Journal of Pharmacy and Pharmacology, 2023, **75**, 143–161
https://doi.org/10.1093/jpp/rgac053
Advance access publication 7 October 2022
Review

JPP Journal of Pharmacy and Pharmacology
OXFORD

Pharmacological and phytochemical potential of *Rubus ellipticus*: a wild edible with multiple health benefits

Pushpa Kewlani[1], Deepti Tiwari[1], Sandeep Rawat[2], and Indra D. Bhatt[1,*]

[1]Centre for Biodiversity Conservation and Management, G.B. Pant National Institute of Himalayan Environment, Kosi-Katarmal, Almora, Uttarakhand, India
[2]Sikkim Regional Centre, G.B. Pant National Institute of Himalayan Environment, Pangthang, Gangtok, Sikkim, India
[*]Correspondence: Indra D. Bhatt, Centre for Biodiversity Conservation and Management, G. B. Pant National Institute of Himalayan Environment, Kosi-Katarmal, Almora, Uttarakhand 263 643, India. Email: id_bhatt@yahoo.com; idbhatt@gbpihed.nic.in

Abstract

Objectives *Rubus ellipticus* (family Rosaceae) is used for its delicious edible fruits in the Himalayan region and other parts of the globe. However, the full potential of the species is yet to be harnessed. The current review focuses on the phytochemical, traditional uses, morphological, molecular and pharmacological potential of *R. ellipticus*.

Key findings The review of the literature reveals that many health-promoting compounds of *R. ellipticus* have been reported from the species along with the different biological properties, such as nephroprotective, anti-inflammatory, analgesic, anti-pyretic, anti-proliferative, cytotoxicity, anti-cancer, wound healing, anti-fertility, anti-plasmodial, anti-microbial and antioxidant. Traditionally, it is used in many formulations, which are validated through primary pharmacological assays. However, several medicinal properties are still need to be validated through detailed pharmacological and clinical studies.

Summary All the information is available in a scanty form, and the complete information is missing on a single platform. Such type of information will help researchers to better utilize the available data for initiating future research on the species as it has the potential to contribute to the food and pharmaceutical industry. The review highlights the need for further studies on the species to harness its potential in nutraceutical, functional food, energy supplement, and beneficial therapeutic drug development program.

Keywords: *Rubus*; berries; nutraceutical; wild edible; Himalaya Raspberry

Introduction

The efforts to address food insecurity and improve health are greatly acknowledged worldwide.[1,2] It is well known that only a few crops are being utilized to fulfill the food and nutrition need. Still, the growing population size and shrinking agricultural land hamper the continuity, and how long it will support is a question of debate. Therefore, there is a need to search for alternative resources to lessen the pressure on crops. In this context, wild resources such as wild edible fruits can play a crucial role in meeting food and nutritional security, as these have regional-specific diversity, adaptability, and applications.[3] These wild edible plants are rich in vitamins and essential nutrients.[4] In addition, they possess valuable phytochemicals used for medicinal purposes.[5]

Indian Himalayan Region (IHR) is known for its rich biodiversity. It supports more than 670 wild edible plant species, many commercially utilized for nutritional supplements and health-beneficial products.[6,7] Among these, Rosaceae is a dominant family of wild edibles in the Himalayan region represented by many valuable species like *Pyrus*, *Prunus*, *Rubus*, *Fragaria*, *Rosa,* and *Potentilla*, which are traditionally being used as food supplements and genetic backup of a wild relative of cultivated crops.[6] The *Rubus* genus represents a diverse group of blackberries, and raspberries have a special consideration among nutritionists due to their appearance, deliciousness, and health benefits.[8] Commercially important species *R. idaeus*, *R. occidentalis*, and many others can easily be hybridized with wild species and produce fertile accessions. The genus is represented by more than 900 species within its 12 subgenera.[9] *Rubus* fruits are gaining research attention due to the presence of high vitamins (ascorbic acid and others), minerals, bioactive compounds, such as anthocyanin, phenolics, and flavonoids[7,10] antioxidants[11] and health-promoting beneficial properties. The beneficial effects of berry phytochemicals have been reported due to their ability to modulate gene expression through nuclear receptors and subcellular signaling pathways and subsequently prevent oxidative damage.[12,13]

Rubus ellipticus Smith (*syn. R. flavus* Buch-Ham. ex D. Don, *R. gowreephul* Roxb.; *R. hirtus* Roxb.; *R. paniculatus* Moon; *R. rotundifolius* Wall.; *R. wallchianus* wight Arn.) is an evergreen shrub distributed throughout the sub-tropical to the sub-temperate region.[14] Geographically, the species is found in south and south-east Asian countries within various habitats, such as hilly terrain, roadside, mountain valleys, forest, and slopes.[15] Its delicious edible fruits are consumed raw in the Himalayan region,[16] while other parts of the plant (leaves, roots, and fruits) play a vital role in Ayurveda, traditional Chinese, and different folk medicine. Different plant parts of this species have been used to cure

Received: January 3, 2022. Editorial Acceptance: June 28, 2022

diarrhea, dysentery, cough, fever, colic, constipation, gastric trouble, vomiting, wounds, and uterine relaxant since ancient times.[17–23] Various health-promoting bioactive compounds have been reported from the species[11,24,25] with many beneficial pharmacological activities.[26–28]

With the increase in the flow of information on the species, there is a need to collect and compile the existing information to highlight its potential. The present review provides information on traditional knowledge, phytochemicals, nutritional, pharmacological potential, and genomic advances of *R. ellipticus*. A detailed study of the available literature will identify the gap areas and provide complete information in one place for improving understanding of the various aspects of this species. Furthermore, the review highlights the potential of the species for the development of nutraceutical, pharmaceutical, and health-promoting products, which will provide baseline information for future research and help to promote the conservation and utilization of *R. ellipticus*.

Approach for Data Collection

For this systematic review, we conducted a literature search related to various aspects of *R. ellipticus* according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), an internationally recognized guideline for reporting reviews. The search was carried out from August 2020 to December 2021 using three online databases: Google Scholar, Wiley, and Scopus. This review included the following search terms '*Rubus ellipticus*' AND 'Himalayan raspberry', 'ethnomedicinal uses' OR 'traditional uses', 'phytochemicals', OR 'secondary metabolites' 'nutritional analysis' OR 'proximate analysis', 'pharmacological activity' OR 'biological activity, 'socio-economic' OR 'molecular aspect'. At the initial stage of the literature search, a total of 3456 references were found for the study, of which 614 were duplicates and excluded.

The selected articles were thoroughly read for eligibility criteria, and 314 articles were retrieved. These findings were further assessed for inclusion (full papers, investigation associated with ethnomedicinal, nutritional and phytochemical, socioeconomic, molecular aspect and pharmacological activities of *R. ellipticus* and exclusion (only abstracts, posters, presentations, not experimental, qualitative data only, and dissertation) criteria. Finally, a total of 123 studies were selected for this review. The procedure of selecting and screening literature for PRISMA analysis is depicted in Figure 1. Some of the papers fall within two categories; therefore, the total of these articles may seem higher than the reviewed papers.

Botanical Description and Distribution

R. ellipticus is an evergreen shrub, which grows up to 6 m long with a purple-brown stem having shaggy long purplish-brown flexuous bristlier or glandular hairs. The leaves of the plant are elliptic, rough, acute at the apex, spiny below and orbicular obviate with leathery leaflets. The inflorescence is ovate, acute, bisexual flower, petals 7–8 mm long, and white flowers with yellow intermixed tomentose in clusters in leaf axils, which are 1–1.5 cm wide. The fruits are succulent drupes, orange-yellow, 6.0 mm long, and 7.0 mm wide.[29,30]

The *Rubus* species are well adapted to different habitats and have evolved mechanisms for natural resistance to biotic and abiotic environmental factors.[31] *R. ellipticus* is commonly preferred to grow in slopes, open forests, and roadsides between 300 and 2600 m.a.s.l. It is native to south-east Asia and distributed in south-western China, India, Bhutan, Nepal, Laos, Myanmar, Pakistan, Philippians, Sri Lanka, Thailand, and Vietnam. However, it is invasive in Hawaii and Australia and naturalized in tropical Africa, tropical South America, West Indies, and England.[32]

Traditional and Ethnobotanical Uses

In Traditional Chinese medicine, the *Rubus* genus has a long history of medicinal use with remarkable therapeutic effects in curing liver and kidney meridians due to its sweet and warm properties. Its roots and bark are applied to reduce sore lower back, improve eyesight and prevent uterine, cervical, and colon cancer in China.[33] Several species of the genus are used to treat wounds, burns, inflammation, microbial infection (anti-microbial), anticonvulsant, muscle relaxant, and radical scavenging, ulcers, gastrointestinal problems, and diabetes.[34] For instance, the plant part of *R. ulmifolius* is used to cure ulcers, abscesses, furuncles, red eyes, vaginal disorders, intestinal inflammations, diarrhoea, and haemorrhoids.[35] The fruits of *R. fruticosus* are used in dermatological problems, such as itching, eczema, scabies,[36] and gynecological disorders.[37] The leaves of *R. idaeus* are consumed as a tablet, tea, or tincture during pregnancy to facilitate labour and easy childbirth[38,39] and uterine relaxant stimulants during confinement.[40]

Different plant parts of *R. ellipticus* are used traditionally to cure various diseases, such as diarrhoea, dysentery, cough, fever, colic, constipation, gastric trouble, vomiting, wounds, uterine relaxant, wound healing agents, analgesics, and antipyrectics (Table 1). Its edible fruits are juicy and delicious and have been considered astringent, febrifuge, stomachic, laxative, and carminative. Fruits are medicinally used to treat indigestion,[41] cholera,[42] blood and heart problems,[43] diabetes, constipation, nausea, tonic, stomach, and abdominal pain disorders.[44–49] Paste of young fruits (10–20 g) is consumed twice or thrice a day as an antacid for treatment of gastritis and in diarrhoea and dysentery.[50] Fruit juice is used for gastrointestinal problems and mouth disorders, such as leukoplakia, cold sores, and mouth ulcers.[51]

The leaves of the species are used in wound healing,[20] diarrhoea, colic, and uterine relaxant,[17] while leaf buds are used to treat peptic ulcers.[72] Its roots are laxative and used in the treatment of paralysis,[67,73] bone fracture, headache, urinary tract infection, stomach-warm, stomach-ache, typhoid, measles, fevers, gastric troubles, wound, and jaundice,[52,58,61,69,74] ulcer, skin infection,[56] Parkinson's disease and other CNS disorders.[62] The root juice is consumed against urinary tract infection, and root paste is applied on the forehead to relieve headache, while root decoction is used for bellyache.[75] In Nepal, some rural communities consume juice of buds and roots to cure diabetes mellitus, whereas the juice of buds and leaves is applied externally for cuts and wounds.[76] Its root is an intoxicant ingredient; root juice treats fevers, gastric troubles, dysentery, and root decoction. It is used as an intoxicant during wine preparation [65,77,78], while shoots are used for stomach warmth, stomach pain, and headache.[52,73] The bark is used in fever, gastric troubles, diarrhea, dysentery, colic,[79] common cold, and blood disorders.[54,72] Peeled young shoots are eaten raw for the sour taste, and fruits are eaten as snacks.[80] The whole plant is used against gastralgia,

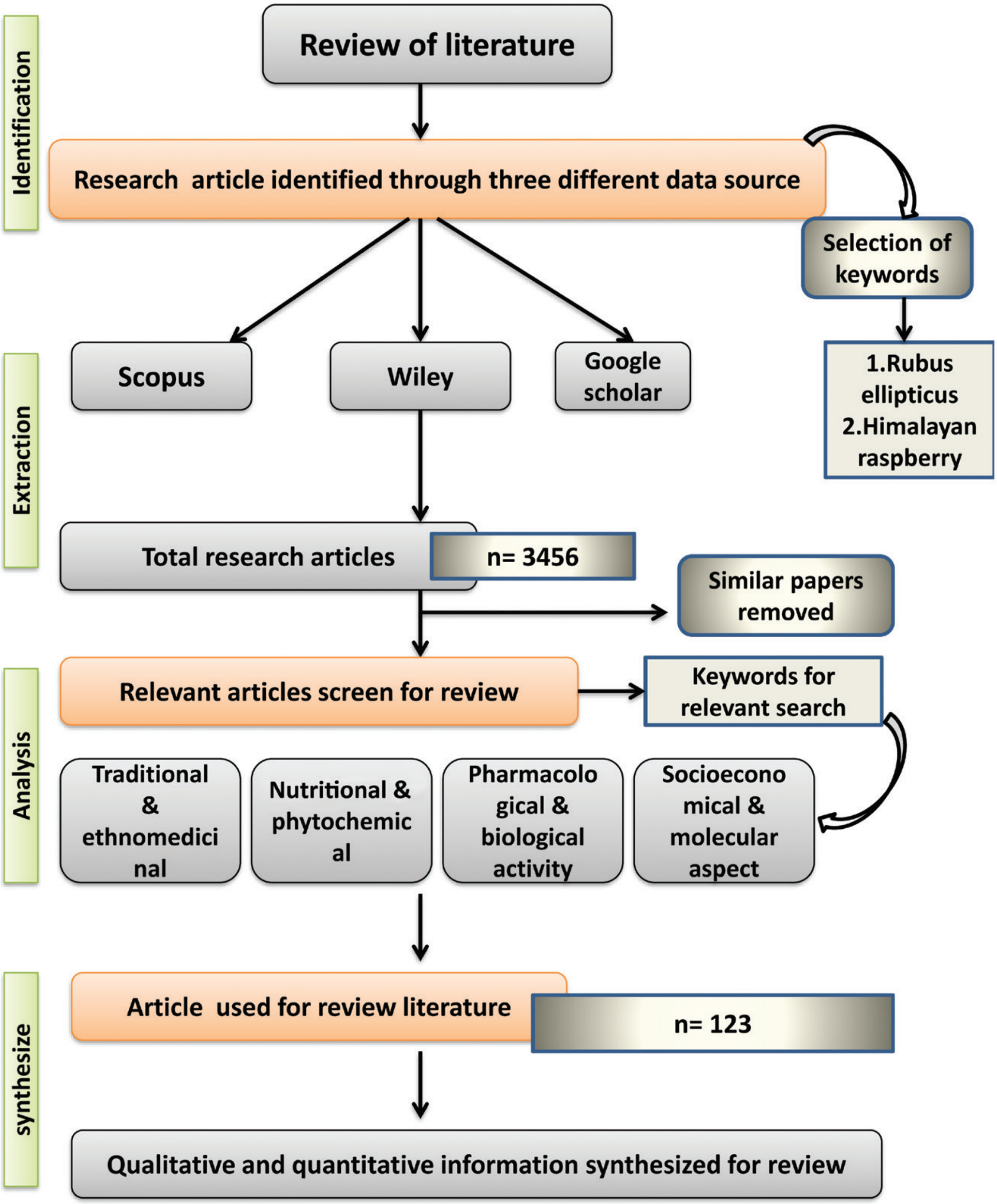

Figure 1 Flow diagram of process for review of the literature used in this study.

cholera, wound healing, anti-fertility, anti-microbial, analgesic, epilepsy, fever, diabetes mellitus, ulcer, skin infections, endocrine and metabolic ailments, colic pain, diarrhea, piles, hyperthermia and helminthic infestation in children.[81–84] All this information on the species can be useful for developing new therapeutic agents after validating traditional knowledge.

Proximate and Nutritional Composition of Fruits

Proximate and nutritional studies of *R. ellipticus* fruits revealed their high nutritive value due to the presence of carbohydrates, crude fibre, fat, protein, lipid, and minerals (Figure 2). A high content of carbohydrate (86.4%) and crude fibre (3.53%) has been reported in the fruits of *R. ellipticus*, along with a significant amount of crude protein (4.37%), crude lipid (2.73%), and high energy value (374.0 Kcal). Sundriyal and Sundriyal reported carbohydrate (72.7%) and fibre (7.90%) in fruits of *R. ellipticus*.[4] Total sugar has been reported as 8.73% in fruits of the species.[84] The reducing (5.66%) and non-reducing (2.90%) sugars are found in the fruit.[85] Similarly, the protein composition of this species makes it a good source of amino acids as a total of 16 amino acids have been identified in *R. ellipticus* fruits.[86]

Moisture content in *R. ellipticus* fruits has been reported from 64.4% to 80.6%, while ash content ranged from 1.30%

Table 1 Traditional and indigenous uses against different diseases and modes of application of *R. ellipticus* in different parts of the world

S. No	Plant part	Geographic region/ community	Dose/mode of administration	Used in disease	References
1.	Young shoot	Dzongu Valley, Sikkim	Chewing raw shoots	Stomach pain	[52]
2.	Root	Dzongu Valley, Sikkim	Decoction	Stomach warm of children	[52]
3.	Root	Dzongu Valley, Sikkim	Paste	Forehead during severe headache	[52]
4.	Root	Sikkim	Root paste is used as a poultice	Bone fracture	[50]
5.	Ripe fruit	Sikkim	Eaten raw	Laxative used in constipation	[50]
6.	Fruits	Sikkim	10–20 g fruits twice and thrice in a day	Gastritis, antacid, diarrhoea, and dysentery	[50]
7.	Root	Western Nepal	Juice	Urinary tract infections	[53]
8.	Bark	Bhutan	–	Common cold and blood disorders resulting from defective air	[54, 55]
9.	Root	Garhwal Himalaya, Uttaranchal	Paste	Skin infections and diseases, and ulcers	[56, 57]
10.	Root	Nepal (Chepang)		Wound, jaundice, typhoid	[58]
11.	Root	East Nepal (Lepcha)	10–20 ml of juice taken orally	Diarrhoea, cholera, gastritis, sore throat	[71]
12.	Root	Bageshwar, Uttarakhand	Decoction (10 ml dose) of 100 g root with water for 5 days	Gastrointestinal problems and fever	[21, 60]
13.	Leaf	Bageshwar, Uttarakhand	Paste	Wound healing	[21]
14.	Fruit	Bageshwar, Uttarakhand	Juice	Cholera	[42, 61]
15.	Fruit	Nainital, Uttarakhand	Eaten Raw	Diabetes, stomach disorders and digestion problems	[48]
16.	Root	Nepal (Chitwan–Panchase–Mustang)	Paste of roots is mixed with various plant species, and 1 spoon (fresh) or 1/2 spoon (dry) is consumed with 1 glass of water once a day	Mental diseases	[62]
17.	Ripe fruits	Udhampur, Jammu & Kashmir	Taken orally act as aperients and juice of tender leaves	Oral ulcer	[63]
18.	Root	Kaski, Central Nepal	Decoction	Typhoid and fever	[64]
19.	Young leaves	Dronagiri, Uttaranchal	Paste of leaves with cold water thrice a day is given orally and same paste with hot water	Acute diarrhoea and constipation	[65]
20.	Root	Panchase, Central Nepal	1–2 spoons of root powder diluted with a half glass of water and drunk twice a day for 2–3 days	Fever	[66]
21.	Root	Almora, Uttarakhand	Root decoction is used with *Girardinia diversifolia* root and bark of *Lagerstroemia parviflora*	Fever, gastric trouble, diarrhoea and dysentery	[61]
22.	Fruit	Ziro valley, Arunachal Pradesh	–	Indigestion	[41]
23.	Fruit	Jasrota hill, Jammu and Kashmir	Juice of fruits	Gastrointestinal problems and mouth disorders	[51]
24.	Root	Hasanur hills, Tamil Nadu	The root paste is taken internally	Paralysis	[67]
25.	Root	Indo Aryan and Gurang communities	Ash of *Eleusine coracana* (L) flour with *R. ellipticus* root paste is externally applied once a day	Wound healing	[66]
26.	Fruit	Gurang community	During fever, typhoid fruits are eaten in jelly form and stored for 3–4 months for a bottle	Fever, typhoid, cut, wound, hypothermia and appetizer	[66]
27.	Young leaves	Gurang community	Chewed once a day for 2–3 days.	Fever, cough, gastritis	[66]
28.	Root	Gurang community	Paste 1 spoon for children and 2 spoons for young people diluted with a half glass of water and drunk once a day for 2–3 days	Hyperthermia	[66]
29.	Root	Kaverpalanchok, Central Nepal	The crushed root is inhaled	Rhinitis and sinusitis	[68]

Table 1. Continued

S. No	Plant part	Geographic region/ community	Dose/mode of administration	Used in disease	References
30.	Root	Kaverpalancho, Central Nepal	The root juice is taken	Gastrointestinal and respiratory problems	[68]
31	Whole plant	Kaverpalanchok, Central Nepal	The crushed plant mixed with *Osbeckia nepalensis* is applied to the skin	Dermatitis	[68]
32	Root	Dolakha, Nepal	Decoction and infusion of root with *Girardinia diversifolia* root and bark of *Pyrus parsia* and *Rhododendron arboreum* is boiled and drunk	Typhoid and stomach pain, gastrointestinal ailments and respiratory tract infections	[69]
33	Root	Taplejung, Nepal	The paste is applied externally in piles and root extract is consumed	Gastritis and diarrhea	[70]
34	Root	Ilam, Eastern Nepal	*R. ellipticus* root juice and *Docynia indica* mixed and 10–15 ml taken thrice a day for 2–3 days.	Diarrhea and dysentery	[71]
35	Root and young shoots	Ilam, Eastern Nepal	Paste taken orally	Throat pain	[71]

to 4.1%. Fruits of *R. ellipticus* contain a wide variety of essential minerals, including Ca (450.1 mg/100 g), Mg (118.72 mg/100 g), K (680.16 mg/100 g), P (1.26 mg/100 g), N (700 mg/100 g), Na (89.43 mg/100 g), Fe (4.249 mg/100 g), Zn (12.77 mg/100 g), Cu (0.020 mg/100 g), Pb (0.02 mg/100 g), Mn (1.948 mg/100 g), Cr (0.47 mg/100 g) which is important for strengthening bone and immune system.[84] Besides, Himalayan raspberry is considered a reservoir of total vitamin C and reported between 4.10 and 44.00 mg/100 g in different studies.[85, 87, 88] A good amount of total sugar (39.0%) and total soluble solids (TSS) ranging between 10.02 and 15.11 Brix,[14] has been reported from the fruits.[89] However, the TSS of ripened fruits varied from 8.33 to 12.20 Brix.[90] TSS has been reported as 16.11 Brix, acidity as 1.97%, ascorbic acid as 5.67 mg/100 g, total sugar as 7.86%, reducing sugar as 5.57%, and non-reducing as 2.18 in the fruits of *R. ellipticus* collected from Sikkim State.[91]

A high variability has been reported among the different genotypes in these qualitative traits of the species. In a large-scale genotype-wide variability study, acidity was recorded between 1.09% and 1.72%, reducing sugar between 2.2% and 4.9%, non-reducing sugars between 4.20% and 11.60%, ascorbic acid between 2.4 and 5.2 mg/100 g and TSS value between 9.60 and 18.60 Brix.[92] Similarly, ascorbic acid among genotypes in Uttarakhand has been reported between 10.65 and 40.15 mg/100 g fresh weight (FW) of fruits.[25] The nutrients present in the species can be used to develop new nutritional products, which may help address the nutritional security of communities in the IHR and other parts of the world.

Bioactive Constituents

Polyphenolics and other chemical compounds

R. ellipticus fruits are a rich source of natural bioactive compounds, such as phenolics, flavonoids, anthocyanins, terpenoids, tannins, saponins, steroids, alkaloids, and β-carotene (Table 2). However, other plant parts of the species are also rich in valuable phytochemicals. For instance, the qualitative analysis of the root bark showed that *R. ellipticus* is a source of polyphenols, alkaloids, glycosides, flavonoids, terpenoids, tannins, coumarins, saponins, carotenoids, etc.[93]

Phenolic acids

The berries of the *Rubus* are increasingly recognized due to their bioactive compounds, such as phenolic, flavonoids, anthocyanin, and carotenoids (Table 2). In *R. ellipticus*, recovery of total phenolic content varied in different solvent extractions, and acidified methanol showed 6.9 mg/g FW, while acidified acetone showed 8.99 mg/g FW.[24] However, methanol extract exhibited total phenolic content as 401.36 mg/g dry weight fruit.[94] Different parts, such as leaf (58.26 mg/100 g in acetone extraction), stem (62.02 mg/100 g chloroform extraction), and roots (80.23 mg/100 g chloroform extraction), exhibited a varied level of total phenolic content.[102] Fruits of *R. ellipticus* have been reported as a rich source of phenolic acids, for example, gallic acid, chlorogenic acid, caffeic acid, ellagic acid, and m-coumaric acid, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid, ferulic acid, vanillic acid, trans-cinnamic acid.[11, 25] Fruits were also found rich in tannin content and reported as 628.32 mg/g DW in methanol[94] and 33.97 mg/g FW in acidified methanol extraction.[11] Similarly, George et al. analyzed total tannin content in leaf, root, and stem in different solvent extraction. Leaf showed higher content in acetone (48.00 g/100), root (52.10 g/100 g), and stem (66.20 g/100 g) in chloroform solvent extraction.[102] Recently, various compounds, such as 2,4-bis-(1,1-dimethylethyl), benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-methyl ester, and n-hexadecanoic acid were isolated in different solvent fractions of *R. ellipticus* fruits.[72] However, in-depth analysis of phenolic composition and other phytochemicals in other plant parts using modern techniques, such as infra-red spectra, high-resolution mass spectrophotometry, and tandem mass spectrophotometry (MS-MS), nuclear magnetic resonance (NMR), optical rotary dispersal and circular dichroism techniques is lacking for accurate compound identification.

Flavonoids

Flavonoids are an important group of compounds known for their taste, colour, fragrance, and aroma. It has multiple health benefits, such as anti-inflammatory, antioxidant, anti-mutagenic, and anti-carcinogenic activities; thus, it is used in nutraceutical, cosmeceuticals, pharmaceutical, and

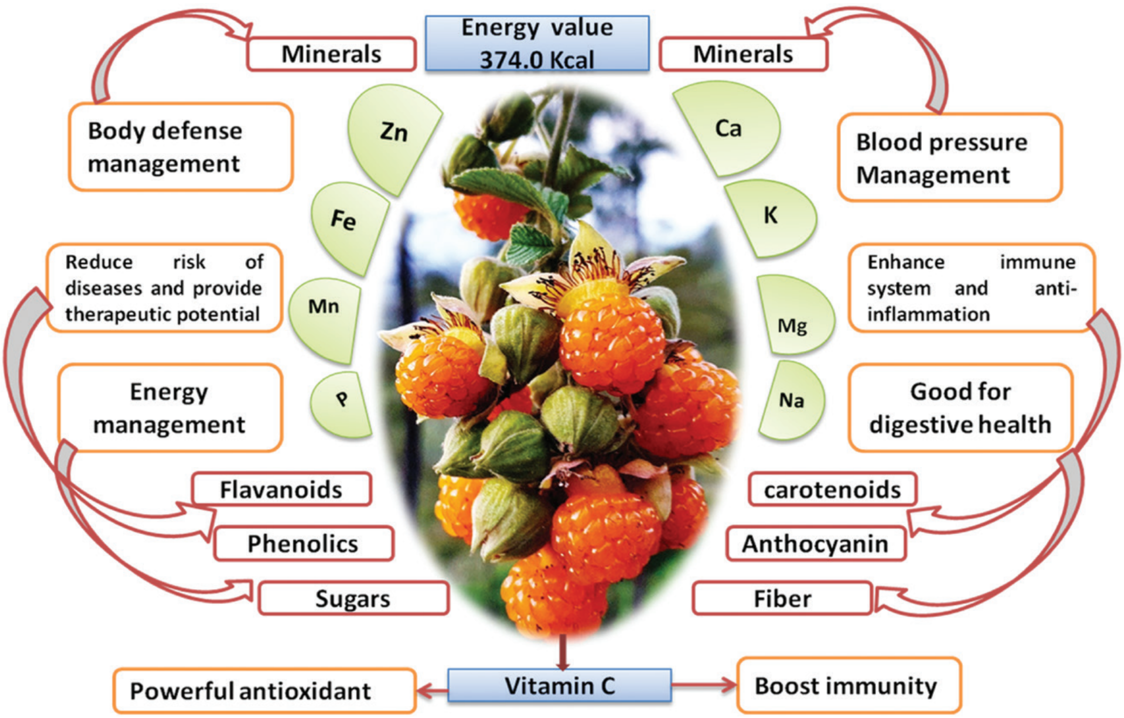

Figure 2 Nutritional components present in fruits of *R. ellipticus* and their major biological significance.

medicinal applications.[103] The total flavonoid in fruits varied in different solvent extraction systems, and 100% methanol extracted 217 mg/g content in dried fruit.[94] The total flavonoid concentration was observed between 2.76 and 4.65 mg/g FW in the sample extracted in 80% acidified methanol and 4.335 mg/g FW in acidified acetone.[24, 25] Among the plant parts of *R. ellipticus*, the leaf showed 1.89 mg/g flavonoid content in acetone extract. In contrast, in the stem and roots, the total flavonoid content was 2.2 mg/g and 3.08 mg/g in petroleum ether extract.[102] The HPLC analysis showed that (+)-catechin, phloridzin, and kaempferol were the main flavonoid compounds in *R. ellipticus* fruits[11, 94] (Table 2). Among these, kaempferol (17.4 mg/g) is a therapeutically important compound in apoptosis, angiogenesis, inflammation, and metastasis.[94]

Anthocyanins, a class of flavonoids, are natural plant pigments and have potent antioxidant, anti-hypertension, anti-diabetic and anti-inflammatory activity.[104] Recovery of total anthocyanin content varied in different solvent extractions. Total anthocyanins were extracted maximum as 0.12 mg/g FW in 80% acidic methanol,[25] followed by 1.71 mg CGE/100 g in 70% methanol,[88] 3.18 ± 0.10 mg/100 g DW in 100% methanol[94] in different studies. The HPLC analysis of anthocyanin revealed that cyanin and delphinidin were prominent anthocyanins, which are the source of antioxidant potential.[11]

Triterpene, terpene glycosides, and triterpenoid saponins

Terpenes are five-carbon isoprene units classified into different subclass based on the number of units, which include monoterpenes (C10), sesqui-terpenes (C15), di-terpenes (C20), sester-terpenes (C25), tri-terpenes (C30) and higher terpenes (>C30), and these terpenes responsible for vast structural and biological diversity.[105] *R. ellipticus* was found rich in various terpenes, such as leaves and roots containing oleanane, ursane, elliptic acid, ursolic acid, and the whole aerial part containing 3-β-hydroxy-urs-12, acuminatic acid, tormentic acid.[40, 95–99] Aswal *et al.* also confirmed the presence of β-sitosterol-β-D-glucoside, 18-dien-28-oic acid-3-0[β-D-glucopyranosyl] (1→4)-α-L-arabinopyranoside in aerial parts of the species.[98] Nine new ursane-type triterpenoids (Rubuside A–G and Rubuside J) and one new lupane-type triterpenoid (H) were isolated and identified along with 29 other known compounds from the roots of *R. ellipticus* var. *obcordatus*.[100]

Carotenoids

Carotenoids are pigments responsible for the red, orange, and yellow colours in fruits and vegetables. Total carotenoids (0.20 mg/100 g) have also been reported in significant quantity in fruits of the species.[84] Total carotenoids in ready-to-serve fruit beverages were recorded as 516 μg/100 ml[106] and 0.2 mg/100 g FW in fruit.[85] Similarly, β carotene was found between 0.52 to 1.81 mg/100g FW among the different genotypes of *R. ellipticus* fruits.[25]

Organic acids

Organic acids are important metabolites that maintain the pH of juice and can metabolize as an energy reservoir. Organic acids have anti-microbial potential and are used as a food preservative.[107] Karuppusamy *et al.* reported ascorbic acid in fruit (44 ± 4.95 mg/100 g), a free radical scavenger.[88] Badhani *et al.* quantified ascorbic acid in fruit using HPLC and varied 10.65–40.15 mg/100 g FW between different genotypes of the species.[25] However, the composition of other organic acids in juice and other parts remains unexplored in fruits and other plant parts.

Table 2 Bioactive constituents present in different plant parts of *R. ellipticus*

Chemical class	Compounds	Source plant part	Reference
Phenolic acid	Gallic acid	Fruit	[11, 24, 25]
	Chlorogenic acid	Fruit	[11, 25]
	Caffeic acid	Fruit	[11, 25]
	Ellagic acid	Fruit	[11,24]
	m-Coumaric acid	Fruit	[11]
	3-Hydroxybenzoic acid	Fruit	[11]
	4-Hydroxybenzoic acid	Fruit	[11]
	Ferulic acid	Fruit	[11]
	Vanillic acid	Fruit	[11]
	trans-Cinnamic acid	Fruit	[11]
Flavonoids and anthocyanins	(+)-Catechin	Fruit	[11, 25]
	Kaemferol	Fruit	[94]
	Phloridzin	Fruit	[11]
	Cyanin	Fruit	[11]
	Delphinidin	Fruit	[11]
Triterpene	Oleanane	Leaves	[95]
	Ursane	Leaves	[95]
	Elliptic acid	Leaves	[96]
	Ursolic acid	Leaves, root	[97]
	3-β-Hydroxy-urs-12	Whole aerial parts	[98]
	Acuminatic acid	Whole aerial parts	[98, 99]
	Tormentic acid	Whole aerial parts	[98]
Terpene glycosides	2α,3β,19α-Trihydroxyolen-12-en-28-oic acid 28-O-β-D-glucopyranosyl ester (24-deoxysericoside)	–	[40]
	28-β-Glucopyranosyl ester of 19α-hydroxyasiatic acid (Niga-ichgoside-F1)	–	[40]
	3-β-Hydroxy-urs-12,18-diene-28-oic-acid-3-O-(β-D-glucopyranosyl(1-4)-α-L-arabino-pyranoside	–	[40]
Triterpenoid saponin	18-Dien-28-oic acid-3-0[β-D-glucopyranosyl](1→4)-α-L-arabinopyranoside	Whole aerial parts	[98]
	Rubuside A–J	Root	[100]
	2R,3,23-trihydrox-yurs-12,18-dien-28-oic acid 28-O-D-glucopyranoside	Root	[100]
	2R,3,23-trihydroxyurs-12,19-dien-28-oic acid 28-O-D-glucopy-ranoside	Root	[100]
	Alpinoside; 11 quadranoside VIII	Root	[100]
	Sericoside	Root	[100]
	Sericic acid	Root	[100]
	Buergericic acid	Root	[100]
	Pinfaensin	Root	[100]
	Rosamutin	Root	[100]
	Kaji-ichigoside F1	Root	[100]
	Nigaichigoside F1 and F2	Root	[100]
	Trachelosperoside A1	Root	[100]
	Pedunculoside	Root	[100]
	Sauvissimoside R1	Root	[100]
	4-Epinigaichigoside F1	Root	[100]
	Ziyuglycoside	Root	[100]
	Euscaphic acid	Root	[100]
	1R,2R,3,19R-tetrahydroxyurs-12-en-28-oic acid	Root	[100]
	19R-hydroxyasiatic acid	Root	[100]
	2R,3,19R-trihydroxyurs-12-en-23,28-dioic acid	Root	[100]
Carotenoids	β-carotene	Fruit	[25]

Table 2. Continued

Chemical class	Compounds	Source plant part	Reference
Organic acids	Ascorbic acid	Fruit	[25]
	4-Dimethylamino-2,2,6,6-tetramethylpiperidinde; 3-piperidinecarboxamide, N,N-diethyl-	Fruit	[101]
Fatty alcohol	1-Octacosanol	Leaves, fruit	[97]
	(e)-9,11-dodecadien-1-ol	Fruits	[101]
Sterols	β-Sitosterol	Leaves	[97, 98]
	β-Sitosterol-β-D-glucoside	Leaves and whole plant	[97, 98]
Saturated fatty acids	Octacosanic acid	Leaves	[97]
Organooxygen compounds	3,3-Diethoxypropylamine	Fruit	[101]
Phenols	[2-(4-Hydroxy-phenyl)-ethyl]-carbamic acid ethyl ester	Fruit	[101]
	2,4-Bis(1,1-dimethylethyl)	Fruit	[72]
Phenylpropanoic acids	Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydrox-methyl ester	Fruit	[72]
Fatty acyls	n-Hexadecanoic acid	Fruit	[72]
Carboxylic acids and derivatives	2-Bromopropionic acid, tridecyl ester	Fruit	[101]
Lactones	Glucurolactone	Fruit	[101]
Organic carbonic acids and derivatives	Carbamic acid, hydroxy-, ethyl ester	Fruit	[101]
Carboximidic acids and derivatives	Acetamide, N-[3-(3-dimethylaminopropylamino)propyl]-2-hydroxyimino-2-phenyl	Fruit	[101]
Organonitrogen compounds	1,3-Propanediamine, N′-[3-(dimethylamino) propyl]-NN dimethyl	Fruit	[101]
	2-Propanamine, N-methyl-1-[4-[2-(1-piperidyl)ethoxyphenyl]	Fruit	[101]
Organoheterocyclic compounds	3-Piperidinamine, 1-ethyl-	Fruit	[101]
Others	7,9-Dimethyl-1,4-dioxa-7,9-diazacycloundecan-8-one	Fruit	[101]
	1-(Diethylamino)ethylidenimino]sulfur pentafluride	Fruit	[101]
	4-Fluoro-n-[2-(4-methyl-piperazine-1-carbonyl phenyl benzamide]	Fruit	[101]
	1,1-(Diethylcarbamoyl)succinimide)	Fruit	[101]
	4(Equat)-N-butyl-1,2(axial)-dimethyl-transdecahydroquinol-4-ol	Fruit	[101]

Other important phytochemicals

One fatty alcohol 1-octacosanol, and two saturated fatty acid, octacosanic acid and n-hexadecanoic acid, along with β-sitosterol and β-sitosterol-β-D-glucoside were isolated from the leaves of *R. ellipticus*.[97] These isolated compounds from the species are well characterized for having various biological activities. 1-Octacosanol is reported to have antifeedant, ovicide, and larvicide activities.[108] Similarly, β-sitosterol exhibits anti-inflammatory, anti-cancer, neuroprotective, anti-diabetic hypo-cholesterolemic, anthelminthic, anti-mutagenic, immune-modulatory genotoxicity, and angiogenic activities.[109]

Pharmacological and Biological Activities

Different plant parts of *R. ellipticus* exhibited various biological activities, including anti-diabetic, nephroprotective activity, anti-inflammatory, analgesic, anti-pyretic, anti-fertility, wound healing, anti-microbial and antioxidant, etc. (Table 3).

Anti-diabetic and α-amylase inhibition properties

After oral administration of petroleum ether, ethanol, and aqueous extracts of *R. ellipticus* fruits (200 mg/kg) for 15 days in alloxan-induced diabetic Wistar albino rats and Swiss albino mice, a significant reduction in serum glucose level has been recorded. However, ethanol extract was observed most potent extract than others.[26] Inhibition of α-amylase is another strategy for controlling the digestion of dietary carbohydrates in diabetes. The methanolic extract of *R. ellipticus* leaves exhibited significant α-amylase inhibition activity with IC_{50} value 269.94 ± 0.11 μg/ml.[110] Li *et al*. extracted triterpenoid compounds from the leaf of *R. ellipticus* and found that euscaphic acid was the most potent α-amylase inhibitor with IC_{50} values of 0.65 mM, compared with positive control acarbose (IC_{50} – 0.82 mM).[100]

Nephroprotective properties

In male albino rats, administration of paracetamol (750 mg/kg body weight) elevated serum creatinine, urea, blood urea nitrogen, and kidney weight with reduced urine volume. Petroleum ether, ethanolic and aqueous extracts of *R. ellipticus* fruits significantly normalized these biochemical parameters of the body. Besides, kidney histology revealed significant improvement after oral administration of all the extracts.[111] Oral administration of petroleum ether, ethanolic and aqueous extracts of *R. ellipticus* fruits (200 mg/kg/day) exhibited significant nephroprotective activity on gentamicin (100 mg/kg/day, 8 days) and cisplatin (7.5 mg/kg/day, 10 days) induced nephrotoxicity in Wistar albino rats and Swiss albino mice by normalizing the increased level of serum creatinine, serum uric acid, blood urea nitrogen, and serum urea levels.[28]

Table 3 Pharmacological and biological activity along with extract/fraction type, dose, experimental model, experimental background, effect, and possible underlying mechanism of *R. ellipticus*

S.N.	Pharmacological activity	Extract/ fractions/ plant parts	Dose and experimental details	Type of assay and model	Experimental background	Allied or related assays conducted	Underlying mechanism/ observed parameters	Reference
1	Anti-diabetic, α-amylase inhibition activity	Various solvent extracts of fruits	200 mg/kg, 15 days	*In vivo*: Wistar albino rats and Swiss albino mice	Alloxan-induced diabetes	Glucose tolerance test	Decrease in the blood glucose level in tested models	[26]
		Methanol extract of leaves	40–1000 µg/ml extract 200 µl of 50 µg/ml α-amylase Acarbose (40–1000 µg/ml)	–	Qualitative screening of phytochemicals, antioxidant activities, and α-amylase inhibition activity	α-Amylase inhibition assay	Significant inhibition of α-amylase inhibition	[110]
2	Nephroprotective activity	Various solvent extracts of fruits	100–200 mg/kg/day, 8 days, gentamicin (100 mg/kg/day, 8 days), cisplatin (7.5 mg/kg/day, 10 days)	*In vivo*: Wistar albino rats and Swiss albino mice	Investigation of nephroprotective activity	Gentamicin and cisplatin-induced nephrotoxicity	Protecting the kidney by normalization of gentamicin and cisplatin-induced increase in serum creatinine, serum uric acid, blood urea nitrogen and serum urea levels	[28]
		Various solvent extracts of fruits	200 mg/kg b. wt. Acetaminophen (APAP) 750 mg/kg	*In vivo*: Wistar albino rats	Investigation of nephroprotective activity	Acetaminophen-induced nephrotoxicity	Fruit extract normalized the increased level of serum creatinine, serum urea, blood urea nitrogen and kidney weight	[111]
3	Anti-inflammatory, analgesic and anti-pyretic	Methanolic leaf extract	200 and 400 mg/kg b. wt, indomethacin (20, 10 mg/kg, 7 h), aspirin (100 mg/kg, 15 min), morphine (10 mg/kg, 120 min), Paracetamol (100 mg/kg, 24 h)	*In vivo*: Wistar albino rats and mice	Anti-inflammatory, analgesic and anti-pyretic activity	Carrageenin-induced paw oedema, croton oil-induced ear oedema, acetic acid-induced writhing test, Eddy's hot plate mediated pain reaction, yeast-induced pyrexia in rats	Reduced paw and ear oedema, latency period increased, writhing responses reduced, rectal temperatures decreased	[59]
		Ethanolic root extract	250 and 500 mg/kg	*In vivo*: Red blood cells of albino rats	Investigation of anti-inflammatory activity	Carregeenin-induced rat paw oedema	Oedema swelling reduced	[81]
4	Tumour, wound healing, anti-proliferative, cytotoxicity	Ethanolic root extract	Tumour: 50–250 mg/kg b. wt, 0.1% carboxy methyl cellulose, 38 days Wound healing: 100 mg/kg and 200 mg/kg, 21 days	*In vivo*: Swiss albino mice, Wistar male rats,	Tumorigenesis	Dalton's lymphoma ascites (DLA) cell lines induced solid tumour, Ehrlich ascites carcinoma (EAC) induced ascites tumour in Swiss albino mice, incision, excision, and *Staphylococcus aureus*-induced infected wound	The dose of 250 mg/kg prolonged the life span of mice with EAC (46.76%); reduced the volume of DLA (2.56 cm^3); complete epithelialization was observed during the 13th and 19th days	[112]
		Various solvent extracts of fruits	Cervical cancer cell lines (C33A, HeLa): 0.667, 1.66, 3.33, 5.0 and 6.67 mg/ml peripheral blood mononuclear cells (PBMCs): 5.0 and 6.67 mg/ml	*In vitro*: C33A, HeLa, PBMCs	Antioxidant and antiproliferative activity	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay	Viability of cervical cancer cell lines reduced, PBMCs remained non-toxic	[24]
		Methanol extract of leaves	104 cells/200 µl/well	*In vitro*: HEK293	Cytotoxicity	MTT assay	Non-toxic to HEK293	[72]
		Methanol extract of fruits	1–10 g/L penicillin, streptomycin (100 U/ml)	*In vitro*: Caco-2	Cytotoxicity	MTT assay	Significantly controlled the viability of Caco-2 cells	[94]

Table 3. Continued

S.N.	Pharmacological activity	Extract/ fractions/ plant parts	Dose and experimental details	Type of assay and model	Experimental background	Allied or related assays conducted	Underlying mechanism/ observed parameters	Reference
5	Anti-fertility activity	90% ethyl alcohol extract of leaves	200 mg/kg PEG 400 (1000–5000 mg/kg, 72 h)	*In vivo*: female albino mice	Validation of anti-fertility activity	–	Decreased implantation sites, increased resorption sites	[113]
		90% ethanolic extract of root and whole plant	50–250 mg/kg body weight	Albino rats	Anti-implantation activity	*In vivo*	Root ethanolic extract showed 60–66% anti-fertility activity at 250 mg/kg dose. Whole plant parts without root extract showed 100% activity at 50 mg/kg dose	[114]
6	Ovi-position deterrent, anti-plasmodial activity	Aqueous extracts of leaves and silver nanoparticles	–	*In vitro*: *Anopheles stephensi*, *Aedes aegypti*, *Culex quinquefasciatus*	Ovicidal, larvicidal, and adulticidal activity	UV-Vis spectroscopy, XRD, FTIR, SEM, TEM and EDX	Biosynthesized AgNPs showed higher toxicity when compared with aq. extract	[115]
		Methanol extract of leaves and stem	500 µg/ml, four days	*In vivo*: *Plasmodium berghei* (ANKA) In vitro: *Plasmodium falciparum* (Pf3D7, PfINDO)	Antimalarial activity	SYBRgreen I fluorescence-based assay, column chromatography, GCMS, RP-HPLC	Significant reduction of parasite load, leaf extract showed significant antimalarial activity against PfINDO	[72]
7	Antimicrobial activity	90% ethanol extract of the root	250–1000 µg/ml extract, gentamycin (10 and 20 µg/ml), ketoconazole (10 µg/ml), 24 h for anti-bacterial, 48 h for anti-fungal	*In vitro*: *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Saccharomyces cerevisiae*, *Aspergillus niger*, *Candida albicans*, *Rhizopus nigricans*	Anti-bacterial and anti-fungal activity	Agar wall diffusion method	Bacterial growth significantly inhibited, anti-fungal activity not observed	[121]
		Petroleum ether and various solvents of roots and fruits	10 and 50 mg/ml, 24 h for anti-bacterial and 7 days for anti-fungal Erythromycin (10 mg/ml), ketoconazole (10 mg/ml)	*In vitro*: *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter gergoviae*, *Salmonella entericatyphim*, *Shigella flexneri*, *Staphyloccus aureus*, *S. epidermidis*, *Streptococcus pyogenes*, *Bacillus cereus*, *Aspergillus flavus*, *A. paraciticus*, *Candida albicans*	Anti-bacterial and anti-fungal activity	Swab method, disc diffusion method	Significantly inhibited bacterial and fungal growth	[86]
		Ethanol extract of leaf	500 µg/ml and 1000 µg/ml, 24 h for anti-bacterial, 40 mg/ml, 48 h for anti-fungal Ampicillin (100 µg/ml), clotrimazole (10 µg/ml)	*In vitro*: *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *E. coli*, *Aspergillus flavus*, *Candida albicans*, *Candida krusei*, *Trichoderma lignorum*	Anti-bacterial, anti-fungal	Swab method, disc diffusion method, evaluated for the presence of bioactive compounds, TLC	Significant inhibition of bacterial and fungal growth	[116]
		Methanol extract of root bark	20 µl, 24 h, neomycin (1 mg/ml)	*In vitro*: *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Salmonella typhi*	Anti-bacterial activity	Disc diffusion method, resazurin microtiter assay	The plants possessed inhibitory effect against only Gram-positive bacteria *Staphylococcus aureus*	[93]
		Ethanolic extract of leaves	1000 µg/ml Streptomycin (30 mcg)	*In vitro*: *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Bacillus cereus*	Anti-bacterial activity	Disc diffusion method	Significant inhibition of bacterial growth	[117]

Table 3. Continued

S.N.	Pharmacological activity	Extract/ fractions/ plant parts	Dose and experimental details	Type of assay and model	Experimental background	Allied or related assays conducted	Underlying mechanism/ observed parameters	Reference
	Antioxidant, radical scavenging activity	Methanol extract from fruits	Gallic acid equivalents (GAE)/100 g	*In vitro*	Antioxidant/radical scavenging activity	DPPH assays, quantitative estimation of polyphenolic compounds	Extract showed significant scavenging activity	[118]
		Acetone extract from fruits	2 ml, 30 min for DPPH and 5 min for H_2O_2, 20 min for FRAP, 90 min for phosphomolybdenum complex assay (PMA)	*In vitro*	Antioxidant/radical scavenging activity	DPPH hydrogen peroxide (H_2O_2) radicals scavenging assays, FRAP, PMA, quantitative estimation of polyphenolic compounds	Significantly scavenge DPPH and H_2O_2 radicals	[49]
		Various solvent extracts of fully ripe fruit	50–200 µg/ml, 30 min for DPPH 100–200 mg/l, 10 min for reducing power assay	*In vitro*	Radical scavenging and reducing power activity	DPPH, reducing power assay, qualitative phytochemical screening	Ethanolic extract exhibits the highest scavenging and reducing power activities	[27]
		Various solvent extracts from fruits	100 µl (for DPPH and PRAA), 50 µl (for ABTS), 30 µl (for FRAP),	*In vitro*	Radical scavenging activity	ABTS, FRAP, PRAA, DPPH, quantitative estimation of phytochemicals, and cytotoxicity	Methanol extracts possessed the most significant activity	[94]
		Methanol extract from leaves	1 ml, 30 min	*In vitro*	Qualitative antioxidant activities	DPPH	Significant free radical scavenging activity	[110]
		Methanol extract of root bark	50–300 µg/ml	*In vitro*	Assessment of phytochemical, antioxidant and anti-microbial activity	DPPH	Significant scavenging capacity	[93]
		80% each of various solvents of fruits	50 µl for ABTS, 0.1 ml for DPPH	*In vitro*	Antioxidant and anti-proliferative activity	DPPH, ABTS, Superoxide anion scavenging activity, ferric reducing activity	Significant scavenging and ferric reducing activity	[24]
		70% methanolic extract of the fruit	2.5 ml, 30 min	*In vitro*	Antioxidant activity	DPPH	Significant scavenging activity	[88]

Anti-inflammatory and analgesic properties

The ethanolic extract of *R. ellipticus* roots significantly ($P < 0.01$) decreased the edema swelling with the dose of 250 and 500 mg/kg after 3 hours (h) in carrageenan (0.1 ml) induced paw edema in albino rats. High concentration dose (500 mg/kg) was more active than 250 mg/kg, which was equally potent as Indomethacin (10 mg/kg) treated animals.[81] The extract in concentrations of 200 mg/kg and 400 mg/kg prevented (45.43% and 66.47%, respectively) the increased thickness of paw edema in the rats. However, standard drug indomethacin (10 and 20 mg/kg body weight) showed a higher inhibitory effect (80.89%) after 7 h. Similarly, in croton oil-induced ear inflammation the methanolic extract significantly reduced the inflammation of ear from 36.66% (200 mg/kg) to 45.78% (400 mg/kg) when compared with the control (76.52%) Indomethacin (10 mg/kg).[59] The analgesic activity of methanolic extract showed significant protection against acetic acid induced writhing in mice. The dose of 200 mg/kg and 400 mg/kg significantly reduced the writhing frequency from 19.40% and 32.84%, respectively when compared with standard drug (73.13% inhibition) Aspirin (100 mg/kg). The dose of 400 mg/kg produced the significant analgesic activity tested by Eddy's hot plate mediated pain reaction which showed the animal could withstand on the hot plate for 11.2, 13.6 and 7.7 second at 30, 60 and 120 min reaction time which is comparable with the standard drug (10 mg/kg) morphine (7.8, 9.6 and 12.4 second).[59] The root contains anti-inflammatory property, which shows potent fibroblast proliferation and anti-ageing. The active ingredient of the roots is kaji-ichigoside F1.

Anti-pyretic properties

The methanolic extract of *R. ellipticus* leaf exhibited strong anti-pyretic properties against yeast (Brewer's yeast) induced hyperpyrexia in rats at the concentration of 200 and 400 mg/kg. A significant reduction in hyperpyrexia was observed in yeast-induced rats body temperature from third to seventh hours after administration, and the activity was comparable to standard drug paracetamol (100 mg/kg).[59]

Anti-tumor, anti-proliferative, cytotoxicity and anti-cancer properties

The methanolic extract of *R. ellipticus* leaf exhibited protective effects against Dalton's lymphoma ascites (DLA) cell lines induced solid tumour and Ehrlich ascites carcinoma (EAC) induced ascites tumour in Swiss albino mice. The dose of 250 mg/kg extract prolonged the life span of mice with EAC (46.76%) and reduced the volume of DLA (2.56 cm^3).[112] Anti-proliferative activity of *R. ellipticus* fruits was analyzed in human cervical cancer cell lines (C33A and HeLa) and one normal cell line (peripheral blood mononuclear cells [PBMCs]) with 80% each of methanol, acid methanol, acetone, acid acetone using MTT ([3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide) assay. It was observed that acetone (EC_{50} value 5.04 mg/ml) and methanol (EC_{50} value 4.9 mg/ml) extracts possessed the highest anti-proliferative activity against C33A. In contrast, none of the extracts showed cytotoxicity to PBMC cells.[24] Also, the methanolic extract significantly controlled the viability of tested cell lines in a dose-dependent manner, and only 50% of Caco-2 cell lines were viable at 10 µg/µl concentration.[94] Sachdeva *et al.* evaluated the cytotoxic activity of the methanolic extract of *R. ellipticus* leaves in the HEK293 cell line and revealed a non-toxic effect on HEK293 with TC50 values of 90 µg/ml.[72]

Wound healing properties

The methanolic extract of *R. ellipticus* leaf (dose 100 mg/kg and 200 mg/kg) exhibited healing properties against *Staphylococcus aureus*-induced wounds in Wistar male rat models. The remarkable healing property of the extract observed in *S. aureus*-induced wound models compared with the control (Betadine, Neomycin) and the complete epithelialization period was reported during the 13th and 19th day.[112]

Anti-fertility properties

Different plant parts of *R. ellipticus* have been used as an abortifacient since ancient times.[119] The ethanolic extract of *R. ellipticus* roots (250 mg/kg) exhibits significant anti-implantation activity during 1–7 days of pregnancy, while the ethanolic extract of the aerial part of *R. ellipticus* (whole plant without root) showed 100% activity even at the lower dose (50 mg/kg body weight) during 1–3 days of pregnancy.[114] The whole plant (without root) extracted with 90% ethanol showed potent anti-fertility activity and at the dose of 250 showed 100% early pregnancy and strong oestrogenic activity.[120] The ethanolic extract of *R. ellipticus* leaves (200 mg/kg) evaluated for anti-fertility activity on male-female albino mice revealed a significant decrease in implantation sites and increased resorption sites.[113]

Ovi-position deterrent and anti-plasmodial properties

R. ellipticus-fabricated AgNPs synthesized using the aqueous leaf extract of *R. ellipticus* are potential ovi-deterrents and showed significant ovicidal, larvicidal, and adulticidal activity against the eggs, larvae, and adults of *Anopheles stephensi*, *Aedes aegypti* and *Culex quinquefasciatus*.[115] The methanolic leaf and seed extract of *R. ellipticus* tested for *in vitro* anti-plasmodial activity against *Plasmodium falciparum* (*Pf*3D7 and *Pf*INDO) and *in vivo* anti-plasmodial effect of methanolic leaf extract against *P. berghei* (ANKA)-infected mice. *R. ellipticus* leaf extract showed remarkable antimalarial activity against *Pf*3D7 with IC_{50} = 14.26 µg/ml. The results of *in vivo* anti-plasmodial activity showed that the oral dose (500 mg/kg) of methanolic extract suppressed *P. berghei* parasitemia by 64% ($P < 0.05$) and significantly reduced the parasite load.[72]

Toxicological properties

Petroleum ether, ethanolic and aqueous extracts of *R. ellipticus* fruit exhibited non toxic neurological and behavioral symptoms up to a dose of 2000 mg/kg on Wistar albino rats and Swiss albino mice.[26] Also, the methanolic extract of *R. ellipticus* leaves administered to Wistar albino rats, and mice up to a dose of 2000 mg/kg showed neither any behavioral change nor the death of tested animals. Moreover, acute oral and dermal toxicity studies of methanolic extract of *R. ellipticus* leaf reported being safe for the tested animals up to a dose of 2 g/kg.[112] The ethanolic extract of *R. ellipticus* roots showed no toxicity and mortality in albino rats.[81] These toxicity studies on *R. ellipticus* suggested that the species is well tolerated by the animals and exhibited a high safety profile.

Anti-microbial, anti-bacterial and anti-fungal properties

In various studies, different plant parts of *R. ellipticus* showed anti-microbial, anti-bacterial, and anti-fungal properties. The ethanolic extract of *R. ellipticus* roots exhibited mild anti-bacterial activity using agar diffusion method at the different concentrations from 250 to 1000 µg/ml exhibited remarkable activity when compared with the standard drug gentamycin (10–20 µg/ml).The significant activity was observed at the 1000 µg/ml against *S. aureus*, *Bacillus subtilis*, *Escherichia coli*, *Shigella* but there was very less antifungal activity against *Saccharomyces cerevisiae*, *Aspergillus niger*, *Candida albicans,* and *Rhizopus nigricans*.[121] The ethanolic extract of *R. ellipticus* fruits (50 mg/ml) has the highest antibacterial activity against food poisoning bacteria viz. *E. coli* (MTCC 729) with an inhibitory zone of 16.0 mm followed by *Streptococcus pyogenes* (MTCC 1925) and *E. coli* (MTCC 443) with an inhibitory zone of 15.0 mm each.[86] The anti-microbial activity of *R. ellipticus* leaf extracted in different solvents was evaluated against bacterial strains (*E. coli* and *S. aureus*) and fungal strains (*C. albicans*) by broth microdilution method. Maximum growth inhibition for anti-bacterial activity was observed in the ethanolic extract of *S. aureus* strain (100%). In contrast, the acetone extract observed maximum anti-fungal activity with growth inhibition (100%). The maximum antibacterial activity of *R. ellipticus* was shown in an aqueous extract of *E. coli* (MIC_{50} as 450 µg/ml). In contrast, acetone was the most suitable solvent for anti-fungal activity against *C. albicans* (MIC_{50} as 240 µg/ml).[122] Similarly, *R. ellipticus* extract was evaluated against eight common foodborne pathogens and fungal strain (*C. albicans*) by broth microdilution method. Maximum growth inhibition of *R. ellipticus* leaf for anti-bacterial activity was observed in the ethanolic extract (1 mg/ml) against *E. coli* strain. In contrast, water extract showed maximum growth inhibition against *B. cereus*, *L. innocua* and *M. luteus*. Comparatively, ampicillin as a controlled drug produced a 26.0 mm zone of inhibition. The maximum antibacterial activity of *R. ellipticus* using the MIC method was exhibited in an aqueous extract for *E. coli* and *B. cereus* (MIC_{50} as 559 µg/ml), *Listeria innocua* (MIC_{50} as 560 µg/ml), and ethanol was the most suitable solvent against *Bacillus cereus* (MIC_{50} as 273 µg/ml) and *E. coli* (MIC_{50} as 527 µg/ml). In contrast, acetone was the most suitable solvent against *Micrococcus luteus* (MIC_{50} as 282 µg/ml).[123] However, significant anti-fungal activity was reported against various fungal strains.[116] Overall, the anti-bacterial and anti-fungal activities of the fruits and roots remain low (MIC_{50} value > 500 µg/ml), which signifies the identification of the most potent molecule as an anti-microbial agent rather than the direct plant extract.

The methanolic extract of root bark of *R. ellipticus* was investigated for antibacterial activities against *S. aureus* (gram-positive), *Klebsiella pneumoniae*, *E. coli,* and *Salmonella typhi* (gram-negative) by using disc diffusion and Resazurin microtiter assay. The methanolic extract of root bark of *R. ellipticus* exhibited significant antibacterial activity against *S. aureus* with a 17 mm zone of inhibition, but no effect was observed with gram-negative strains by disc diffusion method. The MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) values of *R. ellipticus* were reported as 3.125 mg/ml and 12.5 mg/ml by Resazurin microtiter assay.[93] Similarly, the ethanolic extract of *R. ellipticus* leaves has the highest zone of inhibition and maximum activity against *Enterococcus faecalis* and lowest against *E. coli*, which is studied for MIC highest activity against *E. facecalis* (16 mg/ml) at 1000 µg/ml concentration and the minimum of *S. typhi* (10 mg/ml).[117] The whole plant (except the root) of *R. ellipticus* is reported to have antibacterial activity against *S. aureus*, *E. coli*, *Streptococcus faecalis*, *K. pneumoniae*, *Pseudomonas aeruginosa*; anti-fungal activity against *C. albicans*, *Cryptococcus neoformans*, *Trichophyton mentagrophytes*, *Aspergillus fumigates*, *Sporotrichum schenckii*; antiprotozoal activity against *Entamoeba histolytica*, *Giardia lamblia* and anti-viral activity against Ranikhet disease-causing agent, *Vaccinia* virus.[98]

Anthelmintic activity, and anti-enteroviral activity of *R. ellipticus* leaf in three different extracts reported by Panda *et al*.[122] Anthelmintic activity studied by 96-well microplate by relative percentage movement compared with the solvent (Nematode growth medium) showed promising activity over 50% inhibition. The anti-viral activity was tested against EV71 and BrCr, ethanol, acetone and aqueous extract, which showed that aqueous (EC_{50} = 5 ± 5 and EC_{90} = 8 ± 6 µg/ml) and ethanol exract (EC_{50} = 13 ± 6 and EC_{90}: 15 ± 0 µg/ml) are potent inhibitors for enterovirus. The maximum inhibition was observed in aqueous (88 ± 18%) and ethanol (74 ± 1%) extract which showed the *R. ellipticus* is the best inhibitions for enterovirus. It proves that *R. ellipticus* could be a source for broad-spectrum antibiotics.[122]

Antioxidant and radical scavenging activity

Himalayan raspberry has high antioxidant potential measured by *in vitro* assays, such as radical scavenging DPPH (2,2′-diphenyl-1-picryl-hydrazyl-hydrate), the ferric-reducing activity of plasma (FRAP), 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS), superoxide, nitric oxide (NO), hydroxyl radicals, lipid peroxidation and β-carotene bleaching activity (Figure 3; Table 3) as reported by various workers.[27,88,90,93,94,102,110] For instance, Saini *et al*. investigated free radical scavenging activities (DPPH, ABTS, superoxide anion scavenging activity, inhibition of β-carotene bleaching activity) and ferric-reducing activity with different solvent systems and reported that highest DPPH (619.3 ± 32.14 (mg CE/100 g FW) and ABTS (1072.6 ± 42.11 mg BHAE/100 g FW) scavenging activity was found in acetone extract, whereas the highest superoxide anion scavenging activity (1083.0 ± 2.23 mg AAE/100 g FW) and ferric-reducing activity (1389.8 ± 49.22 mg AAE/100 g FW) was exhibited in acidic acetone extract. Inhibition of β carotene bleaching activity was much higher in acetone, acidic acetone, and acidic methanol extract when compared with standard butylated hydroxyanisole (BHA) (10 mg), control and methanol extract.[24]

Sasikumar *et al*. examined polyphenolic compounds and *in vitro* antioxidant activity of ripened fruit extract of *R. ellipticus* and revealed that the total phenolic content (6100 ± 0.082 mg GAE/100 g FW) and total flavonoid content (320 ± 0.120 mg QE/100 g FW) were the major antioxidants. Significant scavenging activity towards DPPH (EC_{50} 9.85 ± 1.33 µg/ml), superoxide anion (EC_{50} 64.65 ± 0.82 µg/ml), hydroxyl ion radicals (EC_{50} 79.98 ± 1.02 µg/ml) and NO (EC_{50} 75.21 ± 1.32 µg/ml) was observed. The reduction capacity of the extract caused significant reducing power (increased OD value 1.435 ± 0.021), strong Fe^{2+} chelation (EC_{50} value

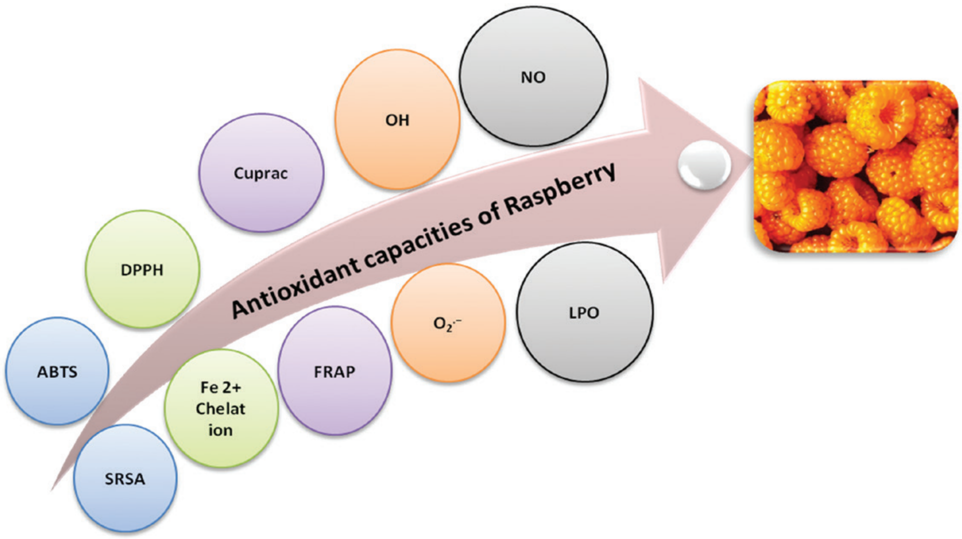

Figure 3 Antioxidant activities of *R. ellipticus* were determined in different assays.

45.24 ± 1.42 μg/ml) and lipid peroxidation (EC_{50} 71.1 ± 0.22 μg/ml). The antioxidant activity of the extract was comparable to butylhydroxytoluene (BHT), ethylenediaminetetraacetic acid disodium salt (EDTA-Na_2) and catechin.[118] Water and acetone extract of *R. ellipticus* fruit was evaluated for free radical scavenging activity (DPPH, $OH^-$and, and H_2O_2), and total antioxidant activity (FRAP and phosphorous-molybdenum (PM) complex). Remarkably highest scavenging activity was reported through the DPPH assay (94.65a ± 9.87%) in acetone extract, whereas the highest total antioxidant activity was shown in acetone extract (76.42c ± 9.11%) through (261.27 ± 17.49 μM AAE/100 g FW) through PM assay.[49] Hexane, ethyl acetate, and methanol extract of *R. ellipticus* were evaluated for free radical scavenging activity through ABTS and FRAP assay. The hexane extract contains the highest scavenging activity against DPPH with an IC_{50} value of 615.08 ± 1.76 μg/ml and ABTS with an IC_{50} value of 163.89 ± 1.32 μg/ml.[124] Similarly, George *et al*. demonstrated that methanol extract showed the highest 57.05 mM Fe(II)/mg extract when compared with hot water (24.35 mM), ethyl acetate (23.05 mM), and petroleum ether (0.44 mM).[101]

Genetic Variability and Genomic Resources for Crop Improvement

There is taxonomic confusion among genetic resources, and comprehensive investigations are required to resolve this issue. For instance, a comparative karyotypic, palynological, and RAPD (random amplified polymorphic DNA) analysis of 12 taxa belonging to subsections *Idaeobatus* in *Rubus* L. revealed that all the taxa except *R. ellipticus* and *R. pinfaensis* could be distinguished from each other by markers. Furthermore, *R. ellipticus* var. *obcordatus* should be treated as *R. obcordatus*, and *R. ellipticus* and *R. pinfaensis* should be combined as *R. ellipticus* to resolve the taxonomical confusion.[125]

The genus *Rubus* is highly variable, and the morphological characteristics vary from young and small canes to spring, and autumn foliage of the same cane; even the plant may respond differently in habitats like shade, moist, sun, and dry conditions and showed high hybridization compatibility among species.[126] Maikhuri *et al*. demonstrated that fruit yield in small, medium and large bushes are 0.475, 0.976, and 2.625 kg/plant, respectively, for *R. ellipticus*.[135] Plant morphological characteristics, such as leaf length (3.32–10.52 cm), leaf width (2.17–9.80 cm), petal length (0.30–1.36 cm); petal width (0.15–1.00 cm), flower diameter (0.56–3.26 cm), flowers/truss (2–23 fruit) vesicles/fruit (5–72), fruit length 0.55–1.92 cm), fruit width (0.64–1.82 cm), fruit weight (0.332–1.43 g) and fruit volume (0.213–1.020 cm^3) significantly varied among genotypes.[14] Among the nine *Rubus* species, a high variation in number of branches/plant (5.8–10.2); leaf length (5.69–8.90 cm); leaf width (2.23–9.81 cm); leaf petiole length (1.02–4.98 cm); petal length (0.43–1.44 cm); petal width (0.32–0.97 cm); plant canopy (12 320.2–73 317.3 cm^2); flower diameter (0.53–3.26 cm); number of trusses/plant (38–115); number of flowers truss/plant (10.4–15.2); number of vesicles/fruit (23–82); fruit length (0.46–1.55 cm); fruit width (0.46–1.11 cm); fruit weight (0.422–2.212 g); fruit volume (1.132–2.471 cm^3) was recorded.[90] Similarly, the species have already reported phytochemical variability in fruits among the different genotypes.[25] The significant variability in morphological traits in *R. ellipticus* offers the scope for identifying and selecting superior genotypes, which could be utilized for elite selection, commercialization, and domestication of this underutilized fruit plant.

Recent advancement in molecular biology has provided a platform to plant breeders to identify the genetic variation of traits among genotypes and identify the function of gene and associated bioactive compounds.[127,128] Genetic diversity analysis of 21 genotypes of *R. ellipticus* using ISSRs (inter simple sequence repeats) and EST-SSRs (expressed sequence tags-based simple sequence repeats) showed high polymorphism (100%), which can be used for future breeding programs.[129] Similarly, the transferability of EST-SSRs was studied in 10 *Rubus* species (including four *R. ellipticus* collections of different geographical origin, *R. ulmifolius*, *R. hypargyrus*, *R. panniculata*, *R. nutans*, *R. macilentus* and *R. strigosus*) revealed a high level of polymorphism (98.36%).[130] Inter-specific and inter-generic cross-transferability among these genotypes and species indicated that in the absence of genomic resources in *R. ellipticus*, inter-specific and inter-generic resource data could be used for genotyping and genetic genomic mapping genetic characterization and phylogenetic analysis. Sharma *et al.* analyzed variability among 21 *R. ellipticus* genotypes from different locations in India using morphological and EST-SSR markers and found a high phenotypic variation in genetic polymorphism (89.7%).[131] Recently, Sharma *et al*. developed 7870 SSRs in the species using transcriptome sequencing of leaf tissue. Among these, 68 randomly selected primers provided 90% amplification in *R. ellipticus*, whereas 95% of primer pairs were informative in the five tested genera of Rosaceae, pear, peach, apple, rose, and strawberry, with 95.3% and 93.5% polymorphism. Such genomic resources can further be harnessed for molecular breeding for variety development in the species in a shorter period.[132]

Economic Importance and Market Potential

Besides edible value, *R. ellipticus* fruits are commercially cultivated to collect nectar sugar as honey.[133,134] The value-added edible products, such as squash, jam, jelly, alcoholic beverages, herbal wines, toothpaste, health beverage, yogurt and 'Haanj' (rice-based alcoholic beverage), and ice cream prepared from *R. ellipticus* fruits have economic benefits.[78,106,124,135–139] Cost-benefit of jam prepared from *R. ellipticus* fruit indicated a net return of 117.0 rupees per person, while fruit has Rs. 50.0/kg in rural areas.[135] Similarly, Negi *et al*. also analyzed the input (Rs. 203.0), and output (Rs. 420.0) costs with a net benefit of Rs. 217.0 per/person per day.[78] Comrep syrup prepared from the ripe fruits of *R. ellipticus* and *R. paniculatus* and roots is used to treat colds and coughs in Northeastern India.[140] Recently, Assam State Biodiversity Board fixed the market value of *R. ellipticus* fruits as Rs. 30.0–40.0/kg, while the global price has been estimated as around $1.54/kg.[141] In Nepal, fresh fruits of species have a price of Rs. 50.0–55.0/kg in the local market to make wine.[142] The Maruzen pharmaceutical and other cosmetic industries use the root of *R. ellipticus* for clinically tested products, like BG80 (cosmetic and pharmaceutical products), to protect skin from UV-induced damage and wrinkle improvement.[143]

Conclusion and Recommendations

R. ellipticus is used for multiple purposes, including edible fruits, processed products, and traditional medicines. The review revealed that *R. ellipticus* is well investigated in pharmacological properties, such as anti-diabetic, nephroprotective, anti-inflammatory, analgesic, anti-pyretic, anti-proliferative, wound healing, anti-fertility, insecticidal, anti-microbial and antioxidant properties. Most of these studies validated its traditional uses, such as gastritis, liver and kidney problems, wound healing, urinary infections, etc.[94] suggesting its huge biological potential. However, many other uses in traditional medicine for many diseases (such as diarrhea, peptic ulcers, heart- and blood-related diseases, typhoid, CNS troubles, etc.) have not been validated through pharmacological activity and need further research. Furthermore, in-depth phytochemical investigations need to be carried out to identify active molecule(s), which are necessarily required for drug or formulation for cosmeceutical or pharmaceutical purposes. While identifying a molecule as a novel drug, identifying the molecular target responding to the drug is the first insight to discovering the molecular mechanism of drug action, which faces multiple hurdles due to the complexity of the biological system. There is a need to understand the role and mechanism of each bioactive compound and the therapeutic effect that can lead to drug development. The pharmacological studies are not entirely explored, only performed through *in vitro* screening and very few animal model-based studies, which do not include comprehensive investigations into the molecular mechanisms of action. Proteomic analysis of the disease prevention mechanism of *R. ellipticus* can generate large data, including the expression of proteins, functioning, interaction and networking with other proteins, their biosynthetic pathways, etc., during drug discovery. Such large data-generating approaches will be more effective in diagnosing multiple targets of *R. ellipticus*-based drugs against complex diseases, such as diabetes, cancers, aging-related degenerations, and blood pressure-associated complications.

Fruits of the species have colossal potential, and various nutritional investigations[84] support that species have huge nutraceutical potential and need popularization for their wide acceptability among society. Fruit sensory characteristics must be further optimized to improve quality-related parameters. The detailed composition of fatty acids, organic acids, sugars, vitamins, etc., needs further investigation. The berries are tasty and nutritional data on berries can be used as health supplements, nutraceuticals, and nutria-cosmetics supplements, which can reduce the risk of health problems such as skin aging and can be used as an immunity booster. As the food industry always demands new products, the Indian Himalayan raspberry can be a source of food supplements and beverages with functional properties and improved livelihood and socioeconomic status.

The selected species might be introduced for mass cultivation. Small fruit size, short shelf-life, long ripening time, and multiple picking efforts are a few major concerns for its domestication. The short shelf-life of fruits can be encountered by processing and value addition of products, which will increase economic benefits from the species. The plantation of the species in degraded land can also help provide a resource for pollinators, which will be beneficial for making honey and other products. In this way, the species could be one of the important means for improving income generation and land stabilization in hilly terrain.

Overall, the edible fruits of the species are a good source of important essential nutrients and metabolites. The wide genetic variability in *R. ellipticus* could help the plant breeders to identify a superior accession among other species and utilize it either as a cultivar or as a suitable parent for the breeding program having desirable vegetative and reproductive traits. Modern advanced sequencing tools and improved computational simulation provide rapid method for accelerated development of genomic information, facilitating identification of molecular targets for drug discovery, trait improvement, and potential parental genotype identification for molecular breeding.[131] Developing varieties with improved traits can improve yield, productivity, and quality of fruits during commercial cultivation. Standardization of fruit quality is necessary for breeding particular plants to investigate variation in traits among genotypes coupled with an enhanced level of bioactive compounds, antioxidant activity, taste, and nutrients. Basic pharmacological assays of solvent extracts indicated the potential of the species against different diseases, such as nephroprotective, anti-inflammatory, analgesic, anti-pyretic, anti-proliferative, cytotoxicity, anti-cancer, wound healing, anti-fertility, anti-plasmodial properties, anti-microbial, antioxidant properties. Furthermore, in-depth research on pharmacological properties, such as identification of potential molecules, identification of drug target, and interaction with potential receptor molecules, can be helpful for its potential application as therapeutics. Overall, it can be concluded that species have immense potential to improve the dietary system of rural people and can be used in developing nutraceutical and energy supplement.

Author Contributions

P.K. and I.D.B. conceived the idea and designed the study. P.K., D.T., and S.R. compiled the database and wrote the manuscript. I.D.B. critically reviewed and improved the MS. All authors contributed to editing and critical revision of the manuscript.

Funding

Support for this research work provided by NMSHE TF-3 phase I&II (Forest resources and plant biodiversity, CSIR-SRF-Direct fellowship, Delhi, India under the grant no-09/560/0001/19-EMR-1, and In-house Project 4 is greatly acknowledged.

Conflict of Interest

The authors declare that they have no conflicts of interest to disclose.

Data availability

In this review paper, no primary data was generated.

References

1. FAO (Food and Agriculture Organization). The State of Food Security and Nutrition in the World. 2018. http://www.fao.org/3/I9553EN/I9553en.pdf (30 December 2021, date last accessed).
2. Berrang-Ford L et al. Mapping evidence of human adaptation to climate change. *Nat Clim Chang* 2021. (In press) http://doi.org/10.21203/rs.3.rs-100873/v1
3. Tardío J et al. Ethnobotanical review of wild edible plants in Spain. *Bot J Linn Soc* 2006; 152: 27–71. http://doi.org/10.1111/j.1095-8339.2006.00549.x
4. Sundriyal M, Sundriyal RC. Wild edible plants of the Sikkim Himalaya: nutritive values of selected species. *Econ Bot* 2001; 55: 377–90. http://doi.org/10.1663/0013-0001(2004)058[0286:WEPOTS]2.0.CO;2
5. Li Y et al. Bioactivities and health benefits of wild fruits. *Int J Mol Sci* 2016; 17: 1258. http://doi.org/10.3390/ijms17081258
6. Samant SS, Dhar U. Diversity, endemism and economic potential of wild edible plants of Indian Himalaya. *Int J Sustain Dev World Ecol* 1997; 4: 179–91. http://doi.org/10.1080/13504509709469953
7. Bhatt ID et al. Nutraceutical potential of selected wild edible fruits of the Indian Himalayan region. *Food Chem* 2017; 215: 84–91. http://doi.org/10.1016/j.foodchem.2016.07.143
8. Schulz M, Chim JF. Nutritional and bioactive value of *Rubus* berries. *Food Biosci* 2019; 31: 100438. http://doi.org/10.1016/j.fbio.2019.100438
9. Wang Y et al. Phylogenetic insights into Chinese *Rubus* (Rosaceae) from multiple chloroplast and nuclear DNAs. *Front Plant Sci* 2016; 7: 968. http://doi.org/10.3389/fpls.2016.00968
10. Nile SH, Park SW. Edible berries: bioactive components and their effect on human health. *Nutrition* 2014; 30: 134–44. http://doi.org/10.1016/j.nut.2013.04.007
11. Belwal T et al. Trends of polyphenolics and anthocyanins accumulation along ripening stages of wild edible fruits of Indian Himalayan region. *Sci Rep* 2019; 9: 1–11. http://doi.org/10.1038/s41598-019-42270-2
12. Seeram NP. Chapter 37. Berries. In: Heber D, Blackburn G, Go V et al. (eds.), *Nutritional Oncology*. 2nd edn. London, UK: Academic Press, 2006, 615–25.
13. Seeram NP, Heber D. Chapter 21. Impact of berry phytochemicals on human health: effects beyond antioxidation. In: Ho CT, Shahidi FS (eds.), *Lipid Oxidation and Antioxidants: Chemistry, Methodologies and Health Effects. ACS Symposium Series 956*. New York, NY: Oxford University Press, 2006. pp. 240–255.
14. Trivedi AK et al. Variability in vegetative characters and yield attributes of Raspberry (*Rubus* spp.) in Uttarakhand Himalayas. *Int J Fruit Sci* 2014; 14: 107–16. http://doi.org/10.1080/15538362.2013.817774
15. Khaniya L et al. *Rubus ellipticus* Sm. *Rubus foliolosus* Weihe & Nees *Rubus fruticosus* L. *Rubus irritans* Focke Rosaceae. In: Kunwar RM, Sher H, Bussmann RW (eds.), *Ethnobotany of the Himalayas. Ethnobotany of Mountain Regions*. Cham, Switzerland: Springer, 2020, 1–17. http://doi.org/10.1007/978-3-030-57408-6_208
16. Parmar C, Kaushal MK. *Rubus ellipticus*. In: *Wild Fruits*. New Delhi, India: Kalyani Publishers, 1982, 84–7.
17. Rojas-Vera J et al. Relaxant activity of raspberry (*Rubus idaeus*) leaf extract in guinea-pig ileum in vitro. *Phytother Res* 2002; 16: 665–8. http://doi.org/10.1002/ptr.1040
18. Rokaya MB et al. Ethnobotanical study of medicinal plants from the Humla district of western Nepal. *J Ethnopharmacol* 2010; 130: 485–504. http://doi.org/10.1016/j.jep.2010.05.036
19. Parihaar RS. Diversity and uses of ethno-medicinal plants associated with traditional agroforestry systems in Kumaun Himalaya. *Indian J Agric Sci* 2014; 84: 1470–6.
20. Singh H et al. An ethnobotanical study of medicinal plants used in sacred groves of Kumaon Himalaya, Uttarakhand, India. *J Ethnopharmacol* 2014; 154: 98–108. http://doi.org/10.1016/j.jep.2014.03.026
21. Singh P, Attri BL. Survey on traditional uses of medicinal plants of Bageshwar Valley (Kumaun Himalaya) of Uttarakhand, India. *Int J Conserv Sci* 2014; 5: 223–34.
22. Shah A et al. Medicinal shrubs used by Gujjar-Bakerwal tribes against various non-communicable diseases in Rajouri district (J&K), India. *Indian J Trad Knowl* 2017; 20: 466–73.
23. Tripathi AN et al. Uses of invasive alien plants in Kumaun Himalayan folk medicinal system. *Int J Herb Med* 2020; 8: 27–31.
24. Saini R et al. Antioxidant and antiproliferative activities of phenolics isolated from fruits of Himalayan yellow raspberry (*Rubus ellipticus*). *J Food Sci Technol* 2014; 51: 3369–75. http://doi.org/10.1007/s13197-012-0836-3.
25. Badhani A et al. Variation in chemical constituents and antioxidant activity in yellow Himalayan (*Rubus ellipticus* Smith) and hill raspberry (*Rubus niveus* Thunb). *J Food Biochem* 2015; 39: 663–72. http://doi.org/10.1111/jfbc.12172
26. Sharma US, Kumar A. Anti-diabetic effect of *Rubus ellipticus* fruit extracts in alloxan induced diabetic rats. *J Diabetol* 2011a; 2: 1–6.
27. Sharma US, Kumar A. In vitro antioxidant activity of *Rubus ellipticus* fruits. *J Adv Pharm Technol Res* 2011c; 2: 47–50. http://doi.org/10.4103/2231-4040.79805
28. Sharma US, Kumar A. Nephroprotective evaluation of *Rubus ellipticus* (smith) fruits extracts against cisplatin and gentamicin induced renal-toxicity in rats. *J Pharm Res* 2011b; 1: 285–7.
29. Upreti K et al. Diversity and distribution of wild edible fruit plants of Uttarakhand. In: Tewari LM, Pangtey YPS, Tewari G (eds.), *Nainital Biodiversity Potentials of the Himalaya*. Nainital, India; Gyanodaya Prakashan, 2010, 157–96.

30. India Biodiversity Portal. https://indiabiodiversity.org/ (28 November 2021, date last accessed).
31. Purgar D et al. A comparison of fruit chemical characteristics of two wild grown *Rubus* species from different locations of Croatia. *Molecules* 2012; 17: 10390–8. http://doi.org/10.3390/molecules170910390
32. Wu K et al. Potential classical biological control of invasive Himalayan yellow raspberry, *Rubus ellipticus* (Rosaceae). *Pac Sci* 2013; 67: 59–80. http://doi.org/10.2984/67.1.5
33. Hao DA et al. *Potentilla* and *Rubus* medicinal plants: potential non-Camellia tea resources. In: *Medicinal Plants Chemistry, Biology and Omics*. (1st edn), Woodhead Publishing, UK. 2015, pp-373–430.
34. Rocabado GO et al. *Rubus* – a review of its phytochemical and pharmacological profile. *Nat Prod Commun* 2008; 3: 423–36. http://doi.org/10.1177/1934578X0800300319
35. Manganelli RU, Tomei PE. Ethnopharmacobotanical studies of the Tuscan Archipelago. *J Ethnopharmacol* 1999; 65: 181–202. http://doi.org/10.1016/S0378-8741(98)00177-9
36. Sher H. Ethnoecological evaluation of some medicinal and aromatic plants of Kot Malakand Agency, Pakistan. *Sci Res Essay* 2011; 6: 2164–73.
37. Hummer KE. *Rubus* pharmacology: antiquity to the present. *HortScience* 2010; 45: 1587–91. http://doi.org/10.21273/HORTSCI.45.11.1587
38. Simpson M. Raspberry leaf: panacea for pregnancy and labour or problem? *Birth* 2010; 12: 54–5.
39. Bowman R et al. Biophysical effects, safety and efficacy of raspberry leaf use in pregnancy: a systematic integrative review. *BMC Complement Med Ther* 2021; 21: 1–11. http://doi.org/10.1186/s12906-021-03230-4
40. Patel AV et al. Therapeutic constituents and actions of *Rubus* species. *Curr Med Chem* 2004; 11: 1501–12. http://doi.org/10.2174/0929867043365143
41. Kala CP. Ethnomedicinal botany of the Apatani in the Eastern Himalayan region of India. *J Ethnobiol Ethnomed* 2005; 1: 1–8. http://doi.org/10.1186/1746-4269-1-11
42. Kumari P et al. Diversity and status of ethno-medicinal plants of Almora district in Uttarakhand, India. *Int J Biodivers Conserv* 2011; 3: 298–326.
43. Gangwar KK et al. Ethnomedicinal plant diversity in Kumaunhimalaya of Uttarakhand, India. *Nat Sci* 2010; 8: 66–78.
44. Wójcik E. Phytochemical investigation of *Rubus plicatus* blackberry. *Acta Pol Pharm* 1989; 46: 386–90.
45. Ajaib M et al. Ethnobotanical studies on useful shrubs of district Kotli, Azad Jammu & Kashmir, Pakistan. *Pak J Bot* 2010; 42: 1407–15.
46. Amjad MS, Arshad M. Ethnobotanical inventory and medicinal uses of some important woody plant species of Kotli, Azad Kashmir, Pakistan. *Asian Pac J Trop Biomed* 2014; 4: 952–8. http://doi.org/10.12980/APJTB.4.201414B381
47. Yaseen G et al. Traditional management of diabetes in Pakistan: ethnobotanical investigation from traditional health practitioners. *J Ethnopharmacol* 2015; 174: 91–117. http://doi.org/10.12980/APJTB.4.201414B381
48. Joshi K, Bhardwaj N. Traditional health care practices: a women centric study in lesser Himalayan region of Uttarakhand (India). *J Pharmacogn Phytochem* 2017; 6: 617–23.
49. Shan S et al. Evaluation of polyphenolics content and antioxidant activity in edible wild fruits. *Biomed Res Int* 2019; 2019: 1381989. https://doi.org/10.1155/2019/1381989
50. Maity D et al. Folk uses of some medicinal plants from North Sikkim. *Indian J Trad Knowl* 2004; 3: 66–71.
51. Singh B et al. Exploring plant-based ethnomedicine and quantitative ethnopharmacology: medicinal plants utilized by the population of Jasrota Hill in Western Himalaya. *Sustainability* 2020; 12: 7526. http://doi.org/10.3390/su12187526
52. Pradhan BK, Badola HK. Ethnomedicinal plant use by Lepcha tribe of Dzongu valley, bordering Khangchendzonga Biosphere Reserve, in north Sikkim, India. *J Ethnobiol Ethnomed* 2008; 4: 22. http://doi.org/10.1186/1746-4269-4-22
53. Uprety Y et al. Plant biodiversity and ethnobotany inside the projected impact area of the Upper Seti Hydropower Project, Western Nepal. *Environ Dev Sustain* 2011; 13: 463–92.
54. Wangchuk P et al. Ethnobotanical authentication and identification of Khrog-sman (lower elevation medicinal plants) of Bhutan. *J Ethnopharmacol* 2011; 134: 813–23. http://doi.org/10.1016/j.jep.2011.01.034
55. Yeshi K et al. Taxonomical identification of Himalayan edible medicinal plants in Bhutan and the phenolic contents and antioxidant activity of selected plants. *J Biol Act Prod Nat* 2017; 7: 89–106. http://doi.org/10.1080/22311866.2017.1325008
56. Uniyal B, Shiva V. Traditional knowledge on medicinal plants among rural women of the Garhwal Himalaya, Uttaranchal. *Indian J Trad Knowl* 2005; 4: 259–66.
57. Jain D et al. Traditional resources and use of aromatic and ethnomedicinal plants in Uttarakhand: compliment of nature. *Int J Herb Med* 2020; 8: 88–95.
58. Tamang R et al. Ethno-medicinal Plants used by Chepang community in Nepal. *J Plant Resour Environ* 2017; 15: 21–30.
59. George BP, Parimelazhagan T, Saravanan S. Anti-inflammatory, analgesic and antipyretic activities of Rubus ellipticus Smith. Leaf Methanol Extract. *Int J Pharm Pharm Sci* 2013; 5: 222–224.
60. Ojha SN et al. Ethnomedicinal knowledge of a marginal hill community of Central Himalaya: diversity, usage pattern, and conservation concerns. *J Ethnobiol Ethnomed* 2020; 16: 1–21. http://doi.org/10.1186/s13002-020-00381-5
61. Rawat N, Upadhaya ML. Diversity of the medicinal plants of Almora district, Uttarakhand and their Ethno-medicinal use. *J Med Plants Stud* 2020; 8: 89–101.
62. De Rus Jacquet A et al. Nepalese traditional medicine and symptoms related to Parkinson' s disease and other disorders: patterns of the usage of plant resources along the Himalayan altitudinal range. *J Ethnopharmacol* 2014; 153: 178–89. http://doi.org/10.1016/j.jep.2014.02.016
63. Bhatia H et al. Ethnomedicinal plants used by the villagers of district Udhampur, J&K, India. *J Ethnopharmacol* 2014; 151: 1005–18. http://doi.org/10.1016/j.jep.2013.12.017
64. Khadka B et al. Folklore medicinal plants used against typhoid and fever in Lwangghalel, Kaski District, Central Nepal. *J Plant Resour Environ* 2020; 18: 258–66.
65. Arya KR. Traditional uses of some common plants in indigenous folklore of Dronagiri: a mythic hill of Uttaranchal. *Indian J Trad Knowl* 2002; 1: 81–6.
66. Subedi R. *Ethnobotanical study of Panchase protected forest, Kaski District, Central Nepal*. Doctoral Dissertation, Kathmandu, Nepal: Central Department of Botany, Tribhuvan University Kirtipur, 2017.
67. Revathi P, Parimelazhagan T. Traditional knowledge on medicinal plants used by the Irula tribe of Hasanur Hills, Erode District, Tamil Nadu, India. *Ethnobot Leafl* 2010; 4: 136–60.
68. Ambu G et al. Traditional uses of medicinal plants by ethnic people in the Kavrepalanchok district, Central Nepal. *Plants* 2020; 9: 759. http://doi.org/10.3390/plants9060759
69. Shrestha PM, Dhillion SS. Medicinal plant diversity and use in the highlands of Dolakha district, Nepal. *J Ethnopharmacol* 2003; 86: 81–96. http://doi.org/10.1016/S0378-8741(03)00051-5
70. Thapa S. Accessing the Himalayan herbs traded in the streets of Itahari by Sherpa community of Taplejung, Nepal. *MOJ Biol Med* 2021; 6: 21–8. http://doi.org/10.15406/mojbm.2021.06.00124
71. Bhattarai KR. Ethnobotanical study of plants used by Thami community in Ilam District, eastern Nepal. *Our Nat* 2018; 16: 55–67.
72. Sachdeva C et al. Assessment of in vitro and in vivo antimalarial efficacy and GC fingerprints of selected medicinal plant extracts. *Exp Parasitol* 2020; 219: 108011. http://doi.org/10.1016/j.exppara.2020.108011
73. Gaire BP, Subedi L. Medicinal plant diversity and their pharmacological aspects of Nepal Himalayas. *Pharmacogn J* 2011; 3: 6–17. http://doi.org/10.5530/pj.2011.25.2

74. Uprety Y et al. Diversity of use and local knowledge of wild edible plant resources in Nepal. *J Ethnobiol Ethnomed* 2012; 8: 1–15. http://doi.org/10.1186/1746-4269-8-16
75. Long CL, Li R. Ethnobotanical studies on medicinal plants used by the Red-headed Yao People in Jinping, Yunnan Province, China. *J Ethnopharmacol* 2004; 90: 389–95. http://doi.org/10.1016/j.jep.2003.10.021
76. Adhikari M et al. Ethnomedicinal uses of plant resources in the Machhapuchchhre rural municipality of Kaski district, Nepal. *Medicines* 2019; 6: 69. http://doi.org/10.3390/medicines6020069
77. Negi VS et al. Traditional healthcare practices among the villages of Rawain valley, Uttarkashi, Uttarakhand, India. *Indian J Trad Knowl* 2011a; 10: 533–7.
78. Negi VS et al. Non-timber forest products (NTFPs): a viable option for biodiversity conservation and livelihood enhancement in central Himalaya. *Biodivers Conserv* 2011b; 20: 545–59. http://doi.org/10.1007/s10531-010-9966-y
79. Shah S et al. Medicinal plant wealth of oak dominated forests in Nainital catchment area of Uttarakhand. *Academia J Med Plant* 2014; 2: 6–13.
80. Punchay K et al. Traditional knowledge of wild food plants of Thai Karen and Lawa (Thailand). *Genet Resour Crop Evol* 2020; 67: 1277–99. http://doi.org/10.1007/s10722-020-00910-x
81. Vadivelan R et al. Evaluation of anti-inflammatory and membrane stabilizing property of ethanol root extract of *Rubus ellipticus* Smith in Albino rats. *J Nat Remedies* 2009; 9: 74–8.
82. Pal S, Palit D. Traditional knowledge and bioresource utilization among Lepcha in North Sikkim. *NeBIO* 2011; 2: 13–7.
83. Chaitanya M et al. Pharmacodynamic and ethnomedicinal uses of weed species in Nilgiris, Tamilnadu State, India: a review. *Afr J Agric Res* 2013; 8: 3505–27.
84. Ahmad M et al. Antioxidant and nutraceutical value of wild medicinal *Rubus* berries. *Pak J Pharm Sci* 2015; 28: 241–7.
85. Bhutia KD et al. Nutraceutical potential of some wild edible fruits of Sikkim, Himalaya, India. *Ethno Med* 2018; 12: 106–12.
86. Saklani S et al. Antimicrobial activity, nutritional profile and phytochemical screening of wild edible fruit of *Rubus ellipticus*. *Int J Med Aromat Plants* 2012; 2: 269–74.
87. Jin C et al. Ethnobotanical studies on wild edible fruits in Southern Yunnan: folk names; nutritional value and uses. *Econ Bot* 1999; 53: 2–14. http://doi.org/10.1007/BF02860785
88. Karuppusamy S et al. Antioxidant activity of selected lesser known edible fruits from Western Ghats of India. *Indian J Trad Knowl* 2011; 2: 174–8.
89. Bajracharya D. Nutritive values of Nepalese edible wild fruits. *Z Lebensm Unters Forsch* 1980; 17: 363–6. http://doi.org/10.1007/BF01087135
90. Trivedi AK et al. Variability in morpho-physiological traits and antioxidant potential of *Rubus* species in Central Himalayan Region. *Ind Crops Prod* 2016; 82: 1–8. http://doi.org/10.1016/j.indcrop.2015.12.022
91. Pandey Y et al. Phyto-chemical constituent of some wild edible fruits of Sikkim Himalaya. *J Pharmacogn Phytochem* 2018; 7: 1045–47.
92. Singh D et al. Expression of genetic variability and character association in raspberry (*Rubus ellipticus* Smith) growing wild in North-Western Himalayas. *Int J Hortic Sci* 2009; 4: 28–31.
93. Khanal LN et al. Assessment of phytochemical, antioxidant and antimicrobial activities of some medicinal plants from Kaski District of Nepal. *Am J Plant Sci* 2020; 11: 1383. http://doi.org/10.4236/ajps.2020.119099
94. Muniyandi K et al. Phenolics, tannins, flavonoids and anthocyanins contents influenced antioxidant and anticancer activities of *Rubus* fruits from Western Ghats, India. *Food Sci Hum Wellness* 2019; 8: 73–81. http://doi.org/10.1016/j.fshw.2019.03.005
95. Xiao-Hong Z et al. Oleanane and ursane glucosides from *Rubus* species. *Phytochemistry* 1992; 31: 3642–4. http://doi.org/10.1016/0031-9422(92)83747-M
96. Dutta S et al. Isolation and structure elucidation of new pentacyclic triterpene acid from the leaves of *Rubus ellipticus*. *Nat Prod Sci* 1997; 3: 108–10.
97. Bhakuni RS et al. Chemical examination of the roots of *Rubus ellipticus*. *Indian Drugs* 1987; 24: 272.
98. Aswal BS et al. Screening of Indian plants for biological activity: part XV. *Indian J Exp Biol* 1996; 34: 444–67.
99. Talapatra SK, Karmacharya B, De SC, et al. Chemical investigation of some medicinal plants of Nepal. *Indian J Chem B* 1989; 28: 356–7.
100. Li W et al. Triterpenoid saponins from *Rubus ellipticus* var. *obcordatus*. *J Nat Prod* 2009; 72: 1755–60. http://doi.org/10.1021/np900237a
101. George E et al. *GC-MS Analysis of Methanolic Extract of Rubus ellipticus: A Wild Edible Fruit in Phytomedicine*. Boca Raton, FL: CRC Press; 2020, 37–43.
102. George BP et al. A comparative study on in vitro and in vivo antioxidant properties of *Rubus ellipticus* and *Rubus niveus*. *Pharmacologia* 2014; 5: 247–55. http://doi.org/10.5567/pharmacologia.2014.247.255
103. Panche AN et al. Flavonoids: an overview. *J Nutr Sci* 2016; 5: 1–15. http://doi.org/10.1017/jns.2016.41
104. Vendrame S, Klimis-Zacas D. Potential factors influencing the effects of anthocyanins on blood pressure regulation in humans: a review. *Nutrients* 2019; 11: 1431. http://doi.org/10.3390/nu11061431
105. Huang AC, Osbourn A. Plant terpenes that mediate below-ground interactions: prospects for bioengineering terpenoids for plant protection. *Pest Manag Sci* 2019; 75: 2368–77. http://doi.org/10.1002/ps.5410
106. Krishna H et al. Changes in phenolic contents and antioxidant capacity of bayberry (*Myrica esculenta* Buch. Ham. ex D. Don) and yellow Himalayan raspberry (*Rubus ellipticus* Smith) based health beverages. *Indian J Trad Knowl* 2016; 15: 417–23.
107. Amrutha B et al. Effect of organic acids on biofilm formation and quorum signaling of pathogens from fresh fruits and vegetables. *Microb Pathog* 2017; 111: 156–62. http://doi.org/10.1016/j.micpath.2017.08.042
108. Zavala-Sánchez MA et al. Bioactivity of 1-octacosanol from *Senna crotalarioides* (Fabaceae: Caesalpinioideae) to control *Spodoptera frugiperda* (Lepidoptera: Noctuidae). *Fla Entomol* 2020; 102: 731–7. http://doi.org/10.1653/024.102.0410
109. Saeidnia S et al. The story of beta-sitosterol – a review. *European J Med Plants* 2014; 4: 590–609. http://doi.org/10.9734/EJMP/2014/7764
110. Subba B et al. Analysis of phytoconstituents, antioxidant, and alpha amylase inhibitory activities of *Persea Americana* Mill, *Rhododendron arboretum* SM. *Rubus ellipticus* SM. from Arghakhanchi District Nepal. *Asian J Pharm Clin Res* 2019; 12: 301. http://doi.org/10.22159/ajpcr.2019.v12i1.29679
111. Sharma US, Kumar A. Therapeutic efficacy of *Rubus ellipticus* (smith) fruits extracts in acute acetaminophen induced nephrotoxicity in rats. *Pharmacologyonline* 2010; 3: 514–24.
112. George BP et al. Antitumor and wound healing properties of *Rubus ellipticus* smith. *J Acupunct Meridian Stud* 2015; 8: 134–41. http://doi.org/10.1016/j.jams.2013.10.002
113. Dhanabal SP et al. Validation of antifertility activity of various Rubus species in female albino rats. *Indian J Pharm Sci* 2000; 62: 58–60.
114. Sharma BB et al. Antifertility screening of plants. Part I. Effect of ten indigenous plants on early pregnancy in albino rats. *Int J Crude Drug Res* 1983; 21: 183–7. http://doi.org/10.3109/13880208309070640
115. AlQahtani FS et al. Green and facile biosynthesis of silver nanocomposites using the aqueous extract of *Rubus ellipticus* leaves: toxicity and oviposition deterrent activity against Zika virus, malaria and filariasis mosquito vectors. *J Asia-Pac Entomol* 2017; 20: 157–64. http://doi.org/10.1016/j.aspen.2016.12.004

116. Shibu Prasanth SCR, Chandran P. Phytochemical and antimicrobial analysis of leaf samples of different *Rubus* species. *Intl J Chem Tech Res* 2017; 10: 359–68.
117. Singh M, Purohit R. Study on phytochemical characterization and antibacterial activity of fruit trees of Chamoli District, Uttarakhand, India. *Int J Pharma Bio Sci* 2019; 9: 226–31.
118. Sasikumar JM et al. In vitro analysis of antioxidant capacity of Indian yellow raspberry (*Rubus ellipticus* Smith.). *Int Food Res J* 2015; 22: 1338–46.
119. Sharma BB et al. *Rubus ellipticus* Smith – a potential antifertility plant. *Indian Vet Med J* 1981; 5: 25–8.
120. Prakash AO. Biological evaluation of some medicinal plant extracts for contraceptive efficacy in females. In: *Future Aspects in Contraception*. Runnebaum B, Rabe T, Kiesel L. (eds.), Dordrecht, the Netherlands: Springer, 1985, 115–28.
121. Vadivelan R et al. Antimicrobial evaluation of the ethanolic root extracts of *Rubus ellipticus* (Smith). *Pharmacist* 2008; 3: 19–21.
122. Panda SK et al. Antimicrobial, anthelmintic, and antiviral activity of plants traditionally used for treating infectious disease in the Similipal Biosphere Reserve, Odisha, India. *Front Pharmacol* 2017; 8: 658. http://doi.org/10.3389/fphar.2017.00658
123. Panda SK et al. Antimicrobial activity of select edible plants from Odisha, India against food-borne pathogens. *LWT* 2019; 113: 108246. http://doi.org/10.1016/j.lwt.2019.06.013
124. Handique JG, Gogoi D. Antioxidant activities of the medicinal plants used for preparation of fermentation cakes of “Haanj”, the rice based alcoholic beverage of Ahom community people of Assam, India. *Int J Pharmacogn Phytochem* 2016; 8: 217–22.
125. Wang XR et al. Karyotypic, palynological, and RAPD study on 12 taxa from two subsections of section Idaeobatus in *Rubus* L. and taxonomic treatment of *R. ellipticus*, *R. pinfaensis*, and *R. ellipticus* var. *obcordatus*. *Plant Syst Evol* 2009; 283: 9–18. http://doi.org/10.1007/s00606-009-0190-8
126. Rana JC et al. Naturally occurring wild relatives of temperate fruits in Western Himalayan region of India: an analysis. *Biodivers Conserv* 3991; 16: 3963. http://doi.org/10.1007/s10531-007-9201-7
127. Pourmohammad A. Application of molecular markers in medicinal plant studies. *Agric Ecosyst Environ* 2013; 5: 80–90.
128. Mattummal R et al. A review on molecular techniques employed for authentication of Indian medicinal plants. *Plant Sci Today* 2019; 6: 465–78. http://doi.org/10.14719/pst.2019.6.4.588
129. Rajinder K et al. Assessment of genetic diversity in *Rubusellipticus* (Smith) using molecular markers. *Proc Indian Natl Sci Acad* 2017; 83: 669–79. http://doi.org/10.16943/ptinsa/2017/49120
130. Thakur R. Studies on development of genic-SSRs in raspberry (*Rubus ellipticus* Smith.) and their transferability across related species. Doctoral Dissertation. Nauni, India: UHF, 2013.
131. Sharma S et al. Genetic variability in *Rubus ellipticus* collections assessed by morphological traits and EST-SSR markers. *J Plant Biochem Biotechnol* 2021; 30: 37–55. http://doi.org/10.1007/s13562-020-00567-8
132. Sharma S et al. Transcriptome sequencing of Himalayan Raspberry (*Rubus ellipticus*) and development of simple sequence repeat markers. *3 Biotech* 2019; 9: 1–15. http://doi.org/10.1007/s13205-019-1685-9
133. Gupta JK, Thakur RK. Nectar sugar production and flower visitors of the bramble, *Rubus ellipticus* Smith (Rosaceae), at Solan, India. *Apidologie* 1987; 18: 223–30.
134. Kala CP. Prioritization of cultivated and wild edibles by local people in the Uttaranchal hills of Indian Himalaya. *Indian J Trad Knowl* 2007; 6: 239–44.
135. Maikhuri RK et al. Wild fruits as a contribution to sustainable rural development: a case study from the Garhwal Himalaya. *Int J Sustain Dev World Ecol* 1994; 1: 56–68. http://doi.org/10.1080/13504509409469861
136. Maikhuri RK et al. Bioprospecting of wild edibles for rural development in the central Himalayan mountains of India. *Mt Res Dev* 2004; 24: 110–3. http://doi.org/10.1659/0276-4741(2004)024[0110:BOWEFR]2.0.CO;2
137. Gairola Y, Biswas S. Bioprospecting in Garhwal Himalayas, Uttarakhand. *Curr Sci* 2008; 94: 1139–43.
138. Rana A, Singh HP. Bio-utilization of wild berries for preparation of high valued herbal wines. *Indian J Nat Prod Resour* 2013; 4: 165–9.
139. Shah S, Lamichhane D. Documentation of indigenous knowledge on plants used by Tamang community of Kavrepalanchok district, Central Nepal. *J Plant Res* 2017; 15: 45–51.
140. Chakraborty T et al. First report on the ethnopharmacological uses of medicinal plants by Monpa tribe from the Zemithang Region of Arunachal Pradesh, Eastern Himalayas, India. *Plants* 2017; 6: 13. http://doi.org/10.3390/plants6010013
141. Tridge. Your Global Sourcing Hub. https://www.tridge.com/ (25 October 2021, date last accessed).
142. Joshi N, Dhakal KS. Utilization pattern and market value of wild fruit and nut species in Nepal. *J Plant Resour Environ* 2017; 15: 52.
143. Maruzen Pharmaceuticals Co., Ltd. https://www.maruzenpcy.co.jp (25 October 2021, date last accessed).