New Collection of Crude Drugs in *Chinese Pharmacopoeia 2010 III. Kadsurae Caulis*

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**Abstract:** The dried cane of *Kadsura interior* (*Kadsurae Caulis*) is recorded in *Chinese Pharmacopoeia 2010* as Dian Jixueteng for the treatment of rheumatism, irregular menstruation, and deficiency of Qi and blood. In this paper, morphological characteristics, chemical constituents, and pharmacological activities in the cane of *K. interior* were summarized. Moreover, some suggestions about application and quality control of *Kadsurae Caulis* were proposed in order to provide a theoretical basis for further scientific use.

**Key words:** biological activities; chemical constituents; *Kadsurae Caulis; Kadsura interior*; morphological characteristics

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**Introduction**

The dried cane of *Kadsura interior* A. C. Smith (Schisandraceae) is recorded in *Chinese Pharmacopoeia 2010* as *Kadsurae Caulis* (Dian Jixueteng) for the treatment of rheumatism, irregular menstruation, and deficiency of Qi and blood. It is a major raw material in the formula of Compound Dian Jixueteng Gao, which is mainly composed of the water extracts from *Kadsurae Caulis*, *Cyathulae Radix*, *Dipsaci Radix*, *Carthami Flos*, and black soybean as a traditional formula with the function of activating blood circulation and treating irregular menstruation (Chen *et al.*, 1993).

Many Chinese herbal medicines exhibit their therapeutic effects via the synergy and integration of multi-components and multi-targets (Wu *et al.*, 2010); And one disease/symptom could be treated via multi-targets by multi-components. Thus different herbs with similar effects for one disease may be a result of a variety of integrated components. Dian Jixueteng has very similar medical function with Jixueteng. Locally, different species including some plants of *Kadsura A. L. Jussieu* have the same name of Jixueteng due to their similarities in appearance or medicinal function. There are about fifteen species from six genera being used as Jixueteng in different areas of China, and the cane of *K. interior* is one of the substitutes. The real Jixueteng is botanically derived from the dried cane of *Spatholobus suberectus* Dunn, which possesses similar medicinal function with Dian Jixueteng, but quite different chemical components from the cane of *K. interior*. The compounds from Jixueteng mainly belong to the classes of flavonoid, steroid, and triterpenoid while the compounds from Dian Jixueteng mainly belong to the classes of lignan and triterpenoid.

In this review, we summarized the research progress in botany, phytochemistry, quality control, biological activities, and application in the cane of *K. interior* under the item of *Kadsurae Caulis* in *Chinese Pharmacopoeia 2010* (Pharmacopeia Committee of P. R. China, 2010) in order to provide scientific evidence for the better utilization of *Kadsurae Caulis*.

**Brief history**

The cane of *K. interior*, basically originated in Fengqing County, Yunnan Province, is accepted as *Kadsurae Caulis* independently in *Chinese Pharmacopoeia 2010*.
In fact, the cane of *K. interior* has been used as the major raw materials of *Kadsurae Caulis* in the formula of Compound Dian Jixueteng Gao for a long history to enrich blood, dredge collaterals, promote blood circulation, and stimulate menstrual discharge.

**Botanical identification and resources**

*K. interior* distributes in the southwest of Fengqing County, Yunnan Province, China and the northeast of Burma, in the woods within 1200−2500 m elevation (Liu, Luo, and Wu, 1996).

*Kadsurae Caulis* is mainly from the dried canes of *K. interior*, harvested in autumn with their branches and leaves removed, then sliced and sun-dried.

The product has a circle, elliptic or irregular inclined section with diameter of 1.8−6.5 cm. It is externally taupe, the outer cork is scaling off, and the exposed surface appears dark purple. The cork is thick, longitudinally furrowed or wrinkled, often accompanied by liverworts and lichens. The texture is too hard to broken. The odor is aromatic and the taste is bitter and astringent.

The characteristic of transverse section is described as follows: cortex narrow, red brown, and fibrous; The xylem is relatively broad, consisting of fine vessels scattered; The pith is small and taupe and shows vacancy.

In some literatures, *Kadsurae Caulis* was usually the mixture of *K. heteroclita* (Roxb.) Craib and *K. interior* (Chen, 2007). The difference in the canes between *K. heteroclita* and *K. interior* is the cork; The cork characteristic of *K. heteroclita* is yellowish-white, soft, and has rich flexibility, sometimes as thick as 7 mm, with longitude furrow and transverse crack.

**Chemical constituents**

Lignans and triterpenoids are mainly bioactive components in the species, and lignans are usually considered as the characteristic components from the plants in the family of Schisandraceae. Main compounds are listed in Table 1 and their structures are demonstrated in Fig. 1.

**Table 1 Chemical constituents (1—34) from cane of *K. interior***

<table>
<thead>
<tr>
<th>No.</th>
<th>Compounds</th>
<th>References</th>
<th>No.</th>
<th>Compounds</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>isointeriorin</td>
<td>Ding and Luo, 1990</td>
<td>19</td>
<td>gomisin A</td>
<td>Yu, Chen, and Situ, 1996</td>
</tr>
<tr>
<td>2</td>
<td>interiorin</td>
<td>Ding and Luo, 1990</td>
<td>20</td>
<td>schizandrin</td>
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<tr>
<td>3</td>
<td>interiorin B</td>
<td>Ding and Luo, 1990</td>
<td>21</td>
<td>(+)-deoxyschizandrin</td>
<td>Yu, Chen, and Situ, 1996</td>
</tr>
<tr>
<td>4</td>
<td>interiorin C</td>
<td>Ding and Luo, 1990</td>
<td>22</td>
<td>ursolic acid</td>
<td>Zhou, Li, and Li, 2008</td>
</tr>
<tr>
<td>5</td>
<td>interiorin D</td>
<td>Ding and Luo, 1990</td>
<td>23</td>
<td>α-amyrin</td>
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</tr>
<tr>
<td>6</td>
<td>interoitherin D</td>
<td>Chen et al, 2002</td>
<td>24</td>
<td>β-amyrin</td>
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</tr>
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<td>7</td>
<td>heterolitin F</td>
<td>Chen et al, 1996</td>
<td>25</td>
<td>germanicol C</td>
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<td>9</td>
<td>schisandrin C</td>
<td>Chen et al, 2002</td>
<td>27</td>
<td>lupenone</td>
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<td>10</td>
<td>kadsurin</td>
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<td>11</td>
<td>schisantherin A</td>
<td>Zhou, Li, and Li, 2008</td>
<td>29</td>
<td>7-oxositosterol</td>
<td>Zhou, Li, and Li, 2008</td>
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<td>13</td>
<td>interoitherin B</td>
<td>Chen et al, 1996;</td>
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<td>formononetin</td>
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<tr>
<td>14</td>
<td>schisantherin D</td>
<td>Chen et al, 1996</td>
<td>32</td>
<td>7-hydroxy-4′,8′-</td>
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<td>16</td>
<td>interoitherin C</td>
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<td>4′,7-dihydroxyflavone</td>
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<td>Chen et al, 1996</td>
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<td>18</td>
<td>angeloylgomisin R</td>
<td>Chen et al, 1996</td>
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</table>
**Lignans**

Lignan is an important type of components in this species. Totally, 21 lignans (1—21) were isolated from the cane of *K. interior*. Among them, seven compounds (1—7) contained special tetrahydrofuran ring spanning the biphenyl linkage. Those are spirobenzofuranoid dibenzocyclooctadienes mostly presented in the plants of *Kadsura* A. L. Jussieu, which could be considered as marker compounds in the plants of *Kadsura* A. L. Jussieu.

**Triterpenoids**

Five triterpenoids (22—26) have been isolated from the cane of *K. interior*. They are ursolic acid, α-amyrin, β-amyrin, germanicol C, and lupenol. Up to now, there were no reports show that the cane of *K. interior* contains those typical triterpenoids as other species in *Kadsura* A. L. Jussieu.

**Other compounds**

Eight compounds including sterioes (27 and 28) and flavonoids (29—34) were isolated and identified.

**Pharmacological research**

**Anti-oxidant**

The EtOH extract from the cane of *K. interior* resulted in decreasing the active products of CCl$_4$-induced lipid peroxidation (LP), such as thiobarbituric acid reactive substances (TBA-RS), conjugated dienes, and fluorescent products in the liver of mice (Yang et al., 1992a). Dibenzocyclooctadiene- type lignans isolated from the cane of *K. interior* potently inhibited LP in rat liver homogenate stimulated by Fe$^{2+}$-ascorbic acid, the CCl$_4$-reduced form of nicotinamide adenine dinucleotide phosphate (NADP), and adenosine diphosphate-reduced form of nicotinamide adenine dinucleotide phosphate (ADP-NADPH) (Yang et al., 1992b). Gomisin J could inhibit lipid peroxide (LPO) induced by hydroxy free radical in rat liver mitochondria scavenge the superoxide anion radical, and also protect the cultured myocardial cells from injury during the development of the calcium paradox (Jin et al., 2000; Peng et al., 1996).

**Antitumor**

Some neolignans were screened as potential antitumor promoters by examining their ability to inhibit Epstein-Barr virus early antigen (EBV-EA) activation (induced by 12-O-tetradecanoylphorbol-13-acetate) in Raji cells. Neokadsuranin and schisandrin C were the most potent compounds. The results suggested that
some neolignans might be valuable antitumor promoters or chemopreventors (Chen et al, 2002).

**Anti-HIV**

Compound 15 was weakly active as an anti-HIV agent (Pu et al, 2008). Interiotherins A (I) and schisantherin D inhibited HIV replication with EC50 of 3.1 and 0.5 μg/mL, respectively (Chen et al, 1996).

Gomisin G exhibited the most potent anti-HIV activity with EC50 and therapeutic index (TI) of 0.006 μg/mL and 300, respectively. Schisantherin D, kadsuranin, and schisandrin C showed good activities with EC50 values of 0.5, 0.8, and 1.2 μg/mL, and TI of 110, 56, and 33.3, respectively. The anti-HIV data indicated that the relative position and types of substituents on the phenolic hydroxy groups of either natural lignans or synthetic biphenyl compounds, rather than the numbers of bromine(s) on aromatic rings are of primary importance. In the cyclooctane ring of natural lignans, the position and substitution of hydroxy groups are also important to enhance the anti-HIV activity (Chen et al, 1997).

**Platelet activating factor (PAF) receptor antagonistic and other activities**

Using [3H] PAF binding to human platelet membrane assay, tigloylgomisin B, angeloylgomisin P, and R-(+)-gomisin M1 showed the antagonistic activities of PAF receptor (Han et al, 1992). Schisanhenol (SAL) and (+)-anwulignan (AN) have the inhibitory effects on platelets aggregation induced by ADP and PAF in vitro. The inhibitory effect of heteroclitin D is the most potent and could be one of the important active components from the medicinal plants of Kadsura A. L. Jussieu (Jiang, Zhang, and Chen, 2005). This study suggested that the extract from the cane of K. interior at proper doses could promote the growth and development of hippocampal neurons (Xiao et al, 2002). Gomisin J could inhibit L-type calcium channels (Zhang et al, 2000).

**Chemical constituents proposed for quality control**

By now, no quality control method for Kadsurae Caulis has been reported yet. The lignan heteroclitin D with notable activities was considered as the standard compound of Kadsurae Caulis in HPLC analysis (Lu, 2006), although the compound was isolated from the cane of K. heteroclitae. The characteristic lignans, especially spirobenzofuranoid dibenzocyclooctadienes, could be recommended as the standard components for the quality control of Kadsurae Caulis and related formula in further study.

**Application**

The canes of K. interior were used as the major raw material of Kadsurae Caulis in the formula of Compound Dian Jixueteng Gao for a long history (Wu, Lu, and Chen, 2010).

Compound Dian Jixueteng Gao, a traditional Chinese patent medicine, is made of the water extract of Kadsurae Caulis, Cyathulae Radix, Dipsaci Radix, and Carthami Flos. It is mainly used for the treatment of blood deficiency, numbness of hands and feet, painful aching of the joints, and irregular menstruation.

**Conclusion**

The cane of K. interior is one of the new crude drugs collected in Chinese Pharmacopoeia 2010. It is one of the main components of Compound Dian Jixueteng Gao. Modern researches indicates that cane of K. interior with plentiful spirobenzofuranoid dibenzocyclooctadienes has obvious pharmacological activities on anti-oxidant, antitumor, anti-HIV, and so on. Researchers are providing more findings from the cane of K. interior, which will be helpful for the improvement of national regulations of traditional Chinese herbs. It also should be emphasized that the canes of both K. interior and K. heteroclitae are used as the major raw materials of Kadsurae Caulis for a long history. Although the cane of K. heteroclitae has not been included in Chinese Pharmacopoeia 2010, its application is also extensive locally. Thus, the resources and the original plants about Kadsurae Caulis should be deeply investigated in future.

**References**


