Liquorice (*Glycyrrhiza glabra*): A Traditional Sweetener and Medicinal Plant

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ABSTRACT

This is a review on a traditional sweetener and medicinal plant widely used in Bangladesh as well as many other countries. As Bangladesh Sugarcrop Research Institute (BSRI) is mandated with research on all kinds of sweetener crop, Liquorice is thus targeted for this purpose. This study gathered various information on Liquorice (*Glycyrrhiza glabra* L.) through different books, journals and e-sources. It mentioned a brief description on the history, origin and distribution, agro-ecology, botanical descriptions including morphology, scientific classification, synonyms and sweetening agents, pharmacological properties, use in soil reclamation, halophyte or salt tolerance activity, drought tolerance activity and finally its cultivation procedure. It concluded with more research demand which can make it a possible cash crop for anywhere of the country specially for the southern coastal areas.

Key words: Liquorice , *glycyrrhiza*, sweetener crop, medicinal plant

INTRODUCTION

Glycyrrhiza glabra is one of the most traditional sweetener and medicinal plant belongs to the family Leguminosae (also known as Fabaceae). The genus *Glycyrrhiza* is derived from the Greek words glykos (sweet) and rhiza (root). It is also called Liquorice, liqeorice, glycyrrhiza, sweet wood, and Liquiritiae radix (in English); sussholz and lakritzenwurzel (in German); reglisse and bios doux (in French); shirin bayan and mak (in Persian); and liquirizia and regaliz (in Italian and Spanish, respectively) (Pastorino *et al*., 2018). This species is a native of Mediterranean areas, but it is now also present in Bangladesh, India, Russia, China and many other countries. The extracts are currently used in pharmaceutical and food industries, as well as in the manufacture of functional foods and food supplements (Hayashi & Sudo, 2009; Herrera, *et al*., 2009).

Liquorice extract and glycyrrhizin is allowed to use in foods by the United States Food and Drug Administration, the Council of Europe, and the Joint FAO/WHO Expert Committee on Food Additives (FAO, 2005). U.S. Flavor and Extract Manufacturers Association has grouped it in Generally Recognized As Safe (GRAS). The use of glycyrrhizin is also used as a flavoring for hydrolyzed vegetable protein, soya sauce, and bean paste to control saltiness (Gloria, 2003).

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Demand for alternate sweeteners are increasing broadly with the increasing rate of health conciseness and world economy. Thus the average growth rate in the 1990s was around 2% which was increased up to 9% in 1997. The world consumption is at that time was 12 million tonnes. Asian production is about 50-55% of the total, and the rest are almost equally from Americas and Europe. More than 70% among all alternate sweeteners is saccharin followed by aspartame 18% and cyclamates 5%. If the consumption is measured in terms of value, aspartame is 62%, followed by saccharin 17%, cyclamates 5%, and others 16%. The high share of Saccharin is cheap and is suitable for use in almost all applications where sweet taste is required. It is also being used for nonfood item, such as pharmaceuticals, animal feed, and toothpaste. Other widely used sweeteners are acesulfame-K and stevioside. These two are especially used in soft drink items (Gloria, 2003).

History

Ozturk *et al*. (2017) reported that Theophrastus has referred to the liquorice plant, mentioning that Romans cultivated it after the thirteenth century and called it as Radix dulis. In England, it was first cultivated in 1562 (Trease and Evans, 1983). Currently, the plant is widely cultivated in different parts of India, Iran, Turkey, Greece, Spain, Russia and many other countries and is traded in Spain, Iraq, Italy, Egypt, Belgium, France, and Germany.

Rittenhouse (1895) mentioned, in United States total imports of Liquorice were about 5,000,000 pounds during 1872. At that time, it was more profitable than that of either sugar cane, sugar beets, rice or cotton. Although the industry was not as large as any of those but it gave higher profit.

Origin and distribution

Glycyrrhiza glabra is native to Eurasia, in central and south-western Asia and the Mediterranean region (Lim, 2015). However, Fiore *et al*. (2005) claimed that it is native to the Mediterranean region, central to Southern Russia and Asia, and now is widely and popularly cultivated throughout Europe and Middle East. According to Hayashi (2009), Hayashi and Sudo (2009), *G. glabra* is found in South Europe (Spain, Italy), Turkey, Iran, Iraq, Central Asia and the north-western part of China; while *G. uralensis* is found in Central Asia, Mongolia, north-western & north-eastern parts of China, and *G. inflata* is found only in the north-eastern part, the Xinjiang Uygur Autonomous Region of China. *G. glabra* is divided into two varieties: *G. glabra* var. typica (Spanish Liquorice) and *G. glabra* var. glandulifera (Russian Liquorice) (Hayashi and Sudo 2009). however, Nomura *et al*., 2002 reported three varieties of *G. glabra* which were the Spanish and Italian Liquorice, assigned to *G. glabra* varity typica; Russian Liquorice to *G. glabra* variety glandulifera and Persian and Turkish Liquorice *G. glabra* varity violacea. Countries producing liquorice including Iran, Afghanistan, the People's Republic of China, Pakistan, Iraq, Azerbaijan, Uzbekistan, Turkmenistan and Turkey are the major producer in the world. In China, commercial Liquorice is produced from the three aforementioned species.

Agro-ecology

The Liquorice plant grows from the shores of the Mediterranean, on the south (latitude 30^0), to Siberia, on the north (latitude 55^0), and from the western shores of Europe to the plains of Persia and farther India. It is also from low levels to 1,500 feet above the sea. Thus it was found to be well adopted of land and variety of soil and climate (Rittenhouse, 1895). It grows well in temperate, warm and subtropical climate. It prefers well-limed, well-drained, composted, loose, friable, sandy and clay soil near to the river. It also prefers full sunlight. It remains dormant in winter, which induces the translocation of assimilates to the underground rhizomes. Frost or drought do not injure the root if it is well established. So, care should be taken for young and tender plants of the first year of plantation which is vulnerable.

BOTANICAL DESCRIPTIONS

Morphology

It is a herbaceous perennial, with stem 0.5-1.5 meter high, woody at base, densely scaly glandular punctuate with stoloniferous roots. Leaves compound, imparipinnate, 7-15 cm long with 9-17 ovate-oblong, oblong-lanceolate, or elliptic leaflets 1.7-4.0 by 0.8-2.0 cm. Stipules caducous, linear, 1-2 mm. Inflorescence open, racemose, many flowered. Flowers 0.8-1.2 cm long. Calyx campanulate, 5-7 mm, 5-toothed, upper 2 teeth mostly joined; corolla purple or pale whitish blue, 9-12 mm, standard ovate or oblong. Fruit oblong, flat, glabrous or sparsely hairy legume, 2-3 cm long, usually containing 2-4, whitish, smooth seeds, 2 mm across (Lim, 2015). The *Glycyrrhiza* is a member of pea family and grows in subtropical climates in rich soil. The *Glycyrrhiza glabra* plant has an extensive root system with a main taproot and numerous runners below the soil level. The main taproot, which is harvested for medicinal use, is soft, fibrous, and has a bright yellow interior (Sharma and Agrawal, 2017a).

Scientific classification

As it was mentioned by (Sharma and Agrawal, 2017a) the Scientific Classification of *Glycyrrhiza* are as follows:
Kingdom: Plantae
Division: Angiospermae
Class: Dicotyledoneae
Order: Rosales
Family: Leguminosae/Fabaceae
Genus: *Glycyrrhiza*
Species: *glabra* Linn

Synonyms

The Synonyms of *Glycyrrhiza* as mentioned by Lim (2015) are as follows:
Glycyrrhiza brachycarpa Boiss.,
Glycyrrhiza glabra var. caduca X.Y. Li,
Glycyrrhiza glabra var. glabra ,
Glycyrrhiza glabra subsp. glandulifera (Waldst. & Kit.) Ponert,
Glycyrrhiza glabra var. glandulifera (Waldst. & Kit.) Regel & Herder,
Glycyrrhiza glabra var. glandulifera (Waldst. & Kit.) Boiss.,
Glycyrrhiza glabra var. glandulosa X.Y. Li,
Glycyrrhiza glabra var. laxifoliolata X.Y. Li,
Glycyrrhiza glabra var. typica L.,
Glycyrrhiza glabra var. violacea (Boiss. & Noe) Boiss.,
Glycyrrhiza glandulifera Waldst. & Kit.,
Glycyrrhiza hirsuta Pall.,
Glycyrrhiza pallida Boiss. & Noe,
Glycyrrhiza pallida Boiss.,
Glycyrrhiza violacea Boiss. & Noe

The genus *Glycyrrhiza* consists of about 30 species, such as *G. glabra, G. uralensis, G. inflata*, *G. aspera, G. korshinskyi, or G. eurycarpa* etc. Like the other plants of Fabaceae, *G. glabra* has the capacity to fix nitrogen, with Rhizobium bacteria through symbiosis at the root level. It is suitable for sandy and clay soils, although it prefers humid soils. Since the Egyptian age, the therapeutic properties of *G. glabra* are well documented (Fiore *et al.*, 2005). The roots are the most used parts whereas the leaves are considered an agrochemical waste. However, different authors studied the phytochemical composition of *G. glabra* leaves and mentioned that certain compounds present in the roots are also present in leaves, although in smaller quantities (Hayashi & Sudo, 2009; Siracusa *et al.*, 2011).

Sweetness agents : Chemistry and extraction

Liquorice has a high nutritional value and was used in foods since ancient times. In food, it is mainly used as a sweetening agent. It also has properties to inhibit the sensation of thirst (Yang *et al.*, 2017). Liquorice oil is approved by the Food and Drug Administration (FDA) and has applications in various food products such as beverages, toothpaste, chewing gum, and cosmetics (Carmines *et al.*, 2005). Liquorice has been traditionally used as a sweetener due to its taste, (Tian *et al.*, 2013; Tong *et al.*, 2015). The main primary active ingredient of roots for its sweet taste is glycyrrhizin, a triterpenoid saponin Gloria (2003). Glycyrrhizin or 20-β-carboxy-11-oxo-30-norolean-12-en-3β-yl-2-O-β-d-glucopyranurosyl--d-glucopyranosiduronic acid (C42H62O16, MW 822.92), is a triterpenoide glycoside (saponin) with glycyrrhetinic acid, which is condensed with O-β-d-glucuronosyl- (1' 2) -β-d-glucuronic acid. It is almost 50 times sweeter than sucrose (Yu *et al.*, 2015). Glycyrrhizin (GL) contains about 10% of the liquorice root on dry weight basis which is a mixture of potassium, calcium, and magnesium salts of glycyrrhizic acid that significantly varies between 2% and 25% (Rizzato *et al.*, 2017) due to geographic sources, harvesting, and processing. After oral administration, glycyrrhizin is

metabolized to 18-glycyrrhetic acid -3-omonoglucuronide and glycyrrhetic acid by intestinal bacteria (Albermann, *et al*., 2010). Ahamed *et al.* (2001) found this as non sugar sweetner for human as well as a sweet taste inducer in insects also.

After harvest, the roots are dried to reduce moisture below 10% level, cleaned and extracted with aqueous ammonia. It is further concentrated in vacuum evaporators, precipitated with sulfuric acid, and crystallized with 95% alcohol providing a crude ammonium glycyrrhizin (AG). Other type treatment yields a white, crystalline mono-ammonium glycyrrhizin (MAG). Both derivatives are the same in terms of sweetness but they differ in solubility and sensitivity to pH. AG is relatively stable and highly soluble in hot or cold water and in alcohol. Glycyrrhizin is 50 times sweeter than sucrose and it has a slow releasing capacity of sweetness followed by a lingering Liquorice -like aftertaste. It produces a sweet and woody flavor, which guides its use as a pure sweetener. Glycyrrhizin increases food flavors, minimize any bitter flavors, and increases the perceived sweetness level of sucrose. It has the great potentiality for providing functional characteristics, for foaming, viscosity control, gel formation, and antioxidant characteristics (Gloria, 2003).

According to Bahmani *et al.* (2014), liquorice can reduce diabetes symptoms, such as polydipsia and frequent urination, but cannot reduce blood glucose. Takii *et al*. (2001) suggested that glycyrrhizin has an antidiabetic effect in noninsulin dependent diabetes mice, reducing the postprandial blood glucose rise. After studying various alternate sweeteners, Wal *et al*. (2018) concluded that Stevia and Mono ammonium glycyrrhizin should be encouraged as besides these two compounds carrying the benefit of natural ingredients. these are also free from the hazardous effects of other chemical based alternatives.

However, It has side-effects also and these are cardiac dysfunction, edema, and hypertension those who receive high doses of glycyrrhizin-based pharmaceuticals or consuming large amounts of Liquorice containing confectionery or health products over a prolonged period of use (Gloria, 2003).

PHARMACOLOGICAL PROPERTIES

Liquorice is one of the oldest and most popular herbal medicines in the world. Many of its historical uses are still practiced today Pastorino *et al*. (2018). A summary of the most important pharmacological activities of *G. glabra* are explained as follows:

Anti-oxidant activity

Antioxidants are defined as any substance that delays or inhibits oxidative damage by blocking the propagation stage in oxidative chain reaction. The anti-oxidant activity of *G. glabra* is one of the major reasons for its uses. Many authors observed the powerful anti-oxidant activity though they differ on its phenolic content. (Rackova *et al*., 2007, Varsha and Sonam (2013), Singh *et al*. (2015), Biondi, *et al*. (2003), Sharma, *et al*. (2016).

Anti-inflammatory activity

Anti-inflammatory substance that reduces inflammation (pain, redness, and swelling) in the body by blocking certain inflammation substances in the body. They are used to treat many different conditions including cancer.

Use of of *G. glabra* in the treatment of inflammatory diseases have been documented since ancient times (Yang, *et al*., 2017). Shalaby, *et al*. (2004) observed a significant decrease in the total cholesterol. Harwansh, *et al*. (2011) reviewed on the treatment of the upper respiratory tract and gastric system diseases. Rackova *et al*. (2007); Yin *et al*. (2017) found the healing action of stomach and mouth ulcers; Xiao *et al*. (2010) used in renal and liver complications. Furthermore, Wang, *et al*. (2017) described the anti-inflammatory effects on endometriosis.

Anti-tussic and expectorant activity

Antitussic mean cough suppressants. They relieve cough by blocking the cough reflex. Similarly expectorants thin mucus. This may help to clear the mucus of cough from airway. The anti-tussic and expectorant effects of liquorice have been reported by different authors, particularly its useful effects on the treatment of sore throat, cough, and bronchial catarrh (Damle, 2014; Fiore *et al*., 2005). Glycyrrhizin helps to expel congestion in the upper respiratory tract and accelerates tracheal mucus secretion (Sharma *et al*., 2016).

Anti-ulcerative activity

Antiulcer agents are commonly used drugs that inhibits gastric acid production, neutralization of acid or protection of the gastrointestinal mucosa from acid injury. The use of *G. glabra* extract as anti-ulcerative is widely known. The benefits of *G. glabra* in the treatment of duodenal and peptic ulcers have been reported since 1970s, and this traditional use is related to the presence of anti-inflammatory saponins (Krausse *et al*., 2004). Reports are also available to to use Glycyrrhizin in gastric and duodenal ulcers for the gastrointestinal system, (Bardhan, *et al*., 1978).

Anti-microbial activity

Different authors reported the anti-microbial properties of *G. glabra*, particularly on Gram positive and Gram negative bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Bacillus subtilis* (Gupta *et al*., 2008; Wang, *et al*., 2015). The antibacterial activity observed is due to the presence of secondary metabolites, namely, saponins, alkaloids, and flavonoids (Fukui *et al*.,1988; Wang, *et al*., 2015).

Anti-viral activity

Antiviral drugs are used to treat viral infections. Most of them are target specific. *G. glabra* is mentioned as effective against a wide range of viruses. Antiviral drugs do not destroy their target pathogen but they resist its development.

Different authors explained the anti-viral activities of *G. glabra* extracts against different viruses has been reported, including herpes simplex, Varicella

zoster, Japanese encephalitis, influenza, and vesicular stomatitis virus (Wang, *et al*., 2015). Different studies have demonstrated that two triterpenoids are responsible for the antiviral activity reported glycyrrhizin and 18β glycyrrhetinic acid (Wang, *et al*., 2015). These compounds have the ability to inhibit virus gene expression and replication, decreasing the adhesion force and stress and reducing HMGB1 binding to DNA (Wang, *et al*., 2015). Fiore *et al.* (2007) mentioned *Glycyrrhiza glabra* derived compound glycyrrhizin and its derivatives reduced hepatocellular damage in chronic hepatitis B and C. They further mentioned a reduction of mortality and viral activity in herpes simplex virus encephalitis and influenza on animal studies. Anagha *et al.* (2014) mentioned Yashtimadhu (*Glycyrrhiza glabra*) is one such plant which has shown remarkable activity against large number of viruses. Cited from ancient Ayurvedic System they further stated *Glycyrrhiza glabra* or Licorice has been proven beneficial against many DNA viruses such as Varicella zoster virus, Kaposi sarcoma-associated herpesvirus, Herpes Simplex Virus^{-1}, Epstein Barr virus, Human Cytomegalo virus, etc and RNA viruses such as Influenza A virus (IAV), H5N1 virus, H1N1 virus, Hepatitis C virus, Newcastle disease virus, Rotavirus, SARS-associated coronavirus, Human Immunodeficiency Virus etc. Omer *et al*. (2014) found 60 mg/100 ml concentration of *Glycyrrhiz*a extract did not produce any toxicity in the embryonated eggs and showed anti-viral activity against the virus. Thus they suggested that the mechanism of action of these active phytochemicals as an antiviral agent would be helpful to elucidate the pathogenesis of the disease.

Hepatoprotective activity

Hepatoprotective or antihepatotoxic activity is the ability of a chemical substance to prevent liver damage. The hepatoprotective activity of glycyrrhizin has also been extensively reported by some authors (Huo *et al*., 2011; Sharma and Agrawal, 2017b). Al-Razzuqi, *et al.* (2012) reported that the aqueous extract of *G. glabra* had a significant effect on liver functions as well as restoring hepatic tissue in acute liver diseases. Therefore they mentioned the aqueous extract of *G. glabra* roots can be used for prevention and treatment of liver disorders.

Anticarcinogenic and antimutagenic activity

The process of antimutagenesis and anticarcinogenesis is to inhibit of tumors both extracellular and intracellular mechanisms. Different studies suggest that the extract of *G. glabra* may be a potential supplemental source for different cancer treatments (Lee, *et al*., 2008; Ohtsuki, *et al*., 1992). This activity was also found on tumour cells (Lee *et al*., 2008), against the human cervix (Lee *et al*., 2008) and chromosomal aberration in bone marrow cells of albino mice (Sharma, *et al*., 2014). According to Wang *et al.* (2017), it also works in breast and ovarian cancer, gastric tumours, leukaemia. and human breast cancer cell lines (Li *et al*., 2016).

Neuro-protective activity

Neuroprotection means the relative preservation of neuronal structure and/or function. It is known to be a strong antioxidant which has broad anti-inflammatory properties. Chakravarthi and Avadhani (2013) and Dhingra and Sharma (2006) suggested

a possible neuro-protective role of liquorice in the prevention of diseases such as Alzheimer. The basis of Alzheimer is the chronic inflammation of certain brain regions. Thus, the anti-inflammatory activity of liquorice might contribute to the observed memory enhancing effects (Yokota *et al*., 1998).

Sedative activity

Sedatives are used to treat anxiety, tension, seizures, panic disorders and sleep disorders. *G. glabra* being able to induce sedative and anxiolytic effects (Hoffmann *et al*., 2016). It is the major inhibitory neurotransmitter in the central nervous system, for anaesthetics and neuroleptic, anxiolytic and anti-convulsant compounds (Simmler *et al*., 2013).

Anti-depressive activity

Antidepressants are used to treat major depressive disorder, including anxiety disorders, some chronic pain conditions and so on. As liquorice extract reversed reserpine induced depression, its antidepressant effect can be associated with the restoration of brain monoamines, such as norepinephrine and dopamine. Liquorice extract may have potential therapeutic value for the treatment of depressive disorders. (Dhingra & Sharma, 2006).

Oestrogenic and androgenic effects

Estrogens and Androgens are hormones produced by the body in greater amounts in females and males respectively. These are for normal sexual development. Since ancient times, the influences of liquorice on the action of cortisol, reduction of testosterone synthesis, and the influence on oestrogen activity are well known (Armanini *et al*., 2002). Kim and Park (2012) reported that isoflavones can influence sexual development and impair oestrous cycling. This can also influence ovarian and hypothalamus and pituitary glands function (Kim & Park, 2012).

Skin effects

The skin effect is usually an undesirable effect which occurs when using alternating electric current signals. The main skin benefits reported for *G. glabra* are based on the antioxidant and anti-inflammatory activities as well as on the ultraviolet (UV) protection (Halder & Richards, 2004). Saeedi, *et al*. (2003) reported the use of liquorice mainly for skin eruptions, including dermatitis, eczema, pruritus, and cysts. In particular, the *G. glabra* flavonoids present depigmenting capabilities and tyrosinase inhibition effects (Solano *et al*., 2006).

Other activities

It is well known that myocardial ischaemia is one of the major diseases in the world. It occurs through blockage of coronary arteries and results in myocardial cell death. The pretreatment with *G. glabra* significantly reduce the risk of ischaemia and improves antioxidant status (Di Paola *et al*., 2009; Ojha *et al*., 2013). The extract of *G. glabra* has been used in the treatment of low bone mass, osteoporosis, fractures, bone defects, osteomalacia, osteogenesis imperfecta, bone disease, and periodontal diseases (Kumar *et al*., 2015).

Use in poultry industry

Liquorice contains bioactive components, such as flavonoids and glycyrrhizin, which have pharmacological properties and medicinal applications, discussed earlier. The Liquorice extract has also been found to show immunogenic and antioxidant activities, which might improve the growth performance, feed efficiency, carcass traits, and blood biochemical indices of the poultry birds. It acts as a potential solution for solving respiratory, digestive, and immune problems in poultry (Alagawany, 2018). Ocampo *et al.* (2016) reported that broiler chickens treated with glycyrrhizin presented better weight gain, final body weight, feed conversion ratio, and lower mortality rate than the non-treated controls. they further mentioned that Glycyrrhizin treated birds gained higher antibody against Newcastle disease virus and other diseases. Alagawany *et al.* (2019) reviewed the updates of current knowledge about the beneficial effect of licorice supplementation in poultry diets, particularly its positive effect on the treatment of high-prevalence diseases of the immune system, liver, and lungs.

Use in soil reclamation

Egamberdieva *et al*. (2015) observed the plant growth, nutrient acquisition and symbiotic interactions between liquorice and rhizobia under salt stress was higher. They also evaluated the interactions between rhizobia and root-colonizing Pseudomonas in liquorice grown in potting soil and observed more biomass, nodule numbers and nitrogen content after combined inoculation. Studies examined the interactions between symbiotic bacteria and root-colonizing Pseudomonas strains in areas where nutrient uptakes in the rhizosphere are remarkably high. Their observations indicated that microbes living in the rhizosphere of liquorice can form a mutualistic association and coordinate their involvement in plant adaptations to stress tolerance. Varganov and Gladyshev (1989) revealed the utility of Liquorice cultivation in stabilization of sand and quick improvement of soil. Mohammad and Rehman (1985) also recorded the similar findings.

Halophyte or salt tolerance activity

Dagar *et al*. (2015) mentioned that the sodic lands could also be reclaimed remarkbly in reducing soil pH and exchangeable sodium percentage by growing *Glycyrrhiza glabra;* Egamberdieva and Mamedov (2015) and Mirkin *et al.* (1971) also supported it.

Drought tolerance activity

Drought, which is increasing due to the climatic change resulting the scarcity of irrigation water. This will limit our plant cultivation. *Glycyrrhiza glabra* can increase the synthesis of glycyrrhizin under this stress. Hosseini *et al*. (2018) mentioned that under drought condition, application of only 23% of the normal water with appropriate choice of genotype can increase the growth and lead to acceptable glycyrrhizin yields. Aprasidi (1978) reported drought resistant varieties of *Glycyrrhiza glabra*. However Mohammad and Rehman (1985) concluded as irrigation is a must for better yield.

CULTIVATION PROCEDURE

Conventional plantation

Rittenhouse (1895) mentioned it needs only be one plowing and harrowing to turn down the grass and weeds. Then it should be laid out in furrows about 25 to 30 inches apart. The buds or cuttings are to be planted in 6 or 8 inches apart in the rows and covered by plowing. Set should be placed in a furrow so that the buds stay each side. It can be covered 3 or 4 inches with a hoe. From time to time, during the growing season, a cultivator should be run between the rows to keep down weeds or grass. The author suggested to cut off the end of the tops during growing season. This could be easily done with a mowing machine. He suggested the same treatment for the second and third year. In the fall of the third year the crop would be ready to harvest. The cost of harvesting are the most expensive part of the systems. In an acre of land, with the row distance of 30 inches and the plants in the rows 6 to 8 inches apart, would contain 20,000 plants. Narrower rows and closer planting is permissible, so that more than 20,000 plants can be grown in an acre suggested by the author.

Douglas *et al*. (2004) found increasing plant populations at establishment had a large effect on production. Maximum root production was achieved with plant populations above 24000 plants/ha. Low plant densities favoured stem production and high densities favoured root production. Sampling roots upto 900 mm showed that the majority of production was from the top 300 mm. Roots harvested from below 300 mm contained less glycyrrhizin than surface roots. Glycyrrhizin concentration increased each year and varies location to location. The minimum international standard of glycyrrhizin is 4% in the roots. By the third harvest amounts of glycyrrhizin with 90% of the glycyrrhizin content in roots in the 300 mm to 600 mm soil layer in different provinces of USA, they reported. These trials showed with fresh root and rhizome yields of 17-28 tha^{-1} in the second and third years of production and with a glycyrrhizin content above the minimum international standard.

In India, many authors mentioned the cultivation technique. Among them, Central Institute of Medicinal and Aromatic Plants (CIMAP) under the Council of Scientific and Industrial Research (CSIR) in Lucknow released few varieties namely EC 111236, EC 124587, EC 21950 and *Mishree*. They mentioned it is propagated through root cuttings, runners or underground stem pieces (10 cm length). The land is to be prepared by ploughing twice and harrowing. A handful amount of 15-20 tonnes of farm yard manure, 250 kg of single superphosphate, 65 kg of muriate of potash and 25 - 50 kg zinc sulphate per hectare are needed to be applied basally.

Planting is done at the end of the winter or in the spring season (February to March) with a spacing of 90 cm between rows and 45-60 cm between plants. Dry condition at the time of planting and in the next few months gives best result for a good crop. Field should be irrigated weekly during summer months (Anonymous, 2018).

According to some other expert, sandy-clay soil was good for its cultivation. January-February season is right time for its sowing. A nursery bed is needed to be prepared at this time. After that seed can be sown in the month of February-March or July-August. It is necessary to level the fields properly until the soil becomes soft. Weeds should be removed properly. Transplanting distance for its field is 90 cm x 45 cm for direct sowing. The seeds are germinated by 10-20 days. Intercrops like carrot, potato cabbage, etc can be grown. Marzi et al. (1993) reported that intercropping had a detrimental effect on Liquorice root growth. De Mastro (1993) also confirmed the result. Light irrigation at regular intervals of 30-45 days during the summer season is also required. Although Marzi *et al.*(1993) reported irrigation has no significant effect. Well drainage system is necessary to avoid root rotting. After two or three years, the plant can be harvested in the month of November to December. It is better to dry the roots in the sun after harvesting.

Another expert Sharma *et al.* (2005) from India mentioned to cultivate it in warmer climatic conditions, sandy loam fertile soils having pH of 6 to 8.2 are ideal for better root development. However the plant survives in places which receives 50-100 cm rainfall annually. Plantation is done by 15-25 cm long stolons having 2 or 3 buds from freshly cut root stock. Old crowns can also be used as planting material. These materials (stolons or root cuttings or crowns) are planted in the field at 6.8 cm deep in the soil and at a distance of 90 cm x 45 cm. Requirement of stem cuttings are 250 - 300 kg per hectare. The cuttings begin sprouting in 15-20 days after planting. Light and frequent irrigation is necessary during spring season. During field preparation, farm yard manure at the rate of 10 tons per hectare should be used to enhance the growth of underground roots. In dry summer season irrigation is requirement of the crop in an interval of 30-45 days. Water logging in field should be avoided, because these may lead to soil borne diseases which causes root rotting. High yields are obtained from 2 to 3 years old crop. Singh *et al.* (1984) mentioned removal of flowers immediately results good quality of Liquorice. To get high yield of glycyrrhizic acid, harvest of the crop should be done in winter. While storing in polythene lined bags, the permissible moisture content of dry roots should be below 10%. CIMAP (1982) informed G. glabra plants were affeced by weevil Myllocerus undecimpustulatus and few records are also found on viral disease.

In vitro culture or micro-propagation

In vitro culture or Micropro-Propagation in Glycyrrhiza glabra is done from nodal segments through axillary bud proliferation (Arya, 2009; Kukreja, 1998). Shah and Dalal (1982) found successful establishment of plantlet using different MS medium and reported 15-20 times higher multiplication rate than stem cuttings.

In conclusion Liquorice as an alternate source of sweeteners can also be an important cash crop. It has a wide range of medicinal value. Literature said that, it does not increases blood sugar level. Thus with the increasing trends of diabetic patients, extracts of it can be a better option for the people. On the other hand, this plant is well tolerant to salt. Thus it can also be a better option for the southern coastal belt of the country. However, the crop demands more research in this climate and socio-economic conditions.

REFERENCES

Ahamed, A.; Seiji T.; Mamiko, O. and Taisano, A. 2001. An Artificial Sweetener stimu lates the sweet taste in insect: Dual effects of glycyrrhizin in phorma regina. *Chem. Senses,* **26**: 507-515.

Alagawany, M.; Elnesr S.S. and Farag, M.R. 2018. Use of liquorice (*Glycyrrhiza glabra*) in poultry nutrition: Global impacts on performance, carcass and meat quality. *World's Poultry Science Journal,* **75**(2): 293-304.

Alagawany, M.; Elnesr, S. S.; Fara, M. R.; El-Hack, M. E. A.; Khafaga, A. F.; Taha, A. E.; Tiwari, R.; Yatoo, M. I.; Bhatt, P.; Marappan, G. and Dhama, K. 2019. Review Use of Licorice (*Glycyrrhiza glabra*) Herb as a Feed Additive in Poultry: Current Knowledge and Prospects. *Animals,* **9**: 536. doi:10.3390/ani9080536

Albermann, M. E.; Musshoff, F.; Hagemeier, L. and Madea, B. 2010. Determination of glycyrrhetic acid after consumption of liquorice and antioxidant activity. *Journal of Natural Products*, **66**(4):477–480.

Al-Razzuqi R. A. M.; Al-Jawad F. H.; Al- Hussaini J. A. and Al-Jeboori A. A. 2012. Hepatoprotective effect of *Glycyrrhiza Glabra* in Carbon Tetrachloride-Induced Model of acute liver injury. *J. Phys. Pharm. Adv.,* **2**(7): 259-263.

Anagha, K.; Manasi, D.; Priya, L. and Meera, M. 2014. Scope of *Glycyrrhiza glabra* (Yashtimadhu) as an Antiviral agent: A Review. *Int. J. Curr. Microbiol. App. Sci*., **3**(12): 657-665.

Anonymous, 2018. Medicinal Plants. Web portal of Ikisan Agri-Informatics and Services. Division Web Portal. Nagarjuna Agricultural Research & Development Institute (NARDI) Nagarjuna Hills, Hyderabad- 500 082. India.

Aprasidi, G.S. (1978). Ref Zh 4 [55] 747. In Rao, K.V.S. 1993. A review on Liquorice *Ancient Science of Life*. **13** (1 & 2): 57-88.

Armanini, D.; Fiore, C.; Mattarello, M. J.; Bielenberg, J. and Palermo, M. 2002. History of the endocrine effects of Liquorice . *Experimental and Clinical Endocrinology & Diabetes*, **110**(06): 257-261.

Arya, Sarita; Rathi, N and AryArya, I.D. 2009. Micropropagation Protocol for *Glycyrrhiza glabra* L. *Phytomorphology,* **59** (1&2) : p.71-76.

Bahmani, M.; Rafieian-Kopaei, M.; Jeloudari, M.; Eftekhari, Z.; Delfan, B.; Zargaran, A., and Forouzan, S. 2014. A review of the health effects and uses of drugs of plant Liquorice (*Glycyrrhiza glabra* L.) in Iran. *Asian Pacific Journal of Tropical Disease*, **4**: S847-S849.

Bardhan, K. D.; Cumberland, D. C.; Dixon, R. A. and Holdsworth, C. D. 1978. Clinical trial of deglycyrrhizinised liquorice in gastric ulcer. *Gut*, **19**(9):779-82. (https://pubmed.ncbi.nlm.nih.gov/361512/)

Biondi, D. M.; Rocco, C. and Ruberto, G. 2003. New dihydrostilbene derivatives from the leaves of *Glycyrrhiza glabra* and evaluation of their antioxident activity, *J. Nat. Prod.,* **66(4)**:477-480.

Carmines, E. L.; Lemus, R. and Gaworski, C. L. 2005. "Toxicologic evaluation of Liquorice extract as a cigarette ingredient," *Food and Chemical Toxicology*, **43** (9):1303-1322.

Chakravarthi, K. K. and Avadhani, R. 2013. Beneficial effect of aqueous root extract of *Glycyrrhiza glabra* on learning and memory using different behavioral models: An experimental study. *Journal of Natural Science Biology and Medicine*, **4**(2): 420-425.

CIMAP. 1982. Annual Report 1981-82. Central Inst. of Medicinal & Aromatic Plants, Lucknow, India, p.41.

Dagar, J.; Yadav, R.; Dar, S. R. and Ahmad, S. 2015. Liquorice (*Glycyrrhiza glabra*): A potential salt-tolerant, highly remunerative medicinal crop for remediation of alkali soils. *Current science*, **108**:1683-1688.

Damle, M. 2014. *Glycyrrhiza glabra* (liquorice)-A potent medicinal herb. *International Journal of Herbal Medicine*, **2**(2): 132-136.

De Mastro, G. 1993. Influence of Temporary Intercropping on the Productivity of Liquorice (*Glycyrrhiza glabra* L.). *Acta horticulturae*, **10:** 523-528.

Dhingra, D. and Sharma, A. 2006. Antidepressant-like activity of *Glycyrrhiza glabra* L. in mouse models of immobility tests. *Progress in Neuro Psychopharmacology and Biological Psychiatry*, **30**(3): 449-454.

Di Paola, R.; Menegazzi, M.; Mazzon, E.; Genovese, T.; Crisafulli, C.; Dal Bosco, M. and Cuzzocrea, S. 2009. Protective effects of glycyrrhizin in a gut hypoxia (ischemia)-reoxygenation (reperfusion) model. *Intensive Care Medicine*, **35**(4): 687–697.

Douglas, J.A.; Douglas, M.; Lauren, D. R. and Martin, R. J. 2004. Effect of plant density and depth of harvest on the production and quality of Liquorice (*Glycyrrhiza glabra*) root harvested over 3 years. *New Zealand Journal of Crop and Horticultural Science,* **32**(4): 363-373.

Egamberdieva, D. and Mamedov, N.A. 2015. Potential Use of Liquorice in Phytoremediation of Salt Affected Soils. In: Öztürk M., Ashraf M., Aksoy A., Ahmad M., Hakeem K. (eds) Plants, Pollutants and Remediation. Springer, Dordrecht.

FAO, 2005. Evaluation of certain food additives. In Sixty-third report of the Joint FAO/WHO Expert Committee on Food Additives. Singapore: World Health Organization.

Fiore, C. M.; Eisenhut, E.; Ragazzi, G. Z. and Armanini, D. 2005. A history of the therapeutic use of liquorice in Europe. *Journal of Ethnopharmacology*, **99**(3): 317-324.

Fiore, C.; Eisenhut, R.; Krausse, M.; Ragazzi, E.; Pellati, D.; Armanini, D.and Bielenberg, J. 2008. Antiviral Effects of *Glycyrrhiza* species. *Phytopthera Research*, **22**: 141-148.

Fukui, H.; Goto, K. and Tabata, M. 1988. Two antimicrobial flavanones from the leaves of *Glycyrrhiza glabra*. *Chemical & Pharmaceutical Bulletin*, **36**(10): 4174-4176.

Gloria, M.B.A. 2003. Sweeteners. in Encyclopedia of Food Sciences and Nutrition (Second Edition) 2003. pp. 42-47.

Gupta, V. K.; Fatima, A.; Faridi, U.; Negi, A. S.; Shanker, K.; Kumar, J. K. and Khanuja, S. P. S. 2008. Antimicrobial potential of *Glycyrrhiza glabra* roots. *Journal of Ethnopharmacology*, **116**(2): 377-380.

Halder, R. M. and Richards, G. M. 2004. Topical agents used in the management of hyperpigmentation. *Skin Therapy Letter*, **9**(6): 1-3.

Harwansh, R. K.; Patra, K. C.; Pareta, S. K.; Singh, J. and Biswas, R. 2011. Pharmacological studies of *Glycyrrhiza glabra*: A review. *Pharmacology*, **2**: 1032-1038.

Hayashi, H. 2009. Molecular biology of secondary metabolism: case study for *Glycyrrhiza* plants. In: Kirakosyan A, Kaufman PB (eds) Recent advances in plant biotechnology. Springer, New York/Dordrecht, pp. 89-103.

Hayashi, H. and Sudo, H. 2009. Economic importance of Liquorice. *Plant Biotechnology*, **26**(1):101-104.

Herrera, M.; Herrera, A. and Arino, A. 2009. Estimation of dietary intake of ochratoxin A from liquorice confectionery. *Food and Chemical Toxicology*, **47**(8): 2002-2006.

Hosseini, M.S.; Samsampour, D.; Ebrahimi, M.; Abadía**,** J. and Morteza, K. 2018. Effect of drought stress on growth parameters, osmolyte contents, antioxidant enzymes and glycyrrhizin synthesis in Liquorice (*Glycyrrhiza glabra* L.) grown in the field. *Phytochemistry*, **156**: 124-134.

Huo, H. Z.; Wang, B.; Liang, Y. K.; Bao, Y. Y. and Gu, Y. 2011. Hepatoprotective and antioxidant effects of Liquorice extract against CCl(4) induced oxidative damage in rats. *International Journal of Molecular Sciences*, **12**(10): 6529-6543.

Kim, S. H. and Park, M. J. 2012. Effects of phytoestrogen on sexual development. *Korean Journal of Pediatrics*, **55**(8): 265-271.

Krausse, R.; Bielenberg, J.; Blaschek, W. and Ullmann, U. 2004. In-vitro anti Helicobacter pylori activity of extractum liquiritiae, glycyrrhizin and its metabolites. *Journal of Antimicrobial Chemotherapy*, **54**(1): 243-246.

Kukreja, A. K.1998. In vitro propagation of liquorice (*Glycyrrhiza glabra* L.) through multiple shoot formation. *Journal of Spices and Aromatic Crops,* **7**(1): 13-17.

Kumar, B. S.; Hemalatha, T.; Deepachitra, R.; Raghavan, R. N.; Prabu, P. and Sastry, T. P. 2015. Biphasic calcium phosphate-casein bone graft fortified with Cassia occidentalis for bone tissue engineering and regeneration. Indian Academy of Sciences. 38.

Lee, C. S.; Kim, Y. J.; Lee, M. S.; Han, E. S. and Lee, S. J. 2008. 18β Glycyrrhetinic acid induces apoptotic cell death in SiHa cells and exhibits a synergistic effect against antibiotic anti cancer drug toxicity. *Life Sciences*, **83**(13-14): 481-489.

Li, Y.; Feng, L.; Song, Z. F.; Li, H. B. and Huai, Q. Y. 2016. Synthesis and anticancer activities of glycyrrhetinic acid derivatives. *Molecules*, **21**(2):199. Lim, T. K. 2015. *Glycyrrhiza glabra. Edible Medicinal and Non-Medicinal Plants*. **22**: 354-457.

Marzi, V.; Ventrelli, A. and De Mastro, Giuseppe. 1993. Influence of Intercropping and Irrigation on Productivity of Liquorice (*Glycyrrhiza glabra* L.). *Acta* Horticulturae, **331**: 71-78. 10.17660/ActaHortic.1993.331.10.

Mirkin, B.M.; Antipov, E.A. and Sangitov, S.I. 1971. *Rastit Resur,* **7** (3): 417- 420. Mohammed, N. and Rehman, S. 1985. Cultivation of Liquorice in irrigated and rainfed sanddunes. *Pakistan J. Agricultural Research*, **6**(3): 176-179.

Nomura, T.; Fukai, T. and Akiyama, T. 2002. Chemistry of phenolic compounds of Liquorice (*Glycyrrhiza* species) and their estrogenic and cytotoxic activities. *Pure Appl. Chem.,* **74**(7):1199-1206. .

Ohtsuki, K.; OhIshi, M. and Nagata, N. 1992. The stimulatory and inhibitory effects of glycyrrhizin and a glycyrrhetinic acid derivative on phosphorylation of lipocortin by A kinase *In vitro*. *Biochemistry International*, **28**(6): 1045 -1053.

Ojha, S.; Golechha, M.; Kumari, S.; Bhatia, J. and Arya, D. S. 2013. *Glycyrrhiza glabra* protects from myocardial ischemia–reperfusion injury by improving hemodynamic, biochemical, histopathological and ventricular function. *Experimental and Toxicologic Pathology*, **65**(1-2): 219-227.

Ocampo, C.L.; Gomez-Verduzco, G.; Tapia-Perez, G.; Gutierrez, O.L. and Sumano, L.H. 2016. Effects of Glycyrrhizic Acid on Productive and Immune Parameters of Broilers. *Rev. Bras. Cienc. Avic.*, **18** : 3.

Omer, M.O.; Al Malki, W.H.; Shahid, I.; Khuram, S. Altaf, I. and Imran S. 2014. Comparative study to evaluate the anti-viral efficacy of *Glycyrrhiza glabra* extract and ribavirin against the Newcastle disease virus. *Phcog Res*., **6**:6-11.

Ozturk, M.; Altay, V. ; Hakeem, K. and Akcicek, E. 2017. Liquorice: From Botany to Phytochemistry (Anglais) Broche. Springer.

Pastorino, G.; Cornara, L.; Soares, S.; Rodrigues F. and Oliveira, M.B.P.P. 2018. Liquorice (*Glycyrrhiza glabra*): A phytochemical and pharmacological review. *Phytotherapy Research*, **32**: 2323-2339.

Pohtam, I; Anuradha, K.N. and Devraj, K.C. 2019. Need for sustainable utilization and conservation of *Glycyrrhiza glabra* Linn: A review. *International Journal of Research and Review*, **6**(11): 271-274.

Rackova, L.; Jancinova, V.; Petrikova, M.; Drabikova, K.; Nosal, R.; Stefek, M. and Kovacova, M. 2007. Mechanism of antiinflammatory action of liquorice extract and glycyrrhizin. *Natural Product Research*, **21**(14): 1234-1241.

Rittenhouse, H. N. 1895. The cultivation of Liquorice root in the United States. *The American Journal of Pharmacy*, Vol. 67.

Rizzato, G.; Scalabrin, E.; Radaelli, M.; Capodaglio, G. and Piccolo, O. 2017. A new exploration of Liquorice metabolome. *Food Chemistry*, **221**: 959-968.

Saeedi, M.; Morteza S.K. and Ghoreishi, M. R. 2003. The treatment of atopic dermatitis with Liquorice gel. *The Journal of Dermatological Treatment,* **14**(3): 153-157.

Shah, P.R. and Dalal, K.C. 1982. Proceedings of Plant Tissue Cult. 5th Meet. 685-686.

Shalaby, A. M.; Ibrahim, H. S.; Mahmoud, E. M. and Mahmoud, A. F. 2004. Some effects of *Glycyrrhiza glabra* (liquorice) roots extract on male rats. *Egyptian Journal of Natural Toxins,* **1:** 83-94.

Sharma, P.C.; Yelne, M.B. and Dennis,T.J. 2005. Database on medicinal plants used in ayurveda. Vol 3. 2nd ed. New Delhi: Central Council for Research in Ayurveda & Siddha, pp.561- 66.

Sharma, V. and Agrawal, R. C. 2017a. *Glycyrrhiza glabra*- A Plant for Future. *Mintage journal of Pharmaceutical & Medical Sciences*, **2**(3): 15-20.

Sharma, V.; Agrawal, R. C. and Shrivastava, V. K. 2014. Assessment of median lethal dose and anti mutagenic effects of *Glycyrrhiza glabra* root extract against chemically induced micronucleus formation in Swiss albino mice. *International J. of Basic & Clinical Pharmacology*, **3**(2): 292-297.

Sharma, V. and Agrawal, R. C. 2017b. In vivo antioxidant and hepatoprotective potential of *Glycyrrhiza glabra* extract on carbon tetra chloride (CCl4) induced oxidativestress mediated hepatotoxicity. *International Journal of Research in Medical Sciences*, **2**(1):7.

Sharma, V.; Katiyar, A. and Agrawal, R. C. 2016. *Glycyrrhiza glabra*: Chemistry and pharmacological activity. In J.M. Merillon & K. G. Ramawat (Eds.), Sweeteners: Pharmacology, biotechnology, and applications Cham: Springer International Publishing, pp.1-14.

Simmler, C.; Pauli, G. F. and Chen, S. N. 2013. Phytochemistry and biological properties of glabridin. *Fitoterapia*, **90**:160-184.

Singh, A.K.; Sharma, A.; Kumar, P. and Virmany, O.P. 1984. Liquorice cultivation. *Current Research on Medicinal and Aromatic Plants*, **6**(3): 98-105.

Singh, V.; Pal, A. and Darokar, M. P. 2015. A polyphenolic flavonoid glabridin: Oxidative stress response in multi drug resistant Staphylococcus aureus. *Free Radical-Biology and Medicine,* **87**: 48-57.

Siracusa, L.; Saija, A.; Cristani, M.; Cimino, F.; D'Arrigo, M.; Trombetta, D. and Ruberto, G. 2011. Phytocomplexes from liquorice (*Glycyrrhiza glabra* L.) leaves-Chemical characterization and evaluation of their antioxidant, anti-genotoxic and anti-inflammatory activity. *Fitoterapia,* **82**(4): 546-556.

Solano, F.; Briganti, S.; Picardo, M. and Ghanem, G. 2006. Hypopigmenting agents: An updated review on biological, chemical and clinical aspects. *Pigment Cell Research,* **19**(6): 550-571.

Takii, H.; Kometani, T.; Nishimura, T.; Nakae, T.; Okada, S. and Fushiki, T. 2001. Antidiabetic effect of glycyrrhizin in genetically diabetic KKAy mice. *Biological & Pharmaceutical Bulletin,* **24**(5): 484-487.

Tian, J.; Liu, W.; Zhen, Z. and Tong, X. 2013. Successful treatment of latent autoimmune diabetes in adults with traditional Chinese medicine: A case report. *Journal of Traditional Chinese Medicine*, **33**(6): 766-769.

Tong, X.; Xie, Q.; Rong, G.; Zhou, S. and Meng, Q. 2015. Detection of consensuses and treatment principles of diabetic nephropathy in traditional Chinese medicine: A new approach. *Journal of Traditional Chinese Medical Sciences*, **2**(4): 270-283.

Trease and Evans.1983. Text book of pharmacognosy. Bailliere and Tindal Publication, Baltimore.

Varnov, L.A. and Gladyshev, A.I. 1989. Cultivation of Liquorice on soil stabilization. *Probl. Osvo. Pustyn.*, **4**: 30-40.

Varsha, A. R. and Sonam, P. 2013. Phytochemical screening and determination of anti-bacterial and anti-oxidant potential of *Glycyrrhiza glabra* root extracts. *Journal of Environmental Research and Development*, **7**(4A): 1552-1558.

Wal, P.; Pal, R.S. and Wa, l. A. 2018. A review on the sugar alternates. *Int. J. Pharm. ci. & Res*., **10**(4): 1595-04.

Wang, L.; Yang, R.; Yuan, B.; Liu, Y. and Liu, C. 2015. The antiviral and antimicrobial activities of Liquorice, a widely used Chinese herb. *Acta Pharm. Sin. B.,* **5**(4): 310-315.

Wang, S.; Shen, Y.; Qiu, R.; Chen, Z. and Chen, W. 2017. 18 β-glycyrrhetinic acid exhibits potent antitumor effects against colorectal cancer via inhibition of cell proliferation and migration *Int. J. Oncol*., **51**(2):615-624.

Wang, X. R.; Hao, H. G. and Chu, L. 2017. Glycyrrhizin inhibits LPS induced inflammatory mediator production in endometrial epithelial cells. *Microbial Pathogenesis*, **109**: 110-113.

Xiao, Y.; Xu, J.; Mao, C.; Jin, M.; Wu, Q.; Zou, J.; … Zhang, Y. 2010. 18β Glycyrrhetinic acid ameliorates acute Propionibacterium acnes induced liver injury through inhibition of macrophage inflammatory protein 1. *The Journal of Biological Chemistry,* **285**(2): 1128-1137.

Yang, R.; Yuan, B. C.; Ma, Y. S.; Zhou, S. and Liu, Y. 2017. The anti-inflammatory activity of Liquorice, a widely used Chinese herb. *Pharmaceutical Biology,* **55**(1), 5-18.

Yin, X.; Gong, X.; Zhang, L.; Jiang, R.; Kuang, G.; Wang, B.; … Wan, J. 2017. Glycyrrhetinic acid attenuates lipopolysaccharide induced fulminant hepatic failure in d galactosamine sensitized mice by up regulating expression of interleukin 1 receptor associated kinase M. *Toxicology and Applied Pharmacology,* **320:** 8-16.

Yokota, T.; Nishio, H.; Kubota, Y. and Mizoguchi, M. 1998. The inhibitory effect of glabridin from Liquorice extracts on melanogenesis and inflammation. *Pigment Cell Research*, **11**(6): 355-361.

Yu, J.Y.; Ha, J.Y.; Kim, K.M.; Jung, Y.S.; Jung, J.C. and Oh, S. 2015. Anti-Inflammatory Activities of Liquorice Extract and Its Active Compounds, Glycyrrhizic Acid, Liquiritin and Liquiritigenin, in BV2 Cells and Mice Liver. *Molecules*, **20**:13041-13054.