

# Ethnopharmacological study about *Glycyrrhiza glabra* L. (Licorice) based on Ayurveda, An Indian System of Traditional Medicine- A Review

**Review Article** 

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# **Abstract**

Glycyrrhiza glabra L. (GG), also known as Yashtimadhu, is a traditional plant which is widely used in Ayurveda. It is used to treat a variety of ailments including cough, asthma, bronchitis, diabetes, gastric ulcers, skin problems, inflammation, anaemia, premature greying of hair and others. Clinical and experimental research suggests that it possesses anti-inflammatory, antiviral, immunomodulatory, hepatoprotective, antimicrobial, antioxidant, anticancer, and cardioprotective activities. We gathered material on the phytochemistry, pharmacology, and toxicity of Glycyrrhiza glabra published before March 2022 from PubMed, Springer, SCOPUS, Google Scholar and Science Direct. To compile this study, we conducted a thorough analysis of the classical Ayurvedic treatises in order to obtain a full account of the qualities, actions, and applications stated in Ayurveda about yashtimadhu in order to demonstrate ancient-modern concordance. GG has been studied for a variety of pharmacological properties, including ulcer healing, anti-ulcerogenic, anti-bacterial, antioxidant potential activity, anti-asthmatic activity, hair growth stimulating activity, and memory enhancing action. Licorice in Ayurveda is generally used in Ayurveda as a rejuvenator and aphrodisiac, as well as for boosting memory, complexion, sound quality, dental health, vision, lactation, and healing cancer, ulcers and wounds. Even though GG is a widely used Ayurveda medicine, there is a lack of evidence regarding the true medicinal potential of the drug. There are innumerable actions mentioned in the Ayurveda classical textbooks. Here, an effort is made to find substantiation for the ancient wisdom through a thorough search with the modern available literature.

**Key Words:** Ayurveda, *Glycyrrhiza glabra*, *Licorice*, *Madhuka*, *Yashti*, *Yashtimadhu*.

# Introduction

Nature has bestowed upon us a diverse botanical life and a vast array of plant species cultivated in various regions of the globe. Plants are the foundation of a complicated traditional medical system. Ayurveda is one of the ancient life sciences practiced in India. In the ayurvedic healing process, plant-based remedies play a significant role. There is no material on the planet that cannot be employed as a potential medication, in broad words (1). Plant-based ayurvedic remedies account for around 90% of the total traditional medicine. Food and spices have a less effect on the body than Ayurvedic botanicals. As a result of these activities, the plant is able to reverse pathophysiological processes (1).

Glycyrrhiza glabra L. (GG) known as yashtimadhu according to Ayurveda is one of the most commonly used traditional drugs in Ayurveda which is

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having a rich medicinal potential (2). In Vedic literature and Samhita, it has been used to treat a variety of ailments. More than 1250 formulations containing *Licorice* are mentioned in the ancient Ayurvedic system. In 50 mahakashyas (group of 10 drugs for specific disease) told by Charaka, GG is one of the most repeated drugs which reflects its wide-scale application in Ayurveda (3). The *Glycyrrhiza* genus has more than 30 species that are found all over the world. Its name comes from the Greek words glykys, which means sweet, and *rhiza*, which means root (4). Similarly, in Ayurveda literature yashtimadhu has a synonym called madhuka which means having a sweet taste (madhura rasa). Licorice has been utilized in traditional Chinese medicine for about 4000 years. The oldest mention of it medicine may be found in the 'code Humnubari' (2100 BC). It was also described in Assyrian herbals as one of the most essential herbs (2000 BC). Hippocrates (400 BC) suggested it as a treatment for ulcers and thirst quenching. Theophrastus and Dioscorides both referenced the medication. Licorice is used as a demulcent, expectorant, anti-tussive, laxative, and sweetener in traditional Siddha medicine (2).

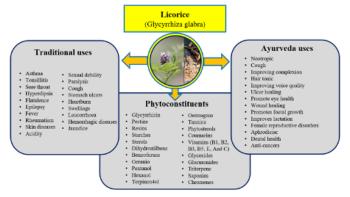
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The Ayurvedic potential of this drug is still unknown to the best of knowledge, just a few evaluations on this plant have been published, particularly in terms of its Ayurvedic value. The goal of



this review was to look at the Ayurvedic literature as well as current scientific information on GG to see whether there was any ancient-modern concordance.

Picture 1. Phytochemicals, Traditional and Ayurveda uses of Licorice



# Materials and methods

A thorough review of the current available Ayurveda classical literature was performed along with the published literature using scientific search engines like PubMed, Springer, SCOPUS, Google Scholar and Science Direct. The following keywords were used to search the literature including "Glycyrrhiza glabra", "Yashtimadhu", "Madhuka", "Glycyrrhiza glabra AND Ayurveda, "yashtimadhu AND Ayurveda", "botany of Glycyrrhiza glabra", "pharmacological activity of Glycyrrhiza glabra", "biological activity of Glycyrrhiza glabra", "traditional uses of Glycyrrhiza glabra". 'toxicology of *Glycyrrhiza glabra*", "Traditional uses of Glycyrrhiza glabra", and "Traditional uses of Yashtimadhu". The plant name, Glycyrrhiza glabra L. corresponds to the latest revision in "The Plant list" and checked in the website (http://www.theplantlist.org/tpl/ search?q=glycyrrhiza+glabra& csv=on).

# Literature review Traditional uses

Egyptian, Chinese, Greek, Indian, and Roman civilizations employed the dried rhizome and root as expectorants and carminatives. Licorice has been used in Chinese medicine since 2800 B.C. It was regarded as a form of classical medicine in Tibet. The Egyptian pharaoh Tutanchamon (1350 B.C.) extolled the therapeutic potential of licorice roots in his tomb (5). Asthma, tonsillitis, sore throat, hyperdipsia, flatulence, epilepsy, fever, sexual debility, paralysis, coughs, stomach ulcers, heartburn, colic, swellings, rheumatism, skin diseases, acidity, leucorrhea, bleeding, hemorrhagic diseases, and jaundice have all been reported to be treated with licorice traditionally in the past (4).In Ayurveda water infusion of powder of GG is used to induce vomiting while doing the emesis procedure (Vamana- one among the panchakarma (Purification of body)). Glycyrrhiza combined with butter is applied in burns and wounds, Glycyrrhiza mixed with cow's milk is used to increase lactation, Glycyrrhiza blended root is used as a wash for greying of hair, and Glycyrrhiza decoction is useful for erysipelas (6). For hoarseness of

voice, a solution of rice milk produced with *Glycyrrhiza* is used; for oedema, a paste of *Licorice*, milk, and *Sesamum indicum* combined with butter is used (6). Traditionally oil of *Licorice* is used as a nasal drop to reduce hair fall and baldness. It also reduces heartburn and acidity. It is used in anaemia along with honey, along with cow's milk to promote lactation, *Santalum album* (Chandana) and milk for hematemesis (7). In Pakistan, licorice root paste mixed with flour and oil is fed to cows, goats, buffaloes, and sheep to boost milk production and fertility (8). GG root sap is used in the manufacture of wine in Turkey's middle region (9).

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In Italy, a decoction of the root is used as a mild laxative (10), while in Nepal, juice from the root and stem is used as a stimulator, astringent, and tonic (11). In Egypt, it is combined with tea to treat a sore throat (12). Licorice was utilized as a flavoring ingredient in the tobacco and confectionery businesses, as well as in the pharmaceutical and beverage sectors to some extent (5). When fresh licorice root is cleaned, it has a vivid yellowish-brown colour on the outside and is eaten fresh or dried as a mouth refresher, teething aid, and tooth cleanser (13). Brewers utilize licorice root to flavour and colour porter beers, and the enzymes in the root also help to maintain the foam heads created by these beers. Licorice powder is used in sweets, baked goods, ice cream, soft drinks, and various herbal beverages, while the powdered root is also used as a sweetener (14).

# **Phytoconstituents**

Licorice contains proteins, amino acids, polysaccharides and simple sugars, mineral salts (such as calcium, phosphorus, sodium, potassium, iron, magnesium, silicon, selenium, manganese, zinc, and copper), pectins, resins, starches, sterols, and gums (15). Also, there have been reports of estrogens, tannins, phytosterols (sitosterol and stigmasterol), coumarins, vitamins (B1, B2, B3, B5, E, and C), and glycosides (15). The saponins in licorice are found as glucuronides, while the aglycones are found as oleananes. The sweet flavour of licorice is due to the triterpene saponins, which are the most prominent components. Due to regional origins, harvesting, and processing, the quantities of these components might vary greatly, altering the medicinal benefits of licorice (16). The chief active element present in roots is glycyrrhizin, a triterpenoid saponin that is approximately 50 times sweeter than sucrose (16). Glycyrrhizin, a combination of potassium, calcium, and the magnesium salts of glycyrrhizic acid that ranges from 2% to 25%, accounts for around 10% of the dry weight of the licorice root. Glycyrrhizin is degraded by intestinal bacteria into 18glycyrrhetic acid 3 omonoglucuronide and glycyrrhizic acid after oral administration (17). The flavonoid component of licorice gives it its yellow colour. Flavanones, flavanonols, chalcones, isoflavans, isoflavavenes, isoflavavones, and isoflavanones are some of the flavonoid's classes discovered. Liquiritigenin (4',7' dihydroxyflavanone) and isoliquiritigenin (2',4,4' trihydroxychalcone) glycosides, such as liquiritin,



isoliquiritin, liquiritin apioside, and licuraside, are the most important flavonoids present in it (18) Isoprenoid-substituted flavonoids, chromenes, coumarins, dihydrostilbenes, coumestans, benzofurans, and dihydrophenanthrenes are minor phenolic compounds. Furthermore, several volatile components, including geraniol, pentanol, hexanol, terpinen4ol, and terpineol, are present in roots, imparting the distinctive odour. Propionic acid, benzoic acid, furfuraldehyde, 2,3 butanediol, furfuryl formate, maltol, 1methyl2formylpyrrole, and trimethylpyrazine are all present in GG essential oil (19).

# Ayurvedic literature of *Glycyrrhiza glabra* Synonyms

There are 22 synonyms of *Licorice* mentioned in ayurvedic literature. Of these *Yashtimadhu, madhuka, yashti, madhuyashti* are commonly mentioned in almost all Ayurvedic works of literature. Synonyms like *Madhuka, Madhuyeshti, madhralata, madhuvalli, madhusrava* are due to their sweet root and stem. *Klitaka* and *klitanaka* synonyms denote the plant found terrestrial. *Vanaprastha, Madhava, Lodrapushpa, Golaphala, Dolaphala, Tiksnasara* explains the morphology (20).

# Morphology

According to Ayurveda, there are two types of Licorice they are sthalaja and jalaja. Sthalaja variety originates inland while Jalaja originates in water and is rare (21) According to the source it has been divided into three types Mishri, Arabi and Turki based on the location they are obtained from like Baluchistan, Arab countries and Turkey respectively. According to Unani it is three types they are Misheya, Arabiya, Turkiya and their sweetness decreases successively (21) Ayurvedic literature explains morphology with its synonyms to some extent. Rajanigandu the ancient ayurvedic literature describe the seven factors by which one can nomenclate the drug. They are Rudhi (specific term), Prabhava (natural power), Desokti (place of origin), Lanchana(special characters), upama (simile), Virya (potency), *Itarahwaya* (Miscellaneous). The synonyms like Vanaprastha (grows wildly), Madhava (blossoms in spring), Lodrapushpa (flowers are cream coloured like those lodra (symplocos racemosa)), golaphala (having round fruits), Dolaphala (fruits hanging in branches), Tiksnasara (having sharp kernel). This reflects the indepth knowledge regarding the plant in Ayurveda classics.

GG is an herbaceous perennial that grows to a height of 1 m and has pinnate leaves that are 7 to 15 cm long. The flowers range in colour from purple to pale white blue and are grouped in a hermaphrodite inflorescence, while the fruits are an oblong legume that is 2 to 3 cm in length and contains multiple seeds (16).

Glycyrrhiza (Fabaceae) has roughly 30 species, including *Glycyrrhiza glabra* L., *Glycyrrhiza uralensis* Fisch., *Glycyrrhiza inflata* Batalin., *Glycyrrhiza aspera* Pall., *Glycyrrhiza korshinskyi* Grig., *and Glycyrrhiza eurycarpa* P.C.Li., *GG*, like other Fabaceae plants, can fix nitrogen at the root level through symbiotic

association with bacteria of the genus Rhizobium, making it suited for sandy and clay soils, however, it prefers wet soils (22).

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#### Ayurveda classification based on action (Vargas)

In Ayurveda, Drugs are categorized into different Vargas (groups) based on the similarity in pharmacological action. In Ayurveda GG is categorized under 11 categories as per Charaka they are jeevaneeya (promotes longevity), sandhaneeya (helps in healing of fractures), varnya (Improves complexion), kanthya (improves voice), Kandughna (relieves itching), chardinigraha (relieves vomiting), shonithasthapana (checks bleeding), mutraviranjaneeya (restores the proper colour of urine), snehopanga (herbs used in oleation therapy), vamanopanga (herbs used in emesis therapy) and asthapanopanga (herbs used in enema therapy) (23). Susrutha categorized GG under Sarivadigana (group of drugs that relieves thirst), Anjanadigana (drugs that can be used as collyrium), Ambashthadigana (promotes healing of ulcers and fractures), Nyagrodhadigana (beneficial for the female reproductive system), Utpaladigana (cures vomiting )groups (24). Vagbhata included it in Sarivadi, Anjanadi gunas which have the same therapeutic action mentioned by Sushruta. More than 1250 Ayurvedic medicines with Licorice as one of their ingredients are mentioned in the ancient Ayurvedic system.

#### Licorice as a rejuvenator (rasayana)

Rasayana is a concept based on the use of herbs as a preventative measure against different illnesses and disorders (25). The term rasayana (rasa + ayana) refers to obtaining sustenance in order to build the best attributes of dhatus, or bodily cells and tissues, which results with a variety of advantages, including longevity, memory, intellect, disease-free living, youth, beauty, complexion, and voice, optimal strength of the body and sense organs, respectability, and brightness (26). As a result, rasayana treatment offers a broad scope for favorable nutrition, immunoenhancement, lifespan, and mental and sensory competence maintenance (27).

GG is one among the potent *rasayana* drug told in Ayurveda which is most commonly used in practice (28). GG is a low-cost, easily accessible herb with excellent immunomodulator effects (29). It is one among the component of some important and commonly used formulations like *Amruthaprasham*, *Brahma rasayana*, *Amalakyadi ghritha* (28).

GG along with Acorus calamus is told as a Kanthya rasayana ie Rasayanas which promote throat health and is good for speech (27). It is widely used as a nutraceutical herb for the sake of gastrointestinal health, soothens and regulates the mucous membranes and reduces muscular spasms (30).

Amalakyadi Ghritha having GG as potent ingredient was studied for its hepatoprotective impact against carbon tetrachloride-induced liver damage in rats. The study found that oral administration of the Amalakyadi Ghritha reduced the levels of marker



enzymes SGPT, SGOT, ACP, and ALP significantly and reduced bilirubin levels in the blood (31).

In an animal study to assess the protective effects of rasayanas on cyclophosphamide and radiation-induced damage, researchers used four rasayanas: Brahma Rasayana, Narasimha Rasayana, Amruthaprasham, and Ashwaganda Rasayana, and discovered that only Brahma Rasayana and Amruthaprasham were found to induce bone marrow cell proliferation in animals. Only Brahma Rasayana and Amruthaprasham were proven to be useful as myeloprotective drugs against chemotherapy and radiation in trials. They also aided in the quick recovery from toxic treatment-induced immunosuppression (32).

Atherosclerosis is a vascular disease marked by a localized thickening of the artery wall in the inner layer (Tunica intima). ROS/RNS are now widely thought to have a role in the start and progression of atherosclerosis. Oxidants are thought to perform a number of functions in the development of atherosclerosis (33). In atherosclerotic apolipoprotein E defective mice, the impact of glabridin, an isoflavan derived from GG roots, on the susceptibility of low-density lipoprotein to the oxidation were only mild (34).

GG contains seven antioxidant compounds, including the isoflavans hispaglabridin A, hispaglabridin B, glabridin, and 4 -O-methylglabridin, the two chalcones isoprenylchalcone derivative as well as isoliquiritigenin, and the isoflavone, formononetin (35).

#### Licorice as a nootropic drug (medhya rasayana)

The term 'Medhya Rasayana' is derived from the Sanskrit words 'medhya', which means intelligence or intellect, and 'Rasayana' which means rejuvenation. Medhya Rasayanas are a class of medicinal plants listed in Ayurveda for improving memory and intelligence (specific action) (36). In order to achieve the medhya effect, various dosage forms like powder, swarasa (extracted juice), paste, and powder along with milk are advised. For getting Medhya effect, fine powder of dried root of licorice is to be taken internally with milk (37). GG powder is combined with honey and consumed with milk acts as aphrodisiac and intellect promoter (7).

In a study conducted in school going children *Licorice* granules is shown to be improving the IQ of students due to Glycyrrhizin which is responsible for improving glucose bioavailability in the brain and, as a result, Increasing the brain's activity. The flavonoids present in *Licorice* by its antioxidant effect prevent oxidative damage in the brain thereby improves brain function (38).

It was discovered that Oral licorice eating twice a day might boost a student's performance.IQ level as compared to placebo therapy with minimal negative effects (39). In both exteroceptive and interoceptive behavioural memory models in mice, licorice has shown potential as a memory enhancer. this may be due to improving acetylcholine levels in the brain and also by mediating gamma-aminobutyric acid (GABA) (40).

Glycyrrhizin found in licorice has shown to have neuroprotective action on kainic acid-injected mouse brain might be attributable to the inhibitions of HMGB1 induction and release, which in turn, mitigates the inflammatory process (41). Glycyrrhizin has neuroprotective properties in the postischemic rat brain after blockage of the middle cerebral artery (MCAO). This mechanism has anti-inflammatory, anti-excitotoxic, and anti-oxidative properties, and it has an anti-inflammatory effect in particular (42).

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GG's 2,2',4'-trihydroxychalcone is a novel selective beta-site amyloid precursor protein (APP)-cleaving enzyme 1 (BACE1) inhibitor that effectively improves memory impairment in mice (43). Glabridin, derived from the roots of *Glycyrrhiza glabra*, has also been shown to increase learning and memory in mice. This might be owing to its antioxidant characteristics, which lower oxidative stress in sensitive brain cells, resulting in less brain damage and improved neuronal function (44). In rats, the aqueous extract of licorice dramatically enhanced spatial learning and memory retention. Also, 300 mg/kg of this extract substantially corrected the amnesia caused by scopalamine (0.5 mg/kg i.p.) (45).

#### Licorice and covid-19

According to Ayurvedic literature GG is potent Antiviral Drug which boosts the immunity of respiratory system. A study on COVID19 patients with moderate disease found that two formulations containing GG accelerated clinical recovery, viral clearance, reduced oxygen requirements, and lowered inflammatory biomarker levels, suggesting that they may play a role in the medical management of COVID-19 patients with moderate disease (46). Insilico studies revealed that when these two formulations containing GG were tested against the corona viral membrane protein for their ability to inhibit the active spike protein, there was interaction between the constituents and different regions of the spike protein, implying that the formulations would be functionally significant against the corona viral protein (46). Glycyrrhizin substantially suppressed the replication of 2 clinical isolates of SARS-associated corona virus (FFM-1 and FFM-2) in Vero cells, according to a 2003 study. The medication was discovered to have an EC50 of 300 mg/ml, inhibiting the virus's cytopathic action while being non-cytotoxic to the host cells. Glycyrrhizin not only stopped viral reproduction, but it also stopped virus adhesion and penetration into cells (47).

# Licorice on cough (Kasa)

Kasa (Cough) is an essential clinical characteristic that can manifest as a separate disease or as a Clinical Feature (Lakshana) in conjunction with other diseases, and it can also manifest as a Sequelae (Upadrava) of an illness (Vyadhi) (48). Licorice according to Ayurveda is a drug of choice for these manifestations and is told in Kasa chikitsa (for the treatment of cough) in ayurvedic literature. In Astangahridaya it is told that licorice is effective in



chronic cough, chronic bronchitis and chest injury (49). In a clinical trial, *Licorice* powder given in a dose of 6gm/day for 90 days showed good improvement in cough (50). A randomized, double-blinded, placebo-controlled clinical trial done on 70 patients complaining of chronic cough Licorice pastille showed promising results by its demulcent and emollient effects on the pharynx and the lungs (51). Animal experiments utilizing chemical stimulation in the unanaesthetized guinea pig and electrical stimulation in the mildly anaesthetized cat, glycyrrhetinic acid and its derivatives were active in antitussive activity, indicating a central antitussive impact (52).

GG has antitussive, demulcent, and expectorant loosening properties due to the presence of glycyrrhizin, an active component. Glycyrrhizin reduces upper respiratory tract congestion and enhances tracheal mucus output (53). Another active component liquiritin apioside is found in the methanolic extract of licorice. inhibits capsaicin-induced cough (53).

Using an ammonia-induced cough model and phenol red secretion paradigm in mice, researchers evaluated the antitussive and expectorant effects of 14 main licorice components and various extracts of licorice. Liquiritin apioside, Liquiritin and Liquiritigenin have shown to have powerful antitussive and expectorant properties (54). In-vivo investigations revealed that glycyrrhizin treatment of ovalbumininduced asthmatic mice improved all known chronic histopathologic lung parameters (55). Liquiritigenin was discovered to protect human lung cells (A549) from *Staphylococcus aureus*-haemolysin-mediated damage research. In a dose-dependent manner, low concentrations of liquiritigenin significantly reduced *Staphylococcus aureus* α-haemolysin synthesis (56).

#### Licorice in improving complexion (Varnya)

Licorice is used to improve complexion and also as a cure for skin disorders in Ayurveda It is included in the group of 10 drugs that improve complexion (varnya mahakashaya) according to Ayurveda (57) this signifies its importance in this regard. It is used in a variety of dosage forms for getting improved complexion (varnya) Ayurveda have advised using of Licorice in a powder form. Licorice powder when applied on the face will improve complexion and also reduces acne blemishes and acne scars (58). Kumkumadi-Lepa a potent formulation with Licorice as the main ingredient in as study showed good results in enhancing complexion and also acts as a depigmenting agent (59).

In a study it is reported that *licorice* power when applied locally on the face has shown to improve complexion(58). Melanin, which is produced by the melanogenesis process in melanocyte cells, is responsible for the skin's colour. Hyperpigmentation or hypopigmentation may result from changes in melanin (60). The anti-melanogenic effect of licorice root extract was demonstrated in B16F10 melanoma cells by a decrease in intracellular tyrosinase and melanin levels. Licorice root extracts in methanol and ethyl acetate showed significant efficacy with IC50 values of 2.1 and 4.7 g/mL being low (61). *GG* extract was also compared

to kojic acid, a commercially available chemical that is already utilized as a tyrosinase inhibitor. Tyrosinase activity was suppressed by the extract by 78.45%, whereas kojic acid inhibited it by 99.67%. Unfortunately, kojic acid is unstable during storage; however, GG did not exhibit any drawbacks during tyrosinase inhibition, suggesting that licorice extract might be used in cosmetic compositions (62). Active chemicals identified from licorice extracts, such as glabrene, isoliquiritigenin, licuraside, isoliquiritin, and licochalcone A, have been found to suppress tyrosinase activity (63). Licochalcone A By activating ERK, A inhibited melanogenesis via the MAPK/ERK pathway. Phosphorylated p38 can activate microphthalmiaassociated transcription factor (MITF), boosting melanin formation, whereas phosphorylated ERK can block MITF activation, inhibiting melanin synthesis(60).

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An herbal face cream, in which GG combined with other herbal extracts, showed multipurpose effects such as whitening, antiwrinkle, anti-ageing, and sunscreen the effect, due to a synergistic effect between all the extracts (64) At a dosage of 150 mg/kg/day, GG extract has been shown to have anti-wrinkle efficacy through an anti-oxidant mechanism (65). The prenylflavonoids dehydroglyasperin C, dehydroglyasperin D, and isoangustone A have been shown to have anti-wrinkle action by scavenging superoxide (66). In 2012, Afnan et al. studied the impact of glycyrrhizinic acid on UV-B photoaging. produced by irradiation of human dermal tissue with a sub-toxic dosage of UV-B (10 mj/cm2) fibroblasts (HDFs) and their potential mode of action Glycyrrhizinic acid's involvement matrix metalloproteinase 1 (MMP1), pro-collagen 1, cellular and molecular biology Inhibition of hyaluronidase, nuclear morphology, cell cycle, intracellular ROS, and caspase 3 The tests were assessed. The obstruction looked to be linked to the main mechanism. modulation of MMP1 activation via NF-kB signaling (67) Dibenzoylmethane acted as a sunscreen, protecting the skin from UV light damage. It served as a UV-A screen, preventing UV light from penetrating important cells and preventing ROS overproduction. The researchers looked at in vivo photoprotection in a mouse model of UV-induced photodamage (68).

The effects of UV-A irradiation on photoaging of human dermal fibroblasts (HDFs) were studied. As a ROS scavenger, Licoricidin inhibited UV-A-induced photoaging. The modulation of MMP-1 is linked to this A moisturizing cream (oil in water) action (69). containing an extract of Beta-vulgaris (1%) and an extract of GG(1%) was created to give UV-A/UV-B protective hydration for use after laser treatment. Furthermore, by increasing melanocytic growth and eliminating obstinate scars and wrinkles, this lotion aided re-pigmentation (70). The anti-irritative effect of licochalcone A formulations on UV-induced erythema development was tested in randomized clinical trials. The formulation resulted in a significant decrease in UV-induced damage. erythema testing, which showed a significant reduction of pro-inflammatory in vitro



responses, includes keratinocyte PGE2 release driven by UVB (71). In the DPPH assay, Licochalcones B and D have shown high scavenging action as well as the capacity to reduce microsomal lipid peroxidation. These phenolic chemicals were found to help protect biological systems from oxidative stress, as well as prevent skin damage (72).

# Licorice as a promoter of hair growth (keshva)

The term "Keshva" denotes anything beneficial to hair. In Bhava Prakash Nighantu, an ayurvedic book, many hair-promoting (Keshya) medications are discussed and in that Licorice is the main ingredient and he also emphasises the importance of Licorice in preserving hair growth (73). In a clinical trial, Licorice power taken in a dose of 3gm twice/day showed a significant reduction in patients having hair fall in 30 days (74). In the treatment of alopecia, Madhukadi lepa is widely used in which *Licorice* is the main ingredient. This topical application (Lepa) contains Yasthimadhu (Glycyrrhiza glabra L.), lotus, Munakka (Vitis vinifera L.), oil, ghee and milk in equal amounts should be applied. This formulation is named after madhuka which is a synonym of *Licorice* in ayurvedic literature (75). Licorice extracts in hair care products have a unique function that promotes hair development. An ethanol extract of licorice was recently studied for its safety, stability, and hair growth activities (GG). Hair growth activity was comparable to the positive control (minoxidil) in hair tonic solutions containing this extract, with high physical and chemical stability and safe topical application (76). The petroleum ether extract of GG roots was found to have promise as a hair growth promoter in female rat studies. Female rats given GG had longer hair than those given either minoxidil or a placebo. In licorice extract-treated mice, 76 per cent of hair follicles were in the anagenic stage (active growth phase of hair), compared to 66 and 45 per cent in minoxidil-treated and control groups, respectively (77). A study on cells previously confirmed the effect on hair growth promotion for a mixture of extracts from Glycyrrhiza uralensis Fisch., Angelica gigas Nakai., Acorus calamus L., Cnidium officinale Makino., Panax ginseng C.A.Mey., Camellia sinensis (L.) Kuntze, Salvia miltiorrhiza Bunge, Zanthoxylum schinifolium Siebold & Zucc., Carthamus tinctorius L., Prunus persica (L.) Batsch, and Scrophularia buergeriana Miq. Human hair dermal papilla cells and C57BL/6J mouse cells were used in the experiment. In a dose- and time-dependent way, the combination significantly boosted the proliferation of human hair dermal papilla cells (78). Silver nanoparticles containing GG extract were shown to have antibacterial properties against pathogen-caused dandruff in a recent study. The solidity of pathogens' membrane was affected by this formulation, according to a protein leakage study (79).

# Licorice on improving voice quality (Swarya)

Due to its Swarya (which improves sound ) quality, Licorice is especially recommended for vocal problems and for improving voice tone and quality (80). Inorder to improve voice, small sticks of licorice of 2-3cm long are to be chewed and its juice should be consumed. Licorice mixed with ghee/honey also serves the same purpose. In hoarseness of voice, payasam (rice-milk) made with Licorice combined with ghee should be consumed (81). GG reduces throat discomfort and had expectorant properties. Glycyrrhiza was thought to be able to promote mucus secretions in the trachea and cause demulcent and expectorant effects this in turn helps in clearing the voice (5).

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# Ulcer healing property of licorice

*Licorice* is one of the potent ayurvedic drugs used to heal ulcers. In mouth ulcers medicated ghee prepared of Licorice is advised to hold in mouth according to person capacity (82) also application of *Licorice* mixed with honey in ulcer site will reduce healing-time (83).

GG extract has been utilized as an antiulcerogeni agent because it inhibits two enzymes: 15hydroxyprostaglandin and delta 13prostaglandin reducta se. As a result of the inhibition of these two enzymes, the quantity of prostaglandin rises. Chenoxolone is another molecule that may be produced from Glycyrrhiza extract. It can suppress gastrin secretion and hence act as an anti-ulcerogenic agent (84).

It is also beneficial in the management of peptic ulcers and duodenal ulcers studies showed that this action may be due to increased production of prostaglandin which protects the gastrointestinal mucosa. Peptic ulcers can be treated with deglycyrrhizinated licorice, a particular licorice extract. GG also plays an essential function in the repair of peptic ulcers caused by Helicobacter pylori (85).

#### Licorice for Acidity (*Amlapitta*)

Acidity is a frequent illness currently caused by digestive impairment and characterized by symptoms such as indigestion, tiredness without exertion, nausea, eructation's with bitter or sour taste, body heaviness, chest and throat burning, and lack of appetite (86). A clinical trial using GG root powder showed significant reduction in cardinal symptoms of acidity. This activity might be attributed to presence of glycyrrhizin, which can aid with this condition by causing mucus formation and tissue thickening in the digestive system. They can also help heal peptic ulcers by interfering with prostaglandins (86).

# Licorice for healthy eyes (Chaksusya)

Licorice is one of the chakshusya (drugs that promote eyesight) drugs told to consume daily in Ayurveda. It is told as beneficial for the eyes (chakshushya hithakara) in Ayurveda (87). Ayurveda advises includes Licorice in dinacharya(daily regimen )for getting its benefits. Ayurvedic classics have given equal importance to Licorice along with triphala in maintaining good eyesight, Licorice act as a drug that nourishes the eyes and is also used in corneal opacities and cataract. The antioxidant, immunostimulant, neuroprotective and antiinflammatory property of the drug helps in this regard (88).



Glabridin inhibited activation of ERK1/2 and the p38 MAPK pathway in retinal pigment epithelial (RPE) cells in vitro, protecting them against oxidative stress and apoptosis. Glabridin substantially reduced retinal damage in vivo by halting retinal degeneration and lowering the accumulation of deposits on the RPE layer caused by NaIO3. Glabridin, according to electroretinogram (ERG) studies, aided in maintaining normal retinal function, and is having protection action against retinal degeneration diseases (89). Vasanjana (VK) prepared with Licorice (GG) Kalka (paste) in Vasa (fat) of the domestic fowl (Gallus gallus) on glucose-induced cataract in ovine (sheep) lenses were found to have in vitro preventive anti-cataract activity in the experimental cataract model induced by high glucose in ovine (sheep) lenses in Vasanjana's anticataract action might be due to its antioxidant and free radical scavenging properties (90).

# Wound healing action of licorice (Vranaropana)

On ulcers, warm clarified butter with licorice can used topically is found to be effective (7). A comparative study of gels prepared with Licorice with betadine showed that Licorice gels helped to heal the wound faster (91). Yashtimadhu gritha (ghee processed with Licorice ) showed excellent results in healing noninfected surgical wounds (92). For effective wound healing Interleukin 2 is required, and glycyrrhizin a phytoconstituent present in licorice has been shown to enhance it (93). In a study done on guinea pigs, it is found that GG herbal creams dramatically enhanced collagen content and epithelialization rate in healing wounds and also reduced inflammation severity (94). A study conducted on the wound healing action of licorice in rabbits found that the extract when applied topically showed a faster wound healing rate when compared with dexpanthanol. Licorice has also been shown to have a cortisol-like impact on wound healing, including the prevention of inflammation via blocking phospholipase A2 (the first step in the creation of inflammatory prostaglandins and leukotrienes) (93). It found that licorice root extract when applied topically can reduce the time needed for induced oral mucosal lesions to heal in rabbits, Vitamin E, B complex, pantothenic acid, lecithin, biotin, niacin, manganese, calcium, calcium salts, proteins, and nucleic acids are all found in licorice, and they may help in wound healing (95). M. A. Takhshid et al found that there was a dose-dependent healing effect was seen with licorice extract in acetic acid-induced ulcerative colitis in rats (96).

# Licorice in Mother and Child care

In Ayurveda, *Licorice* has a wide range of actions in the male and female reproductive system. Milk boiled by adding Sugar, *Gmelina arborea* and licorice promotes foetal growth (*Charaka Samhita*). Licorice is said to be a drug that possesses the quality of *stanya vardhaka* (improves lactation) according to Ayurveda. Lactation was discovered to be enhanced by combining *Licorice* with cow's milk (7). In a clinical trial done on 25 patients *yastimadhu* along with *ashwagandha* 

(Withania Somnifera (L.) Dunal) and milk added with sugar helped to prevent IUGR in females also there were adverse effects seen in course of the treatment (97).

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#### Licorice and female reproductive disorders

Licorice has been shown to have a variety of medicinal qualities, including the ability to increase cortisol action, inhibit testosterone production, especially in women, exert estrogen-like activity, and reduce body fat mass (98). Compared to estradiol and glabridin, licorice extract caused an increase in creatine kinase (CK) activity, a known marker for estrogenresponsive genes, that was higher than expected based on the levels of glabridin in the extract, implying the presence of other components that may contribute to this strong estrogen agonist activity. The results showed that glabrene and isoliquiritigenin (2',4',4-3 hydroxy chalcone) (ILC) in licorice extract had a greater affinity for the human estrogen receptor (IC50, 1 and 0.5 M) than glabridin (IC50, 5 M). Glabrene's in-vivo stimulatory effects were tissue-specific and similar to those of estradiol. The effect of increasing glabrene and ILC concentrations on breast tumour cell proliferation was biphasic. At low doses (10 nM-10 M), both displayed estrogen receptor-dependent growthpromoting action, and estrogen receptor-independent antiproliferative activity at concentrations >15 M (99).

In a study Mean blood pressure was considerably lower with spironolactone therapy in a trial of 32 women with the polycystic ovarian syndrome (PCOS), but it was unaltered in women taking spironolactone plus licorice. Symptoms of volume depletion were reported by 20% of women treated with spironolactone and none of the women treated with licorice. The activation of the renin-aldosterone system was consistently lower when spironolactone was combined with licorice than when spironolactone was used alone. Metrorrhagia was less common in the combination treatment group. The findings showed that the mineralocorticoid characteristics of licorice might minimize the frequency of adverse effects associated with spironolactone's diuretic action in PCOS patients (100).

#### Licorice as Aphrodisiac (Vrisya)

Vajikarana, also known as Vrishya chikitsa, in Ayurveda deals with aphrodisiacs, virility, and boosting progeny's health. According to Charak Samhita, correct usage of these compositions bestows good body, potency, strength, and complexion, as well as sexual exhilaration and potency (101).

In ancient Indian scriptures, the sexual style of humans is frequently linked to and defined in terms of the sexual relationship style of animals. The following are some frequent examples: *Chataka* (Sparrow) - Several short-span conjugations with a limited amount of semen produced, *Gaja* (Elephant) - Long-term conjugation with considerable semen discharge every now and then. *Vrusha* (Bull) - Seasonal conjugation that is consistent and produces more sperm. Regular



vigorous dynamic conjugation with average quantitative semen in *Ashwa* (Horse) (101).

GG is one of the ingredient in aphrodisiac Ayurvedic Preparations like Trikantakadhyo Modaka, Gokshuradi Leha, Madanvardhano Modak, Makardhwajo Rasa, Gokshuradi Modak, Rativruddhikaro Modak(102). Shathavari Ghritha when consumed along with milk and licorice powder is an excellent aphrodisiac (103).

Charaka Samhita, an Ayurveda classical test has clearly mentioned licorice as a potent aphrodisiac and rejuvenator. Rats were used to test the aphrodisiac effect of an aqueous extract of GG roots and rhizomes. For 28 days, 150 mg/kg and 300 mg/kg/day were given orally through gavage. Mount latency, intromission delay, mounting frequency, and intromission frequency were measured on days 0, 7, 10, 14, 21, and 28 before and throughout the trial. Mount delay and intromission latency were both dramatically lowered by the extract. The extract also raised mounting and intromission frequency considerably (104).

# Licorice for oral health

Yastimadhu is widely used in diseases of teeth (dantha roga). According to Ayurveda to prevent dental caries and maintain oral hygiene chewing yastimadhu sticks daily having nine inches is advised. Studies have shown that glycyrrhizol A, glycyrrhizol B, 5-O-methylglycryol, isoglycyrol, 6,8-diisoprenyl-5,7,40trihydroxyisoflavone and gancaonin G which are phytochemicals present in yastimadhu showed antimicrobial activity (105) against Mutants group of streptococci, Streptococcus sanguis, Lactobacillus spp. and Actinomyces spp which are responsible for the formation of dental caries (106). A study found that MAIDS mice (mice infected with the LP-BM5 murine leukaemia virus) are 100 times more vulnerable to C. Albicans infection than normal mice, and glycyrrhizin treatment enhanced MAIDS mice's resistance to C. Albicans infection (107). In an in vitro investigation, Motsei et al. tested licorice extracts against Candida albicans and they found that freshwater extract of GG had an antifungal impact on C. Albicans (108).

Lee et al. demonstrated that a phytochemical present in licorice namely Liquiritigenin (LG) can protect mice against disseminated candidiasis by activating the CD4 Th1 immune response (109). Raw polysaccharides from GG have been demonstrated to have high anti-adhesive properties against *P. gingivalis* in aqueous extracts (110). A study on over-the-counter Canker Melts GX patches containing licorice extract change the course of aphthous ulcers by lowering lesion length, size, and discomfort, resulting in faster healing (111). Another study found that using a dissolving oral patch containing a licorice extract for up to 8 days improved ulcer size and discomfort compared to using a placebo patch in a randomized, double-blind clinical experiment with 23 patients (112).

# Anti-cancer activity of licorice

Ayurvedic remedies are more effective in treating chronic illnesses that were previously unsuitable for Western therapeutic approaches (113). *Licorice* pacifies the body humours due to the antioxidant, antiangiogenic, increases different hormone enzyme activities thereby protects non-tumorous cells from radiation, and interferes with DNA replication (113). In a study conducted to evaluate the effect of *Licorice* in oral mucositis, it is found that *Licorice* (GG) is beneficial in alleviating mucositis in a considerable and clinically important way, speeding up the resolution of mucositis and discomfort (114).

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A study to assess the protective impact of Licorice (Glycyrrhiza glabra L.) against adverse effects of radiation/chemotherapy in head and neck cancers, it was discovered that Yashtimadhu ghrita exhibited promising results in reducing radiation and chemotherapy side effects. by its anti-inflammation, anti-ulcer, and skin-regeneration properties (115). Glycyrrhiza's 18-glycyrrhetinic acid and glycyrrhizic acids are responsible for the anti-cancer-property, which causes a mitochondrial permeability transition and tumour cell death (116). Intestinal carcinoma cell line (Caco-2) and prostate carcinoma cell line were used to examine the anti-cancer efficacy of licorice methanolic extracts of 0, 12.5, 25, 50, and 100 g/ml (PC-3). The methanolic extract inhibited the growth of Caco-2 and PC-3 cells. Licorice extract includes a variety of phytoestrogen chemicals, making it a potent chemopreventive agent. As a result, it could be able to fight cancers including breast cancer, ovarian cancer, and stomach tumours. One study found that combining licorice extract with cisplatin reduced cisplatin-related toxicity (117).

Glycyrrhizinic acid inhibits the proliferation of cancer cells via inducing AKT/mTOR signaling in endometrial and breast cancer cells (118). In an adiposedependent way, the ethanolic extract has antiproliferative actions against MCF-7. In albino mice, licorice hydroethanolic extract suppressed micronuclei development and chromosomal abnormality in bone marrow cells, indicating antimutagenic potential. Furthermore, it inhibited thromboxane A2 production in lung cancer cells (119). A pentacyclic triterpenoid derived from the licorice root, 18-glycyrrhetinic acid, exerts significant inhibitory effects on colorectal cancer cell growth in a dose-dependent and time-dependent manner, both in vivo and in vitro experiments in a timedependent way (120). In cancer cells, activation of the PI3Kor AKI signaling pathways increases cell survival, outgrowth, and migration. The expression of MMP 1, 2, 3, 9, 12, 13, and MTI-MMP is downregulated when these pathways are inhibited, and cancer cell proliferation and invasion are suppressed. Glycyrrhetenic acid also prevents metastasis by disrupting the actin cytoskeleton and inducing Fas or DNA fragmentation-mediated apoptosis. Furthermore, it exhibits toxicity only toward tumour cells. Its antitumour activity is greater than that of several currently available anti-tumour drugs. Matrix metalloproteinase (MMP) expression is also increased by glycyrrhetenic acid (84).

The in-vivo (mice) and in-vitro growth of Ehrlich ascites tumour cells were both reduced by aqueous



licorice root extract (121). The suppression of angiogenesis in in-vivo experiments, peritoneal and chorioallantoic membrane assays, validated GG 's angio-inhibitory efficacy. Licorice extract inhibited VEGF production and neovascularization produced by cytokines. The findings showed that licorice root extract might be used as a cancer treatment supplement. Licorice extract decreased the development of mouse colon carcinoma in BALB/C mice implanted with CT-26 colon cancer cells and reduced cisplatin-induced toxicity without causing any side effects. Furthermore, licorice extract treatment greatly decreased cisplatininduced oxidative stress (122). In various animal models, dibenzovlmethane (DBM), a minor -diketone ingredient of licorice and sunscreens, was found to have anti-neoplastic effects in chemically produced skin and mammary malignancies (123).

#### Toxicity and side effects of licorice

Licorice is told in Ayurveda as one of the vamanopaga (drugs that induce vomiting) overuse of this will lead to vomiting. Licorice has abortifacient action also, so it is not advised to take during pregnancy. The recommended daily dosages of licorice root for ulcer and gastritis therapy range from 1 to 15 g. Higher dosages given for longer periods, on the other hand, may raise the danger of hyperkalemia, as well as induce significant elevations in blood pressure and apparent mineralocorticoid excess (4). Pseudoaldosteronism is a condition in which a person becomes abnormally sensitive to a hormone in the adrenal cortex as a result of too much glycyrrhizin. Headaches, lethargy, high blood pressure, and even heart attacks are all symptoms of this illness. It may also contribute to water retention, which can result in leg inflammation and other issues (124).

#### Conclusion

Licorice, an important and widely used drug in Ayurvedic practice. Ayurveda uses it for its multifarious activity against a number of systematic and non-systematic diseases. It shows various medicinal properties like anti-inflammatory, antiulcer, anticancer, antioxidant, nootropic, antitussive, wound healing and others. It also improves voice, complexion, hair growth, eye health, lactation and foetal health. It is considered as a drug which possesses rejuvenate and aphrodisiac property. All these properties can be attributed due to presence of phytochemicals such as glycyrrhizin, glycyrrhetic acid, glabridin, liquiritin, isoliquiritigenin, isoflavones and others. Licorice is told in various other contexts of diseases in ayurveda along with suitable adjuvants. This area is unexplored till now and only small amount of literature is used nowadays to treat the ailments using Licorice so more strong double-blind randomized controlled trials and deep literary reviews are still needed. There's also a lot of room to experiment with different licorice formulations in a variety of illnesses.

#### **Authors Contributions**

Amal S Chandran, Syam R J, Jojan J Jerone and Sreeja Kaimal V contributed to Conceptualization; Data curation; Methodology; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing; with Amal S Chandran and Syam R J taking the lead in preparing the manuscript. The manuscript was read and approved by all the authors.

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