



International Journal of Indian Medicine

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International Journal of Indian Medicine

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Systemic review of Yashtimadhu (*Glycyrrhiza glabra* Linn); A potent Ayurvedic herb against Covid-19 pandemic.

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Abstract:

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. COVID-19 pandemic is the defining global health crisis of our time and the greatest challenge we have faced till date. Ayurveda is a science of life main focus of Ayurveda to cure the disease root cause and maintain the health of healthy individuals. Yashtimadhu (*Glycyrrhiza glabra*), also known as liquorice and sweet wood, liquorice has been described as 'the grandfather of herbs'. which is a natural herb for cough and has expectorant properties. It can also reduce infection of the upper respiratory tract. Yashtimadhu or liquorice has been included in Indian pharmacopeia as well as in literatures of many other ancient civilizations namely Greek, Roman, Egyptian and Chinese. In Ayurveda Yashtimadhu is one of the important plant which is been referred in many texts with many therapeutically uses. Glycyrrhizin does not allow the virus cell binding. Thus, it is found to have a prominent antiviral activity. Recent researches suggest that liquorice can be used to neutralize the activeness of COVID-19 and it can be used as an antiviral drug.

Keywords: Yashtimadhu, *Glycyrrhiza glabra*, COVID-19, SARS-CoV-2

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How to cite this article: Gulhane CM, Agarkar Deepali, Thakar AB. Systemic review of Yashtimadhu (*Glycyrrhiza glabra* Linn); A potent Ayurvedic herb against Covid-19 pandemic ?. Int. J Ind. Med. 2020;1(1):20-26.

Introduction:

The SARS-CoV-2 belongs to the largest family of the RNA viruses and its genome ranges from 27 to 32 kilobases in size (~125 nm or 0.125 µm).^[1] The virus that causes SARS-CoV-2 is mainly transmitted through droplets generated when an infected person coughs, sneezes, or exhales. These droplets are too heavy to hang in the air, and quickly fall on floors or surfaces.^[2] Human pathogenic SARS-CoV-2 bind to their target cells through angiotensin-converting enzyme 2 (ACE2), which is recognized by epithelial cells of the lung, intestine, kidney and blood vessels. The general symptoms observed in the infected individuals are fever, cough, dyspnoea and lesion in the Lungs. In the advanced stage, the symptoms of this virus show pneumonia which progresses to severe pneumonia and acute respiratory distress syndrome (ARDS) which results in to the need for life-support to sustain the patient's life.^[3] Liquorice (Yastimadhu) is one of the most popular medicinal herbs in India and also in abroad. The root of *Glycyrrhiza glabra* (liquorice) contains a substance called glycyrrhizin which is 50 times sweeter than sugar. In Indian medicinal system first *Yashtimadhu* is mentioned as 'Madugha' in Atharvaveda,^[4] in charaka samhita *Klitaka* (*Yashtimadhu*) has been mentioned as being of two types viz. *Anupa* and *Sthalaja*.^[5] Dhanvantari nighantu, the first among the Nighantus has dealt *Yashtimadhu* and *Klitana* separately in which *Klitana* is stated to be 'Tallakshanam' i.e. possessing the same properties as that of *Yashtimadhu*. *Yashtimadhu* itself is divided as *Sthalaja* and *Jalaja* and to the latter synonyms, *Madhuparni* and *Madhulika*. *Klitana* is different from *Yashtimadhu* but resembles it closely in qualities and properties. *Sthalaja* and *Jalaja* are the two varieties of *Yashtimadhu*. Both types are *Madhura*, *Shitala* and acts as *Pittashamaka*.^[6] It has Antacid, Anti-ulcerogenic, Anti-inflammatory, Anti-oxidant, Anti-angiogenic (in cancer or Tumors), Anti-proliferative (in cancer

or Tumors), Anti-asthmatic, Antibacterial, Antiviral, Analgesic, Anti-arthritic, Antitussive, Aphrodisiac, Expectorant and Immuno-modulator properties.^[7] In some studies it shows that licorice root extract is effect against HIV, RSB, herpes viruses and severe acute respiratory syndrome-related corona virus which causes a serious type of pneumonia.^[8]

Aim and objective:

1. To review the *Yashtimadhu* in literature
2. To review the Anti SARS-COV effect of *Yashtimadhu* and its active components.

Review of Yastimadhu**Nirukti^[9]**

1. *Klitaka*- It cures male infertility.
2. *Madhuka*- It is sweet like honey.
3. *Yashtimadhu*- It is sweet like honey.

Botanical name: *Glycyrrhiza glabra* Linn.

- Glycyrrhiza - Glykas = Sweet
- Rhiza = Root
- Glabra - Smooth and hairless

Natural order: Leguminosae

Leguminosae - Legume = pulse pod

Classical names: *Madhuka*, *Yashtimadhu*, *Madhulika*, *Yasthahya*, *Madhu*, *Klitaka*, *Klitana*, *Yasthi*.

Plant Description

- Type of Plant- Herbaceous Perennial Plant
- Native Range- India, Asia, Southern Europe
- Height (grows up to)-Grows up to 1 meter in height
- Habitat (type of environment)- Dry, hot and sunny climates with low annual rainfall are best for liquorice growth. However, adequate soil moisture is also necessary for its growth.
- Roots- Stolonerous
- Leaves- Pinnate leaves (70 to 150 mm long) bearing 9–17 leaflets
- Flowers- Purple to pale whitish blue (8 to 12 mm long)

- Fruits- Oblong pod (20 to 30 mm)
- Seeds- Fruits contains several seeds

Rasapanchaka (properties)^[10]

- Rasa** (Taste)- *Madhura* (Sweet)
- Guna** (Characteristics)- Heavy and slightly oily.
- Veerya** (Potency)- *Sheeta* (cold)
- Vipaka** (Post digestion effect)- *Madhura* (Sweet)
- Actions on Doshas** - Reduces *Vata* and *Pitta*, may increase *Kapha*.
- Parts Used** : Roots

Indications

- *Aamvatahara* (Aamvatahara)
- *Amlapittahara* (Hyperacidity)
- *Arshogna* (haemorrhoids)
- *Ashmarihara* (Urinary calculi)
- *Kasahara* (reduce cough)
- *Kshatahara* (heal wound)
- *Kshayahara* (Anti TB)
- *Raktapittahara* (Raktapittahara)
- *Sirorogahara* (head diseases)
- *Shwasahara* (Anti asthmatic) etc.

Therapeutic uses^[11]

- Piles:** After application of *Kshara*, *Ghrita* mixed with *Yashtimadhu* should be applied on haemorrhoides.

- Consumption:** In case of pain in head, sides and shoulders the parts should be sprinkled with milk and decoction of *Madhuka*.
- Hoarseness of voice:** *Payasa* (rice-milk) prepared with *Yashtimadhu* and mixed with *Ghrita* should be taken.
- Hiccough:** Pressed snuff should be used of *Madhuka* mixed with honey or *Pippali* mixed with fine sugar.
- Thirst:** Thirsted caused by wasting is quenched with *Ghrita* extracted from milk meat-soup or decoction of *Madhuka*.
- Retention of urine:** *Madhuka*, *Darvi* and seeds of *Ervaru* should be taken with rice water.
- Accidental wound:** Pain of the accidental wound is removed by applying locally warm *Ghrita* mixed with *Yashtimadhu*

Chemical constituents: chemical analysis of the *G. glabra* extracts revealed the presence of several organic acids, liquiritin, rhamnoliquiritin, liquiritigenin, prenyllicoflavone A, glucoliquiritin apioside, 1-methoxyxyphaseolin, shinpterocarpin, shinflavanone, licopyranocoumarin, glisoflavone, licoaryl coumarin, glycyrrhizin, isoangustone A, semilicoisoflavone B, licoriphenone, and 1-methoxyficifolinol, kanzonol R and several volatile components.^[12]

Table no. 1 Pharmacological properties of *Glycyrrhiza glabra*. (*Yashtimadhu*)

Sr.no.	Activities	Research title
1.	The choloretic effects ^[13]	The choloretic effects of licorice: identification and Determination of the pharmacologically active components of <i>Glycyrrhiza glabra</i> .
2.	Anti-ulcer and antioxidant activity ^[14]	Anti-ulcer and antioxidant activity of GutGard.
3.	WoundHealing activity ^[15]	Glycyrrhizic Acid Ammonium Salt in Rats
4.	Wound Healing activity ^[16]	Evaluation of <i>Glycyrrhiza glabra</i> (Licorice) on wound healing in Rats

5.	Wound Healing activity ^[17]	Healing potential of liquorice root extract on dermal wounds in Rats
6.	Antiulcerogenic and toxicological studies ^[18]	Antiulcerogenic and Toxicological Studies of <i>Glycyrrhiza glabra</i> Roots Available in Local Market of Karachi.
7.	Anti-Helicobacter pylori activity ^[19]	In vitro anti-Helicobacter pylori activity of a flavonoid rich extract of <i>Glycyrrhiza glabra</i> and its probable mechanisms of action.
8.	Anti-Staphylococcal and wound healing activities ^[20]	Anti-Staphylococcal and wound healing activities of <i>Ganoderma praelongum</i> and <i>Glycyrrhiza glabra</i> formulation in mice.
9.	Alleviates symptoms of functional dyspepsia ^[21]	An extract of <i>Glycyrrhiza glabra</i> (GutGard) alleviates symptoms of functional Dyspepsia: A Randomized, Double-Blind, Placebo-Controlled Study.
10.	Healing effect ^[22]	The healing effect of licorice (<i>Glycyrrhiza glabra</i>) on Helicobacter pylori infected peptic ulcers

Antiviral activity of Yashtimadhu

In vitro studies revealed antiviral activity against HIV-1, SARS related coronavirus, respiratory syncytial virus, arboviruses, vaccinia virus and vesicular stomatitis virus. **Mechanisms** for antiviral activity of *Glycyrrhiza* spp. include.^[23]

1. Reduced transport to the membrane and sialylation of hepatitis B virus surface antigen,
2. Reduction of membrane fluidity leading to inhibition of fusion of the viral membrane of HIV-1 with the cell,
3. Induction of interferon gamma in T-cells,
4. Inhibition of phosphorylating enzymes in vesicular stomatitis virus infection and reduction of viral latency.
5. Glycyrrhizin inhibits SARS-associated coronavirus (SARS-CoV) replication in Vero cells with a selectivity index of 67. In addition to inhibition of virus replication, glycyrrhizin is able to inhibit adsorption and penetration of the virus during the early steps of the replicative cycle.^[24] Study also show that glycyrrhizin induces nitrous oxide synthase in Vero cells and that virus replication is inhibited when a nitrous oxide donor (DETA Nonoate) is added to the culture medium

Adverse effect: Reported adverse effects of glycyrrhizin include aldosterone-like effects (pseudohyperaldosteronism), which are related to its inhibition of conversion of cortisol to cortisone. This has been associated with hypokalemia, hypertension, decreased plasma renin and aldosterone levels, myopathies, oedema and/or muscle weakness in people taking excessive amounts of glycyrrhizin containing products.^[25]

Discussion

Researches shows that glycyrrhizin, a major active constituent liquorice root which is the most frequently used Chinese herb, potently inhibited the replication of clinical isolates of SARS virus.^[26] Thus glycyrrhizin was found to have bioactivity in inhibiting the replication, absorption and penetration of SARS-CoV. In some studies shows glycyrrhizin could interact with ACE2, Therefore, these compounds as well as herbs containing these ingredients may have the capacity to inhibit the infection of SARS-CoV-2.^[27] COVID-19 is a RNA based infected virus, which is formed by nucleocapsid protein (N-protein), spike protein (S-protein), (E) the envelope protein, (M) the membrane protein. The nucleocapsid protein (N-protein) is a structural protein that binds to the coronavirus

RNA genome, thus creating a shell (or capsid) around the enclosed nucleic acid. These most of the proteins of COVID 19 are formed by the amine(-NH₂) and carboxyl (-COOH) functional groups. Some chemical reaction oriented strategies are developed to neutralize the effect of amine(-NH₂) and carboxyl (-COOH) functional groups to protect the adverse effect of corona virus on human body. This investigation reveals that the extracted components of natural plants, especially hydroxyl (OH) groups react chemically to deactivate the active components of the virus by esterification process.^[28] In case study licorice was selected as a sample to neutralize the activity of virus proteins.^[29] In vitro studies proved that *Glycyrrhiza glabra* at 100µg/ml concentration, showed immunostimulatory effects. It increases production of TCD69 lymphocytes and macrophages from human granulocytes.^[30] *Glycyrrhiza glabra* has been reported to display an anti-inflammatory activity similar to a steroid hormone (hydrocortisone) by inhibiting phospholipase A2 enzyme activity, which is crucial for various inflammatory processes. Moreover, an in vitro study demonstrated that glycyrrhizic acid suppresses the activity of cyclooxygenase and the formation of prostaglandin E2, preventing platelet aggregation indirectly.^[31]

Conclusion

Yashtimadhu Glycyrrhiza glabra have been evaluated number of times for different pharmacological activities. glycyrrhizin was the most efficient in controlling viral replication. Thus, it can be a good prophylactic measure. The mechanism of glycyrrhizin's activity against SARS-CV is unclear, But Glycyrrhizin are affects cellular signalling pathways such as protein kinase C; casein kinase II and transcription factors such as activator protein. It also regulates the synthesis of nitrous oxide synthase and help in the production

of nitrous oxide, Nitrous oxide inhibits the replication of several viruses.

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Financial support and sponsorship

Nil.

Conflicts of interest

Nil.