Anatolian Journal of Biology
ISSN: 2687-444X
2020 2:69-73

Mini Review

Bioactivities of *Toxicodendron succedaneum* (L.) Kuntze Extracts and Isolated Compounds

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Received 02 December 2020; accepted 28 December 2020
Available online 31 December 2020

Abstract

Toxicodendron succedaneum (L.) Kuntze (synonym: *Rhus succedanea* L.) is a tree in the family of Anacardiaceae. *T. succedaneum* has been using to treat diarrhea, nose and gum bleedings, vomiting, dysentery, cough, tuberculosis, fever, asthma, liver ailments, and ear infections in traditional medicines. Phytochemicals such as agathisflavone, rhusflavone, robustaflavone, succedaneaflavanone, and volkensiflavone were isolated from this plant species. The purpose of this review is to analyze, summarize, and document available bioactivity studies of *T. succedaneum*. The Web of Science, Scopus, ScienceDirect, and PubMed (databases) were used to search relevant published papers between 1900 and November 2020. So far, *in vivo* is the highest level of scientific evidence available for the reported bioactivities. Various parts of *T. succedaneum* disclosed such as antibacterial, anticancer, anti-diabetic, anti-inflammatory, antioxidant, and antiviral activities. Anticancer, antioxidant, and antiviral compounds have been identified from this plant species. Further bioactivity and phytochemical studies should make it possible to obtain additional scientific evidence. This minireview work will be useful for future researches involving this plant species.

Keywords: Toxicodendron succedaneum, *Rhus succedanea,* Anacardiaceae, Sri Lanka, Siddha Medicine, bioactivities.

1. Introduction

Toxicodendron succedaneum (L.) Kuntze (synonym: *Rhus succedanea* L.) is a tree in the family of the *Anacardiaceae*. It is originally from Asia (Japan, Taiwan, Laos, Malaysia, Cambodia, India, Bangladesh, China, Mongolia, Korea, Indonesia, Vietnam, and Thailand) and was introduced to South America (Cuba) [1]. It is called Katkadahasingi (கற்கடகசிங்கி) in Tamil/Siddha Medicine, Karkatashringee in Ayurveda, and Wild varnish tree and Japanese wax tree in English [2]. *T. succedaneum* has been using to treat diarrhea, nose and gum bleedings, vomiting, dysentery, cough, tuberculosis, fever, asthma, liver ailments, and ear infections in traditional medicines [2]–[4]. Noticeably, galls are applied to prepare antidiabetic preparations in Sri Lankan Siddha Medicine [5]–[8]. Phytochemicals, including 5-hydroxy-2-methyl-4H-pyran-4-one, 7"-O-3-glucoside, agathisflavone, amentoflavone, benzeneacetaldehyde, linalool, cupressuflavone, GB-1a, GB-2a, hinokiflavone, lilac aldehyde, morelloflavone, neorhusfiavanone, p-anisaldehyde, p-cresol, rhusflavanone, rhusflavone, robustaflavone, spicataside, succedaneaflavanone, trimethoxybenzene, and volkensiflavone have been isolated from this plant species [9]–[12].

The purpose of this work is to analyze, summarize, and document available bioactivities studies of *T. succedaneum*. This work would be beneficial for future bioactivities and phytochemical studies using this plant species.

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Table 1: Reported bioactivities of *T. succedaneum*

Level of scientific evidence	Bioactivity	Part used	Extract / compound	Assay / model	Dose / concentration	Reference
In vivo	Anticancer	Sap	10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone	Fischer 344 rat	1 mg/kg	[14]
In vivo	Anti-inflammatory	Gall	Water	Carrageenin-induced paw oedema	50 mg/kg	[16]
In vitro	Antibacterial	Gall	Water	*Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis*	300 µg/disc	[17]
In vitro	Antibacterial	Gall	Hexane, Methanol	*Eschericia coli, Micrococcus luteus, Salmonella typhi, Staphylococcus aureus*	100 µg	[22]
In vitro	Anticancer	Leaf	Methanol	Prostate cancer cell line DU145, Prostate cancer cell line LNCaP	500 µg/ml	[15]
In vitro	Anticancer	Sap	10'(Z),13'(E),15'(E)-heptadecatrienylhydroquinone, 10'(Z)-heptadecenylhydroquinone, 10'(Z),13'(E)-heptadecadienylhydroquinone	NS	NS	[24]
In vitro	Anticancer	Sap	10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone	Leukemia HL-60 cell	0.9 µM (EC_{50})	[14]
		Sap	10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone	Topoisomerase-II-deficient cell HL-60/MX2	9.6 µM (EC_{50})	
In vitro	Antidiabetic	Leaf	NS	Aldose reductase inhibitory	2.47 µg/ml (IC_{50})	[18]
		Stem	NS	Aldose reductase inhibitory	NS	
In vitro	Antihepatitis	Seed	Robustaflavone	Hepatitis B virus	0.25 µM (EC_{50})	[21]
In vitro	Antihepatitis	Seed	Robustaflavone	Hepatitis B virus replication in 2.2.15 cell	0.25 µM (EC_{50})	[25]
In vitro	Antioxidant	Gall	Methanol	ABTS	224.83 mmol/100 g dry weight	[23]
		Gall	Methanol	DPPH radical scavenging	236.49 mmol/100 g dry weight	
		Gall	Methanol	FRAP	104.45 lmol/g dry weight	
In vitro	Antioxidant	Gall	Water	DPPH radical scavenging	27.33 µg/ml (IC_{50})	[13]

Level of scientific evidence	Bioactivity	Part used	Extract / compound	Assay / model	Dose / concentration	Reference
		Gall	Water	NO radical scavenging	32.63 µg/ml (IC_{50})	
In vitro	Antioxidant	Sap	10'(Z),13'(E),15'(E)-heptadecatrienylhydroquinone, 10'(Z),13'(E)-heptadecadienylhydroquinone, 10'(Z)-heptadecenylhydroquinone	NS	NS	[24]
In vitro	Antiviral	Seed	Agathisflavone	HIV-1 acutely infected primary human lymphocyte	33.6 µM (EC_{50})	[21]
		Seed	Agathisflavone	HIV-1 reverse transcriptase	100 µM (IC_{50})	
		Seed	Amentoflavone	HIV-1 acutely infected primary human lymphocyte	94 µM (EC_{50})	
		Seed	Amentoflavone	HIV-1 reverse transcriptase	119 µM (IC_{50})	
		Seed	Hinokiflavone	HIV-1 acutely infected primary human lymphocyte	4.1 µM (EC_{50})	
		Seed	Hinokiflavone	HIV-1 reverse transcriptase	62 µM (IC_{50})	
		Seed	Robustaflavone	HIV-1 acutely infected primary human lymphocyte	100 µM (EC_{50})	
		Seed	Robustaflavone	HIV-1 reverse transcriptase	65 µM (IC_{50})	
		Seed	Agathisflavone	Respiratory virus (Influenza A), Respiratory virus (Influenza B)	NS	[20]
		Seed	Amentoflavone	Herpes virus (HSV-1)	17.9 µg/ml (EC_{50})	
		Seed	Amentoflavone	Herpes virus (HSV-2)	48 µg/ml (EC_{50})	
		Seed	Amentoflavone	Respiratory virus (Influenza A)	NS	
		Seed	Amentoflavone, Rhusflavanone	Respiratory virus (Influenza B)	NS	
		Seed	Rhusflavanone	Herpes virus (HSV-2)	NS	
		Seed	Rhusflavanone	Respiratory virus (Measles)	NS	
In vitro	Antiviral	Seed	Robustaflavone	Herpes virus (HSV-1)	8.6 µg/ml (EC_{50})	[19]
		Seed	Robustaflavone	Herpes virus (HSV-2)	8.5 µg/ml (EC_{50})	
		Seed	Robustaflavone	Respiratory virus (Influenza A)	2 µg/ml (EC_{50})	
		Seed	Robustaflavone	Respiratory virus (Influenza B)	0.2 µg/ml (EC_{50})	

2. Materials and methods

The Web of Science, Scopus, ScienceDirect, and PubMed databases were employed to search for relevant published articles from 1900 to November 2020. The scientific name (*Rhus succedanea* L.) was obtained from A Checklist of Medicinal Plants of Sri Lanka by Sugathadasa et al. (2008). Then it was validated using [1]. It was found that *Rhus succedanea* L. was a synonym of *Toxicodendron succedaneum* (L.) Kuntze. Therefore, both scientific names *Rhus succedanea* L. and *Toxicodendron succedaneum* (L.) Kuntze were used as search terms in the literature review process. Then the findings were limited to subjects such as Pharmacology, Toxicology, Pharmaceutics, Medicine, Biochemistry, Genetics, Molecular Biology, Chemistry, Agriculture, Biology, and Multidisciplinary.

3. Results and discussion

3.1. Reported bioactivities of *T. succedaneum*

Table 1 presents information such as the level of scientific evidence, bioactivity, part used, extract/compound, assay/model, dose/concentration, and reference of reported studies. So far, *in vivo* is the highest level of scientific evidence available at the moment for reported bioactivities. Different parts of *T. succedaneum* unveiled such as antibacterial, anticancer, antidiabetic, antihepatitic, anti-inflammatory, antioxidant, and antiviral activities [13]–[25]. However, more scientific evidence is available for anticancer activity. Further, gall has been used in most of the studies and in a greater number of studies, and water and methanol have been used as solvents to prepare the extracts. Anticancer, antihepatitic, antioxidant, and antiviral active compounds have been identified in this plant species. All over, eight bioactive compounds have been discovered in *T. succedaneum.* Robustaflavone exhibited both antihepatitic and antiviral effects. Only two traditional medicinal use for treating liver disorders and diabetes have scientific evidence at the moment. Only riveting investigations, based on the lowest concentration/dose used are discussed below.

3.2. Reported *in vivo* activities

3.2.1. Anticancer activity

10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone that was isolated from sap orally administered to Fischer 344 rat at a dose of 1 mg/kg exhibited anticancer activity [14].

3.2.2. Anti-inflammatory activity

In a study conducted by Kumar et al., 50 mg/kg of water gall extract orally directed to Carrageenin-induced paw edema animal models showed significant anti-inflammatory activity [16].

3.3. Reported *in vitro* activities

3.3.1. Antibacterial activity

Hexane and methanol gall extracts (100 µg) unveiled antibacterial activities against *Escherichia coli, Micrococcus luteus, Salmonella typhi, and Staphylococcus aureus* [22].

3.3.2. Anticancer activity

Up to now, three active anticancer compounds (10'(Z),13'(E),15'(E)-heptadecatrienylhydroquinone, 10'(Z)-heptadecenylhydroquinone, and 10'(Z),13'(E)-heptadecadienylhydroquinone) isolated from sap. Anyhow,10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone (Half maximal effective concentration, EC50 0.9 µM) showed the best anticancer activity in leukemia HL-60 cell line [14], [24].

3.3.3. Antidiabetic activity

Lee et al. (2008) studied the antidiabetic activity of leaf extract in aldose reductase inhibitory assay exhibited inhibitory activity at the half-maximal inhibitory concentration, IC_{50} 2.47 µg/ml [18].

3.3.4. Antihepatitic activity

Until now, only one antihepatitic active compound identified from T. succedaneum. In two studies conducted independently by Lin et al. (1997) and Zembower et al. (1998), robustaflavone isolated from seeds unveiled the antihepatitic effects at EC50 0.25 µM in both hepatitis B virus assay and hepatitis B virus replication in 2.2.15 cell line [21], [25].

3.3.5. Antioxidant activity

An extract prepared using water and gall revealed the antioxidant properties in DPPH radical scavenging assay at IC_{50} 27.33 µg/ml [13].

3.3.6. Antiviral activity

Overall, five antiviral compounds have been identified from this plant species, and they are agathisflavone, amentoflavone, hinokiflavone, robustaflavone, and rhusflavanone [19]–[21]. Among these compounds, robustaflavone discovered in seeds showed the best antiviral activity at IC_{50} 0.2 µg/ml in respiratory virus (Influenza B) assay [19].

3.4. Toxicity studies

10′(Z),13′(E),15′(E)-heptadecatrienylhydroquinone (1 mg/kg) isolated from sap injected to rats for 28 days and no adverse side effects and mortality were observed [14].

4. Conclusion

On one hand, there are only two pieces of scientific evidence available for the ethnomedicinal uses of *T. succedaneum.* On the other hand, there is a range of traditional medicinal uses for this plant species. Hence, further bioactivity and phytochemical studies should make it possible to obtain additional scientific evidence. Also, the active compounds for the other

traditional medicinal uses should be isolated. This minireview work will be useful for future researches involving this plant species.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgments

This work received no funding. The authors are grateful to their family members for their support to deliver this work.

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