PHARMACOLOGICAL STUDIES OF YASHTIMADHU (GLYCYRRHIZA GLABRA L.) IN VARIOUS ANIMAL MODELS - A REVIEW

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ABSTRACT

Plants are one of the most important sources of medicines. Yashtimadhu [Glycyrrhiza glabra] is one such plant which symbolizes all that is wondrous in nature because, the whole plant has been used as traditional medicine for household remedy against various human ailments from antiquity. The objective of this paper is to review the literature regarding various pharmacological actions. The canvas of the pharmacological activities of Yashtimadhu is very vast. When these activities were compiled Yashtimadhu stands out strongly as a drug of choice in various disorders. This paper reviews the available data on use of Yashtimadhu [Glycyrrhiza glabra] in various disorders as evidenced in these topics.

KEYWORDS: Glycyrrhiza glabra, glycyrrhizin, isoliquiritigenin, Licorice, flavonoids.

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INTRODUCTION-

The increasing use of medicinal herbs among the general public has increased the need for scientific-based research to determine the mechanism of action of herbs. In India, the licorice root carries the ancient Sanskrit name of 'Yashtimadhu' (sweet stalk) and it has been a mainstay of Ayurvedic and other traditional medicines. In ancient Ayurvedic System, more than 1250 preparations are described containing Yasthimadhu as one of its Constituents. In traditional Ayurvedic medicine, herbs were used as special foods, serving to eliminate the excesses as well as strengthen the deficiencies, restore and rejuvenate. (Korhalkar A. et al., 2012). Research on the herbs is a developing area in modern biomedical sciences. Scientists who are trying to develop newer drugs from natural resources are looking towards the Ayurveda, the Indian traditional system of medicine. Several drugs of plant, mineral, and animal origin are described in the Ayurveda for their healing properties. Most of these drugs are derived from plant origin. Some of these plants have been screened scientifically for the evaluation of their pharmacological activity in different models, but the potential of most remains unexplored. The available data on some of the major points on the pharmacological activity of Yasthimadhu [Glycyrrhiza glabra L.] in the various disorders is described below.

1] Regulation of gastrointestinal motility

This study explained the gastrointestinal effects of isoliquiritigenin, a flavonoid isolated from the roots of Glycyrrhiza glabra in vivo & in vitro. The results indicated that isoliquiritigenin plays a dual role in regulating gastrointestinal motility, both spasmogenic and spasmylytic (Chen G, et al., 2009).

2] Anti-obesity action–

Licorice flavonoid oil (LFO), was investigated for anti-obesity action in diet-induced obese rats. The addition of 2% LFO in a high-fat diet significantly decreased the weight of abdominal adipose tissue and the levels of hepatic and plasma triglycerides. The enzymatic activities of acetyl-CoA carboxylase and fatty acid synthase, the rate-limiting enzymes in the fatty acid synthetic pathway, were significantly decreased by LFO, whereas the enzymatic activity of acyl-CoA dehydrogenase, the rate-limiting enzyme in the fatty acid oxidative pathway, was significantly increased (Kamisoyama et al., 2008).

The effects of hydrophobic flavonoids from Glycyrrhiza glabra on abdominal fat accumulation and blood glucose level in obese diabetic KK-A(y) mice, were investigated. The results indicated that licorice hydrophobic flavonoids have abdominal fat-lowering and hypoglycemic effects, possibly mediated via activation of peroxisome proliferator-activated receptor-gamma (PPAR-gamma) (Nakagawa K, et al., 2004).

3] Antioxidant action-

The following is a summary of the scientific evidence in support of the capacity of Glycyrrhiza glabra as antioxidant activity.

Spices such as cloves (Syzygium aromaticum), licorice (Glycyrrhiza glabra), mace (arl of Myristica fragans), and greater cardamom (Amomum subulatum) were tested for their antioxidant properties in vitro. The metal chelating activity, bleomycin dependent DNA oxidation, diphenyl-p-picryl hydrazyl (DPPH) radical scavenging activity and the ferric reducing /antioxidant power (FRAP) were measured in rat liver homogenate in presence of spices. The results showed that the spices tested were strong antioxidants and may have beneficial effects on human health (Yadav AS., et al., 2007).

As cancer chemopreventive agents, a new chalcone derivative a novel group of neolignan lipid esters, and seven known phenolic compounds (formononetin, glabridin, hemileiocarpin, hispaglabridin B, isoliquiritigenin, 4'-O-methylglabridin, and paratocarpin B) were isolated from the roots and stolons of licorice (Glycyrrhiza glabra). All isolates were tested in an authentic
peroxynitrite anti-oxidant assay. Of these compounds, hispaglabridin B, isoliquiritigenin, and paratocarpin B were found to be the most potent anti-oxidant agents. Furthermore, isoliquiritigenin was demonstrated to prevent the incidence of 1, 2-dimethylhydrazine-induced colon and lung tumors in mice when administered at a dose of 300 mg/kg (Chin YW, et al., 2007).

DHC-1, a herbal formulation derived from Bacopa monniera, Emblica officinalis, Glycyrrhiza glabra, Mangifera indica and Syzygium aromaticum was studied for its antioxidant activity. The protective effect of DHC-1 in isoproterenol-induced myocardial infarction and cisplatin-induced renal damage were studied. The results suggested that DHC-1 possesses a protective effect against both damaged heart and kidneys in rats. This beneficial effect may be attributed, at least in part, to its antioxidant activity (Bafna PA, et al., 2005a).

Pepticare, a herbomineral formulation of the Ayurveda medicine consisting of the herbal drugs: Glycyrrhiza glabra, Emblica officinalis and Tinospora cordifolia, was tested for its anti-ulcer and anti-oxidant activity in rats. Effects of various doses of Pepticare were studied on gastric secretion and gastric ulcers in pylorus-ligation and on ethanol-induced gastric mucosal injury in rats. It was concluded that Pepticare possesses anti-ulcer activity, which can be attributed to its anti-oxidant mechanism of action (Bafna PA, et al., 2005b).

Rabbits were treated (orally) with a preparation of Glycyrrhiza glabra L. for 30 days and in parallel were exposed to vibration stress (30 days). The licorice preparation reduced catalase activity in the peripheral blood and increased animal resistance to vibration stress (Oganesyan KR., 2002). The hypcholesterolemic and antioxidant effects of Glycyrrhiza glabra root powder were examined in hypercholesterolemic male albino rats. Administration of Glycyrrhiza glabra root powder (5 and 10 gm% in diet) to hypercholesterolemic rats resulted in significant reduction in plasma, hepatic total lipids, cholesterol, triglycerides and plasma low-density lipoprotein and VLDL-cholesterol accompanied by significant increases in HDL-cholesterol levels. The root powder administration to hypercholesterolemic rats also decreased hepatic lipid peroxidation with a concomitant increase in superoxide dismutase (SOD) and catalase activities and total ascorbic acid content. The normo-cholesterolemic animals when fed with Glycyrrhiza glabra root powder at 10 gm% level, registered a significant decline in plasma lipid profiles and an increase in HDL-cholesterol content. The antioxidant status of these animals also was improved upon treatment (Visavadiya NP, et al., 2006).

4) Protective activity –

It was concluded that Glycyrrhiza glabra is a potential antioxidant and attenuates the hepatotoxic effect of CCl4 by acting as an in vivo antioxidant and thereby inhibiting the initiation and promotion of lipid peroxidation or by an accelerated scavenging of free radicals and their products by conjugation with GSH aided by GST (MG Rajesh, et al., 2004).

Another study evaluated the potential beneficial effect of glycyrrhizin in a mouse model of carbon tetrachloride (CCl4 (4)-induced liver injury. Glycyrrhizin diminished these alterations. These results suggested that glycyrrhizin alleviated CCl (4)-induced liver injury, and this protection was likely due to the induction of heme oxygenase-1 and the downregulation of proinflammatory mediators (Lee CH, et al., 2007).

In the study by Zhan, the protective effects of Isoliquiritigenin (ISL) were investigated in transient middle cerebral artery occlusion (MCAO)-induced focal cerebral ischemia-reperfusion injury in rats. Pretreatment with ISL significantly reduced the cerebral infarct volume and edema and produced significant reduction in neurological deficits. These findings indicated that ISL had the protective potential against cerebral ischemia injury and its protective effects were may be due to the
amelioration of cerebral energy metabolism and its antioxidant property (Zhan C, et al., 2006).

The research done by Liu, compared rectal and oral treatments with glycyrrhizic acid for trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats. There were significant pathological changes in colon in TNBS-treated groups, and rectal glycyrrhizic acid significantly attenuated colitis. These results suggested that rectally administered glycyrrhizic acid had significant protective effects against TNBS-induced colitis in rats, and the rectal route could be a complementary treatment for inflammatory bowel disease (Liu Y, et al., 2011).

The effect of *Glycyrrhiza glabra* extract as a natural antioxidant and melatonin (MEL) on ochratoxin A (OTA)-induced histopathological damages on the testes and oxidative stress was evaluated in male rats. The serum total antioxidant power (TAOP) and total thiol molecules (TTM) production were assessed. Both the biochemical and histopathological examinations showed that MEL and *Glycyrrhiza glabra* extract exerted a protective effect on OTA-induced damages. This data suggested that OTA contamination in animal feeds and human foods could cause reproductive abnormalities (Malekinejad H, et al., 2011).

The study was carried out to evaluate the cerebroprotective effect of the aqueous extract of the roots of *Glycyrrhiza glabra* Linn in hypoxic rats. Extract at the tested doses promoted the locomotor activity and spatial behavior significantly, which was impaired in hypoxic rats. The extract administration restored the decreased levels of brain enzymes such as glutamate and dopamine and decreased acetyl cholinesterase (AChE) activity significantly. Levels of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase were restored to near normalcy by administration of ethanol extract of *Glycyrrhiza glabra*. The study suggested that ethanol extract of *Glycyrrhiza glabra* possessed a cerebroprotective effect in hypoxic rats, which may be mediated by its antioxidant effects (P. Muralidharan, et al., 2009).

Another study indicated that the DNA was protected from the deleterious effects of gamma radiation by glycyrrhizic acid in vitro, ex vivo, and in vivo conditions of radiation exposure. The results showed that the glycyrrhizic acid protected bone marrow cells from the radiation-induced damages. It was suggested that glycyrrhizic acid could be a potential drug for the protection of the hemopoietic system from radiation-induced lesions. These results indicated that glycyrrhizic acid offered radioprotection by the scavenging of free radicals (Nitin Gandhi, et al., 2004).

Yu XQ, et al study was designed to evaluate whether glabridin modulated the cerebral injuries induced by middle cerebral artery occlusion (MCAO) in rats and staurosporine-induced damage in cultured rat cortical neurons and the possible mechanisms involved. Findings indicated that glabridin had a neuroprotective effect via modulation of multiple pathways associated with apoptosis (Yu XQ, et al., 2008).

5] Anti-inflammatory activity-

Glycyrrhizin was evaluated on an animal model of spinal cord injury (SCI) induced by the application of vascular clips. The results demonstrated that treatment with glycyrrhizin extract reduced the development of inflammation and tissue injury events associated with spinal cord trauma (Genovese T, et al., 2009).

This study compared the antiarthritic activities and underlying mechanism of LE and rLE (Licorice and Roasted Licorice Extracts) in the CIA mouse model of human RA. The data suggested that supplementation with LE and rLE might be beneficial in preventing and treating both acute and chronic inflammatory conditions (Ki RimKim, et al., 2010).

The anti-inflammatory activities of glycyrrhizin given at 10 mg/kg i.p. 5 min prior to carrageenan in mice model were evaluated in
this study. Glycyrrhizin exerted potent anti-inflammatory effects in this model. The results indicated that prevention of the activation of NF-kappaB and STAT-3 by glycyrrhizin reduced the development of acute inflammation (Menegazzi M, et al., 2008).

6] Immunostimulating –

The uses of ISCOMs (Immunostimulating complexes) formulated with saponins from plants (Aesculus hippocastanum and Glycyrrhiza glabra) collected in Kazakhstan, with antigens from the poultry coccidian parasite Eimeria tenella, were evaluated for their potential use in developing a vaccine for control of avian coccidiosis. The results of this study indicated that these ISCOMs were an effective antigen delivery system which may be successfully used, with low toxicity, for preparation of highly immunogenic coccidia vaccine (Berezin VE, et al., 2008).

7] Learning and memory-

Glabridin was isolated from the roots of Glycyrrhiza glabra and its effects on cognitive functions and cholinesterase activity were investigated in mice. Glabridin and piracetam were administered daily for 3 successive days to different groups of mice. Both remarkably reduced the brain cholinesterase activity in mice compared to the control group. Therefore, glabridin appeared to be a promising candidate for memory improvement (Cui YM, et al., 2008).

The study was undertaken to investigate the effects of Glycyrrhiza glabra, on learning and memory. The elevated plus-maze and passive avoidance paradigm were employed to evaluate learning and memory parameters. Three doses of aqueous extract of Glycyrrhiza glabra were administered for 7 successive days in separate groups of mice. Glycyrrhiza glabra showed promise as a memory enhancer in both exteroceptive and interoceptive behavioral models of memory (Parle M, et al., 2004).

Another study investigated the effect of chronic treatment with glabridin on cognitive function in control and streptozotocin (STZ)-induced diabetic rats. The results showed that glabridin prevented the deleterious effects of diabetes on learning and memory in rats due to its combination of antioxidant, neuroprotective and anticholinesterase properties (Hasanein P., 2011).

8] Relaxes smooth muscle-

The tracheal relaxation effects of isoliquiritigenin, was investigated, on guinea-pig tracheal smooth muscle in vitro and in vivo. Result indicated that isoliquiritigenin relaxes guinea-pig trachea through a multiple of intracellular actions, including sGC activation, inhibition of PDEs, and associated activation of the cGMP/PKG signaling cascade, leading to the opening of BKCa channels and [Ca2+]i decrease through PKG-dependent mechanism and thus to tracheal relaxation (Liu B, et al., 2008).

Licochalcone A, a flavonoid found in licorice root (Glycyrrhiza glabra), is known for its anti-microbial activity and inhibition of cancer cell proliferation. This study investigated whether Licochalcone A inhibits rat vascular smooth muscle cell (rVSMC) proliferation. The data provided that Licochalcone A could regulate rVSMC proliferation and suggested that Licochalcone A inhibited the proliferation of rVSMCs by suppressing the PDGF-induced activation of the ERK1/2 pathway and Rb phosphorylation, resulting in cell cycle arrest (Park JH, et al., 2008).

9] Accelerating metabolism processes of the marrow stem cells-

The effect of long-term exposure of vibration and feeding rabbits with liquorice (Glycyrrhiza glabra L) on peripheral blood indicators was studied. It was found that biological active substances of licorice accelerate metabolism processes of the marrow stem cells, enlarge organism compensatory abilities, in that way providing organism resistance to vibration (Minasian SM, et al., 2007).
10] Antiviral effects-

Animal studies demonstrated a reduction of mortality and viral activity in herpes simplex virus encephalitis and influenza A virus pneumonia. In vitro studies revealed antiviral activity against HIV-1, SARS related coronavirus, respiratory syncytial virus, arboviruses, vaccinia virus and vesicular stomatitis virus (Fiore C, et al., 2008).

11] Antifibrotic effects -

Study investigated whether a combination regimen of *Salvia miltiorrhiza* (S), *Ligusticum chuanxiong* (L) and *Glycyrrhiza glabra* (G) exerted in vivo antifibrotic effects on rats with hepatic fibrosis. Fibrosis was induced in rats by dimethylnitrosamine (DMN) administration for 4 weeks. The results showed that SLG exerted antifibrotic effects in rats with DMN-induced hepatic fibrosis (Lin YL, et al., 2008).

12] Antiallergic effects-

In this study, the main components (glycyrrhizin, 18β-glycyrrhetinic acid, isoliquiritin, and liquiritigenin) were isolated from licorice, and their anti-allergic effects, such as antiscratching behavior and IgE production-inhibitory activity, were evaluated both in vitro and in vivo. These components inhibited the production of IgE in ovalbumin-induced asthma mice but liquiritigenin had little effect. The study suggested that the antiallergic effects of licorice were mainly due to glycyrrhizin, 18β-glycyrrhetinic acid, and liquiritigenin, which could relieve IgE-induced allergic diseases such as dermatitis and asthma (Shin YW, 2007).

The study evaluated glycyrrhizin a major constituent of Glycyrrhiza glabra, for its efficacy on asthmatic features in a mouse model of asthma. The results demonstrated that glycyrrhizin alleviated asthmatic features in mice and it could be useful towards developing a better therapeutic molecule in the future (Ram A, et al., 2006).

Glycyrrhiza glabra, Allium cepa and Clerodendrum serratum with hydroalcoholic (50:50) solvent were evaluated for acute toxicity and Anti asthmatic activity. Saponins and flavonoids were the major reason for antioxidant activity as confirmed by DPPH free radical scavenging activity test and were responsible for treating oxidative stress during asthma (Tulsiani Puja, 2012).

13] Cholinesterase-inhibiting activity-

This study estimated the acetyl cholinesterase- inhibiting activity of extracts of *Glycyrrhiza glabra*, and compared these values with a standard acetyl cholinesterase-inhibiting drug, metrifonate. Aqueous extract of *Glycyrrhiza glabra* and metrifonate were administered to young male Swiss albino mice. Acetyl cholinesterase enzyme was estimated in brains of mice. *Glycyrrhiza glabra* and metrifonate significantly decreased acetyl cholinesterase activity as compared with their respective vehicle-treated control groups (Dhingra et al., 2006a).

14] Immunomodulatory properties-

Standardized ethanol extracts of *Allium sativum*, *Glycyrrhiza glabra*, *Plantago major* and *Hippophae rhamnoides* were assessed for their effects on cellular immunity in laying hens. Birds had blood samples taken and both specific and non-specific immune cell responsiveness were evaluated by a leukocyte proliferation assay, carbon clearance test and SRBC phagocytosis in monocyte-derived macrophage cultures. Licorice and sea buckthorn clearly enhanced the macrophage membrane function. Small concentrations (20 µg/mL) of licorice proved the co-mitogenic potential for both T and B avian lymphocytes (Dorhoi A, et al., 2006).

15] Antidepressant-like activity

This study investigated the effects of aqueous extract of *Glycyrrhiza glabra*, on depression in mice using forced swim test (FST) and tail suspension test (TST). The dose of 150 mg/kg of the extract significantly reduced the immobility times of mice in both
FST and TST, without any significant effect on locomotor activity of mice. This suggested that antidepressant-like effect of liquorice extract seems to be mediated by increase of brain noradrenaline and dopamine, but not by increase of serotonin (Dhingra D. et al., 2006b).

Other study evaluated the potential of methanolic extract of Glycyrrhiza glabra as an adjuvant in treatment of Parkinson's disease and depression. In acute study Glycyrrhiza glabra extract (30 and 100 mg/kg i.p.) significantly inhibited haloperidol-induced catalepsy in mice in dose dependent manner. Similar inhibitory effect of Glycyrrhiza glabra extract was also observed in chronic study (15 days) which indicated that there was no development of tolerance. The Glycyrrhiza glabra extract reduced duration of catalepsy also. These observations indicated that Glycyrrhiza glabra has a good potential as an adjuvant of anti-Parkinsonian and antidepressant drugs (SB Kasture et al., 2008).

16] Increased resistance to stress-

This study observed the effect of continuous vibration and treatment with licorice root (Glycyrrhiza glabra L.) on peripheral blood red cells in rabbits. Active substances of licorice root accelerated metabolism in cells of the bone marrow erythroid stem, enhanced compensatory reserve of the organism, and increased animal's resistance to stress (Adamyan TI., et al., 2005).

17] Antimutagenic properties-

The antimutagenic effect of the bioactive compounds from fruits of Morus alba L. (MA), Punica granatum L. (PG), Diospyros kaki L. (DK), Cydonia oblonga Mill. (CO) and roots of Glycyrrhiza glabra (GG) were investigated. The antimutagenic effects were studied on mutations induced by genotoxicants (X-rays, N-methyl-N-nitrosourea, cyclophosphamide, NaF) and aging in bone marrow cell chromosomes from mice and rats. The antimutagenic properties of the complex mixtures were considerably greater than those of the separate components. More antimutagenic activity of the mixture was revealed when mutagenesis was the result of X-rays and the natural aging processes (Alekperov UK., 2002).

18] Protection of DNA and microsomal membranes-

The radioprotective effect of the root extract of Glycyrrhiza glabra L on lipid peroxidation in rat liver microsomes and plasmid pBR322 DNA was investigated. The extract was found to protect microsomal membranes, as evident from reduction in lipid peroxidation, and could also protect plasmid DNA from radiation-induced strand breaks (Shetty TK, et al., 2002).

19] Antiulcerogenic effect-

Extracts from the plants Iberis amara, Melissa officinalis, Matricaria recutita, Carum carvi, Mentha x piperita, Glycyrrhiza glabra, Angelica archangelica, Silymbum marianum and Chelidonium majus, singly and combined in the form of a commercial preparation, STW 5 (Iberogast) and a modified formulation, STW 5-II, were tested for their potential antiulcerogenic activity against indometacin induced gastric ulcers of the rat as well as for their antisecretory and cytoprotective activities. All extracts produced a dose dependent antiulcerogenic activity associated with a reduced acid output and an increased mucin secretion, an increase in prostaglandin E2 release and a decrease in leukotrienes (Khayyal MT, et al., 2001).

20] Hepatoprotective and antihepatocarcinogenic –

Liver protective and antihepatocarcinogenic effects of combination use of Gly and Mat (Matrine), a component extracted from Sophora flavescens Ait, Glycyrrhizin (Gly), a major active constituent of licorice (Glycyrrhiza glabra) root, were tested, as compared to effects of Gly or Mat alone. The results showed that compared with Gly or Mat alone, Gly + Mat reduced the mortality of acetaminophen overdose mice more effectively, attenuate acetaminophen-induced hepatotoxicity, and reduced the
number and area of γ-GT positive foci, thus protecting liver function and preventing HCC from occurring (Xu-ying et al., 2009).

21] Improve efficiency of chemotherapy and surgical treatment-

Experiments on animals with Lewis lung carcinoma and Ehrlich tumor showed that licorice (Glycyrrhiza) extract and glyciram prepared from this plant improved the antitumor effect of cyclophosphamide. Glyciram reduced the toxic effect of the cytostatic on peripheral blood leukocytes. Licorice extract inhibited the growth of Ehrlich tumor and development of metastases in mice with Lewis lung carcinoma. Glyciram administered to mice after removal of Lewis lung carcinoma produced an antimetastatic effect and prevented relapses (Goldberg ED, et al., 2008).

22] Antithrombotic effect-

Here the in vivo effects of Glycyrrhizin upon two experimental models of induced thrombosis in rats are reported. Intravenous administration of Glycyrrhizin caused a dose-dependent reduction in thrombus size on a venous thrombosis model that combines stasis and hypercoagulability. It was observed that Glycyrrhizin doses of 180 mg/kg body weight produced 93% decrease on thrombus weight. Glycyrrhizin was also able to prevent thrombosis using an arteriovenous shunt model. In contrast with heparin, Glycyrrhizin did not potentiate the inhibitory activity of antithrombin III or heparin cofactor II towards thrombin. Altogether, data indicate that Glycyrrhizin is an effective thrombin inhibitor in vivo, which may account for its other known pharmacological properties (Mendes-Silva W.et al., 2003).

23] Reduce ocular hypertension –

This study evaluated the hypotensive effects of glycyrrhizin on a rabbit model of ocular hypertension (OH) induced by triamcinolone acetonide (TA). The administration of Glycyrrhizin could suppress OH induced by TA in rabbits, and improve their electrophysiological parameters. These results indicated that TA-induced ocular metabolism changes could be compensated by Glycyrrhizin (Song Z, 2011).

24] Anticonvulsant Activity -

The anticonvulsant activity of ethanolic extract of roots and rhizomes of Glycyrrhiza glabra in mice was assessed using maximum electroshock seizure (MES) test and pentylenetetrazol (PTZ) using albino mice. The lithium-pilocarpine model of status epilepticus was also used to assess the anticonvulsant activity in rats. The ethanolic extract of Glycyrrhiza glabra did not reduce the duration of tonic hindleg extension in the MES test even in the dose of 500 mg/kg. However, the extract significantly and dose-dependently delayed the onset of clonic convulsions induced by pentylenetetrazol (Shirish D et al., 2002).

25] Restores the impaired production of β-defensins-

In this paper, the decreased production of antimicrobial peptides by EK influenced by Gr-1(+) CD11b (+) cells was shown to be restored by glycyrrhizin. Also, sepsis stemming from P. aeruginosa burn-site infection was not demonstrated in burn mice treated with glycyrrhizin. These results suggested that through the improved production of antimicrobial peptides in tissues surrounding the burn area, sepsis stemming from P. aeruginosa wound infection is controllable by glycyrrhizin in severely burned mice (Tsuyoshi Yoshida, 2010).

26] Modulate rat cardiac performance-

The direct cardiac activity of glycyrrhizin and glycyrrhetinic acid was explored. The effects of synthetic glycyrrhizin and glycyrrhetinic acid were evaluated on the isolated and Langendorff perfused rat heart. The intracellular signaling involved in the effects of the two substances was analyzed on isolated and perfused heart and by Western blotting on cardiac extracts. Under basal conditions, both glycyrrhizin and glycyrrhetinic
acid influenced cardiac contractility and relaxation. Glycyrrhizin induced significant positive inotropic and lusitropic effects starting from very low concentrations, while both inotropism and lusitropism were negatively affected by glycyrrhetinic acid. Both substances significantly increased heart rate (Maria L. Parisella et al., 2012).

27] Antitumor and antimetastatic effects –

Experiments on mice inoculated with metastasizing Lewis lung carcinoma showed that the antitumor and antimetastatic effects of cyclophosphan (cyclophosphamide) are potentiated by the extracts of phytopreparations based on Baikal scullcap (Scutellaria baikalensis), rhodiola (Rhodiola rosea), common licorice (Glycyrrhiza glabra), and their principal acting components-baikalin, paratyrrosyl, and glycyrram (Razina T.G, 2000).

28] Antitussive activity –

This study analyzed the water-extracted polymeric fraction (WE) of Glycyrrhiza glabra. This arabinogalactan protein enriched fraction, ≥ 85% of which gets precipitated with Yariv reagent, consisted mainly of 3- and 3,6-linked galactopyranosyl, and 5- and 3, 5-linked arabinofuranosyl residues. Peroral administration of this polymer, in a dose of 50 mg/kg body weight decreases the number of citric acid induced cough efforts in guinea pigs more effectively than codeine. It does not induce significant change in the values of specific airway resistance or provoked any observable adverse effects (Saha S et al., 2011).

29] Prevention of hepatorenal damage –

Protective role of Glycyrrhiza glabra rhizomes (roots) at three dose levels (100, 75, & 50 mg/kg/bw) against sublethal dose (300 mg/kg/bw) of acetaminophen (paracetamol) induced hepatorenal damage has been assessed in mice. Parameters of study were glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), bilirubin, alkaline phosphatase (ALP) as liver function tests, creatinine and urea as kidney function tests and histology for pathology. Glycyrrhiza glabra could antagonize acetaminophen induced both, hepato and nephrotoxicity in dose dependent manner. No protection provided by a single dose of Glycyrrhiza glabra (1.5 gm/kg/bw) against lethal dose of acetaminophen (1 gm/kg/bw) (Sharma A. et al., 2011).

30] Antiandrogenic activities-

This study was carried out to investigate different aspects of antiandrogenic properties of Glycyrrhiza glabra. Immature male rats, castrated rats without any treatment received only vehicle; castrated rats plus T replacement; three castrated groups with T replacement plus various doses of G. glabra extract (75, 150 and 300 mg/kg). Those receiving the doses of 150 and 300 mg/kg showed a significant reduction in prostate weight, total T and VP epithelium/stroma ratio (V/V). These results in SV and levator ani were shown in response to 300 mg/kg of extract. Increasing in T metabolism, down-regulation of androgen receptors or activation of oestrogen receptors could be involved mechanisms. This study showed that alcoholic extract of Glycyrrrhiza glabra has antiandrogenic properties (Zamansoltani F. et al., 2009).

CONCLUSION

Yashhtimadhu (Glycyrrhiza glabra) still remains a mainstay of Ayurvedic and other traditional medicines. But only some of its uses are supported by clinical data. So it becomes relevant to search the evidence based data and to classify and to analyze it. In last two decades more and more bioactive compounds have been recognized and promising results have been established through various pharmacological studies on animal models as well as clinical studies. Mechanisms of action of its major constituents such as glycyrrhizin (glycyrrhizic acid, glycyrrhizinic acid), isoliquiritigenin, Licorice flavonoid oil (LFO), hydrophobic flavonoids, formononetin, glabridin, hemileiocarpin, hispaglabridin B, 4′-O-methylglabridin, paratocarpin B. Licochalcone A., 18 β-glycyrrhetinic acid, isoliquiritin, liquiritigenin, glyciram etc have been discussed in this review which could help the researchers.
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