Research Progress on Chemical Constituents and Pharmacological Activities of *Chrysosplenium* spp. (*Saxifragaceae*)

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Abstract  Plants of *Chrysosplenium* (*Saxifragaceae*) were usually reported as traditional Chinese herbal medicines. The active ingredients such as trimethoxyflavones separated from *C. nudicaule* have significant inhibitory effect on human erythroleukemia K562 cell. The pharmacological activities of other species in this genus were also frequently reported and chemical constituents & pharmacological activities of this genus is worthy of in-depth research. In order to reveal the research progress of active components and bioactive ingredients such as flavonoids, volatile oil and terpenoids in *Chrysosplenium* spp, the major chemical constituents and pharmacological activities of *Chrysosplenium* were discussed in this paper.

Keywords  *Chrysosplenium*; chemical constituents; pharmacological activities; research progress

The genus *Chrysosplenium* Linnaeus contains more than 65 species of perennial herbs and the genus is mainly distributed in the northern hemisphere with high diversity in China. As traditional Chinese medicine, the genus plants were used to treat inflammation, fever and liver disease. The chemical constituents of 90% ethanol extract isolated from *C. nudicaule* and *C. carnosum* have higher anti-tumor activity. Flavonoids and volatile oil are the main ingredients in most *Chrysosplenium* individuals and the minor components were pentacyclic triterpenoids, triacontane and a mount of L-arabinose. Moreover, flavonoids and triterpenoids from the genus plants showed stronger bioactivities. The chemical composition of the genus and pharmacological studies have been reported frequently. This article systematically reviews the chemical constituents and pharmacological activities of *Chrysosplenium* spp. The active ingredients such as trimethoxyflavones separated from *C. nudicaule* have significant inhibitory effect on human erythroleukemia K562 cell. The pharmacological activities of other species in this genus were also frequently reported and chemical constituents & pharmacological activities of this genus is worthy of in-depth research. In order to reveal the research progress of active components and bioactive ingredients such as flavonoids, volatile oil and terpenoids in *Chrysosplenium* spp, the major chemical constituents and pharmacological activities of *Chrysosplenium* were discussed in this paper.

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Chemical composition

Chrysosplenium is rich in bioactive chemical constituents but only a few Chrysosplenium species have been covered. The valuable chemical compositions of the genus are highly methylated and hydroxylated flavonoids such as chrysosplenol A B C & D chrysosplenol B A B C & D kaempferol and quercetin. Furthermore triterpenoids triacontane and L-arabinose were also covered in Chrysosplenium.

1.1 Flavonoids

Chrysosplenium species have quite a few flavonoids including 3-OMe-flavonoids. Flavonol and flavonol glycosides are the major medicinal compounds in Chrysosplenium. Flavonoids were given in Tab. 1; the main skeleton of flavonoids was showed in Fig. 1 A and 3-OMe-flavonoid in Fig 1 B.

![Main skeleton of flavonoids](image)

A) main skeleton of flavonoids;
B) the structure of 3-OMe flavonoid in C.nudicaule and C.grayanium

Tab.1 The main flavonoids of Chrysosplenium

<table>
<thead>
<tr>
<th>No.</th>
<th>Compounds</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4’-dihydroxy-7’-trimethoxyflavone</td>
<td>[14]</td>
</tr>
<tr>
<td>2</td>
<td>3’-dihydroxy-7’-trimethoxyflavone-4’-glucoside</td>
<td>[14]</td>
</tr>
<tr>
<td>3</td>
<td>7’-pentaflavonol-3’-methoxyflavone</td>
<td>[14]</td>
</tr>
<tr>
<td>4</td>
<td>7’-pentaflavonol-3’-methoxyflavone-6’-glucoside</td>
<td>[14]</td>
</tr>
<tr>
<td>5</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone</td>
<td>[14]</td>
</tr>
<tr>
<td>6</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone-6’-glucoside</td>
<td>[14]</td>
</tr>
<tr>
<td>7</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone</td>
<td>[14]</td>
</tr>
<tr>
<td>8</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone-3’-glucoside</td>
<td>[14]</td>
</tr>
<tr>
<td>9</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone</td>
<td>[14]</td>
</tr>
<tr>
<td>10</td>
<td>7’-pentaflavonol-3’-trimethoxyflavone-6’-glucoside</td>
<td>[14]</td>
</tr>
</tbody>
</table>

Chrysosplenium.
1.2 Volatile oil

151 essential oils have been reported[21] and some are used as natural cosmetics and medicine[22]. For example[22], a large amount of hexadecanoic acid was separated from *C. cavaleriei* and *C. macrospermum* [14] and hexadecanoic acid is the main raw material of common cosmetics. The basis was shown in Tab. 2.

1.3 Triterpenoids

The triterpene derivatives[11] isolated from *C. nudicaule* [2], *C. carnosum* and *C. grayanum* [11] were found to have good anti-cancer effects [23]. The main structure of these triterpenoids was put in Fig. 2.

1.4 Other components

Melissane and a minute amount of L-arabinose were the component of *Chrysosplenium* [24]. L-arabinose is a natural L-monosaccharide which has hypoglycemic effect to prevent diabetes[25] and L-arabinose also retards fat synthesis[26].

![Structure of triterpenoids](image)

**Fig. 2** Structure of triterpenoids

<table>
<thead>
<tr>
<th>No.</th>
<th>Compounds</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E)-2-Hexenal</td>
<td>[17]</td>
</tr>
<tr>
<td>2</td>
<td>(E)-β-Damascenone</td>
<td>[17]</td>
</tr>
<tr>
<td>3</td>
<td>(Z)-13-Doospermamide</td>
<td>[17]</td>
</tr>
<tr>
<td>4</td>
<td>(Z)-9,11-Octadecadienal</td>
<td>[17]</td>
</tr>
<tr>
<td>5</td>
<td>10-Heneicosene</td>
<td>[17]</td>
</tr>
<tr>
<td>6</td>
<td>14-β-Pregna</td>
<td>[17]</td>
</tr>
<tr>
<td>7</td>
<td>1-Methyl-naphthalene</td>
<td>[17]</td>
</tr>
<tr>
<td>8</td>
<td>6,8-Dimethyl-naphthalene</td>
<td>[17]</td>
</tr>
<tr>
<td>9</td>
<td>4,6,14-Tetramethyl-hexadecane</td>
<td>[17]</td>
</tr>
<tr>
<td>10</td>
<td>6-Dihydroxy-4-methyl-2-oxacyclohexadien-1-one</td>
<td>[17]</td>
</tr>
<tr>
<td>11</td>
<td>6-Dimethyl-Naphthalene</td>
<td>[17]</td>
</tr>
<tr>
<td>12</td>
<td>6-Di-tert-Butyl phenol</td>
<td>[17]</td>
</tr>
<tr>
<td>13</td>
<td>6-Dimethylcyclohexano</td>
<td>[17]</td>
</tr>
<tr>
<td>14</td>
<td>2-Hexen-4-olide</td>
<td>[17]</td>
</tr>
<tr>
<td>15</td>
<td>2-Hexenoic acid</td>
<td>[17]</td>
</tr>
<tr>
<td>16</td>
<td>2-Methoxyethyl phthalate</td>
<td>[17]</td>
</tr>
</tbody>
</table>

**Tab. 2** The volatile constituents in *Chrysosplenium*.
3 Pharmacological activities

*Chrysosplenium* had obvious physiological activity in antibacterial[24][25] anti-tumor[26][27][28] and cytotoxic effect[29]. Furthermore it also played an effective role in the treatment of glycogen cataract[30].

3.1 Anti-bacterial

5[4′-di-hydroxy-3′][6′] 3′-trimethoxy-flavone-7-O-β-D-glucose showed strong bacteriostatic ability to *Staphylococcus aureus* and *Bacillus subtilissimus*. Veronicafolin had high antibacterial with *S. aureus* B. subtilissimu S. *typhias* and *E. coli*. 3.2 Anti-tumor

All triterpenoids separated from *C. nudicaule* C. *grayanum* and *C. carnosum* showed high effectiveness to gastric cancer cells (ST-KM[31] Kato-III[32] NKPS & KKLS) Lewis (PC-3 PC-8  PC-18 & QC-9) osteosarcomas (MG63 & Oste) colon adenocarcinoma cells (SW-480 & Colo320 DM) and malignant melanomas[33]. Quercetins could block the G1 / S phase in the human colon cancer cell (Colo320 DM) cycle. It is worth considering that 6[4′][7′] 3′-trimethoxy-5′ 5′ 4′-trihydroxy flavone (separated from *C. nudicaule*) inhibited the growth of cancer cells with an IC50 value of 8.33 μg/
ml after 72 incubation\textsuperscript{[20]}. The anti-tumor mechanism of flavonoids is that cellular cleavage and proliferation was markedly inhibited. Furthermore\textsuperscript{[20]} 3-OMe-flavonoids could protect DNA from free radical attack\textsuperscript{[20]} it also showed anti-oxidant potential\textsuperscript{[20]}.

3.3 Antiviral

Tsuchiya \textsuperscript{[23]} reported that the generous flavonoids in Chrysosplenium species like chrysosplenol B and C had specific antiviral activity against rhinovirus for their 3-OMe. It is suggested that this genus be used as a remedy for flu. However\textsuperscript{[20]} both the flavonoids were rare in nature. Another flavonoid\textsuperscript{[20]} Oxyayanin A might be applied to general cold virus.

3.4 Cytotoxic action

The LD\textsubscript{50} (Lethal median dose) of Oxyayanin A (isolated from C.\textit{grayanum}) for KB cells was 1.99 ± 0.75 μg/mL\textsuperscript{[20]}. Three triterpenoids of \textit{C. carnosum} exhibited strong inhibitory activities against B16F10 cells’ growth with an IC\textsubscript{50} ranging from 15.7 to 18.3 μmol/L\textsuperscript{[21]}.

3.5 Cataract preventing

Accumulation of polyols leads to cataracts\textsuperscript{[20]} but chrysosplenoid D could effectively cut off the pathway by which crystalline aldose reductase was used to reduce aldose to polyols\textsuperscript{[20]}. Therefore\textsuperscript{[20]} it could reduce the incidence of cataracts.

3.6 Insecticidal activity

Methanolic extract of \textit{Chrysosplenium macrophyllum} had intense killing effects on \textit{Caenorhabditis elegans}\textsuperscript{[20]}. In addition\textsuperscript{[20]} the main chemical composition of \textit{C. davidianum} and \textit{C. cavaleriei} are similar to \textit{C. macrophyllum}\textsuperscript{[20]} both \textit{Chrysosplenium} plants may be used as biological pesticides\textsuperscript{[11]}.

4 Conclusion

\textit{Chrysosplenium} plants play a unique role in traditional medicine\textsuperscript{[20]} however\textsuperscript{[20]} only a few researchers have conducted pharmacological studies on the genus in the past 30 years. Recently\textsuperscript{[20]} many new species of this genus had been covered\textsuperscript{[20-28]} but pharmacological studies on these new species have not been undertaken yet. Based on previous research\textsuperscript{[20]} the new \textit{Chrysosplenium} species may have more potential efficacy. In order to present a clinical anti-tumor and anti-virus effect\textsuperscript{[20]} \textit{Chrysosplenium} plants acting as traditional medicines are worth further studying and developing.

References

\begin{itemize}
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