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The Potential and Outgoing Trends in Traditional, Phytochemical, and Ethnopharmacological Activity of *Rumex nepalensis* : A Comprehensive Review

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ABSTRACT

Rumex, a genus of polygonaceae family, is very prevalent worldwide. There are about 200 species of this genus, many of which are beneficial and used as vegetables and for their medicinal properties. *Rumex nepalensis* Spreng. (Polygonaceae) commonly-known as Nepal Dock has wide-spectrum therapeutic potencies and is extensively used for centuries in traditional medicine systems. Root, seed, leaf, fresh plant juice, aerial parts, etc. are the parts generally used. The leaves of this plant are edible and a rich source of natural antioxidants. Extracts and metabolites from this plant exhibit pharmacological activities including anti-inflammatory, antioxidant, antibacterial, purgative, analgesic, antipyretic, anti-algal, central nervous system depressant, wound healing, and skeletal muscle relaxant activity. Due to its remarkable biological activities, it has the potential to act as a rich source of the drug against life-threatening diseases. However, more studies are needed to scientifically validate the traditional uses of this plant, besides isolating and identifying their active principles and characterizing the mechanisms of action. We present herein a critical account of its ethnobotany, traditional uses, phytoconstituent profile, and major pharmacological activities reported in recent years and therefore will provide a source of information on this plant for further studies.

INTRODUCTION

The evolution of mankind has happened along with their surrounding herbs and medicinal plants from the ancient period. Approximately 270,000 plant species have been discovered by a human, while there is a possibility of the existence of close to 400,000 species in mother earth [1]. No synthetic substitute is currently available for about 121 major plant-based drug molecules, comprising 45 from tropical and 76 from subtropical areas. A recent study by World Health Organization claimed 80% dependency of the world population on ethno medicines to some extent [2]. Medicinal plants are nature's gift for answering a limitless range of fatal diseases among human beings, therefore medicinal plants are getting more consideration currently than ever, especially in the line of medicine and pharmacology. The bioactive phytochemical constituents of the plant are being explored worldwide for their broad-spectrum medicinal potencies. Medicinal plants are explored as a source to isolate pure active principles or in the form of phyto complex, where there is a synergistic combination of active ingredients and other substances like enzymes, resins, essential oils, tannins to facilitate their actions. The health-promoting properties of medicinal plants are usually derived from the interaction of all the substances naturally present in the phyto complex. However, the emphasis on the use of total herbs as medicines and food supplements is gradually replacing the techniques to isolate the biologically active novel compounds and molecules as leading drug molecules. [3]

The *Rumex* species, belonging to the Polygonaceae family, comprise about 200 species widely distributed around the World. The name *Rumex* originated from the Latin word for dart, alluding to the shape of the leaves [4]. There have been numerous ethnobotanical and ethnopharmacological literature reports dealing with the occurrence and traditional uses of *Rumex* species [5-7]. *Rumex nepalensis* spreng. is a tall robust annual or perennial herb found in the temperate Himalayas from Kashmir to Bhutan and in Western Ghats, Nilgiris, and Palni Hills at altitudes between 1200 and 2700. It is well known for various medicinal activities in folklore medicine [8,9]. The use of the plant for various therapeutic purposes is well known in Indian traditional medicine. The roots of the plant have been claimed to be used as a hepatoprotective, purgative, analgesic as well as hypotensive in folklore medicine. The tribal people of the Himalayas also use the roots to relieve mental tension and disturbance. The present study was undertaken to investigate the psychopharmacological activities of methanol extract of *R. nepalensis* roots in rats and mice [10-13]. It is a common weed in pastures and the plants are known to become dominant and outcompete desirable

pasture species and degrade pasture quality. It regenerates from taproots and establishes quickly as seedlings. Once established, tough taproots become difficult to remove and are not readily killed by tillage. These characteristics have often made farmers regard this species as the most difficult weed [1]. The general issue of Rumex spp is that they are weeds of grassland, particularly in disturbed areas with high fertility. [14]

Traditionally *R. nepalensis* roots are used as purgative, to cure dysentery, venereal diseases and as a coloring agent. The fresh leaves are used for the treatment of colic and syphilic ulcers [15]. *Rumex nepalens* is has been investigated for antihistaminic, anticholinergic, antibradykinin, anti prostaglandin [16], anti-inflammatory [17], purgative, antibacterial [18], and antipyretic [19] activities. *Rumex nepalensis* contain mainly anthraquinones, naphthalene derivatives, and tannins [20-22]. Anthraquinones are reported to possess numerous biological activities such as antifungal [23], anti-inflammatory [17], antioxidant [24], genotoxicity and anti-genotoxicity [25], and anticancer [26], whereas naphthalene derivatives possess anti-inflammatory and antioxidant activities [17, 27]. In addition, anthraquinones are also used as natural dyes for textile and as foodstuffs [25, 28]. Recently reported anthraquinone (chrysophanol, physcion, emodin, endocrocin, chrysophanol-8-*O*-b-D-glucopyranoside, and emodin-8 *O*-b-D-glucopyranoside) and naphthalene (nepodin as well as nepodin-8-*O*-b-D-glucopyranoside) derivatives of *R. nepalensis* roots to possess COX-1, COX-2 inhibitory, and anti-inflammatory activities; and among these compounds, emodin and nepodin exhibited potent COX-1 and COX-2 inhibitory activity. A significant antioxidant activity of nepodin and nepodin-8-*O*-b-D-glucopyranoside was also observed against the DPPH and ABTS radicals. [17]

Vernacular names

English-Sheep sorrel, Nepal duck, Hindi-Jangli palak, Amlya, Amlora, Bhilmora, Malori, Sanskrit-Amlavetasa, Kashmiri-Aliphiri, Bengali-Pahari palang, Pakistani-Shalkhay, Hoola, Nepali-Halhale sag, Ban haldi, Halya, Halye, Uttarakhandi- Kathura, Tamil-Sukkankeerai, Manipuri-Torongkhongchak. [29]

Botanical description

R. nepalensis is an erect plant with long taproots, erect stems (50- 100 cm tall) which are branched, glabrous, grooved, green, or pale brown. Basal leaves, petiole 4-10 cm, leaf blade broadly ovate (10-15 cm long and 4-8 cm wide), both the surfaces of leaf are glabrous or

abaxially minutely papillate along veins, base cordate, margin entire, apex acute; cauline leaves shortly petiolate, ovate-lanceolate; ocrea fugacious, membranous, inflorescence paniculate with bisexual pedicellate flowers. Outer tepals are elliptic, ca. 1.5 mm; inner tepals enlarged in fruit; valves broadly ovate, 5-6 mm, valves all or 1 or 2 with tubercles, base truncate, each margin with 7 or 8 teeth, apex acute; teeth 1.5-3 mm, apex hooked or straight. Achenes brown, shiny, ovoid, sharply trigonous, ca. 3 mm, base truncate, apex acute[30, 31]. Part of this plant that is used in its propagation is a seed. Vashistha *et al*.[30] studied the phenological observations of this plant and found that the growth initiation occurs in May, senescence occurs in October, wherein flowering (reddish) occurs in between June and July flower, and fruiting takes place from August to September. [32,33]

Traditional Medicine Uses

R. nepalensis has served as the basis of traditional medicine systems in India, Nigeria, China, and Indonesia. *R. nepalensis* is used for various therapeutic purposes and is well known in Indian traditional medicine. Plant of *R. nepalensis* is consumed fried in olive oil or sautéed with butter or lard or are used as filling for pie [34]. The leaves of this plant are diuretic, astringent and demulcent. It also soothes the irritation caused by Urtica dioica L. [35]. This plant is used for the treatment of scurvy as it is rich in vitamin C [36] and also for the treatment of rheumatism. Infusion of leaves is purgative [37], the juice of the leaves is applied externally to relieve headache and is also used for its astringent qualities [38]. Its leaf extract has antiseptic properties and is used to stop bleeding. It is also used against allergy caused by leaves of *Acacia nilotica* (L.) Willd ex Delile [39] and also for the treatment of syphilic and colic ulcers. Leaf extract is applied to cure skin sores. The aqueous extract is used as a wash for reducing body pain. Leaf powder mixed with butter is used to treat scabies [40, 41]. Infusion of leaves is used in dysmenorrhoea and stomach aches [42, 43]. Crushed leaf extract is applied externally on cuts, boils, blisters, and wounds as an anti-allergic [43-45]. This plant is also used to treat skin infections in Jimma [46]. *R. nepalensis* acts as a favorite source of fodder for cows, horses, and sheep [47]. Leaves are crushed and the solution is made and used as a pesticide to kill pests. Also, leaves are crushed and paste is made with milk, churned curd, or with the urine of a cow, and applied on the area around the snake bite on the body [45]. The fresh young leaves of *R. nepalensis* are rubbed over the affected areas after injury from stinging nettles [48]. Root juice of *R. nepalensis* is orally given on empty stomach as an effective cure for jaundice [49, 50]. The roots of the plant are traditionally used for the treatment of pain, inflammation [51], bleeding, constipation, and

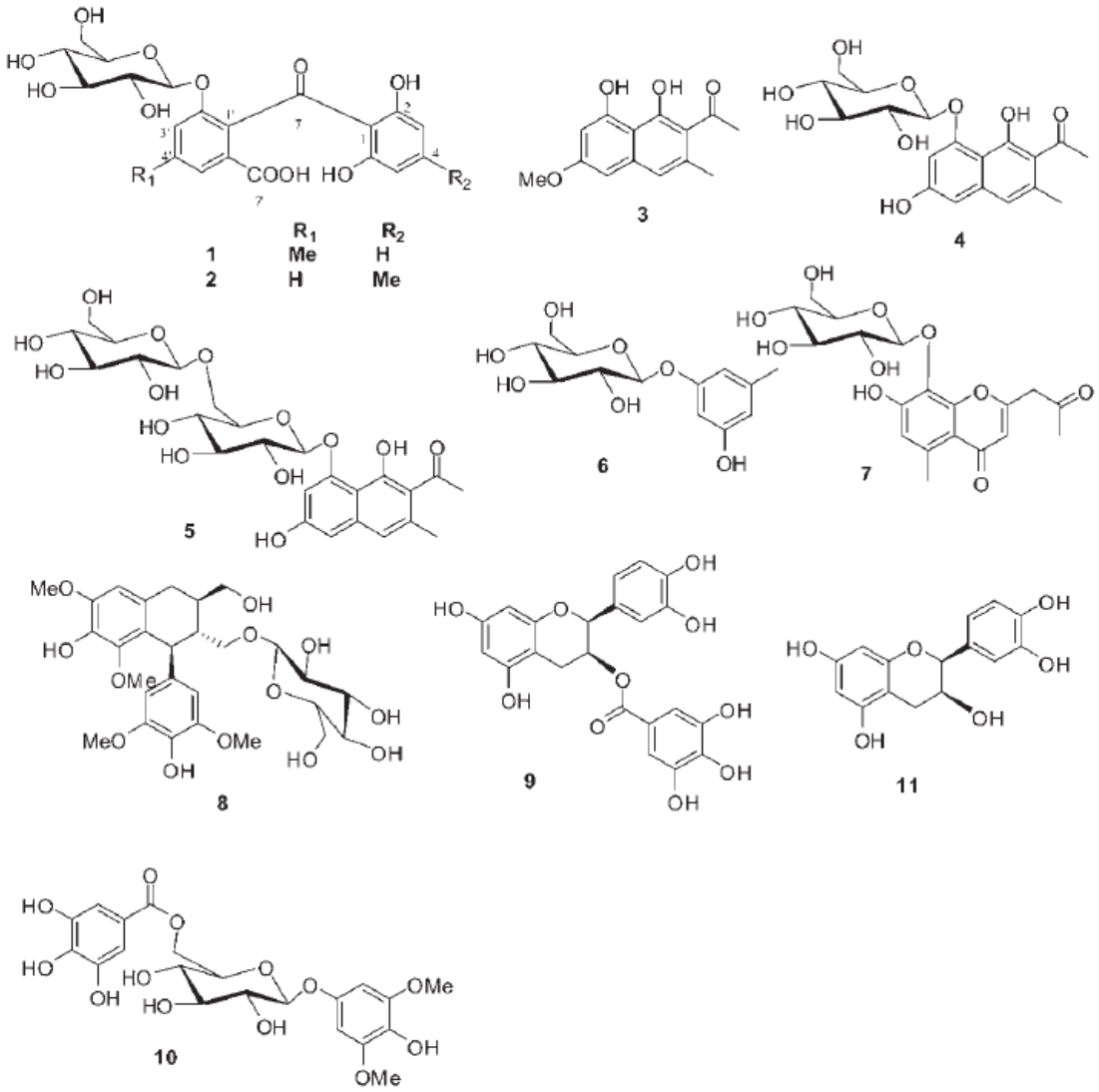
tinea in Chinese folk medicine. The pounded root is given to animals in case of diarrhea [42] and dysentery [40, 41]. The root of *R. nepalensis* is also used as an astringent [35], purgative [52]. A decoction is applied to dislocated bones and to reduce body pain. A paste of the root is applied to swollen gums, pimples, and ringworm [38, 51, 53] and applied externally to relieve headaches [54, 55]. Methanolic root extract is applied in joint pain, paralysis and significantly possesses hypotensive effect and also shows the property of muscle relaxant and tranquilizer activity [56]. Traditional medicine practitioners of Bale used *R. nepalensis* to treat diarrhea, blackleg, and swelling. In Ethiopia, this plant is used to treat colic in livestock and as an antidote for poisoning as well as a laxative [57]. The roots of the plant have been used in folklore medicine to relieve mental tension and disturbance [48]. The root is crushed and the juice is applied to the scalp to prevent hair loss [45]. Half a spoon of the grounded floral parts and root extract is used to cure joint pain. It also cures body aches. Roots grounded powder is applied on the burned body part to avoid infection and for immediate healing [58]. The roots of the plant are also used in traditional Chinese medicine for the treatment of emostasis [59]. Crushed fresh root and leaf with water are taken orally to treat tonsillitis [60]. In South Africa, a strong decoction of leaf in tablespoon doses 3 times daily to treat bilharziasis. [61]

Phytochemical constituents

R. nepalensis has been reported to contain phytochemicals like phenols, flavonoids, anthraquinones, naphthalenes, saponins, cardiac glycosides, stilbene glycosides, triterpenoids, anthraquinone glycosides, tannic acid and sterols, tannins, steroids, reducing sugar, saponin, and sitosterols. Investigation of the *n*-butanolic extract of the roots of *R. nepalensis* yielded two *seco* anthraquinone glucosides, nepalensides A and B, and the seco nor derivative aloesin. The *seco*-anthraquinones are probably formed by the decomposition and oxidation of the anthraquinones chrysophanein and pulmatin [59]. Emodin, Chrysophanol, physcion, citreoresin, endocrocin, emodin-8-*O*-*β*-D- Glucopyranoside, chrysophanol – 8 – *O* – *β* D Glucopyranoside, chrysophanol -8-*O*-*β*-D-(6'-*O*acetyl) glucopyranoside and emodin-8-*O*-*β*-D-(6'-*O*-acetyl) glucopyranoside, were isolated from the roots of *R. nepalensis* [62]. From the roots of *R. nepalensis*, aloesin, rumexoside, oriental side, and torachrysone were isolated [59]. Later, Gautam *et al*. reported nepodin and its glucoside from the plant [63]. Liang *et al*. identified nepodin-8-*O*-β-Dglucopyranoside, torachrysone, torachrysone-8-*O*-β-D-glucopyranoside, and two naphthalene acyl glucoside, rumexneposides A and B and Epicatechin and epicatechin-3-*O*-gallate were then detected in the roots of the plant [60]. An

investigation of the EtOAc fraction of *R. nepalensis* roots and the ethanolic extract of *R. hastatus* roots also resulted in the isolation of resveratrol [64]. From the roots of *R. nepalensis*, (3,5-dimethoxy-4-hydroxyphenol)-1-*O*-β-D-(6-*O*-galloyl) glucose, orcinol-glucoside, a lignan derivative, lyoniresinol 3α-*O*-β-D-glucopyranoside was isolated [60]. It is reported that anthraquinones have several pharmacological properties like antifungal, anti-inflammatory, antioxidant, and anticancer, whereas naphthalene derivatives possess anti-inflammatory and antioxidant activities. [3]

Investigation of the n-BuOH extract of the roots of *Rumex nepalensis* afforded two new seco-anthraquinone glucosides, nepalensides A (1) and B (2), along with nine known compounds, torachrysone (3), rumexoside (4), oriental side (5), orcinol glucoside (6), aloesin (7), lyoniresinol 3_-O-_-D-glucopyranoside (8), (−)-epicatechin-3-O-gallate (9), (3,5-dimethoxy-4-hydroxyphenol)- 1-O-_-D-(6-O-galloyl) glucose (10), and (−)-epicatechin (11). [65]



Nutritional and elemental compositions

In *R. nepalensis*, elements like O, Si, C, and K are reported from all plant organs, whereas, Na in stems and leaves, Mg in petioles and flowers, Si in stems, Cl in stems, leaves, petioles, and flowers, Ca in roots, petioles and flowers, Fe in petioles and Al is found in all plant organs except in roots and flowers[51]. Hameed *et al.* [66] reported 19.1% fats and oils in flowers whereas stem contains 18.69%. Further, authors reported the plant as highly fibrous as fruits 50.83% fibers while flowers contain 48.43% fibers. [65]

Reported Activity

Psychopharmacological Activities

The methanol extract of *Rumex nepalensis* Spreng. (Family – Polygonaceae) was assessed for different psychopharmacological activities in rats and mice by evaluation of general behavior, exploratory behavior, muscle relaxant activity, and phenobarbitone sodium-induced sleeping time. The extract at doses 200 mg/kg and above exhibited a reduction in spontaneous activity (general behavioral profile), a decrease in exploratory behavioral pattern in the Y-maze and Head-dip tests, a reduction in muscle relaxant activity in rotarod, 30° inclined screen, and traction tests, and also potentiated phenobarbitone sodium-induced sleeping time. [67]

Purgative Activity

The roots of *R. nepalensis* possess a purgative activity by increasing intestinal peristalsis and gastro-intestinal motility and thereby, seem to be providing support to the traditional medicinal practice. The anthraquinones present in the plant extract may be responsible for its purgative activity. The methanol extract of *Rumex nepalensis* Spreng. roots at the oral dose of 100–400 mg/kg exhibited significant and dose-dependent purgative activity. [68]

Antibacterial Activity

The antibacterial property of *Rumex nepalensis* Spreng. was evaluated against some strains of bacteria. The methanol extract of the roots showed significant concentration-dependent antibacterial activity [69]. The methanolic extract of *Rumex nepalensis* was tested for antibacterial efficacy against four bacterial strains and antifungal activity against three fungal strains by well diffusion method. In the present study Ampicillin 10µg/well (antibacterial) and Fluconazole 10µg/well (antifungal) were used as a reference standard. The methanolic

extract possessed some antimicrobial activity against all the test organisms at a concentration of 400µg/well. [70]

Anti-inflammatory activity

Evaluation of the topical anti-inflammatory activity of chloroform and ethyl acetate extracts of *Rumex nepalensis* roots in a TPA-induced acute inflammation mouse model demonstrated a significant reduction in ear edema. The extracts were further tested on purified enzymes for COX-1 and COX-2 inhibition to elucidate their mechanism of action, and a strong inhibition was observed. Six anthraquinones and two naphthalene derivatives were isolated from the ethyl acetate extract. Among the isolated compounds, emodin was found to be a potent inhibitor with slight selectivity towards COX-2, and nepodin exhibited selectivity towards COX-1. Emodin, endocrocin, and nepodin also exhibited significant topical anti-inflammatory activity in mice. Interestingly, nepodin showed better radical scavenging activity than Trolox and ascorbic acid against DPPH and ABTS radicals. The strong radical scavenging activity of chloroform and ethyl acetate extracts could be explained by the presence of nepodin as well as by the high phenolic content of the ethyl acetate extract. Thus, the anti-inflammatory effect of *R. nepalensis* roots was assumed to be mediated through COX inhibition by anthraquinones and naphthalene derivatives and through the radical scavenging activities of naphthalene derivatives. [71, 72]

Antimicrobial activity

Two herbaceous plants named *Urtica diocia* and *Rumex nepalensis* were selected for checking their antimicrobial activity. Also observing their opposite action on humans when extracts were applied on the skin. The extracts were prepared in 95 percent ethyl acetate, 70 percent methanol, and boiled water. After drying the leaves and roots of selected plants, the *U. diocia* extracts were prepared by using 95 percent ethyl acetate and boiled water while the *R. nepalensis* extracts were prepared in 70 percent methanol. *U. diocia* has an inflammatory response when applied to the skin while the Rumex has opposite action by removing the symptoms of Urtica extracts when applied to skin. The antimicrobial activity was also tested for both plants extracts against selected strains of organisms which were *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *Klebsiella pneumonia*, and MRSA (Methicillin-resistant *Staphylococcus aureus*) for extracts of *Rumex nepalensis*. The clear zone on nutrient agar when leaves extract of *R. nepalensis* were applied against these organisms which were *E.coli* 15mm, *Pseudomonas aeruginosa* 15mm, *Candida albicans* 13mm, MRSA 9mm, and

Klebsiella pneumoniae 7mm. Roots extracts of *R. nepalensis* show 19mm *E.coli*, 9mm *Pseudomonas aeruginosa*, 16mm *Candida albicans*, 12mm MRSA, and 12mm for *Klebsiella pneumoniae* clear zones have appeared on nutrient agar. *E.coli*, *Pseudomonas aeruginosa*, *Bacillus cereus*, MRSA and *Enterococcus faecalis* were tested for the extracts of *U. diocia*. The *U. diocia* extracts in boiled water were sensitive against these selected organisms but the ethyl acetate extracts shows the clear zone which was 9mm *E.coli*, 10mm *Pseudomonas aeruginosa*, 19mm *B. cereus*, 17mm MRSA, and 13mm *E. faecalis* due to leaves extract of *U. diocia* while roots extracts of *U. diocia* shows 10mm E.coli, 12mm *Pseudomonas aeruginosa*, 13mm *B. cereus*, 7mm *E. faecalis* zones appeared against these organisms. Only MRSA is resistive to roots extracts of *U. diocia.* [73]

Pancreatic Lipase inhibitory activity

Rumex nepalensis Spreng. (Polygonaceae) is an edible plant rich in anthraquinones that significantly inhibits Pancreatic Lipase (PL), a key enzyme in dietary fat digestion. The effectiveness of Ultrasonic assisted extraction (UAE) of *R. nepalensis* was investigated using ethyl acetate as a solvent. Further, optimization of extraction conditions required for maximizing the PL inhibitory activity was determined using response surface methodology with Box-Behnken design (BBD with three-factor, 17 experimental runs). Extraction time (A, min), solid: solvent ratio (B, g/mL), and temperature (C, °C) were selected as the variables. The optimum conditions were established as extraction time (37 min), solid: solvent ratio (1:10.5), and extraction temperature 33°C. However, to date, no HPTLC reports are available for the simultaneous quantification of chrysophanol and physcion from *R. nepalensis.* Thus, chrysophanol and physcion were quantified in various extractives of *R. nepalensis via.* A validated HPTLC method and a positive correlation were obtained with PL inhibition activity (Pearson's r = 0.801 and 0.755 for chrysophanol and physcion respectively), which justified the PL inhibition potential of *R. nepalensis* derived anthraquinones.[74]

Abortifacient activity

The hydro-alcoholic leaves extract of *Rumex nepalensis* Spreng was evaluated for its abortifacient activity in Swiss albino rats. The mature female rats were mated overnight to male rats in mating cages. Two different dosage regimens (300 mg/kg, 600 mg/kg) of the extract were administered. Laparotomy was performed on the rats to assess the uterus and ovary, the viable, non-viable, adsorbing sites, and corpora lutea. Differences between the experimental and control groups were compared using one-way analysis of variance

(ANOVA), followed by Dunnett's T-test to determine their level of significance. This study revealed that *Rumex nepalensis* Spreng had antiimplantation and abortifacient activities at both 300 and 600 mg/kg doses, which was statistically significant as compared with the controls. It was relatively safe up to the dose of 5000 mg/kg, where no mortality and organ toxicity was manifested. Phytochemicals identified were alkaloids, flavonoids, saponins, tannins, steroids, and anthraquinones. The study showed that *R. nepalensis* had a significant abortifacient activity that testifies its traditional dibs. Therefore, the use of this plant should be avoided in pregnant women to minimize unintended abortion and further studies are needed to know its mechanism of activity and to identify the phytochemicals corresponding to this activity. Checking its efficacy on other species is also needed. [75]

Anti-ulcer activity

Rumex nepalensis (RN) Spreng has been used to treat ulcer disease in Ethiopian folk medicine. This study determined the anti-ulcer activity of hydroalcoholic root crude extract and solvent fractions of *R. nepalensis* in rats. The effect of *R. nepalensis* crude hydromethanolic extract and solvent fractions at doses (100, 200, 400 mg/kg/day) and repeated dosing (200 mg/kg/day for 10 and 20 days) was examined on ulcers in rats in pyloric ligation-, cold restraint stress-, and acetic acid-induced ulcer models. Cimetidine (100 mg/kg/day) and/or Omeprazole (20 mg/kg/day) were used as standard drugs and served as a positive control. Data were analyzed by one-way ANOVA post hoc followed by a Tukey HSD test with SPSS software version 24.0, and $P \leq 0.05$ was considered as statistically significant. In the pylorus ligation-induced ulcer model, pretreatment with the crude extract significantly reduced the degree of gastric secretions, pH, total acidity, and ulcerations in a dose-dependent manner. Gastroprotection offered by the *R. nepalensis* 400 mg/kg test extract was comparable to that of the standard. Among fractions, the ethyl acetate fraction at 400 mg/kg had the highest protection of ulcer but the chloroform fraction was ineffective. In the cold restraint stress-induced ulcer model, *R. nepalensis* at 200 and 400 mg/kg reduced the lesion index significantly ($P<0.01$). With relevant chronic ulcer model treatment, a dose of *R. nepalensis* at 200 and 400 mg/kg healed ulcers significantly with a curative ratio of 53.22% and 54.59%, respectively. From this study, it is concluded that hydromethanolic crude extract and solvent fractions of *R. nepalensis* root showed promising anti-ulcer activity. This upholds its folkloric use. Thus, it is considered as a possible source to develop a new anti-ulcer agent. [76]

Gold Nanoparticles using *Rumex nepalensis* leaf extract

The biosynthesized gold nanoparticles were characterized by UV-vis spectroscopy, scanning electron microscopy (SEM), energy dispersive x-ray (EDX), and x-ray diffraction (XRD) analysis. SEM showed spherical in the shape of nanoparticles and XRD revealed crystalline nature with an average size of 8.63 nm. Fourier transform infrared spectroscopy (FTIR) revealed the involvement of biomolecules in the reduction of gold ions to gold nanoparticles. Biosynthesized gold nanoparticles were applied against common pathogenic bacterial strains along with plant extracts (aqueous and methanolic). Gold nanoparticles demonstrated much higher activity as compared to both leaf extracts and positive control (Ampicillin). The current study demonstrated that an aqueous leaf extract of *R. nepalensis* can be utilized to fabricate gold nanoparticles with smaller spherical size and significant antibacterial activity. Moreover, this green approach to synthesize AuNPs using *R. nepalensis* leaf extract, being cost-effective and eco-friendly, can be scaled up. [77]

CONCLUSION AND FUTURE PERSPECTIVES

This review aimed to enlighten the valuable application of this unique and valuable plant species. It carries high nutritional and medicinal values for humans and animals. The literature was analyzed to congregate the phytochemical and pharmacological information on *R. nepalensis*, which reaffirmed that this plant is a good source of phytocomplexes and medicinally important pure compounds for the treatment of various diseases. *R. nepalensis* demonstrated various medicinal, pharmacological, and phytoremediation activities which give immense importance to this herb. However, further clinical trials should be performed to verify efficacy and any side effects or toxicity of purified plant extracts. It is essential to conduct in-depth and comprehensive pharmacological studies at the molecular level to investigate the unexploited potential of this plant. For these reasons, wide pharmacological and chemical studies, together with human metabolism, might be the focus of future studies. Besides, the isolation of pure compounds with pharmacological activities and deciphering the underlying mechanisms hold significance in contemporary and future research. Recently, the plant extract was also being used by the researchers to produce nanoparticles, but again more studies are required to use its potential via nanotechnologies [78]. This plant could also be improved, through the use of conventional breeding techniques, and genetic engineering approaches for metal tolerance or the metabolism of organic chemicals. Therefore, there is huge room for research in these directions.

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