Biological Activities of Extracts from Sumac (*Rhus* spp.): A Review

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Abstract. Sumac is the common name for a genus (*Rhus*) that contains over 250 individual species of flowering plants in the family Anacardiaceae. These plants are found in temperate and tropical regions worldwide, often grow in areas of marginal agricultural capacity, and have a long history of use by indigenous peoples for medicinal and other uses. The research efforts on sumac extracts to date indicate a promising potential for this plant family to provide renewable bioproducts with the following reported desirable bioactivities: antifibrogenic, antifungal, antiinflammatory, antimalarial, antimicrobial, antimutagenic, antioxidant, antithrombin, antitumorigenic, antiviral, cytotoxic, hypoglycaemic, and leukopenic. As well, the bioactive components can be extracted from the plant material using environmentally benign solvents that allow for both food and industrial end-uses. The favorable worldwide distribution of sumac also suggests that desirable bioproducts may be obtained at source, with minimal transportation requirements from the source through processing to end consumer. However, previous work has focussed on only a few members of this large plant family. In addition, not all of the species studied to date have been fully characterized for potential bioactive components and bioactivities. Thus, there remains a significant research gap spanning the range from lead chemical discovery through process development and optimization in order to better understand the full potential of the *Rhus* genus as part of global green technology based bioproduct and bioprocess research programs.

Key words: Biological activities, Extracts, *Rhus* spp., Sumac, Sustainable bioproducts

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Introduction

A central tenet of green chemistry is the ability to obtain a commercially viable product with desirable properties from a widely available renewable feedstock using environmentally benign processes [1]. In particular, there is significant interest in obtaining extracts with particular biological activities from plants using green technologies [2,3]. However, there is a tension in the use of agriculturally optimum land worldwide for producing biologically sourced industrial- and health-based chemicals, versus the production of food products for human consumption [4,5]. Thus, efforts are underway to identify and investigate potential industrially valuable crops rich in bioactive components that can grow in marginal lands with little or no fertilizer or irrigation inputs [5,6].

Sumac is the common name for a genus (*Rhus*) that contains over 250 individual species of flowering plants in the family Anacardiaceae [7]. This genus is found in temperate and tropical regions worldwide, with representative members by geographic location given in Table 1. In general, sumac can grow in non-agriculturally viable regions, and various species have been used by indigenous cultures for medicinal and other purposes, suggesting potential for commercializing the bioactivity of these plants without competing for food production land uses [8]. For example, *R. glabra* (smooth sumac) is traditionally used by native peoples of North America in the treatment of bacterial diseases such as syphilis, gonorrhea, dynsentery, and gangrene [9]. *R. coriaria* (tanner's sumac), which grows wild in the region from the Canary Islands over the Mediterranean region to Iran and Afghanistan, is commonly used as a spice by

grinding the dried fruits with salt, and is also widely used as a medicinal herb in the Mediterranean and Middle East, particularly for wound healing [10].

Over the past few decades, a number of publications have reported on the biological activities of extracts from sumac. However, no comprehensive review has been performed to summarize the state-of-the-art, especially in light of the recent focus on the use of bioproducts in a sustainable world economy. Thus, in the current work, we critically review the known biological activity of extracts from sumac species, and suggest future research avenues that warrant exploration. In addition, we found that the research to date has focussed on only a few members of this large plant family. Because of this, the review is timely in helping to suggest increasing our breadth of research and development efforts for obtaining bioactive extracts from sumac using green technologies, by building on the promising findings from the selected members of the *Rhus* genus investigated to date. If there are generalizable bioactive properties within the genus to be discovered, the favorable worldwide distribution of sumac suggests that desirable bioproducts may be obtained at source, with minimal transportation requirements from source through processing to end consumer. This makes sumac an appealing genus on which to possibly focus substantial green chemistry research efforts, as its ability to grow on marginal land, produce potentially useful bioactive products, and ubiquitous nature warrant its consideration as a potential signature species for biproducts and bioprocesses research programs.

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Bioactivity of Sumac Extracts

Sumac extracts have been shown to exhibit a wide range of biological activities, which are summarized in Table 2 and discussed in more detail below.

Antimicrobial, Antifungal, and/or Antiviral Activity

Sumac extracts are most notable for their antimicrobial activities, although some limited information is available on their antifungal and antiviral activities. As part of a screening of 100 medicinal plants in British Columbia (Canada), crude methanolic extracts of *R. glabra* branches exhibited both the widest zones of inhibition in a disc assay, and the broadest spectrum of inhibition (active against all of the following 11 species of bacteria tested: *Bacillus subtilis*, *Enterobacter aerogenes*, *Escherichia coli* DC2, *Klebsiella pneumoniae*, *Mycobacter phlei*, *Pseudomonas aeruginosa* H187, *Serratia marcescens*, *Staphylococcus aureus* meth^{S}, *Staphylococcus aureus* meth^{R} P00017, and *Salmonella typhimurium* TA98) [11]. To obtain the crude extracts, the plant material was air dried and ground in a Wiley mill with a 2 mm mesh, followed by extraction with methanol and filtration through cheesecloth, cotton wool, and a paper filter. Similarly, in a follow-up study, the same methanolic extracts from *R. glabra* branches inhibited the following nine fungal strains tested: *Aspergillus flavus*, *A. fumigatus*, *Candida albicans*, *Fusarium tricuictum*, *Microsporum cookerii*, *M. gypseum*, *Saccharomyces cerevisiae*, *Trichoderma viridae*, and *Trichophyton mentagrophytes* [12]. While the *R. glabra* extract had the strongest antibiotic activity among the 100 plants surveyed, it was only

moderately inhibitory of the fungi although it exhibited a broad spectrum of activity.

To better understand the compounds likely responsible for the observed antimicrobial activity of *R. glabra*, ground dried branches were exhaustively extracted with methanol and fractionated with hexane, chloroform, chloroform/methanol (3:2 v/v) and water [13]. All fractions were tested against Gram positive and Gram negative bacteria, with the most active fraction being chloroform/methanol (3:2 v/v). Subsequent column chromatography allowed the isolation and purification of the following three compounds, which were found to be the only active constituents against the bacteria: methyl gallate (**1**; minimum inhibitory concentration (MIC) of 13 μg/mL), 4-methoxy-3,5-dihydroxybenzoic acid (**2**; MIC of 25 μg/mL), and gallic acid (**3**; MIC of >1000 μg/mL) (Fig. 1).

The majority of the antimicrobial studies on sumac have focussed on *R. coriaria*, and specifically, on the fruits because of their widespread use in the Mediterranean and Middle East as a dried spice. All of the studies have used either ethanol or water based extracts. Fruits of *R. coriaria* extracted with 95% (v/v) ethanol exhibited a broad range of antimicrobial activity by inhibiting the growth of all of the following Gram positive and Gram negative species tested: *Bacillus cereus*, *Escherichia coli* strains B, 01111, 2759, and 25922, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Shigella dysentariae*, *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus pyogenes*, *Enterococcus faecalis*, and *Yersinia enterocoltica* [14]. The observed antimicrobial activity was

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

ascribed to the tannins in the ethanolic extracts, with MICs in the range of 10 to 26 mg/mL depending on the bacterial species.

Subsequent work also investigated the inhibitory effect of 97% (v/v) ethanol extracts from ripened and unripened *R. coriaria* fruits against six Gram positive (*Bacillus cereus*, *B. megaterium*, *B. subtilus*, *B. thuringiensis*, *Listeria monocytogenes*, and *Staphylococcus aureus*) and six Gram negative (*Citrobacter freundii*, *Escherichia coli* strains Type I and O157:H7, *Hafnia alvei*, *Proteus vulgaris*, and *Salmonella enteritidis*) bacteria [15]. The extract was found to be effective against all tested bacteria, with the Gram positives more sensitive. *Bacillus* spp. were the most sensitive, with MICs at about 500 µg/mL, followed by *S. aureus* (1000 µg/mL), and *L. monocytogenes* (1500 µg/mL). Among the Gram negative bacteria, *S. enteritidis* and *E. coli* Type I were the most resistant (MICs up to 3000 µg/mL), followed by *E. coli* O157:H7 (2500 µg/mL), *H. alvei* (2000 µg/mL), *P. vulgaris* (1500 µg/mL), and *C. freundii* (1000 µg/mL). Ripened fruits were also found to have a significant higher antimicrobial activity compared to unripened fruits.

Most recently, additional work using dried *R. coriaria* seed, found an antibacterial effect of a combined ethanol/methanol extract against *Pseudomonas aeruginosa* [16]. As well, hydroalcoholic extracts of *R. coriaria* fruits prepared by a cool percolation method using 80% (v/v) ethanol were tested against representative Gram positive and negative bacteria such as *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, *Proteus vulgaris*, and *Shigella flexneri* [17]. The sumac extract exhibited

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

antibacterial activity against all the species tested, with MICs ranging from 0.05 mg/mL (*B. cereus*) to 0.20 mg/mL (*E. coli* and *S. flexneri*) on a weight/volume percentage.

Water extracts of *R. coriaria* fruits, like the ethanolic extracts, also display antimicrobial activity. Water extracts (1 hour at 25°C following by 2 minutes of boiling) of dried *R. coriaria* fruits at 0.1 to 5% (w/v) exhibited antimicrobial activity against the following bacteria: *Bacillus cereus*, *B. megaterium*, *B. subtilis*, *B. thuringiensis*, *Listeria monocytogenes*, *S. aureus*, *C. freundii*, *E. coli* (Type I and O157:H7), *H. alvei*, *P. vulgaris*, and *S. enteritidis* [18]. Both ripened and unripened fruits displayed similar antibacterial effectiveness (in contrast to ethanolic extracts obtained by the same research group, where ripened fruits had a significant higher antimicrobial activity compared to unripened fruits [15]), but differences in antimicrobial activity were found between the various bacteria. The *Bacillus* group was, in general, found to be more sensitive among Gram positive bacteria with *B. subtilis* being the most sensitive (MICs from 0.25-0.32% (w/v)). *L. monocytogenes* was the most resistant among Gram positive strains with a MIC of 0.67% (w/v). *P. vulgaris* was the most sensitive Gram negative strain (MIC of 0.63% (w/v)), with *S. enteritidis* and *E. coli* having the highest resistance. Overall, Nasar-Abbas *et al.* [18] found that water extracts from *R. coriaria* fruits had the greatest effectiveness against Gram positive bacteria, with Gram negative strains being more resistant, and a four to five log cycle reduction in *Bacillus* spp. after one hour exposure to a 1.0% (w/v) sumac extract. Other microbial species tested had a two to three log cycle reduction after the one hour exposure period.

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Similarly, Gulmez *et al.* [19] reported that a water extract (45°C for 12 hours) from *R. coriaria* fruits exhibited antimicrobial activity at a concentration of 8% (w/v) – particularly towards coliforms (total and fecal) – on poultry meat during storage. In contrast to the conventional alcoholic and aqueous extracts from sumac, which appear to have substantial antimicrobial activity, a hydrodistillation extract of dried *R. coriaria* fruits was found to be ineffective as an antimicrobial agent [20].

To the best of our knowledge, only one study has examined the broad spectrum antiviral properties of sumac extracts, and the work focussed on biflavonoids isolated from the seed kernels of *R. succedanea* [21]. Six biflavonoids (robustaflavone (**4**), amentoflavone (**5**), agathisflavone (**6**), volkensiflavone (**7**), succedaneaflavanone (**8**), and rhusflavanone (**9**)) were isolated from *R. succedanea* seeds and tested for inhibitory activities against a number of viruses including respiratory viruses (influenza A, influenza B, respiratory syncytial, parainfluenza type 3, adenovirus type 5, and measles) and herpes viruses (HSV-1, HSV-2, HCM, and VZV) (Fig. 2). The results indicated that **4** exhibited strong inhibitory effects against influenza A and influenza B viruses with EC_{50} values of 2.0 μg/mL and 0.1 μg/mL, respectively. **5** and **6** also demonstrated significant activity against influenza A and B viruses. **4** and **5** showed moderate anti-HSV-1 and anti-HSV-2 activities with EC_{50} values of 18 μg/mL (HSV-1) and 48 μg/mL (HSV-2), and 8.5 μg/mL (HSV-1) and 8.6 μg/mL (HSV-2), respectively. **9** demonstrated inhibitory activities against influenza B, measles, and HSV-2 viruses, while **8** exhibited inhibitory activities against

influenza B virus and VZV. It is also of note that **5** has been reported in *R. retinorrhoea* leaves [22] and **6** in *R. semialata* leaves [23], suggesting that other *Rhus* species may contain antiviral constituents.

The literature strongly suggests the potential for useful antimicrobial, antifungal, and antiviral agents to be obtained from sumac extracts, but the work to date has been too focussed on one primary species and plant part (fruits of *R. coriaria*) given its regional use as a spice. This focus is understandable, but (as with the other bioactive properties discussed below) future efforts should survey the worldwide sumac species to determine if these properties are generalizable across the *Rhus* genus. In addition, since the bioactivities appear to be ascribed to polar compounds extractable with protic solvents, additional studies are required on whether these properties occur in extracts from other plant parts (*e.g.*, stems/branches, roots, and leaves), and what the optimum extraction and storage conditions are to obtain the highest quality yields of desired functionality. The use of other green solvent systems, particularly sub- and super-critical fluids (*e.g.*, CO_2, water), also warrants investigation.

Antioxidant Activity

Developing new, safe, and naturally derived antioxidants for food and health applications is a major goal in sustainable bioproducts. Synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are widely used in spite of concerns regarding their toxicology and a sustainable supply [24]. Most of the research performed on sumac extracts has examined

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

antioxidant activity, and there appears to be potential for commercial development of the products from a number of species. However, as with other areas of bioactivity, the work to date has been focussed on a limited number of species (*R. verniciflua* and *R. succedanea* in Asia, *R. coriaria* in the Mediterranean/Middle East, and *R. hirta* in northeastern North America). More breadth in worldwide species is required to better understand the potential of sumac as a commercial source of natural antioxidants.

Crude ethanol extracts from *R. verniciflua* wood have exhibited strong antioxidant activity using cultured neuronal cells [25]. The unfractionated ethanol extract showed both antioxidant and cytotoxic effects on mouse thymocytes. Results from deoxyribose, DNA nicking, and glucose/glucose oxidase enzyme assays indicated that the extract contained a strong scavenging activity of oxygen free radicals, particularly hydroxyl radicals, but also exhibited cytotoxicity at higher concentrations towards the thymocytes.

In further studies on the same extract, the crude ethanol extract was separated using column chromatography into three water-eluted fractions and three organic solvent fractions (30% ethanol in water (v/v), absolute ethanol, and 5% acetic acid in water (v/v)) to better understand the source of the observed bioactivity in the *R. verniciflua* wood [26]. The water eluted fractions were the most protective against reactive oxygen species generated by iron and enzymes. As well, one of the water eluted fractions (shown to contain the flavonoids fustin (**10**), quercitin (**11**), butein (**12**), and sulfuretin (**13**)) protected against thymocyte apoptosis mediated by hydroxyl radicals, and these compounds were

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

attributed to the antioxidant activity (Fig. 3). **10** and **13** have also been reported in the wood of *R. copallina* [27], *R. glabra* [27-29], and *R. typhina* [27], suggesting that these species may also yield extracts with antioxidant behaviour. **11** has also been found in the leaves of *R. coriaria* [30] and *R. typhina* [31,32].

Kitts and Lim investigated the antioxidant, cytotoxic, and antitumorigenic activities of a fractionated ethanol extract derived from branches of *R. verniciflua*, and gel electrophoresis results suggested that the active component of a Sephadex G-150 fractionated extract was a copper containing protein, possibly a plant laccase (benzenediol:oxygen oxidoreductase EC 1.10.3.2) [33]. Antioxidant activity of the extract was observed in both aqueous and lipid in vitro oxidation reactions using DPPH, Fenton reaction deoxyribose, and lipid emulsion test systems, and cultured mouse brain neurons were protected against glucose oxidase induced hydroxyl radical in the presence of 4.9 μM (58% protection) and 22.7 μM (95% protection) fractionated *R. verniciflua* extract. In addition, 2.5 μM fractionated extract led to 70% tumor cell death after 24 hours incubation in the HeLa and CT-26 cell lines.

In terms of direct practical industrial antioxidative application, the only study using *R. verniciflua* wood involved a 75% ethanol (v/v) extract obtained at 80°C for 3 h and evaluated in frying oil of Yukwa base (rice snack) [34]. Additions of 400 and 1000 mg/L of sumac extract to the frying oil indicated a superior antioxidative action compared to BHA and α-tocopherol. Other work at stabilizing food products with sumac extracts includes the use of a methanol

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

extract from *R. coriaria* fruits tested in sunflower oil stored at 70°C by measuring peroxide values after regular intervals [35]. Along with rosemary and Turkish sage, sumac extracts were found to be most effective in stabilizing sunflower oil, followed by wild thyme and black thyme.

Antioxidant properties for stabilizing peanut oil were also reported on the methanol extracts of *R. coriaria* fruits and leaves [36,37]. Fruit extract additions to peanut oil at from 1 to 5% (w/v) generally inhibited the formation of hydroperoxide during the initial 7 days after addition [36], but that by 28 days of storage, the sumac extract had substantially lower antioxidant potential than compared to BHA controls. Similar results were observed with leaf extracts [37], whereby the addition to peanut oil at 4% (w/v) had a limited effect relative to the BHT controls.

Other work has examined the antioxidant and free radical scavenging activities of *R. coriaria* fruit extracts obtained by extraction with 80% methanol (v/v), and further fractionated using *n*-hexane, ethyl acetate, and water [38]. The ethyl acetate fraction exhibited greater antioxidant activity than the corresponding BHA and BHT controls as measured using the DPPH assay, but tests using the linoleic acid peroxidation assay indicated lower activity than the synthetic controls.

Candan's group has also examined the antioxidative ability of chloroform partitioned methanol extracts from *R. coriaria* fruits for lipid peroxidation, free radical scavenging, superoxide radical scavenging, and xanthine oxidase activity

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

[39,40]. The IC_{50} value for lipid peroxidation was estimated at 1200 µg/mL in the Fe^{2+}-ascorbate system, while those for superoxide scavenging ability in the xanthine-xanthine oxidase method and hydroxyl radical scavenging activity in the deoxyribose decomposition method with 283 µg/mL and 3850 µg/mL, respectively [39]. As well, the fractionated extract was an uncompetitive inhibitor of xanthine oxidase and scavenger of superoxide radical *in vitro* with IC_{50} values of 173 µg/mL and 232 µg/mL, respectively [40].

In the only aqueous extraction study regarding the antioxidative behaviour of *R. coriaria* fruits, a water extract (25°C for 24 hours) was more effective than BHT in preserving sausage, decreasing formation of putrescine, histamine, tyramine, and thiobarbituric acid reactive substances during storage [41].

Other than *R. verniciflua* and *R. coriaria*, only two other sumac species (*R. hirta* and *R. succedanea*) have been investigated for their extracts' antioxidant activities. A methanolic extract from the fruits of *R. hirta* performed similarly to green teas for scavenging superoxides produced by a NBT/xanthine oxidase (XO) assay, and greater than green tea and ascorbic acid for peroxyl radical scavenging using a DCF/AAPH assay [42]. Of the 35 native plant species from the boreal forest region of northeastern North America that were tested based on their historical use by indigenous peoples for treating diabetes and its complications, *R. hirta* exhibited the lowest IC_{50} (3.7 µg/mL) in the DPPH assay, and the highest percent inhibition in the NBT/XO (44.5%) and DCF/AAPH (31.5%) assays.

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

An antioxidant directed HPLC fractionation of the 80% ethanol (v/v) extract from the sap of *R. succedanea* was used to isolate three heptadecenyl compounds (**14**, **15**, and **16**; see Fig. 3 for structures) with antioxidative and cytotoxic activities against five cancer lines (cervix epitheliod carcinoma [HeLa], hepatoma cell line [Huh7], colorectal cancer cell line [HCT116], colon adenocarcinoma [LoVo], and rat C6 glioma cells) with IC_{50} concentrations ranging from 0.9 to 6.4 μg/mL [43].

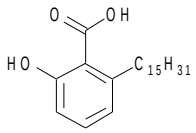
With a number of studies indicating that sumac extracts display considerable antioxidant behaviour, and with a few applied examples, we argue that this genus may offer promise for a natural source of commercial antioxidants. However, more species breadth is required in delineating the possible generality of obtaining viable natural antioxidants from sumac, as well as studies that consider the agronomic growth potential, optimized extraction and processing methods, and corresponding economic aspects at the feasibility level.

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Anticlotting Activity

Limited work has been done on the antithrombin activity of sumac extracts, with only a single report of 6-pentadecylsalicylic acid (**17**) being isolated from air-dried stems of *R. semialata* after methanol extraction and subsequent column chromatographic purification [44]. The compound showed antithrombin activity at 50 μg/mL using the amidolytic method, and prolonged clotting time in a dose-dependent manner in the clotting assay of thrombin-fibrinogen interaction. As

with other areas of potentially bioactive agents from sumac, significantly most breadth in research efforts worlwide is required to determine not only the feasibility of obtaining commercially viable products from the plants, but also in whether all members of the genus display similar bioactive possibilities.



17

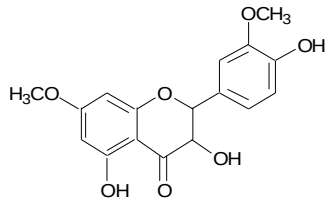
Antifibrogenic, Antiinflammatory, Hypoglycemic, and/or Leukopenic Activities

Antifibrogenic activity of *R. verniciflua* was assigned to **12** [45], which was isolated from the bark by drying and pulverizing, extracting with hot methanol for 3 hours, subsequently dissolving the methanol extract in water:methanol (3:2 v/v), and partitioning with *n*-hexane followed by dichloromethane. The dichloromethane extract was separated by Sephadex LH-20 column chromatography (dichloromethane:methanol, 20:1 v/v) to yield five fractions, the fourth was further chromatographed to give pure **12** in 0.035 w/w% yield. Testing of the isolated **12** on liver fibrosis in rats indicated the compound had antifibrotic effects, and dose levels of 10 to 25 mg/kg/day showed a significant reduction of hydroxyproline and malondialdehyde levels in rats. The expression of α1(I)collagen and tissue inhibitor of metalloproteinase-1 (TIMP-1) mRNAs in liver was reduced in a dose-dependent manner in rats given **12** compared with corresponding carbon tetrachloride controls. Thus, **12** appears to act as an antifibrogenic agent by inhibition of collagen accumulation and lipid

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

peroxidation, and by down regulation of the expression of both α1(I)collagen and TIMP-1 mRNA.

From the roots of *R. undulata*, apigenin dimethyl ether (**18**) was isolated and found that, at a dose of 75 mg/kg, this compound exhibited 81% inhibition of the phlogistic response (carrageenan induced edema) in a rat [46].



18

Methanol extracts of *R. coriaria* fruits were recently studied for potential hypoglycemic activity [47]. The crude extracts were further fractionated by ethyl acetate and *n*-hexane, and the ethyl acetate extracts exhibited significant hypoglycemic activity through α-amylase inhibition (87% inhibition at 50 μg/mL), with lower activity from the *n*-hexane fraction (77% inhibition at 250 μg/mL). The higher biological acitivity in the ethyl acetate extract was attributed to the presence of flavonoids as tentatively identified by thin-layer chromatography, while dominantly terpenoids were found in the *n*-hexane fraction.

The exudate that can be obtained from the stem bark of lac tree (*R. vernicifera*) has been used mainly as a material for traditional paint and lacquer in East Asian countries [48]. The lacquer polysaccharide is an acidic

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

heteropolysaccaride with a 1,3-β-linked D-galactopyranosidic main chain having complex branches with 4-*O*-methyl-β-glucoronic acid in the terminal [49,50]. Studies on isolated chinese laquer polysaccharide from *R. vernicifera* have found significant bioactivity against leukopenia [51,52]. In addition to the material properties of this product, further work is required to better understand its range of potential bioactivities.

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

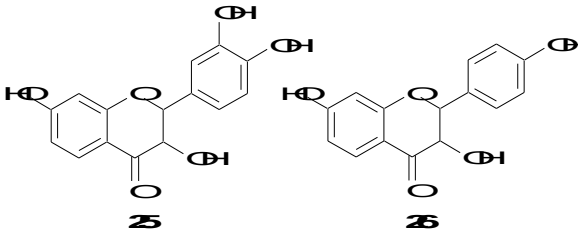
Antimalarial Activity

Work with dried and ground leaves of *R. retinorrhoea* from Saudi Arabia, which were extracted using dichloromethane, suggests that a modest antimalarial activity can be obtained [22]. Partitioning of the dichloromethane extract between hexane and acetonitrile, followed by silica gel column chromatography (benzene/ethyl acetate) yielded the following five flavonoids, 7-*O*-methylnaringenin (**19**), eriodictyol (**20**), 7,3'-*O*-dimethylquercetin (**21**), 7-*O*-methylapigenin (**22**), 7-*O*-methylluteolin (**23**), and the biflavone (2S,2"S)-7,7"-di-*O*-methyltetrahydroamentoflavone (**24**) (Fig. 4). The biflavone **24** exhibited moderate antimalarial activity with an IC_{50} of 0.98 μg/mL against *Plasmodium falciparum* (W2 clone) and weak activity against *P. falciparum* (D6) with an IC_{50} of 2.8 μg/mL, but was not cytotoxic. **19** showed weak antimicrobial activity against *Candida albicans*, *C. krusei*, *Staphylococcus aureus*, *Mycobacterium smegmatis*, *M. intracellulare*, and *M. xenopi*. Given the global interest in environmentally and economically sustainable antimalarial treatments, further work is needed on ascertaining whether this desirable bioactivity can be obtained from the numerous sumac species indigenous to malarial regions of sub-Saharan Africa (see Table 1).

Antimutagenic, Cytotoxic, and/or Antitumorigenic Activities

Park *et al.* examined the heartwood of *R. verniciflua*, and following an initial methanol extraction, the following four flavonoids were separated by ethyl acetate fractionation and column chromatography: **10**, **13**, fisetin (**25**), and garbanzol (**26**) [48]. The crude methanolic extract was applied to rats, and

prevented the activation of hepatic microsomal cytochrome P_{450} enzymes and inhibition of hepatic glutathione S-transferase, leading to further isolation efforts to identify the specific compounds responsible for the observed bioactivity. When the individual flavonoids were subjected to the Ames test, it was observed that **13** might effectively prevent the metabolic activation, or scavenge the electrophilic intermediates, capable of causing mutation. In contrast, **10** showed a dose-independent antimutagenic activity with mutagenic and antimutagenic behaviour. However, a 1:1 (w/w) mixture of **10** and **13** exhibited dose-dependent antimutagenicity, indicating that **13** inhibited the mutagenicity of **10**.

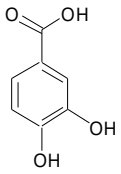


10, **13**, and **25** have also been reported in the wood of *R. copallina* [27], *R. glabra* [27-29], and *R. typhina* [27], suggesting that these species may also yield extracts with antitumorigenic behaviour.

Similarly, Son *et al.* prepared a flavonoid containing chloroform-methanol fraction from a crude acetone extract of *R. verniciflua* wood that contained the following compounds: **10**, **12**, **13**, **25**, and protocatechuic acid (**27**) [53]. The fraction exhibited selective growth inhibition and apoptosis-inducing effects in mouse tumorigenic hepatic cells. Additional work on a chloroform-methanol

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

fraction from a crude acetone extract of *R. verniciflua* woods suggested that these flavonoids may also be responsible for inhibiting the growth of human lymphoma cells [54].



27

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Conclusions

The research efforts on sumac extracts indicate a promising potential for the plant family to provide renewable bioproducts with the following desirable bioactivities: antifibrogenic, antifungal, antiinflammatory, antimalarial, antimicrobial, antimutagenic, antioxidant, antithrombin, antitumorigenic, antiviral, cytotoxic, hypoglycaemic, and leukopenic. As well, the bioactive components can be extracted from the plant material using environmentally benign solvents (*e.g.*, ethanol, water) that allow for both food and industrial end-uses. Furthermore, a substantial opportunity exists to investigative the use of other green solvents (*e.g.*, sub- and super-critical liquids, ionic liquids) for obtaining bioactives and other phytochemicals from sumac, and in processing the residue for complete biomass conversion.

However, as this overview demonstrates, the previous work has focussed on only a few members (eight) of this large plant family (*ca.* 250 species). In addition, not all of the species studied to date have been fully characterized for

potential bioactivities. Thus, there remains a significant research gap spanning the range from lead chemical discovery through process development and optimization in order to better understand the full bioactive potential of the *Rhus* genus as part of global green technology based bioproduct and bioprocess research programs.

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Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

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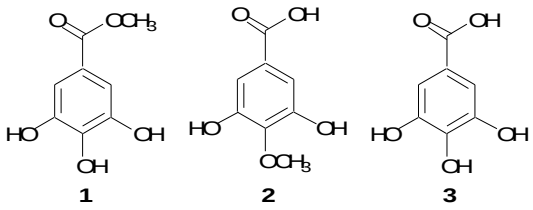

Fig. 1. Compounds exhibiting antimicrobial activity in sumac extracts.

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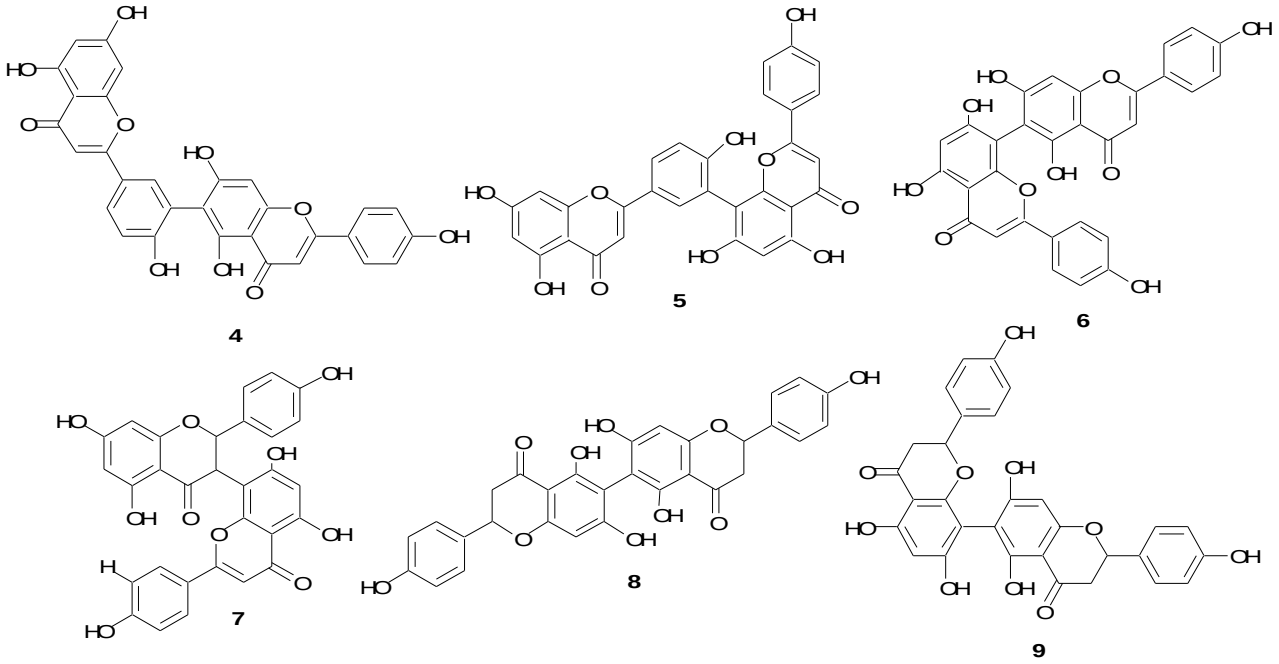

Fig. 2. Compounds exhibiting antiviral activity in sumac extracts.

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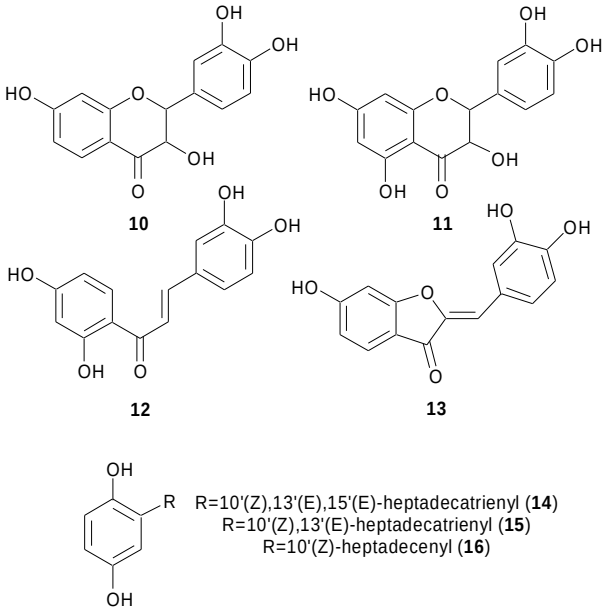

Fig. 3. Compounds exhibiting antioxidant activity in sumac extracts.

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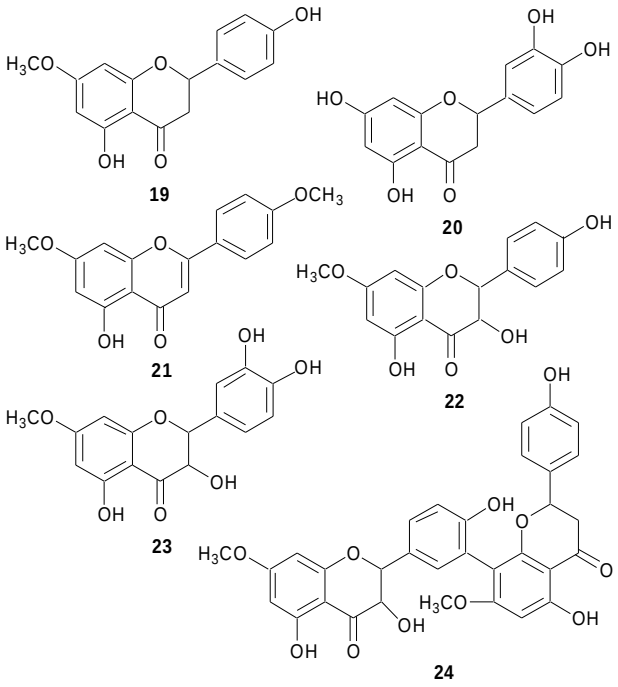

Fig. 4. Compounds exhibiting antimalarial activity in sumac extracts.

Table 1. Summary of the geographic distribution of representative members of the sumac genus (*Rhus* spp.). Adapted from ref. 7.

Asia	**Africa (cont'd)**
R. chinensis (Chinese Sumac)	*R. lucida*
R. hypoleuca	*R. macowanii*
R. javanica	*R. magalismontana*
R. punjabensis (Punjab Sumac)	*R. maricoana*
R. verniciflua	*R. marlothii*
Australia	*R. microcarpa*
R. taitensis	*R. montana*
Mediterranean	*R. natalensis*
R. coriaria (Tanner's Sumac)	*R. nebulosa*
R. pentaphylla	*R. pallens*
R. tripartita	*R. pendulina*
Mexico and Central America	*R. pentheri*
R. muelleri (Müller's Sumac)	*R. pondoensis*
Pacific Ocean	*R. populifolia*
R. sandwicensis	*R. problematodes*
Africa	*R. pterota*
R. acocksii	*R. pygmaea*
R. albomarginata	*R. pyroides*
R. angustifolia	*R. quartiniana*
R. batophylla	*R. refracta*
R. baurii	*R. rehmanniana*
R. bolusii	*R. rigida*
R. burchellii	*R. rimosa*
R. carnosula	*R. rogersii*
R. chirindensis	*R. rosmarinifolia*
R. ciliata	*R. rudatisii*
R. crenata	*R. scytophylla*
R. cuneifolia	*R. sekhukhuniensis*
R. dentata	*R. stenophylla*
R. discolor	*R. tenuinervis*
R. dissecta	*R. tomentosa*
R. divaricata	*R. transvaalensis*
R. dracomontana	*R. tridactyla*
R. dregeana	*R. tumulicola*
R. dura	*R. undulata*
R. engleri	*R. volkii*
R. erosa	*R. wilmsii*
R. fastigiata.	*R. zeyheri*
R. gerrardii	**North America**
R. glauca	*R. aromatica* (Fragrant Sumac)
R. gracillima	*R. choriophylla* (Mearns Sumac)
R. grandidens	*R. copallina* (Winged Sumac)
R. gueinzii	*R. glabra* (Smooth Sumac)
R. harveyi	*R. integrifolia* (Lemonade Sumac)
R. horrida	*R. lanceolata* (Prairie Sumac)

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

R. incisa	*R. laurina* (Laurel Sumac)
R. kirkii	*R. michauxii* (Michaux's Sumac)
R. keetii	*R. microphylla* (Desert Sumac)
R. krebsiana	*R. ovata* (Sugar Sumac)
R. laevigata	*R. trilobata* (Skunkbush Sumac)
R. lancea	*R. typhina* (Staghorn Sumac)
R. leptodictya	*R. toxicodendron*
R. longispina	*R. vernix*
R. lucens	*R. virens* (Evergreen Sumac)

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007

Table 2. Summary of reported biological activities of compounds and fractions extracted from sumac.

Biological activity	Species	Plant part	Compound(s) and/or extract type	Reference
antifibrogenic	*R. verniciflua*	bark	butein	45
antifungal	*R. glabra*	branches	methanol extract	12
antiinflammatory	*R. undulata*	roots	apigenin dimethyl ether	46
antimalarial	*R. retinorrhoea*	leaves	7-O-methylnaringenin, eriodictyol, 7,3'-*O*-dimethylquercetin, 7-*O*-methylapigenin, 7-*O*-methylluteolin, and (2S,2"S)-7,7"-di-*O*-methyltetrahydroamentoflavone	22
antimicrobial	*R. retinorrhoea*	leaves	7-*O*-methylnaringenin	22
	R. glabra	branches	(a) methyl gallate, 4-methoxy-3,5-dihydroxybenzoic acid, and gallic acid (b) methanol extract	(a) 13 (b) 11
	R. coriaria	seed	ethanol and methanol extracts	16
		fruits	(a) water extract (b) ethanol:water (19:1 v/v) (c) hydrodistillation extract (d) water-soluble fraction of methanol extract partitioned against chloroform (e) ethanol: water (4:1 v/v)	(a) 18,19 (b) 14,15 (c) 20 (d) 40 (e) 17
antimutagenic	*R. verniciflua*	heartwood	garbanzol, sulfuretin, fisetin, fustin, and mollisacasidin	48
		branches	protocatechuic acid, fustin, fisetin, sulfuretin, and butein	53
antioxidant	*R. verniciflua*	branches	(a) ethanol extract fractionated on Sephadex G-150 (activity ascribed to laccase, benzenediol:oxygen oxidoreductase) (b) fustin, quercitin, butein, and sulfuretin (c) crude Ethanol extract further fractionated using prep-LC with acetonitrile:water gradient	(a) 33 (b) 26 (c) 25
		bark	ethanol:water (3:1 v/v) extract	34
	R. succedanea	sap	10'(Z),13'(E),15'(E)-heptadecatrienylhydroquinone, 10'(Z),13'(E)-heptadecadienylhydroquinone, and 10'(Z)-heptadecenylhydroquinone	43
	R. coriaria	fruits	(a) methanol extract (b) water extract (c) water-soluble fraction of methanol extract partitioned against chloroform	(a) 36 (b) 41 (c) 39
		leaves	methanol extract	37

		whole plant	ethyl acetate and methanol fractions after initial defatting (petroleum ether), extraction with aqueous:methanol (1:4 v/v), and partitioning (*n*-hexane/ethyl acetate)	38
	R. hirta	fruits	methanol extract	42
antithrombin	*R. verniciflua*	stems	6-pentadecylsalicylic acid	44
antitumorigenic	*R. verniciflua*	branches	(a) ethanol extract fractionated on Sephadex G-150 (activity ascribed to laccase, benzenediol:oxygen oxidoreductase) (b) protocatechuic acid, fustin, fisetin, sulfuretin, and butein	(a) 33 (b) 54
antiviral	*R. succedanea*	fruits	robustaflavone, amentoflavone, agathisflavone, volkensiflavone, succedaneaflavone, and rhusflavanone	21
cytotoxic	*R. verniciflua*	branches	ethanol extract fractionated on Sephadex G-150 (activity ascribed to laccase, benzenediol:oxygen oxidoreductase)	33
hypoglycaemic	*R. coriaria*	fruits	methanol extract further fractionated with ethyl acetate and hexane	47
leukopenic	*R. vernificera*	sap	polysaccharide extracts	51,52

Nature Precedings : hdl:10101/npre.2007.631.1 : Posted 6 Aug 2007