An Update on Secondary Metabolites from Glycyrrhiza Species

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Abstract: Secondary metabolites have been obtained from the Glycyrrhiza species (Fabaceae) including G. glabra, G. echinata, G. uralensis, G. triphylla and G. macedonica. These compounds 1-25 belong to the classes, steroid, saponin, flavonoid, flavonoid glycoside, triterpenic acid, coumarin, phenolic derivative, chalcone and chalcone glycoside. This review will describe the isolated compounds 1-25, obtained from Glycyrrhiza species with their biological activities up to 1966.

Keywords: Glycyrrhiza glabra, Glycyrrhiza echinata, Glycyrrhiza uralensis, Glycyrrhiza triphylla, Glycyrrhiza macedonica, Licorice.

INTRODUCTION

The role of natural products is always very important in the discovery and development of new pharmaceuticals. They may be as clinically useful drugs, as starting material to produce synthetic or semi-synthetic drugs, or as lead compounds from which a new synthetic drug can be designed [1]. Plants are extensively used medicinally all around the world and are an important aspect of various traditional medicine systems. The application of phytherapy has increased, especially in developed countries during the past few decades [2]. Despite advancements in synthetic chemistry, about 80% of the world’s populations still depend upon medicinal plants for the treatment of diseases [3,4].

The genus Glycyrrhiza belongs to the family Fabaceae. Glycyrrhiza consists of about 30 species belong to Asia, North and South America, Europe as well as Australia, including G. uralensis, G. aspera, G. glabra, G. korshinskyi, G. inflata and G. eurycarpa. Glycyrrhiza glabra includes three varieties: Persian and Turkish liquorices assigned to G. glabra var. violacea, Russian liquorice is G. glabra var. glabulifera, and Spanish and Italian liquorices are G. glabra var. typical [5]. G. uralensis, G. inflata and G. glabra are the only species mentioned in the Chinese Pharmacopoeia, their Chinese name is gan-cao, which means “sweet herb”. It is also known as liquorice, kannoh, sweet root and yasti-madhu [5,6]. It is a perennial herb, which is 3-5 feet in height, smooth rising from thick rhizome.

Glycyrrhiza plant is used as galactagogue, emmenagogue, laxative, contraceptive, anti-asthmatic drug and antiviral agent. It has been suggested for dyspepsia and gastric and duodenal ulcers as well as an anti-inflammatory agent during allergic reactions in folk medicines [7]. Glycyrrhiza root powder has exhibited significant hepatoprotective action against ascorbate dependent oxidation endogenous polyenic lipids in rat liver [8]. The ethanolic extract of Glycyrrhiza showed anticonvulsant activity against pentylenetetrazol (PTZ) and lithium pilocarpine induced seizures in mice. It also exhibited anti-carcinogenic and anti-hepatotoxic activities [9,10].

Phytochemical Analysis of the Genus Glycyrrhiza

Phytochemical analysis of the aerial parts of the genus Glycyrrhiza revealed the presence of various secondary metabolites, 1-25 isolated from Glycyrrhiza glabra, G. echinata, G. uralensis, G. triphylla, G. macedonica and Liquorice up to 1966. These compounds belong to the classes, steroid 1, saponins 2, flavonoids 3-4, flavonoid glycosides 5-6, triterpenic acids 7-15, coumarins 16-17, phenolic derivatives 18-19, chalcones 20-21 and chalcone glycosides 22-25. Their structures are represented in Figure 1 and their detail is also mentioned in Table 1.

Steroids

Zayed and co-workers in 1964 isolated β-sitosterol (1) from G. glabra, which was a very common compound present in plants [11]. It has potential to reduce blood cholesterol levels and benign prostatic hyperplasia (BPH) [12,13].

Saponins

Kobert and co-workers in 1915 isolated glycyrrhizin (2) from Glycyrrhiza species [14]. Glycyrrhizin (2) is also called glycyrrhizic acid (2). It is exceedingly sweet
(Figure 1). Continued.

Figure 1: Structures of Secondary Metabolites obtained from *Glycyrrhiza* species.
and the main sweet tasting compound from Liquorice root. It is also used to prevent liver carcinogenesis in patients with chronic hepatitis C [15]. Baytop in 1954 also isolated it from roots and juice of *G. glabra* and *G. echinata* [16].

**Flavonoids**

Litvinenko and co-workers in 1963 isolated liquiritigenin (3) from the ethanolic extract of the roots of *G. glabra* [17]. It is an estrogenic compound. Reiners in 1964 isolated 3 from methanolic extract of Liquorice root [18]. It was also isolated by Litvinenko in 1963 from *G. uralensis* [19] while Litvinenko and Obolentseva in 1964 again isolated it from *G. glabra* and *G. uralensis* [20]. Reiners in 1966 isolated 7-hydroxy-4′-methoxyisoflavone (4) from the roots of Liquorice [21].

**Flavonoid Glycosides**

Shinoda and Ueeda in 1934 isolated a glucoside, liquiritin (5) from the extraction of the powder root of *G. glabra* L. with methanol [22]. Litvinenko in 1963 isolated liquiritin (5) and neoliquiritin (6) from *G. uralensis* [19]. Litvinenko and Obolentseva in 1964

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of Compound</th>
<th>Class of Compound</th>
<th>Glycyrrhiza species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>β-Sitosterol (1)</td>
<td>Steroid</td>
<td><em>G. glabra</em></td>
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<tr>
<td>2</td>
<td>Glycyrrhizin or glycyrrhizic acid (2)</td>
<td>Saponin</td>
<td><em>G. species, G. glabra and G. echinata</em></td>
<td>14,16</td>
</tr>
<tr>
<td>3</td>
<td>Liquiritigenin (3)</td>
<td>Flavonoid</td>
<td>Liquorice, G. uralensis, G. glabra and G. uralensis</td>
<td>17-20</td>
</tr>
<tr>
<td>4</td>
<td>7-Hydroxy-4′-methoxyisoflavone (4)</td>
<td>Flavonoid</td>
<td>Liquorice</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>Liquiritin (5)</td>
<td>Flavonoid glycoside</td>
<td><em>G. glabra, G. uralensis, Liquorice, G. glabra and G. uralensis</em></td>
<td>19,20,22</td>
</tr>
<tr>
<td>6</td>
<td>Neoliquiritin (6)</td>
<td>Flavonoid glycoside</td>
<td><em>G. uralensis, G. glabra and G. uralensis</em></td>
<td>19,20</td>
</tr>
<tr>
<td>7</td>
<td>Glabridin (7)</td>
<td>Triterpenic acid</td>
<td>Liquorice</td>
<td>24</td>
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<tr>
<td>8</td>
<td>Meristotropin (8)</td>
<td>Triterpenic acid</td>
<td>G. triphylla</td>
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<tr>
<td>9</td>
<td>Macedonic acid (9)</td>
<td>Triterpenic acid</td>
<td>G. macedonica</td>
<td>26</td>
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<tr>
<td>10</td>
<td>Echinatic acid (10)</td>
<td>Triterpenic acid</td>
<td>G. echinata</td>
<td>27</td>
</tr>
<tr>
<td>11</td>
<td>Liquoric acid (11)</td>
<td>Triterpenic acid</td>
<td>G. glabra</td>
<td>28</td>
</tr>
<tr>
<td>12</td>
<td>Glycyrrhetic acid or Uralenic acid (12)</td>
<td>Triterpenic acid</td>
<td><em>G. glabra and G. uralensis</em></td>
<td>28,29</td>
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<td>13</td>
<td>11-Deoxyglycyrrhetic acid (13)</td>
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<td>Liquiritic acid (14)</td>
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<td><em>G. glabra</em></td>
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<td>Triterpenic acid</td>
<td>G. glabra</td>
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<td>16</td>
<td>Herniarin (16)</td>
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<td>Liquorice</td>
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<td>Coumarin</td>
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<td>Ferulic acid (18)</td>
<td>Phenolic derivative</td>
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<tr>
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<td>Sinapic acid (19)</td>
<td>Phenolic derivative</td>
<td>Liquorice</td>
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<td>20</td>
<td>2,4,4′-Trihydroxychalcone (20)</td>
<td>Chalcone</td>
<td><em>G. glabra</em></td>
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<td>21</td>
<td>Isoliquiritigenin (21)</td>
<td>Chalcone</td>
<td><em>G. uralensis, G. glabra and G. uralensis</em></td>
<td>19,20</td>
</tr>
<tr>
<td>22</td>
<td>Neoisoliquiritin (22)</td>
<td>Chalcone glycoside</td>
<td><em>G. uralensis, G. glabra and G. uralensis</em></td>
<td>19,20</td>
</tr>
<tr>
<td>23</td>
<td>Licurazid (23)</td>
<td>Chalcone glycoside</td>
<td><em>G. uralensis, G. glabra and G. uralensis</em></td>
<td>19,20</td>
</tr>
<tr>
<td>24</td>
<td>Isoliquiritin (24)</td>
<td>Chalcone glycoside</td>
<td><em>G. glabra and G. uralensis</em></td>
<td>20</td>
</tr>
<tr>
<td>25</td>
<td>Licuraside (25)</td>
<td>Chalcone glycoside</td>
<td><em>G. glabra</em></td>
<td>36</td>
</tr>
</tbody>
</table>

*Table 1: Secondary Metabolites from *Glycyrrhiza* Species*
again isolated licoritit (5) and neoliquiritin (6) from G. glabra and G. uralensis [20]. Licoritit (5) has significant antidepressant-like effects [23].

**Triterpenic Acids**

Beaton and Spring in 1957 isolated glabric acid (7) from Licorice root [24]. Kir'yalov and Naugol' naya in 1963 isolated meristotropac acid (8) from G. triphylla [25]. They also isolated macedonic acid (9) from the roots of G. macedonica and echinatic acid (10) from G. echinata [26,27]. Elgamal and co-workers in 1965 isolated liquoric acid (11) and glycyrrhetic acid (12) from the roots of G. glabra [28]. Kir'yalov and Naugol’ naya in 1964 again isolated glycyrrhetic acid (12) from the alcoholic extract of the roots of G. uralensis, which is also known as uralenic acid (12) [29]. Canonica and co-workers in 1966 isolated 11-deoxy glycyrrhetic acid (13), liquiritic acid (14) and isoglabrolide (15) from G. glabra [30,31].

**Coumarins**

Reiners in 1964 isolated two coumarins, herniarin (16) and umbelliferone (17) from the methanolic extract of Licorice root [18]. Herniarin (16) may be used as a reference material in the analysis of coumarin compounds whereas umbelliferone (17) has antioxidant properties.

**Phenolic Derivatives**

Reiners in 1964 obtained two phenolic derivatives, ferulic acid (18) and sinaptic acid (19) from the methanolic extract of Licorice roots [18]. Ferulic acid (18) is an antioxidant; its small amount can inhibit melanin production in the process of skin whitening [32].

**Chalcones**

Litvinenko and co-workers in 1963 obtained 2,4,4’- trihydroxychalcone (20) from the ethanolic extract of the roots of G. glabra [17]. Litvinenko in 1963 also isolated isoliquiritigenin (21) from G. uralensis [19] whereas Litvinenko and Obolentseva in 1964 isolated again from G. glabra and G. uralensis [20]. It is potent GABA-A benzodiapine receptor positive allosteric modulator [33].

**Chalcone Glycosides**

Litvinenko in 1963 isolated neoisoliquiritin (22) and licurazid (23) from G. uralensis [19]. Litvinenko and Obolentseva in 1964 reported neoisoliquiritin (22) and licurazid (23) again with isoliquiritin (24) from G. glabra and G. uralensis [20]. Licurazid (23) has antitumor potential [34] whereas isoliquiritin (24) has antioxidant, anti-inflammatory and anti-depression activities [35]. Litvinenko and Kovalev in 1966 also isolated licursaide (25) from G. glabra [36].

**CONCLUSION**

The genus *Glycyrrhiza* has been considerable attention since the last decade. Therefore this review describes secondary metabolites, 1-25 obtained from various species of the genus *Glycyrrhiza* up to 1966. Regarding this survey, it is assumed that much more phytochemical and pharmacological investigation with biological activities of whole plants and their isolated secondary metabolites has ever been carried out on *Glycyrrhiza* species.

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**REFERENCES**


