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## SCIENTIFIC, PHYTOCHEMICAL, AND PHARMACOLOGICAL STUDY OF PLANT *GLYCYRRHIZA GLABRA* LINN.

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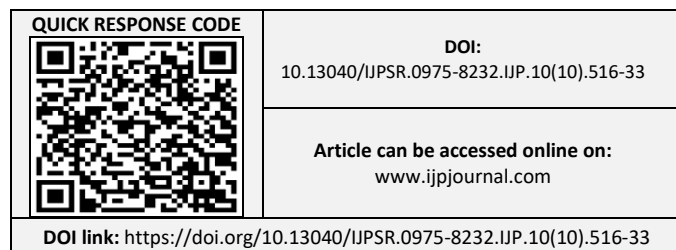
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**ABSTRACT:** There is a bigger need for herbal cures and solutions in today's world of increasing ailments. Different work habits lead to different diseases. Although very simple, the allopathic curative method involves several negative side effects. Therefore, this is the area of interest that compelled us to use allopathic or synthetic pharmaceuticals that are derived from plants. Fabaceae is a family of plants that includes the species *Glycyrrhiza glabra*. Glycyrrhiza is a well-known herb used in Western herbal therapy that has been grown in Europe, Asia, and the Middle East for over 4,000 years. We concentrate on the body of knowledge about plants with medicinal value. This article summarizes the many applications, chemical makeup, pharmacological effects, and phytochemistry of *G. glabra*. The scientific names and categories of phytochemicals serve as examples of native *G. glabra* compounds. Glycyrrhizin, a triterpenoid saponin that is more than 50 times sweeter than sucrose, is the major chemical in the root that is active. The digestive medicine *Glycyrrhiza glabra* flavonoids extract has a variety of pharmacological effects on living things and aids in gastrointestinal system lubrication. Licorice has a variety of benefits, including the ability to lighten skin, enhance memory, control diabetes, boost immune function, and have hepatoprotective and antiviral qualities. This article summarizes recent studies on the plant, including its bioactive components and traditional use, in order to thoroughly investigate its health benefits.

**INTRODUCTION:** *Glycyrrhiza glabra*, a medicinal plant, is fused in traditional medicine worldwide for its ethnomedicinal value in treating various diseases<sup>1</sup>. Root, a common liquid genus species, contains glycyrrhizine and Glycyrrhizinic acid as its chemical constituents<sup>2</sup>. Extracts are used to treat various diseases such as eye, throat, peptic ulcer, liver, immunodeficiency, cough, tuberculosis, respiratory, endocrine, kidney, psoriasis, eczema, haemorrhoids, epilepsy, and heart diseases<sup>3</sup>.

*Glycyrrhiza glabra*, a sweet wood plant native to the Mediterranean and Asia, was used in ancient civilizations as carminatives, and expectorants. The English word 'Glycyrrhiza' is derived from the 'Greek' words 'glykos' meaning 'sweet' & 'rhiza' meaning 'root'. *Glycyrrhiza glabra* Linn. is a member of the 'Fabaceae' family and has various vernacular names in different languages<sup>4,5,6</sup>.

Liquorice is commonly used for post-childbirth lactation. Liquorice is used to treat oral cavity issues and hoarseness and is recommended for mental development as a memory booster. Glycyrrhiza, a genus of 20 species, is distributed globally a species native to North Africa, is the primary source of confectionery liquorice, grown in India, Spain, Iran, Russia, and China<sup>6</sup>. This compound is used as a laxative, galactagogue, anti-asthmatic, antacid, and antiviral agent in various



therapeutic oils, including those used for conditions like rheumatism, paralysis, and epilepsy. Liquorice, a key component in the "Liquorice compound powder," accelerates the action of senna and is used in treating peptic ulcers<sup>7-9</sup>. *Glycyrrhiza glabra* L, an indigenous perennial in Asia and Europe,

contains a triterpenoid saponin called Glycyrrhizin, which is 50-200 times sweeter than sucrose, with the monoglucuronide being sweeter<sup>10-12</sup>. *Glycyrrhiza* species like *G. uralensis* also produce glycyrrhizin<sup>13,14</sup>.



FIG. 1: DIFFERENT FORMS OF *G. GLABRA* ROOTS & POWDER FORMATION

TABLE 1: SCIENTIFIC CLASSIFICATION OF *GLYCYRRHIZA GLABRA* LINN

Kingdom	Plantae
Division	Angiospermae
Class	Dicotyledoneae
Subclass	Magnoliidae
Order	Rosales
Superorder	Rosanae
Family	Leguminosae
Genus	Glycyrrhiza
Species	Glabra linn

**Collection and Processing of *Glycyrrhiza glabra*:**

Liquorice root was dried and powdered, then dissolved in sterile water, incubated, and filtered.

The mixture was then stored at 4°C until needed and then filtered<sup>15-17</sup>.

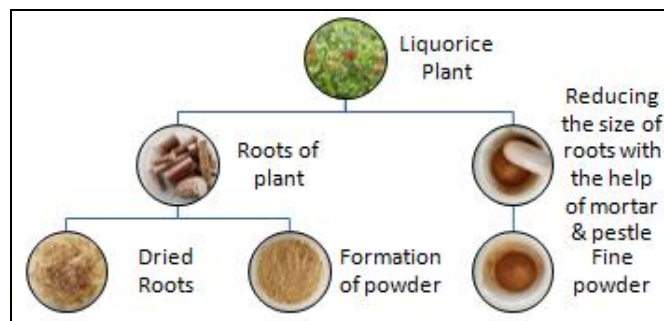


FIG. 2: FLOW CHART FORMATION OF LIQUORICE POWDER FROM ROOTS

TABLE 2: LIQUORICE & THEIR VERNACULAR NAMES<sup>18</sup>

S. no.	Language	Common names
1	Hindi/ Gujarati	Jethi-madh, Jothi-madh, and mulaithi, Jashtimadh, Yashti-madhu
2	English	Licorice, liquorice, sweet wood
3	Tibetan	Sin mnar
4	Urdu	Asl-us-soos, asal-ul-sus muqqashar, asal-us-sus nim kofta
5	Persian	Beikh-e-mahak, bikhe-mahak, bikhemahak, mahak, and mazhn
6	Malayalam	Malayalam, Iratimadhuram
7	Telugu/ Tamil/ Kannada	Atimadhuranu, Yashtimadhukam/ Vatalam/Yastimadhuka
8	Arab	Aslussiesa
9	France	Boisdoux
10	Germany	Sussholz

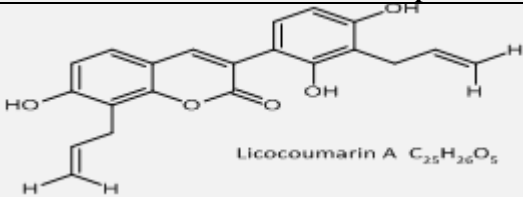
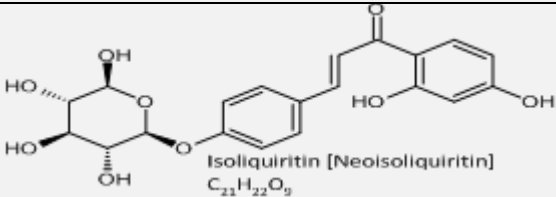
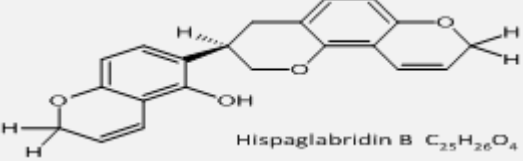
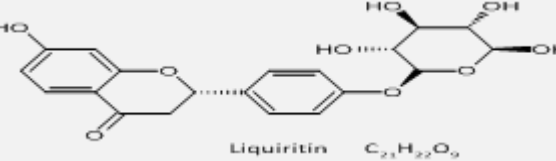
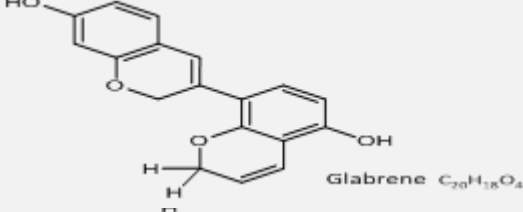
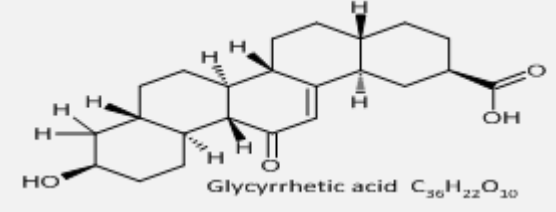
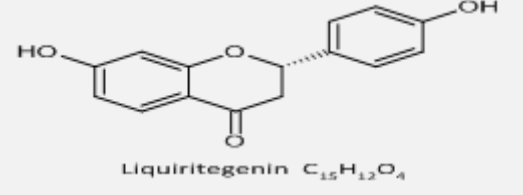
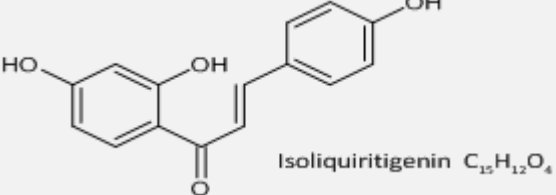
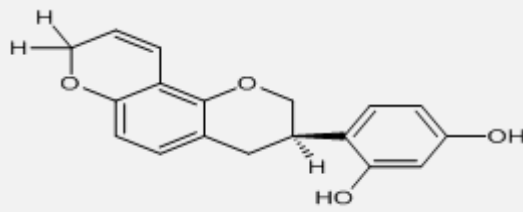
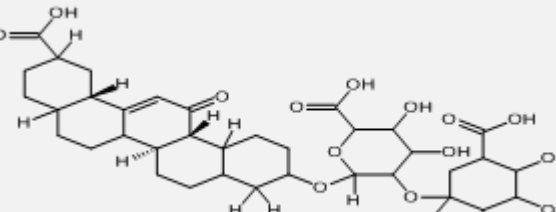
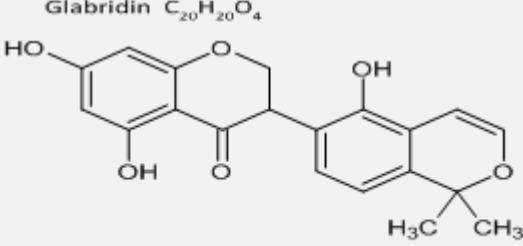
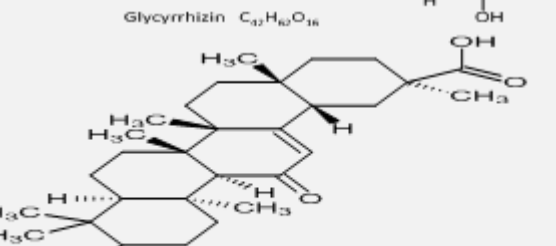
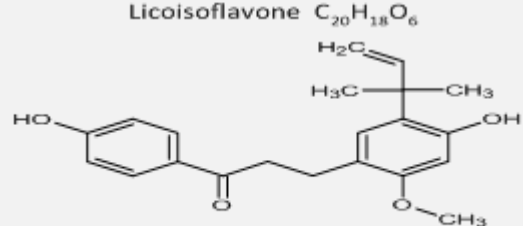
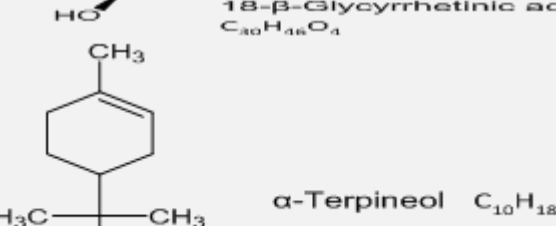
**Phytochemical Reviews:** *Glycyrrhiza glabra* roots are utilized to extract various substances, including a water-soluble, physiologically active complex

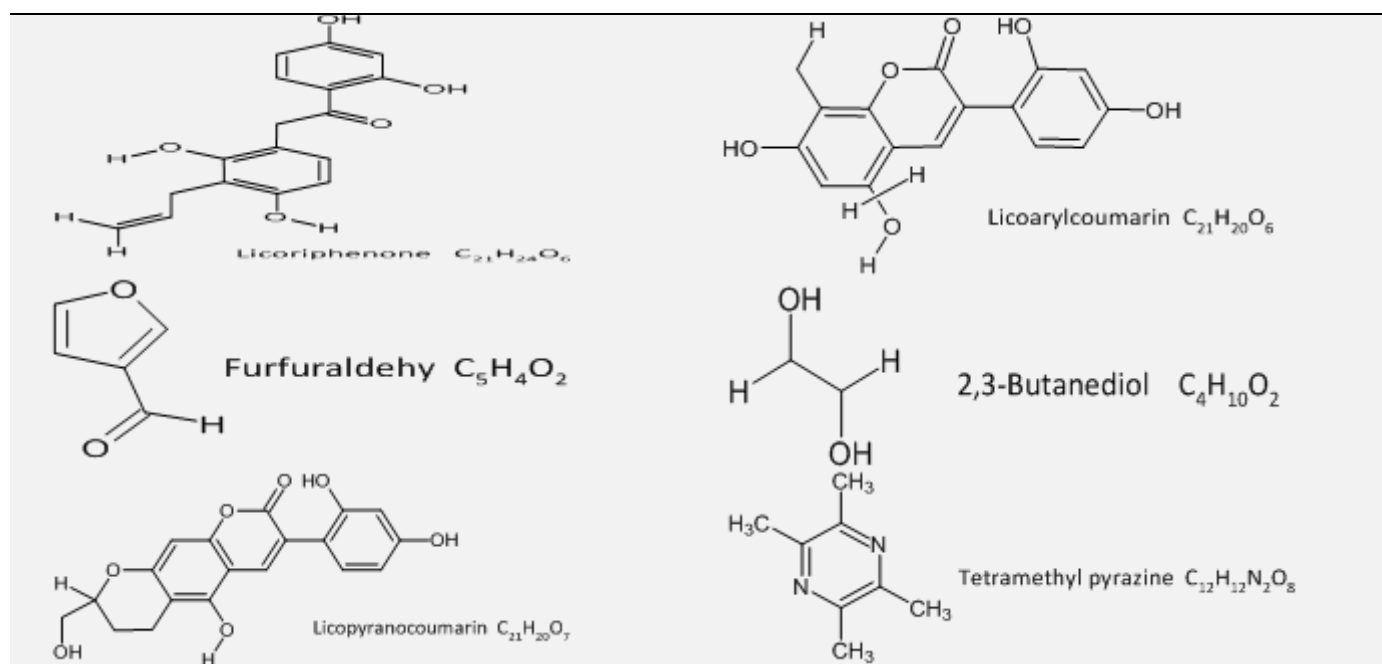
that constitutes 40-50% of the dry material weight. This complex comprises various substances including triterpenes, saponin, flavonoids,

polysaccharides, pectins, amino acids, mineral salts, asparagines, bitters, essential oils, fat, estrogen-producing hormone, gums, mucilage, protein, resins, starches, sterols, volatile oils, tannins, glycosides<sup>19-21</sup>. Sinmar distinctive yellow color is attributed to the presence of flavonoid-

containing chemicals like liquiritin and isoliquiritin<sup>22</sup>. The antioxidant properties of isoflavones, including glabridin, hispaglabridins A & B, glabrene & glabridin both possessing estrogen activity<sup>23</sup>.

**TABLE 3: CHEMICAL CONSTITUENTS & THEIR STRUCTURES**

Compound / Chemical formula/ Chemical Structure	
 Licocoumarin A $C_{25}H_{26}O_5$	 Isoliquiritin [Neoisoliquiritin] $C_{21}H_{22}O_9$
 Hispaglabridin B $C_{25}H_{26}O_4$	 Liquiritin $C_{21}H_{22}O_9$
 Glabrene $C_{20}H_{18}O_4$	 Glycyrrhetic acid $C_{30}H_{22}O_{10}$
 Liquiritigenin $C_{15}H_{12}O_4$	 Isoliquiritigenin $C_{15}H_{12}O_4$
 Glabridin $C_{20}H_{20}O_4$	 Glycyrrhizin $C_{47}H_{60}O_{16}$
 Licoisoflavone $C_{20}H_{18}O_6$	 18-β-Glycyrrhetic acid $C_{30}H_{48}O_4$
 Licochalcone A $C_{21}H_{22}O_4$	 α-Terpineol $C_{10}H_{18}O$



**Procedure for Extraction of Isoliquiritigenin Flavonoid:** Dried, roots powdered, then extracted using ethanol-water (1:1) mixture at room environment. Filtration, resulting in hydroalcoholic extract, after being combined and evaporated. The extract underwent acid hydrolysis in a 5% HCl

solution, resulting in a reaction mixture that was extracted with ethyl acetate<sup>24</sup>. The ethyl acetate extract was fractionated on silica gel using a mixture of ethyl acetate and chloroform solvent system as an eluent<sup>25, 26</sup>.

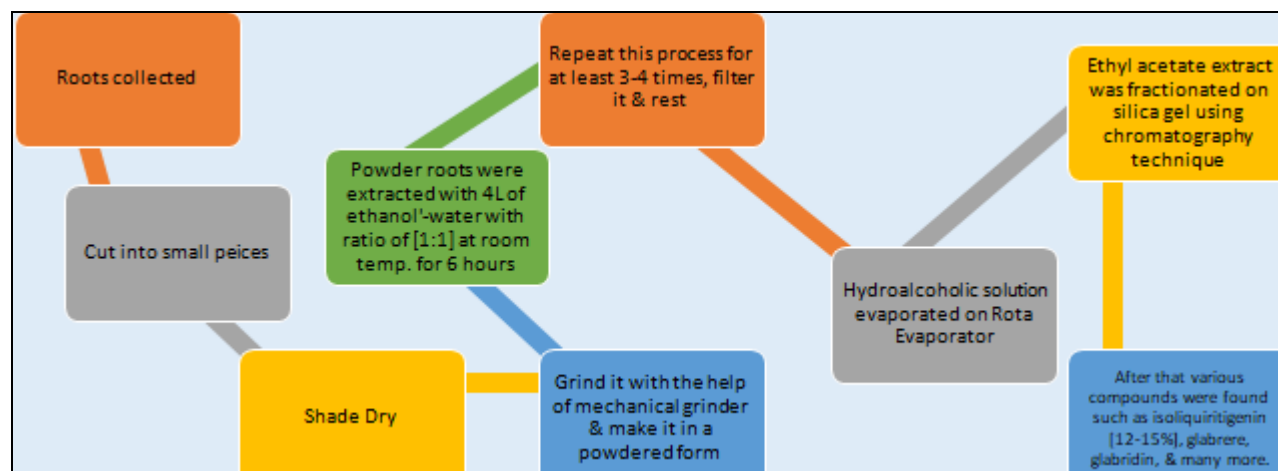


FIG. 3: FLOW CHART OF EXTRACTION PROCESS

TABLE 4: VARIOUS PHARMACEUTICAL PREPARATIONS UTILIZED IN *GLYCYRRHIZA GLABRA* LIN<sup>27</sup>

S. no.	Name	Manufacturer	Composition	Therapeutic Uses	Ref.
1	Gut gard	Natural Remedies	<i>Glycyrrhiza glabra</i> extract [ $>10\%$ flavonoids content]	Promotes GIT, soothes heart burn, antioxidant support	(28)
2	Liquorice root 500mg	Pure Science supplements	10% <i>Glycyrrhiza glabra</i> extract of root, deglycyrrhizinated Liquorice	Supports digestive, and respiratory function, expectorant & demulcent	(29)
3	Health aid Liquorice [GG 50ml]	Health aid	Each 1ml Liquorice liquid: Liquorice extract 1:3 [equivalent of 330mg of Liquorice herb]	Dry cough, promotes clear & comfortable breathing	(30)
4	Solaray Liquorice 450mg-100 capsules	Nutraceutical	Liquorice [ <i>Glycyrrhiza glabra</i> (root), Gelatin & mag. stearate	Health supplement	(31)

5	Nature sunshine Licorice roots	Nature sunshine	Liquorice root 792mg	Supports glandular system, specifically adrenal glands & liver (32)
6	Chewable DGL Licorice tablets	Nature Garden	Deglycyrrhizinated Licorice 380 mg [ <i>Glycyrrhiza glabra</i> ] (root), L-Glycine 50mg	Health supplement (33)
7	Banyan botanicals licorice root powder	Banyan Botanicals	<i>Glycyrrhiza glabra</i> extract	demulcent, dry cough, relives breathing, balanced adrenals, proper kidney works (34)
8	Nature republic cotton armpit cream	Nature republic	<i>Glycyrrhiza glabra</i> root extract component	Claims to whiten, brighten, deodorize underarm, give powdery fragrance (35)
9	Himalaya clear complexion whitening face wash	Himalaya	Pomegranate, saffron, liquorice, dhupa fat	Removes dark spots, cleanses & clarifies impurities (36)
10	Liquorice extract- with retinol	Seattle	Retinol, liquorice	Anti-aging cream & removes wrinkles (37)

### Pharmacological Reviews of Licorice:

**Antitussive/Expectorant Activity:** Licorice powder extracts effect on treat of sore throat, cough, and bronchial catarrh by acting as an expellant, accelerating tracheal mucus secretion<sup>38</sup>. Liquiritinapioside, an active compound in mulaithi methanolic extract effectively inhibit capsaicin-induced cough<sup>39</sup>. Noscough® syrup, containing noscapine and licorice, is an opioid antitussive that reduces bradykinin-induced cough in humans that can be linked to COVID-19 symptoms<sup>40, 41</sup>. Bradykinin & cytokine storms may contribute to worse COVID-19 outcomes, suggesting that mediating these pathways may improve relieving symptoms. Noscapine is a safe candidate with potential benefits in modulating both pathways<sup>30, 42</sup>. liquoriceunlike diphenhydramine, has no sedative effects, no anticholinergic effects, making it beneficial for the elderly, and has antiviral effects against various viruses, including SARS. Phaseol in, liquorice may reduce COVID-19 inflammatory response by inhibiting CXCL8 and IL2RA activation. *In-silico* analysis reveals noscapine and hydroxychloroquine conjugates have binding affinity for SARS-CoV2 protease, crucial in COVID-19 pathogenesis. , liquorice with its ingredients like Glycerol and Glyasperin Fhas been shown to potentially reduce COVID-19 symptoms and potentially block SARSCoV-2 replication *in-vitro*<sup>43</sup>.

**Immunomodulatory Activity is a Crucial Aspect of Immune Function:** Swine flu, a low-mortality species-specific respiratory disease has spread widely among humans due to the Influenza-A

H1N1 virus, which has the ability to cross species barriers and stimulate macrophages<sup>44</sup>. N-acetylmuramoyl peptide, a glycyrrhizin analogue with potential *in-vitro* immunostimulant properties<sup>45</sup>. Animal studies show glycyrrhizic acid efficacy against influenza-virus inhibits replication, a potential immunomodulator<sup>46</sup>. Glycyrrhizin consumption is safe for children aged 5-11 with a daily intake of 2mg/kg/day for children aged 10 years old<sup>47</sup>. Overconsumption of glycyrrhizin in 8-year-old children may cause adverse effects on mineral corticoid activity including hypertension, hypokalemia, hypertensive encephalopathy, rhabdomyolysis & cardiac arrest, using liquorice in foods for its health benefits<sup>48</sup>. Clinical trials show glycyrrhizin's inhibitory effect against chronic hepatitis C, HIV-1, herpes-virus, epstein-barr virus, and influenza virus. It is potent in inhibiting SARS-CoV replication in Vero cells, limiting virus adsorption, penetration<sup>49, 37</sup>. Sweet wood active compound N-acetylmuramoyl has potent immunomodulatory activity, immobilizing viruses, and stimulating macrophages, with potential for *in vitro* immune stimulation<sup>50</sup>. Sweet wood & ginger extracts in fish feed effectively stimulate growth, prevents heavy metal contamination in Nile tilapia ponds, either alone or in combination. *G. glabra* root extract's immunomodulatory activity, linked to glycyrrhizin phenolic compound, increased lymphocyte and macrophage production from human granulocytes *in-vitro*<sup>51, 52</sup>.

**Eye Inflammatory Activity:** A study on 60 cases of herpetic keratitis, keratoconjunctivitis, and fascicular keratitis found that eye drops with 5%

sodium glycyrrhizinate, glycyrrhetic acid, or herb extract effectively treated nodules and inflammation<sup>53</sup>. Bacterial keratitis is treated with antibiotics but local administration is preferred due to blood-ocular barrier restrictions. High solubility of DG-Hes enhances antioxidant properties by preventing keratitis progression<sup>54</sup>. DG-Hes ophthalmic solution demonstrated strong antibacterial activities *in-vitro/vivo*, i.e., similar to levofloxacin eye drops. *In-vivo* tests showed clinical scores, corneal test & histopathological observation. The physical mixture of DG-Hes showed stronger antibacterial activities. DG-Hes exhibited stronger antibacterial activities compared to physical mixtures indicating micelle formation gives positive effect. It also demonstrated good *in-vivo* eye tolerance in rabbits. The DG-Hes ophthalmic solution significantly improved DG-He bioavailability and antibacterial activities, suggesting the potential for a new ophthalmic solution formulation for other ophthalmologic drugs<sup>55, 56</sup>.

**Hepatoprotective Activity:** The aqueous extract of *Glycyrrhiza glabra* roots was found to prevent and treat liver disorders in rabbit models with a dose of 2gm/kg/day orally for 7 days<sup>57</sup>. This study compares the efficacy of Gly and Mat alone and their combination in China for liver function protection and tumor treatment. It aims to determine if concomitant use reduces side effects like Na-H<sub>2</sub>O retention, and hypokalaemia, and enhances hepatoprotective & anti-hepatocarcinogenic effects<sup>58</sup>. The study investigated Gly+Mat hepatoprotective effects using an acetaminophen-induced hepatotoxicity animal model highlighting the potential risks of over dosage of PCM, i.e., a common analgesic & antipyretic drug<sup>59</sup>. Jatimadhu's beneficial effects stem from its glycyrrhizin & glycyrrhizic acid proved to inhibit the growth and cytopathology of various RNA/DNA viruses<sup>60</sup>. The study found that combining Gly+Mat can reduce acetaminophen overdose mortality in mice attenuate hepatotoxicity, reduce GT positive foci, protecting liver function and preventing HCC while also reducing sodium Na-H<sub>2</sub>O retention<sup>34</sup>.

**Antiulcerogenic Activity:** GutGard™ showed dose-dependent anti-ulcer activity in a pylorus ligation ulcer model, decreasing gastric content,

total acidity, & ulcer index. Its antioxidant properties may contribute to its antiulcerogenic properties and its effects on gastric ulcers in rats were studied. A licorice extract was demonstrated potent antioxidant activity and antiulcerogenic properties supporting its ethnomedical use in treating gastric ulcers through cytoprotective mechanisms<sup>61, 62</sup>. *H. pylori* causes gastroduodenal diseases including ulcers and stomach cancers. Glycyrrhizin reduces hepatocellular carcinoma risk, i.e., beneficial for chronic hepatitis C treatment possibly due to its bactericidal effect<sup>63</sup>. Recent studies in Japan attribute Anti-*H. pylori* activity to glycyrrhizin a constituent of liquorice used for peptic ulcers. Overconsumption can cause pseudo-aldosteronism and a maximum dosage of 100 mg glycyrrhizin a day is considered safe and its metabolites<sup>64, 65</sup>.

**Antiobesity/ hypolipidemic/ Antidyslipidaemic Activity:** A study on dyslipidaemic hamsters found that ethanolic extract and its fractions significantly reduced LDL and VLDL levels with the ethanolic extract by showing significant antidyslipidaemic activity<sup>66</sup>. Obesity a result of imbalance between energy intake and expenditure is linked to lifestyle-related diseases like hyperlipidemia, hypertension, arteriosclerosis, Type-2 diabetes and cancer<sup>67</sup>. Obesity is increasing due to excess energy in adipose tissue leading to fatty liver disease. Strategies for prevention and treatment include diet therapy, exercise, weight loss drugs, appetite suppressants, and food supplements, in addition to diet therapy and exercise. Recent studies are exploring functional food ingredients or herbal extracts, the root of *Glycyrrhiza glabra* Linn suppresses weight gain and body fat accumulation caused by high-fat diets<sup>68</sup>. Licorice species including *Glycyrrhiza uralensis* Fischer, *G. glabra* Linne, and *G. inflata* Batalin, contain flavonoids with anti-obesity effects, and strong anti-adipogenic activity. Supercritical fluid extraction effectively prepared glabridin-rich licorice extract by protecting against high-fat diet-induced weight gain and adiposity and ameliorating hepatic steatosis through gene regulation in hepatic metabolism<sup>69</sup>.

**The Activity of Reducing Blood Sugar Levels or Preventing Diabetes:** Sweetwood extract effect on lipid profile and liver enzymes in albino mice was

found to be anti-lipidemic and anti-hyperglycemic, addressing Type 2 diabetes. PPARs classified as PPAR- $\alpha$ , PPAR- $\gamma$ , and PPAR- $\delta$ , regulate gene expression in glucose and lipid metabolism found in liver, muscle, and kidney<sup>70, 71</sup>. Diabetes with long-term health complications is a significant issue with Type 2 diabetes being the most prevalent and expected to increase by 5.4% in 2025<sup>72</sup>. Diabetes mellitus is a chronic metabolic disorder with high glucose levels due to insulin non-secretion leading to the discovery of metformin (hypoglycemic drug)<sup>73</sup>. Isoliquiritigenin and liquiritigenin, flavonoids found in licorice root have antioxidant, anti-inflammatory, and antitumor properties<sup>74</sup>. LTG, an estrogenic compound acts as an agonist for the subtype of oestrogen receptor<sup>75</sup>. The study focused on obtaining antidiabetic compounds from structural modifications at C-4, C-2 and 4 positions on ISL and C-7, C-4 positions on LTG reporting its antidiabetic activity<sup>76,77</sup>.

ISL and LTG have been previously reported as anti-inflammatory, hepatoprotective, antimycobacterial, & antitumor agents<sup>77, 78</sup>. Bioactive compounds either alone or in combination have shown enhanced antidiabetic activities with rutin and silymarin therapy reducing glucose levels and increasing antioxidant activity in diabetic rats. Another discovery discovered that piperine and quercetin significantly enhance curcumin's antidiabetic potential suggesting that combining these compounds could be more effective<sup>79</sup>. Future research in diabetic disease management should explore the combination of bioactive compounds with foods or synergistic efficacy comparing results to metformin and evaluating antihyperglycemic activity in diabetic rats<sup>78</sup>. The combined formulation of pure and NF showed more antidiabetic effect on diabetic rats, as insulin deficiency leads to decreased protein production resulting in decreased body weight<sup>79,80</sup>.

**The Text Discusses the Activity of Skin Lightening, Whitening, and Tightening:** Liquiritin in liquorice extract induces skin lightening is safe and effective. Glabridin inhibits tyrosinase activity in B16 murine melanoma cells without affecting DNA synthesis. Glabrene, Licochalcone A and Isoliquiritin are known to inhibit tyrosinase activity<sup>81</sup>. *Glycyrrhiza glabra*'s ethanolic extract enhances skin viscoelastic and

hydration properties, possibly due to its UV protective, antioxidant and anti-inflammatory properties<sup>82</sup>. Liquorice extract due to its effective tyrosinase inhibition activity can be utilized in the creation of depigmenting cosmetic formulations<sup>35, 83</sup>. Licorice extracts contain active compounds that can stimulate or suppress melanogenesis. Glabridin, a key ingredient that inhibits tyrosinase activity in murine melanoma cells, while other compounds like glabrene and isoliquiritin also inhibit tyrosinase activity<sup>35, 84</sup>. Liquiritin, a depigmenting agent effective in treating melasma, while licorice extracts are safe and have few side effects by making them the most commonly used pigment-lightening agent in cosmetics<sup>35</sup>. Licorice extract rich in flavonoids can be used in facial foundations and moisturizers for topical anti-inflammatory properties potentially reducing skin redness and hyperpigmentation<sup>85</sup>. Liquiritin promotes skin lightening by dispersing melanin but its clinical results are modest due to its modest concentration in most cosmetics<sup>86</sup>.

**It has been found to have Anticancer and Antimutagenic Properties:** Jothi-madh root extract has antimutagenic properties by inhibiting micronuclei development in bone marrow cells, and causing mitochondrial permeability transition leading to tumor cell apoptosis in human cervix and uterus<sup>87</sup>. The *in-vivo* inhibition of Ehrlich ascites tumour cell growth by the methanolic extracts of *G. glabra* with the corresponding reduction in cell number, body weight and ascites volume<sup>88</sup>. Glycyrrhizin and glycyrrhetic acids are effective in treating gastric cancer, while glycyrrhizin suppresses thromboxane A2 in lung cancer cells with low toxicity<sup>89</sup>.

Jothi-madhhydromethanolic extract demonstrated antimutagenic properties in albino mice inhibiting micronuclei formation and chromosomal aberration in bone marrow cells and thromboxane A2 in lung cancer cells<sup>90</sup>. Glycyrrhetic acid and its derivatives 3-oxy-18 $\alpha$ -glycyrrhetic acid inhibited transplanted myeloma and had antileukemic activity in mice. They also inhibited morphological changes in liver and Ehrlich as cites carcinoma, inhibited Jitian sarcomas and prevented liver carcinoma development. Jothi-madh components were found to increase PGR and GREB1 expression in MCF7 breast cancer cells, with

intrinsic activity comparable to E2 ubiquitin-conjugating enzymes. Jothi-madh, a natural product with flavonoids and saponins has been found to have no anti-non-small-cell lung cancer activity, antioxidant, antiinflammatory and anti-cancer properties. Recent studies shows that glycyrrhizic acid can inhibit the proliferation of endometrial and breast cancer cells and possess anticancer properties through various mechanisms. Combining clinical chemotherapy drugs with licorice compounds reduces side effects and enhances anticancer effects. The flavonoid-rich part of licorice exhibits cytotoxic effects against human oral squamous cell carcinoma cell lines. Licorice inhibits tumor cell proliferation, angiogenesis, and apoptosis in MCF-7 breast cancer cells. Isoliquiritigenin inhibits prostate cancer growth and is effective in cancer prevention. Lic A suppresses oxidation making it a potential anti-cancer and antiproliferative agent<sup>91,92</sup>. Glycyrrhizin stimulates endogenous defense mechanisms and enhances phagocytic activity in neutrophils<sup>46</sup>.

**Antimicrobial Activity:** Licorice leaves ethanol extracts of 4 & 8mg have been found to be effective against *Candida albicans*, *Bacillus subtilis*, and *Staphylococcus aureus*<sup>93</sup>. Root extracts in ether, chloroform, and acetone were found to be effective against both gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*)<sup>94</sup>. The root ethanolic extract showed antimycobacterial activity against *Mycobacterium tuberculosis* H37Ra and H37Rv strains<sup>95</sup>. Glabridin was found to be effective against *Mycobacterium* while hispaglabridin was inactive. Glabridin a potent antimycobacterial molecule has been found to be effective in treating coughs and chest ailments with its 1,3-positions of free phenolic hydroxyls potentially influencing its activity.<sup>(95)</sup>

**The Text Focuses on the topic of Antimalarial Activities:** Further study in *In-vitro* studies showed its antiplasmodial activity against *P. falciparum* and HeLa cells, while *in-vivo* studies inhibited *P. berghei* growth<sup>96</sup>. Licorice containing licochalcone exhibits antimalarial properties with an oral dose of 1000 mg/kg in mice completely eliminating malarial parasites<sup>97</sup>. Chinese pharmacopoeia uses *Glycyrrhiza* species, including *G. glabra*, *G.*

*uralensis*, and *G. inflata*, as sources of Gan Cao. Chalcone licochalcone A, isolated from all species, shows antimalarial activity<sup>98</sup>. Malaria, a global public health threat, is primarily caused by *Plasmodium* species, including *P. falciparum*. The disease mortality is primarily due to *P. falciparum* infections, with multiple drug classes and modes of action<sup>99</sup>. Quinoline-like compounds and artemisinin-based combination therapies are used to treat malaria, promoting the search for antimalarial agents from diverse botanic sources due to their effectiveness. Medicinal herbs with antioxidant, antifungal, anticarcinogenic, anti-inflammatory and cytotoxic properties commonly used in traditional herbal formulas for various diseases<sup>100</sup>. GLR and its metabolites have anti-malaria properties due to two complementary activities, a membrane effect and cholesterol sequestration, stable complexes with HMGB1 proteins. GLR has antiplasmodial properties and low toxicity to human red blood cells making it a less hemolytic saponin<sup>101</sup>.

**Antiviral Activity:** Glycyrrhizin a compound with strong antiviral properties inhibits virus cell binding making it effective against HIV-1, Japanese encephalitis, yellow fever viruses, in controlling viral replication and potential use as a prophylactic measure was evaluated against two SARS isolates<sup>102, 103</sup>. Licorice extract has been found to inhibit the growth of various viruses including Herpes simplex, Varicella zoster, Japanese encephalitis, influenza, vesicular stomatitis virus, and type A influenza virus<sup>104-106</sup>. A study on SARS patients at Frankfurt University in Germany found that glycyrrhizin compared to other antiviral agents was most effective in controlling viral replication making it a potential prophylactic measure<sup>107</sup>.

GL, a compound isolated from licorice roots has been confirmed to have antiviral activity, targeting release step of infectious anti-HCV particles, suggesting potential use in treating chronic hepatitis C patients. Recent studies of licorice extracts inhibit Gram-positive and Gram-negative bacteria<sup>108</sup>. The antiviral efficacy of 6-azouridine, glycyrrhizic acid, mycophenolic acid, pyrazofurin, and ribavirin on SARS-COV, finding glycyrrhizic acid superior in viral adsorption and penetration<sup>109, 110</sup>. Licorice extracts rich in triterpenoids and flavonoids are being explored as potential



alternatives to synthetic fungicides for treating dental caries, periodontal disease, digestive anabrosis and tuberculosis<sup>111</sup>.

**Memory Enhancer Activity is a Type of Cognitive Enhancement:** The study examined the impact of *Glycyrrhiza glabra* on learning and memory in mice finding significant improvement in learning and memory at a dose of 150 mg/kg<sup>112</sup>. Dementia is a severe mental disorder affecting intellectual abilities and memory often caused by Alzheimer's disease. Central cholinergic pathways play a role in learning and memory processes. Centrally acting antimuscarinic drugs can impair learning and memory in animals and humans<sup>113</sup>. The study followed neuropsychopharmacology parameters for testing learning and memory, using diluted librice extract, scopolamine hydrobromide and diazepam injections. Oral and intravenous administration was done at 1 ml/100 g of mouse<sup>114</sup>. Chronic inflammation in Alzheimer's disease patients brains may be inhibited by anti-inflammatory drugs like indomethacin, a non-steroidal anti-inflammatory drug has been shown to protect against memory loss and amyloid deposits, supporting the hypothesis<sup>115</sup>. Glycyrrhizin and its metabolites cause pseudoaldosterone syndrome by inhibiting aldosterone metabolism and suppressing 5'-reductase due to its similar structure to adrenal cortex hormones<sup>116, 117</sup>.

**Anticoagulant Activity:** *Glycyrrhiza glabra* extract enhances bleeding time and blood loss *in-vivo* indicating its effectiveness as an antithrombotic agent<sup>118</sup>. Glycyrrhizin a plant-based anti-inflammatory compound has been found to inhibit thrombin, prolong clotting time and increase plasma recalcification duration, while not affecting platelet aggregation or collagen induced agglutination<sup>118</sup>. Thrombin serine proteinase crucial for blood coagulation and hemostatic processes. Glycyrrhizin, a thrombin inhibitor, has shown effective antithrombotic activity in rats, without potentiating antithrombin III or heparin cofactor II<sup>119</sup>. High doses of GL (360 mg/kg) increase APTT by 4.3fold while doses of 180 mg/kg reduce venous thrombus formation and prolong coagulation time by 1.5-fold<sup>119</sup>. The study identifies a heparin-like anticoagulant activity for GL, but cautions against its broad specificity. High doses of GL increase APTT without antithrombic action, but thrombus

inhibition and bleeding effect are linked. GL also produces pseudoaldosteronism, hypertension, salt retention, and hypokalemia<sup>118, 120</sup>. Glycyrrhizin, a thrombin inhibitor reduces thrombus size in rats with dose-dependent effects, with doses ranging from 180-360 mg/kg decreasing thrombus weight by 35-90%, respectively<sup>121, 122</sup>.

**Antioxidant Activity:** Glycyrrhiza root extract when mixed with DPPH demonstrated potent antioxidant properties with a maximum scavenging effect of 67.22% at a concentration of 500 µg/ml<sup>123</sup>. Licochalcones B and D found in Glycyrrhiza can prevent microsomal lipid peroxidation and safeguard biological systems from oxidative stress<sup>124</sup>. Glycyrrhiza glabra's retrochalcone has a 100 times more potent anti-oxidant capacity than vitamin E protecting red blood corpuscles from oxidative hemolysis<sup>125</sup>. Antioxidant activity observed likely due to phenolic content with flavonoids and isoflavones like glabridin, hispaglabridin A and 30-hydroxy-4-O-methylglabridin being the responsible compounds. The study revealed a significant antioxidant activity of the dihydrostilbene derivatives found in *G. glabra* leaves<sup>126</sup>.

The antioxidant activity of GA was also examined using the CIDNP technique. This method is highly informative for studying free radical reactions/biochemical processes<sup>127</sup>. GA molecules effectively capture paramagnetic species, surpassing natural antioxidants through reactions with reactive oxygen species, solvated electrons and radical xenobiotics<sup>128</sup>. Drug encapsulated in GA micelles or gel nanoparticles inhibits free radical formation in drug molecules and potentiates the therapeutic activity of other drugs and antioxidants. It increases the solubility and bioavailability of natural antioxidants and lipophilic molecules. Glycyrrhizin has promising prospects for combination therapy, especially with Vitamin C, a potent antioxidant<sup>28</sup>.

**The Statement is About the Analgesic Activity:** The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience linked to tissue damage or its description<sup>129</sup>. Analgesics are medications that numb the central and peripheral nervous systems to alleviate pain<sup>130</sup>. The hydroalcoholic root extract of

licorice, as proven through formalin and light tail-flick tests, effectively inhibits white globule immigration, inflammatory mediator production and neutrophil production<sup>131</sup>. Isoliquiritigenin, a flavonoid from *Glycyrrhiza glabra* roots inhibited uterine contraction and attenuated pain in mice aligning with its traditional use for dysmenorrhea treatment<sup>132</sup>.

It shifted Ca<sup>2+</sup> concentration-response curves, similar to verapamil suggesting relaxant activity through voltage-dependent L-type Ca<sup>2+</sup> channel blockade. Nitric oxide an agonist of apoptosis may control menstrual bleeding and synthesis of prostaglandins. Its inducible calcium-independent activity in menstrual phase endometria is six times higher than proliferative or late-secretory endometrial<sup>133</sup>. Analgesic activity of isoliquiritigenin was evaluated in vivo. This study investigated the analgesic activity of isoliquiritigenin using the acetic acid-induced writhing method and hot-plate method revealing that isoliquiritigenin up-regulates anti-inflammatory heme oxygenase-1 expression in RAW264.7 macrophages<sup>134</sup>. The reduced nociceptive behavior in animals treated with isoliquiritigenin is not due to skeletal muscle relaxant effect as it did not affect their performance in the rotating rod test<sup>135</sup>.

**Antidepressant Activity:** Anti-depressant effects in mice through forced swim and tail suspension tests with 150 mg/kg dose reducing immobility time without compromising locomotor activity<sup>136, 137</sup>. Liquiritin, a metabolite of *G. uralensis* has been shown to enhance memory and act as an antidepressant in mouse immobility tests and chronic stress tests<sup>138</sup>. The study found that licorice extract improves memory and learning in mice by increasing 5-Hydroxytryptamine and norepinephrine levels in the hypothalamus, hippocampus & cortex, antagonizing scopolamine-induced amnesia<sup>138</sup>. The study found that licorice extract when administered at doses of 225mg/kg body wt. and 150 mg/kg body wt. enhanced dendritic intersections and arborization in hippocampal pyramidal neurons, suggesting potential therapeutic applications<sup>91, 139</sup>.

**The Activity is Designed to Stimulate Hair Growth:** Female wistar rats were used for hair growth promotion studies with their dorsal skin

denuded and treated with paraffin oil, minoxidil solution or *G. glabra* root extract daily for 30 days. Animals treated with petroleum ether extract of *G. glabra* roots exhibited longer hair compared to those treated with minoxidil or control<sup>92</sup>. Licorice's hydro-alcoholic extract promotes hair growth with a 2% concentration showing better stimulatory activity than Minoxidil. Its efficacy and safety analysis suggest it can safely be used in herbal Alopecia treatments<sup>140</sup>.

**The Statement Suggests that the Substance has Antiallergic Properties:** Allergic diseases such as asthma, rhinitis and atopic dermatitis have become the most prevalent health issues<sup>141</sup>. Mast cells and cell surface-bound IgE release histamine, cytokines and prostaglandins<sup>89</sup>. Licorice-derived compounds like glycyrrhizin, 18-β-glycyrrhetic acid, isoliquiritin, and liquiritigenin exhibit anti-allergic properties, anti-scratching properties and IgE production inhibitory activity<sup>142</sup>. Liquiritin, glycyrrhizic acid and liquiritin are effective in inhibiting pro-inflammatory mediators in BV2 cells including iNOS, COX2, TNF-α, IL-1 β, IL-4, IL-5, and IL-6<sup>143</sup>. Glycyrrhizin inhibits MUC5AC gene transcription in NCI-H292 cells, reducing mucus hyperproduction and frequency of scratching behavior with doses ranging from 50 mg/kg to 18-β-glycyrrhetic acid<sup>144, 145</sup>.

**Antispasmodic Activity:** Licorice when hydrolyzed by heat and converted into isoliquiritigenin, exhibits strong solid spasmolytic activity<sup>146</sup>. Glycoumarin inhibited smooth muscle contraction in male ICR mice by inhibiting phosphodiesterases and increasing intracellular cyclic AMP effect induced by stimulants like carbachol, KCL, barium chloride and calcium ionophore 3<sup>147</sup>. Licorice alcoholic extract exhibits antispasmodic properties by reducing ileum contraction irrespective of beta-adrenergic, opiodic, and NO receptors<sup>142</sup>. Licorice's antispasmodic effects were studied in mice and it was found that glycoumarin effectively inhibits phosphodiesterase acting as an effective antispasmodic agent.

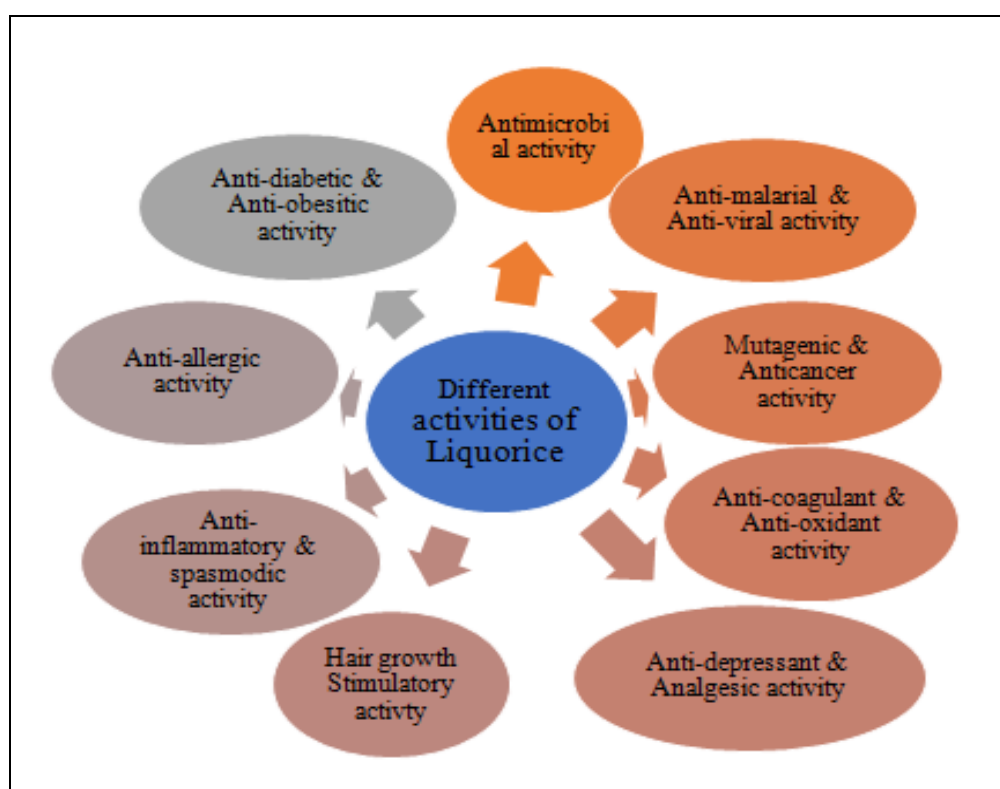
The antismooth muscle mechanism of 1 is similar to papaverine's, inhibiting carbachol-induced contractions. Its relaxant activity depends on licorice and roots with 1 content significantly

influencing relaxant effects. It inhibits intestinal tube contraction activity more strongly than isoliquiritigenin<sup>148</sup>.

**Antiinflammatory Activity:** B-Glycyhrritinic acid the major antidepressant activity is primarily derived from the metabolite of glycyrrhizin<sup>9, 149</sup>. B-glycyhrritinic acid a compound with antiinflammatory properties has been found to be more potent in various animal models<sup>150-152</sup>. Glycyhrritinic acid when crushed in H<sub>2</sub>O effectively treats sore throat cough by inhibiting glucocorticoid antitussive and expectorant effects and potentiating their effects in skin and lung. The

co-administration of them with glycyrrhetic acid has been observed<sup>153</sup>. NO, an inflammatory mediator produced by iNOS enzyme stimulated by inflammatory stimuli like bacterial LPS and induced by NF-kB, the main transcription factor in inflammatory response<sup>25</sup>.

Licorice constituents show steroid-like anti-inflammatory activity similar to hydrocortisone by inhibiting phospholipase A2 activity enzyme crucial for various inflammatory process<sup>154</sup>. Over 80% inhibition rate and higher NO production inhibition compared to indomethacin indicating good anti-inflammatory activity<sup>155</sup>.



**TABLE 4: SUMMARY OF PHARMACOLOGICAL ACTION WITH ANIMAL MODEL**<sup>89, 156</sup>

S. no.	Activity/ Chemical composition	Animal model & cell lines	Ref.
1.	Antitussive activity (Glycyrrhizin, Liquiritinapioside)	G. glabra extract- reduced cough caused by SO <sub>2</sub> gas in experiment.	(29,39-43)
2.	Immunomodulatory activity (Glycyrrhetic acid & N-acetylmuramoyl)	In-vivo phagocytosis, determination of cellular immune	(37,47,49-52,90)
3.	Anti-inflammatory activity (Glycyrrhetic acid, liquiritoside, Licochalcone-a)	doses of 100, 200, or 300mg/kg inhibited rat paw oedema, with a maximum inhibitory action of 46.86%.	(9,59,149,153,155,157,158)
4.	Hepatoprotective activity (Glycyrrhetic acid, liquiritoside, Licochalcone-a)	in-vivo damage of hepatocytes in rats induced by PCM and acute liver injury in rabbit models induced by CCL <sub>4</sub> .	(34,57,151,158,159)
5.	Antiulcerogenic activity (Glabridin, Glabrene, Glycyrrhizinic acid)	The agar well diffusion method was utilized to study the microorganisms, specifically Helicobacter pylori.	(63,65,160-162)
6.	Antimicrobial activity (Liquiritigenin, Glabrol, Glabrene, hispaglabridin A and B)	Micro-organisms used: E. coli, B. subtilis, P. aerogenosa, S. aureu, Entamoeba histolytica protozoa	(94,95,163)
7.	Antiobesity & Hypolipidemic activity/ Antidyslipidaemic activity	Fractions significantly reduced LDL and VLDL levels in HFD-fed hamsters to varying degrees.	(67-69,164)
8.	Antihyperglycemic/ Antidiabetic activity	Male albino rats of Wistar strain	

	(Amorfrutin, Glycycoumarin, 18- $\beta$ -glycyrrhetic acid)		(70,72–80,165)
9.	Skin lightening/whitening activity	Glabridin, hydrophobic fraction of liquorice extract,	(35,81,82,84–
10.	Anticancer/Antimutagenic activity	inhibit tyrosinase activity in B16 murine melanoma cells. The Ames test was conducted on <i>S. typhimurium</i> TA 98 reverants, revealing the presence of Trp-p-1 and Trp-p-2 genes.	86,166,167) (87–92,168)
11.	Antimalarial activity	Micro-organism used: <i>Plasmodium falciparum</i> , <i>Plasmodium yoelii</i>	(96–101)
12.	Antiviral activity (Glycyrrhetic acid)	Herpes simplex 1 & vesicular stomatitis virus	(102–107, 110, 111, 169)
13.	Memory Enhancing/Learning activity	Three-month-old Wistar albino rats were subjected to elevated-plus maze and Morris water-maze tests.	(112,114–117)
14.	Anticoagulant activity	Dose of 250mg hydromethanoliclicorice extract exhibits FXa inhibitory effects in vitro	(118,120,170,1 71)
15.	Antioxidant activity (Licochalcones B D & C, Licochalcone, glabridin)	scavenging activity & reduction capability of 1,1-diphenyl-2-picrylhydrazyl radical; also against NO <sub>2</sub> & superoxide radicals	(28,123,127,12 8,172–174)
16.	Analgesic activity	glycaemia coumarin, glycerin, and glycyrrhizin in ammonium salt, exhibits anti-inflammatory properties.	(129–135)
17.	Antidepressant activity (Glycyrrhizin)	extracts orally to male mice at doses of 75, 150, and 300 mg/kg for 7 consecutive days.	(91,92,136– 138,168)
18.	Hair growth stimulatory activity	Glycyrrhiza possesses good hair growth-promoting activity	(91,140,168)
19.	Antiallergic activity	inhibiting pro-inflammatory mediators in BV2 cells, including iNOS, COX2, TNF- $\alpha$ , IL-1 $\beta$ , IL-4, IL-5, and IL-6.	(89,141– 144,175)
20.	Antispasmodic activity	extract of aerial parts was inactive against ACh- and histamine-induced spasms in guinea pig ileum.	(142,146,147,1 76,177)

**CONCLUSION:** Basically, liquorice plant having various enormous benefits. As Glycyrrhetic acid, a biologically active component of liquorice utilized as a plant-based medicine for various disease conditions due to its neuroprotective, anti-inflammatory, antiviral, and anti-carcinogenic properties. Clinical studies have shown that licorice has pharmacological effects against disease conditions. Liquorice is known for its numerous health benefits, including treating glucose intolerance, improving insulin sensitivity, stressing adipose tissue formation, enhancing energy expenditure, and having anti-cancer and antimicrobial effects. Due to work habits and different types of imbalanced diets leads to alopecia and liquorice's profound role in hair growth adjuvants activity studied by scientists is also a great invention.

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