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Review

Review of the application of the traditional Chinese medicinal herb, *Ranunculus sceleratus* Linn.

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Ranunculus sceleratus **Linn. is a wetland plant and a widely used traditional Chinese medicinal herb that has been researched intensively. It has many pharmacological effects, such as antibiosis, antiphlogosis, and the relief of articular effusion. *R. sceleratus* also has water purifying effects because it can adsorb large amounts of nitrogen and phosphorus, decompose suspended organic particles, and accumulate heavy metals such as Fe and Zn, while it may also be used to monitor any variation in these levels. These activities of *R. sceleratus* are attributable to its secondary metabolites including alkaloids, sterols, tannins, flavonoids, and tryptamine derivatives. The functional chemicals produce by *R. sceleratus* might be applied to the control of harmful algae in the future.**

Key words: Environmental restoration, functional metabolites, potential application, *Ranunculus sceleratus*, traditional Chinese medicinal herb.

INTRODUCTION

Ranunculus sceleratus Linn. is an annual or perennial herbaceous plant, which is often found on damp terrain, riversides, and small water bodies. This species originated in the northern hemisphere and it is widely distributed in China. *R. sceleratus* biosynthesize and releases functional chemicals including ranunculin, protoanemonin and anemonin. Accidental ingestion of *R. sceleratus* can cause respiratory failure and even subsequent death in human (Xiang et al., 2010). In traditional Chinese medicine, the whole plant of *R. sceleratus* is collected during the late spring or early summer, and then rinsed (Wu et al, 1999). The fresh or dry plant can be used to treat cancer of the esophagus and the breast (Li, 1999). In addition to its medicinal value, *R. sceleratus* has other potential applications. Recent studies suggest that it is capable of purifying organic sewage and the industrial wastewater containing an abundance of heavy metals. *R. sceleratus* has also been considered as a potential bio-indicator of eutrophication in aquatic habitats (Xu et al., 2004). In this report, we reviewed the literature on possible applications of *R. sceleratus* to elucidate its potential value.

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BIOLOGICAL AND ECOLOGICAL CHARACTERISTICS OF *R. sceleratus*

The white fibrous roots of *R. sceleratus* are distributed mainly in the upper soil layer, about 10 to 25 cm deep in the soil. The diameter of the rhizosphere is ca. 18 cm. The taproot may rot during development. The fine roots have many root hairs and they contain a hollow cavity surrounded by the epidermal parenchyma. This means that roots have a very soft texture. The stems of *R. sceleratus* are light green, robust, and smooth. The aerial regions of *R. sceleratus* possess an abundance of trichomes (konar et al., 1972). The adult plant generally reaches a height of 40 to 60 cm without any obvious intermediate nodes. The stem has a hollow cavity that extends from the top to the bottom, with a diameter of 0.3 to 0.8 cm. The upper stems branch during the spring. *R. sceleratus* possesses stalked simple tripartite leaves. The leaves can have a variety of shapes including circles, kidney-shapes, and hearts. The length and width of leaves ranges from 3 to 4 and 1.2 to 4 cm, respectively. The leaves are arranged alternately on stems. The flower has a diameter of 6 to 8 mm with five sepals, which are

Table 1. The biological characteristics of *R. sceleratus* Linn (Teaching and Research Section, 1990).

Plant height	Branches per plant	Flowering period	Fruiting period	Petals per flower	Flower diameter	Receptacle area	Lobes per leaf
20-40 cm	41-423	Early spring	March-April	5	6-8 mm	10-32 mm^2	2-3
Plant length							
Achene	Leaf	Root	Pedicel	Sepal	Pedal	Anther	Receptacle
1-1.2 mm	3-15 cm	10-25 cm	1-2 cm	2-3.5 mm	1.5-3 mm	0.2 mm	3-10 mm
The reproduction and seed output (Mean)							
Fruits per plant (270.8 seeds per fruit)		Dry weight per seed		Seed yield		Total reproduction capacity	
3223 ind./m^2 (individual/m^2)		1.85×10^{-4} g/ind.		8.728×10^5 ind. / m^2		161.5 g/m^2	

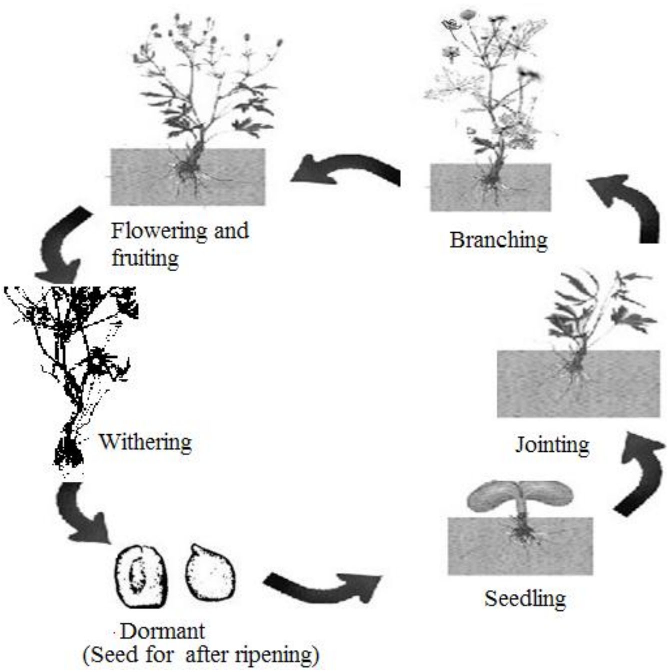


Figure 1. The life cycle of *R. sceleratus* Linn. The life cycle of the species is divided into six stages, including seedling, jointing, branching, flowering-fruiting, withering, and dormant, according to morphological features (Wu et al., 1999).

covered with tiny hairs (Xu and Andre, 1972). There are five obovate petalines, which are flat, open and yellow, while the flower is reflexed. The flower contains multiple stamens and pistils. The anthers are elongated and oval, and the flowers produce a small ovary. *R. sceleratus* flowers mainly between April and June. The fruit are characterized as an etaerio of achenes that are suborbicular with a diameter of 1 cm. Both sides are covered with wrinkles and the apex has a short beak. *R. sceleratus* usually produces fruits from May to August. A single seed appears dark green. (Quantitative biological traits are shown in Table 1).

R. sceleratus emerges in February to form fascicular assemblages (Qian and Dong, 1999) and it is commonly found in wetlands, by streams or ditches, and sometimes water bodies. Its life cycle is shown in Figure 1. It is distributed widely in the northern hemisphere, including China. *R. sceleratus* grows well and acquires a large biomass in both warm climates and cold periods. It will still germinate at 5°C, even when this temperature persists for 5 to 7 days. It grows very well in temperatures exceeding 10°C and it reaches its optimal state at 20°C. The habitat preferences of *R. sceleratus* are determined by the fertility, available water, and adequate light. With fertile soil, adequate water, and sufficient light, *R. sceleratus* develops well and branches vigorously, with a strong stem, to produce numerous seeds (Yang et al., 2006). In aquatic and terrestrial habitats, *R. sceleratus* displays no significant differences, apart from its leaf configuration. The leaves are very smooth and terminate with a circle in aquatic habitat, whereas they are coarse, hairy, and sharp in terrestrial habitat (Qian and Dong, 1999). Yang et al. (2006) found that *Schoenoplectus trigueter* L. promotes the growth of *R. sceleratus*. When accompanied by *S. trigueter*, *R. sceleratus* grows rapidly and produces many branches, buds, flowers and seeds.

REACTIVE CHEMICALS PRODUCED BY *R. sceleratus*

Many studies have confirmed the role of *R. sceleratus* as a traditional Chinese medicine, especially as an antibiotic, antiphlogostic, diarrhea cure, and mastitis remedy. It is also suitable for water purification purification (luan et al., 2008; Shi et al., 2009; Zhao et al., 2008) and the removal of heavy metals. These functions are attributable to specific amino acids and sugars, which can be used as medical value assessment indices (Table 2), and their metabolic products. Misra and Dixit (1979, 1980) discovered that protoanemonin and anemonin extracted from *R. sceleratus* leaves had a strong antimicrobial function. The stems of *R. sceleratus* contain numerous flavonoids, which were identified by Dong et al.

Table 2. Amino acid and sugar contents of *R. sceleratus* Linn.

Plant part	Amino acid (%)						
	Cystine	Lysine	Histidine	Serine	Methionine	Proline	Glutamic acid
The aerial part	19.60	18.14	9.29	2.10	8.14	3.46	2.45
Root	24.12	17.40	9.04	8.71	7.53	3.18	0
Seed	12.85	5.48	1.70	14.91	22.08	2.64 (threonine)	4.91 (tyrosine)

Plant part	Sugar (%)			Plant part	Sugar (%)		
	Sucrose	Glucose	Fructose		Sucrose	Glucose	Fructose
The aerial part	19.97	19.75	52.05	Root	67.46	4.76	27.77

(2007). It is well-known that flavonoids compound, which are important secondary metabolites in plants, have many roles in fat reduction, anti-thrombotic and anti-arrhythmic therapy, and as antioxidants. Tricin (ca. 0.0204 mg/g) is a functional component in most types of buttercups and it was detected in *R. sceleratus* (Dong et al., 2007). Tricin has a potent resistance to exterior oxidation and it can be used to treat cancer in humans. During experimental pharmacodynamic screening for anti-HBV effects, Gao et al. (2005) isolated and identified six functional chemicals including stigmasa-4-ene-3,6-dione, stigmasterol, isoscopoletin, scoparone, protocatechuic aldehyde, and protocatechuic acid. Most of the active chemicals that have been identified and isolated are shown in Table 3.

POTENTIAL APPLICATIONS OF *R. sceleratus*

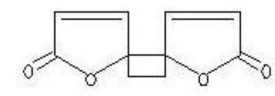
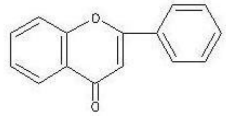
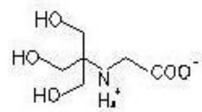
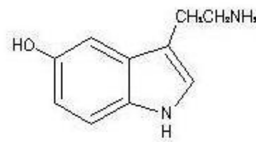
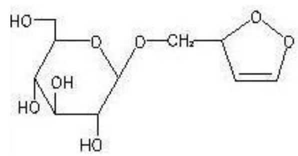
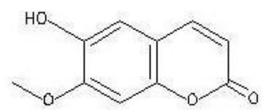
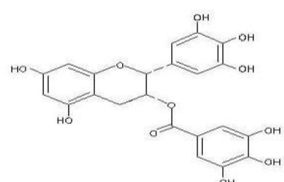
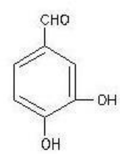
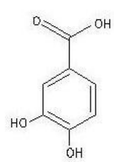
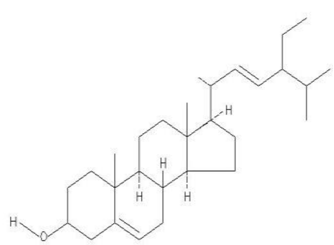
Medicinal value and use in disease therapy

R. sceleratus is a common traditional Chinese medicinal herb with excellent therapeutic effects, which was recorded in the earliest Chinese literature in this area. This medicinal herb has a bitter flavor, good nature, and specific toxicity. It is capable of promoting blood circulation by removing blood stasis, expelling cold, relieving swelling, and removing excessive heat from the liver and the gall bladder. It can also cure internal abscess, malaria, scrofula, snake or scorpion venom, and acute icteric hepatitis (PRI, 2003). Du (2009) used fresh *R. sceleratus* to relieve hydrops articulation of the knee, with an 80% percent cure rate. This was attributed to the activity of protoanemonin from *R. sceleratus*. This chemical greatly stimulates the affected region and it also altered the blood circulation in the sore region, resulting in the elimination of inflammation and swelling, and the recovery of abnormal tissue. During the 1980s, many researchers demonstrated that *R. sceleratus* has antifungal properties. Misra *and* Dixit (1980) also showed that a leaf extract of *R. sceleratus* produced a very strong antibacterial effect. Subsequent chemical analyses identified and isolated protoanemonin and anemonin. Both compounds had no effects on other plants, whereas they killed harmful fungi at a low concentration. It was suggested that antibiotics could be developed from *R. sceleratus* in the future to cure human diseases caused by fungi. Chagas disease is a common epidemic disease and second in frequency only to malaria in Latin America. It is caused by *Trypanosoma cruzi*. Schinella et al. (2002) screened 18 plant species and two types of bacterium to determine their inhibitory effects on *T. cruzi*. Methanol extracts of the aerial part of *R. sceleratus* and the root of *Coptis deltoidea* at a concentration of 250 µg/ml had significant inhibitory effects on *T. cruzi*. The inhibitory rates were 97 and 100%, respectively. If both extracts were mixed, the suppression rate of *T. cruzi* could be very significant. Therefore, a novel mixture of extracts from *R. sceleratus* and other species could provide a good alternative for treating specific human diseases.

Environmental remediation

R. sceleratus has great potential in the field of phytoremediation. It adsorbs many heavy metals from its surroundings, such as Fe and Zn. Hu et al. (2007) found that *R. sceleratus* accumulated Fe and Zn (Guo et al., 2002) and its roots had the greatest capacity for Fe adsorption. However, an excess of this element destroyed the membrane system and enhanced the permeability of the plasma membrane of *R. sceleratu*. Zhou et al. (2002) also verified that *R. sceleratus* can remove five heavy metal elements (Cd, Cr, Cu, Zn, and Pb) from the soil. Thus, *R. sceleratus*, especially its aerial parts, could adsorb a great deal of nitrogen, phosphorus, and organic matter from eutrophic water systems. *R. sceleratus* also had a good performance when used to treat different types of polluted sewage. After the application of *R. sceleratus*, the mean removal rate of chemical oxygen demand (CODcr), total nitrogen (TN), total phosphorus (TP) from sewage were found to reach 74.1, 73.4, and 74.5%, respectively (Wang et al., 2009). Pollutants were completely removed by a combination of

Table 3. Important active chemicals in *R. sceleratus* Linn.

Chemical	Chemistry formula	Chemical abstracts service (CAS)	Chemistry structure	Source	Concentration (mg/g)
Anemonin	$C_{10}H_2O_4$	508-44-1		Plant	unknown
Flavone derivatives	$C_{15}H_{10}O_2$	84-54-8		Stem	14.96-26.02
Tricin	$C_6H_{13}NO_5$	5704-04-1		Stem and leaf	0.0204
5-hydroxy tryptamine	$C_{10}H_{12}N_{20}$	28721-19-9		Plant	unknown
Ranunculin	$C_9H_{14}O_8$	124064-70-6		Plant	unknown
Isoscopoletin	$C_{10}H_8O_4$	776-86-3		Plant	unknown
Scoparone	$C_{22}H_{18}O_{11}$	989-51-5		Plant	unknown
Protocatechuic aldehyde	$C_7H_6O_3$	139-85-5		Plant	unknown
Protocatechuic acid	$C_7H_6O_4$	99-50-3		Plant	unknown
Stigmasterol	$C_{29}H_{48}O$	83-48-7		Plant	unknown

R. sceleratus and *Rumex acetosa* Linn. (Shi et al., 2008). Therefore, *R. sceleratus* has often been used as the main species in the design of constructed wetland in parks (Guo et al., 2010; Luan et al., 2008). *R. sceleratus* can assimilate several typical pollutants, such as nutrient elements and heavy metals, during its growth and reproduction. It also supports the growth of the microbial rhizosphere. This co-existing relationship will be beneficial for nitrification, denitrification and pollution purification.

Biological monitoring of environmental change

Biological species that can be used to monitor pollution status have been widely reported. Environmental pollution can be measured based on micronucleus occurrence and formation, as well as chromosomal aberration, in indicator organisms. Guo (1985) showed that *R. sceleratus* could be a useful indicator organism for monitoring environmental pollution, because of its micronucleus responses to environmental mutagenic pollutant. *R. sceleratus* was cultured in two different types of sewage, that is, a wastewater containing heavy metals and nitrate from a watercress field, and another containing ClO^- and mercury from the a plant. The micronuclei of the apical meristematic region were then observed in *R. sceleratus*. With increasing concentrations of pollutants, the rate of micronucleus formation was enhanced and it was greater with the sewage from the chemical plant compared with that from the watercress field. Therefore, *R. sceleratus* could be very valuable as a biological monitoring organism for evaluating environmental pollution.

Ornamental value

R. sceleratus is an annual or perennial wetland herb, and a highly decorative species. Many light yellow flowers are produced on the cymes at the anthesis stage in *R. sceleratus*. During the fruiting period, the receptacles are elongated and amplified, with a cylindrical form. The numerous obovate achenes are closely clustered on the receptacle. Because of its attractive features, *R. sceleratus* has been planted in shallow wetlands and lakes. *R. sceleratus* is also found in the parks, urban residential areas, and a wide range of the waterscapes, where it contributes to the attractive scenery. It has also been utilized as a barrier in the waterscape on beaches and lake shores.

RESEARCH PROSPECTS

R. sceleratus is very common in China. However, there has been little development of its utilization for environmental protection such as sewage treatment and the control of harmful algae. *R. sceleratus* has been widely used in traditional Chinese medicine, but it also has great potential in eutrophication remediation and heavy metal removal. These functions probably rely on specific secondary metabolites. Thus, we should try to build a functional chemical database of *R. sceleratus* and its spectrum of effects. It would facilitate the development of its potential allelopathic effects for the inhibition of the main algae found in water bloom and red tide. The development of potential applications for *R. sceleratus* demands further investigations and studies.

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