



## Review Article

# Topical Honey Application for Treatment of Herpes Labialis: A Review

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### ABSTRACT

**Introduction:** Cold sores – herpes labialis infects 90% of people worldwide, of whom only 30% will experience recurrent herpes labialis, which can last up to 10 days. The common treatment protocol for treating herpes labialis is antiviral drugs. Honey is readily available home remedy, herbal and biocompatible extract with antibacterial, antiviral & immune stimulatory effects. The present review is focussed to analyse the efficacy of topical application of honey in treating herpes labialis.

**Methods And Analysis:** The primary focus of the search was on randomised control trail of honey versus acyclovir in the treatment of herpes labialis. The randomised control trail, clinical trials without randomization and other experimental studies were considered.

**Discussion:** Honey is found to have antiviral properties, which is used in the treatment of herpes labialis. The component called NO (nitric oxide) has antiviral property. Reduction in signs and symptoms of herpetic lesions by honey application is due to inhibition of prostaglandin at lesion site.

**Conclusion:** It is concluded that the mean duration healing time of honey is little lesser than acyclovir with the time period of 3-4 days. Pain reduction is comparable with acyclovir and acceptability of honey is good.

**Key Words:** Herpes Labialis, Acyclovir, Honey.

## Introduction

Herpes labialis is also known as cold sores or fever blisters, primarily affects the lip, caused by herpes simplex virus 1 (HSV-1). HSV-1 belongs to herpeviridae family, contains 9 types of viruses that are harmful for humans (HSV-1, HSV-2, varicella zoster virus, cytomegalovirus, Epstein Barr virus, HHV-6, HHV-7, simian herpes virus B). Of all manifestation of herpes labialis, stage 3 and 4 blisters and ulcers are painful, which are going to produce more discomfort for the patient. The existing line of treatment for herpes includes pain control, supportive care & definitive treatment<sup>1</sup>. 2% viscous lidocaine, liquid diphenhydramine, 0.1% didonine hydrochloride, benxydaimine, analgesic is used for pain control. Hydration, ice chips or popsicles, soft bland diet, antipyretics as supportive care and Definitive treatment: antiviral medication like topical acyclovir 5% cream (6 times per day for 10 days), 3% pencicloyir cream, oral acyclovir tablet 400mg TDS-10 days, severe cases IV 5mg per kg infused over 1 hour kept for 8 hourly for 10 days. Valacyclovir prodrug of acyclovir has 3-5 times the bioavailability of acyclovir. Acyclovir inhibits viral replication and is activated by virally produce thymidine kinase<sup>1</sup>.

The adverse effects of antiviral drugs are tingling and burning sensation in each application. When orally taken

causes headache, nausea, malaise & CNS manifestation (tremors, lethargy, disorientation, hallucinations, convulsions & coma in higher doses). In IV line causes rashes, sweating, emesis and fall in Blood pressure. Ayurvedic products like honey, aloe Vera, curcumin (turmeric) were used for herpes labialis infection with less adverse effect<sup>1</sup>.

Honey is readily available home remedy, inexpensive, herbal and biocompatible with fewer side effects. Honey has antibacterial, antiviral and immune stimulatory effects. There are different types of honey with varying composition. The kanuka honey was brought into the eyes of the world with tremendous advantages. The present review has carried out to analyse the efficacy of topical application of honey in herpes labialis.<sup>2</sup>

## Materials And Methods

The following sources were searched from 2004 to 2017 PUBMED and Google database, to explore the role of honey in comparison of acyclovir in treating herpes labialis. The following key words were used herpes labialis, acyclovir and honey. The primary focus of the search was on randomised control trail of honey versus acyclovir in the treatment of herpes labialis. The randomised control trail, non-randomised clinical trials

without randomization and other experimental studies were considered. The outcome measures used were improvement in signs and symptoms of herpes labialis like pain, ulcer healing time.

## Discussion

Honey is the nectar collected by honey bees, is a sweet natural gift of nature<sup>4</sup>. It is used as food and medicine for treatment of various systemic diseases. Honey is found to have antiviral properties, which is used in the treatment of herpes labialis.<sup>5</sup> The component called NO (nitric oxide) has antiviral property against RNA and DNA of several viruses. Many drugs are available for treating herpes simplex virus, including foscavir, famciclovir, Valacyclovir and acyclovir<sup>1</sup>. Though topical acyclovir ointment has poor penetration, the intravenous and oral forms decrease both healing time and viral shedding<sup>1</sup>. In addition, acyclovir has been used to suppress recurrence of genital herpes. It has been known that acyclovir inhibits viral enzyme DNA polymerase. Though acyclovir is a safe drug, it may induce nephrotoxicity and neurotoxicity. Honey was used as an alternative treatment to manage recurrent episodes of herpetic lesions<sup>5</sup>.

## Honey And Its Types

Honey is comprised of water, sugar, amino acids, enzymes, Vitamins, minerals, flavonoids, phenolic acids, ascorbic acid, carotenoid-like substances, organic acids and several other compounds. D-fructose and D-glucose are the predominant sugars; sucrose occasionally exceeds 1 % of the total sugar content while maltose may be found at levels three times higher than that of sucrose<sup>4</sup>. The mineral fraction of honey is mainly composed of potassium and smaller amounts of magnesium, sodium, calcium, phosphorous, iron, manganese, cobalt and copper. Enzymes such as invertase, amylase, catalase and glucose oxidase are also present. Proline is the major amino acid constituent comprising about half the content of total free amino acids<sup>4</sup>. The beneficial role of honey is attributed to its antibacterial property with regards to its high osmolality, acidity (low pH) and content of hydrogen peroxide and non-peroxide components i.e., the presence of phytochemical components like methylglyoxal (MGO). Most types of honey generate Hydrogen peroxide, which thus attributes the antimicrobial activity. But the peroxide activity in honey can be destroyed easily by heat or the presence of catalase<sup>4</sup>.

Honey is collected from different geographical location has its own unique properties. Raw honey can be sourced from any plant, but it is unique in that it hasn't undergone any heat processing before it is sold, resulting in a 'raw' or uncooked product with bioactive

compounds. Kanuka honey is derived from the flower pollen of *kanzearicoides* is found along north and south island of New Zealand. The bee's native to the area where the kanuka trees flower help in extracting the nectar and producing the honey. The kanuka honey contains an ingredient called arabinogalactan protein (type 2) this component acts as antiviral, as they are present in the nectar of kanuka flowers.

Manuka honey is derived from plant *leptospermum scoparium*; these trees are found in New Zealand. The key ingredient of Manuka honey is methylglyoxal that gives antibacterial property; it is heat stable in order to express the total antibacterial property, it is given a score called unique Manuka factor (UMF) score to indicate its antibacterial potency.

Recently it was identified as nitric oxide (NO) metabolites, nitrite and nitrate in various honeys. It is known that NO is an important active molecule that plays a role in host defence against bacteria, protozoa and tumour cells. NO has antiviral effects against DNA and RNA of several viruses. NO may inhibit herpes simplex virus ocular lesion<sup>5</sup>. Prostaglandin is the immune mediators for simulating recurrent herpes labialis. It involves HSV- 1&2 infections by suppressing the T- Cell function allowing for clinical recurrence. Prostaglandin increases adhesion between cells infected with herpes cells and uninfected cells<sup>5</sup>. They are potent immune suppressive agents lower in antibody titre in thymus dependent and thymus independent during primary & secondary immune responses. Prostaglandins are mediators for pain and inflammation. Honey lowers prostaglandin concentration in various biological fluids such as plasma and urine<sup>5</sup>. Therefore reduction in signs and symptoms of herpetic lesions by honey application is due to inhibition of prostaglandin at lesion site<sup>5</sup>.

Two randomized clinical trial and one non randomized clinical trial estimated the efficacy of honey in recurrent herpes labialis. Two randomized control trail compared 5% acyclovir and honey, primary outcome is healing time and secondary outcome is pain acceptability of the intervention. The mean duration of healing of acyclovir is 5 days and honey is little lesser than acyclovir with the time period of 3 – 4 days. Pain reduction is comparable with acyclovir and acceptability of honey is good with visual mean analogue scale score of 81.9<sup>2</sup>.

Duration of pain, occurrence of crust and mean healing time with honey treatment were better than with acyclovir. Symptoms of pain tingling and burning were reduced and resolved completely within 24 hrs. With the use of acyclovir, no pain relief was seen in first 24 hrs.

No side effects were encountered with repeated application of honey, and the patients reported greater satisfaction with honey application than with acyclovir treatment<sup>4</sup>.

### Antimicrobial Activity

The enzymatic glucose oxidation reaction and its physical properties play important factors in antimicrobial activity. Other factors include high osmotic pressure, low pH (acidic environment), low protein content, high carbon to nitrogen ratio and low redox potential due to the high content of reducing sugars.

Honey is a supersaturated sugar solution which has low water activity to support the growth of bacteria and yeast. The natural acidity pH of honey will inhibit many pathogens. The minimum pH value for some infected wounds ranges from 4.0 - 4.5. Glucose oxidase is an enzyme secreted by the bees, which converts glucose in the presence of water and oxygen to gluconic acid and hydrogen peroxide. The resulting acidity and hydrogen peroxide preserve and sterilize the honey.

Transition ions and ascorbic acids rapidly decompose hydrogen peroxide to oxygen and water. Dilution of honey results in a 2,500 - 50,000 increase in enzyme activity, not all honey are created equal in antimicrobial activity due to differences in levels of peroxide and non-peroxide production<sup>4</sup>.

### Antibacterial Activity

The antibacterial activity of honey is associated with the release of hydrogen peroxide, from oxidation of glucose to glucolactone and then to gluconic acid in presence of the enzyme glucose oxidase. Manuka honey which has been demonstrated to be effective against several human pathogens like *E. coli*, Methicillin resistant staphylococcus aureus, beta haemolytic streptococci and enterococci<sup>4</sup>.

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### Antiviral Activity

The antiviral property of honey is exerted by flavonoids such as chrysin which has inhibitory effects against HSV-1. Apigenin is an antiviral substance against HSV-2. Experiments performed on monkey kidney cell culture infected with the rubella virus shows anti-rubella activity. Important flavonoids of honey such as chrysin, acacetin and Apigenin can even inhibit the human immunodeficiency virus (HIV-1) activation via inhibition of viral transcription<sup>4</sup>.

### Conclusion

Based on the search undertaken from different resources we conclude that the mean duration healing time of acyclovir is 5 days and honey is little lesser than acyclovir with the time period of 3 - 4 days. Pain reduction is comparable with acyclovir and acceptability of honey is good. Further Randomised clinical control trials study with large sample may strongly support the efficacy of honey in treating Herpes labialis.

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