

Phytochemicals and pharmacological review on licorice (*Glycyrrhiza glabra*)

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ABSTRACT: Licorice (*Glycyrrhiza glabra*) known to possess various pharmacological activities. Licorice carry 20 triterpenoids and 300 flavonoids. Mechanism of anticancer activity include antioxidant activity, arrest of cell cycle, progression and cell death. Pharmacological experiments have been carried out and reported that different extracts and pure compounds from this species exhibit a various biological activities. Different phytochemicals including glycyrrhizin and glycyrrhetic acid, glabrin A and B, isoflavone have been identified and associated with various biological activities reported namely antioxidant, antiviral, antimicrobial, anticancer, antiinflammatory activity and hepatoprotection. Side effects and toxicity of licorice are very less. There is brief discussion here on constituent and their pharmacological potential of *G. glabra* in order to explain its importance and challenges which will be faced in future to formulate a new products that will be useful for human health and wellness.

KEYWORDS: Licorice, antioxidant, anticancer, glycyrrhizic acid, chalcone

I. INTRODUCTION

Licorice is the dried, peeled or unpeeled root or rhizome of *Glycyrrhiza glabra* belonging to family fabaceae which is also called as pea family or legume family due to its unique characteristics of this family i.e (single chambered legume). Licorice is native to Eurasia, in central and south-western Asia and the Mediterranean region. It is found in south Europe, Turkey, Iran, Iraq. Licorice is one of the most widely used and extensively researched medicinal plant of the world. Licorice is the one of the main drug in *Susruta*. Those who are consuming it for a longer period it will rejuvenate them. Romans cultivated it after sixteen centuries called as *radix dulcis*. Active ingredient in licorice is mainly glycyrrhizin, a triterpenoid glycoside, which constitutes up to 14 percent of total soluble solid

content. Recent advents in molecular biology and biotechnology led to the efforts to improve/increase the yield of compounds which are of economic importance. Licorice mostly contain 20 triterpenoid and 300 flavonoids such as liquiritin, Isoliquiritigenin, liquiritigenin, glycyrrhizic acid, polysaccharides. Active compound isolated from licorice which is glycyrrhizic acid is an inhibitor of lipoxygenase and cyclooxygenase, inhibit the protein kinase C, and downregulate the epidermal growth factor receptor. Licorice polyphenols include apoptosis in cancer cells. Licorice root extract mostly used in food industry as sweetening agents, a flavor potentiator and flavor modifier.

(2) Plant anatomy/classification of plant::

- Kingdom: plantae
- Sub kingdom: Tracheobionta_vascular plant
- Super division: spermatophyta_seed plant
- Division: magnoliophyta_flowering plant
- Class: magnoliopsida_Dicotyledons
- Subclass: rosidae
- Order: fabales
- Family: fabaceae
- Genus: *Glycyrrhiza* L., licorice
- Species: *Glycyrrhiza glabra*

(3) Vernacular names

- Arabic: sus, irissus, ribel_sus
- English: licorice, licorice root, liquorice
- French: réglisse,
- German: lakritze, subholz
- Hindi: Mulathi, jethimadh, mithilakdi
- Italian: liquirizia
- Portuguese: alcacuz, pau_doce
- Spanish: alcacuz, licorice, irozuz, regaliz
- Swedish: lakritsro

(4) Biodiversity of licorice :

Glycyrrhiza genus contains more than 30 species which is widely distributed all over the world. *Glycyrrhiza* genus plants are widely found

in Mediterranean southern regions and central Russia and Asia. Large scale commercial cultivation is available in Spain England. Many species of licorice are found through out the world specially in Europe, Syria, UK, USA, Italy, German, Europe, Afghanistan, Northern India (Punjab and Himalaya regions).

(5) Occurrence :

1. There are various varieties of *G. glabra* are known to relate trade drugs. *G. glabra* var. typical the plant of Spanish is source height about 15m with published blue flowers the underground root or thin rhizome that penetrate the soil upto a depth of 1m or more
2. *G. glabra* var *glunder* ground was found in Russian and grown in central and southern Russian. The underground part of this species consist of large root but no stolen.
3. *G. glabra* var. *violacea* is Persian licorice which have violet flowers. It is found in Iran, Iraq in the valleys of Tigris
4. *G. lepidota* found throughout the California and requires a rich soil of low or moist land in the valleys.

(6) Botanical descriptions:

Licorice is eternal, strong, herbaceous plant having height upto 1.5 m. and having an extensive root system which consist of tap root, root branches and long runners. The woody stalk bears a loose foliage with Unpaired pinnate, narrowly lanceolate leaves covered with glandular sticky hairs The erect 10 to 15 cm long blossom clusters grow from the leaf axil and bears numerous blue lilac, blue violet or white pink blossom. (6)

The genus name *Glycyrrhiza* derived from Greek Glycy for sweet and rhiza for root. the species name *glabra* was derived from Latin *glabra* which means smooth or bald and refers to smooth husk. (6)

(7) Family descriptions:

Family Fabaceae have another name which is leguminosae family (bean family). It is known as third largest family among angiosperms. Fabaceae family contains many important species regarding genetic studies and genomic model system. Fabaceae have more than 19000 species out of which Caesalpiniaceae, Mimosaceae, and Papilionaceae are important subfamily. Leaves of this family are simple to compound. Flowers are actinomorphic to zygomorphic, bisexual and have single superior carpel. The most common

identifying point of the family fabaceae is its fruit which is one chambered pod (a legume.) (27)

(8) Ecology:

It tends to grow best in a area which is dry, sunny, hot climate, that allow to receive a relatively low annual rainfall between 500mm to 650mm. while the climate may be hot and dry. plant refer to grow in adequate soil moisture. licorice is able to grow in the area of mean annual rainfall fall between 400mm to 1100mm. the mean annual temperature range from 5.7 to 25 degree. soil ph varies from 5.5 to 8.2. (4)

(9) Chemical constituent :

Glycyrrhiza genus contains more than 30 species which is widely distributed all over the world.

Glycyrrhiza glabra root of ethanolic extract contain alkaloids, glycosides, carbohydrates, starches, phenol, proteins, pectin, mucilage, saponins, lipids, tannins, sterols and steroids. Licorice root have triterpenoids saponins (27.99mg/100g(DWB)) which is nothing but *glycyrrhizin*, a mixture of potassium and calcium salts of 18β-*glycyrrhizic acid*. The total phenolic contents of the ethanolic extract of *Glycyrrhiza glabra* root was found to be 405.02 Mg/100g(DWB) while the total flavonoids contents was 114.91Mg/100g(DWB).

Antioxidants content of licorice root (mg/100g on dry weight basis) (3)

Component	Mg/100g(DWB)
Total phenols	405.02
Total flavonoids	114.91
Tannis	47.54
Saponin	27.99
Carotenoids	11.78
Vitamin c	1.20

The ethanolic extract of *Glycyrrhiza glabra* root shows a various heavy metals such as cadmium: 0.28 ± 0.03 , lead: 0.48 ± 0.12 , arsenic: 0.47 ± 0.05 and mercury: 0.33 ± 0.08 mg/kg (40). *Glycyrrhiza glabra* shows the various trace element also which is present as percentage in it such as potassium :0.66, calcium 1.87, sulphur 0.09, iron 0.14, aluminium 0.05, phosphorous 0.06, silicon 0.12, magnesium 0.17 and sodium 0.04% (50).

The chemical composition of licorice also contains the protein, fat, moisture ash and fiber, and carbohydrates

Components	Percentage
Ash	5.42
Crude proteins	7.97
Ether extract	1.35
Crude fiber	37.6
Nitrogen free extract (by difference)	47.66
Moisture	9.04

The plant contained many amino acids included aspartic, glutamic, threonine, serine, proline, glycine, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine, histidine, tyrosine and lysine, it was found that that proline was the major free amino acid in the licorice. The other one were aspartic acid, glutamic, valine and the other amino acids. The amino acids in the methanolic extract of *G.glabra* are aspartic (91.96 mg/100 ml) proline (77.14 mg/100 ml) and glutamic acid (27.05). HPLC analysis of the organic acids in the licorice methanolic extract, tea and infusion forms revealed that the plant contained acetic, fumaric, butyric, propionic, malic, citric and tartaric acids. Methanolic extract of licorice contain tartaric acid followed by butyric acid, malic acid, propanoic acid and citric acid. (51)

II. MATERIAL AND METHOD

(1) Phytochemistry:

(Hayanshueta et al 2016) carried out studies on nutritional value of *G.glabra* and concluded that liquorice is a source of protein, amino acid, poly saccharides and simple sugar, mineral salts (such as calcium, sodium, potassium, phosphorus, iron, magnesium, silicon, selenium, zinc, copper), pectins, resins, sterols and gums.

Oestrogen, phytosterol, (sitosterols and stigmasterol), tannin, coumarins, vitamins (B1, B2, B3, B5, E and C), glycoside have been reported by Wang, Qian, et al, 2015, Rizzato et al, 2017, and they were isolated a large no. of biological comp mostly triterpenes, saponin (for sweet taste) and flavanoid. Licorice saponin present as glucuronides, and aglycone part is oleananes. The content of the compound may differ due to geographic sources, processing, harvesting which effect the therapeutic effects of licorice.

(J.y. yoet al 2015) reported that the glycyrrhizin is the main constituent of root and it constitute 10% of liquorice root dry weight. The mixture of potassium, calcium, magnesium salt of glycyrrhizin acid that varies from 2% to 25%. glycyrrhizin is metabolized to 18_ glycyrrhetic acid 3_ amonoglucoronide and

glycyrrhetic acid by intestinal bacteria. Yellow colour of licorice is because of flavonoids content. the flavanoid of different classes such as flavones, flavanone, chalcones, isoflavans, isoflavones, isoflavone.

(Rizzato et al 2017) reported that Glabridin is the major isoflavone and found in the range of 0.08% to 0.35% of root dry weight flavanoids, coumarins, chromene, benzofuran dihydrophenanthrene are the minor phenolic compounds. The geraniol, pentanol, hexagon, terpinen_4_ol, alpha_ terpineol are the some volatile which is present in it which confers the characteristic odour. Some essential oil is also present in it.

(2) Pharmacological activity :

Antioxidant activity:

Extract of *G.glabra* root shows a antioxidant activity because it contain potent flavonoids. (Vava et al, Hesham and Shgru, Lateef et al, Franceschelli et al (2012) have reported that isoflavones glabridin, hispaglabridin A and B flavonoids like luteolin, licochalcone possess a antioxidant properties which is confirmed by cerebroprotective effect in hypoxic rats by using essential oil of *G.glabra* which exhibit a DPPH radical scavenging activity (8.1%) at a dose of 400 µg/ml, where as methanolic extract exhibit a (91.3%) scavenging activity at a dose of 62.5 µg. Licochalcone act by not only reduces the super oxide radicals but also reduces the activity of inducible nitric oxide synthase (iNOS). (4)(6) The study was carried out by using ethanolic extracts of *Glycyrrhiza glabra* var. *glandulifera* and found that there antioxidant activity by using the DPPH (1,1-diphenyl-2-picrylhydrazyl) method. The extracts showed good antioxidant activity, with a median inhibitory concentration (IC₅₀) of 588 ± 0.86 to 2190 ± 1.73 units/l (42). antioxidant activity of root extract of *G.glabra* evaluated with DPPH scavenging assay and reported that methanolic extract of *G.glabra* shows a potent antioxidant activity with maximum scavenging effects as 67.22% at a concentration of 500 µg/ml. The calculated IC₅₀ for the methanolic extract of *Glycyrrhiza glabra* was 359.45 µg/ml (10)(23)

Anticarcinogenic and antimutagenic activity:

18beta glycyrrhetic acid and glycyrrhetic acid shows the anticancer activity by inducing mitochondrial permeability transition, leading to the apoptosis of tumour cells. 18beta glycyrrhetic acid increases the formation of reactive oxygen

species, nitric oxide production and lots of mitochondrial membrane potential hence it is useful in tumour in breast, ovarian cancer gastric tumour and in treatment of leukemia. glycyrrhetic acid derivative can be used by inducing the apoptosis of HL₆₀ cell through the activation of extrinsic and intrinsic apoptosis pathway.(22) it also certain specific constituent shows the anticancer activity such as licochalcone A by cancer cell growth in a dose dependent way by blocking cell cycle progression at the G₂/M transition inducing apoptosis and second one is isoliquiritigenin which suppresses pulmonary metastasis in mice. another one is glabridin which induced apoptosis in dose dependently in H_{9c7} cell through caspase₃, caspase₈, caspase₉ activation and RA PR cleavage (7)(8)

This activity of licorice is due to 18 beta glycyrrhetic and glycyrrhizic acid that induce mitochondrial permeability transition and leads to apoptosis of tumour cells. (V sharma ,Agarwal and shrivastava 2014) reported that hydro methanolic root extract of *G. glabra* shows the antimutagenic activity by suppressing micro nuclei formation and chromosomal aberrations in bone marrow cells of albino mice. Glycyrrhizin and glycyrrhetic acid are most effective in gastric cancer treatment. glycyrrhizin suppressing the thromboxane A₂ in lung cancer cell with low toxicity.(22)

(Wang et.al.2017), reported that 18 beta glycyrrhetic acid shows an anti tumour activity in various organs such as breast, ovary, gastric tumours and leukaemia. In liver they act by inhibiting the proliferation of Hep G₂ cells without affecting normal liver cell line and 18 beta glycyrrhetic acid acts by increasing the formation of reactive O₂ species, nitric oxide production, loss of mitochondrial potential. glycyrrhetic acid derivative shows a cytotoxicity activity in breast cancer cell line and human leukemia by inducing the apoptosis of H₁₆₀ cells by activation of extrinsic and intrinsic pathways. (24)(25)

(Y.y.xiao et al, yu.et.al, 2017) reported that licochalcone A shows a cytotoxic activity by exploring the MKN₂₈, AGS, MKN₄₅ Gastric cancer cells and human cancer cells and human gastric epithelial immortalized cells. Licochalcone A inhibits gastric cancer cells growth in a dose dependent manner by blocking cell cycle progression at the G₂/M transition, inducing apoptosis. Methanolic extract of licorice which contains licocoumarin was documented to stimulate the phosphorylation of Bcl₂ and halt the G₂/M

cycle in Cancer cell line and induce human mono blast leukaemia 0937 cell apoptosis. (18)

Antimicrobial activity:

(Gupta et.al,Wang, yang,yuang, liu, 2015) shows the antimicrobial activity of *G. glabra* on gram positive and negative bacteria such as staphylococcus aureus, Escherichiacoli, pseudomonas aeruginosa, candida Albicansand, bacillus subtilis and these antibacterial activity is due to presence of secondary metabolite such as saponin, alkaloid, flavonoids, they act by decreasing the bacterial gene expression, inhibiting of bacterial growth and reduced the bacterial toxin production.(16). In vitro studies have been carried out and reported that ethanolic extract of licorice shows inhibitory activity on streptococcus pyogenes.

Glabridin is effective against mycobacterium tuberculosis and anti tubercular phenolic compound was reported as licoisoflavone and licochalcone A.(Chakotiya.et.al,2017) reported that *G. glabra* was therapeutically active against multi drug resistant strain of *p.aeruginosa* and hydroalcoholic extract shows a reduction in microbial load in blood due to presence activity of ergosterol, licochalcone and glabridin.(30)

(Cao.et.al,2016),reported that 18 beta glycyrrhetic acid, glabridin, gangrene are effective against *Helicobacter pylori* infection by inhibiting proteins synthesis, DNA gyrase, dehydrofolate reductase(26)

The isoflavonoid, glabridin, glabrol, and their derivative are responsible in vivo inhibition of mycobacterium smegmatis, shigella, salmonella, E.coli, S.mutant, lactobacillus dophilus and aspergillus Niger due to liquiritigenin, liquiritin, licochalcone A(33).

Hepatoprotective activity:

Secondary metabolite derived from licorice were reported to treat various liver diseases by lowering the serum liver enzymes level or by improving the tissue pathology in hepatitis patients. (Al razzaque et.al,Sharma,Agarwal) carried out study by using aqueous and hydro methanolic extract of *G. glabra* in a single dose of 2mg/kg showed that glycyrrhetic acid prevents the drug induced liver injury and ensures the description of bile acid metabolism in human by inhibiting the free radical generation and lipid peroxidation. they also concluded that glycyrrhizin modifies the intracellular transport and suppresses the hepatitis B virus surface antigen and prevents the

oxidative and hepatic damage caused by aflatoxin through increasing cyp1A1 and glutathione s-transferase activity also by metabolic deactivation of hepatotoxin (4)(7)

Antidiabetic activity: Treatment of non insulin dependent mice with glycyrrhizin was evaluated and reported that it will leads to decrease the blood glucose levels after one week of feeding test. glycyrrhizin reduced the lipid and blood glucose levels by acting various mechanisms by inhibiting 11 β -HSD. And reported that intra peritoneal administration of glycyrrhizin at a specific dose of 50mg/kg decreased the 11 β -HSD in a subcutaneous adipose tissue, liver, kidney, abdominal muscle. (23) (Sen et al) was carried out a comparison study between glycyrrhizin and antidiabetic drug glibenclamide and reported that STZ diabetic efficacy was significantly stimulated by glycyrrhizin by regulating glucose intolerance behaviour and blood glucose levels by in enhancing glycohaemoprotein, cholesterol triglyceride levels and reduced the level of serum insulin (20) Glycyrrhetic acid and glycyrrhizin bind to mineral corticoid receptor with less affinity than that of aldosterone and bind to glucocorticoids receptor with less than affinity than that of dexamethasone. their use in association with spironolactone is used to avoid major side effects in treatment of (PCOD) to increase anti androgen activity of spironolactone and limit its hypotensive properties hence mineral corticoid activities of licorice can decrease the incidence of spironolactone diuretic side effects. (23)

Effects of licorice on body weigh: Studies were carried out on rats by pre_treating them with licorice infusion and tea forms and concluded that after 4 weeks the mean value of body gains for control and pre treated Rats group with licorice infusion and tea were 118.5, 132.6, 121.7 gm respectively. And reported after 8 weeks, the group of male rats which drank licorice infusion were found to increased in weight than that of control. (36)

Effect of licorice in orodental diseases: Aqueous extract, ethanolic extract, supercritical fluid extract of licorice shows a potent inhibitory activity against gram positive and gram negative bacteria (S aureus, E. coli, streptococcus mucus, Paurogenosa, C. albicans, B. subtilis) shows good antibacterial activity. (Sedighiniaf. et al, sug J A et al, Segal R et al, Lingrajat. al, saleem D et al) carried an in vitro

study to check the antimicrobial activity of deglycyrrhizinate licorice root extract (DG_CRE) on streptococcus mutants UA159 in plank tonic and biofilm culture and they reported that it shows antimicrobial activity against S. mutant in plankton phase. they also reported that antifungal activity of licochalcone A reduced the biofilm growth compared to control group by reducing number of colony forming units. (5)

Anti inflammatory activity: Use of G. glabra for the treatment of inflammation have been used since ancient time. (R. yang, yuan, Ma, zhou, harwanshh, patra, pareta, Singh and biswas) had been evaluated the anti inflammatory activity of G. glabra in Male rats after 4 weeks after four week of food intake by lowering the total cholesterol and triglycerides level and in the level of serum liver enzymes due to its contribution In increasing the secretion of serotonin and prostaglandin in stomach that led to a decrease of gastric inflammation. glycyrrhizin shows the anti inflammatory effects as similar to the glucocorticoids and mineral corticoids it is reported that glycyrrhizin inhibit the granuloma formation in liver and inflammatory cytokines formation. glabridin also shows the activity on Raw cells. (4)(8). Nirmala and salvaraj carried out studies by using hydroalcoholic extract against carrageenan induced rat paw and they found that this extract prevent the leukocytes migration in a dose dependent manner. (31)

Antitussive and expectorant activity: Licorice extract have been useful in treatment of sore throat cough, bronchial catarrh. These effects are due to presence of glycyrrhizin which will help in to expel the congestion in upper respiratory Tract and accelerated tracheal mucus secretion. (9)

Antiulcerative activity: Licorice extract used in treatment of spasmodic pains of chronic gastritis, it is used as adjuvant. Glycyrrhizin which is the active component from the extract have been reported for this activity which were act by increasing the concentration of prostaglandin in digestive tracts, promoting the stomach mucus secretion. (Jafarian, Ghazviani, Ram, lachaki, shreedhara) carried out a study in aqueous extract of licorice and they have been reported that it also prolongs the lifespan of stomach surface cell, demonstrating an antipepsin effect. The two most important enzymes prostaglandin, 15 hydroxyprostaglandin dehydrogenase and prostaglandin reductase increase the prostaglandin

which stimulate the mucous secretion and cell proliferation leading to ulcer healing.(4)(8)

Antiviral activity:The mechanism of this compound by inhibiting the adsorption and penetration of the virus in early steps of replicative cycle. due to immunostimulant properties of glycyrrhizin it induces the synergistic effect with duck hepatitis virus (DHV) vaccine due to activation of T.lymphocyte proliferation and hence they are used in treatment alone or in combination with DHV vaccine for an immune stimulation and anti viral effect against DHV(Damle 2014,)reported that, kaposi sarcoma associated herpes virus can be treated by using licorice extract containing glycyrrhizic acid. Glycyrrhizin effects the cellular signalling pathways such as proteins kinase, casein kinase, transcription factor such as activator proteins 1, nuclear factor kB. glycyrrhizin decreases the expression of pro inflammation cytokines affecting Coxsackie virus,B3_induced myocarditis. And hence glycyrrhizin has been used to treat patients with HIV_1.

They also reported that glycyrrhizin can be given intravenously for the treatment of acute onset autoimmune hepatitis.

(Huang.et.al,2017) reported that glycyrrhizin can be used as a novel therapeutic method to control porcine epidemic diarrhoea virus (PEDV) infection by inhibiting the infection of vero cells and decreasing the m_RNA levels of pro inflammatory cytokines.(34)

Antidepressive activity:(TST,Dhinga, and sharma in 2016) had been found that licorice extract showed the significant antidepressant effects in mice during forced swim test (FST) and tail suspension test (TST).in FST model, mice were found to swim in a restricted space and induced a immobility and shows a state of depression. The TST model also induced the state of immobility and the licorice extract have been applied to these models and study the anti depression activity and concluded that extract may interact with alpha 1 adrenoceptors and dopamine D2 receptors, and this increasing the N.E and dopamine in mice receptors. Licorice extract reversed the reserpine induced depression by restoration of brain monoamine such as N.E and dopamine because use of reserpine produce a significant depression by depleting biogenic amines in brain.(17)

Sedative activity:Gamma _aminobutyric acid (GABA) receptor is a target for anaesthetic, neuroleptic, antibiotic and anticonvulsant compounds.(Hoffmann,Beltran, Ziemba, halt, Gisselmann in 2016) carried out study and concluded that G.glabra act as modulator of GABA receptor by its ability to induce sedative and anxiolytic effects. (Tin et.al 2013) reported that glabridin potentiated GABA _ Induced responses by positive modulation of GABA receptors. Exhibiting sedative and hypnotic effects also glabridin could produces the hypnotic effects as it as able to cross the blood brain barrier.(29)

Effects of licorice on skin :Due to antioxidant, anti-inflammatory and UV protection activity of G.glabra it has beneficial effects on skin .studies have been carried out by S castangia in 2015 and they have been found that flavonoids(alpha keto group) shows the depigmenting capabilities by tyrosine inhibition.also concluded that licorice extract by scavenging DPPH Free radicals they can inhibit them 80% and protect fibroblasts against oxidative stress.(12)Tyrosine inhibitor prevents the pigmentation disorder such as melasma, age spot etc. Hence studies has been carried out by(y.j Kim, E banks, wickets and bio assay 2009) by using licorice extract and concluded that glabridin, glabrene, isoliquiritigenin, licochalcone and liquiritin compounds capable of inhibiting the tyrosinase activity. Grippaudo and Di Risso (2016) reported that topical applications of glycyrrhetic acid with combination of fractional carbon dioxide laser for the benign treatment of hand hyperpigmentation for 4 weeks. The treatment of human keratinocytes with 18_ beta_glycyrrhetic acid and glabridin was reported that they directly and indirectly inhibit or prevent the DNA damage, avoiding the apoptosis activation caused by UV B radiation. (Saumenda, Raj, suwakanta, jashaabirbiswajit, 2104) reported that hydro alcoholic extract of licorice promotes hair growth, being safety used in herbal formulations for the treatment of various type of alopecia.(19)

Effects on smooth muscle:Studies was carried out by using hydro alcoholic extract of licorice rhizome and epinephrine on mechanical activity of isolated colon of the male rats and found that activity of tissue in presence of extract and epinephrine was reduced (p<0.05) as compared to control group. .licorice as compared to control group when treated with propranolol but there is no change in activity.when treated with phenylephrine and extract

compared to control group and result was concluded that hydroalcoholic extract of licorice had modifying effect on colon motility synergistic effects with adrenergic receptors and independent of alpha adrenergic receptors. Isoliquiritigenin was found to be a potent relaxant, it inhibited the contraction where induced by cch, KCl, BaCl₂, IC₅₀ values of 4.96 ± 1.97 µM, 4.03 ± 1.34 µM, 3.7 ± 0.58 µM mechanism of action of licorice root extraction on duodenal motility in vitro was evaluated on rats by using treated with acetylcholine (10⁻⁵) as muscarinic receptor antagonist and muscarinic antagonist (10⁻⁴), and beta adrenoceptor agonist epinephrine (10⁻⁶) and beta adrenoceptors antagonist (propranolol) and inhibitors of the NE synthase enzyme.

Oestrogenic and androgenic effects of licorice

Studies have been carried out by (G. Sharma et al., 2012) found the ethanolic extract of licorice showed the oestrogenic effect by its agonist activity on MCF-7 breast cancer cells, this action is mediated by 18 β -glycyrrhetic acid and glabridin is used for the treatment of menopausal symptoms and in concentration between 2.5 and 25 µg per animal, glabridin induces the similar effects as the administration of oestradiol in a concentration of 5 µg per animal. Glabrene and glabridin are equal to 17 β oestradiol activity for the stimulation of the specific activity of creatine kinase (Power and Setzer, 2015) reported that in vitro stimulatory effects of glabrene are similar to those of oestradiol and isoliquiritigenin and formononetin stimulates the sperm during fertilization hence used in infertility treatment. (Tung, Shoyama, Wada, Tanaka, 2015) reported that ethanolic extract of *G. glabra* shows the antiandrogenic effect by increasing the testosterone metabolism, down regulating androgen receptors and activating estrogenic receptors. (21)

Neuroprotective effects of licorice

(Chakraborty and Avadhani 2013) carried out a study with aqueous root extract of *G. glabra* on one month old Male wistar albino mice at a dose between 75 and 300 mg/kg for the learning and memory outcomes. This study concluded that there is a significant improvement of learning and memory in mice, but the mechanism is unknown but they suggest that due to neuroprotective effects of licorice. Hence they can use for the prevention of Alzheimer's disease. The anti-inflammatory activity of licorice contributes for

the enhancing the memory effects and due to its protective actions.

It may be attributed to its antioxidant properties due to which reduction in brain damage and improvement of neural function and memory has been seen. In a simple word the both anti-inflammatory and antioxidant activities with neuroprotective role could lead to memory enhancing effects. Hassanein carried out a study of the chronic treatment cognitive function of diabetic Rats with glabridin and concluded that there is an improvement of learning and memory in non-diabetic rats and reversal of learning and memory defects in diabetic rats and these were due to antioxidant, neuroprotective and anti-cholinesterase properties of glabridin and hence it can be used in treatment of dementia diabetic patients. (22)

Methanolic extract of licorice shows potent antifungal activity towards *Chaetomium funicola* M002 and *Arthrinium sacchari* M001 and this activity is due to glabridin. Licochalcone has been shown to have potent antiplasmodial activity. Christen et al. concluded the efficacy of chalcone for in vitro antileishmanial activity was evaluated and also effective against *Babesia* and *Theileria* parasites. Glycyrrhizin has been proved to prolong thrombin and fibrinogen coagulation time and increase the time for recalcification of plasma in vitro and hence it is considered to be the first plant-based thrombin inhibitor. Polysaccharides part of *G. glabra* shown immune-stimulating activity by stimulating macrophages and hence raises the immune response. The hydroalcoholic licorice extract found to attend the efficacy of colon motility by its synergism with B-adrenergic receptors only without affecting alpha adrenergic receptors. Rhizome of licorice extract reduces the contraction force of duodenum which is induced by acetylcholine without affecting the B-adrenergic, cholinergic pathways. *G. inflata* extract has been reported to induce spinocerebellar ataxia type 3 (SCA3) by increasing the nuclear factor erythroid-2 related factor 2 antioxidant responsive element (NFE2L2-QRE) peroxisome proliferator-activated receptor gamma activities.

III. RESULT AND DISCUSSION :

Pharmacokinetics of *G. glabra* extract and its metabolites:

Glycyrrhizin and glycyrrhetic acid are the inhibitors of 11 β -HSD1 and 11 β -HSD2 to which it converts the active glucocorticoids into inactive glucocorticoids and glycyrrhizin prevents

the activity of 11beta _HSDI due to which it reduced the properties of active peroxisome proliferator activated reported organisms and glucocorticoids properties due to which is increased expression of lipoprotein lipase in all tissue after glycyrrhizin administration.

Glycyrrhizin shows the impaired oral bioavailability in humans. Glycyrrhetic acid after oral administration are more relevant than glycyrrhizin acid as they show 200_1000 time stronger 11_beta HSD inhibition glycyrrhetic acid is rapidly absorbed and transmitted the level by carrier molecules where it is metabolized by lysosome B_D glucuronidase to 3_mono _glucuronide 18 beta glycyrrhetic and sulfate conjugates and then degrade to glycyrrhetic acid and reabsorbed due to which it delay the plasma clearance the plasma clearance is the dose dependent hence at high doses it exceeds the serum protein binding saturation but at low doses it is not dose dependent. Isbrucker and Burdock reported that when we examine the activity of glycyrrhizin in alone and in combination with 18_beta_glycyrrhetic acid in rats and it is concluded the pure glycyrrhizin single therapy is more and it shows of significant variation in Tmax,AUC,Cmax of glycyrrhetic plasma clearance of glycyrrhizin and decrease in chronic hepatitis c and liver cirrhosis, due to their capacity limit of liver for their metabolism and excretion in bile.

Dose, side effects and contraindications :

Administration of liquorice for longer period of time may increase the risk of hyperkalemia, increased B.P, excess mineralocorticoid in the body. LD50 value for glycyrrhizin in rat and mice was found to be 44.4g/kg for subcutaneous and (1.42_1.70)g/kg for intra peritoneal and 1.42_18.0g/kg) for oral route of administration and also reported that people with kidney and heart problems are more prone to toxication also administration of high doses of glycyrrhizin causes pseudo hyperaldosteronism due to which person become hyper sensitive to adrenal cortex hormone and thus shows various adverse effect such as heart attack high ,headache, fatigue, water retention and also it is contraindications in pregnancy. Glycyrrhizin is contraindicated with contraceptive specially prednisolone.

IV. CONCLUSION:

Literature studies indicate that G.glabra has been used for various biological activity hence it is very intentionable one there is a still need to do

more 3 to identify more specific active constituent which are responsible for biological activity licorice has been used as a traditional medicine and flavouring and sweetening agent in food industry due to the presence of flavonoids it shows varies biological activity different phytochemicals including glycyrrhizin 18beta glycyrrhetic acid globin A and B or isoflavone have been identified and associated with various biological activities reported namely antioxidant antiviral, antimicrobial, anticancer, antiinflammatory and hepatoprotection side effects. and toxicity of licorice are very less which is hypertension and fluid retention. there is a still need to carry out double blind randomized controlled trial there is an immense scope to explore formulation of licorice with different constituent

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