Review Article

Toxicodendron radicans (Poison Ivy): Phytochemistry, Pharmacology and Toxicology

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Received: 08-01-2021; **Revised:** 17-02-2021; **Accepted:** 25-02-2021; **Published on:** 20-03-2021.

ABSTRACT

Toxicodendron radicans (Family: *Anacardiaceae*) is very toxic plant associated with contact dermatitis. The toxic contact dermatitis is due to the presence of toxic molecule, urushiol. *T. radicans* mediated contact dermatitis secondarily facilitates the growth of various aerobic and anaerobic bacteria. Moreover, this plant is very much useful in homeopathic system of medicine for the treatment of various inflammatory conditions such as musculoskeletal problems, arthritis, carpal tunnel syndrome, pain in muscle, tendon and joint in the body. Pharmacologically the homeopathic preparation of *T. radicans* seen to be associated with anti-inflammatory and antineoplastic activity. Thus, in this review, the attempt has been made to review its medicinal use, phytochemicals, pharmacology and toxicity.

Keywords: *T. radicans*, medicinal use, phytochemistry, pharmacology, toxicity.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2021.v67i01.009

DOI link: http://dx.doi.org/10.47583/ijpsrr.2021.v67i01.009

INTRODUCTION

Medicinal plants play an active role in survival of mankind all over the world. Furthermore, a number of plant species, has also been identified in last few years with promising therapeutic potential. Although, research on a huge number of terrestrial plants has been done for their medicinal properties however, in plant kingdom, Anacardiaceae family remained unexplored[1-9].

T. radicans is belongs to the family of Anacardiaceae[10]. It is a toxic plant distributed throughout the United States, Canada, Ontario and Mexico over the Rocky Mountains and in West Indies[11]. Its nature is like climbing vine that grows on trees with the help of other support[12]. It has several vernacular names: In Latin: *Rhus radicans* L., *R. humilis* Salisb. *R. verrucosa* Scheele; In English: poison ivy; In French: sumac veneneux; In German: giftsumach[10]. The leaves of this plant were used in Homeopathic medicine[10]. In homeopathic System of Medicine this plant is used for the treatment of various inflammatory conditions[13]. Urushiol was the principle constituents present in this plant[14,15]. *T. radicans* mediated contact dermatitis was due to the presence of this toxic molecule[14,15]. In this review, the attempt has been made to review its medicinal use, phytochemicals, pharmacology and toxicity.

Medicinal Use

Historically, *T. radican* has been used as herbal medicines for skin conditions, paralysis, and arthritis[16]. The acrid oil of this plant used for itching in North America[16]. In homeopathic *T. radicans* was recommended for vesicular dermatoses like varicella, erisipelas, herpes simplex, contact dermatitis[16]. In homeopathy this plant has been used for the treatment of various musculoskeletal problems, arthritis, carpal tunnel syndrome, and painful conditions of muscle, tendon and joint in the body[17].

History

T. redicans was first introduced in London in 1640 and this plant was not used in the medicinal purpose till 1798[18]. A great physician of Valenciennes, Du Fresnoy was first demonstrated that this plant can be useful for the treatment of herpetic eruptions and palsy[18]. After Du Fresnoy's success this plant was gained popularity in general practice and then used in the treatment of paralysis, rheumatism, amaurosis, and other chronic and eruptive diseases[18]. In general purpose the milky juice was used as indelible ink and varnishing agent for finishing boots and shoes[18].

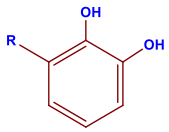
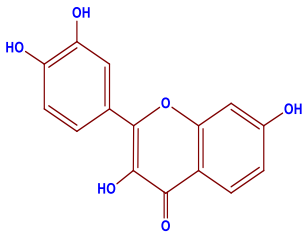
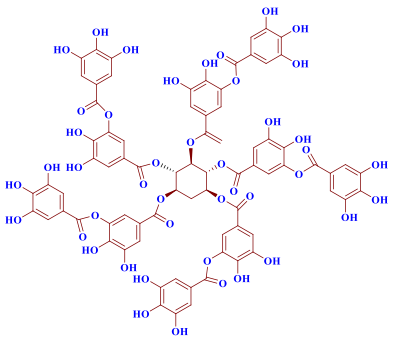
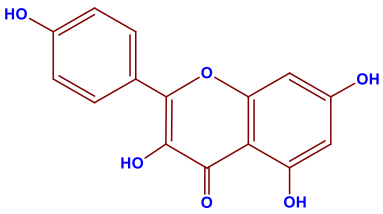
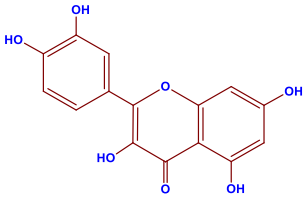
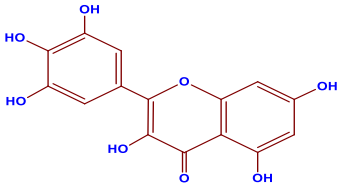
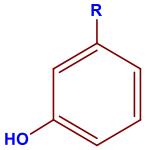
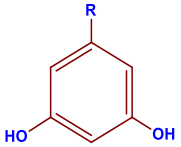
Botanical Description

T. redicans is a less erect herb and grows up to 2 to 4 feet[18]. These species grows at a height of 1500m above sea level being popular in suburban and exurban areas of U.S and New England. Roots are reddish with branches[19,18]. Leaves are alternate, compound, deciduous, pinnate, trifoliate, yellowish green, veined, thin and long petioles[18-20]. Folioles are oval and 3 inches long. The leaflets are acute and intended angularly, 10-16 cm long and 5-10 cm wide[19]. The surface of the leaves of T. *redicans* are smooth with no teeth along its edges. Propagation occurs dioeciously by means of vegetative as well as sexually method in the month of May to July. The mature leaflets are variously dentate, crenate, and sinuate[18]. The lateral leaflets are unequal[18]. Species of T. *redicans* grows on wide range of soils ranging from acidic to alkaline medium; however, it can also grow in areas with seasonal flooding and having brackish water[21]. These plants are too much sensitive to CO_2 levels. Being sensitive acts as a marker for carbon dioxide levels in ecosystem. Higher the CO_2 level in atmosphere greater will be the rate of plant growth[22]. Stems are erect covered with gray, brown bark[19]. Flowers are polygamous, small, yellowish-green, milky juice with nauseous odor[19,18]. Fruits are smooth, rounded, 4-6 mm in diameter, pale brown in colour and produced in clusters like grapes[18,20]. The nutlets are gibbous, straight and tuberculate [18].

Phytochemistry

All parts of the *T. radicans* were containing urushiol (1) as a principle toxic compound[23,24,20]. Other constituents including rhoitannic acid, volatile principle toxicodendric acid [18], fisetin (2), gallotannic acid (3), kaempherol (4), heneicosandicarbonic acid, quercetin (5), urushenol, myricetin (6)[25], cardanol (7) and cardol (8)[23] were also reported to present in *T. radicans*. Keeler and Tu (1983) reported that the leaves contain numbers of pentadecylcatechol including 3-n- pentadecylcatechol, 3-n- pentadecyl-8'-catechol, 3-n- pentadecyl-8'-11'-catechol, 3-n- pentadecyl-8'-11'-14'-catechol[26]. Two new pentadecylcatechol analogues compounds, 3-(tridecafluoroundecyl)-catechol and 3-(nonafluoropentadecyl)-catechol were identified in the leaves[27]. The leaves were also containing some non-toxic glycoside of fisetin, rhamnose and gallic acid[28].

Table 1: Important chemical constituents of *T. radicans*

 Urushiol (**1**) R=$(CH_2)_7$-CH=CH-CH_2-CH=CH-CH_2-CH=CH_2	 Fisetin (**2**)
 Gallotannic acid (**3**)	 Kaempferol (**4**)
 Quercetin (**5**)	 Myricetin (**6**)
 Cardanol (**7**) R=$(CH_2)_7$-CH=CH-$(CH_2)_5$ –CH_3	 Cardol (**8**) R=$(CH_2)_{14}$-CH_3

Pharmacology

Anti-inflammatory activity

Inflammation is the response to body aggression by a pathogen agent, an allergen, a toxic compound, a tissue lesion, etc. It is generally a phenomenon with fever and tiredness, with local symptoms, pain, and edema. New anti-inflammatory substances are still vitally necessary due to intolerable side effects such as gastric ulceration, of the marketed anti-inflammatory drugs[29-34]. Inflammation is a well-known symptom of many diseases such as arthritis, diabetes, obesity, cancer, neurodegenerative diseases, autoimmune disorders, dementia, scleroderma, allergy, asthma, bronchitis, inflammatory bowel disease, and cardiovascular diseases[35-40].

Homeopathic *T. radicans* extract was used to treat various inflammatory conditions[13]. *In vivo* study revealed that homeopathic Rhus significantly reduced the carrageenan-induced paw oedema, vascular permeability and stress induced gastric lesions[13]. It reduced the inflammatory processes by interfering the involvement of histamine, prostaglandins and other inflammatory mediators[13].

Antineoplastic activity

According to a World Health Organization (WHO) report, by 2030 there will be 21 million new cases of cancer and 13 million deaths due to this disease. Cancer is one of the leading causes of deaths worldwide[41-43]. A number of natural products have been reported to exhibit significant anti-cancer actions. Developing prospects of using phytochemicals have shown a recent therapeutic concept for the utilization of phytochemicals as pharmacological alternatives against human malignancies in a drug repositioning approach[44-45].

From the ancient times, *T. radicans* has been used in homeopathic medicine for the treatment of tumor in America, Asia and Europe [46]. Heine (2008) demonstrated that low homeopathic dilution of Rhus showed antineoplastic activity against tumor cell line (Hep G2) as well as in animals[46.]

Toxicity

The main toxic effect associated with *T. radicans* was contact dermatitis[14,15]. Urushiol was present in *T. radicans*[24] and was a potent allergen as well acts as a potent skin irritant[47]. The contact dermatitis was developed due to the presence of urushiol[48,49]. Poison ivy containing urushiol causes severe allergic reaction (SAR) causing contact dermatitis which in extreme cases leads to fatal condition leading to Anaphylaxis. 15-20% of the population shows no allergic reaction to urushiol. Duration of rashes may last up to 5-12 days normally but in chronic cases it may extend up to a month. Urushiol mediated contact hypersensitivity depending on the CD4+ T cells and CD8+ T cells [50,51] and the IFN-γ, TNF-α, and inducible protein 10 plays an important role in this CD4+ T cells and CD8+ T cells dependent contact hypersensitivity [51].

The oral ingestion of Rhus produced lesions like maculopapular eruptions, erythroderma, vesiculobullous lesions and erythema multiform-like lesions[52]. In many patients it was also produced leucocytosis with neutrophilia and abnormalities in liver function[52]. From a case study showed that it causes severe pruritic, erythematous, vesicular and bullous dermatitis[53]. After poisonous infection with ivy dermatitis secondarily facilitated the growth of aerobic, anaerobic bacteria in infection sites[54]. The most predominant bacteria were including *Staphylococcus aureus*, β-haemolytic *Streptococci* spp., *Prevotella* spp., *Porphyromonas* spp., *Fusobacterium* spp., *Bacteroides fragilis*[54,55].

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Source of Support: None declared.

Conflict of Interest: None declared.