply the drug as soon as possible after noticing the symptoms of an aphthous ulcer, 4 times a day, preferably following oral hygiene, after breakfast, lunch, dinner and at bedtime. They were asked to take out the agent from bottle on a clean fingertip and apply to the site of the ulcer. The hygroscopic and viscous quality makes it a better to use in oral mucosa whereas other oral topical agents require vehicle. They were instructed to apply the agent after drying the ulcer with a soft piece of clean cotton.

**Evaluation of efficacy:**

The subjects were explained about the VAS pain scale which consists of a horizontal straight line with marking from 0 to 10 shown in Figure 1. Zero means no pain to 10 that means severe or unbearable pain. The patients were given marker and asked to encircle the severity of pain in VAS scale.<sup>6</sup>The ulcer size was assessed by using calibrated William's probe. The degree of erythema and exudation was evaluated on a 4-point scale ranging from 0 to 3 based on the methods of Greer et al.<sup>7</sup> with some modification shown in Table 2. The screening was done on 3<sup>rd</sup> and 6<sup>th</sup> visit and patients reading were taken and recorded.

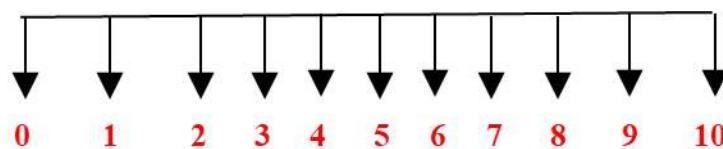


Figure 1 shows Visual analogue scale (VAS)

Criteria	0	1	2	3
Erythema	No erythema	Light red/pink	Red but not dark in colour	Very red, dark in colour
Exudates	No exudation	Light exudation	Moderate exudation	Heavy exudation with pseudo -membrane

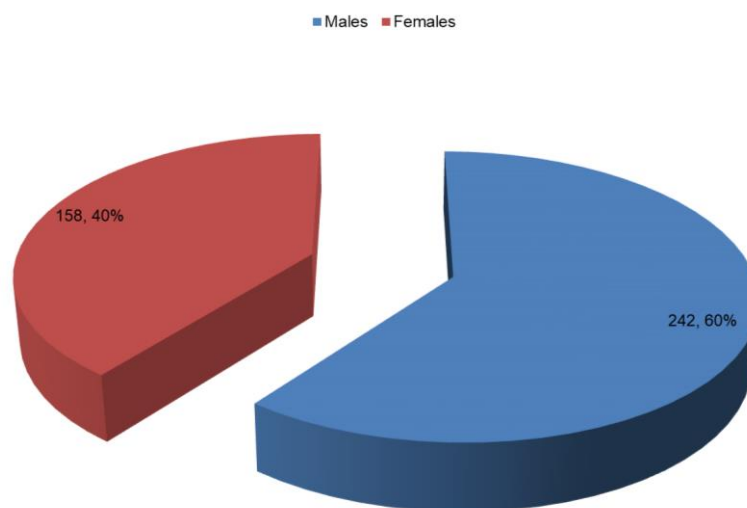
**Table 2 shows scale for erythema and exudates**

### Statistical method:

All randomized subjects were analyzed in terms of demographic and baseline characteristics. A P-value < 0.05 was taken to indicate statistical significant. A comparison between 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> visit was done by using Wilcoxon Signed Rank test.

### Results:

A total of 400 patients with minor recurrent aphthous stomatitis were enrolled in this study. They were randomly selected and patients were clinically evaluated and later compared the topical efficacy of 100% natural honey in the treatment of recurrent minor aphthous ulcers. The mean age of the subjects was about (26.18 ±5.172) 26 years, which may reflect the subject population mostly affected. The number of males (242) patients was dominated as compared to females (158) in the present study shown in Figure 2.



**Figure 2 shows Gender distribution**

The various parameters were recorded during the course of treatment. The number, size, pain, burning sensation, exudates, erythema and recurrence of the ulcer were evaluated.

### Reduction in number of ulcers:

In total of 400 patients, 93% of patients had solitary ulcers and 26% had multiple ulcers on the first visit. The number of ulcers reduced on the 2<sup>nd</sup> visit of the patient as 39% had solitary ulcers and even a single patient did not have multiple ulcers in the oral cavity. The highly significant difference was seen in the reduction in number of ulcer between 1<sup>st</sup> and 2<sup>nd</sup> visit which was on 3<sup>rd</sup> day and zero ulcers was seen on the 3<sup>rd</sup> visit shown in Tables 3 and Figure 3.

Number of Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value <sup>#</sup>
Solitary	374 (93.5%)	39 (9.8%)	39 (9.8%)	<0.001**
Multiple	26 (6.5%)	-	-	<0.001**
Zero	-	361 (90.3%)	361 (90.3%)	1.000 <sup>NS</sup>

**Table 3 shows reduction in number of ulcers with statistically significant P value**

### Reduction in ulcer size

On the first day, the size (mm) of the ulcer was recorded for all the patients. The application of honey was explained to the patient from the first day (3 times daily) and patient was recalled on 2<sup>nd</sup> and 3<sup>rd</sup> visit which was on 3<sup>rd</sup> and 6<sup>th</sup> day. The size of the ulcer was again recorded, the honey showed significant improvement between first and 2<sup>nd</sup> visit and a maintained greater effectiveness between 2<sup>nd</sup> and 3<sup>rd</sup> visit of treatment. The P value was less than 0.001, which was statically significant between the visits shown in Tables 4.

Size of Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value
1	137	13		.00
2	263	280	26	.00
3		107	16	.00
4			358	

**Table 4 shows reduction in size of ulcer with statistically significant P value**

### Reduction in Pain/Burning Sensation of Ulcer

The pain and burning sensation were recorded on the first, 2<sup>nd</sup> and 3<sup>rd</sup> visit by using VAS Scale, which starts from 0-10 (0-no pain and 10 severe pain). The highly significant reduction in pain and burning sensation was seen between first and 2<sup>nd</sup> visit and 3<sup>rd</sup> visit hardly patient experienced pain. The P value was <0.001, which is highly statically significant shown in Table 5.

Pain in Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value
1	269	20	19	.00
2	129	226	19	.00
3	2	153	27	.00
4		1	354	.00

**Table 5 shows Comparison of pain score between different visits.**

### Reduction in Erythema and Exudates in Ulcer

The erythema and exudates were also recorded on the first, 2<sup>nd</sup> and 3<sup>rd</sup> visit. Around 99% of patients had erythema on first, 2<sup>nd</sup> visit and 99% of patients had exudates on first visit and 1% on 2<sup>nd</sup> visit. The highly statistical significant difference was seen in the reduction of exudates. The highly significant reduction of erythema was seen on 3<sup>rd</sup> visit of patient and P value was <0.0001, which showed highly statistical significant value shown in Table 6 and 7.

Erythema In Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value
1	399	396	399	.00
2	1	4	1	.00
				.00

**Table 6 Comparison of the erythema levels between the different visits**

Exudates In Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value
1	398	3	1	.00
2	2	397	399	.00
				.00

**Table 7 Comparison of the exudation levels between the different visits**

### Recurrence in Ulcer

The recurrence of ulcer was followed up to 1 year. Only multiple ulcers have greater recurrence rate as compared to single ulcer patients. The highly statistically significant result was found shown in Table 8 i.e. there were less recurrence cases in present study.

Recurrence In Ulcer	1 <sup>st</sup> Visit	2 <sup>nd</sup> Visit	3 <sup>rd</sup> Visit	P Value
1	174	396	1	.00
2	225	4	160	
3	1		239	

**Table 8 Depicting decrease in recurrence of recurrent aphthous ulceration**

### Discussion:

Nature and natural products are a miracle gift to mankind from god. From several years these products have been used in folk medicine. *Apis mellifera* (*A. mellifera*) is one of the oldest traditional medicines considered important in the treatment of several human ailments. These products were not well-known for centuries and they came when people realized about the adverse effect of allopathy. They started to search new products with least or no harmful effect and this led to the rise of the alternative and complementary medicine. Among the natural medicated products, honey holds a composition that can help in treating grave disease. Honey and its products have been tried in diabetic foot to one of the most incurable malignancy like oral squamous cell carcinoma.<sup>8,9</sup>

Since ancient times, it is known that honey possess antimicrobial and wound-healing property. Due to its antibacterial activity, maintenance of moist wound condition and its high viscosity helps to provide a protective barrier and to check infections. Wound repair is also credited to its immunomodulatory effect. Honey also contains various enzymes which are responsible for production of hydrogen peroxide because of which it shows the property of antioxidants. Honey also shows hygroscopic property, which means that it can draw moisture out of the environment and dehydrate bacteria, and its high sugar content and low-level pH can also prevent the microbes.<sup>10</sup>

For treatment of RAU, topical medications have played a crucial role in reducing ulcer pain and accelerating ulcer healing. Natural honey has recently been found to have a significant role in management of minor aphthous ulcers.<sup>11, 12,13</sup> The present study aimed at evaluating the potential of this agent in reducing the size of the ulcer, pain, erythema and exudation. In the present study, the number of RAU in female patients dominated which is

consistent with the earlier studies. The most common site of occurrence was Labial mucosa followed by buccal mucosa and tip of the tongue. This is similar to studies done earlier. The common age of occurrence of RAU was in young adult and it is similar to that mentioned in literature. To study the effect of honey various parameters were considered. Starting with the size of ulcer which was measured with the help of William's probe on each visit showed considerable decrease in size on 2<sup>nd</sup> visit i.e: 3<sup>rd</sup> day with complete resolution of ulcer on 3<sup>rd</sup> visit i.e: 6<sup>th</sup> day was observed. This is consistent with the study done by Mohamed SS et al.<sup>14</sup> Another parameter for the research was pain score measured by VAS showed significant improvement in pain and burning sensation which is consistent with El-Haddad S A et al.<sup>15</sup> This indicates that honey has a significant therapeutic effect. Next parameter considered was erythema and exudation which also showed significant improvement which is similar to the observations of Samet et al. The recurrence of ulcer was significantly reduced as seen in Samet et al study.<sup>16</sup>

Nearly 100 % honey was well tolerated during the study period with negligible adverse effects. When administered for a period of 1 year whenever the ulcer developed, is not associated with any adverse effects. This shows a tremendous scope for further research for use of honey in management of an intractable condition like RAU.

In this study, we have demonstrated that honey reduces aphthous ulcer erythema and exudation, lesion size and pain with a good safety record. Furthermore, because honey is easy to use without any unfavorable taste and was easy for patients to carry, a large number of patients showed preference for it over other agents. The agent is easily available in market.

According to literature reviewed honey being nature's gift to human is still in its budding stage in India. Efficient collaborations with pharmacologists and medical doctors, pathologist's and microbiologists are crucial to see the complete development of interesting phenolic compounds into an exploitable product.

### **Conclusion:**

Honey being nature's gift to human can help in many fields of medicine. Honey as hygroscopic, anti-inflammatory, anti-bacterial and anti-oxidant agent is most appropriate topical agent. Honey is safe, effective, economical and easily available agent. Thus, the investigator concluded that the holistic and novel agent honey is of enormous help in the management of minor recurrent aphthous ulcer.

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