Rhus Aromatica: A Plant of Phytochemical and Pharmacological Importance – Review

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Abstract- *Rhus Aromatica Linn. (Anacardiacea), commonly known as sumac, has been used as a spice, condiment, appetizer, and as a souring agent for centuries. A broad range of nutritionally and medicinally significant phytochemical components have been identified from various parts of sumac such as tannins, flavonoids, anthocyanins, organic acids, flavones, proteins, fiber, volatile oils, nitrates, and nitrites. The role of plant in leather and textile industry as tanning agent and as a colouring agent is significant. It also prevents wood decay and has considerable potential for future research.*

Keywords- Rhus Aromatica, Phytochemical, pharmacological.

I. INTRODUCTION

The genus Rhus (sumac) comprises more than 250 species and is well characterized by phenolics and triterpenes. Rhus species grow in temperate and tropical regions worldwide and have been used as spice or medicinal herbs for hundreds of years[1]. Rhus aromatica Aiton (Anacardiaceae), the fragrant sumac, is an aromatic, deciduous, small bushy shrub with yellowish catkin like flowers preceding dark red berries. The stem is growing 6 to 12 feet high, leaves alternate and trifoliate. The shrub is native in the rocky regions of Eastern United States. Aqueous extracts of plant root or stem bark exhibited antiinflammatory and anti-microbial effects. Also inhibition of muscarinic receptor mediated contraction of human bladder was demonstrated. These properties support the traditional use of Rhus aromatic for the treatment of urinary incontinence, overactive bladder, cystitis, functional bladder problems and certain types of uterine hemorrhages [2-4].

Sumac has long been used as a seasoning spice, either in pure form or in combination with other spices, as a drink, appetizer, sauce, and also as a natural acidulant in food recipes [5]. It is worth noting that Rhus Aromatica has an attractive economic importance due to its increasing use in cosmetic and pharmaceutical industries, coloring or preservation of foods, veterinary practices and animal skins processing technology [6,7]. In the past, the leaves, bark, roots and branches of Rhus Aromatica were used in dyeing as mordant natural dyes. In addition, Rhus Aromatica possesses high fixation, retention and fungal resistance properties, and is useful against wood decay [8]. So far, a big deal of nutritionally and medicinally considerable metabolites (such as phenolic acids, tannins, anthocyanins, organic acids, proteins, essential oils, fatty acids, fiber, and minerals) have previously been identified from various parts of Rhus Aromatica [9].

Figure -1: Different Stages of Rhus Aromatica

(A) Flower in Stage

(B) Fruiting Stage

(C) Mature Fruit Stage

(D) Seeds of Rhus Aromatica

II. HISTORY AND DISTRIBUTION

It is widespread in Spain, Southern Italy and Turkey and from the Middle Eastern countries to Afghanistan. In Iran, Rhus Aromatica is traditionally used as a table spice especially along with rich dishes[10].

III. BOTANICAL DESCRIPTION

Bud Arrangement:

This plant Bud Color - Yellow, pubescent, covered by leaf scar. Bud Size - Small. Leaf Type and Shape - Trifoliate. Leaf Margins - Acute to acuminate, crenate-serrate. Leaf Surface - Hairy, pubescent. Leaf Length - 1½ to 3 inches; leaflets 1 to 2 inches. Leaf Width - 1½ to 3 inches; leaflets 1/2 to 1 inch. Leaf Color - Soft green as leaflets unfold, then turning semi-glossy, deep green in summer, and yellow to red in autumn.

Flowers and Fruits:

Flower Type - Polygamous or dioecious, male buds are 1 inch catkins, female are short panicles at the ends of branches. Flower Color - Yellowish. Fruit Type - Hairy-clustered drupes, 1/4 inch in diameter, females only. Fruit is red colour.

Form :

Growth Habit - Ascending, branchlets pubescent, rounded mounds. Texture - Medium, summer; medium, winter. Crown Height - 3 to 9 feet. Crown Width - 6 to 10 feet. Bark Color - Gray-brown, aromatically fragrant when bruised, leaf scars circular, distinctly raised. Root System - Fibrous, spreading and also flower are polygamous or dioecious - yellowish-green, male catkins form in late summer and persist as 1" long ornamental buds in winter -male and female flowers bloom in March to April [11].

Fruit:

This plants fruits are red (when present) -Aug. and persistent into early winter; noticeable but not overly attractive[12,13].

IV. PHYTOCHEMICAL STUDIES

Recent phytochemical studies of Rhus Aromatica L. have proved its richness in strong antioxidants called tannins [14]. The leaves contain up to 25-33% tannins [15]. Hydrolysable tannins, condensed tannins and gallic acid derivatives have been found [16]. The hydrolysable gallotannins have not been structurally characterized by Nuclear magnetic resonance or physicochemical mass spectrometry. They have been extensively used in tanning leather. [17,18]. Gallic acid, protocatechuic acid, linolenic acid, p-OH-benzoic acid, and vanillic acid were the phenolic acids found in the leaves of this herb. In vitro testing has indicated that gallic acid is the active principle of sumac [19]. Anthocyanins like cyanidin, peonidin, pelargonidin and petunidin have also been reported in the leaf of Rhus Aroma. The flavonoids detected in this herb are quercetin and kaempferol glycosides [20,21]. Echium amoenum L. is considered as a promising source of bioactive compounds with various beneficial biological activities. It has been reported that the petals of Echium amoenum L. is rich in rosmarinic acid (RA), a potent antioxidant , Cyaniding, delphinidin, anthocyanins, gamma linolenic acid (GLA), alpha-linolenic acid (ALA), delta6-fatty acyl desaturase, delta8-sphingolipid desaturase and flavonoids [17,18,21] . The Cyaniding 3-glucoside, the most common anthocyanin, which is present in petals of Echium amoenum L. attenuates prostaglandin production and cyclooxygenase-2 expressions by inhibiting activation and translocation of c-Jun and NFκB factors into nucleus (Petersen & Simmonds, 2003) and reducing intracellular reactive oxygen species (ROS) levels via activating the glutathione (GSH) antioxidant system [22] Its neuroprotective effect was related to attenuation of brain superoxide levels resulted from blocking apoptosis-inducing factor release in mitochondria [23].

In the light of the significance of sumac uses in food seasoning, folklore medicine and industry Rhus Aromatica has long been investigated to expose its chemical composition. R. aroma plant is known as an abundant source of tannins (condensed and hydrolysable), phenolic acids, anthocyanins, gallic acid derivatives, flavonoid glycosides, organic acids[25]. Parts like leaves, fruits, and seeds of Rhus aroma were reported to contain a number of phyto constituents as shown in Figure 2. The presence of gallotannins (mainly hydrolysable tannins) is a characteristic property of the Rhus genus, mostly Rhus Aromatica species, which is an abundant source of tannins with different isomers and conjugations; besides, it contains other metabolites or phytochemicals, which have been described in various parts of the plant. Tannins are polyphenolic secondary metabolites of plants (MW's: 500 to 3,000), containing sufficient hydroxyls and carboxyls' groups. Which form hydrogen bonds in solutions. Tannins are astringent and bitter compounds, which can form strong complexes with various macromolecules that bind to and can precipitate proteins and other organic compounds including amino acids. They play a vital role in protecting plants from predation; and perhaps also as pesticides, as well as in plant growth regulation [26]. Lately, these substances have gained attention as they may trim down the risk of chronic diseases, by reinforcing the defenses against reactive oxygen species [27] The tannin compounds are widely distributed in many plant species, where they play a role in protection from predation, and plant growth regulation [28]. Structurally, tannins are divided into two classes: hydrolysable and condensed ones. Rhus Aromatica has been reported as one of the major commercial hydrolysable tannin sources [29]. The methanol extracts from Rhus Aromatica fruits were reported as a rich source of natural antioxidants phenolics, mainly tannins, which has an inhibitory function in the migration of vascular smooth muscle cells, suggesting an atheroprotective role for this chemical. In vitro and in vivo studies have shown that tannins have anticarcinogenic effects [30]. The aqueous and aqua methanol extracts of Rhus Aromatica leaves and fruits were investigated using HPLC to reveal the presence of gallotannins derivatives, namely gallic acid (1), methyl gallate (2), digallic acid (3), tri-gallic acid (4), and ellagic acid, together with mono- (5), di- , tri- , tetra- (6), penta- (7), deca-, undeca- and dodecagallolyl glycoside derivatives as representative tannins present in Rhus Aromatica [31]. Some of the above-mentioned galloylglucose derivatives were reported to have the ability to reduce blood urea nitrogen and blood pressure [32]. In fact, the galloylated glucose derivatives were previously studied in Rhus Aromatica leaves using UV, paper chromatography, and IR measurements, in addition to the column chromatography technique which was used to uncover the existence of flavonoid glycosides [33]. Flavonoid dimers (with antiviral activity) like amenthoflavone (8), agathisflavone (9), hinokiflavone (10), and sumaflavone (11) have also been identified in the leaves and fruits via LC and LC-MS (Van Loo et al., 1988; Abu Reidah et al., 2014). Other anthocyanins were also established: cyanidin (12), peonidin (13), pelargonidin (14), and petunidin (15) structures and coumarates, anthocyanins were peonidin-3-glucoside, petunidin-3-glucoside (coumarate), delphinidin (coumaroyl) glucosides, and cyanidin coumaroyl glucoside. However, the presence of cyanidin-3-glucoside (16), delphinidin-3-glucoside (17) and delphinidin (18) has already been reported from the fruits of Rhus Aromatica [33]. Furthermore, some other phenolics have been isolated from Rhus aromatica, including gallic acid, methyl gallate, kaempferol (19), myricetrin (20), quercetin (21), p benzoic acid, vanillic acid isoquercitrin, protocatechuic acid (22), kaempferol 3-galactoside, quercetin 3-glucoside (isoquercitrin) (23), quercetin 3-rhamnoside, myricetin 3- rhamnoside (24), myricetin 3-glucoside (25), myricetin 3- glucuronide, myricetin 3-rhamnoglucoside, have also been already identified in the Rhus Aromatica leaves and fruits [34]. The separation of gallotannins and flavonoids was carried out by HPLC-ESI-MS, which allowed the structure resolution of the isobaric flavonoid glycosides. Lately, a detailed profiling of phytochemical compounds has been carried out by analyzing the hydromethanolic extract of the fruits using HPLC-DADESI-MS/MS technique, where more than 200 phytochemical components have been tentatively identified. Curiously, the occurrence of the conjugated form of aglycone with hexose malic moieties (24 compounds) has been very recently identified for the first time in the Palestinian Rhus Aromatica [35,36]. In the same work, five cyanidin derivatives have been newly detected anthocyanins in the fruit epicarps. Moreover, the following flavonoid glycosides have been also identified: quercetin rhamnofuranoside (26), rutin (27), and kaempferol 3 glucoside (Astragalin) (28). Butein (29) is a recently identified chalconoid derivative from Rhus Aromatica. Notably, this compound exhibited a significant anti-breast cancer activity. Another galloyl derivative compound was also characterized in the fruits: O-galloyl arbutin (30). Minerals are essential chemical elements for supporting the human health, indispensably obtained from the diet. Once minerals intake is inadequate, deficiency symptoms may take place [37]. However, minerals like potassium, calcium and magnesium were found to be predominant in sumac. Other minerals have also been explored, namely sulfur, cadmium, phosphor, lead, titanium, vanadium, copper, silicon, barium, chromium, lithium, brome, aluminum, chloride, manganese, iron, sodium, zinc, strontium, and nitrogen [38]. On the other hand, β-caryophyllene (31) a bicyclic sesquiterpene has been recently described to be a major essential oil component isolated from Rhus Aromatica [39]. An anti inflammatory effect for this terpenoid has been described elsewhere [40]. Interestingly, Rhus Aromatica fruits were found to possess various fatty acids, including azelaic, tetradecanoic, elaidic, stearic, eicosadienoic, arachidic, and tetracosanoic acids, with oleic (ω 9), palmitic, and linoleic (ω 6) acids being as major fatty acids in sumac. The polyunsaturated fatty acid (ω 6+ ω 3) contents of the total fatty acids were found to be between 34.84 and 37.36% (Dogan and Akgul, 2005). The main fatty acids of sumac were found to be: oleic (33.78-52.57%), palmitic (17.00-29.80%), linoleic (11.60-21.90%), linolenic (0.33-1.33%) and stearic (17 %) acids. On the other hand, linoleic (49.35- 60.60%), oleic (24.60-32.05%), palmitic (8.30-13.60%), stearic (1.60-3.00%) and linolenic (0.46-0.74%) acids were described to be major fatty acids of Rhus Aromatica seeds [41].

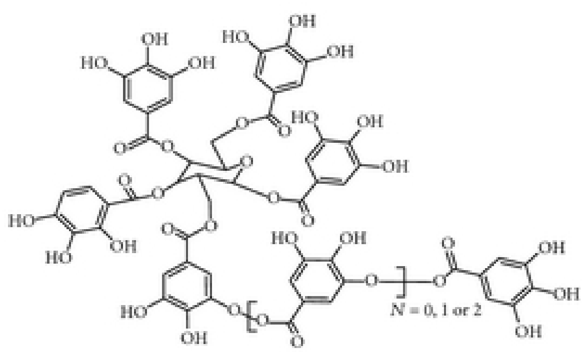

Figure 2: Rhus Aromatica Phytochemical Structure

V. PHARMACOLOGICAL STUDIES

Anti Diabetic Property:

Results of the recent studies have clearly indicated that the methanol extract of the fruits have potential hypoglycemic activity [42]. The crude extract has been further fractionated and the ethyl acetate extract has exhibited significant hypoglycemic activity through α-amylase inhibition (87% inhibition at 50 µg/mL), compared to the *n*-hexane fraction (77% inhibition at 250 µg/mL). The higher biological activity of the ethyl acetate extract has been attributed to the presence of flavonoids as tentatively identified by thin-layer chromatography[43].

Antimicrobial effects:

In recent years, an explosive spread of multiple drug resistance bacterial pathogens has become a serious concern worldwide in terms of public health and economic issues. The majority of the antimicrobial studies on sumac have focused 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. Ethanol extracts of the ripe and unripe fruits of the plant have exhibited a broad range of antimicrobial activity by inhibiting the growth of Gram positive and Gram negative species such as *Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa, Shigella dysentariae, Staphylococcus aureus, S. epidermidis, Streptococcus pyogenes, Enterococcus faecalis,* and *Yersinia enterocolitica*[44]. The observed antimicrobial activity has been ascribed to the tannins in the ethanol extracts, with MICs in the range of 10 to 26 mg/mL depending on the bacterial species. Ripe fruits were also found to have a significant higher antimicrobial activity compared to unripe fruits. Dried seeds have shown antibacterial effect against *Pseudomonas aeruginosa* [45]. The antibacterial activity of *R. coriaria* leaf methanol extract has been also shown against Gram positive and Gram-negative bacteria along with antimycotic activity against some *Candida* species[46] . Xanthones and aromatic components isolated from the seeds have been active against *Candida albicans* and *Aspergillus flavu* [47].

Antioxidant activity:

Developing safe, new and naturally derived antioxidants for food and health applications is a major goal in sustainable bio-products. Synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are widely used in spite of concerns regarding their toxicity and a sustainable supply [48]. An antioxidant is defined as ‘any substance that, when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate [49,50]. Antioxidants are of interest to biologists and clinicians because they help to protect the human body against damages induced by reactive free radicals generated in atherosclerosis, ischemic heart disease, cancer, Alzheimer's disease, Parkinson's disease and even in the aging process[51,52]. There are many evidences that natural products and their derivatives have efficient anti-oxidative characteristics, consequently linked to anti-cancer, hypolipidemic, anti aging and anti inflammatory activities[49-54] .

Antioxidant properties for stabilizing peanut oil have been also reported for the methanol extracts of Rhus Aromatica fruits and leaves. Fruit extract addition to peanut oil from 1 to 5% (w/v) has inhibited the formation of hydroperoxide during the initial 7 day after addition, but at 28 days of storage, the antioxidant potential of sumac extract has substantially lowered compared to BHA controls.

Hypolipidemic Activity:

Positive effects of sumac consumption on antioxidant status and cholesterol level in rabbits have been demonstrated in a recent study, suggesting that the plant may have a lowering effect on blood cholesterol level in animals and human beings [55]. On the other hand, Shafiei and coworkers showed that the sumac extract was able to decrease high serum lipid concentrations and could adjust the elevated cardiac lipid levels in the hypercholesterolemic conditions. Additionally, Valiollahi and others have shown that the triglyceride and cholesterol level decreased significantly in broiler chicks that consumed sumac; also, the LDL level decreased significantly and HDL levels increased in the same group [56]. Similarly, Santiago et al., reported reduced serum cholesterol concentrations in rats consuming d-limonene. It was recently monitored that the acute consumption of sumac might have a protective effect on some of the risk factors caused by high fat food stress, such as atherosclerosis, oxidative stress and liver enzymes [57]. Again, a significant decrease in the blood levels of total cholesterol, LDL-C, and fibrinogen compared to the high cholesterol diet group have been described elsewhere[58], a protective effect demonstrated on some risk factors including atherosclerosis and oxidative stress, followed consuming the Sumac with food.

Anti ischemic property:

Sumac leaves extract demonstrated cardiovascular protective effect. This property was investigated by using isolated rabbit heart and thoracic aorta preparations. Different factors such as free radical and ROS scavenging, tissue necrosis factor (TNF)-α inhibition, cycloxygenase pathway activation, and endothelial nitric oxide synthase activation were found to be responsible for cardiovascular protective effect. Sumac leaves contain hydrolysable gallotanins which are mainly responsible for anti ischemic property[59].

Anti migratory property:

Dry sumac was ground and tannins were extracted. Cultured rat carotid vascular smooth muscle cells were treated with tannins. Transmembrane migration assay was used to measure vascular smooth muscle cells migratory activity in response to platelet derived growth factor BB. Sumac significantly reduced vascular smooth cell migration by 62%, thus possesses potent anti migratory activity, and may possibly have atheroprotective effect [60].

Antifungal property:

Candidia albicans was susceptible at 625 mg/L MIC to methanol extract of Rhus coriaria leaves [61]. Dilution method was used to determine total fungal counts in spice samples. Three different nutritive media were chosen such as potato dextrose agar, coke rose, and czapek dox agar. Sumac showed very low affinity to be contaminated with moulds thus demonstrated antifungal effect [62].

DNA protective effect:

Sumac strongly reduced DNAmigration after treatment of the cells with H2O2 by 30%. DNA-migration due to endogenous production of oxidized pyrimidines and purines was also significantly decreased by 36% and 52%, respectively. The most significant decrease in damage due to oxidation of purines and pyrimidines was found in liver and in lymphocytes. Supplementation of drinking water clearly decreased comet formation due to oxidized DNA bases. Cells sensitivity towards anti benzo[a]pyrene-7,8- dihydro-diol-9,10-epoxide (BPDE) were also changed as BPDE-induced comet formation was markedly reduced by 69%. Overall glutathione *S*-transferase (GST) activity in plasma and the two isoenzymes GST–π and GST-α were clearly enhanced by 40%, 26%, and 52%, respectively, suggesting that sumac protects against genotoxic carcinogens which are degraded by these enzymes [63] .

VI. CONCLUSION

The above collected information regarding the uses and pharmacological activities of Rhus Aromatica is immensely useful for further studies. In the present scenario, ethnobotanical and traditional uses of natural compounds, especially of plant origin have received much attention, as they are well tested for their efficacy and are generally believed to be safe for human use. It is best classical approach in the search of new molecules for management of various diseases. Thorough screening of literature available on Rhus Aromatica depicted the fact that it is a popular remedy among the various ethnic groups, AYSUH and traditional practitioners for treatment of various ailments. Researchers are exploring the therapeutic potential of this plant as it has more therapeutic properties which have not been investigated. This review will be helpful in the development of polyherbal formulation as well as for conducting further research to explore the therapeutic potential of Rhus aromatic..

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