A Summary of Extraction, Synthesis, Properties, and Potential Uses of Juglone: A Literature Review

Discussion Paper

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Abstract

This literature review summarizes the state of current information on the extraction, synthesis, properties, and potential uses of juglone, a natural product produced by the walnut tree (Juglandacea). Juglone (5-hydroxy-1,4-naphthoquinone) is known primarily for its allelopathic effect against certain plants and toxicity towards marine organisms. It has a wide variety of potential uses in medicine, and as a biocide for organic farming and pest control. This summary also provides historical uses of juglone and the walnut tree in British Columbia and worldwide, current applications in the agroforestry management, a brief background on the biosynthesis, and mode of toxicity of juglone.

KEYWORDS: biocide; juglans spp.; juglone; natural product; walnut tree

The history of research

The detrimental effect of the walnut tree has been observed for at least two millennia (Willis 1985; Jose 2002). Walnut trees were known for killing or damaging plants that grew nearby—this effect is commonly referred to as "walnut wilt"; however, the cause of walnut wilt remained largely unknown for centuries. It was not until the 1850s that juglone (then termed "nucin") was first isolated from the walnut tree (Vogel & Reischauer 1856), and in 1881 the first scientific report on juglone's allelopathic effect was published (Stickney & Hoy 1881). In 1887, juglone was for the first time synthesized and characterized (Bernthsen & Semper 1887) and in 1928 the compound was identified and confirmed to be toxic to other plants (Davis 1928). Despite these findings, the allelopathic nature of the walnut tree and toxicity of juglone were questioned and heavily debated over many decades because of the incidence of varying results obtained by different research groups (MacDaniels & Muenscher 1941; MacDaniels & Pinnow 1976; De Scisciolo et al. 1990), but also because of the availability of anecdotal evidence and old myths. It appeared that the allelopathic effect of juglone was affected by many causes, including edaphic factors such as pH, texture, and organic matter (De Scisciolo et al. 1990; von Kiparski et al. 2007). One research group was able to isolate bacteria that could degrade juglone in soil (Inouye & Leistner 1988) and another study showed that certain *Pseudomonas* species are capable of using juglone as their only source of carbon (Schmidt 1988).

Numerous natural processes reduce juglone persistence in the environment, and allelopathy depends on the juglone concentration in the soil in the locations where the

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compound meets the roots of the target plant (von Kiparski et al. 2007). Still, juglone's persistence in the field has on several occasions been recommended for use in walnut alley agroforestry system management (von Kiparski et al. 2007). The allelopathic nature of juglone and the walnut tree is acknowledged by the majority of research groups in the scientific community; this acceptance likely comes from the large extent of research done on the topic (Lee & Campbell 1969; Sherman 1971; Soderquist 1973; Willis 1985; Jose & Gillespie 1998; Jose 2002; Terzi 2008; Li et al. 2010); however, some scientists still consider allelopathy a controversial concept, even though the toxicity of juglone is widely recognized (Macías et al. 2007).

Historical uses and reported properties

The use of walnut tree has historically been and still is widespread geographically around the world, especially within the field of traditional medicine (Leclerc 1976; Bruneton 1993). For example, the hulls of the walnut have been used as a remedy for parasites, ringworm, and other fungal infections, itchy and restless feet, to heal ulcers, skin eruptions and cracks in the palms of the hands (Morton 1974; Kirtikar et al. 1975). In the early 1900s, American doctors prescribed juglone for the treatment of various skin diseases (Soderquist 1973) and in southern America it was common practice to throw fresh, unripe husks from the walnut tree into ponds to stun fish so they could be easily collected (Gries 1943). In the Indian, Greek, and Arab cultures, the walnut tree has been used extensively to treat common illnesses and cancer (Sharma et al. 2009). In some countries, parts of the walnut tree have been used as a toothbrush and as a dye for colouring lips and hair (Alkhawajah 1997); juglone has been also been reported as an active ingredient in hair colour (Ghosh & Sinha 2008). Elixirs from parts of the walnut tree were reported to be astringent and keratolytic (Bézanger-Beauquesne et al. 1990), antifungal (Nahrstedt et al. 1981), antimicrobial (Clark et al. 1990; Sharma et al. 2009), antidiarrheal, anthelmintic, depurative and tonic (Wichtl 1994), antihemorrhagic (Dorland 1981), anti-scrofulous (Fournier 1948), hypoglycemic (Neef et al. 1995), diuretic, laxative, blood purifying, and detoxifying (Haque et al. 2003; Bhatia et al. 2006; Stampar et al. 2006). Other reported effective uses: antiviral against Vesicularis Stomatitis Virus (Husson et al. 1986), vascular protective (Perusquia et al. 1995), inhibitory to tumours (Bhargava & Westfall 1968), and sedative for animals (Westfall et al. 1961; Auyong et al. 1963; Girzu et al. 1998a). Still, what may be of the highest significance to agroforestry system management is the effect that juglone exerts on neighbouring plant life (von Kiparski et al. 2007). The most commonly reported symptoms of walnut toxicity range from stunting of growth via partial or total wilting to death of the affected plant (Leuty 2010). Such adverse effects are selective to specific genera of plant life and are discussed below (see the "Effects on various plant species"). However, toxicity is not limited to the Plant kingdom, as select members of the Protista, Fungi, and Animal groupings may also be controlled or killed by juglone or its extracts. Before we discuss these effects, we summarize the origins and localization of this quinone metabolite, with a specific focus on the geography of western Canada.

Origins in nature

Juglone is produced by the numerous species of walnut tree, including the black walnut (*Juglans nigra*), English or Persian walnut (*J. regia*), and Japanese walnut (*J. sieboldiana*), and also by the butternut (*J. cinerea*) and hickory tree (*Carya ovata*) (Soderquist 1973). Several research groups have reported finding juglone in plant families such as Proteaceae (Moir & Thomson 1973), Caesalpiniaceae (Nageshwar et al. 1984; Lee & Lee 2006), and

Fabaceae (Marichkova & Kumanova 1981). Most studies refer to the use of *Juglans nigra* for isolation of juglone and allelopathic studies because this particular species produces the largest amount of juglone (Cassens 2005; Leuty 2010).

Juglone in British Columbia

Since the arrival of the early settlers, different kinds and varieties of nuts have been grown in the more temperate areas of British Columbia. Tree nuts can be grown in the same areas where tree fruits grow: southern Vancouver Island, the Fraser Valley, the Okanagan and West Kootenay, and even in the Peace River area. The most successful kinds of nuts in British Columbia include butternuts, buartnuts, chestnuts, filberts, heartnuts, and walnuts. Of the walnuts, the Carpathian, Japanese, and black are predominant commercially. Early attempts at commercial walnut production in the Fraser Valley, the Okanagan, and the Kootenays were thwarted by silver-thaws, winter injury, competing land uses, and the non-precocious nature of the walnut; however, this has changed as agricultural techniques have improved.

Localization of production

Juglone (or its precursors) is produced mainly in the walnut tree's roots and hulls (Lee & Campbell 1969), but it is also found in fresh leaves (Lee & Campbell 1969; Bruneton 1993; Girzu et al. 1998a, 1998b; Solar et al. 2006), stem bark (Mouhajir et al. 2001), husks (Binder et al. 1989; Buttery et al. 2000; Fukuda et al. 2003; Stampar et al. 2006), and inner root bark (Hedin et al. 1979). In addition, juglone can be found in the soil surrounding the walnut tree (De Scisciolo et al. 1990), but no juglone has been found to occur in the edible walnut itself (Ikekawa et al. 1967). Table 1 shows the juglone content in various parts of the walnut tree.

Table 1: Juglone content in various parts of the walnut tree, including seasonal variation (Lee & Campbell 1969)

Juglone content		Seasonal variation in juglone content		
Tree part	**mg/g dry wt**	**Month**	**mg/g dry hulls**	**mg/g dry leaves**
Leaves	1.23	June	9.3	2.9
Hulls	6.71	July	10.3	2.8
Roots	7.73	August	11.5	2.5
		September	10.9	1.8

Toxic forms of juglone

As with most plants that produce toxic secondary metabolites, juglone is stored in a non-toxic form in the walnut tree. In 1943, juglone was shown not to be present in the inner root bark and husks, but rather in the α–hydrojuglone form that is non-toxic and upon exposure to air becomes oxidized to juglone (Gries 1943). Less than a decade later, Daglish's group discovered that juglone is stored in the walnut tree as the 5-glucoside of 1,4,5-tri-hydroxynaphthalene (Daglish 1950). The glucoside was demonstrated to be extremely labile and easily hydrolyzed to glucose and α–hydrojuglone. Figure 1 illustrates the conversion of the glucoside to juglone, a proposed two-step process with ß-glucosidase (a common soil enzyme) catalyzing the hydrolysis in the first step and fast chemical oxidation in the second step (Duroux et al. 1998).

Transport and potential biological pathways

A compound can travel to the target organism through several routes. These include evaporation or rainwash from leaf surfaces, secretion from roots, and decaying tree material (Soderquist, 1973). The *root theory*, first proposed in the first half of 20th century, stipulates that the juglone is released via plant roots (Cook 1921; Massey 1925). In 1958, Bode's group suggested a different route called *leaf theory*, indicating the release via leaves (Bode 1958). The most likely pathway encompasses a combination of both theories, since juglone is produced in several parts of the walnut tree (roots, hulls, fresh leaves, husks, and inner root bark). Furthermore, juglone toxicity depends on its accumulation and concentration in the soil where it comes in contact with the roots of the target plant (von Kiparski et al. 2007). This accumulation of the quinone can, via active planning and agroforestry management, be applied to limit or control growth of certain species, whether plant, insect, or fungal, in the specific geographical proximities to juglone-producing trees.

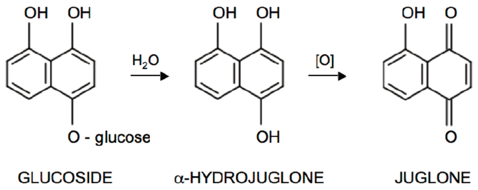

Figure 1: Conversion of glucoside to juglone in the walnut tree (Soderquist 1973).

Chemical class and composition

Juglone is a naphthoquinone, an aromatic organic compound that is commonly found in nature—the most widespread naphthoquinones are juglone, lawsone, plumbagin, and lapachol (Babula et al. 2009). It has a distinct phenyl group and is not the only phenolic compound produced by the walnut tree; other phenolic compounds include flavonoids, terpenoids, other naphthoquinones and examples are gallic acid, caffeic acid, myricetin, and quercetin (Nahrstedt et al. 1981; Hirakawa et al. 1986; Wichtl & Anton 1999; Sharma et al. 2009). Juglone is also the compound responsible for yellow pigmentation in the walnut tree (Inbaraj & Chignell 2004).

Juglone was historically known as a secondary metabolite and allelochemical—that is a compound classified as not required for the growth, development, and reproduction of an organism where it is produced, but instead is believed to have a biological effect often on other organisms. This notion has been challenged with a study suggesting that juglone may also play a role in plant development, thus making it a primary metabolite (Duroux et al. 1998). Further evidence is needed to support this process and additional studies are currently under way.

Biosynthesis

The biosynthesis of juglone has not been fully established, but the shikimate pathway has been suggested as a likely candidate (Babula et al. 2009), since various key precursors include 1,4-naphthoquinone (Müller & Leistner 1976; Dey & Harborne 1997; Seigler 1998), o-succinylbenzoic acid (Dansette & Azerad 1970; Seigler 1998) [Figure 2], and 2-succinyl-

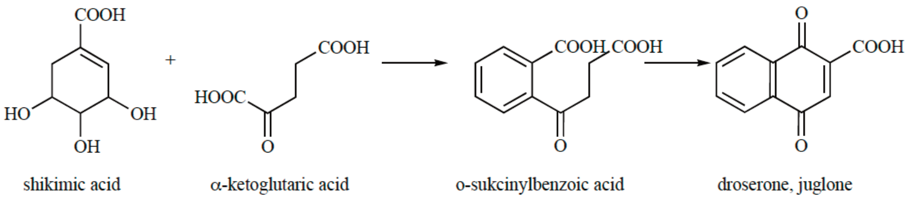

Figure 2: Biosynthesis of juglone (Babula et al. 2009).

benzoate (Dey & Harborne 1997). Figure 2 illustrates the biosynthesis of juglone with o-succinylbenzoic acid as the key precursor.

Mode of toxic action

The mechanism for the toxic effects of juglone is still not fully understood, and the mode of action may be different in various organisms. Several pathways have been suggested including cell death, cell cycle disruption, DNA modifications (predominantly rapid dividing cells), inhibition of mRNA synthesis, alkylation of thiol or amine groups of essential proteins, and decreasing levels of p53 (tumour suppressor) (O'Brien 1991; Paulsen & Ljungman 2005). H^+-ATPase inhibition is a possible mechanism (Hejl & Koster 2004) as well as K^+ channel blocking (Varga et. al. 1996). Juglone can also be reduced by enzymes in the mitochondria or cytoplasm to form a semiquinone radical (Inbaraj & Chignell 2004). Juglone can be regenerated in a process called redox cycling and this produces hydrogen peroxide, which is a strong oxidant and can cause oxidative damage to the cell (Inbaraj & Chignell 2004). The high toxicity of juglone compared to other naphthoquinones has been suggested to correlate with its high redox potential of -93mV (O'Brien 1991). Juglone also has high electrophilicity and thiol reactivity, which can cause irreversible protein complexation, especially in cysteine-rich proteins that are important for mitosis (von Kiparski et al. 2007; Fila et al. 2008).

Properties of juglone as related to various living organisms and plant species

Many naphthoquinones, including juglone, have been demonstrated to exhibit a broad range of toxic effects that are associated with inhibition of growth, photosynthesis and respiration, reduced water transport in plants, larval development dysfunction, mitochondrial damage in insect muscles, sedative/depressant/carcinogenic/mutagenic/lethal effects on fish and animals, antimicrobial, antifungal, cytotoxic, and anti-parasitic effects (Westfall et al. 1961; Auyong et al. 1963; Krajci & Lynch 1978; Clark et al. 1990; Galey et al. 1991; Hejl & Koster 2004; Cassens 2005; Paulsen & Ljungman 2005; Kong et al. 2008; Babula et al. 2009; Leuty 2010).

More recent studies (summarized below) have focussed on the toxicity of juglone and other naphthoquinones toward insects (Mitchell & Smith 1988; Ahmad 1992; Thiboldeaux et al. 1994, 1998), microorganisms (Krajci & Lynch 1978; Clark et al. 1990; Preira et al. 2007; Kong et al. 2008; Sharma et al. 2009), marine organisms (Marking 1970; Faimali et al. 2006; Wright et al. 2007a), and animals (Westfall et al. 1961; Auyong et al. 1963; Galey et al. 1991; Cassens 2005) as opposed to plants. Further studies on juglone for medicinal purposes have also been conducted recently (Krajci & Lynch 1978; Clark et al. 1990; Kong et al. 2008; Babula et al. 2009).

Effects on various plant species

Allelopathic studies have been done on various vegetables, field crops, fruit trees, ornamental species, and medicinal plants (Cook 1921; Massey 1925; Pirone 1938; Reinking 1943; Strong 1944; Brooks 1951; Sherman 1971; MacDaniels & Pinnow 1976; Scott & Sullivan 2007; Li et al. 2010). Many species are reported to be negatively influenced by the walnut tree, but some appear unaffected (Funt & Martin 1993; Leuty 2010). Table 2 provides examples of plant species having an immunity to juglone as well as those most affected by the compound. Plants such as asparagus, cabbage, tomato, magnolia, alfalfa, eggplant, potato, peonies, and blueberries, and trees, including white birch, linden, and white pine, are all negatively affected by the compound, whereas onion, beets, parsnip, lima beans, snap beans, various *Prunus* fruit trees, raspberry, squash, and corn are not affected. Various flowers species (alliums, crocus, daffodils, hyacinth, and tulips) are hardly affected.

Table 2: Influence of juglone on some plants (Funt & Martin 1993; Leuty 2010)

Negatively affected	Unaffected or hardly affected
Asparagus officinalis (asparagus) *Betula papyrifera* (white birch trees) *Brassica oleracea* (cabbage) *Lycopersicon esculentum* (tomato) *Magnolia* x *soulangiana* (saucer magnolia) *Medicago sativa* (alfalfa) *Solanum melongena* (eggplant) *Solanum tuberosum* (potato) *Paeonia* (some peonies) *Pinus strobus* (white pine) *Tilia americana* (linden trees) *Vaccinium* (blueberries)	*Allium cepa* (onion) *Beta vulgaris* (beets) *Pastinaca sativa* (parsnip) *Phaseolus zinnia* (lima and snap beans) *Prunus* spp. (cherries, nectarine, peach, and plum) *Rubus occidentalis* (black raspberry) Most squashes *Zea mays* (sweet corn) Most of the hardy, fall-planted bulbs, including alliums, crocus, daffodils, hyacinth, tulips, and a series of ornamental plants

In some agronomic crops, including maize (*Zea mays* L.) and soybeans (*Glycine max* L. Merr), juglone has been shown to inhibit shoot and root growth rates, leaf photosynthesis, transpiration, respiration and stomatal conductance (Hejl et al. 1993; Jose & Gillespie 1998).

Effects on commercial and private agriculture in British Columbia

Plants that are commonly found in British Columbia that are sensitive to the presence of walnut in the landscape and garden include tomato, potato, pea, pear, apple, cucumber, watermelon, bean, garden cress, corn, and many ornamental ericaceous species such as rhododendron and azalea.

Effects on various insects

Studies show that the saturniid moth *Actias luna,* which prefer members of the Juglandaceae as their host, had more rapid larvae growth on a juglone-rich diet compared to a non-juglone diet. On the other hand, the moth *Callosamia promethea,* which is not naturally in contact with Juglandaceae*,* experienced reduced growth rates and a 3.6-fold decrease in consumption rate when fed juglone-supplemented diets (Thiboldeaux et al. 1994). Another study revealed that *C. promethean* experienced partial loss of epithelial structure, an increase in glutathione disulfide, and a small decrease in glutathione when fed walnut foliage (Thiboldeaux et al. 1998). Some herbivore insects that naturally consume juglone and other pro-oxidant allelochemicals produce special enzymes to prevent the generation of free-radical oxygen during quinone reduction (Ahmad 1992). Juglone also inhibits ecdysone 20-monooxygenase activity in protein extracts from larval *Aedes aegypti, Drosophila melanogaster,* and *Manduca sexta.* (Mitchell & Smith 1988).

Effects on microorganisms

Juglone has been shown to inhibit a broad spectrum of microorganisms including bacteria, algae, and fungi (Krajci & Lynch 1978). One study showed antimicrobial activity against *Pseudomonas aeruginosa, Burkholderia cepacia, Staphylococcus aureus, Bacillus subtilis, Mycobacterium smegmatis, Candida albicans, Saccharomyces cerevisiae, Helminthospo-*

rium sp., *Pycnoporus sanguineus,* and *Microsporum gypseum* (Clark et al. 1990; Preira et al. 2007; Sharma et al. 2009). The antifungal activity of juglone has also been compared to other known antifungal agents, such as griseofulvin, clotrimazole, tolnaftate, triacetin, zinc undecylenate, selenium sulfide, liriodenine, and liriodenine methiodenine (Clark et al. 1990). Clark et al. (1990) determined that juglone exhibited moderate antifungal activity similar to zinc undecylenate and selenium sulfide, which are commercially available antifungal agents. Furthermore, the compound's antimicrobial activity was established to be low to moderate, with moderate activity against Gram-positive and acid-fast bacteria and no to low activity against Gram-negative bacteria. Another study showed that juglone potentially can inhibit three key enzymes from *Helicobacter pylori*, a Gram-negative bacterium that causes several human diseases (Kong et al. 2008). Several algae species are inhibited by juglone, including *Anabaena variabilis* and *Anabaena flos-aquae* (significantly inhibited), *Nostoc commune* (moderately inhibited), and *Scenedesmus acuminatus* (slight inhibition) (Krajci & Lynch, 1978; Randall & Bragg 1986).

Effects on marine organisms

Marking (1970) discovered that juglone was an effective fish toxicant. His studies showed juglone was highly toxic to nine species of fish, including rainbow trout (*Salmo gairdneri*), northern pike (*Esox lucius*), goldfish (*Carassius auratus*), carp (*Cyprinus carpio*), white sucker (*Catostomus commersoni*), black bullhead (*Ictalurus melas*), channel catfish (*Ictalurus punctatus*), green sunfish (*Lepomis cyanellus*), and bluegill (*Lepomis macrochirus*) at concentrations ranging from 27 to 88 parts per billion over a 96-hour period. In a study conducted to screen natural product biocides for the control of non-indigenous species, juglone scored high. For example, in five out of six taxonomic groups tested, juglone was among the most toxic (Wright et al. 2007a).

Effects on animals

Lethal doses (LD_{50}) of 0.25 mg juglone/100 g bodyweight in mice and rats have been reported and injection of 0.07 mg juglone/kg body weight in rabbits resulted in tranquilization for 2–3 hours (Westfall et al. 1961). In this study, a difference between the crude and the purified extract was noted, further indicating influence of other compounds in the crude extract. Laminitis in horses that were in contact with debris from walnut trees has also been reported (Galey et al. 1991; Cassens 2005; Belknap 2010).

Applications in agroforestry management

Various examples of the compound and its inhibitory role in nature, as mentioned above, can be applied as specific case studies in the agroforestry management system. The evaluation of both nutrient and non-nutrient resource interactions provides information needed to sustainably manage agroforestry systems. Improved diagnosis of appropriate nutrient usage can help increase crop yields and also reduce financial and environmental costs. To achieve this, a management support system that allows for site-specific evaluation of nutrient-production imbalances needs to be established.

Since juglone is not particularity water soluble, it does not readily leach through soil settings but instead can persist underneath the tree canopy where living roots are located. After walnut trees are removed from a site or die, toxicity can persist for up to 1 year following removal owing to the persistence of juglone in the soil.

Linking crop performance to appropriate nutrient application and compound inhibition, along with quantifying existing nutrient cycles and interactions, will not only have the economic advantage of increasing yields but will also diminish financial and environmental costs, as well as negative competition impacts (Issac & Kimaro 2011). Common examples of such linkages, using intercropping systems via vector analysis, are found in field trials of cocoa and pigeon pea but are easily applied to corn, flax, wheat and barley, among others.

Known medicinal properties

Juglone has antifungal properties similar to some commercially available antifungal agents used to treat infections, such as athlete's foot and ringworm (Clark et al. 1990). One study showed that juglone inhibits three key enzymes from *Helicobacter pylori*, a bacterium that can cause gastritis, peptic ulceration, and gastric cancer in humans. This bacterium affects approximately 50% of the world's population and antibiotic resistance is a rising problem. Juglone could become a new antibacterial agent to treat infections from this bacterium (Kong et al. 2008). Recent data suggest juglone could be a promising chemo-preventive agent for human intestinal neoplasia (Sugie et al. 1998) and anti-tumour properties have been reported (Bhargava & Westfall 1968; O'Brien 1991; Paulsen & Ljungman 2005; Xu et al. 2010). Finally, juglone has been noted to block K channels in human lymphocytes—a state often associated with lymphocyte depolarization (Varga et al. 1996).

Common extraction methods

Typical juglone extraction methods use leaves, hulls, and bark material from the black walnut tree and maceration in an organic solvent followed by solvent evaporation, or from the soil beneath the walnut tree. The best extraction solvents for fresh walnut hulls appeared to be petroleum ether or hexane (more expensive), whereas for leaf and bark material chloroform was the most frequently used solvent. Yield appears to depend on temperature; the higher the temperature, the lower the yield.

Common synthesis methods

Juglone is most commonly synthesized from 1,5-dihydroxynaphthalene by oxidation (Figure 3; Table 4).

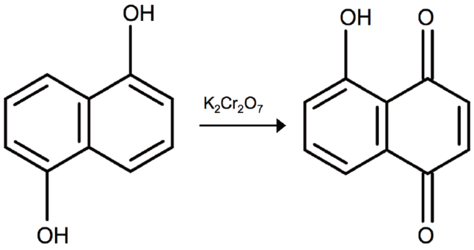

Figure 3: Oxidation of 1,5-naphthalenediol (also known as 1,5-dihydroxynapthalene) to juglone.

Table 3: Summary of synthesis procedures

Reactant	Yield	Reference
Sodium dichromate $Cr_2O_7^{2-}$	~10%	Jesaitis & Krantz (1972)
$C_6H_5IO_2$ C_6H_5IO $C_6H_5(OCOCH_3)_2$ $C_6H_5I(OCOCF_3)_2$ $C_6F_5I(OCOCF_3)_2$ $C_6F_{13}I(OCOCF_3)_2$	30% 47% 26% 58% 76% 91%.	Barret & Daudon (1990)
tert-butyl hydroperoxide	70%	Taylor & Flood (1983)

Characterization of juglone

Table 4 presents the chemical characteristics of the juglone molecule.

Table 4: Chemical characteristics of juglone molecule

		Reference
Formula	$C_{10}H_6O_3$	National Institute of Standards and Technology
Molecular weight	174.15 g/mol	National Institute of Standards and Technology
Chemical Abstracts Service Registry No.	481-39-0	National Institute of Standards and Technology
International Union of Pure and Applied Chemistry nomenclature	5-hydroxy-1,4-naphthoquinone	
Melting point	151°C	Jesaitis & Krantz (1972)
	153–154°C	Barret & Daudon (1990)
	155°C	Budavari (1997)
	161–163°C	Aldrich Chemical Company
Aqueous solubility	52 mg/L	Weidenhamer et al. (1993)
K_{ow}	≈2	Wright et al. (2007b)
pK_a	8.85	Palit et al. (1986)
K_H	2.58×10^{-8} atm m^3 mol^{-1}	von Kiparski et al. (2007)
Infrared (IR)	3300–3600, 1670, 1645 cm^{-1}	Barret & Daudon (1990)
Nuclear magnetic resonance (NMR)	($CDCl_3$, 60MHz) ppm: 7.5 (s), 7.2 (m), 6.8 (s)	Barret & Daudon (1990)
UV-visible	l_{max}: 420 nm in methanol	Girzu et al. (1998b)
	209, 249, and 421 nm	Wright et al. (2007b)
Gas Chromatography retention time	9.1 min	Girzu et al. (1998b)
Redox potential	–93mV	Wright et al. (2007b)
Physical properties	Yellow insoluble solid Photodegradable	Wright et al. (2007b)

Stability of juglone

Numerous studies have explored the fate of juglone in the environment, including the degradation of juglone in soil (De Scisciolo et al. 1990; von Kiparski et al. 2007), effect of wood-dwelling organisms (Curreli et al. 2004), fate in natural waters (effect of pH, microbial activity, photolysis, salinity, and octanol:water partitioning) (Wright et al. 2007b), and degradation in different solvents (Sharma et al. 2009).

Juglone is reported to degrade in certain solvents and aquatic conditions that include acetonitrile, methanol, acidic solutions, alkaline solutions, and saline water (Marking 1970; Girzu et al. 1998b; Hadjmohammadi & Kamel 2006; Wright et al. 2007b); however, juglone is reported to be more persistent under acidic conditions (De Scisciolo et al. 1990; Wright et al. 2007b).

Potential uses

The use of natural products is associated with preservation of the environment, thus supporting a sustainable natural resource management. Juglone is a natural product that has shown a multitude of properties that are deemed beneficial in the fields of medicine, farming, and aquaculture. In British Columbia, especially in the regions where juglone-growing species are readily found (southern Vancouver Island, the Fraser Valley, the Okanagan and

West Kootenay, and Peace River area), the presence of walnut trees in particular has a natural inhibiting effect on several species, and hence acts as a natural agroforestry growth-limiting factor. Furthermore, even if these trees are removed or die, the toxicity can persist for up to 1 year owing to the persistence of juglone in the soil. As such, a juglone derivative, or even juglone itself (readily available as a compound), can be used for site-specific growth control in the areas where it is deposited or sprayed. The use of juglone compound in such cases would not be geographically limiting; the main impact factor would be the cost and the ease of application.

Uses in medicine

The use of juglone in medicine is limited because of its sedative effect on animals, though it could be used externally (fungal, bacterial, and viral infections). More studies are needed on juglone and its anti-tumour properties.

Herbicide

A likely potential use of juglone is as a herbicide. Juglone could possibly be used in weed management, as it is harmful to many weeds but not to all cultivated plants (Topal et al. 2007; Shrestha 2009). Black walnut extracts have also been suggested as a pre- and post-emergence bioherbicide (Shrestha 2009). Similarly, it can be applied to various crops, especially in Canadian agricultural environments. As noted previously, the use of mapping and intercropping systems to manage or improve yields of specific plant species with the aid of natural herbicide, even if marginally cost effective, can be considered an organic alternative.

Biocide

Invasive marine species transported in ballast water are a well-studied global threat on ecosystems and environments alike. Several treatment methods are suggested and these include chemical (ozone, bleach, chlorination, glutaraldehyde), UV radiation, heat, and filtration, but they all have implications (Faimali et al. 2006; Wright et al. 2007a). An effective treatment method with low environmental impact would be ideal and juglone, along with a few other naphthaquinones, are suggested as potential candidates. These compounds show significant toxicity towards both eukaryotes and prokaryotes, and methods for fish culture and treatment of aquatic pests, both using juglone, were patented in 2000 (Patent No. 6,164,244 and No. 3,602,194; Cutler et al. 2000, 2002). Juglone was identified for commercial use because of its broad toxic effects at low concentrations (Wright et al. 2007a). Other positive properties of juglone include biodegradability with non-toxic degradation products, enhanced degradation in sunlight, and short half-lives ranging from a few hours to less than 2 days in natural saline waters (Wright et al. 2007b). The potential for additional applications is not limited only to agroforestry practices, given quinone's effectivness and short half-life.

Conclusion

Juglone is a compound with a long history and multitude of uses throughout various geographic locations; such longevity of usage has yielded a set of well-defined characteristics that include select toxicity towards plant species, microorganisms, and animals, specific stability in various chemical conditions, defined purity, well-established isolation methods, and agreed-upon chemical structure. Its applications in agroforestry management are closely tied to the scope of available data, and given that the compound has been well characterized to date, it is indicative that its uses can be applied to various crop management methodologies worldwide. In British Columbia, Canada, walnut trees have been used as natural biocide and herbicide supplements in the areas in which they can grow—this scope could be expanded with a simple cost-analysis model and complementary data sets that show juglone's effectiveness as a natural agroforestry management factor. What remains to be further explored are the biosynthesis pathways as well as additional insights into the mechanisms of action, including the pathways of juglone's byproducts and secondary products. Having insight into its modes of action would potentially increase the spectrum of juglone use, in addition to allowing the scientific and commercial communities alike a better understanding of its versatile pathways, some with potential for cross-application in other sectors of the industry, especially agriculture and aquaculture. Although the future uses of juglone remain to be seen, the amount of data and research conducted to date indicate a high demand for such a resourceful agent.

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References

Ahmad, S. 1992. Biochemical defense of pro-oxidant plant allelochemicals by herbivorous insects. Biochemical Systematics and Ecology 20:269–296.

Alkhawajah, A.M. 1997. Studies on the antimicrobial activity of *Juglans regia*. American Journal of Chinese Medicine 25:175–180.

Auyong, T.K., B.A. Westfall, & R.L. Russell. 1963. Pharmacological aspects of juglone. Toxicon 1:235–239.

Babula, P., V. Adam, L. Havel, & R. Kizek. 2009. Noteworthy secondary metabolites naphthoquinones: Their occurrence, pharmacological properties and analysis. Current Pharmaceutical Analysis 5:47–68.

Barret, R., & M. Daudon. 1990. An efficient synthesis of juglone. Synthetic communications 20(18):2907–2912.

Belknap, J.K. 2010. Black walnut extract: An inflammatory model. Veterinary Clinics of North America: Equine Practice 26(1):95–101.

Berntsen, A., & A. Semper. 1887. Ueber die constitution des juglons und seine synthese aus naphtalin. Berichte der Deutschen Chemischen Gesellschaft 20:934–941.

Bézanger-Beauquesne, L., M. Pinkas, M. Torck, & F. Trotin. 1990. Plantes Médicinales des Régions Tempérées. 2nd ed. Maloine, Paris. p. 58.

Bhargava. U., & B. Westfall. 1968. Antitumor activity of *Juglans nigra* (black walnut) extractives. Journal of Pharmaceutical Sciences 57:1674–1677.

Bhatia, K., S. Rahman, M. Ali, & S. Raisuddin. 2006. In vitro antioxidant activity of *Juglans regia* L. bark extract and its protective effect on cyclophosphamide-induced urotoxicity in mice. Redox Report 11:273–279.

Binder, R.G., M.E. Benson, & R.A. Flath. 1989. Eight 1,4-naphtoquinones from *Juglans regia*. Phytochemistry 28:2799–2801.

Bode, H.R. 1958. Beiträge zur Kenntnis allelopathischer Erscheinungen bei einigen Juglandaceen. Planta 51:440–480.

Brooks, M. 1951. Effects of black walnut trees and their products on other vegetation. West Virginia University, Morgantown, WV. Agricultural Extension State Bulletin No. 347.

Bruneton, J.P. 1993. Phytochimie. Plantes médicinales. 2nd ed. Lavoisier, Paris. pp. 348; 556–558.

Budavari, S. 1997. The Merck index: An encyclopedia of chemicals, drugs, and biologicals. 12th ed. Whitehouse Station, NJ.

Buttery, R.G., D.M. Light, Y. Nam, G.B. Merrill, & J.N. Roitman. 2000. Volatile components of green walnut husks. Journal of Agricultural and Food Chemistry 48:2858–2861.

Cassens, L.D. 2005. Laminitis caused by black walnut wood residues. Purdue Extension, West Lafayette, IN. http://www.ces.purdue.edu/extmedia/FNR/FNR-254.pdf (Accessed February 2011).

Clark, A.M., T.A. Jurgens, & C.D. Hufford. 1990. Antimicrobial activity of juglone. Phytotherapy Research 4(1):1–14.

Cook, M.T. 1921. Wilting caused by walnut trees. Phytopathology 11:346.

Curreli, N., A. Rescigno, A. Rinaldi, B. Pisa, F. Sollai, & E. Sanjust. 2004. Degradation of juglone by *Pleurotus sajor-caju*. Mycological Research 108:913–918.

Cutler, H.G., N.A. Belson, R. Dawson, & D.A. Wright. 2000. Method for treating aquatic pests. US Patent 6,164,244, pp. 164–244.

Cutler, H.G., S.J. Cutler, R. Dawson, & D.A. Wright. 2002. Method of controlling zoological and aquatic plant growth. US Patent 3,602,194, pp. 340–468.

Daglish, C. 1950. The determination and occurrence of hydrojuglone glucoside in the walnut. Biochemical Journal 47:458–462.

Dansette, P., & R. Azerad. 1970. A new intermediate in naphthoquinone and menaquinone biosynthesis. Biochemical and Biophysical Research Communications 40(5):1090–1095.

Davis, E.F. 1928. The toxic principle of *Juglans nigra* as identified with synthetic juglone, and its toxic effects on tomato and alfalfa plants. American Journal of Botany15:620–621.

De Scisciolo, B., D.J. Leopold, & D.C. Walton. 1990. Seasonal patterns of juglone in soil beneath *Juglans nigra* (black walnut) and influence of *J. nigra* on understory vegetation. Journal of Chemical Ecology 16:1111–1130.

Dey, P.M., & J.B. Harborne. 1997. Plant biochemistry. Academic Press, San Diego, CA.

Dorland, N.W. 1981. Dorland's illustrated medical dictionary. 26th ed. W.B. Saunders Company, Philadelphia, PA. p. 691.

Duroux, L., F.M Delmotte, J.M. Lancelin, G. Keravis, & C. Jay-Allemand. 1998. Insight into naphthoquinone metabolism: Beta-glucosidase-catalyzed hydrolysis of hydrojuglone beta-D-glucopyranoside. Biochemical Journal 333:275–283.

Faimali, M., F. Garaventa, E. Chelossi, V. Piazza, O.D. Saracino, F. Rubino, G.L. Mariattini, & L. Pane. 2006. A new photodegradable molecule as a low impact ballast water biocide: Efficacy screening on marine organisms from different trophic levels. Marine Biology 149:7–16.

Fila, C., C. Metz, & P. van der Sluijs. 2008. Juglone inactivates cysteine-rich proteins required for progression through mitosis. Journal of Biological Chemistry 283:21714–21724. http://www.jbc.org/content/283/31/21714.full.pdf [June 2012].

Fournier, P. 1948. Le Livre des Plantes Médicinales et Vénéneuses de France, tome III Lechevalier, Paris. p. 104.

Fukuda, T., H. Ito, & T. Yoshida. 2003. Antioxidative polyphenols from walnuts (*Juglans regia* L.). Phytochemistry 63:795–801.

Funt, R.C., & J. Martin. 1993. Black walnut toxicity to plants, humans and horses. Ohio State University, Columbus, OH. Extension Fact Sheet HYG-1148–93.

Galey, F.D., H.E. Whiteley, T.E. Goetz, A.R. Kuenstler, C.A. Davis, & V.R. Beasley. 1991. Black walnut (*Juglans nigra*) toxicosis: A model for equine laminitis. Journal of Comparative Pathology 104:313–326.

Ghosh, P., & A.K. Sinha. 2008. Hair colors: Classification, chemistry and a review of chromatographic and electrophoretic methods for analysis. Analytical Letters 41:2291–2312.

Girzu, M., A. Carnat, A.-M. Privat, J. Fialip, A.-P. Carnat, & J.-L. Lamaison. 1998a. Sedative effect of walnut leaf extract and juglone, an isolated constituent. Pharmaceutical Biology 36(4):280-286.

Girzu, M., D. Fraisse, A.-P. Carnat, A. Carnat, & J.-L. Lamaison. 1998b. High performance liquid chromatographic method for the determination of juglone in fresh walnut leaves. Journal of Chromatography A 805:315–318.

Gries, G.A. 1943. Juglone, the active agent in walnut toxicity. Northern Nut Growers Association Annual Report 34:52–55.

Hadjmohammadi, M.R., & K. Kamel. 2006. Determination of juglone (5-hydroxy 1,4,-naphthoquinone) in *Pterocarya flaxinifolia* by RP-HPLC. Iranian Journal of Chemistry and Chemical Engineering 25:73–76.

Haque, R., B. Bin-Hafeez, S. Parvez, S. Pandey, I. Sayeed, M. Ali, & S. Raisuddin. 2003. Aqueous extract of walnut (*Juglans regia* L.) protects mice against cyclophosphamide-induced biochemical toxicity. Human and Experimental Toxicology 22:473–480.

Hedin, P.A., V.E Langhans, & C.H. Graves. 1979. Identification of juglone in pecan as a possible factor of resistance to *Fusicladium effusum*. Journal of Agriculture and Food Chemistry 27:92–94.

Hejl, A.M., A.E. Frank, & A.R. James. 1993. Effects of juglone on growth, photosynthesis and respiration. Journal of Chemical Ecology 19(3):559–567.

Hejl, A.M., & L.L. Koster. 2004. Juglone disrupts root plasma membrane H+-ATPase activity and impairs water uptake, root respiration, and growth in soybean (glycine max) and corn (*Zea mays*). Journal of Chemical Ecology 30(2):453–469.

Hirakawa, K., E. Ogive, J. Motoyoshiya, & M. Yajima. 1986. Napthaquinones from Juglandaceae. Phytochemistry 25:1494–1495.

Husson, G.P., R. Vilagines, & P. Delaveau. 1986. Recherche des propriétés antivirales de quelques extraits d'origine naturelle. Annales Pharmaceutiques Francaises 44:41–48.

Ikekawa, T., W.E. Lin, M. Hamada, T. Takeuchi, & H. Umezawa. 1967. Isolation and identification of the antifungal active substance in walnuts. Chemical and Pharmaceutical Bulletin 15(2):242–245.

Inbaraj, J.J., & C.F. Chignell. 2004. Cytotoxic action of juglone and plumbagin: A mechanistic study using HaCaT keratinocytes. Chemical Research in Toxicology 17(1):55–62.

Inouye, H., & E. Leistner. 1988. Biochemistry of quinones. In: The quinonoid compounds. S. Patai and Z. Rappoport (editors). John Wiley & Sons, New York, NY. Vol. 2, pp. 1293–1349.

Isaac, M., & A. Kimaro. 2011. Diagnosis of nutrient imbalances with vector analysis in agroforestry systems. Journal of Environment Quality 40(3):860.

Jesaitis, R.G., & A. Krantz. 1972. Juglone: An organic chemistry-ecology interaction experiment. Journal of Chemical Education 49:436–437.

Jose, S. 2002. Black walnut allelopathy: Current state of science. In: Chemical ecology of plants: Allelopathy in aquatic and terrestrial ecosystems. A.U. Mallik and Inderjit (editors), pp. 149–172. Birkhauser-Verlag, Switzerland.

Jose, S., & A.R. Gillispie. 1998. Allelopathy in black walnut (*Juglans nigra* L.) alley cropping. II. Effects of juglone on hydroponically grown corn (*Zea mays* L.) and soybean (*Glycine max* L. Merr) growth and physiology. Plant and Soil 203:199–205.

Kirtikar, S., B. Basu, E. Blatter, J. Cauis, & K. Mhaskar. 1975. Juglandaceae. Indian Medicinal Plants 3:2347–2349.

Kong, Y., L. Zhang, Z. Yang, C. Han, L. Hu, H. Jiang, & X. Shen. 2008. Natural product juglone targets three key enzymes from *Heliobacter pylori*: Inhibition assay with crystal structure characterization. Acta Pharmacologica Sinica 29(7):870–876.

Krajci, W.M, & D.L. Lynch. 1978. The inhibition of various micro-organisms by crude walnut hull extracts and juglone. Microbios Letters 4:175–181.

Leclerc, M. 1976. Précis de Phytothérapie. 5th ed., pp. 105–106. Masson, Paris.

Lee, C.H., & H.S. Lee. 2006. Color alteration and acaricidal activity of juglone isolated from *Caesalpinia sappan* heartwoods against *Dermatophagoides* spp. Journal of Microbiology and Biotechnology 16(10):1591–1596.

Lee, K.C., & R.W. Campbell. 1969. Nature and occurrence of juglone in *Juglans nigra* L. Journal of Horticultural Sciences 4:31–35.

Leuty, T. 2010. Walnut toxicity. Ontario Ministry of Agriculture, Food and Rural Affairs, Toronto, Ont. http://www.omafra.gov.on.ca/english/crops/facts/info_walnut_toxicity.htm [February 2011].

Li, Q., J. Cai, Z. Jiang, & S. Zhang. 2010. Allelopathic effects of walnut leaves leachate on seed germination, seedling growth of medicinal plants. Allelopathy Journal 26(2):235–242.

MacDaniels, L.H., & W.C. Muenscher. 1941. Black walnut toxicity. Northern Nut Growers Association Annual Report 31:172–179.

MacDaniels, L.H., & D.L. Pinnow. 1976. Walnut toxicity, an unsolved problem. Northern Nut Growers Association Annual Report 67:114–122.

Macías, F.A., J.M. Molinillo, R.M. Varela, & J.C.G. Galindo. 2007. Allelopathy: A natural alternative for weed control. Pest Management Science. 63:327–348.

Marichkova, L., & B. Kumanova. 1981. Isolation of flavonoids and some accompanying substances from the above-ground part of some *Astragalus centralpinus* family Leguminosae (Russian). Problemy Farm 9:63–74.

Marking, L.L. 1970. Juglone (5-hydroxy-1,4-naphthoquinone) as a fish toxicant. Transactions of the American Fisheries Society 99(3):510–514.

Massey, A.B. 1925. Antagonism of the walnuts (*Juglans nigra* L. and *J. cinera* L.) in certain plant associations. Phytopathology 15:773–784.

Mitchell, M.J. & S.L. Smith. 1988. Effects of chitin synthetase inhibitor plumbagin and its 2-demethyl derivative juglone on insect ecdysone 20-monooxygenase activity. Experientia 44:990–991.

Moir, M., & R.H. Thomson. 1973. Naphthoquinones in *Lomatia* species. Phytochemistry 12:1351–1353.

Morton, J.L. 1974. Folk remedies of the low country, pp. 85–86. E. A. Seemann Publishing, Inc., Miami, FL.

Mouhajir, F., J.A. Pedersen, M. Rejdali, & G.H.N. Towers. 2001. Phenolics in Moroccan medicinal plant species as studied by electron spin resonance spectroscopy. Pharmaceutical Biology 39:391–391.

Müller, W., & E. Leistner. 1976. 1,4-Napthtoquinone, an intermediate in juglone (5-hydroxy-1,4-naphthoqinone) biosynthesis. Phytochemistry 12(3):407–410.

Nageshwar, G., M. Radhakrishnainah, & L.L. Narayana. 1984. Chemotaxonomy of Caesalpin. Current Science 53:813–814.

Nahrstedt, A., U. Vetter, & F.J. Hammerschmidt. 1981. Composition of the steam distillation product from the leaves of *Juglans regia*. Planta Medica 42:313–332.

Neef, H., P. Declercq, & G. Laekeman. 1995. Hypoglycaemic activity of selected european plants. Phytotherapy Research 9:45–48.

O'Brien, P.J. 1991. Molecular mechanisms of quinone cytotoxicity. Chemico-Biological Interactions 80:1–41.

Palit, D.K., T. Mukherjee, & J.P. Mittal. 1986. Photophysics and laser flash photolysis of hydroxyquinones: Studies on juglone and naphthazarin. Journal of Indian Chemical Society 63:35–42.

Paulsen, M.T., & M. Ljungman. 2005. The natural toxin juglone causes degradation of p53 and induces rapid H2AX phosphorylation and cell death in human fibroblasts. Toxicology and Applied Pharmacology 209(1):1–9.

Perusquia, M., S. Mendoza, R. Bye, E. Linares, & R. Mata. 1995. Vasoactive effects of aqueous extracts from five Mexican medicinal plants on isolated rat aorta. Journal of Ethnopharmacology 46:63–69.

Pirone, P.P. 1938. The detrimental effect of the walnut to rhododendrons and other ornamentals. Nursery Disease Notes 11:13–16.

Preira, J.A., I. Oliviera, A. Sousa, P. Valentao, P.B. Andrade, I.C.F.R. Ferreira, F. Ferreres, A. Bento, R. Seabra, & L. Estevinho. 2007. Walnut (*Juglans regia* L.) leaves: Phenolic compounds, antibacterial activity and antioxidant potential of different cultivars. Food Chemistry and Toxicology 45:2287–2295.

Randall, V.D., & J.D. Bragg. 1986. Effects of juglone (5-hydroxy-1,4-naphthoquinone) on the algae *Anabaena flos-aquae*, *Nostoc commune* and *Scenedesmus acuminatus*. Proceedings of the Arkansas Academy of Science 40:52–55.

Reinking, O.A. 1943. Possible back walnut toxicity to tomato and cabbage. Northern Nut Growers Association Annual Report 34:56–58.

Schmidt, S.K. 1988. Degradation of juglone by soil bacteria. Journal of Chemical Ecology 14(7):1561–1571.

Scott, R., & W.C. Sullivan. 2007. A review of suitable companion crops for black walnut. Agroforestry Systems 71:185–193.

Seigler, D.S. 1998. Plant secondary metabolism. 2nd ed., pp. 82–85. Kluwer Academic Publishers, Norwell, MA.

Sharma, N., P. Gosh, U.K. Sharma, S. Sood, A.K. Sinha, & A. Gulati. Microwave-assisted efficient extraction and stability of juglone in different solvents from *Juglans regia*: Quantification of six phenolic constituents by validated RP-HPLC and evaluation of antimicrobial activity. Analytical Letters 42:2592–2609.

Sherman, R.R. 1971. An ecological evaluation of the allelopathic influence of *Juglans nigra* on *Lycopersicon esculentum*. MSc thesis. Michigan State University, East Lansing, MI.

Shrestha, A. 2009. Potential of a black walnut (*Juglans nigra*) extract product (NatureCur®) as a pre- and post-emergence bioherbicide. Journal of Sustainable Agriculture 33:810–822.

Soderquist, C.J. 1973. Juglone and allelopathy. Journal of Chemical Education 50(11):782–783.

Solar, A., M. Colaric, V. Usenik, & F. Stampar. 2006. Seasonal variations of selected flavonoids, phenolic acids and quinones in annual shoots of common walnut (*Juglans regia* L.). Plant Science 170:453–461.

Stampar, F., A. Solar, M. Hudina, R. Veberic, & M. Colaric. 2006. Traditional walnut liquor-cocktail of phenolics. Food Chemistry 95:627–631.

Stickney, J.S., & P.R. Hoy. 1881. Toxic action of black walnut. Transactions of the Wisconsin Horticultural Society 11:166–167.

Strong, M.C. 1944. Walnut wilt of tomato. Michigan Agriculture Experiment Station Quarterly Bulletin 26:194–195.

Sugie, S., K. Okamoto, K.M.W. Rahman, T. Tanaka, K. Kawai, J. Yamahara, & H. Mori. 1998. Inhibitory effects of plumbagin and juglone on azoxymethane induced intestinal carcinogenesis in rats. Cancer Letters 127(1–2):177–183.

Taylor, R.T., & L.A. Flood. 1983. Polystyrene-bound phenylselenic acid: Catalytic oxidations of olefins, ketones, and aromatic systems. Journal of Organic Chemistry 48:5160–5164.

Terzi, I. 2008. Allelopathic effects of juglone and decomposed walnut leaf juice on muskmelon and cucumber seed germination and seedling growth. African Journal of Biotechnology 7(12):180–1874.

Thiboldeaux, R.L., R.L. Lindroth, & J.W. Tracy. 1994. Differential toxicity of juglone (5-hydroxy-1,4-naphthoquinone) and related naphthoquinones to saturnid moths. Journal of Chemical Ecology 20:1631–1641.

Thiboldeaux, R.L., R.L. Lindroth, & J.W. Tracy. 1998. Effects of juglone (5-hydroxy-1,4-naphthoquinone) on midgut morphology and glutathione status in Saturniid moth larvae. Comparative Biochemistry and Physiology Part C: Pharmacology, Toxicology and Endocrinology 120(3):481–487.

Topal, S., I. Kocaçaliskan, O. Arslan, & A.Z. Tel. 2007. Herbicidal effects of juglone as an allelochemical. Phyton 46(2):259–269.

Varga, Z., L. Bene, C. Pieri, S. Damjavonich, & R. Gasper, Jr. 1996. The effect of juglone on the membrane potential and whole-cell K^+ currents of human lymphocytes. Biochemical and Biophysical Research Communications 218:828–832.

Vogel, A., Jr., & C. Reinschauer. 1856. Uever einen neuen organischen Körper in den Fruchtschalen der *Juglans regia*. Neues Repertorium Für die Pharmacie 5:106–110.

von Kiparski, G.R., L.S. Lee, & A.R. Gillespie. 2007. Occurrence and fate of the phytotoxin juglone in alley soils under black walnut trees. Journal of Environmental Quality 36:709–717.

Weidenhamer, J.D., F.A. Macias, N.H. Fischer, & G.B. Williamson. 1993. Just how insoluble are monoterpenes. Journal of Chemical Ecology 19:1799–1807.

Westfall, B., R.L. Russel, T.K. Auyong. Depressant agent from walnut hulls. American Association for the Advancement of Science 134:1617.

Wichtl, M. 1994. Herbal drugs and phytopharmaceuticals, p. 282. Medpharm, Stuttgart.

Wichtl, M., & R. Anton. 1999. In: Plantes therapeutiques, pp. 291–293. Tec. & Doc, Paris.

Willis, R.J. 1985. The historical bases of the concept of allelopathy. Journal of the History of Biology 18:71–102.

Wright, D.A., R. Dawson, S.J. Cutler, H.G. Cutler, C.E. Orano-Dawson, & E. Graneli. 2007a. Napthaquinones as broad spectrum biocides for the treatment of ship's ballast water: Toxicity to phytoplankton and bacteria. Water Research 41:1294–1302.

Wright, D.A., C.L. Mitchelmore, R. Dawson, & H.G. Cutler. 2007b. The influence of water quality on the toxicity and degradation of juglone (5-hydroxy 1,4-naphthoquinone). Environmental Technology 28:1091–1101.

Xu, H.L., X.F. Yu, S.C. Qu, R. Zhang, X.R. Qu, Y.P. Chen, X.Y. Ma, D.Y. Sui. 2010. Anti-proliferative effect of juglone from juglans mandshurica maxim on human leukemia cell HL-60 by inducing apoptosis through the mitochondria-dependent pathway. European Journal of Pharmacology 645(1–3):14–22.

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Test your Knowledge

How well can you recall the main messages in the preceding article?
Test your knowledge by answering the following questions.

A Summary of Extraction, Synthesis, Properties, and Potential Uses of Juglone: A Literature Review

1. Which geographical regions of British Columbia have historically supported the growth of nut trees, specifically Carpathian, Japanese, and black walnuts?
    - a) Only Fraser Valley and Okanagan areas
    - b) Vancouver Island, Fraser Valley, Okanagan, West Kootenay, and Peace River
    - c) Fraser Valley, Okanagan, West Kootenay, and Rocky Mountain areas

2. What is a common chemical name for organic compounds juglone, lawsone, plumbagin, and lapachol?
    - a) Terpenoid
    - b) Naphthoquinone or quinone
    - c) Quiche

3. Walnut trees can produce all of the phenolic compounds mentioned below except what?
    - a) Benzene
    - b) Terpenoids
    - c) Naphthoquinones or quinones

ANSWERS: 1=b; 2=b; 3=a