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## Plant Profiler

### Elder (*Sambucus nigra*)



#### Synonyms / Common Names / Related Terms

Almindelig hyld, baccae, baies de sureau, battree, black berried alder, black elder, black elderberry, boor tree, bountry, boure tree, Busine (Russian), Caprifoliaceae (family), cyaniding-3-glucoside, cyaniding-3-sambubioside, devil's eye, elderberry, elderberry anthocyanins, elderberry bark agglutinin, elderberry juice, ellanwood, ellhorn, European alder, European elder, European elder fruit, European elderberry, European elderflower,

frau holloe, German elder, Holunderbeeren, Holunderblüten, inking elder, lady elder, nigrin b, old gal, old lady, peonidin 3-glucoside, peonidin 3-sambubioside, peonidin monglucuronide, pipe tree, Rubini® (elderberry extract), Sambreo, *Sambuci flos*, *Sambucipunct Sambucus*, sambuco (Italian), *Sambucus sieboldiana* (Japanese), *Schwarzer holunder* (German), sieboldin-b, suco (Spanish), sureau noir (French), sweet elder, tree of doom, yakori bengestro.

**Note:** Several species of *Sambucus* produce elderberries. Most scientific literature pertains to *Sambucus nigra*. Other species with similar chemical components include the American elder or common elder (*Sambucus canadensis*), antelope brush (*Sambucus tridentata*), blue elderberry (*Sambucus caerulea*), danewort (*Sambucus ebulus*), dwarf elder (*Sambucus ebulus*), red-fruited elder (*Sambucus pubens*, *Sambucus racemosa*), and *Sambucus formosana*. American elder (*S. canadensis*) and European elder (*S. nigra*) are often discussed simultaneously in the literature, since they have many of the same uses and contain common constituents.

**Note:** This review does not include *Sambucus nigra* agglutinin (SNA) affinity chromatography.

### Bioactive products found in *Sambucus nigra*

### Mechanism of Action

#### Pharmacology:

- **Constituents:** There are multiple chemical and biochemical studies of chemical constituents in *S. nigra*. The bark contains  $\alpha$ -amyrenone,  $\alpha$ -amyrin, betulin, oleanolic acid, beta-sitosterol<sup>12</sup>, as well as nigrin b, a lectin similar to ricin, and other type 2 ribosome inactivating proteins (RIPs) that are less toxic to cells and animals<sup>13</sup>. The flowers/leaves contain flavonoids including quercetin (up to 3%), rutin, hyperoside<sup>14</sup>, and anthocyanins<sup>11</sup>, as well as essential oils (responsible for the muscat aroma characteristic of elder flowers)<sup>15</sup>, mucilage, tannins (3%), organic acids, glycoside (0.042% by weight), plastocyanin<sup>16</sup>, and sambunigrin (0.042% by weight). High amounts of N-phenylpropenoyl-L-amino acid amides were found in the flowers of *Sambucus nigra*.<sup>17</sup>
- The fruit contains the protein *Sambucus nigra* agglutinin Ivf or SNAIVf, which is homologous to type 2 ribosome inactivating protein (RIP)<sup>18</sup>, while the bark contains a novel type 2 RIP (SNLRP), consisting of an A-chain with N-glycosidase activity and a B-chain devoid of carbohydrate binding activity normally present<sup>19,20</sup>. Two additional RIPs were further identified in bark (SNAI and SNAI')<sup>19</sup>, demonstrating the complexity of Type 2 RIP/lectins in *S. nigra*. The lectin isolated from bark is tetrameric with two distinct subunits and is rich in glutamine/glutamic acid, valine, and leucine.<sup>21</sup> The fruit type 2 RIP lectin is 10 amino acids

longer than the bark lectin.<sup>22</sup> Elder RIPs with N-glycosidase activity are reported to inhibit protein synthesis in rabbits but not in plants.<sup>5</sup>

- Quercetin is also present in elder and has been shown to be a potent inhibitor of xanthine oxidase.<sup>23</sup> *S. nigra* has been shown to bind heavy metals.<sup>24</sup>
- **Experimental assays:** The lectin of *S. nigra* has been used in multiple experimental clinical assays, due to its carbohydrate binding properties and its ability to precipitate highly sialylated glycoproteins<sup>25</sup>, including the use of *S. nigra* agglutinin binding to identify pregnant women at risk for pre-term delivery (by detecting fibronectin in cervicovaginal secretions using a glycoprotein lectin immunoabsorbent assay)<sup>26</sup>; distinguishing normal from stone-forming kidneys (using N-acetylneuraminic acid-calcium binding ratios)<sup>27</sup>; examining colorectal carcinoma by examining rates of colonic mucin sialylation (by comparing alpha 2,6-linked sialic acid versus sialyl-Tn antigen)<sup>28</sup>; evaluating ulcerative colitis by monitoring differences in sialylation in Asian versus European colitis patients<sup>29</sup>; examining increased beta-galactoside alpha 2,6-sialyltransferase activity (by detection of dioxigenin-conjugated *S. nigra* agglutinin)<sup>30</sup>; evaluating SNA levels in women with breast and ovarian cancer<sup>31</sup>; glycohistochemically identifying microglial cells from Alzheimer's disease samples<sup>32</sup>; measuring decreased sialylation of glycoproteins in nasal glands of patients with sinusitis<sup>33</sup>; monitoring elevated serum sialic acids associated with increased cardiovascular mortality<sup>34</sup>; and enriching stem cell samples/depleting T-cells in bone marrow harvests<sup>35</sup>.
- **Anti-inflammatory effects:** *S. nigra* is reported to modulate the inflammatory cytokines IL-1 and TNF-alpha<sup>3,36</sup>; increase human basophil secretion of IL-4, IL-13, and histamine<sup>9</sup>; alter function of human neutrophils<sup>37</sup>, and inhibit macrophage release of proinflammatory cytokines and nuclear transcription factor kB and phosphatidylinositol 3-kinase<sup>4</sup>.
- **Antioxidant effects:** Elderberries contain flavonoids (flavone, flavonone, isoflavone derivatives and anthocyanins), which are reported to possess antioxidant activity and to protect against oxidative stressors, such as hydrogen peroxide, 2-amidinopropane, dihydrochloride (AAPH), ferrous sulfate, and ascorbic acid.<sup>38,39,40,41</sup>
- **Antiproliferative effects:** *S. nigra* agglutinin has been reported to inhibit nuclear protein transport in neuroblastoma cells, suggesting a functional significance of sialation.<sup>42</sup>
- **Antiviral effects:** Based on laboratory and animal study, *S. nigra* may possess antiviral effects by inhibiting influenza virus types A and B and herpes simplex virus-1<sup>43</sup>, reducing hemagglutination of red blood cells, and inhibiting replication of several strains of influenza A and B<sup>6</sup>. A case report exists of an HIV positive women, taking no HIV drugs, who experienced a viral load drop from 17,000 to 4,000 after ingestion of Sambucol<sup>®</sup> with olive leaf extract.<sup>8</sup> The report also included a placebo controlled, double-blind study of Sambucol associated with a rapid recovery from influenza and inhibited replications of nine other strains of the flu virus by elderberry. The mechanism is believed to be rendering viruses nonfunctional by staining and coating them.
- **Diuretic effects:** In a rat study, diuretic effects and sodium excretion were associated with an extract of *S. nigra* flowers.<sup>7</sup>
- **Glucose/insulin metabolism:** *In vitro* research<sup>10</sup> refutes earlier study<sup>44</sup>, and reports stimulation of glucose metabolism and promotion of insulin secretion from beta cells.
- **Respiratory effects:** The combination herbal product Sinupret<sup>®</sup>, which contains elder, has been studied for its effects on bronchitis. There is a lack of reliable human evidence

evaluating elder monotherapy as a treatment for bronchitis, however, and a mechanism of action is unclear.

- **Vascular effects:** The multi-ingredient product OptiBerry IH141 has been shown to possess antiangiogenic properties via inhibition of H<sub>2</sub>O<sub>2</sub> and TNF-alpha-induced Vascular Endothelial Growth Factor.<sup>1</sup> In another study, elderberry extracts were associated with significantly impaired angiogenesis in human dermal microvascular endothelial cells.<sup>2</sup>

### Pharmacodynamics/Kinetics:

- **Absorption:** Anthocyanins, which are potent flavonoid antioxidants found in elder, are not absorbed in their unchanged glycosylated forms in humans.<sup>45</sup> The maximum concentration of anthocyanins found in blood after injection of a highly concentrated solution was 35mg/mL at one hour, followed by a quick decay.<sup>39</sup>
- **Elimination:** The elimination of plasma anthocyanins appears to follow first-order kinetics, and most anthocyanin compounds are excreted in urine within four hours after ingestion.<sup>45</sup> After ingestion of about 30mL of elderberry extract (147.3mg total anthocyanins), the t<sub>1/2</sub> was 1.74 hours.<sup>46</sup> The urinary excretion rate of intact anthocyanins was fast, and appeared to be monoexponential with high variability.
- At a dose of 3g/kg, *S. nigra* extract did not modify the growth rate of rats.<sup>3</sup>
- Flowers are believed to be safe for use in food, provided HCN levels are below 25ppm.

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