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Glycyrrhiza glabra: A Potent Herb from Traditional to Modern Medicine

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Review Article

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ABSTRACT

Introduction: *Glycyrrhiza glabra*, an ayurvedic herb has had much medical importance since ancient times. It has anti-inflammatory action, anti-diabetic action, anti-viral, anti-cancer, expectorant as well as antitussive characteristics, antimicrobial, anti-ulcer, and hepatoprotective action. The primary medicinal components are the root, leaves, and rhizomes. Ayurvedic plants have possessed varieties of medicine values from ancient times, and *Glycyrrhiza glabra* has been chosen for evaluation based on its chemical components and pharmacological activity.

Methods: Methodology used to define the anti-inflammatory action, anti-diabetic action, anti-viral, anti-cancer, expectorant, antitussive characteristics, antimicrobial, anti-ulcer, and hepatoprotective action with a focus on *Glycerrhiza glabra* potential activity in various modern pathophysiological conditions.

Results: General pathophysiological aspects to target with *Glycerrhiza glabra.*

Discussion: The primary goal of the review is to demonstrate the various chemical components and pharmacological activity of *Glycyrrhiza glabra* with targeting various anti-inflammatory pathways like JACK-STAT, MAPK, COX2, and TXA-2 as well as anti-viral, anti-diabetic, expectorant and antitussive, anti-cancer, antimicrobial, anti-ulcer and hepatoprotective.

INTRODUCTION

A huge proportion of the population in underdeveloped nations uses plant products as medicine [1]. *Glycyrrhiza glabra* medicinal plants which been included in Ayurveda for a long time and have flavoring ingredients, and it is also known in English as Yashti-madhuka, licorice, and sweet food [2]. *Glycyrrhiza* is a Greek term that means "sweet root," and it is a soft and fibrous taproot that is used in medicine [3]. Sugar, resin, starch, asparagine, Glycyrrhetic acid, Glycyrrhizic acid, and Glycyrrhizin are all constituents of *Glycyrrhiza glabra*[4,5]. The root and rhizomes of *Glycyrrhiza glabra* have possessed medicinal activity such as an anti-inflammatory, antioxidant, antispasmodic, and expectorant[6]. It also has hepatoprotective properties. *Glycyrrhiza glabra* components such as Glycyrrhizin and Glabridin suppress neutrophils' production caused by reactive oxygen species where inflammation was caused[7].

The anti-oxidant in *Glycyrrhiza glabra* reduces the levels of NFkB, TNF-, and IL-17, all of which are implicated in the generation of inflammatory cytokines [8,9]. The major medicinal components are the leaves, roots, and rhizomes [10,11]. It also has laxative, contraceptive, and sexual enhancement properties[12]. Different biological active properties have been discovered in *Glycyrrhiza glabra* extract [13].

LITERATURE REVIEW

Components of *Glycyrrhiza glabra*

Different components containing water-soluble and Main biological compounds can be isolated from the root of the *Glycyrrhiza glabra* plant. These compounds include triterpenoid, glycosides, saponin, polysaccharides, tannins, essential oil, resins, proteins, steroids, and other different compounds [14,15]. Glycyrrhizin, which is roughly 60 times sweeter than sugar, is found in saponin. The dried root contains flavonoid components such as liquid, isoliquertin, liquiritigenin, rhamnoliquirilin, and additional recent flavonoid compounds such as glucoliquiritin apioside, phenyllicoflavoneA, shinflavanone, shinpterocarpin, and 1-methoxyphaseolin[16]. Volatile substances like hexanol, linalool oxide A and B, tetramethyl pyrazine, terpine-4-ol, geraniol, and different others may be isolated from the root. *Glycyrrhizin*, as well as Glycyrrhetic acid, exist in 18 alpha and 18 beta stereoisomers. Glycyrrhizin may show different salt complexes as well as formed naturally as calcium and potassium salts. Carbenoxolone, a glycyrrhetic acid derivative, is used to prevent peptic ulcers [17,18].

Anti-inflammatory action

Glycyrrhiza glabra has anti-inflammatory properties that are achieved by blocking the pro-inflammatory factors listed below.

Action of Glycyrrhetic acid and glycyrrhizin on COX-2 and TXA2

COX-2 is more prevalent in inflammatory disorders such as rheumatoid arthritis. CoX-2 activation transforms Arachidonic Acid (AA) into Prostaglandin H2 (PGH2). PGH2 is not stable and is transformed into PGE2, PGI, and TXA2 through the catalysis of Prostaglandin E Synthase (PGES), Prostacyclin Synthase (PGIS), and Thromboxane Synthase (TXAS)[19]. PGE2 has pro-inflammatory and immunosuppressive properties. PGI and TXA2 have mechanisms that contribute to the etiology of inflammatory disorders [20]. The COX-2 and TXA2 pathways are more important in the development of RA [21,22].

Glycyrrhiza glabra has anti-inflammatory effects and inhibits COX's[23]. Glycyrrhetic acid inhibited the activity of many molecules, including COX-2, TXA's, and NF-kB. GA inhibits the entire COX-2 and TXA2 pathway. In Figure 1 shows a pictorial representation of inhibition of inflammation-causing factor-like COX2, PGE2, TXA2. Glycyrrhetic acid and glycyrrhizin's major pharmacological target [21].It gives proof of anti-inflammatory and anti-tumor effects of GA and GL, as COX-2 and TXA-2 are the primary pathways for the development of RA [24,25].

Action of *Glycyrrhiza glabra* in p38/MAPK signaling pathway

The root of *Glycyrrhiza glabra* has many active substances such as flavonoid, saponin, Glycyrrhetic acid, and other anti-inflammatory substances[26,27]. *Glycyrrhiza glabra* extract can operate in a variety of ways. It inhibits mitochondrial lipid peroxidation, phospholipase(A2), and reduces oxidative rate, reactive substance, and free radical production, all of which have pro-inflammatory effects. *Glycyrrhiza glabra* extract inhibits the lipopolysaccharide-induced inflammation and also aids in the suppression of NFkB and p38/MAPK signaling pathways, both of which are important for the activation of pro-inflammatory cytokines (IL-1, IL-6, TNF-alpha) [28-30]. and also represent in Figures 2 and 3 respectively. Suppressing the p38/MAPK signaling pathway lowers cytokine production, inflammation, and protects against bone and cartilage loss [31].

Inhibition of JAK-STAT signaling pathway

The JAK-STAT signaling pathway is the primary mechanism behind the causes of inflammation, such as in RA [32]. Tyrosine kinase, JAK-1, JAK-2, and JAK-3 are all linked with the Jak family cytokine receptor. Increased levels of pro-inflammatory cytokines like IL-1, IL-6, IL-17, and TNF-alpha can be detected. JAK-1 and JAK-2 activation lead to the phosphorylation of Signal Transducer and Activator of Transcription (STAT). The STAT dimer will translocate into the nucleus and bind to interferon-gamma at the target location [33]. The transcription of macrophages will cause the activation of cytokine resulting in synovial tissue damage [34]. The JAK-STAT signaling pathway because inflammation is inhibited by the *Glycyrrhiza glabra* extract describe as a flow chart in Figure 4.

Figure 1. Flow diagram showing inhibition of inflammation causing factor like COX2, PGE2, TXA2.

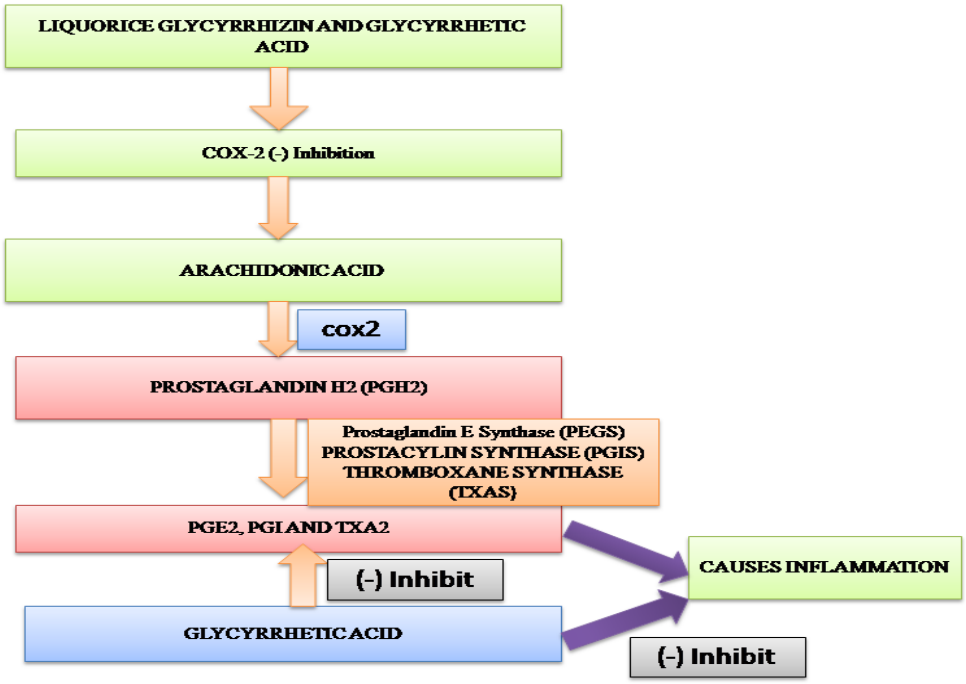


Figure 2. Glycyrrhiza glabra extract action in pro-inflammatory mediators.

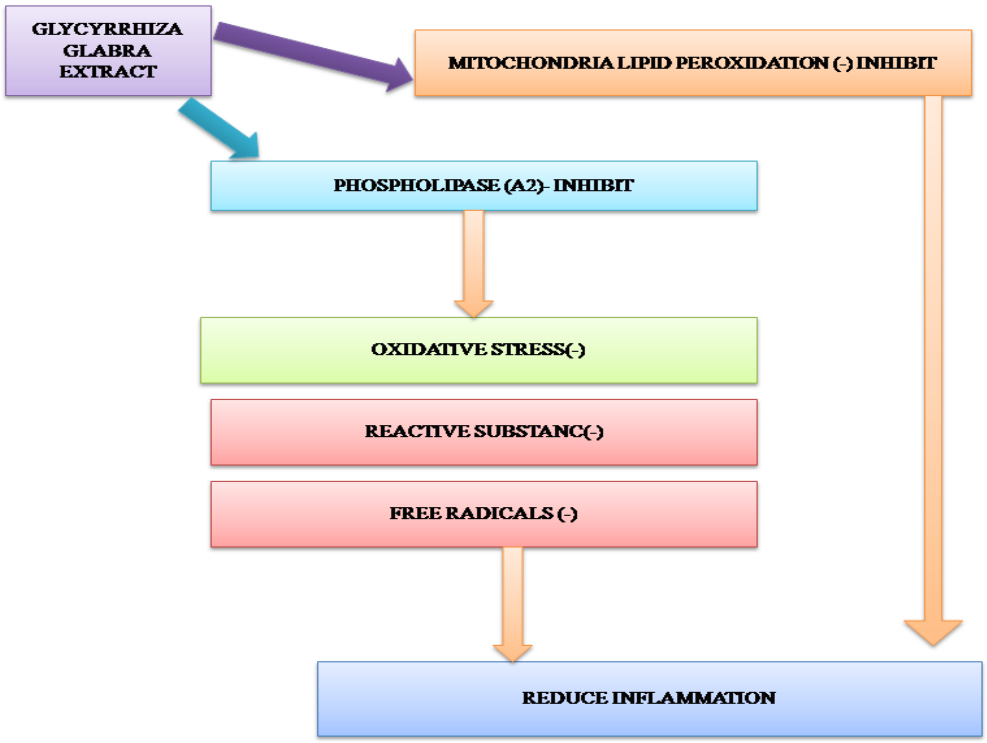


Figure 3. Flow diagram for pro-inflammatory cytokines inhibition.

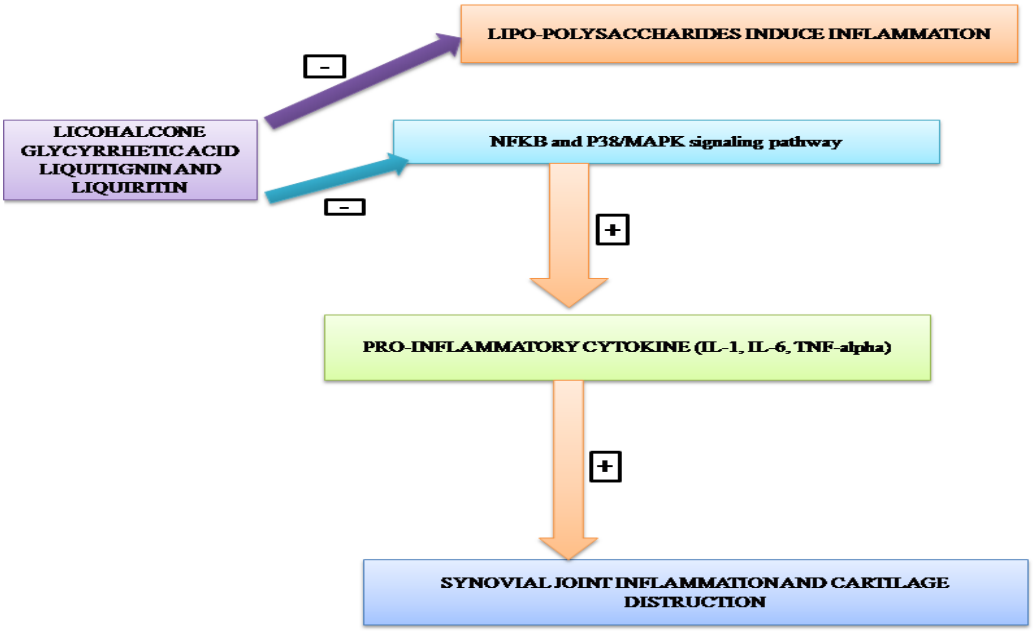
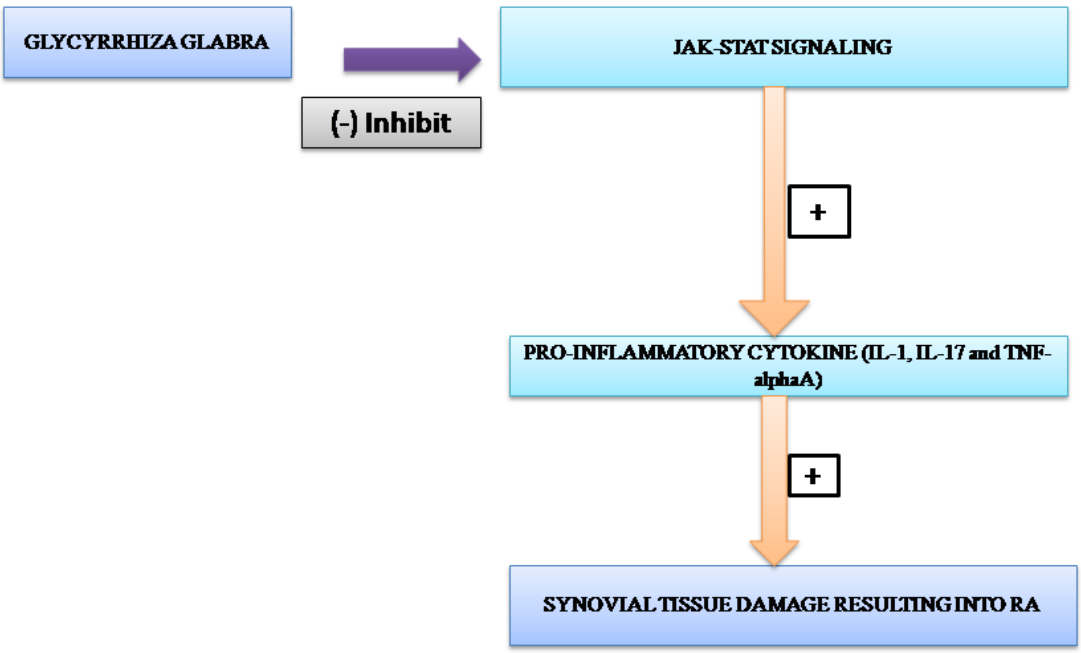


Figure 4. Flow diagram of JAK-STAT inhibition by *Glycyrrhiza glabra*.



Anti-diabetic activity

Diabetes is defined by a rise in blood glucose levels over time, commonly known as diabetes mellitus [35-37]. The major cause of a rise in blood glucose levels is a lack of glucose metabolism caused by faulty insulin production from pancreatic β-cell [38]. It will cause an increase in thirst, appetite, and urination [39,40]. Diabetes can lead to a variety of complications, including foot ulcers, stroke, heart failure, and kidney problems if left untreated for an extended length of time. *Glycyrrhiza glabra* root has a variety of medicinal properties [41,42]. Since it has anti-diabetic properties, *Glycyrrhiza glabra* can be used to treat diabetes on a long-term basis [43,44]. According to recent research, the *Glycyrrhiza glabra* ethanolic root contains phenolic compounds that are responsible for suppressing α-amylase as it aids in the hydrolysis of disaccharides, which aids in the management of diabetes [45].

Anti-viral activity

Glycyrrhiza contains antiviral properties that protect against virus fusion. It was discovered that *Glycyrrhiza* was most significant in limiting viral replication and may also be employed as a preventive measure. It has been utilized over the last year for patients who have been exposed to the Human immunodeficiency virus and chronic hepatitis virus [46,47]. According to much research, the root of *Glycyrrhiza glabra* was employed against the herpes simplex virus, fully deactivating the virus [48-50]. *Glycyrrhiza glabra* components such as Glycyrrhizic acid were utilized to deactivate herpes simplex virus particles [51]. Animal studies revealed that *Glycyrrhiza glabra* and its constituents help prevent herpes simplex virus encephalitis and lower the mortality rate [52]. Other studies suggest that Glycyrrhizic acid can assist to prevent the activation of many viruses *in vitro* [53,54]. Glycyrrhizin is also important in the prevention of several viral diseases like herpes simplex virus, poliovirus, SARS, Arboviruses, and flaviviruses [51,52,55-62].

Anti-cancer activity

The extract compounds of *Glycyrrhiza glabra* reduced the *in-vivo* and *in-vitro* proliferation of Ehrlich ascites tumor cells, as well as angiogenesis *in-vitro*, peritoneal, and chorioallantoic assays [63]. On the other sector, there is a wealth of evidence on the anticancer effects of its many constituents, both in-vivo and in-vitro study. Glycyrrhetic acid would trigger the proapoptotic cycle by altering mitochondrial permeability transition, which might be useful in promoting tumor cell death [64,65]. *Glycyrrhiza* alcoholic extract influences apoptosis and G1 cell cycle capture in MCF-7 human breast cancer cells [66].

When given at a dosage of 300 mg/kg, the *Glycyrrhiza glabra* extract isoliquiritigenin reduced the development of 1,2-dimethylhydrazine-induced colon and lung cancers in the case of mice [67]. The hydromethanolic extraction root of *Glycyrrhiza glabra* has antimutagenic activity and works by suppressing micronuclear production and chromosomal abnormality in albino mouse bone marrow [68,69].

Expectorant and antitussive activity

Glycyrrhiza glabra extract and powder are useful in avoiding infectious throat, cough, and bronchial catarrh. Because of glycyrrhizin, it has been showing antitussive, demulcent, and expectorant losing characteristics that aid in the relief of upper respiratory tract congestion and the acceleration of tracheal mucus secretion [70]. Liquiritin apioside, an active methanolic component of *Glycyrrhiza glabra*, aids in the suppression of capsaicin-induced cough [71]. It will relieve throat discomfort and have an expectorant effect. It stimulates bronchial mucus production and has demulcent and expectorant properties [72,73].

Antimicrobial activity

Glycyrrhiza glabra alcoholic root extract has antibacterial activity when tested against *E coil*, *Pseudomonas fluorescence*, *B cereus*, *Enterococcus faecalis*, and *Staphylococcus aureus*, with a maximum inhibition zone of 15 mm and the lowest inhibition zone of 22 mm [74]. *Pseudomonas aeruginosa*, *S.typi*, *Vibrio mimicus*, and *Salminnella paratypi* were evaluated against *Glycyrrhiza glabra* methalonic extract. Except for *Pseudomonas aerugenosa*, the methalonic extract demonstrated strong antibacterial activity against all experimental microorganisms. The strongest suppression is against *Staphylococcus aureus*, having a 22 mm inhibition zone [75]. *Glycyrrhiza glabra* extract, in combination with Glycrrhizic acid, inhibited the replication of various viruses, including hepatitis A, B, and C viruses along with Herpes simplex virus, Epstein-barr virus, Human immunodeficiency virus, SARS coronavirus, Influenza virus, Human cytomegalovirus, and varicella-zoster virus [76-87]. The coumarin extracts of *Glycyrrhiza glabra*, licopyranocoumarin, and Glycocoumarin, inhibit the development of large cells in HIV-infected cell culture. Licochalcone-A has anti-HIV properties [88,89]. Forty-two patients with haemophilia producing HIV-1 were treated with *Glycyrrhiza* extract for HIV management, and it was discovered that they improved in liver function, clinical function, and immunological function [90]. Glycyrrhizinic acid is used to treat pruritis, dermatitis, and cysts caused by parasite infection of the skin [91,92].

Anti- ulcer activity

According to clinical trials, carbaxolone, a *Glycyrrhiza* extract, has the most potent action against duodenal and stomach ulcers when taken a minimum dose of 100 mg thrice daily. *Glycyrrhiza* extract is beneficial for increasing the number of prostaglandins in the digestive system, which is beneficial for mucus secretion from the stomach and enhances the survival of higher cells in the stomach, as well as having anti-pepsin properties [93-97].

Hepatoprotective activity

Chronic hepatitis is a possible consequence of liver cirrhosis termed liver failure [98]. *Glycyrrhiza glabra* improves liver function and lowers serum aminotransferases when compared to a placebo. Prolonged usage of *Glycyrrhiza glabra* helps prevent hepatocellular cancer in chronic hepatitis C. According to in vitro research, *Glycyrrhiza glabra* developed intracellular transport and inhibited the surface antigen of the hepatitis B virus [99,100]. The formulation of 450 E1 can be reduced by Glycyrrhetic acid, Aglycone glycyrrhizin, and liver preservation [101]. *Glycyrrhiza* protects the oxidative and hepatic damage caused by flatoxin by arising the amount of CYP1A1 and Glutathione-S-transferase and also inhibits anticarcinogenic activity by rendering hepatoxin metabolic inactive [102]. In a mouse liver tissue investigation, the researchers discovered that hydromethanolic root components of *Glycyrrhiza glabra* protects against hepatotoxicity produced by carbon tetrachloride [103].

DISCUSSION AND CONCLUSION

Glycyrrhiza glabra is an old Ayurvedic medicinal plant that has been used in medicine. It has a variety of constituents, each with its unique therapeutic use. This plant's primary parts are the root, leaves, and rhizomes, which are utilized for medicinal purposes. The primary goal of the review is to demonstrate the various chemical components and pharmacological activity of *Glycyrrhiza glabra* with targeting various anti-inflammatory pathways like JACK-STAT, MAPK, COX2, and TXA-2 as well as anti-viral, anti-diabetic, expectorant and antitussive, anti-cancer, antimicrobial, anti-ulcer and hepatoprotective. To demonstrate the general mechanism of action with target specified enzyme or substrate to inhibit or overcome the unwanted action with the use of a natural agent of *Glycyrrhiza glabra*.

REFERENCES

1. Tene V, et.al. An ethnobotanical survey of medicinal plants used in Loja and Zamora chinchipi, Equador. J Ethnopharmacol. 2007;111: 63-81.
2. Rajandeep Kaur, et al.Glycyrrhiza glabra: A phytopharmacological review.2009.
3. Olukoga A, et.al. Historical perspectives on health. The history of liquorice: the plant, its extract, cultivation, and commercialization and etymology. J R Soc Health. 1998; 118:300–304
4. Ayurvedic pharmacopoeia of India Part-I.1:168-169.
5. Chopra's indigenous drugs of India. Academic publishers Kolkata, Second edition.1994;184-186.
6. Syrovets T, et.al. Acetyl-boswellic Acids are novel catalytic inhibitors of human topoisomerases I and II . Mol Pharm. 2000; 58: 71-81.
7. Akamatsu H, et.al. Mechanism of anti- inflammatory action of glycyrrhizin: effect on neutrophil functions including reactive oxygen species generation. Planta Medica.1991; 57:119-121.
8. Kamanli A, et al. Plasma lipid peroxidation and antioxidant levels in patients with rheumatoid arthritis.Cell Biochem Funct. 2004; 22: 53-7.
9. Mahajan A, et al. Antioxidants and rheumatoid arthritis. J Indian Rheumatol Asso.2004; 12: 139-42.
10. Asl MN, et al. Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. Phytother Res. 2008; 22: 709-724.
11. Usmanghani K, et al. Researches on Materia Medica.1997: 29-35.
12. Asl MN, et al. Review of pharmacological effects of Glycyrrhiza sp and its bioactive compounds. Phytother Res. 2008; 22: 709-724.
13. Pastorino, G, et al. Liquorice (Glycyrrhiza glabra): A phytochemical and pharmacological review. Phytother Res. 2018; 32: 2323–2339.
14. Hoffmann D .The new holistic herbal, 2nd edn. Element, Shaftesbury.1990.
15. Obolentseva GV, et al. Pharmacological and therapeutic properties of licorice preparations (a review). Pharm Chem .1999;J33:24–31.
16. The wealth of India, A Dictionary of Indian Raw Materials and Industrial Products, First supplement series, published by National Institute of Sciences Communication and Information Resources, CSIR, New Delhi. 2005; 3: 195-198.
17. Washington DC, et al. Food Chemicals Codex, fifth ed. National Academy Press, 2003; 25.
18. Isbrucker RA,et al. Regulatory Toxicology and Pharmacology. 2006; 46: 167–192.
19. Cathcart MC, et al. The role of prostacyclin synthase and thromboxane synthase signaling in the development and progression ofcancer. Biochimica et biophysica acta. 2010; 1805:153-166.
20. Huang RY, et al. Cigarette smoking, cyclooxygenase-2 pathway and cancer. Biochimica et biophysica acta. 2011; 1815:158-169.
21. Huang QC, et al. The cyclooxygenase-2/thromboxane A2 pathway: a bridge from rheumatoid arthritis to lung cancer? Cancer Lett. 2014; 354:28-32.
22. Wang MJ, et al. Determination of role of thromboxane A2 in rheumatoid arthritis. Discov Med. 2015; 19:23
23. Craig WJ. Health-promoting properties of common herbs. Am J Clin Nutr. 1999; 70:491S-499S.
24. Huang RY, et al. 4-Methylnitrosamino-1-3-pyridyl-1-butanone (NNK) promotes lung cancer cell survival by stimulating thromboxane A2 and its receptor. Oncogene. 2011; 30:106-116.

25. Huang RY, et al. Thromboxane A2 exerts promoting effects on cell proliferation through mediating cyclooxygenase-2 signal in lung adenocarcinoma cells. J Cancer Res Clin Oncol. 2014; 140:375-386.
26. Asan-Ozusaglam, et al. Evaluation of biological activity and antioxidant capacity of Turkishlicorice root extracts. Rom Biotechnol Lett. 2014, 19:8994–9005.
27. Yatoo, M.I, et al. Anti-inflammatory drugs and herbs with special emphasis on herbal medicines for countering inflammatory diseases and disorders-A review. Recent Pat. Inflamm. Allergy Drug Discov. 2018; 12: 39–58.
28. Karkanis A, et al. Phytochemical composition, health effects,and crop management of liquorice (Glycyrrhiza glabra L.): A medicinal plant Food Rev Int. 2016; 34: 1–22.
29. Sohail M, et al. Investigating the antioxidant potential of licorice extracts obtained through different extraction modes. J Food Biochem. 2018;42. b. Thakur, et al. Pharmacological perspective of Glycyrrhiza glabra Linn: A mini-review. J Anal Pharm Res. 2017; 5: 00156.
30. Yatoo, M.I, et al. Anti-inflammatory drugs and herbs with special emphasis on herbal medicines for countering inflammatory diseases and disorders-A review. Recent Pat Inflamm Allergy Drug Discov. 2018; 12: 39–58.
31. Schett G, et al. The p38 mitogen-activated protein kinase (MAPK) pathway in rheumatoid arthritis. Ann Rheum Dis. 2008; 67: 909–916.
32. Ivashkiv LB, et al. The JAK/STAT pathway in rheumatoid arthritis:pathogenic or protective? Arthritis Rheum .2003; 48: 2092–2096.
33. Tang M, et al. Interferon-gamma-mediated osteoimmunology. Front Immunol. 2018; 9: 1508. [Crossref] [Google Scholar][Pubmed]
34. Morelli M, et al. Selective immunomodulation of inflammatorypathways in keratinocytes by the Janus Kinase (JAK) inhibitor tofacitinib: implications for the employment of JAK-targeting drugs in psoriasis. J Immunol Res. 2018; 2018: 1–18.
35. Vickers A, et al. ABC of complementary medicine: Herbal medicine Bmj. 1999; 319:1050-1053.
36. Drug Discovery from Natural Products. RSC Drug Discovery.2012.
37. Predny, et al.Black cohosh Actaea racemosa: an annotated bibliography. Gen. Tech. Rep. SRS–97. Asheville, NC: U.S. Department of Agriculture Forest Service, Southern Research Station.90-99.
38. Jarald E, et al. Diabetes and Herbal Medicines. Iran. J. Pharmacol. Ther.2008; 7:97-106.
39. FioreC, et al. A history of the therapeutic use of liquorice in Europe. J Ethnopharmacol.2005; 99: 317-324.
40. Agarwal A, et al. An Evaluation of the Efficacy of Licorice Gargle for Attenuating Postoperative Sore Throat: A Prospective, Randomized, Single-Blind Study. Anesthesia & Analgesia.2009; 109, 77-81.
41. Yang L, et al.The determination of flavonoid in 6 kinds of licorice root by HPLC. Acta Pharmaceutics Sinica.1990;25: 840-848.
42. Visavadiya NP, et al. Evaluation of antioxidant and anti-atherogenic properties of Glycyrrhiza glabra root using In vitro models. Int J Food Sci. Nutr. 2009;60:135-149.
43. Fenwick, Gr, et al. Liquorice, Glycyrrhiza glabra L.—Composition, uses and analysis. Food Chemistry.1990.38:119-43.
44. Kataria R, et al. Pharmacological activities on Glycyrrhiza glabra–a review. Asian J Pharm Clin Res .2013;6:5-7.

45. Karthikeson.P.S, et al. Anti-Diabetic Activity of Glycyrrhiza glabra - An In vitro Study. Int. J. Pharm. Sci. Rev. Res.2017; 44: 80-81.
46. De Clercq E. Current lead natural products for the chemotherapy of human immunodeficiency virus (HIV) infection. Med Res Rev. 2000; 20: 323-349.
47. Badam L, et al. In vitro studies on the effect of glycyrrhizin from Glycyrrhizin glabra on some RNA and DNA viruses. Indian J Pharmacol. 1994;26: 194-199.
48. Pompei R, et al. Glycyrrhizic acid inhibits virus growth and inactivates virus particles. Nature.1979; 281:689–90.
49. Hirabayashi K, et al. Antiviral activities of glycyrrhizin and its modified compounds against human immunodeficiency virus type 1 (HIV-1) and herpes simplex virus type 1 (HSV-1) in vitro. Chem Pharm Bull (Tokyo). 1991; 39:112–5.
50. Pompei R, et al. Antiviral activity of Glycyrrhizic acid. Experientia. 1980;36:304.
51. Pompei R, et al. Glycyrrhizic acid inhibits virus growth and inactivates virus particles. Nature.1979;281:689–90.
52. Fiore C, et al. Antiviral effects of Glycyrrhiza species. Phytother Res.2008; 22:141–8.
53. Van Rossum TG, et al. Review article: Glycyrrhizin as a potential treatment for chronic hepatitis C. Aliment Pharmacol Ther. 1998;12:199–205.
54. Cohen JI. Licking latency with licorice. J Clin Invest.2005;115:591–3.
55. Pompei R, et al. Glycyrrhizic acid inhibits influenza virus growth in embryonated eggs. Microbiologica.1983; 6:247–50.
56. Utsunomiya T, et al. Glycyrrhizin, an active component of licorice roots, reduces morbidity and mortality of mice infected with lethal doses of influenza virus. Antimicrob Agents Chemother. 1997; 41:551–6.
57. Lampi G, et al. Enhancement of antiherpetic activity of glycyrrhizic acid by physiological proteins. Antivir Chem Chemother. 2001;12:125–31.
58. Cinatl J, et al. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. Lancet.2003; 361:2045–6.
59. Crance JM, et al. Interferon, ribavi-rin, 6-azauridine and glycyrrhizin: antiviral compounds active against pathogenic flaviviruses. Antiviral Res. 2003;58:73–9.
60. Briolant S, et al. In vitro inhibition of Chikungunya and Semliki Forest viruses replication by antiviral compounds: synergistic effect of interferon-alpha and ribavirin combination. Antiviral Res. 2004; 61(2):111–7.
61. Hoever G, et al. Antiviral activity of glycyrrhizic acid derivatives against SARS-coronavirus. J Med Chem. 2005;48:1256–9.
62. Takei M, et al. Glycyrrhizin in-hibits R5 HIV replication in peripheral blood monocytes treated with 1-methyladenosine. Pathobiology. 2005; 72:117–23.
63. Sheela ML, et al. Angiogenic and proliferative effects of the cytokine VEGF in Ehrlich ascites tumor cells is inhibited by Glycyrrhiza glabra. Int Immunopharmacol.2006; 6:494–498.
64. Salvi M, et al. Glycyrrhetinic acid induced permeability transition in rat liver mitochondria. Biochem Pharmacol.2003; 66:2375–2379.
65. Fiore C, et al. On the mechanism of mitochondrial permeability transition induction by glycyrrhetinic acid. Biochim Biophys Acta.2004;1658:195–201.

66. Jo EH,et al. Chemopreventive properties of the ethanol extract of Chinese licorice (Glycyrrhiza uralensis) root: induction of apoptosis and G1 cell cycle arrest in MCF-7 human breast cancer cells. Cancer Lett. 2005; 230: 239–247.
67. Chin YW, et al. Pereira MA and Kinghorn AD. Anti-oxidant constituents of the roots and stolons of licorice (Glycyrrhiza glabra). J Agric Food Chem 2007; 55 : 4691–4697.
68. Sharma V, et al. Assessment of median lethal dose and antimutagenic effects of Glycyrrhiza glabra root extract against chemically induced micronucleus formation in swiss albino mice. Int J Basic Clin Pharmacol.2014; 3:292–297.
69. Sharma V, et al. Evaluation of Anticlastogenic effects of Glycyrrhiza glabra root extract against cyclophosphamide induced chromosomal aberration in swiss albino Mice. J Appl Pharm Sci.2015; 5:127–132.
70. Hikino H, et al. Recent research on oriental medicinal plants. Economic and medicinal plant research,1985;1:53–85.
71. Kamei J, et al. Anti-tussive principles of Glycyrrhiza radix, a main component of Kampo preparations Bakumondo-to. E J Pharm. 2003; 69:159–163.
72. Morris DJ, et al. Medicinal uses of licorice through the millennia: the good and plenty of it. Molecular and Cellular Endocrinology 1991; 78: 1-6.
73. Glabra. Monograph. Alternative Medicine Review. 2005; 10: 230-234.
74. Rodino S, et al.Comparative studies on antibacterial activity of licorice, elderberry and dandelion. Dig J Nanomater Biostructures .2015; 10: 947-955.
75. Krausse R, et al. In vitro anti-Helicobacter pylori activity of extractum liquiritiae, glycyrrhizin and its metabolites. J. Antimicrob Chemother. 2004; 54: 243–246.
76. Baba M, et al. Antiviral activity of glycyrrhizin against varicella-zoster virus in vitro. Antiviral Res .1987; 7: 99–107.
77. Cinatl J. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. Lancet 2003; 361: 2045–2046.
78. Ghannad MS, et al. The Effect of aqueous extract of Glycyrrhiza glabra on Herpes simplex virus 1. Jundishapur J Microbiol 2014; 7: e11616.
79. Crance JM, et al. Inhibition of hepatitis A virus replication in vitro by antiviral compounds. J Med Virol 1990; 31: 155–160.
80. Ito M, et al. Mechanism of inhibitory effect of glycyrrhizin on replication of human immunodeficiency virus (HIV). Antiviral Res 1988; 10: 289-298.
81. Lin JC. Mechanism of action of Glycyrrhizic acid in inhibition of Epstein-Barr virus replication in vitro. Antiviral Res 2003; 59: 41–47.
82. Numazaki K, et al. Effect of glycyrrhizin in children with liver dysfunction associated with cytomegalovirus infection. Tohoku J Exp Med 1994;172: 147–153.
83. Pompei R, et al. Glycyrrhizic acid inhibits virus growth and inactivates virus particles. Nature 1979; 281: 689–690.
84. Takahara T, et al. Effects of glycyrrhizin on hepatitis B surface antigen: a biochemical and morphological study. J Hepatol 1994; 21: 601–609.

85. Utsunomiya T, et al. Glycyrrhizin, an active component of licorice roots, reduces morbidity and mortality of mice infected with lethal doses of influenza virus. Antimicrob. Agents Chemother. 1997; 41: 551-556.
86. Van Rossum T GJ, et al. Review article: Glycyrrhizin as a potential treatment for chronic hepatitis C. Aliment Pharmacol Ther 1998; 12: 199–205.
87. Van Rossum TGJ, et al. Intravenous glycyrrhizin for the treatment of chronic hepatitis C: a double-blind, randomized, placebo-controlled phase I/II trial. J Gastroenterol Hepatol 1999; 14: 1093-1099.
88. Hatano T, et al. Anti-human immuno-deficiency virus phenolics from licorice. Chem Pharm Bull 1988; 36: 2286-2288.
89. De Simone F, et al.Anti-HIV aromatic compounds from higher plants.In: Bioactive compounds from natural sources: Isolation, characterization and biological properties. 2001: 325.
90. Mori K, et al. Effects of glycyrrhizin (SNMC: Stronger neo minophagenin hemophilia patients with HIV-1 infection.Tohoku J Exp Med 1989; 158:25-35.
91. Saeedi M, et al. The treatment of atopic dermatitis with licorice gel. J Dermatol Treat.2003; 14:153–157.
92. Indian drug manufacturer's association and Regional Research Laboratory. 89–97.
93. Adel M, et al. Licorice: A possible anti-inflammatory and anti-ulcer drug. AAPS Pharm Sci Tech 2005; 6: 74-82.
94. Horwich L, et al. Treatment of gastric ulceration with carbenoxolone sodium: clinical and radiological evaluation. Br Med J. 1965; 2: 1274-1277.
95. Fraser PM, et al. Clinical trial of a new carbenoxolone analogue (BX24), zinc sulphate, and vitamin A in the treatment of gastric ulcer. 1972; 13: 459-463.b.Montgomery RD,et al. A controlled trial of carbenoxolone sodium capsules in the treatment of duodenal ulcer. 1968, 9: 704-706.
96. Montgomery RD, et al. A controlled trial of carbenoxolone sodium capsules in the treatment of duodenal ulcer.Gut.1968; 9: 704-706.
97. Doll R, et al. Treatment of gastric ulcer with carbenoxolone: antagonistic effect of spironolactone.Gut.1968; 9: 42-45.
98. Acharaya SK, et al. Preliminary open trial on interferon stimulator (SNMC) derived from Glycyrrhiza glabra in the treatment of subacute hepatic failure. Ind J Med Res.1993; 98: 69-74.
99. Sato H, et al. Therapeutic basis of Glycyrrhizin on chronic hepatitis B. Antiviral Res.1996; 30: 171-177.
100. Van Rossum TG, et al. Glycyrrhizin as a potential treatment of chronic hepatitis C. Aliment Pharmacol Ther.1998;12: 199-205.
101. Jeong HG, et al. Hepatoprotective effects of 18β –glycyrrhetinic acids on carbon tetrachloride-induced liver injury, inhibition of cytochrome P450 2E1 expression. Pharmacol Res.2002; 46: 221-227.
102. Chan HT, et al. Inhibition of Glycyrrhizic acid on alfatoxin B1-induced cytotoxicity of hepatoma cells. Toxicology.2003;188: 211-217.
103. Sharma V, et al. In vivo antioxidant and hepatoprotective potential of Glycyrrhiza glabra extract on carbon tetra chloride (CCl4) induced oxidative stress mediated hepatotoxicity. Int J Res Med Sci.2014; 2:314–320.