

# *Glycyrrhiza glabra*: Medicine over the millennium

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### Abstract

*Glycyrrhiza glabra* Linn. is an age-old plant used in traditional medicine across the globe for its ethnopharmacological values to cure varieties of ailments from simple cough to hepatitis to more complex like SARS and cancer. The present paper is an effort to highlight the role of a few major constituents of this plant, which have multifaceted pharmacological actions and could be used as templates for designing new pharmacophores using modern chemical and bioanalytical tools.

**Keywords:** Bioactive constituents, *Glycyrrhiza glabra*, Licorice/Liquorice, Pharmacophores, Glycyrrhizin.

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Liquorice roots

### Introduction

The widespread use of herbal remedies and healthcare preparations, as those described in ancient texts such as the Vedas, the Bible, and those obtained from traditional/folklore practices, has been traced to the occurrence of natural products with medicinal properties. Plants synthesize and accumulate a variety of compounds, which provide protection to the plant and are useful to humans as medicinal agents. In most developing countries the use of medicinal plants has been observed as a normative basis for maintenance of good health. Approximately 80% world population relies on herbal medicines as over the counter (OTC) herbal formulations and proprietary herbal drugs<sup>1,2</sup>. Industrialized societies are involved in extraction of bioactive constituents from medicinal plants and use them directly or indirectly as new drugs<sup>3,4</sup>.

*Glycyrrhiza glabra* Linn. (Family: *Fabaceae*) is a medicinal plant found in Asia, the Mediterranean and parts of southern Europe. Commonly known as Licorice/Liquorice, Sweet wood, *Mulahatti* and *Yastimadhu*. The underground unpeeled or peeled stems or



*Glycyrrhiza glabra* plant

roots are used for the treatment of upper respiratory tract ailments including coughs, hoarseness, sore throat and bronchitis. Ayurveda considers licorice to be a “*rasayana*” with implicated use in treatment of respiratory and digestive disorders. It is also considered as an anti-stress and anabolic agent. Licorice the most prescribed herb after Ginseng in China is used for ailments related to spleen, liver and kidney. Japanese use the herb as an antiviral agent<sup>5</sup>.

The present review highlights the contribution of *G. glabra* in complementary and modern medicine for the development of new drugs. There is a co-relation established between the bioactivity of the herb and the bioactive compounds responsible under separate headings for facilitating the readers as per their research interests. The paper also deals with use of licorice in polyherbal formulations as a variety of them have been evaluated during clinical studies<sup>6</sup>.

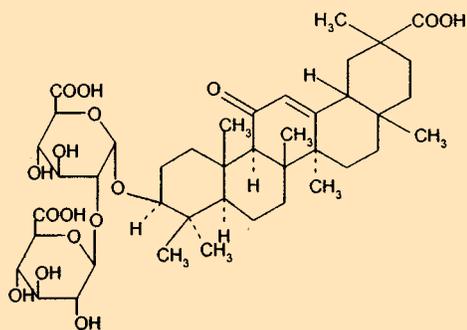
## Bioactive constituents

Liquorice has Glycyrrhizin as the major water-soluble constituent responsible for its sweet taste. Glycyrrhizin is a triterpenoid saponin that is present within a range of 2-14% in different species. The Glycyrrhizin content varies between 5.5-6.4% on weight basis<sup>7</sup>, 3-3.5% in *Radix glycyrrhizae*<sup>8</sup>. Other phytochemicals present in liquorice are: Liquiritigenin, Liquiritin (Flavanones), Isoliquiritigenin, Isoliquiritin (Chalcones), Genistein, Glicoricone, Glisoflavone, Isoangustone A (Isoflavones); Glycyrrhizoflavanone, Glyasperin F, Licoisoflavanone (Isoflavanones); Glyasperin C, Glyasperin D, Glabridin, Licoricidin (Isoflavans); Glycocoumarins, Lipocoumarins, Glycyrin (3-aryl coumarins) and others (Licocoumarone, Licoriphenone, Isoglycyrol)<sup>9</sup>.

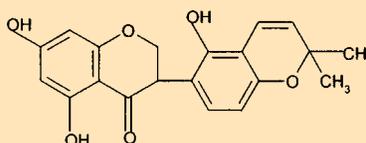
## Pharmacological and other properties

Traditionally the plant has been recommended as a prophylaxis for gastric and duodenal ulcers and dyspepsia as an anti-inflammatory agent during allergic reactions<sup>9</sup>. In folk medicine, it is used as a laxative, emmenagogue, contraceptive, galactagogue, anti-asthmatic drug and antiviral agent.

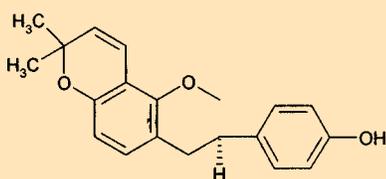
The voluminous studies carried out by ethnobotanists, phytochemists and experimental pharmacologists on its bioactivities suggest that the plant may be a source of new drugs and therapeutic formulations for the treatment of a variety of diseases and ailments (Table 1) could be manufactured. Summary of various activities is given here:



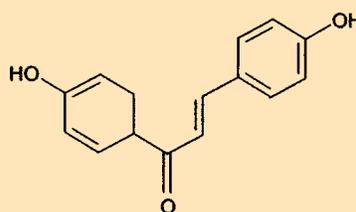
Glycyrrhizin



Licoisoflavanone



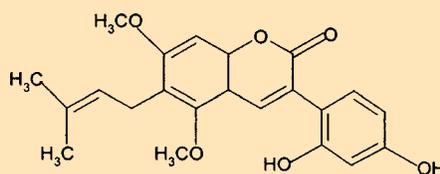
Glabridin



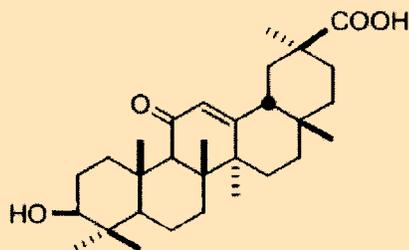
Isoliquiritigenin



Liquiritigenin



Glycyrin



Glycyrrhetic acid

### Antitussive and demulcent

The liquorice powder and extract was found to be useful for the treatment of sore throat, cough and bronchial catarrh. It is antitussive and expectorant loosening and helping to expel congestion in the upper respiratory tract as it accelerates tracheal mucus secretion<sup>10</sup>. The demulcent action is attributed to glycyrrhizin. It has been recently found that Liquiritin apioside is an active compound present in the methanolic extract of liquorice. The compound inhibits capsaicin-induced cough<sup>11</sup>.

### Thrombin inhibitor

Glycyrrhizin, an already known anti-inflammatory compound, has also been found as the first plant based inhibitor of thrombin. It prolonged the thrombin and fibrinogen clotting time and increased plasma recalcification duration. The thrombin induced platelet aggregation was found to be inhibited by the action of glycyrrhizin but Platelet Aggregating Factor (PAF) or Collagen induced agglutination was not affected by glycyrrhizin<sup>12,13</sup>.

### Antiulcerative

Licorice has been used as an antiulcerative since early 1970's. The extracted glycyrrhizin from licorice is referred to as Deglycyrrhizinated licorice (DGL) and is generally used for the treatment of ulcers. Carbenoxolon sodium, hemisuccinate sodium and glycyrrhetic acid (GA) isolated from liquorice have been used to treat a variety of peptic ulcers. Fraction FM-100 isolated

from licorice roots exerts the anti-ulcerogenic effect by inhibiting the secretion of gastrin<sup>14</sup>. Carbenoxolone and Pirenzepine were found to have a similar, but rather limited, efficacy in speeding the healing of chronic gastric ulcers. Both the drugs differed with respect to tolerability. Some antiulcer compounds like glycyrin, formononetin, glyasperin D, 6,8-diprenylorobol, gancaonin I, dihyrlicoisoflavone A and gancaonol B possess weaker anti-*Helicobacter pylori* activity which may be useful chemoprotective agents for peptic ulcers in *H. pylori* infected individuals<sup>15</sup>.

### Antimicrobial

Multi-drug resistant microorganisms pose a serious global threat in clinical medicine today due to the rapid spread as well as chronic infections caused by them. Each species of the genus *Glycyrrhiza* Linn. is characterized by isoprenoid phenols, which have selective antimicrobial spectrum. Glabridin, glabrene and glabrol are the main phenols present in *G. glabra*, licoricidin, licorisoflavan in *G. uralensis* Fisch., licochalcone A in *G. inflata* Batal. and *G. eurycarpa* P C Li and Glyasperin E in *G. aspera* Pallas. Glicophenone and glicoisoflavanone present in *G. glabra* are two new phenolic compounds having potential activity to control Methicillin resistant *Staphylococcus aureus* (MRSA)<sup>16,17</sup>. Effective Minimal Inhibitory Concentration (MIC) of licochalcone A is 16µg/ml for MRSA and 3µg/ml for food borne pathogens like *Clostridium* spp. and *Bacillus subtilis*<sup>18</sup>. Some compounds

like glabridin, glabrene, licochalcone A, licoricidin and licoisoflavone B exhibited *in vitro* activity against the growth of Clarithromycin and Amoxicillin resistant *H. pylori*<sup>19</sup>. Further the mechanism of antimicrobial activity of licochalcone A is via inhibition of NADH cytochrome c reductase in the bacterial respiratory electron transport chain<sup>20</sup>. *G. glabra* extracts have been evaluated and implicated in oral mouth washes against oral pathogens and oral candidal thrush<sup>21,22</sup>. A variety of compounds isolated from *Glycyrrhiza* include glabridin, gabrin, glabrol, glabrene, hispaglabridin A, hispaglabridin B; 40-methylglabridin and 3-hydroxyglabrol have exhibited potential *in vitro* antimicrobial activity<sup>23,24</sup>. Glycyrrhizinic acids have been used as a cure to atopic dermatitis, pruritis and cysts due to parasitic infestations of skin<sup>25</sup>.

### Antiviral

There is an ever increasing database of natural products in treating and preventing medical problems. Plant purified chemicals have been subjected to extensive screening but a few studies have been initiated on crude plant materials and herbal preparations to be used in healthcare systems. Glycyrrhizin has a prominent antiviral activity, as it does not allow the virus cell binding<sup>26,27,28</sup>. β-Glycyrrhizic acid has been found to inhibit HIV-1 reproduction in MT-4 cells<sup>29,30</sup>. Replications of flaviviruses like the Japanese encephalitis virus, yellow fever virus were inhibited by high non-cytotoxic concentrations. Recently antiviral activities of ribavirin, 6-azauridine, pyraziofurin, mycophenolic

Table 1 : Pharmacological activity of major chemical components of *Glycyrrhiza glabra*

Activity	Phytochemicals									
	Glycyrrhizin	Glabridin	Glycyrrhetic acid	Isoliquiritigenin	Licochalcones	Glabrene	Glycerin	Liquiritigenin		
Antitussive/ Demulcent	+	-	-	-	-	-	-	-		
Antithrombin	+	-	-	+	-	-	-	-		
Antitumor	-	-	+	-	-	+	-	-		
Antimicrobial	+	+	-	+	-	+	-	-		
Antiviral	+	-	+	-	+	-	-	-		
Antioxidant	-	+	-	+	-	-	-	-		
Antidiabetic	+	-	-	-	-	+	-	-		
Hepatoprotective	+	-	-	-	-	-	-	-		
Anticancer	+	-	+	-	-	-	-	-		
Drug- delivery	+	-	-	-	-	-	-	+		
Tyrosinase inhibitor	+	-	+	-	-	+	-	+		
Phytoestrogens	-	+	-	-	+	-	-	-		
Immunostimulating	-	-	+	-	-	-	-	-		

+ Indicates the presence of activity of the compound; - indicates activity not reported

acid and glycyrrhizin against two clinical isolates of SARS (Severe Acute Respiratory Syndrome) virus (FFM-1 and FFM-2) from patients with SARS, admitted to clinical center of Frankfurt University, Germany were evaluated and it was observed that Glycyrrhizin was the most effective in controlling viral replication and could be used as a prophylactic measure<sup>28</sup>. Glycyrrhizin has been previously used to treat patients suffering from HIV-1 and chronic hepatitis C virus<sup>27,29,31</sup>. Thus, it would not be out of place to work on the chemistry of Glycyrrhizin and make it an efficient pharmacophores for use as an antiviral drug.

### ***Antioxidant and Antiinflammatory***

Glycyrrhiza root powder has exhibited a marked hepatoprotective action by antioxidant activity of liver against ascorbate dependent oxidation of endogenous polyenic lipids in rat liver<sup>32</sup>. A variety of phytochemicals present in root extracts of Glycyrrhiza exhibit a potential antioxidant activity. Licochalcones B and D exhibit a potential activity by inhibiting the microsomal lipid peroxidation. Retrochalcones exhibit mitochondria lipid peroxidation and prevent red blood corpuscles from oxidative hemolysis. Isoflavones like glabridin, hispaglabridin A and 3'-hydroxy-4-O-methylglabridin present in Glycyrrhiza were found to have a very potential antioxidant activity NADH dependent peroxidation injury<sup>33,34</sup>. More recently dehydrostilbene derivatives like  $\alpha$ ,  $\alpha$ -Dihydro-3, 5,4- trihydroxy-4, 5- diiodopentenylstilbene have been isolated and found to possess antioxidant activity<sup>35</sup>.

### ***Antidiabetic***

Type 2 (non- insulin dependent) diabetes mellitus, an insulin resistant syndrome, is a growing health concern in the modern society. Peroxisome proliferation activated receptors (PPAR's) are ligand dependent transcriptional factors regulating the expression of a group of genes that play an important role in glucose and lipid metabolism. The PPAR receptors are classified as PPAR- $\alpha$ , PPAR- $\gamma$  and PPAR- $\delta$ . The PPAR- $\alpha$  is found in liver, muscle and kidney. PPAR- $\gamma$  is associated with adipose tissue, adrenals and small intestine whereas PPAR- $\delta$  is expressed ubiquitously. PPAR- $\gamma$  serves as a predominant target for insulin sensitizing drugs like Pioglitazone and Rosiglitazone. Ethyl acetate extract of licorice using GAL-4-PPAR- $\gamma$  chimera assay, exhibited a significant PPAR- $\gamma$  binding activity which was attributed to six phenolic compounds, viz. dehydroglyasperin, glyasperin B, glyasperin D, glycoumarin, glycyrin, glycol and isoglycyrol<sup>36</sup>. Pioglitazone and Glycyrin were found to suppress the increased blood glucose level in mice after sucrose loading during the oral sucrose tolerance test. Pioglitazone, a potent PPAR- $\gamma$  agonist ameliorated the insulin resistance and type-2 diabetes mellitus. Similarly glycyrin also exhibited a potent PPAR- $\gamma$  ligand binding activity and therefore reduces the blood glucose level in knockout diabetic mice (KK- A<sup>y</sup>). This finding is of much significance as licorice has also been traditionally used as an artificial sweetening agent and could be helpful in insulin resistance syndrome prevalent in the modern society. Glycyrrhizin has also exhibited antidiabetic activity in non-insulin dependent diabetic model<sup>37</sup>.

### ***Hepatoprotective***

Chronic hepatitis (viral as well as non-viral) is a slowly progressive liver disease that may evolve into cirrhosis with its potential complications of liver failure or hepatocellular carcinoma. Current therapy with the alpha-interferon is directed as viral clearance, but sustained response is only achieved in 20-40% of patients without cirrhosis and is less than 20% in patients with cirrhosis who have greatest need of therapy. In Japan glycyrrhizin has been used for more than 60 years as treatment for chronic hepatitis under the name of Stronger Neo-Minophagen C (SNMC) clinically as an anti-allergic and antihepatitis agent<sup>38</sup>. Glycyrrhizin induced a significant reduction in serum aminotransferases and improved the liver histology when compared with the placebo. It has also been implicated that long-term usage of glycyrrhizin prevents development of hepatocellular carcinoma in chronic hepatitis C. *In vitro* studies have indicated that glycyrrhizin modifies the intracellular transport and suppresses hepatitis B virus (HBV) surface antigen (HbsAg)<sup>39,40</sup>. It has been found that 18 $\beta$ -glycyrrhetic acid (GA), an aglycone of glycyrrhizin decreases the expression of P450 E1 thereby protecting the liver<sup>41</sup>. GA also prevents the oxidative and hepatic damage caused by aflatoxins by increasing the CYP1A1 and Glutathione-S-transferase (GST) activities and may also contribute to anti-carcinogenic activity by metabolic deactivation of the hepatotoxin<sup>42</sup>. It has also been experimentally investigated that Glycyrrhizin and its analogues have a mitogenic effect via epidermal growth factor receptors subsequently stimulating

the MAP (Mitogen Activated Protein) kinase pathway to induce hepatocyte DNA synthesis and proliferation<sup>43</sup>.

### Anticancer

Herbal therapies are being looked at with much hope to combat cancers despite little understanding of the biological diversity underneath. *G. glabra* extract has been used in herbal formulations for combating cancers like PC-SPEs, a polyherbal composition used for prostate cancer. The licorice extract induced the Bcl2 phosphorylation and G2/M cycle arrest in tumour cell lines as done by clinically used anti-microtubule agent Paclitaxel. 1-(2,4-dihydroxyphenyl)-3-hydroxy-3-(4'-hydroxyphenyl)1-propanone ( $\beta$ -hydroxy-DHP) was identified in the licorice extract, which induced Bcl2 phosphorylation in breast and prostate tumour cells, G2/M cell cycle arrest, apoptosis demonstrated by Annexin V and TUNEL assay, decreased cell viability demonstrated by tetrazolium (MTT) assay, and altered microtubule structure<sup>44</sup>. 70% Methanol soluble fraction of licorice acetone extract was found to induce apoptosis in human monoblastic leukaemia U937 cells. The compound was identified to be licocoumarone also responsible for antioxidant and antimicrobial activity<sup>45</sup>. Activator protein-1 (AP-1) is a nuclear transcription factor. Blocking of tumour promoter induced AP-1 activity could be used to arrest the induced cellular transformation. It was found that Glycyrrhizin induced AP-1 activity in untreated cells whereas inhibited TPA (12-O-tetradecanoylphorbol-13-acetate) induced AP-1 activity in TPA treated cells.

This mechanism could serve as a model for development of new chemo-protective agents<sup>46</sup>.

### Drug delivery agent

Transdermal delivery of drugs is an attractive proposition as it has several advantages over the intravenous or oral administration due to sensitivity of drugs. The principal barrier is the *stratum corneum*, the outermost layer of the skin comprising keratin rich cells embedded in multiple layers. A common or simple approach would be to enhance the permeability of the skin by use of penetration enhancers or accelerators, which could induce a reversible permeability of *stratum corneum*. It has been found that glycyrrhizin extracted from *Glycyrrhiza glabra* var. *glandulifera* (roots) enhanced the percutaneous absorption of diclofenac sodium using excised abdominal rat skin. The results showed that the efficiency of glycyrrhizin as an enhancer agent is greater in gel formulations than in the emulsions. The enhancer with the concentration of 0.1%w/w in gel increased diclofenac sodium flux value to tenfold compared with the control gel<sup>47</sup>. Liquiritigenin and daidigenin have also been reported to be drug delivery agents as they have good transepithelial flux through human intestinal epithelial cell lines (Caco-2)<sup>48</sup>.

### Other pharmacological activities

The phytochemicals present in *Glycyrrhiza* sp. are subjected to different screens for newer pharmacological activities. The ethanolic extract of *Glycyrrhiza* exhibited anti-

convulsant activity against pentylene tetrazol (PTZ) and lithium pilocarpine induced seizures in mice<sup>52</sup>. A variety of plant extracts contain compounds, which have activity similar to ovarian steroid hormones and commonly referred to as phytoestrogens. There is an increasing demand for phytoestrogens as these have beneficial effects mimicking the critical benefits of estrogen but avoiding the deleterious effects on breast and uterus. The licorice extract and its major isoflavan Glabridin act as estrogen receptor (ER) agonist under *in vitro* and *in vivo* conditions. The enzyme creatine kinase is a biomarker for estrogen responsive genes. Glabrene and isoliquiritigenin have a higher affinity for human ER as compared to glabridin<sup>53</sup>. The common finding during premenstrual syndrome (PMS) is the increased ratio of estrogen to progesterone ratio. Liquorice is believed to be beneficial during PMS by reducing the estrogen level and increases the progesterone level<sup>54</sup>. Estrogen and progestin inhibit serotonin re-uptake through allosteric interaction with the serotonin transporter (SERT) in a non-genomic mechanism. Reduction or blocking of serotonin uptake at synapse helps in alleviation of the depression. HEK-293 cells have demonstrated that the isoflavans glabridin and 4'-O-methylglabridin (4'-OMeG) and the isoflavene glabrene inhibited serotonin re-uptake, whereas resorcinol, the isoflavan 2'-O-methylglabridin (2'-OMeG) and the isoflavones genistein and daidzein were inactive in reducing the serotonin re-uptake. Thus, the extracts and their phytochemicals could serve as phytoestrogens to ameliorate mild to moderate depression in pre- and post-menopausal women by affecting the

serotonergic systems blocking serotonin re-uptake<sup>55</sup>.

Radiation therapy has a lot of side effects during the oncological treatment. Compounds, which can reduce the radiation-induced side effects, are being sought and are referred to as radioprotective agents. Licorice extract has been found to be radioprotective to gamma radiation by preventing lipid peroxidation in rat liver microsome and protect the plasmid DNA from radiation induced strand breaks<sup>56</sup>. It is implicated to be anti-mutagenic against Ethylmethane sulfonate (EMS)<sup>57</sup> and prevented DNA damage induced by benzo- $\alpha$ -pyrene<sup>58</sup>. The licorice extract is not only antidiabetic in nature but is also used extensively as an artificial sweetener and flavour enhancer in Japan and USA and called as EMLE (enzymatically modified liquid extract). The major components of EMLE again happens to be glycyrrhithinic acid, liquiritic acid and glycyrrhizin<sup>59</sup>.

Licorice has been widely used in immunomodulating preparations<sup>60</sup>. Autoimmune diseases have an elevated level of immune complexes (IC). Steroids or immunosuppressive drugs generally perform the treatment of these disorders have severe side effects. Licorice root extracts have been widely used in Kampo medicines; studies have indicated that glycyrrhizin present in licorice extracts modulates the clearance of IC under the state of dysfunction<sup>61</sup>. Glycyrrhizin also restores the impaired interleukin IL-2 production in the thermally injured mice<sup>62, 63</sup>. Nitric oxide (NO) is a signal molecule synthesized by the enzyme Nitric oxide synthase (NOS). GA has been found to be an elicitor of nitric oxide. It functions as a biological response

modifier for immunochemotherapeutic usefulness by macrophageal expression of NO production<sup>64</sup>.

### ***Cosmeceutical –Tyrosinase inhibition***

The synthesis of melanin is under the metabolism of aromatic amino acids that is predominantly regulated by the enzyme Tyrosinase via DOPA. Hyper pigmentation is due to excess of melanin biosynthesis. A variety of natural compounds have been used as a sunscreen agents like the Para-aminobenzoic acid (PABA), Vitamin C and kojic acid in cosmeceutical and medicinal treatments but their instability has restricted their efficient use. Glabrene is a unique compound possessing not only inhabiting melanogenesis but also anti-inflammatory in nature<sup>49</sup>. Glabrene specifically inhibits the T1 and T3 tyrosinase isoenzyme activity and, therefore, Isoliquiritigenin and glabrene may serve as skin lightening agent for the medicinal and cosmeceutical purposes<sup>50</sup>. Glycyrrhizin and glycyrrhetinic acid (GA) have been found to have a significant inhibitory effect on melanogenesis. Glycyrrhetinic acid as stearyl glycyrrhetinate is being used as a sun care and sunscreen agent. A synthetic derivative of GA has been found to have a prominent inhibitory potential to melanogenesis. However, there is a need to establish the toxicological safety of the analog of GA for skin applications<sup>51</sup>.

### **Toxic and side effects of Licorice**

Despite a vast range of biological effects like antiinflammatory, antiallergic,

antioxidant, antiviral of the phytochemicals present in Glycyrrhiza extracts there is a flip side too. Prolonged use of glycyrrhiza leads to pseudoaldosteronism<sup>65, 66</sup>, hypertension<sup>67, 68</sup> and hyperkalemia<sup>69, 70</sup>. Licorice extract and glycyrrhizin have also been reported to induce changes in Cytochrome P<sub>450</sub> linked activities resulting in accelerated metabolism of co-administered drugs and adverse effects due to change in cytochrome profiles such as toxicity/cytotoxicity<sup>71</sup>.

### **Future approaches**

The vast range of biological effects like antiinflammatory, antiallergic, antioxidant, antiviral of the phytochemicals present in extracts has been of immense importance in phytotherapeutics. Thus, there is an immense need to modify the natural glycyrrhizin to reduce these side effects thereby generating the advanced versions of the bioactive compounds to be used as drugs in future. High throughput methods help in generating newer versions of a natural product template and generate a library of compounds or analogs, which could be further screened for a particular activity, safety and toxicology. The screening for a particular activity can be achieved using automated high throughput assay system to arrive to a “lead” molecule suitable for the development into a new drug<sup>72</sup>. Glycyrrhizin, glycyrrhetinic acid, glabridin and isoliquiritigenin hold a strong promise in designing future drugs. Derivatives of these compounds are being generated to evaluate their pharmacological purposes for future drug use. Glycyrrhizin sulfate has been

synthesized and investigated for anti-HIV activity in comparison with the parent compound glycyrrhizin. Glycyrrhizin sulfate was found to have nearly four folds of the potential antiviral activity in MT-4 cells compared to glycyrrhizin in molar terms<sup>73</sup>. Glycyrrhizin derivatives have also been synthesized for the development of a stable sunscreen compound with a potential tyrosinase inhibitory activity<sup>51</sup>. Penta-O-cinnamate of glycyrrhizin is the basic structure for the preparation of Niglizin which has a pronounced antiinflammatory activity combined with antiulcer and hepatoprotective action. N-acetylmuramoyl peptide (MDP) is glycyrrhizin analog having potential *in vitro* immunostimulating properties<sup>74</sup>. There are ample chances of arriving to pharmacophores with least toxic side effects using combinatorial chemistry. The advances in drug discovery with tools like the high throughput systems, proteomics, genomics and informatics (Bio/Chem. and Pharmaco) have further enhanced the evaluation of these newly generated compounds for their future medical applications.

## Conclusion

Phytochemistry has regained its strength in the drug discovery process in the past few years, as nature is the best inventive chemist providing ample chemical structural diversity, which could be further remodeled using current tools. *Glycyrrhiza glabra* is one of those ancient plants, which have been used in the traditional pharmacopoeias for its multifaceted actions against a variety of systemic and non-systemic ailments. The chemical foundations of these have been

discovered in the last millennium and this plant is promising in providing new molecules, which could be of immense medicinal applications in the present millennium.

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