

REVIEW

***Glycyrrhiza glabra* L. (Liquorice)**

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Abstract: Medicinal plants are being used for treating various diseases. According to World Health Organization 80% of the world population depends on indigenous medicinal plant remedies. Herbal medicine employs fruits, vegetables, as dry materials or their extracts for the treatment of different diseases and health maintenance. *Glycyrrhiza glabra* (Liquorice) has been used in Europe since prehistoric times. It is well documented in written form starting with the ancient Greeks. Glycyrrhizin is the major active constituent obtained from liquorice roots, one of the most widely used in herbal preparations for the treatment of liver complaints. The plant is used as anti-inflammatory, spasmolytic, laxative, anti-depressive, anti-ulcer and anti-diabetic. The present review focuses *Glycyrrhiza glabra* distribution, ethno botany, ethno pharmacology, chemical constituents, medicinal uses, cultivation and trade. Plant requires a lot of attention as it has been reduced in population due to over-use in Baluchistan. The plant conservationists should consider this herb as priority species and should start its cultivation on the commercial scale to fulfill the requirements of the local markets and pharmaceutical industries as well as reduce the pressure on the wild plants.

Keywords: *Glycyrrhiza glabra* L. natural constituents, medicinal uses, conservation and sustainable marketing, Pakistan.

INTRODUCTION

Liquorice is a perennial herb native to the Mediterranean region, central to southern Russia and Asia Minor to Iran. The distribution of *Glycyrrhiza* species in Pakistan i.e. Baluchistan (Shahrig and Harnai), Ziarat (1980m) and Booni (2200m), Parkusap (2450m), Chapali (2600m) and Chunarhun valley in Tehsil Mustuj, Chitral. It has been introduced into the Punjab and Sind plains. Ali (1977) reported in *Flora of West Pakistan* that *Glycyrrhiza* is a genus of about 30 species but in Pakistan it is represented by three species, *G. triphylla*, *G. uralensis*, *G. glabra*.

The local names of *Glycyrrhiza glabra* L. *Jashtimadhu* (Bangla); *Muleti* (Punjabi); *MithiKathi* (Sindhi); *Khosha Walgi* (Pushto); *Rub-us-soos* (Arabic); *Bikhemahaka* (Persian); *Moyo* (Chitrali). Vernacular names: Liquorice (English); *Bois doux* (French), *Regalizia* (Spanish). Pharmaceutical and Trade names: *Liquirtiae radix*. *Radix Liquirtiae* (Latin); Parts used, rhizomes, rootlets and stolons.

Dymock (1972) stated that it grows wild in Afghanistan Iran and Saudi Arabia. It is widely distributed in Eurasia, extending to Australia, North America and temperate regions of South America. In Eurasia around 20 spp. occur, among them five confined to Europe. Other highly exploited species are *G. uralensis* that extends from western to eastern Siberia, as well as across central Asia to Mongolia i.e. *G. echinata* with an area extending from

the Balkans across Asia Minor to South-eastern Russia and western Siberia and *G. palliflora* native to Far East and China (Lange, 1998). *G. asperima* (Russia, Central Asia); *G. astragalina* (Chili); *G. bucharica* (Central Asia); *G. echinata* (Sicily, Syria).

It has been well known in pharmacy for many years. In old Chinese pharmacy, it was considered as drugs of the first class and to it was ascribed the rejuvenating property when consumed for long periods. In ancient Egypt, Greece and Rome licorice was frequently used. It was referred by Theophrastus. Its use from then, till today, proves its efficacy. The material of commerce comes from wild plants and "semi wild" plants cultivated in the former U.S.S.R., Turkey, Iran, China, India, Pakistan, Afghanistan, Syria, Italy and Spain (Bruneton, 1995; Karnick, 1994; Leung and Foster, 1996; Wichtl and Bisset, 1994).

The licorice grows in subtropical climates in rich soil to a height of 1.4m. It has oval leaflets, white to purplish flower clusters and flat pods. Below ground, it has an extensive root system with a main taproot and numerous runners. The main taproot, which is harvested for medicinal use, is soft, fibrous, and has a bright yellow interior. It is valuable herbal drug. It can be cultivated on marginal lands of Pakistan.

Cultivation

Liquorice grows naturally in different parts of Baluchistan, Chitral and Hindu Kush Himalayan areas. Its roots from Chitral are thick and quality is similar to Chinese liquorice and most suited for commercial exploitation (Zaidi, 1999; Rizvi and Saeed, 2005; Rizvi *et*

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al., 2007). In Pakistan no attention is being paid to the systematic cultivation and collection of medicinal plants neither any authentic data is available except some limited publications published in *Pakistan Journal of Forestry*. There is no national overview in the country with regard to which species should be cultivated though numerous suggestions have been made at the institutional level and even promoted through research and development in this respect (Williams and Ahmed, 1999). Cultivation trials of various medicinal plants were made at Pakistan Forest Institute (PFI) and the yield of roots of *G. glabra* was 4200 lbs/acre, while the active principle glycyrrhizin was 1.2% with 10% glucose (Zaman *et al.*, 1972). The Baluchistan province offers a very suitable habitat for its cultivation (Said, 1978). Medicinal plants can provide better income to the local people than the traditional crops of the areas, if the markets system for the medicinal plants is improved and cultivation of medicinal plants is done on scientific lines. *Foeniculum vulgare* and other plants were cultivated, but not on large scale. This herb should be cultivated at Arkari; Golengol valleys in Chitral (Marwat, 1997). It requires a deep well cultivated fertile moisture-retentive soil for good production. Plants are hardy to about -15°C (Huxley, 1992). It preferred a sandy soil with abundant moisture and did not flourish in clay (Grieve, 1979). The herb thrived in a maritime climate (Chiej, 1984). Liquorice is often cultivated for its edible root, widely used in medicine and as flavouring. *Glycyrrhiza glandulifera* grows in Russia and produces adventitious roots up to 10cm thick (Brouk, 1975). This species has a symbiotic relationship with certain soil bacteria, these bacteria form nodule on the roots and fix atmospheric nitrogen. Some of this nitrogen is utilized by the growing plant but some can also be used by other plants growing nearby. Mohammad and Rehman (1985) reported that liquorice was grown at irrigated and rainfed sand dune areas of Mastung during 1981-82 and after 1 year the survival percent for these two areas were 92 and 85%, respectively. Growth of roots and rhizomes enhanced significantly in the first two years. It was concluded from the study that this plant could prove a suitable forage plant for sand dune stabilization in Mastung area. Generally, rhizomes and roots are dug up in October preferably from the plants, which have not borne the fruits. Buds and rootlets are removed and the drug is washed. Some pieces are peeled and divided into small pieces. The drug is dried first under sun and then in shades during which it loses about 50 % of its weight.

Propagation

Pre-soak the seed for 24 hrs in warm water and then sow in spring or autumn in a greenhouse. Prick out the seedlings into individual pots when they are large enough to handle and grow them on for their first winter in a greenhouse. Plant out in late spring or early summer when in active growth. Division of the root is done in spring or autumn. Each division must have at least one growth bud.

Autumn divisions can either be replanted immediately or stored in clamps until the spring and then be planted out (Huxley, 1992). According to some other studies the propagation of the plant was done with young pieces of stolons and each piece exhibit 2-3 buds of aerial shoot. The plant requires a soil 1.4m deep or more, having a light, loamy and stone-free texture. It is grown continuously on the same land. The pieces of stolons are planted in March at 0.91m distance. The fertilizers are used when the green parts are developing. The crop is kept free of weeds. The roots are harvested 3-4 years after planting when they show sufficient growth. The plants are produced from runners or underground stems which are cut into pieces 4 inches long, each with at least 2 buds. Dry conditions at planting time and for the next two months give best chance for a good crop. If cold weather prevails in May or June, some percentage of the crop may fail to grow. This forms one of the chief hazards of liquorice occupying the land for a period of five, or sometimes four years. A yield of two tons of roots per acre for bailing, plus 3-4 cwt of trimmings is considered satisfactory (Chopra and Chopra, 2006).



Fig. 1: *Glycyrrhiza glabra* in the field.

Microscopic evaluation

Stolon- T.S showed cork was consisted of 10-20 or more layers of tabular cells, outer layer with reddish-brown amorphous contents, inner 3 or 4 rows had thicker, colorless walls; secondary cortex usually of 1-3 layers of radially arranged parenchymatous cells contained isolated prisms of calcium oxalate; secondary phloem with abroad

band, cells of inner part cellulosic and outer lignified, radially arranged groups of about 10-50 fibers, surrounded by a sheath of parenchyma cells, each usually had prisms of calcium oxalate about 10-35 μ long; cambium formed tissue of 3 or more layers of cells; secondary xylem distinctly radiated with medullary rays, 3-5 cells wide, vessels 80-200 μ in diameter with thick, yellow, those of phloem; xylem parenchyma of two kinds, those between the vessels had thick pitted walls without inter-cellular spaces, the remaining with thin walls; pith of parenchymatous cells in longitudinal rows, with inter cellular spaces. **Root-** T.S showed structure of closely resembling that of stolon except that no medulla was present; xylem tetrarch; usually four principal medullary rays at right angles to each other; in peeled drug cork showed phelloderm and sometimes without secondary phloem; all parenchymatous tissues had abundant, simple oval or rounded starch grains, 2-20 μ in length (Vispute and Khopade, 2011).

Trade

Crude plant-based drugs worth of about Rs. 120 million per year in Pakistan (Marwat, 1997). This is a good indicator of the potential economic value of medicinal plants. Aromatic and medicinal plants have market of considerable size both nationally and internationally. The main markets of crude herbal drugs are in KP (Mingora, Dir and Peshawar), Punjab (Rawalpindi, Bahawalpur, Lahore, Faisalabad and Multan) and Sindh (Sukkar, Hyderabad and Karachi). Peshawar market acted as supply Centre of herbal drugs to various herbal markets in the country. This market received liquorice from Afghanistan. The consumption of *Glycyrrhiza glabra* (roots) in Pansar Markets of Pakistan was 2506t /annum and approximate value in 000(Rs), 16289 were recorded. *Glycyrrhiza glabra* (rhizome) was consumed 6500kg @ Rs 24/kg in 1997. The traders were unwilling to disclose exact volumes of trade for fear that information will be passed on to the tax authorities (Khan, 1985). However, it is known that trade in herbal materials is monopolized by wholesale drug dealers in most of the markets with the remaining shopkeepers and dispensers relied on the wholesalers for their supplies, export of herbal products from Pakistan was constraint by quality considerations, which often fail to conform to the standards required by the importing countries. Exports were made sporadically to Dubai, France, Germany, Hong Kong, Korea, India, Italy, Japan, Saudi Arabia, Singapore, Sri Lanka, Switzerland, UK and USA and are largely channeled through the Karachi market. Around ten companies were involved with the export of medicinal plants (Williams and Ahmed, 1999). Medicinal plants are not only used exclusively in the indigenous system of medicines but find extensive use in the allopathic system of medicine including *Glycyrrhiza*. Leading drug dealers in Pakistan imported more than 90% of the herbs from Sri Lanka, China, India and Afghanistan. The present export price of

glycyrrhizic acid is about \$120/kg while that of glycyrrhetic acid about \$250/kg. The demand for these two drugs together in the European countries is estimated to be over 2500kg/ year. To produce these quantities of active principles, 300 tons of *Glycyrrhiza* roots will be required. It could be cultivated on waste/marginal lands (Shinwari *et al.*, 2003).

Ethno pharmacology

The dried rhizome and root have been used as expectorant and carminative by the Egyptian, Chinese, Greek, Indian and Roman civilizations. The *Materia Medica* mentioned as bronchitis, emollient, emmenagogue, expectorant demulcent, diuretic, haemoptysis, laryngitis, laxative etc. It is beneficial in sore throat, soreness, cough, influenza, cold, bronchodilator, ophthalmia, anti-syphilitic, and anti-dysenteric. It is effective in gastric imbalance, indigestion, vomiting, diarrhea, parched throat, swollen abscesses and act as diuretic (Usmanghani, 1997).

Ethno botanical studies

Men collected liquorice roots in September to November in tehsil Mustuj, District Chitral and about 1kg roots were boiled in 2L water for 45min. The yellowish white and sweet decoction was cooled and used as purgative and for cough. This was also used as a purgative for cows, goats and sheeps. It increased the milk production in cows and goats. *Glycyrrhiza glabra* locally called *Khāwāsā* was used as a cough suppressant, throat dryness and as a tonic in southern Baluchistan. The local people said that snakes were attracted to the plants and that by rubbing against it they could spread their poison. Thus, it is extremely important to remove the root bark before it is chewed. In the not too distant past this plant was common in the wild throughout Baluchistan, but due to over-exploitation it is now rare. Currently the best place to find wild populations is between Kalat and Nushki (Goodman and Ghafoor, 1992). Zaman and Khan (1970) described the ethno botanical uses of this plant in Pakistan and some of the uses agree with Usmanghani (1997); Goodman and Ghafoor (1992). Blatter *et al.* (1919) mentioned that in Baluchistan it is mixed with other drugs for derangements of the blood.

Systemic uses of liquorice: Oral doses

Liquorice can be orally used for gastric, duodenal and esophageal ulceration, inflammation, cathartics, mouth ulcer, spasmolytic, anti-tussive, demulcent, expectorant and constituents made it an ideal herb for respiratory disorderness. It is used in asthma, acute and chronic bronchitis and chronic cough. It is effective in Addison's disease. Liquorice extracts can be used topically for inflammatory skin disorder, mouth ulcers and oral hygiene. It is used in the prevention of carcinogenesis and depression. This is not yet verified for oral doses of liquorice (Bone, 1990).

Other uses

Licorice covered the acrid taste of many nauseous drugs such as senna, aloes, chloride of aluminium, senega, hyoscyamus and turpentine. It was employed in dyeing and tobacco industries. It is used as flavoring agent. Ammoniated *Glycyrrhiza* is used as a flavoring agent in beverages, confectionery and pharmaceuticals. It is also consumed in candy industry (Anilkumar *et al.*, 2012). Spasmolytic activity of glycyrrhizin (8%) was 1/500 that of papaverine. Antidyslipidemic activity of *Glycyrrhiza glabra* was observed in high fructose diet induced dyslipidaemic Syrian golden hamsters. Glycyrrhizin usually exists as salts of glycyrrhizic acid (glycyrrhizinic acid) and ammonia, iron or barium; the amount is 6-14%. Glycyrrhizin is a nonhemolytic saponin with foaming property (Vispute and Khopade, 2011).

Chemical constituents and scientific studies

Liquorice consisted of the dried roots of *G. glabra*. It had 2 to 9% sweet saponin known as glycyrrhizin. It has been investigated as a therapy for patients with human immuno-deficiency virus (HIV). A study showed the effects of glycyrrhizin in 42 hemophilia patients with HIV-1 infection. Patients showed improvement in their clinical symptoms (oral candidiasis, lymph node swelling & rash), immunological functions and liver functions (Mori *et al.*, 1990). Another study showed the long-term efficacy in 84 patients with chronic hepatitis C (Arase *et al.*, 1997). The Pharmacopoeia Licorice root had not less than 4% glycyrrhizic acid. Its water-soluble extractive content must be not less than 20% (Bruneton, 1995; IP, 1996; Ph.Eur.3, 1998; Wichtl and Bisset, 1994). The *Japanese Pharmacopoeia* required not less than 25% dilute ethanol-soluble extractive (JP XII, 1993). Glycyrrhetic acid (GA), the aglycone of glycyrrhizin (GL), is also present in the roots about 0.5 to 0.9%. Flavonoids impart yellow color to the roots. Liquiritin is the main flavonoid glycoside present in the roots, on heating is converted to isoliquiritigenin.

In the late 1940s a Dutch doctor named Revers' study led to the investigation of glycyrrhizin and glycyrrhetic acid as the constituents responsible for ulcer healing and GA also showed local anti-inflammatory activity. The English scientists developed a semi-synthetic derivative called carbenoxolone (CB), which was effective for gastric and duodenal ulcers. It caused the same side-effects as liquorice and glycyrrhizin and its use rapidly diminished when cimetidine, the first of the acid inhibitors, became available. CB was chemically and pharmacologically similar to GL. CB showed mineralocorticoids properties. However, it only had a weak affinity for steroid receptors in tissues and probably acted by potentiating the effects of endogenous hormones. Some patients developed side-effects such as hypertension, oedema and hypokalemia. CB enhanced the defense mechanism and inhibited bacterial adherence to the injured urothelium. A CB gel

was used to treat mouth ulcer. De-glycyrrhizinized (DGL) was not completely free of GL it was a concentrated extract of liquorice (a soft extract) with a GL content not exceeding 3%. It had high level of flavonoids. It had spasmolytic effect in duodenal ulcer patients. In animal studies it prevented ulcer development, inhibited gastric acid secretion and protected the gastric mucosa against damage from aspirin and bile. DGL was widely used in the UK, in combination with conventional antacids, which may also contribute to the observed clinical effects (Bone, 1990).

A deglycyrrhizinized licorice (DGL) preparation was developed to provide some of the therapeutic benefits of licorice while reducing risk (D'Imperio *et al.*, 1978; Morgan *et al.*, 1982). DGL might be useful in maintenance therapy for patients with gastric ulcers, although its superiority compared to conventional drugs was questioned. In a two-year comparison study of a DGL product (Caved-S® tablets; two twice per day) and cimetidine, 400mg at night, 12% (4 of 34) of the DGL subjects had ulcer recurrence compared with 10% (4 of 41) of the drug group in the first year of treatment; in the second year, 29% (9 of 31) for DGL and 25% (8 of 32) for cimetidine (Morgan *et al.*, 1982). After termination of treatment in two years, ulcers recurred rapidly: 2 of 22 DGL patients and 7 of 23 cimetidine patients. The study concluded that long-term maintenance therapy was safe and reasonably effective. Licorice root had triterpenoid saponins (4-24%), mostly glycyrrhizin; flavonoids (1%), mainly the flavanones liquiritin and liquiritigenin, chalcones isoliquiritin, isoliquiritigenin and isoflavonoids (formononetin); amines (1-2%) asparagine, betaine, and choline; amino acids; 3-15% glucose and sucrose; starch (2-30%); polysaccharides; sterols; coumarins; resin and volatile oils (0.047%) (Bruneton, 1995; Bradley, 1992; Budavari, 1996; Leung and Foster, 1996; List and H'rhammer, 1973-1979; Newallet *et al.*, 1996; Wichtl and Bisset, 1994).

An extensive review of liquorice chemistry was published (Tang & Eisenbrand, 1992). Five pentacyclitriterpenoids were isolated from the minor constituents of local liquoriceroots (Elgamal *et al.*, 1990). An unusual biflavonoid named licoagrodin was isolated from the hairy root cultures of *G. glabra* along with three prenylatedretrochalcones, licoagrochalcones B, C, D, a prenylatedaurone, licoagroaurone and four known prenylated flavonoids, licochalcone C, kanzonol Y, glyinflanin B and glycyrdione A. From the glycosidic fraction, aiso flavone glycoside, licoagroside A, and a maltol glycoside, licoagroside B were isolated together with four known isoflavone glycosides, two flavone C-glycosides, and three other glycosides (Li *et al.*, 2000). The isoflavonesglabridin and hispaglabridins A and B had antioxidant activity and bothglabridin and glabrene possessed estrogen like activity (Kataria *et al.* 2013).

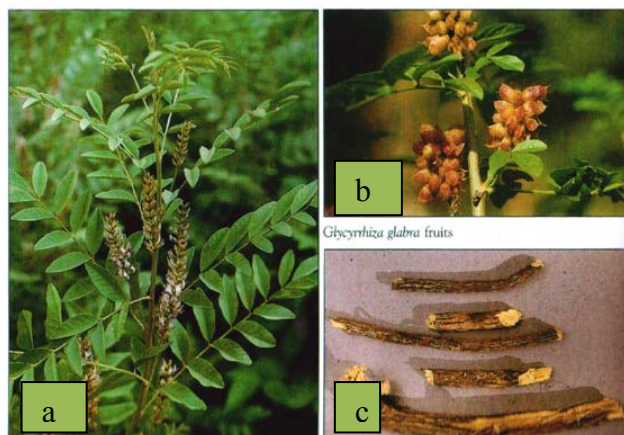


Fig. 2: *Glycyrrhiza glabra* (a) flowers, (b) fruits and (c) roots

Pharmacology: Glycyrrhizin and glycyrrhetic acid (GA)

In the 1950s, various studies led to the use in France of GA and liquorice for the treatment of rheumatoid arthritis. GA did not inhibit prostaglandins synthesis. It might inhibit the migration of white cells into sites of inflammation. Another more recent addition to the possible mechanism of the constituent glycyrrhizin's anti-inflammatory activity is due in part to its anti-thrombin action. GA but not GL showed a significant and special anti-tumour promoting activity by inhibiting the binding of tumour promoters to test cells. GA inhibited the growth of cultured mouse melanoma cells, but was cytostatic and not cytotoxic. It induced phenotypic reversion i.e., the cancer cell became more like a normal cell. GL but not GA inhibited virus growth and in some instances inactivated virus particles. It was active against herpes simplex virus, varicella-zoster virus and human immunodeficiency virus (AIDS virus). GL also induced interferon production *in vivo* and *in vitro*, but GA had only weak activity. Both GL and liquorice will be active as topical anti-viral agents especially for herpes simplex and shingles (Bone, 1990). Human studies have investigated efficacy in sub acute hepatic failure (Acharya *et al.*, 1993), chronic hepatitis C (Arase *et al.*, 1997), infectious hepatitis (Chang and But, 1986), hemophilia with HIV-1 infection (Mori *et al.*, 1990) and inhibition of HIV replication in patients with AIDS (Hattori *et al.*, 1989). In Japan, a preparation of GL, cysteine and glycine was used by injection for the treatment of acute and chronic hepatitis. GL was only active by injection as a protective agent for the liver. However, *in vitro* studies on hepatocytes showed that both GL and GA, were equally hepatoprotective. The clinical significance of oral doses of GL or liquorice in liver disease remained to be established. Oral doses of GA had an anti-tussive effect similar to codeine. GL inhibited bacteria plaque formation by *Streptococcus mutans*. In Chinese medicine, liquorice was considered to have an anti-toxic activity, and the

protective effect of GL against saponin toxicity was demonstrated. Long-term administration of GL to mice did not induce tumours (Bone, 1990). Studies revealed its effects in its traditional context as a component of multi-herb formulas, on testosterone secretion in patients with polycystic ovary syndrome (Takahashi *et al.*, 1988), on treating anxiety (Chen *et al.*, 1985) and on gastric and duodenal ulcer (Chang and But, 1986). The Commission E reported that glycyrrhizic acid and the aglycone of glycyrrhizic acid enhanced the healing of gastric ulcers. Secretolytic and expectorant effects were confirmed in tests on rabbits. In the isolated rabbit ileum, an antispasmodic action has been observed at concentrations of 1:2500-1:5000. The pseudo-aldosterone-like effects were attributed to the glycyrrhizic acid. The findings showed that the glycyrrhetic acid, the hydrolytic metabolite of glycyrrhizic acid, was the primary active component that caused inhibition of peripheral metabolism of corticoid, which binds to mineral corticoid receptors in the same way as aldosterone (Heikens *et al.*, 1995). The Commission E approved the internal use of licorice root for catarrhs of the upper respiratory tract and gastric or duodenal ulcers. The German Standard License approved licorice root infusions for loosening mucus, alleviating discharge in bronchitis, and as an adjuvant in treating spasmodic pains of chronic gastritis (Bradley, 1992; Braun *et al.*, 1997; Wichtl and Bisset, 1994). In France, licorice preparations might be used to treat epigastric bloating, impaired digestion and flatulence (Bruneton, 1995). The WHO recognized medicinal uses as being described in pharmacopeias and in traditional systems of medicine e.g., demulcent for sore throats, expectorant in treatment of cough and bronchial catarrh; prophylaxis, gastric and duodenal ulcers, dyspepsia; anti-inflammatory, rheumatism, arthritis, liver toxicity and to treat tuberculosis and adrenocorticoid insufficiency (WHO, 1999).

Antineoplastic action

Glycyrrhetic acid and its derivatives, 3-oxy-18- α -glycyrrhetic acid at 80mg/kg inhibited the transplanted Oberling-Guerin myeloma in rats. It was equipotent to that of cortisone 50mg/kg once daily. 18 α -Glycyrrhetic acid had antileukemic activity in mice, which was probably an adrenocorticomimetic action. Glycyrrhizin and liquiritin were able to elicit morphological changes of tumor cells in ascetic carcinoma of the liver in rats and Ehrlich ascites carcinoma in mice. Glycyrrhizin could inhibit the subcutaneously transplanted Jitian sarcomas, prevented the development in male mice of liver carcinoma induced by polyoxybenzidine as well as prevented liver carcinoma induced by 0.06% methylaminoazobenzene. The antineoplastic mechanism still unclear. In a study of the ultramicrostructural morphology of the liver cells of mice given glycyrrhizin showed an excellent restorative action. Dramatic reduction of transaminases (GOT and GPT) secreted by

liver cells had been obtained from the clinical use of glycyrrhizin. It was believed that glycyrrhizin enhanced the detoxicant action and resistance of the cells (Chang and But, 1986).

Antidiuretic action

Glycyrrhizin antidiuretic action was confirmed in rats wherein the reduction of sodium excretion was accompanied by a mild decrease in potassium excretion. Similar effects were observed in adrenalectomized rats and it suggested that the antidiuretic action of glycyrrhizin was mediated by adrenocortical hormones. Glycyrrhetic acid and its salts had antidiuretic effect. Some authors reported that the herb could increase the renal tubular reabsorption of sodium and chloride resulted in antidiuresis. The mode of action of the herb was different from that of deoxycorticosterone in that it probably acted directly on the renal tubules (Chang and But, 1986).

Analgesic action

FM 100 had a significant analgesic action in writhing mice. However, its action was weaker in pain threshold experiment on mice, wherein pressure was applied on the animal's tails. The action of the oral medication was even weaker.

Anticonvulsant action

A weak anticonvulsant action was shown by FM 100 against convulsions induced by pentylenetetrazole. FM 100 had analgesic, antispasmodic and gastric secretion inhibitory action. When used with paeonin (*Paeonia lactiflora*), which had sedative, antispasmodic and anti-inflammatory actions, a significant synergistic action was achieved. Hence, the use of the traditional prescription *Paeonia-Glycyrrhiza* decoction was justified.

Protective action on the function of the ear vestibule

Glycyrrhizic acid could combine with the alkaline group of streptomycin to reduce the damage on the vestibular nerve without affecting the antibacterial activity of the latter (Chang and But, 1986).

Compatibility of <Gancao> with other herbs

According to the concept of "Shiba Fan" (eighteen incompatible drugs) in traditional Chinese medicine, four herbs are incompatible with <Gancao> i.e., *Sargassum fusiforme*, roots of *Euphorbia peginensis*, *E. kansui* and flower buds of *Daphne genkwa*. In experiments it was shown that when the herb was used together with the flower buds of *D. genkwa*, a conflicting effect was resulted. Extract of these two herbs was much more toxic than their individual extracts. Moreover, the diuretic and cathartic actions of *genkwa* were inhibited. Low dosage of <Gancao> and the root of *E. peginensis* had decreased toxicity, whereas high dosage had increased toxic reactions. Another study showed that the combined use of <Gancao> and the root of *E. kansui* in guinea pigs caused

death. The roots of *D. genkwa*, *E. peginensis* and *E. kansui* in guinea pigs also caused toxic reactions or death. These findings served as a basis for some investigators to conclude that the four herbs were not incompatible with <Gancao> could increase toxic effects.

Eye inflammatory diseases

Sixty cases of herpetic keratitis, keratoconjunctivitis, and fascicular keratitis were treated with eye drops of the 5% sodium glycyrrhizin ate or the 8-12% suspension of glycyrrhetic acid or the 10-30% herb extract three to four times daily. In 4 cases of episcleritis and 5 cases of scleritis, the nodules disappeared in 3-17 days, and the inflammation subsided in 6-34 days. The therapeutic effects were also satisfactory in 6 cases of spring catarrhal keratitis but it relapsed upon discontinuation of medication. This was successfully controlled by repeating the treatment (Chang and But, 1986).

CONCLUSION

Pakistan is beautiful country where numbers of medicinal plants are naturally growing but no sustainable use of these plants. If these plants are systemically arranged for uses, post-harvest processing, storage and effective control and regulate the commerce in order to make a significant in the world market.

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