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Review

Insights into the Bioactivities and Chemical Analysis of *Ailanthus altissima* (Mill.) Swingle

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Abstract: Many species of the so-called exotic plants coexist with native species in a balanced way, but others thrive very quickly and escape human control, becoming harmful—these are called invasive alien species. In addition to overcoming geographic barriers, these species can defeat biotic and abiotic barriers, maintaining stable populations. *Ailanthus altissima* is no exception; it is disseminated worldwide and is considered high risk due to its easy propagation and resistance to external environmental factors. Currently, it has no particular use other than ornamental, even though it is used to treat epilepsy, diarrhea, asthma, ophthalmic diseases, and seborrhoea in Chinese medicine. Considering its rich composition in alkaloids, terpenoids, sterols, and flavonoids, doubtlessly, its use in medicine or other fields can be maximised. This review will focus on the knowledge of the chemical composition and the discovery of the biological properties of *A. altissima* to understand this plant better and maximise its possible use for purposes such as medicine, pharmacy, or the food industry. Methods for the extraction and detection to know the chemical composition will also be discussed in detail.

Keywords: *Ailanthus altissima*; biological properties; analytical techniques; potential applications

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1. Introduction

Since ancient times humans have taken advantage of the existing flora, especially trees, for various food, wood and non-wood products. Over the years, trees have been planted to provide these services. Consequently, humans' ability to plant trees and transport goods worldwide has led to a greater expression of non-native trees [1]. The spread of many non-native tree species has shown in recent years an increase in the number of publications highlighting its potential constraints either regionally or globally (e.g., *Eucalyptus globulus* [2] and *Acacia* spp. [3]). Other studies have also noted the conflicts that some invasive alien species (IAS), including some non-native species, can cause in the ecosystem [4,5].

IAS are recognised for triggering various impacts, such as habitat modification, the alteration of community structure, and affecting ecosystem processes. Thus, they are considered one of the most significant global threats to biodiversity. However, these species can also be quite helpful to humans, providing a complex number of services, which makes it difficult to assess their positive and negative effects. For this reason, the importance of evaluating and investigating some IAS that have several adverse effects has been growing [6].

The IAS *Ailanthus altissima* (Mill.) Swingle, known as the "Tree of Heaven", was introduced into Europe and worldwide in the 18th century. This plant spreads and is distributed mainly in cities, agricultural fields, and transportation corridors. In cities, it was reported to cause problems from its roots such as damaging infrastructures plus allergic reactions and respiratory problems in humans. It is more frequent in the southern and submeridional zones whereas, in Europe, it has a closed distribution area in the Mediterranean [7]. Through this area, there can be modifications in the structure of the local vegetation and damage to the stability of the ecosystem [8]. In some warm regions of Europe, *A. altissima* can also cause damage to walls and other structures, as reported by Almeida et al. [9], where this species appeared and spread on a wall of a historic monument in Coimbra, Portugal.

Nowadays, this species has been the subject of several pharmacological investigations, showing its positive effects. Traditional Chinese medicine uses it to treat certain disorders such as epilepsy, diarrhea, asthma, ophthalmic diseases, and seborrhoea. Traditional medicine practitioners use different parts of the plant for different types of health problems. The bark, for example, is prescribed for dysentery, menorrhagia and spermatorrhea. For intestinal problems that last a few months, it is advisable to boil some bark with water and then drink the liquid together with gin. Other bark remedies can be made with other ingredients and plants, such as root onions and Chinese pepper (*Zanthoxylum simulans*) for rectal problems, especially after childbirth. In addition, it can also be used as an astringent, parasiticide, a narcotic substance, and a drug to relieve spasms [6,7]. On the other hand, *A. altissima* may have applications in agriculture as an environmentally friendly compound, since its extracts have strong herbicidal and insecticidal properties [10].

This work aims to review (1) the characteristics of the species *A. altissima*, (2) describe all its biological activities to date, and (3) detail studies performed on chemical extractions and consequently the analytical methodologies used. In addition, we intend to alert the possible uses of *A. altissima* biomass in the most diverse areas, showing that this IAS can benefit humans and the environment.

2. Taxonomy and Morphology

Ailanthus altissima is an accepted name with original publication details in J. Wash. Acad. Sci. 6: 495 (1916) and many synonyms [11]. It belongs to the family Simaroubaceae [6], which consists mainly of trees and shrubs, distributed in tropical and warm regions, comprising 30 genera and 150 species. The term for the genus *Ailanthus* is an Ambonese word derived from ailanto, meaning "tree of heaven" [12]. About 5–10 species of trees from this genus are known and characterised by being deciduous with rapid growth, large spreading branches, pinnate leaves with pointed leaflets, where the terminal leaflet is usually present, small yellow to greenish flowers, and the fruits samaras stretched into a long wing, where the seed lies in the middle (Figure 1C). In the root sprouts, the emerging leaves vary in the number of divisions (from unifoliate to compound pinnately) and are yellowish-green at first. In addition, the genus *Ailanthus* has a fine, satiny wood and is known for its medicinal values [12].

Regarding the morphology of the species in the study, *A. altissima* (Figure 1) is described as a tree growing up to 30 m in height with a trunk of greyish, smooth, or cracked bark, and in the oldest specimens and branches, a reddish-brown colour. Its leaves (30–100 cm) are alternate, compound, odd-pinnate (on the shoots) and paripinnate (arranged at the ends of the branches), and glabrous or with scattered hairs on the upper side of the margin. Each leaf can have 5–12 pairs of leaflets (or 4 to 35 leaflets [13]) of very variable size, petiolate, from narrowly lanceolate to ovate-lanceolate, with gradually narrowed apex, and an entire margin. Each of these leaflets has two to four glandular teeth near the base, with 1–8 openings as extrafloral nectaries—an important characteristic to identify *A. altissima* [6,13,14].

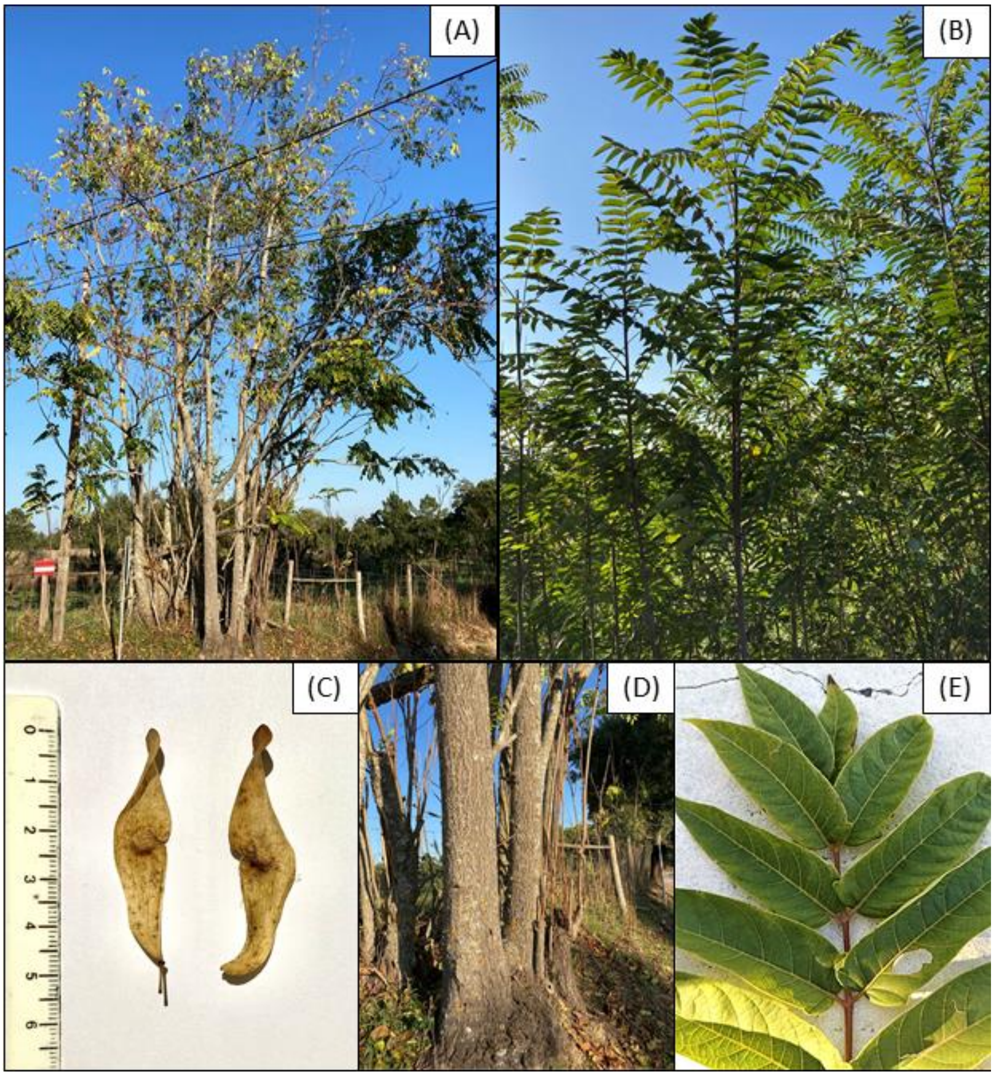

Figure 1. Some examples of *A. altissima* in the Castelo Branco region (Portugal); (**A**) an old plant; (**B**) a younger plant; (**C**) the samaras with seeds in the middle; (**D**) the trunk of the first plant and (**E**) part of a leaf with its leaflets.

A. altissima is a tree with both female and male terminally located inflorescences, where the latter are larger, pluriflor, and emit an unpleasant scent. In addition, unlike the female flowers, the male flowers have 10 well-functioning stamens, each with a fertile anther; the female flowers have abortive anthers. It is due to these facts that *A. altissima* is considered a dioecious tree [7,13,15]. Flowers have a tiny cupular and five-lobed calyx, a corolla with five sepals, lanceolate and green, five distinct petals that are hairy at the base, greenish to yellowish-green, and an annular and lobed gland disc (different types of nectaries); female flowers have five free carpels that generally develop into five separate winged fruits. The fruits (samaras) can vary from greenish-yellow to reddish-brown, and are arranged in clusters and dispersed by the wind [6,7,13,14]. In the samaras, the seeds are found and these, depending on the location of the trees, vary considerably in colour, size, weight, and thickness [6].

Concerning roots, the main root can develop several lateral roots, from pre-existing primordia or root sprouts. The root system has a highly variable and asymmetric spatial extent, in which lateral roots have been reported to reach a length of 27 m from the parent tree. The nectaries' primary function is to eliminate excess sugar from the plant. *A. altissima* has floral and extrafloral nectaries, which excrete different forms of sugar until October. These nectaries are located on the leaves, pseudostipules, and cataphylls. Trees of the genus *Ailanthus* have a rapid stem elongation, which leads to the fact that these trees can grow to heights of 25–45 m [7,12].

3. History and Distribution

The species *A. altissima* is a tree originating in northern and central China, which has spread to all continents except Antarctica. In China, it grows as a native tree, forming part of the broadleaf forests. At the same time, in other continents, namely North America and Europe, it has gained an expansion facilitated by seed transfer. This expansion was mediated by humans, which began in 1740 when a missionary, Pierre d'Incarville, introduced *Ailanthus* to France from Nanking to Paris. After that, it was introduced in London and then a little all over the European continent. In 1784, it was introduced to North America, more specifically to Philadelphia, from European seeds [6,7,13]. Subsequent to its introduction, *A. altissima* began to be planted in landscaped parks because of its tropical appearance, fast growth, and significant tolerance to urban life and pollution, which led to its use as an ornamental plant [6]. Although the male flowers release a nasty odour, they continue to promote shade as an ornamental plant. The species was also used for shelterbelts plantations in Austria in the 1950s to control erosion on hillsides, afforestation and reforestation in south-eastern Europe, and in some cases the reclamation of landfills and mine waste [7]. On the other hand, in China it is used in folk medicine, as firewood and wood, and as a food source for bees, where the honey is appetising but initially has a bad smell [6,7].

According to the review of Kowarik and Säumel [7] about the habitats, the tree of heaven can grow on three different sites: urban, transportation corridors, and forests. It grows on both anthropogenic and natural sites and on stony soils and rich alluvial bottoms. In urban areas, within the temperate to southern zone, i.e., Mediterranean cities, it has a substantial expansion, colonising walls, fence lines, and sidewalk cracks, among others [7]. Peculiarly in New York, *A. altissima* was less frequent in an open habitat than in soil sites with a limited surface [16]. *A. altissima* mainly colonises—outside the cities, road and railway edges, and medians of the highways. It can also invade the borders of agricultural fields and old fields from the roadside edge. In forests, *A. altissima* is invasive in several types, from riverine forests and some mesic and xeric forests in Europe to hemlock forest, oak, and maple forests in temperate North America. Furthermore, it has been reported to invade forests and riverbanks on the Danube, along streams and riverbeds in the most diverse areas of the world, such as southwestern France, southern Switzerland, Japan, and North America [7,17,18].

4. Biology and Ecology

According to Kowarik and Säumel's review [7], *A. altissima* is a short-lived tree that can reach more than 100 years. These authors also mentioned the existence of trees in Germany that were 130, 121, and 113 years old. In terms of germination and seed establishment, information varies widely in the literature. This species is characterised by not forming a long-term seed bank but can establish temporary seed banks in the soil. It has also been observed that a seed in contact with water influences its initiation, duration, and germination rate. In addition, the germination rate was reported to decrease with altitude. The same was observed on a germination experiment when comparing soil types (sand with gravel and peat substrates). The germination rate is much lower on sand and higher on peat substrates [7]. Considering seed establishment, the combination of litter, weed competition, and insect herbivory were studied. It was concluded that litter (without weed competition) delays germination but does not affect seedling biomass.

On the other hand, with weed competition, seedling growth was reduced but neutralised by the litter. However, the litter showed damage to the seedling performance by increasing herbivory [19,20]. In terms of stem elongation, *A. altissima* is one of the fastest-growing trees in North America and Great Britain. The height and diameter increase until the trees reach 5 to 10 years, and then from 10 to 20 years, it starts to decrease. In Hu's [13] review, he states that as young as 1 year old, seedlings can reach 1–2 m in height. On average, the height increment in trees between 20 and 25 years can be less than 8 cm per year [7].

A. altissima is a different tree from many other tree species. One of the requirements for the buds to open is high temperature, leading the seasonal development to start later and last longer (until late fall) [7]. As mentioned before, altitude influences the germination rate and in the case of the flowering stage this is also an essential factor to take into account. The flowers appear at different stages depending on altitude. In North America, they appear from mid-April to July; in the French Mediterranean, they start in mid-May; and in Central Europe, flowering occurs mainly in July. The ripening occurs in September-October, and soon after this, there is the abscission of the samaras, which can vary in time depending on the individual and the years. The fruits can be almost all released in some years before the end of February, and in others, a large part of them can remain on the tree until the beginning of May [6,7].

The reproduction of *A. altissima* occurs by seeds and by root suckers. In sexual reproduction, the seedlings give rise to flowers after 3 weeks of germination and large amounts of light. The flowers usually develop non-viable seeds, at this stage. However, *Ailanthus* is pollinated by bees, beetles, and other insects [7].

In vegetative reproduction, what occurs is the growth of new shoots from a mother plant. These shoots are known to have a great length and can reach up to 27 m or more. Alternatively, *A. altissima* can propagate itself through vegetative regeneration. It consists of originating shoots from pre-existing buds in the hypocotyl, axillary buds of the cataphylls, the roots, and adventitious buds on a cutting section [6,7]. The dispersal of *A. altissima* seeds, which give rise to new individuals, is achieved through the dispersal of samaras. This dispersion can occur from the following types of vectors: the wind, in which the samaras are moved individually or aggregated in groups by water (through river corridors) and animals (such as rodents and birds) [7].

The response to ecological factors is another critical issue to mention when it comes to this IAS. It was found that *A. altissima* is tolerant to several abiotic factors, contributing to its extensive spread. Among the several factors, the following stand out: temperature, frost, drought, soils, and air pollution [6]. First, this species is temperature tolerant, although it adapts better to high temperatures, equivalent to its distribution. Regarding low temperatures, it was observed in a study that old trees survived at −33 °C; however, they suffered some damage. Kowarik and Säumel also mentioned that trees in the early stages of life might be more susceptible to the cold [7]. Drought is another factor to which *Ailanthus* is tolerant, presenting mechanisms that contest the lack of water, such as the closing of the stomata and the reallocation of food reserves to the lateral roots from the main root. Another fundamental factor is the soil. *A. altissima* grows in various soil types: from barren, rocky soils to saline and alkaline soils; it also tolerates dry, humid, and nutrient-rich or nutrient-poor soils. *A. altissima*'s tolerance to pollution is attributed to the high antioxidant capacity of the leaves. It is pretty tolerant of major components of air pollution such as SO_2. However, it is sensitive to ozone [7,21] and cold, which can inhibit some seedlings and limit their occurrence and distribution.

Furthermore, this species of *Ailanthus* has allelopathic effects on other plant species by producing a wide variety of active compounds and becoming resistant to herbivores and pathogens. All these ecological factors and the biological characteristics of *A. altissima*, make it a very competitive species and justify its wide distribution worldwide. Due to its tolerance to several factors, it is established in different habitats. It is widely dispersed and able to establish seedlings at long distances [6].

5. Chemical Characterization

Plants of the *Ailanthus* genus are phytochemically characterised by being rich in alkaloids, terpenoids, sterols, flavonoids, and other compounds. These compounds nowadays are widely studied since they are responsible for several pharmacological activities [12]. The bark of *A. altissima* has always been used in traditional medicine and, nowadays, it is known for being very rich in several compounds. It contains oleoresin, resin, ceryl alcohol, ailanthin, isoquercetin, tannins, ceryl palmitate, and saponins [7]. Two hundred and twenty-one compounds have been isolated and identified from the dry bark, such as alkaloids, quassinoids, phenylpropanoids, triterpenoids, and volatile oils. The main active compounds of dry bark are alkaloids (Figure 2), 32 of which have already been isolated. Quassinoids (Figure 3) are also one of the characteristic compounds of dry bark, with 40 isolated to date [22]. As reported by Pijush Kundu [12], the root bark essentially has alkaloids and terpenoids. Some ligands, coumarins, phenylpropanoids, and new terpenoids have also been identified and isolated [12,23–25]. The leaves of this species are characterised by having some percentage of tannins, quercetin, isoquercetin, alkaloids, and mainly flavonoids. These were widely used in traditional Indian medicine to treat seborrhoea and scabies [7,12].

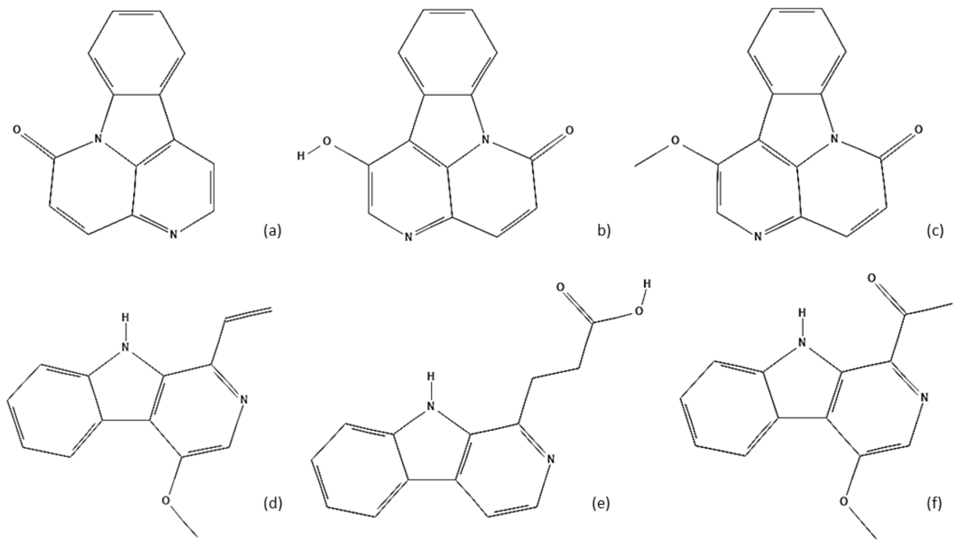

Figure 2. Some examples of alkaloids identified in *A. altissima*: (**a**) Canthin-6-one; (**b**) 1-Hydroxycanthin-6-one; (**c**) 1-Methoxycanthin-6-one; (**d**) 4-methoxy-1-vinyl-β-carboline; (**e**) β-carboline-1-propionic acid; (**f**) 1-Acetyl-4-methoxy-β-carboline.

Regarding the fruits of *A. altissima*, not much is known about its constituents, but they was widely used in China as a medicine for bleeding and as an antibacterial. On the other hand, in India it was used as an emmenagogue and to treat eye diseases [12,26]. Jian-Cheng Ni et al. [27] mentioned that previous studies have shown that only four quassinoid glycosides and several stigmasterols (Figure 4) [28] were identified from fruits. However, they elucidated the structure and isolated four new compounds: two phenylpropionamides, piperidine, and a phenolic derivative. In addition to these new compounds, 13 phenols, 10 flavonoids, and a phenylpropionamide were also isolated. According to Clair and Bory [29], the composition of *A. glandulosa* (syn. of *A. altissima*) extrafloral nectar diverge according to the nectary type. These authors also declared that the three essential nectars' sugars are sucrose, fructose, and glucose in the leaf nectaries. It is the high amount of fructose that characterizes this species. Furthermore, bound lipids (monogalactosyldiacylglycerol) and oleic, palmitic, and linoleic acids have been isolated in the secretion of glandular trichomes in cataphylls and in young stems [7,29].

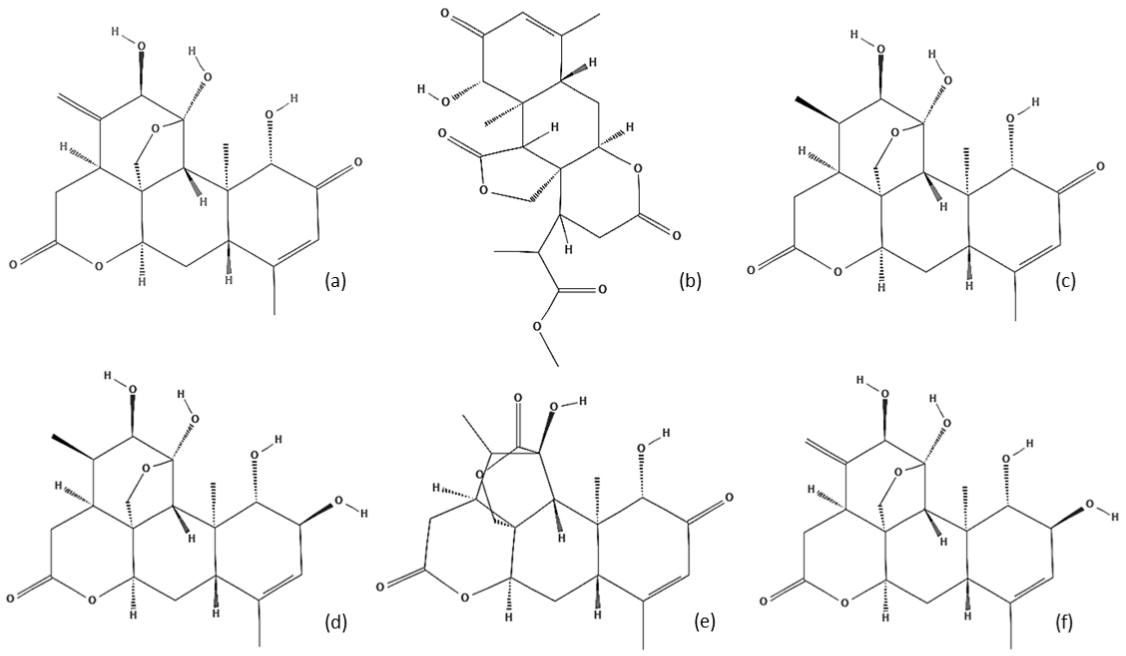

Figure 3. Some examples of the main *A. altissima* quassinoids identified: (**a**) Ailanthone; (**b**) Ailantinol A; (**c**) Chaparrinone; (**d**) Chaparrin; (**e**) Shinjudilactone; (**f**) Shinjulactone A.

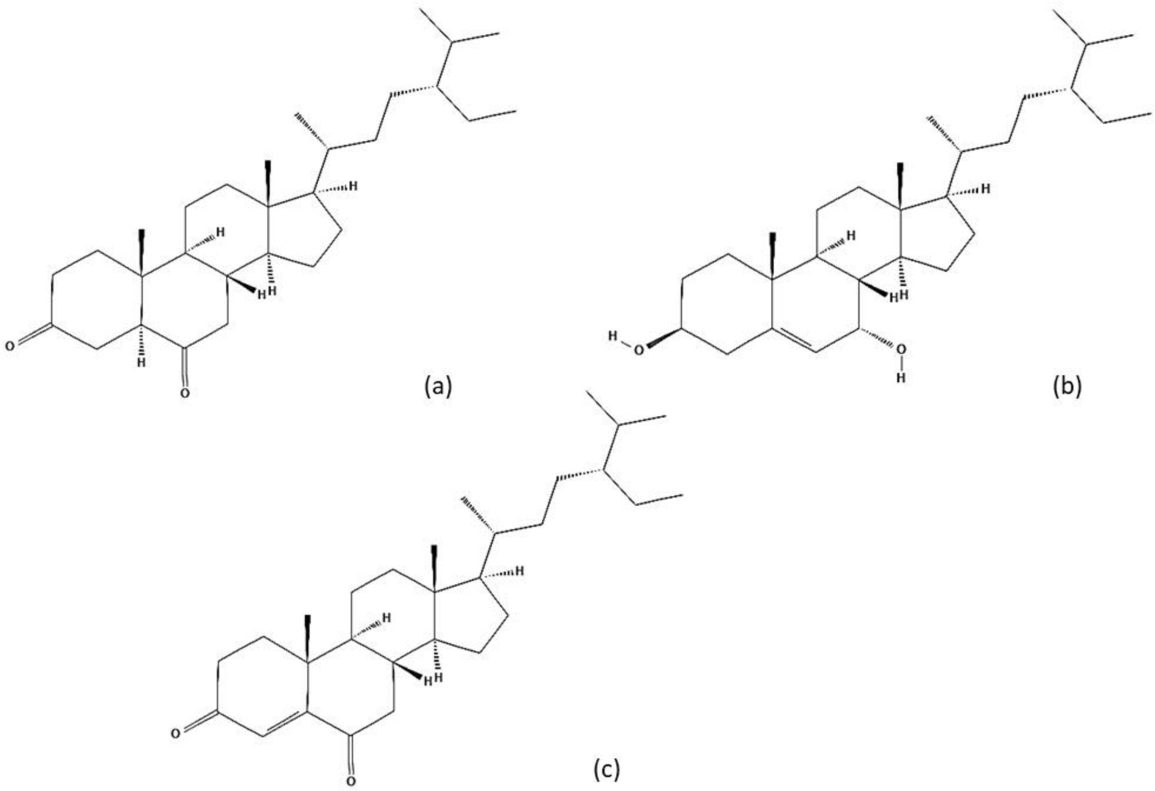

Figure 4. Some examples of steroids identified in *A. altissima*: (**a**) 5α-Stigmastane-3,6-dione; (**b**) Stigmast-5-ene-3β,7α-diol; (**c**) Stigmast-4-ene-3,6-dione.

The quassinoids class has been the main target of many studies due to their bioactivities and phytotoxic impacts. The most widely studied active compound in this group of terpenoids is ailanthone. This has been identified as an effective phytotoxic agent, capable of being used as a herbicide [7,30]. In addition to ailantthone, other derivatives have been isolated and studied (such as ailanthione, ailanthinol B, and chaparrin). There is an increasing demand for the isolation of new quassinoid derivatives to investigate their potential applications, mainly in pharmacology [31–33]. Table 1 summarises the main compounds by classes of compounds and which parts of the plants were used to identify the chemical compounds. These results are based on the review by Pijush Kundu and Subrata Laskar [12].

Table 1. The main compounds identified in *A. altissima* grouped by the major classes and which part of the plant was used for their isolation.

	Compounds	**Parts Used (Source)**
Alkaloids	1-Ethyl-4-methoxy-β-carboline	Root bark
	β-Carboline-1-propionic acid	Root bark
	Methyl-4-methoxy-β-caboline carboxylate	Root bark
	1-(1′-2′-Dihydroxyethyl)-4-methoxy-β-carboline	Root bark
	1-(2′-Hydroxyethyl)-4-methoxy-β-carboline/Crenatine	Root bark
	4-Methoxy-1-vinyl-β-carboline/Dehydrocrenatine	Dried leaves
	1-Methoxycarbonyl-4,8-dimethoxy-β-caboline	Leaves
	1-Methoxycarbonyl-β-carboline/1-caromethoxy-β-carboline	Leaves
	1-(1-Hydroxy-2-methoxy)-ethyl-4-methoxy-β-carboline	Root bark
	1-Carbamoyl-β-carboline	Root bark
	1-Acetyl-4-methoxy-β-carboline	Root bark
	Canthine-6-one	Root bark, leaves and wood
	1-Hydroxycanthine-6-one	Root bark
	1-Methoxy-canthine-6-one	Root bark, dried leaves and wood
	5-Hydroxymethylcanthine-6-one	Root bark
	Canthine-6-one-3-N-oxide	Wood
	1-Methoxycanthine-6-one-3-N-oxide	Root bark
Terpenoids	Ailanthone	Stem bark
	Chapparinone	Seed
	Chapparin	Aerial part
	Shinjulactone and Shinjulactone B	Stem bark
	Shinjulactone A	Seed
	Shinjulactone C, D, E, F, M, N, G, H, I, J, K and L	Root bark
	$\Delta^{13(18)}$ -Dehydroglaucarubinone	Stem bark
	$\Delta^{13(18)}$ -Dehydroglaucarubolone	Stem bark
	Ailantinol A e B	Stem bark
	Ailantinol C, D, E, F, G and H	Aerial part
	Shinjuglycoside A, B, C and D	Seed
	Shinjuglycoside E and F	Root bark
	Shinjudilactone	Root bark
	Cycloart-25-ene-3β-24R-diol and Cycloart-25-ene-3β-24S-diol	Fruits
	9,19-Cyclolanost-23(Z)ene-3β,25-diol	Fruits
	Ailantholide	Seed
	3-epi-ursolic acid	Fruits
	12β, 20 (S)-dihydroxy dammar-24-en-3-one	Fruits

Table 1. *Cont.*

	Compounds	Parts Used (Source)
Steroids	b-Sitosterol	Leaves and fruits
	b-Sitosterol glucoside/Daucosterol/Sitosterol-3-Ob-D-glucoside	Leaves and fruits
	Ailanthusterol A and B	Seed
	5α-Stigmastane-3,6-dione	Fruits
	5α-Stigmastane-3β, 6β-diol	Fruits
	6α-Hydroxy-stigmast-4-en-3-one	Fruits
	Stigmast-4-ene-3β, 6α-diol	Fruits
	Stigmast-4-ene-3,6-dione	Fruits
	6β-Hydroxy-stigmast-4-ene-3-one	Fruits
	Stigmast-4-ene-3β, 6β-diol	Fruits
	3β-Hydroxy-stigmast-5-en-7-one	Fruits
	Stigmast-5-ene-3β, 7α-diol	Fruits
	Stigmast-5-ene-3β, 7α, 20ζ-triol	Fruits
Flavonoids	Quercetin	Leaves
	Kaempferol	Leaves
	Isoquercetin/Quercetin-3-O-glucoside	Leaves
	Kaempferol-3-O-glucoside	Leaves
	Rutin	Leaves
	Luteolin-7-O-b-(600 galloylglucopyranoside)	Leaves
Miscellaneous compounds	1-O-b-D-Glucopyranosyl-(2S,3R,4E,9E)-2-(20-R-hydroxyhexadecenoy)-4,9-octadecadiene-1,3-diol	Fruits
	Ceryl alcohol	Leaves
	Ethyl gallate	Leaves
	Altissimacoumarin A and B	Bark
	Coumarin	Bark
	Isofraxidin	Bark
	Scopoletin	Bark

6. Biological Properties

For a long time, in the history of science, plants and parts of them were explored and used for medicinal purposes. *A. altissima* offers a promising natural alternative for food safety and bioconservation as well as for its antioxidant properties. Several studies report the pharmacological effects: antimicrobial (antibacterial and antiviral), antioxidant, cytotoxic, anti-inflammatory, antipyretic, analgesic, anti-progestogenic, and many others [34–37].

6.1. Antimicrobial Activity

Research on the bactericidal efficiency of phytochemicals as viable alternatives for chemical antibiotics has been conducted. An essential feature of extracts from plant origin is their antimicrobial activity, which contributes to alternative synthetic antibiotics [38].

Natural products derived from *A. altissima* may contribute to the development of new antimicrobial agents used as growth inhibitors of *Listeria monocytogenes*, *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and some important foodborne pathogens and spoilage bacteria [39].

Methanolic extracts from leaves and hydrodistilled residues were strong and efficient against Gram-positive bacteria: *S. aureus*, *B. subtilis*, *Enterococcus faecium*, and *Streptococcus agalactiae* [40]. The same was reported by Rahman [39]; methanolic extracts of *A. altissima* leaves were most effective against Gram-positive bacteria, namely *L. monocytogenes* (ATCC 19,116, ATCC 19,118 and ATCC 19,166), *S. aureus* (ATCC 6538 and KCTC 1916), and *B. subtilis* (ATCC 6633), and two Gram-negative bacteria, *P. aeruginosa* (KCTC 2004) and *E. coli* (ATCC 8739). The zones of inhibition of methanol extract and its derived different polar subfractions against the tested bacteria were found in the 12.1–23.2 mm range, and the minimum inhibitory concentration (MIC) values were recorded between 62.5 and 500 mg/mL [39]. However, their extracts were ineffective against Gram-negative bacteria, such as *E. coli* (ATCC 43,888), *Salmonella enteritidis* (KCTC 12,021), and *Salmonella typhimurium* (ATCC 2525). The MIC values of the methanolic extract against the tested bacteria were found in the 125–500 mg/mL range. In addition, the MeOH extract and its ethyl acetate (EtOAc) subfraction were compared with the standard antibiotics, tetracycline and streptomycin; in some cases, these showed greater antibacterial activity compared to streptomycin, but in other cases tetracycline showed greater activity than the solvent fractions. Aissani et al. [41] observed in aqueous and methanolic extracts of the bark and wood strong antimicrobial activity against *P. aeruginosa* (ATCC 9027) strains and isolated strains with an inhibition zone of 12 $\pm$ 0.3 mm. Zhao et al. [28] showed that the extract from fruits was weakly active against *E. coli*, *S. aureus*, *P. aeruginosa*, and *S. typhiuriun*, with inhibition zones of 6.87–7.51 mm, using the concentration of ethanol extract of 1.2 mg/mL. The plant's chemical composition can be variable due to variations in origin, species, growth, harvesting, and processing conditions, thus altering the biological activities.

Several studies show that antibacterial activity can be attributed to the occurrence of some specific components such as total polyphenol contents [42], namely gallic acid, rutin [43], and epicatechin [44]. The resistance of Gram-positive bacteria towards plant extracts has been previously reported [44–46]. The results obtained encourage the use of species as a food preservative and for pharmaceutical purposes.

6.2. Antioxidant Activity

Scientific research is interested in quantifying and using antioxidants mainly due to their potent biological activity. [47]. Although antioxidant compounds may be synthesized, there is a growing interest in the natural compounds from different plants [48,49]. Taking this into account, Luis et al. [50] performed a research to determine the phenolic, flavonoid, and total alkaloid content on four different extracts (methanolic, ethanolic, hydroalcoholic, and acetone) of *A. altissima* (steams, stalks, and leaves) to establish a correlation to the antioxidant activity of these extracts. To assess their antioxidant activity, DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) assay and the β-carotene bleaching test were used.

It was possible to quantify the total amount of phenolic compounds, 268.15 mg/g of dry extract in all extracts. The most important finding of this research is the potential antioxidant properties of *A. altissima*, since it is abundant in phenolic, flavonoid, and alkaloid compounds. Lungu et al. [51] have identified the presence of flavonoids (ranging around 5.34 to 5.41 g of rutin equivalents per 100 g of dry weight) in leaf extracts of *A. altissima*. The extraction method by reflux or ultrasound did not have a significant effect on the final concentration.

Moreover, the antioxidant activity was performed by the DPPH assay and the 2,2-AzinoBis (3-ethylbenzthiazoline-6-Sulphonic acid) (ABTS) radical scavenging assay. Once again, the extraction method did not affect the obtained concentrations, meaning that values are approximately 0.16 mM Trolox equivalent of extract for DPPH and around 9 mM Trolox equivalent when ABTS was used. In summary, results showed that flavonoids were in higher amounts than other compounds and are responsible for the antioxidant properties of the ethanolic leaf extracts [51]. Another study with leaves from different localities in Tunisia found that the main phenolic compounds in methanolic extracts were gallic acid, chlorogenic acid, HHDP-galloylglucose, epicatechin, rutin, hyperoside, and quercetin-3-galloyl hexoside [40]. Once again, the typical antioxidant activity assays (DPPH and ABTS) were used, as well as the ferric reducing antioxidant power (FRAP) assay and the 2-deoxyribose method, which was used for the determination of the scavenging effects of the methanolic extracts on hydroxyl (OH) radicals. Results showed good antioxidant activity of the methanolic extracts.

Altogether, leaves from the Bousalem region showed better antioxidant activity than those from other regions, with EC_{50} values of 14.78 μg/mL, 8.64 μg/mL, and 4.42 μg/mL when using the DPPH assay, ABTS assay, and the OH scavenging test, respectively. Regarding the leaf hydrodistilled residues, results were similar in efficacy to the DPPH and ABTS test. However, when using the OH radical test, the hydrodistilled residues showed a better antioxidant activity for the species that came from Bab Saâdoun [40]. The DPPH test to assess the antioxidant activity of *A. altissima* leaves was also used by Rahman et al. [39]. Methanolic extracts presented an IC_{50} value of 35.46 μg/mL and its ethyl acetate fraction possessed an even lower IC_{50} value (16.45 μg/mL). Recently, research was conducted to evaluate the physicochemical parameters and pharmacological bioactivity of *A. altissima* seed oil. El Ayeb-Zakhama et al. [52] were able to show that the seed oil presents antioxidant activity. The DPPH assay determined that the IC_{50} was 24.57 μg/mL, although the concentration of polyphenols was considered low (1.067 mg gallic acid equivalent/100 g oil). In addition, the study also showed that this seed oil presents moderate antimicrobial activity against Gram-positive bacteria.

6.3. Anti-Inflammatory Effects

Inflammation can lead to detrimental effects of different pathologies such as neurodegenerative and cardiovascular diseases, cancer, diabetes, and others [21]. It is also essential to find compounds that can tackle this problem by inhibiting the pro-inflammatory molecules and associated pathways [53].

El Ayeb-Zakhama et al. [52] reported that *A. altissima* seed oil could induce anti-inflammatory effects on edema (in vivo experiment), by reducing it more than 60% after 3 h, via the administration of doses of 0.2 and 1 g/kg. The same study also demonstrates the analgesic capacity of the oil due to its complex composition. The acute toxicity study and the analgesic effect of the seed oil was compared with a widely marketed drug, acetylsalicylic acid (ASL), in which the average lethal dose of the oil was estimated to be more than 2 g/kg and the analgesic effect was almost as potent as ASL at a dose of 1 g/kg. Other research [54] has suggested that the ethanolic extract of *A. altissima* (leaves and branch) can inhibit inflammatory mediators, both in vitro and in vivo, mainly by the inhibition of cyclooxygenase-2 (COX-2). By extracting canthin-6-one, an alkaloid, from the stem barks of *A. altissima*, Cho et al. [55] has proven this compound's potential effect in exerting anti-inflammatory effects of macrophages dysregulating pro-inflammatory cytokines and pathways. This same family of compounds was the target of the research conducted by Kim et al. [56], amongst other compounds. The authors reached the same conclusion regarding the anti-inflammatory properties. Kang et al. [57] have shown the potent inhibitory effects of *A. altissima* decoction on the decrease of cytokine levels, such as tumour necrosis factor (TNF) and interleukin (IL)-6 and IL-8 as well as on the reduction of histamine levels, by using both in vitro and in vivo models.

Moreover, the nuclear factor kappaB (NF-κB) pathway can also be inhibited by *A. altissima* compounds. Kim et al. [58] used the ethanolic extract of *A. altissima* leaves to assess the anti-inflammatory properties in astrocytes, where inflammation was induced by lipopolysaccharide. Results showed that the anti-inflammatory mechanism functions through the inhibition of COX-2 and other cytokines and the inhibition of the NF-κB pathway. These findings may lead to the use of *A. altissima* as a new therapeutic approach to neuroinflammatory diseases.

Overall, studies about the anti-inflammatory effects of the *A. altissima* compounds, whether they come from the leaves, bark, or seed oil, all conclusions favour the beneficial effects against pro-inflammatory molecules.

6.4. Phytotoxic Effects/Phytochemical Activity

Recent studies have demonstrated the potential of plant phytotoxins, such as ailanthone from *A. altissima*, as bioherbicides.

A. altissima has produced phytotoxic compounds and the main toxin identified is the ailanthone quassinoid, first isolated by Heisey and Heisey [30]. Both tested the herbicidal effect of the methanol extracts from the stem and bark of *A. altissima* on 17 weed and crop species and found that their application provided a strong herbicidal effect on all tested species. Numerous studies confirmed that quassinoids have a wide range of biological activities, including antileukemic and anticancer, antiamoebal, antimalarial, insecticidal and antifeedant, antiviral, antifungal, antitubercular, and herbicidal activities [59]. It is considered that the bioactivity of quassinoids is based on the plasma membrane NADH oxidase inhibition [60]. The phytotoxic effect seemed to correlate better with the extracts of higher phenolic contents; such results have previously been reported in *Psychotria leiocarpa* [61]. Phytochemical studies have shown that the main allelochemicals are ailanthone, ailantinone, chaparrin, and ailantinol with the first component being the most potent allelochemical. Moreover, both the methanolic extract and the hydrodistilled residue presented a significant phytotoxic activity [40]. Lungu et al. [51] extracts showed an excellent inhibitory action on the germination of seeds and growth of lettuce seedlings.

Regarding inhibiting progestin, Ahmed et al. [62] analysed 13 Chinese plant species, including *A. altissima*, in which they used the extract of the stem part. With the treatment of the T47D human breast cancer cell line with 314.46 ng/mL of progesterone and with three different levels of concentration of 10 μg/mL, 20 μg/mL and 40 μg/mL of ethanolic extracts, it was possible to verify that these concentrations could significantly prevent the action of the hormone in a dose-dependent manner.

Despite all the beneficial effects, some reports depict the contrary. *A. altissima* has been reported to negatively affect human health, with effects such as allergies, dermatitis and myocarditis. In addition, this invasive tree can also produce toxic and noxious environments for other species in the neighbourhood from the soil since the main compound responsible for its allelopathy (ailanthone) is present in high concentrations in the root bark and when released into the soil [6,7,63].

6.5. Anti-Tumour and Anti-Viral Activity

Anti-tumour activity is one of the fields that has contributed to more research on the effects that the bioactive compounds of *A. altissima* exert. Several studies with the dried bark, show that its active compounds exert antitumor effects in several cell lines, for example in A549, MDA-MB-231, LAPC4, A375, B16, and SGC-7901 among others. These in vitro studies lead us to state that ailanthone specifically may be a good inhibitor for cancers such as melanoma, acute myeloid leukaemia, lung, liver, breast, bladder, osteosarcoma, and prostate cancer [22,64,65]. In the work of Ding et al. [65] the different mechanisms of the action of ailanthone that justify its inhibitory effects were described and explained. The main basis of these effects is the mechanism of apoptosis. Apoptosis can be triggered by regulation of Bcl-2 family proteins, transcription factors such as β-catenin, tumour suppressor genes, and by the PI3K/AKT/mTOR and JAK/STAT3 pathways. Arylanthone induces apoptosis by the downregulation of Bcl-2 and the downregulation of the Bax proteins. It also induces this cell death through the downregulation of p53 (tumour suppressor protein) and miR-195, which consequently leads to inhibition of the JAK/STAT3 signalling pathway. On the other hand, the signalling pathway which is responsible for cell proliferation, differentiation, and metabolism that can lead to anti-apoptosis is PI3K/AKT/mTOR. In this pathway ailanthone has a suppressive effect, inducing apoptosis through the phosphorylation of PI3K and AKT. The review work of these authors is very interesting in that they warn of the problem that there are few studies evaluating the cytotoxicity of ailanthone in normal cells. Importantly, a preclinical study by Tang et al. [66] assessed the safety of ailanthone in Kumming rats and classified the mean lethal dose of ailanthone (27.3 mg/kg) as level 2 (severe) from the Globally Harmonised System of Classification and Labelling of Chemicals.

Furthermore, they warn that research into this active compound from *A. altissima* is still very early, as there are no studies on the bioavailability and side effects of ailanthone. Researchers are advised to focus on comparing the efficacy of ailanthone with other existing chemotherapy drugs and also to conduct in vivo and clinical trials [65].

Regarding the antiviral activity, some studies demonstrated that the main compound responsible for this effect is the main compound of *A. altissima*: ailanthone. In the review by Li et al. [22] the authors summarize all the existing pharmacology considering the dried bark of this species. They state that the active compound shows moderate inhibitory effects against the tobacco mosaic virus (TMV). In a study conducted by Tan et al. [67] these effects reached IC_{50} values of 0.30 mmol/L. However, they mention that the mechanism of action leading to this activity is not yet well elucidated.

6.6. Potential and New Applications

Desami et al., 2019 [68], and Caser et al., 2020 [69], provide new insights into *A. altissima* extracts and their phytotoxicity as potential natural herbicide use as a sustainable solution for weed management in horticultural crops.

The methanolic extracts of *A. altissima* showed antibacterial activity against different food pathogens; simultaneously, antioxidant properties indicated a potential use of extracts from this plant as food preservatives [39]. However, toxicity studies must be developed concerning the uses in the food industry and given the presence of alkaloids. The papermaking potential of this species, and its use as a fiber alternative for pulp production for the paper, was also evaluated [70,71]. The results of the paper are close to those of the reference ones. Regarding the growth and longevity of the *A. altissima* tree, other wood applications could be studied for this species.

7. Analytical Techniques for the Determination of Active Compounds

Over the last years several extraction techniques associated with different analytical methods have been reported for the chemical characterisation of *A. altissima*. For this purpose, it is crucial to consider that this type of plant possesses a complex and high number of compounds among which there are several fatty acids, volatile compounds, antioxidants, and alkaloids, among others [50,52,72]. These compounds were studied to check if they had any biological activity; this could help understand mechanisms of action, develop pharmacological formulations, and apply them to different research fields. Therefore, it is essential to identify and quantify the main compounds to improve this species' knowledge and possible uses.

In a study carried out by El Ayeb-Zakhama et al. [52], compounds were extracted from the seeds in a powder format using a Soxhlet apparatus. The authors used hexane (400 mL) as a solvent and the extraction time was 8 h, after which the solvent was evaporated using a rotary evaporator set at 40 °C. The collected oil was analysed by (1) gas chromatography coupled with a flame ionisation detector (GC-FID) and (2) gas chromatography coupled with mass spectrometry with headspace solid-phase micro-extraction (HS-SPME-GC/MS). The GC-FID equipment was used to determine the sterols fraction and the profile of fatty acids after transformation into methyl esters by adding 1 mL of n-hexane for each 40 mL of previously extracted oil, to which was then added a solution of sodium methoxide (2M). After performing this step, the mixture was heated to 50 °C in a thermal bath, followed by the addition of HCl (2N).

On the other hand, the analysis of volatile compounds was carried out by HS-SPME-GC/MS. The fatty acids profile revealed a predominance of linoleic and oleic acids, observing a polyunsaturated/saturated ratio of 11.86. Regarding the level of sterols, a predominant presence of β-sitosterol was observed, which is associated with high antioxidant activity and the control of cholesterol levels. Lastly, concerning the volatile fraction, a significant percentage of non-terpenes were observed in seed oil which could not be observed in oils from other parts of the same plant species.

Luis et al. [50], developed an analytical method to determine phenolic compounds with antioxidant activity by reversed-phase HPLC coupled to an ultraviolet detector (UV) using a Phenomenex Kinetex Luna 2.6 µm PFP 100A reversed column, performing the monitoring of the compounds at a wavelength of 280 nm, with the extraction of the compounds of different parts of *A. altissima* being performed with Soxhlet equipment for methanol, acetone, and ethanol extractions, with hydroalcoholic extractions carried out through refluxing, followed by evaporation under vacuum to a final volume of 150 mL. The authors verified that a greater final concentration of phenolic compounds was obtained when methanol was used for extraction, with lower concentrations of phenols observed in stems and stalks compared with extracts from leaves. In addition, hydroxycinnamic acids were revealed to be predominant, ferulic acid being the one whose percentage was higher, finding that the antioxidant activity levels were closely related to the total phenolic content, with an R2 of 0.86.

He et al. [72] developed a method to evaluate the active components of *A. altissima* with the help of an HPLC-UV. The goal was to perform the fingerprinting and quantification from samples of different sources, proceeding to the extraction of the compounds after performing the drying and pulverization of the stem bark using ethanol (75%) for 1 kg of content, being later evaporated in a vacuum. In this study, concentrations ranged from 6.44 µg/mL to 825 µg/mL for ailanthone, one of the main quasinoids with anti-inflammatory, anti-microbial, and anti-allergic activity in *A. altissima*, used as quality control, with the UV detector set to a wavelength of 250 nm. The samples from different sources revealed 19 similar compounds among the 10 different samples studied with a degree of similarity never exceeding 1.5%, with the predominance of compounds differing in accordance with the source.

Mastelić et al. [73] described for the first time the application of GC-MS to identify volatile compounds present in leaves of different ages. For extraction, Clevenger-type equipment was used for the hydrodistillation of the plant for 3 h, adding 1 mL of pentane to the graduated part, after which the pentane layer was separated and dried with sodium sulfate before analysis. The authors report that the composition of volatile compounds was dependent on the plant's age and its drying process. A higher prevalence of oxygenated aliphatic compounds was observed in younger plants while older plants revealed a greater prevalence of sesquiterpene compounds.

To evaluate the herbicidal activity of ailanthone in *A. altissima* bark, Pedersini et al. [74] isolated this compound with solvents and purified it by Biogel P2. A higher concentration of ailanthone 92% *w*/*w* was obtained when dichloromethane was used. Three obtained fractions were subsequently fractionated by gel permeation chromatography using a Biorad Biogel P2 resin with a UV detector operating at 313 nm. Later, an HPLC coupled with a UV-VIS detector set at 256 nm was used to determine ailanthone in three different species.

Li et al. [75] isolated canthin-6-one to evaluate its antifungal activity. This study was performed by quantifying the different protein expressions in *Fusarium oxysporum* f. sp. *cucumerinum* (Foc) by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). Extraction of the compound was carried out with three times ethanol (70%) at room temperature. The obtained extract was evaporated by vacuum and subsequently dissolved in water before partitioning with other solvents, namely n-hexane, ethyl acetate and butanol. Canthin-6-one present in 32 µg/mL revealed an elevated downregulating effect on the expression of glutamine synthetase, thus affecting the synthesis of glutamine and glutamate, apart from downregulating the transport of amino acids, affecting the growth of the fungus.

To characterise the volatile compounds from leaves and flowers, Yifan et al. [76] quantified them through a dynamic headspace sampling coupled with GC-MS. The compounds were extracted with 150 mL of distilled water for 4 h by pumping air through a SuperQ volatile collection trap equipment and then eluted with 100 mL methylene chloride. The authors observed the presence of fifty-three compounds belonging to groups such as terpenoids, fatty acids, benzenoids, and nitrogen-containing compounds. The percentage of fatty acids present in the total emissions from the leaves was higher than in flowers, which were found to have a higher percentage of terpenoids in the overall emissions for volatile compounds compared to leaves, namely monoterpenoids.

To evaluate the phytotoxic activity of leaves, Lungu et al. [51] studied the composition of this species with GC-MS after extracting water-ethanol (70%; V/V) by reflux and ultrasound for one hour. The extract was then centrifuged, and the supernatant was filtered. Twenty-seven different compounds were identified, of which some fatty acids and polyphenols were estimated to contribute to the phytotoxic activity.

Caboni et al. [77] identified the nematicidal activity of (E,E)-2,4-decadienal and (E)-2-decenal extracted from wood, leaf, bark, and root parts. These two compounds were extracted with methanol (1:10 w/w) with ultrasound for 15 min. After this process, the obtained solution was filtered and centrifuged. A GC-MS was used to determine the presence of these two compounds and the authors claimed their presence in wood parts only. The nematicidal activity revealed EC_{50} values of 11.70 mg/L for (E,E)-2,4-decadienal and 20.43 mg/L for (E)-2-decenal when applied against the nematode *Meloidogyne javanica.*

Additionally, Albouchi et al. [40] studied the composition of essential oils extracted from *A. altissima* leaves from three different regions of Tunisia. The dried material was extracted by hydrodistillation of Quickfit apparatus for 3 h, in which the distillate obtained was extracted with *n*-pentane (twice) and the organic layer was concentrated and consequently analysed by GC-FID and GC-MS. The three essential oils were characterised as containing a high percentage of non-terpenic compounds and some of the sesquiterpene hydrocarbons and oxygenated monoterpenes. The majority of 139 compounds identified were tetradecanol, heneicosane, tricosane, docosane, α-curcumene, α-gurjunene, methyl decanoate, α-terpinen-7-al, geranial, α-guaiene,α-humulene, and (E)-β-farnesene. In the same study, methanolic extracts of dried and ground leaves and the residual leaves (remained after hydrodistillation) were further analysed for their content of phenolic and flavonoid compounds. The total phenolic content was performed by the Folin–Ciocalteu method, and these were characterised by high-performance liquid chromatography with a photodiode array detector and tandem mass spectrometry (HPLC-PDA-MS/MS). Total flavonoid content was performed with the $AlCl_3$ colorimetric method. Comparing the two methods of total content determination, it was possible to verify a higher content of phenols in the dried leaves than the hydrodistilled residue and a higher content of flavonoids in the hydrodistilled residue compared with the dried leaves. Furthermore, from the methanolic extracts antioxidant, antimicrobial, and phytotoxic activities were analysed.

To quantify the phenolic compounds, Vidovic et al. [78] incubated the leaves in methanol with 0.1% chloride acid for 50 min. After this period, water and chloroform were added to the resulting supernatant and the sample was stirred for 45 min at 4 °C, followed by centrifugation and separation of the liquid phase. This process was repeated without the addition of chloroform. After extraction, the compounds were analysed by HPLC-DAD using wavelengths of 520 nm for anthocyanins, 340 nm for flavones and flavanones, 320 nm for resveratrol, coniferyl alcohol, hydroxycinnamic acid and its respective derivatives, 360 nm for flavonols and ellagic acid, and 280 nm for isoflavones, catechins, benzoic acids, and the respective derivatives.

The evaluation of the phenolic compounds' content, flavonoids, and non-flavonoids was also performed by Poljuha et al. [79], using a new HPLC procedure equipped with a C_{18} column using wavelengths of 360 nm and 310 nm to identify flavonoids and phenolic acids, respectively, which was faster (26 min) and used fewer solvents than other works. The extractions in deionised water were performed after maceration and respective extraction for 48 h, followed by filtration. The extractions in methanol were performed for a period of 72 h without maceration. The supernatants were evaporated to 140 mL, reconstituted with water to a final volume of 500 mL, and then stored at 4 °C until analysis. No flavonoid content was obtained from fresh leaves when water extraction was performed, while the content of both groups of compounds was higher when methanol was used for extraction.

8. Conclusions

Nowadays, *A. altissima* can be a valuable species to satisfy some human services, considering it is an IAS and presents some negative effects. There have been distinct investigations with different plant parts to explain its traditional use in medicine and unveil its potential for pharmacology and the food industry. It is a species that can present some variation in its morphology according to its location and is tolerant to diverse factors, which enable its propagation. In addition, biologically, it displays methods of reproduction that greatly favour its spread. Regarding antimicrobial activity, the studies performed so far have demonstrated that the methanolic extracts of the leaves show great effectiveness against Gram-negative bacteria. The methanolic and aqueous extracts of the bark and wood has also demonstrated strong antimicrobial activity. These results are very much in line with its traditional use in medicine, where it is used as an astringent and parasiticide. The antioxidant activity has been performed already with different parts of the plant extracted with different solvents. Most studies have shown that methanolic extracts of the leaves contain phenolic compounds and flavonoids. Furthermore, *A. altissima* showed anti-inflammatory effects due to the chemical composition of the leaves, bark, and seed oils. The results of some studies demonstrating the potent inhibitory effect of the extracts of this species, such as the decoction that reduces cytokine levels and interleukins and TNF, support the use of the plant boiled together with other ingredients to treat problems such as dysentery, intestinal bleeding, and others.

According to the literature, the main extracts for analysing the biological activities of *A. altissima* are essentially made from the leaves, seeds (e.g., essential oil), and bark. However, extracts from other plant parts have been rarely investigated, such as flowers and stems. Moreover, new compounds have been discovered, but few are known about their possible activities.

The novelty of this work is the detailed description of the major biological activities and analytical techniques that have been used to date using different plant extracts of *A. altissima*. Other articles describe only the characteristics of this species, or the chemical compounds, or only the bioactivities of one plant extract, while in this paper, we compiled all the information overall about *A. altissima* to better understand what possible investigations could be carried out.

This review also shows that knowledge about the phytochemical composition and biological activities of *A. altissima* has been growing, leading it to be a promising species for future research.

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References

1. Castro-Díez, P.; Alonso, Á.; Saldaña-López, A.; Granda, E. Effects of widespread non-native trees on regulating ecosystem services. *Sci. Total. Environ.* **2021**, *778*, 146141. [CrossRef]
2. Krumm, F.; Vitkova, L. *Introduced Tree Species in European Forests: Opportunities and Challenges*; European Forest Institute: Joensuu, Finland, 2016; ISBN 9789525980318.
3. Castro-Díez, P.; Godoy, O.; Saldaña, A.; Richardson, D.M. Predicting invasiveness of Australian acacias on the basis of their native climatic affinities, life history traits and human use. *Divers. Distrib.* **2011**, *17*, 934–945. [CrossRef]
4. De Wit, M.P.; Crookes, D.J.; Van Wilgen, B.W. Conflicts of interest in environmental management: Estimating the costs and benefits of a tree invasion. *Biol. Invasions* **2001**, *3*, 167–178. [CrossRef]
5. Dickie, I.A.; Bennett, B.M.; Burrows, L.E.; Nuñez, M.A.; Peltzer, D.A.; Porté, A.; Richardson, D.M.; Rejmánek, M.; Rundel, P.W.; van Wilgen, B.W. Conflicting values: Ecosystem services and invasive tree management. *Biol. Invasions* **2014**, *16*, 705–719. [CrossRef]
6. Sladonja, B.; Sušek, M.; Guillermic, J. Review on Invasive Tree of Heaven (*Ailanthus altissima* (Mill.) Swingle) Conflicting Values: Assessment of Its Ecosystem Services and Potential Biological Threat. *Environ. Manag.* **2015**, *56*, 1009–1034. [CrossRef] [PubMed]
7. Kowarik, I.; Säumel, I. Biological flora of Central Europe: *Ailanthus altissima* (Mill.) Swingle. *Perspect. Plant Ecol. Evol. Syst.* **2007**, *8*, 207–237. [CrossRef]
8. Constán-Nava, S.; Bonet, A.; Pastor, E.; Lledó, M.J. Long-term control of the invasive tree *Ailanthus altissima*: Insights from Mediterranean protected forests. *For. Ecol. Manag.* **2010**, *260*, 1058–1064. [CrossRef]
9. Almeida, M.T.; Mouga, T.; Barracosa, P. The weathering ability of higher plants. The case of *Ailanthus altissima* (Miller) Swingle. *Int. Biodeterior. Biodegrad.* **1994**, *33*, 333–343. [CrossRef]
10. Kožuharova, E.; Lebanova, H.; Getov, I.; Benbassat, N.; Kochmarov, V. *Ailanthus altissima* (Mill.) Swingle—A terrible invasive pest in Bulgaria or potential useful medicinal plant? *Bothalia J.* **2014**, *44*, 213–230.
11. International Plant Nutrition Institute. International Plant Names Index. Available online: http://www.ipni.org (accessed on 1 October 2021).
12. Kundu, P.; Laskar, S. A brief resume on the genus *Ailanthus*: Chemical and pharmacological aspects. *Phytochem. Rev.* **2010**, *9*, 379–412. [CrossRef]
13. Hu, S.Y. Ailanthus. *Arnoldia* **1979**, *39*, 29–50.
14. Castroviejo, S. (coord. gen.). In *Flora Iberica*; Real Jardín Botánico, Spanish National Research Council: Madrid, Spain, 1986–2012.
15. Bashir, A.; Mohi-ud-din, R.; Farooq, S.; Bhat, Z.A. Pharmacognostic Standardization and Phytochemical Evaluation of *Ailanthus altissima* (Mill.) Swingle leaves. *J. Drug Deliv. Ther.* **2019**, *9*, 179–183.
16. Pan, E.; Bassuk, N. Establishment and Distribution of *Ailanthus altissima* in the Urban Environment. *J. Environ. Hortic.* **1986**, *4*, 1–4. [CrossRef]
17. Arnaboldi, F.; Conedera, M.; Maspoli, G. Distribuzione e potenziale invasivo di *Ailanthus altissima* (Mill.) Swingle nel Ticino centrale. *Boll. Soc. Ticin. Sci. Nat.* **2002**, *90*, 93–101.
18. Tabacchi, E.; Planty-Tabacchi, A.M. Recent changes in Riparian vegetation: Possible consequences on dead wood processing along rivers. *River Res. Appl.* **2003**, *19*, 251–263. [CrossRef]
19. Facelli, J.M.; Pickett, S.T.A.; Facelli, J.M. Indirect Effects of Litter on Woody Seedlings Subject to Herb Competition. *Oikos* **1991**, *62*, 129. [CrossRef]
20. Facelli, J.M. Multiple indirect effects of plant litter affect the establishment of woody seedlings in old fields. *Ecology* **1994**, *75*, 1727–1735. [CrossRef]
21. Ranft, H.; Dässler, H.-G. Rauchhärtetest an Gehölzen im SO_2-Kabinenversuch: Fume-Hardiness Test Carried out on Woods in a SO_2-Cabin-Trial. *Flora* **1970**, *159*, 573–588. [CrossRef]
22. Li, X.; Li, Y.; Ma, S.; Zhao, Q.; Wu, J.; Duan, L.; Xie, Y.; Wang, S. Traditional uses, phytochemistry, and pharmacology of *Ailanthus altissima* (Mill.) Swingle bark: A comprehensive review. *J. Ethnopharmacol.* **2021**, *275*, 114121. [CrossRef]
23. Du, Y.Q.; Yan, Z.Y.; Chen, J.J.; Wang, X.B.; Huang, X.X.; Song, S.J. The identification of phenylpropanoids isolated from the root bark of *Ailanthus altissima* (Mill.) Swingle. *Nat. Prod. Res.* **2021**, *35*, 1139–1146. [CrossRef]
24. Yang, X.L.; Yuan, Y.L.; Zhang, D.M.; Li, F.; Ye, W.C. Shinjulactone O, a new quassinoid from the root bark of *Ailanthus altissima*. *Nat. Prod. Res.* **2014**, *28*, 1432–1437. [CrossRef]
25. Zhang, D.D.; Bai, M.; Yan, Z.Y.; Huang, X.X.; Song, S.J. Chemical constituents from *Ailanthus altissima* (Mill.) Swingle and chemotaxonomic significance. *Biochem. Syst. Ecol.* **2020**, *93*, 104174. [CrossRef]
26. Ni, J.C.; Shi, J.T.; Tan, Q.W.; Chen, Q.J. Two new compounds from the fruit of *Ailanthus altissima*. *Nat. Prod. Res.* **2019**, *33*, 101–107. [CrossRef] [PubMed]
27. Ni, J.C.; Shi, J.T.; Tan, Q.W.; Chen, Q.J. Phenylpropionamides, piperidine, and phenolic derivatives from the fruit of *Ailanthus altissima*. *Molecules* **2017**, *22*, 2107. [CrossRef] [PubMed]
28. Zhao, C.C.; Shao, J.H.; Li, X.; Xu, J.; Zhang, P. Antimicrobial constituents from fruits of *Ailanthus altissima* SWINGLE. *Arch. Pharm. Res.* **2005**, *28*, 1147–1151. [CrossRef]
29. Bory, G.; Clair-Maczulajtys, D. Composition du nectar et rôle des nectaires extrafloraux chez l'*Ailanthus glandulosa*. *Can. J. Bot.* **1986**, *64*, 247–253. [CrossRef]

30. Heisey, R.M.; Heisey, T.K. Herbicidal effects under field conditions of *Ailanthus altissima* bark extract, which contains ailanthone. *Plant Soil* **2003**, *256*, 85–99. [CrossRef]
31. De Feo, V.; De Martino, L.; Quaranta, E.; Pizza, C. Isolation of phytotoxic compounds from tree-of-heaven (*Ailanthus altissima* swingle). *J. Agric. Food Chem.* **2003**, *51*, 1177–1180. [CrossRef]
32. Tan, Q.W.; Ni, J.C.; Shi, J.T.; Zhu, J.X.; Chen, Q.J. Two novel quassinoid glycosides with antiviral activity from the samara of *Ailanthus altissima*. *Molecules* **2020**, *25*, 5679. [CrossRef]
33. Wang, Y.; Wang, W.J.; Su, C.; Zhang, D.M.; Xu, L.P.; He, R.R.; Wang, L.; Zhang, J.; Zhang, X.Q.; Ye, W.C. Cytotoxic quassinoids from *Ailanthus altissima*. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 654–657. [CrossRef]
34. Okunade, A.L.; Bikoff, R.E.; Casper, S.J.; Oksman, A.; Goldberg, D.E.; Lewis, W.H. Antiplasmodial activity of extracts and quassinoids isolated from seedlings of *Ailanthus altissima* (Simaroubaceae). *Phyther. Res.* **2003**, *17*, 675–677. [CrossRef] [PubMed]
35. Fukamiya, N.; Lee, K.H.; Muhammad, I.; Murakami, C.; Okano, M.; Harvey, I.; Pelletier, J. Structure-activity relationships of quassinoids for eukaryotic protein synthesis. *Cancer Lett.* **2005**, *220*, 37–48. [CrossRef] [PubMed]
36. Al-Snafi, A.E. The pharmacological importance of *Antirrhinum majus*—A review. *Asian J. Pharm. Sci. Technol.* **2015**, *5*, 313–320.
37. Swingle, M. Analgesic, antipyretic and antiulcer activities of *Ailanthus altissima*. *Phytopharmacology* **2012**, *3*, 341–350.
38. Ghannoum, M.A.; Rice, L.B. Antifungal agents: Mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. *Clin. Microbiol. Rev.* **1999**, *12*, 501–517. [CrossRef] [PubMed]
39. Rahman, A.; Kim, E.L.; Kang, S.C. Antibacterial and antioxidant properties of *Ailanthus altissima* swingle leave extract to reduce foodborne pathogens and spoiling bacteria. *J. Food Saf.* **2009**, *29*, 499–510. [CrossRef]
40. Albouchi, F.; Hassen, I.; Casabianca, H.; Hosni, K. Phytochemicals, antioxidant, antimicrobial and phytotoxic activities of *Ailanthus altissima* (Mill.) Swingle leaves. *S. Afr. J. Bot.* **2013**, *87*, 164–174. [CrossRef]
41. Aissani, N.; Jabri, M.; Mabrouk, M.; Sebai, H. Antioxidant Potential and Antimicrobial Activity of *Ailanthus altissima* (Mill.) Swingle Extracts against *Pseudomonas aeruginosa*. *J. Mol. Biol. Biotech.* **2018**, *3*, 3.
42. Končić, M.Z.; Kremer, D.; Gruz, J.; Strnad, M.; Biševac, G.; Kosalec, I.; Šamec, D.; Piljac-Žegarac, J.; Karlović, K. Antioxidant and antimicrobial properties of *Moltkia petraea* (Tratt.) Griseb. flower, leaf and stem infusions. *Food Chem. Toxicol.* **2010**, *48*, 1537–1542. [CrossRef]
43. Chanwitheesuk, A.; Teerawutgulrag, A.; Kilburn, J.D.; Rakariyatham, N. Antimicrobial gallic acid from *Caesalpinia mimosoides* Lamk. *Food Chem.* **2007**, *100*, 1044–1048. [CrossRef]
44. Betts, J.W.; Kelly, S.M.; Haswell, S.J. Antibacterial effects of theaflavin and synergy with epicatechin against clinical isolates of *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. *Int. J. Antimicrob. Agents* **2011**, *38*, 421–425. [CrossRef]
45. Tian, F.; Li, B.; Ji, B.; Yang, J.; Zhang, G.; Chen, Y.; Luo, Y. Antioxidant and antimicrobial activities of consecutive extracts from *Galla chinensis*:The polarity affects the bioactivities. *Food Chem.* **2009**, *113*, 173–179. [CrossRef]
46. Hosni, K.; Hassen, I.; Sebei, H.; Casabianca, H. Secondary metabolites from *Chrysanthemum coronarium* (Garland) flowerheads: Chemical composition and biological activities. *Ind. Crop. Prod.* **2013**, *44*, 263–271. [CrossRef]
47. Polumbryk, M.; Ivanov, S.; Polumbryk, O. Antioxidants in food systems. Mechanism of action. *Ukr. J. Food Sci.* **2013**, *1*, 15–40.
48. Olszowy, M. What is responsible for antioxidant properties of polyphenolic compounds from plants? *Plant Physiol. Biochem.* **2019**, *144*, 135–143. [CrossRef] [PubMed]
49. Pisoschi, A.M.; Pop, A.; Cimpeanu, C.; Predoi, G. Antioxidant Capacity Determination in Plants and Plant-Derived Products: A Review. *Oxid. Med. Cell. Longev.* **2016**, *2016*, 9130976. [CrossRef] [PubMed]
50. Luís, Â.; Gil, N.; Amaral, M.E.; Domingues, F.; Duarte, A.P. *Ailanthus altissima* (Miller) Swingle: A source of bioactive compounds with antioxidant activity. *BioResources* **2012**, *7*, 2105–2120. [CrossRef]
51. Lungu, L.; Savoiu, M.R.; Manolescu, B.N.; Farcasanu, I.C.; Popa, C.V. Phytotoxic and Antioxidant activities of leaf extracts of *Ailanthus altissima* swingle. *Rev. Chim.* **2016**, *67*, 1928–1931.
52. EL Ayeb-Zakhama, A.; Chahdoura, H.; Ziani, B.E.C.; Snoussi, M.; Khemiss, M.; Flamini, G.; Harzallah-Skhiri, F. *Ailanthus altissima* (Miller) Swingle seed oil: Chromatographic characterization by GC-FID and HS-SPME-GC-MS, physicochemical parameters, and pharmacological bioactivities. *Environ. Sci. Pollut. Res.* **2019**, *26*, 14137–14147. [CrossRef]
53. Yeung, Y.; Aziz, F.; Guerrero-Castilla, A.; Arguelles, S. Signaling Pathways in Inflammation and Anti-inflammatory Therapies. *Curr. Pharm. Des.* **2018**, *24*, 1449–1484. [CrossRef]
54. Jin, M.H.; Yook, J.; Lee, E.; Lin, C.X.; Quan, Z.; Son, K.H.; Bae, K.H.; Kim, H.P.; Kang, S.S.; Chang, H.W. Anti-inflammatory Activity of *Ailanthus altissima* in Ovalbumin-Induced Lung Inflammation. *Biol. Pharm. Bull.* **2006**, *29*, 884–888. [CrossRef]
55. Cho, S.-K.; Jeong, M.; Jang, D.; Choi, J.-H. Anti-inflammatory Effects of Canthin-6-one Alkaloids from *Ailanthus altissima*. *Planta Med.* **2018**, *84*, 527–535. [CrossRef] [PubMed]
56. Kim, H.M.; Lee, J.S.; Sezirahiga, J.; Kwon, J.; Jeong, M.; Lee, D.; Choi, J.-H.; Jang, D.S. A New Canthinone-Type Alkaloid Isolated from *Ailanthus altissima* Swingle. *Molecules* **2016**, *21*, 642. [CrossRef]
57. Kang, T.-H.; Choi, I.-Y.; Kim, S.-J.; Moon, P.-D.; Seo, J.-U.; Kim, J.-J.; An, N.-H.; Kim, S.-H.; Kim, M.-H.; Um, J.-Y.; et al. *Ailanthus altissima* swingle has anti-anaphylactic effect and inhibits inflammatory cytokine expression via suppression of nuclear factor-kappaB activation. *In Vitro Cell. Dev. Biol. Anim.* **2010**, *46*, 72–81. [CrossRef] [PubMed]
58. Kim, S.R.; Park, Y.; Li, M.; Kim, Y.K.; Lee, S.; Son, S.Y.; Lee, S.; Lee, J.S.; Lee, C.H.; Park, H.H.; et al. Anti-inflammatory effect of *Ailanthus altissima* (Mill.) Swingle leaves in lipopolysaccharide-stimulated astrocytes. *J. Ethnopharmacol.* **2021**, 114258. [CrossRef] [PubMed]

59. Fiaschetti, G.; Grotzer, M.A.; Shalaby, T.; Castelletti, D.; Arcaro, A. Quassinoids: From traditional drugs to new cancer therapeutics. *Curr. Med. Chem.* **2011**, *18*, 316–328. [CrossRef] [PubMed]
60. Morré, D.J.; Grieco, P.A.; Morré, D.M. Mode of action of the anticancer quassinoids—Inhibition of the plasma membrane NADH oxidase. *Life Sci.* **1998**, *63*, 595–604. [CrossRef]
61. Corrêa, L.R.; Soares, G.L.G.; Fett-Neto, A.G. Allelopathic potential of *Psychotria leiocarpa*, a dominant understorey species of subtropical forests. *S. Afr. J. Bot.* **2008**, *74*, 583–590. [CrossRef]
62. Ahmed, H.M.; Yeh, J.-Y.; Tang, Y.-C.; Cheng, W.T.-K.; Ou, B.-R. Molecular screening of Chinese medicinal plants for progestogenic and anti-progestogenic activity. *J. Biosci.* **2014**, *39*, 453–461. [CrossRef]
63. Lawrence, J.; Colwell, A.; Sexton, O. The Ecological Impact of Allelopathy in *Ailanthus altissima* (Simaroubaceae). *Am. J. Bot.* **1991**, *78*, 948–958. [CrossRef]
64. Chen, Y.; Zhu, L.; Yang, X.; Wei, C.; Chen, C.; He, Y.; Ji, Z. Ailanthone induces G2/M cell cycle arrest and apoptosis of SGC-7901 human gastric cancer cells. *Mol. Med. Rep.* **2017**, *16*, 6821–6827. [CrossRef]
65. Ding, H.; Yu, X.; Hang, C.; Gao, K.; Lao, X.; Jia, Y.; Yan, Z. Ailanthone: A novel potential drug for treating human cancer. *Oncol. Lett.* **2020**, *20*, 1489–1503. [CrossRef] [PubMed]
66. Tang, S.; Ma, X.; Lu, J.; Zhang, Y.; Liu, M.; Wang, X. Preclinical toxicology and toxicokinetic evaluation of ailanthone, a natural product against castration-resistant prostate cancer, in mice. *Fitoterapia* **2019**, *136*, 104161. [CrossRef] [PubMed]
67. Tan, Q.W.; Ouyang, M.A.; Wu, Z.J. A new seco-neolignan glycoside from the root bark of *Ailanthus altissima*. *Nat. Prod. Res.* **2012**, *26*, 1375–1380. [CrossRef]
68. Demasi, S.; Caser, M.; Vanara, F.; Fogliatto, S.; Vidotto, F.; Negre, M.; Trotta, F.; Scariot, V. Ailanthone from *Ailanthus altissima* (Mill.) Swingle as potential natural herbicide. *Sci. Hortic.* **2019**, *257*, 108702. [CrossRef]
69. Caser, M.; Demasi, S.; Caldera, F.; Dhakar, N.K.; Trotta, F.; Scariot, V. Activity of *Ailanthus altissima* (Mill.) Swingle Extract as a Potential Bioherbicide for Sustainable Weed Management in Horticulture. *Agronomy* **2020**, *10*, 965. [CrossRef]
70. Baptista, P.; Costa, A.P.; Simões, R.; Amaral, M.E. *Ailanthus altissima*: An alternative fiber source for papermaking. *Ind. Crop. Prod.* **2014**, *52*, 32–37. [CrossRef]
71. Ferreira, P.J.T.; Gamelas, J.A.F.; Carvalho, M.G.V.S.; Duarte, G.V.; Canhoto, J.M.P.L.; Passas, R. Evaluation of the papermaking potential of *Ailanthus altissima*. *Ind. Crop. Prod.* **2013**, *42*, 538–542. [CrossRef]
72. He, Q.; Xiao, H.; Li, J.; Liu, Y.; Jia, M.; Wang, F.; Zhang, Y.; Wang, W.; Wang, S. Fingerprint analysis and pharmacological evaluation of *Ailanthus altissima*. *Int. J. Mol. Med.* **2018**, *41*, 3024–3032. [CrossRef]
73. Mastelić, J.; Jerković, I. Volatile constituents from the leaves of young and old *Ailanthus altissima* (Mill.) swingle tree. *Croat. Chem. Acta* **2002**, *75*, 189–197.
74. Pedersini, C.; Bergamin, M.; Aroulmoji, V.; Baldini, S.; Picchio, R.; Pesce, P.G.; Ballarin, L.; Murano, E. Herbicide activity of extracts from *Ailanthus altissima* (Simaroubaceae). *Nat. Prod. Commun.* **2011**, *6*, 593–596. [CrossRef]
75. Li, Y.; Zhao, M.; Zhang, Z. Quantitative proteomics reveals the antifungal effect of canthin-6-one isolated from *Ailanthus altissima* against *Fusarium oxysporum* f. sp. *cucumerinum* In Vitro. *PLoS ONE* **2021**, *16*, e0250712. [CrossRef] [PubMed]
76. Jiang, Y.; Ye, J.; Jiang, B. Characterization of volatile constituents from the flowers and leaves of *Ailanthus altissima* by dynamic head-space collection/GC-MS. *Asian J. Chem.* **2014**, *26*, 6737–6739. [CrossRef]
77. Caboni, P.; Ntalli, N.G.; Aissani, N.; Cavoski, I.; Angioni, A. Nematicidal activity of (E,E)-2,4-decadienal and (E)-2-decenal from *Ailanthus altissima* against *Meloidogyne javanica*. *J. Agric. Food Chem.* **2012**, *60*, 1146–1151. [CrossRef] [PubMed]
78. Vidović, M.; Morina, F.; Milić, S.; Jovanović, S.V. An improved HPLC-DAD method for simultaneously measuring phenolics in the leaves of *Tilia platyphyllos* and *Ailanthus altissima*. *Bot. Serbica* **2015**, *39*, 177–186.
79. Poljuha, D.; Sladonja, B.; Šola, I.; Dudaš, S.; Bilić, J.; Rusak, G.; Motlhatlego, K.E.; Eloff, J.N. Phenolic composition of leaf extracts of *Ailanthus altissima* (simaroubaceae) with antibacterial and antifungal activity equivalent to standard antibiotics. *Nat. Prod. Commun.* **2017**, *12*, 1609–1612. [CrossRef]