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Aesculus species: a review on biologically active compounds and their possible applications

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Abstract

Horse chestnut (*Aesculus hippocastanum* L.) is a specific tree of Eastern Europe, including Balkan Mountains. It is an ornamental tree, but its seeds are valuable for their important content of triterpenoid saponins, especially β-aescin (or β-escin). Other biologically active compounds found in *A. hippocastanum* are flavonoids, anthocyanidins and their glycosides. In this review, the biologically active compounds from *Aesculus* species, especially *A. hippocastanum*, have been reported. The classification, extraction and purification methods of biologically active compounds from these species were emphasized. Moreover, the main biological activities of both *Aesculus* extracts and purified compounds, including the treatment of chronic venous insufficiency, vascular protection and venotonic effect, as well as anti-inflammatory and antioxidant activities, were reviewed.

Keywords: *Aesculus hippocastanum* L., horse chestnut, triterpenoids, saponins, triterpene glycosides, aescins, escins, β-aescin, β-escin, chronic venous insufficiency

1. Introduction

Aesculus hippocastanum L. (horse chestnut or European horsechestnut) is one of the *Aesculus* species originated from Europe, but it is cultivated all over the world. The tree belongs to the genus Aesculus and is valuable even as ornamental tree or for its useful seeds [1-4]. It was used for the treatment of chronic venous inefficiency, varicose veins, inflammation of the veins, haemorrhoids, diarrhoea, fever, prostate disorders, rheumatism and neuralgia [5-8]. Among seeds, other parts of the horse chestnut tree is used for above mentioned applications, such as bark and leaves, all as extracts or other preparations [8, 9]. There are many formulations based on *A. hippocastanum* such as external elastic compresses, sprain, bruise, topical gels, as well as shampoos, foam baths, creams or lotions for skin care and toiletries [9].

There are other *Aesculus* species that were studied both for their composition regarding biologically active compounds and various biological activities. It is the case of *A. californica* (Spach) Nutt. (California buckeye or California horse-chestnut, United States of America), *A. chinensis* Bunge (China), *A. glabra* Willd. (Ohio buckeye or American buckeye, Midwest of the USA), *A. indica* Colebr. (Indian horse chestnut or *Han dun*, temperate regions of Asia), *A. pavia* L. (red buckeyes or scarlet buckeye, originated from the southeast of the USA), *A. sylvatica* W. Bartram (eastern USA), and *A. turbinata* Blume (Japanese horse chestnut or *Tochinomi*, Japan.) [10-16]. An up-to-date survey on the biologically active compound composition and the possible applications is presented below.

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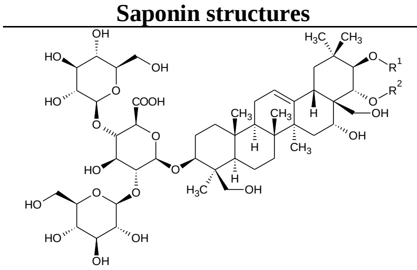
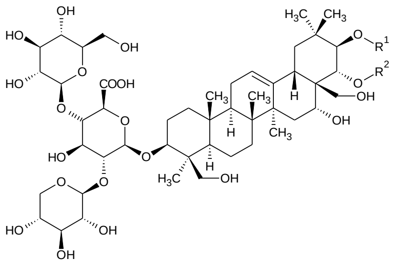
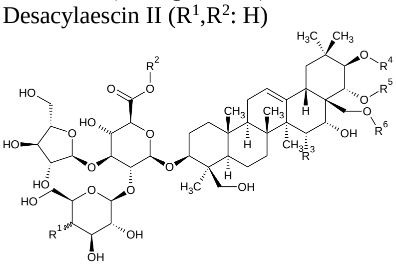
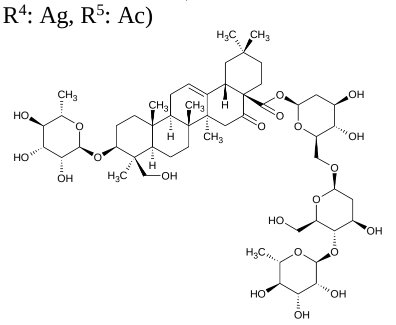
2. Biologically active compounds from *Aesculus* species

The *A. hippocastanum* seeds are the most important part of the tree. Carbohydrates are the most concentrated components of seeds. They comprise of water-soluble and non-water-soluble saccharides (6.6% and 18.1%, respectively), lignin 9.7%, hemicellulose and cellulose (10.8% and 3.6%, respectively). Proteins and lipids were found in concentrations of approximately 34.4% and 13.1%, while ash was at 3% [17]. Moreover, Mediterranean varieties having white or pink flowers had a protein content of 2.64% and 1.82%, while the lipid contents were 4.13% and 5.10%, respectively [18].

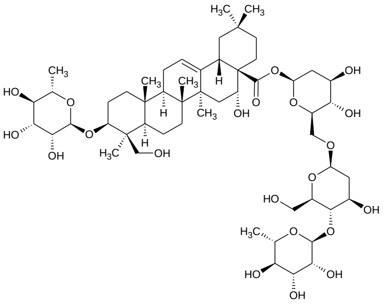
By far, the most important biologically active compounds are saponins with aescins (or escins) as representatives. They provide the main biological activities of the *Aesculus* species. Flavonoids and anthocyanins (and proanthocyanins) are antioxidant compounds that have also been found in various parts of the tree. Fatty acid glycerides are mainly separated from *Aesculus* seeds, while carbohydrates are the major constituents [3-5, 8, 9, 17, 19, 20].

Saponins or triterpenoid glycosides have steroid-based aglycones. Aglycones have saccharide moieties attached through one or more hydroxyl groups. *Aesculus* species have various contents of such saponins, the most important being aescin Ia (with the synonyms β-aescin or β-escin), as well as Ib, IIa, and IIb. They were found in *A. hippocastanum* and *A. turbinata* [21-26]. Desacylaescins have also found in these species. On the other hand, aesculosides, vaccarosides, and paviosides have also been found in *A. galabra*, *A. sylvatica*, *A. californica*, *A. pavia* and *A. turbinata* [10, 12, 14, 15, 27-29]. A survey on the saponin structures found in *Aesculus* species is presented in Table 1.

Table 1. Structures of the main saponins found in *Aesculus* species

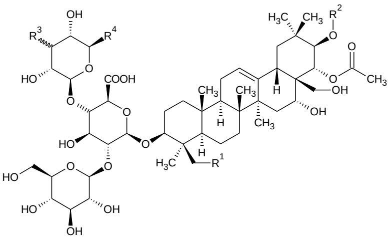
Saponin structures	*Aesculus* species
 Aescin Ia (R^1: tigloyl, R^2: acetyl) Aescin Ib (R^1: angeloyl, R^2: acetyl) Desacylaescin I (R^1,R^2: H)	*A. hippocastanum*, *A. turbinata* [21-26]
 Aescin IIa (R^1: Tg, R^2: Ac) Aescin IIb (R^1: Ag, R^2: Ac) Desacylaescin II (R^1,R^2: H)	*A. hippocastanum*, *A. turbinata* [21-26]
 Aesculioside G1 (R^1: βOH, $R^{2,5}$: H, R^3: OH, R^4: Tg, R^6: Ac) Aesculioside G2 (R^1: βOH, $R^{2,5}$: H, R^3: OH, R^4: Ag; R^6: Ac) Aesculioside G3 (R^1: βOH, $R^{2,3,5}$: H, R^4: Tg, R^6: Ac) Aesculioside G4 (R^1: βOH, $R^{2,3,5}$: H, R^4: Ag, R^6: Ac) Aesculioside G5 (R^1: αOH, $R^{2,5,6}$: H, R^3: OH, R^4: Ag) Aesculioside G6 (R^1: βOH, $R^{2,6}$: H, R^3: OH, R^4: Tg, R^5: Ag) Aesculioside G7 (R^1: βOH, $R^{2,6}$: H, R^3: OH, R^4: Ag, R^5: Tg) Aesculioside G8 (R^1: βOH, $R^{2,3,6}$: H, R^4: Tg, R^5: Tg) Aesculioside G9 (R^1: βOH, $R^{2,3,6}$: H, R^4: Tg, R^5: Ag) Aesculioside G10 (R^1: βOH, $R^{2,3,6}$: H, R^4: Ag, R^5: Tg) Aesculioside G11 (R^1: βOH, R^2: Me, $R^{3,6}$: H, R^4: Ag, R^5: Tg) Aesculioside G12 (R^1: βOH, R^2: Me, $R^{3,6}$: H, R^4: Ag, R^5: Ag) Aesculioside G13 (R^1: αOH, $R^{2,6}$: H, R^3: OH, R^4: Tg, R^5: Ac) Aesculioside G14 (R^1: αOH, $R^{2,6}$: H, R^3: OH, R^4: Ag, R^5: Ac) Aesculioside G15 (R^1: αOH, $R^{2,3,6}$: H, R^4: Tg, R^5: Ac) Aesculioside G16 (R^1: αOH, $R^{2,3,6}$: H, R^4: Ag, R^5: Ac)	*A. galabra*, *A. sylvatica*, *A. californica*, *A. pavia* [10, 12, 14, 15, 27]
	*A. pavia* [28]

Vaccaroside A



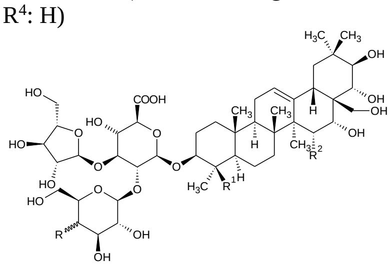
A. pavia [28]

Vaccaroside B



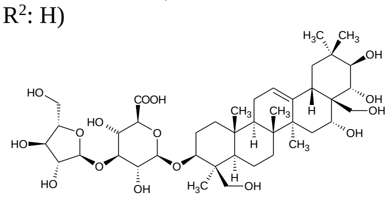
Pavioside A (R^1: H, R^2: Tg, R^3: αOH, R^4: CH_2OH)
Pavioside B (R^1: H, R^2: Ag, R^3: αOH, R^4: CH_2OH)
Pavioside C (R^1: H, R^2: Tg, R^3: βOH, R^4: CH_2OH)
Pavioside D (R^1: H, R^2: Ag, R^3: βOH, R^4: CH_2OH)
Pavioside E (R^1: H, R^2: Tg, R^3: αOH, R^4: H)
Pavioside F (R^1: H, R^2: Ag, R^3: αOH, R^4: H)
Pavioside G (R^1: OH, R^2: Tg, R^3: αOH, R^4: H)
Pavioside H (R^1: OH, R^2: Ag, R^3: αOH, R^4: H)

A. pavia [29]



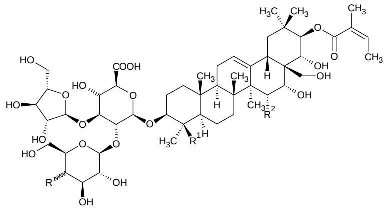
Aesculioside Ia (R: βOH, R^1: Me, R^2: OH)
Aesculioside Ib (R: αOH, R^1: CH_2OH, R^2: OH)
Aesculioside Ic (R: βOH, R^1: Me, R^2: H)
Aesculioside Id (R: αOH, R^1: CH_2OH, R^2: H)

A. turbinata [27]



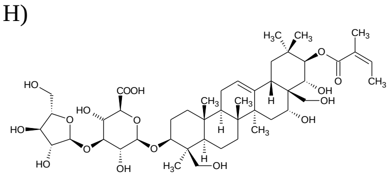
Aesculioside Ie

A. turbinata [27]



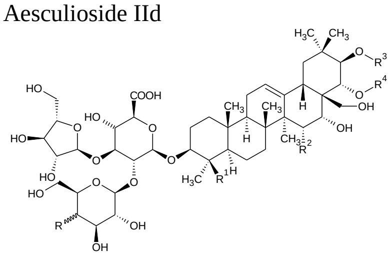
Aesculioside IIa (R: βOH, R^1: Me, R^2: OH)
Aesculioside IIb (R: αOH, R^1: CH_2OH, R^2: H)
Aesculioside IIc (R: βOH, R^1: Me, R^2: H)

A. turbinata [27]



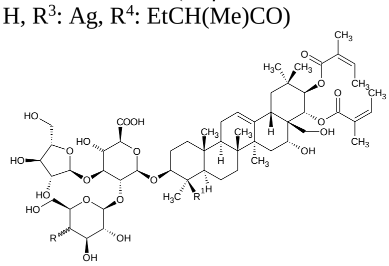
Aesculioside IId

A. turbinata [27]



Aesculioside IVa (R: βOH, R^1: Me, R^2: OH, R^3: Ag, R^4: EtCH(Me)CO)
Aesculioside IVb (R: αOH, R^1: CH_2OH, R^2: H, R^3: Ag, R^4: EtCH(Me)CO)
Aesculioside IVc (R: βOH, R^1: Me, R^2: H, R^3: Ag, R^4: EtCH(Me)CO)

A. turbinata [27]



Aesculioside derivative a (R: αOH, R^1: CH_2OH)
Aesculioside derivative b (R: βOH, R^1: Me)

A. turbinata [27]

* Tg=tigloyl: *trans*-MeCH=C(Me)CO; Ag=angeloyl: *cis*-MeCH=C(Me)CO; Ac=acetyl: MeCO

Flavonoids are valuable compounds that have antioxidant activity. Some compounds from this class was found in *Aesculus* species, as well as catechins and procyanidins (especially trimers). Examples of these structures are presented in Tables 2 and 3.

Table 2. Structures of the main flavonids found in *Aesculus* species

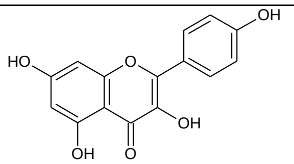
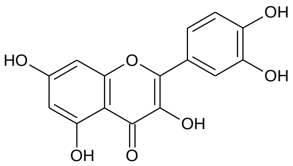
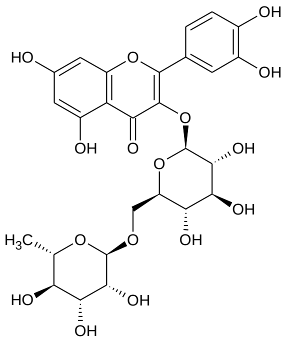
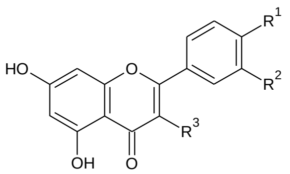
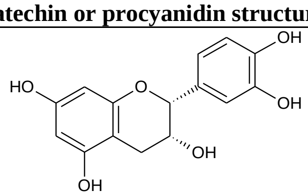
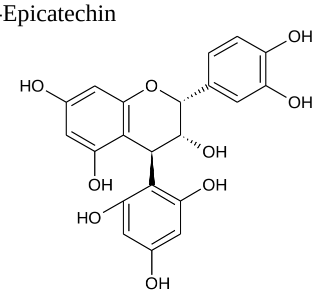
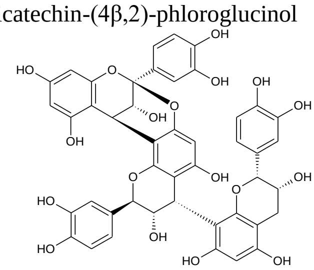
Flavonoid structures	***Aesculus* species**
 Kaemferol	*A. hippocastanum* [30]
 Quercetin	*A. hippocastanum* [30]
 Rutin	*A. hippocastanum* [30]
 Flavonoid derivative 1 (R1: OH, R2: Glc, R3: Xyl-Rha-Glc) Flavonoid derivative 2 (R1: OH, R2: Glc, R3: Xyl(1-2)Glc) Flavonoid derivative 3 (R1,2: OH, R3: Xyl(1-2)[Glc(1-3)]Glc) Flavonoid derivative 4 (R1,2: OH, R3: Xyl(1-2)Glc) Flavonoid derivative 5 (R1: OH, R2: Glc-nicotinoyl, R3: Xyl(1-2)Glc) Flavonoid derivative 6 (R1: OH, R2: Glc-3-hydroxy-2-oxoindolin-3-ilacetil, R3: Xyl(1-2)Glc) Flavonoid derivative 7 (R1: H, R2: OH, R3: Xyl(1-2)[Glc(1-3)]Glc) Flavonoid derivative 8 (R1: H, R2: OH, R3: Xyl(1-2)Glc) Flavonoid derivative 9 (R1: OMe, R2: OH, R3: Xyl(1-2)[Glc(1-3)]Glc) Flavonoid derivative 10 (R1: OMe, R2: Glc, R3: Xyl(1-2)[Glc(1-3)]Glc) Flavonoid derivative 11 (R1,2: OH, R3: Glc-Rha) Flavonoid derivative 12 (R1: OH, R2: 2-oxoindol-3-ylacetyl, R3: Xyl(1-2)Glc) Flavonoid derivative 13 (R1: H, R2: OH, R3: Glc-Rha)	*A. hippocastanum, A. chinensis, A. turbinata* [16, 19, 31]

Table 3. Structures of some catechins and procyanidins found in *Aesculus* species

Catechin or procyanidin structures	***Aesculus* species**
 (-)-Epicatechin	*A. hippocastanum* [32]
 Epicatechin-(4β,2)-phloroglucinol	*A. hippocastanum* [33]
 Epicatechin-(4β,8;2β,7)-catechin-(4β,8)-epicatechin	*A. hippocastanum, A. turbinata* [33, 34]

Fatty acids, as triglycerides, were found in the seed oils of *A. hippocastanum*. The main compounds were oleic and linoleic acids (43.2-59.4% and <35.2%, respectively), but other monounsaturated fatty acids were identified at lower concentrations (gondoic, erucic and nervonic acids) [18, 30, 35].

The most concentrated compounds in *Aesculus* species are carbohydrates (amylose and amylopectin). However, they are less important from the biological activity point of view. There are some studies regarding the chemical changes and characteristics of *Aesculus* starch subjected to various processing conditions [13, 36-38].

Another interesting compound found in *A. hippocastanum* is plastoquinone-8, a structure resembling with coenzyme Q10 [39].

3. Biological activities of *Aesculus* species

The main biological activities of *Aesculus* species are due to the presence of saponins, especially aescins. They provide vascular and venotonic effects, as well as anti-inflammatory properties [5, 20]. On the other hand, the presence of flavonoids and procyanidins furnish antioxidant properties and related biological activities. A survey on the main biological activities and applications of *Aesculus* compounds and extracts is presented in Table 4.

Table 4. The main biological activities and applications of bioactive compound and extracts from *Aesculus* species

Aesculus species	Biological activity
A. hippocastanum (standardized extract to 20% aescins)	Anti-inflammatory, decreasing platelet aggregation, increasing venous contractions and protecting venous endothelium relaxation, treating varicose veins, venous ulcers, leg-tiredness, swelling, and the hardening of the skin caused by lipidermatosclerosis [9]
A. hippocastanum (seed extract)	Treatment of chronic venous insufficiency [6]
A. hippocastanum (fresh seed extract)	Treatment of chronic venous insufficiency [7]
A. hippocastanum (various medicinal preparations)	Treatment of chronic venous insufficiency [8]
A. hippocastanum (flower extract)	Wound healing [40]
A. hippocastanum (seed extract and β-aescin)	Virucidal, antiviral and immunomodulatory activities against viruses HSV-1, VSV and Dengue virus [41]
A. hippocastanum (aescins and desacetylaescins)	Anti-inflammatory effects [21]
A. hippocastanum (seeds)	Treatment of diabetic nephropathy [42]
A. hippocastanum (aescins)	Protective effects on endotoxin-induced liver injury [22]
A. hippocastanum (extracts)	Cosmetic skin-care products [4]
A. hippocastanum (seed extract)	Genotoxic and antioxidant activity [43]
A. hippocastanum (seed extract)	Increase the antioxidative defense system of the body and prevent lipid peroxidation [44]
A. hippocastanum (leaves extract)	Biosynthesis of antibacterial silver nanoparticles [45]
A. hippocastanum (bark extract)	Emulsion stabilizer [46]
A. californica (aesculiosides)	Cytotoxicity to human non-small cell lung tumor (A549) [10]
A. glabra (aesculiosides)	Cytotoxicity against A549 and PC-3 cancer cell lines [12]
A. pavia (saponosides)	Cytotoxicity against various carcinoma cell lines [14, 28, 29]
A. turbinata (aescin derivatives)	inhibitory activities on porcine epidemic diarrhea virus replication [47]
A. turbinata (seeds)	Antioxidant activities [16]
A. turbinata (aescins)	Inhibitory effect on pancreatic lipase [26]
A. turbinata (seed shells)	Anti-obesity effects [34]

4. Conclusions

In this review an up-to-date survey on the chemical composition, biological activities and applications of compounds and extracts from various parts of *Aesculus* species was performed. Saponins (e.g. aescins), flavonoids, catechins and procyanidins from *A. hippocastanum*, *A. galabra*, *A. sylvatica*, *A. californica*, *A. chinensis*, *A. pavia* and *A. turbinata* were emphasized. Moreover, the biological activities and applications of both purified compounds and *Aesculus* extracts were systematically presented. This review can be useful for identifying new possible applications of *Aesculus*-based formulations in the pharmaceutical, cosmetic and even food fields.

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