REVIEW ARTICLE

A C G publications

*Rec. Agric. Food. Chem.*2:2 (2022) 59-74

records of agricultural and food chemistry

Himalayan Yellow Raspberry (*Rubus ellipticus* Smith.): A Plant with Multiple Medicinal Purposes

Rakesh Kumar Joshi[1*], Lucas Fornari Laurindo[2], Preeti Rawat[3], Ricardo de Alvares Goulart[4] and Sandra M. Barbalho[2,4,5]

[1]*Department of Education, Government of Uttarakhand, India*
[2]*Department of Biochemistry and Pharmacology, School of Medicine, University of Marília (UNIMAR), Avenida Higino Muzzi Filho, 1001, Marília, São Paulo, Brazil*
[3]*Department of Chemistry, Bakht Darshan Government PG College, Jaiharikhal, Pauri, Uttarakhand, India*
[4]*Postgraduate Program in Structural and Functional Interactions in Rehabilitation – UNIMAR – Marília–SP, Brazil;*
[5]*School of Food and Technology of Marilia (FATEC) – Marilia – SP, Brazil*

(Received September15, 2022; Revised November30, 2022;December07, 2022)

Abstract: Herbal medicinal plants or products remain very popular around the world despite the large amounts of conventional drugs to treat several illnesses. Among the plethora immensity of medicinal plants, there is *Rubus ellipticus*, also known as yellow Himalayan raspberry. The traditional use of the plant is for the treatment of cough, fever, constipation, diarrhea, relief of stomach worms in children, and healing of bone fracture. Due to the broad spectrum of possible actions of *R. ellipticus*, this study aimed to investigate the effects of this plant on health. Google Scholar, PubMed and Embase were searched to perform this review and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were followed. No Clinical trials were found, however, some *in vitro* and animal studies were included in this review. *R. ellipticus* present many bioactive compounds such as ascorbic acid, ellagic acid, ursolic acid, quercetin, kaempferol, and anthocyanins. These compounds are possible responsible for the antioxidant, anti-inflammatory, anti-proliferative, anti-microbial, anti-diabetic, antipyretic, analgesic activities, and wound healing effects. For these reasons, the consumption of this fruit could reduce oxidative stress and anti-inflammatory processes and, therefore, reduce diabetes and metabolic-related diseases such as cardiovascular diseases and cancer. *R. ellipticus* also has huge economic importance due to its nutritional value and can be used in the food, cosmetics, and pharmaceutical industries.

Keywords: *Rubus ellipticus*; anti-inflammatory; antioxidant; antimicrobial; anticancer.

1. Introduction

Herbal medicinal plants or products remain very popular around the world despite the large amounts of conventional drugs to treat several illnesses. Although the number of bioactive compounds can be enormous in different plants, most are still not chemically defined. Despite that, the relevance of

* Corresponding author e-mail: raakeshjoshi@rediffmail.com

The article was published by ACG Publications
https://www.acgpubs.org/journal/records-of-agricultural-and-food-chemistryJuly-December 2022 EISSN:2792-0763
DOI: http://doi.org/10.25135/rfac.13.2209.2576
Available online: December 30,2022

medicinal plants and products grows every year mainly due to the low costs when compared to conventional therapies and due to low side effects resulting from their use [1]. Surveys among adult, elderly and pediatric patients show that between 15- 45% of them use herbal medicine for health issues, besides prescribed usual medicine Complementary herbal medicines are more frequent among women and the elderly and the use is intended for the treatment of acute and chronic diseases[2-7]. Among the plethora immensity of medicinal plants, there is *Rubus ellipticus*. This is a yellow Himalayan raspberry corresponding to an evergreen shrub belonging to the Rosaceae family. It is native to Indonesia, China, Sri Lanka and the Indian subcontinent. The genus *Rubus* includes over 750 species. Common use of the plant is for the treatment of cough, fever, constipation, diarrhea, relief of stomach worms in children, and healing of bone fracture [8-9]. The root paste is used for the treatment of bone fracture (as poultice), to promote wound healing, and is applied on forehead for severe headache. The root juice is used against urinary tract infection, diarrhea, fever, hyperglycemia, and gastric problems. Roots and young shoots are used to colic pain relief. Root decoction is used to treat warm, and the inner root bark is used as a renal tonic and antidiuretic Ripe fruits show laxative effects, young fruits paste is used for the treatment of gastritis, and cancer, diarrhea. The fruit juice is used treat fever and for colic, sore throats and colds [10-13]. The leaves exhibit anticonvulsant effects against electrically induced convulsions. The fruit and leaf extract of *R. ellipticus* present anti-inflammatory, antioxidant, antimicrobial, central and peripheral analgesic and antipyretic effects, and anticancer activity [14-17].

The leaves possess derivatives of ellagic acid, kaempferol and quercetin. The root bark presents starch, proteins, lipids, saponins tannins glucosides and mucilage. Fruit is rich in phenols, flavonoids, glycosides, vitamin C, pectin, and tannins [17]. Under the optimized conditions, Kewlani et al founds even bioactive compounds in the fruits (catechin, ascorbic acid, vanillin, caffeic acid, m-coumaric acid, p-coumaric acid, and cinnamic acid), and catechin presents the highest concentration. The authors suggest that the use of these fruit in the nutraceutical, food, cosmetic, and medicinal industries will result in a wide range of benefits [18].

Due to the broad spectrum of possible actions of *R. ellipticus*, this study aimed to investigate the effects of this plant on health.

2. Methods

2.1 Literature Search and Inclusion of the Studies

The focal question for this review was "Which are the described effects of *Rubus ellipticus* on health?"A literature survey was done in Pubmed, Cochrane, Embase, and Google Scholar databases to find the studies performed with *R. ellipticus* and health promoting effects. The keywords that were used in the search were *R. ellipticus* and biological activity or phytochemicals or pharmacological properties or antioxidant or anti-inflammatory or antimicrobial or anticancer or health benefits. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [19-20] was pursued and the flow diagram is seen in Figure 1. Only studies published in English language were included. The search did not restrict time. Exclusion criteria were non-English language studies, unpublished data, and poster presentations. We did not find studies with *R. ellipticus* in humans.

3. Botanical Aspects

R. ellipticus is a shrub of 1–3 m tall with many thorns. Its branches are brownish, pubescent, with curved, sparse prickles and dense, brownish bristles or glandular hairs. Leaves are imparipinnate, foliolate; subsessile, and rachis purplish bristly, with prickles. The flowers present calyx pubescent, sparsely bristly; intermixed yellowish tomentose; the petals are white or pink, longer than sepals and densely pubescent. Aggregate fruits are golden yellow, glabrous or drupelets at apex and with 7 mm in diameter and 6 mm long. There are several seeds, very small (1 to 1.5 mm in diameter) [17]. Figure 2 shows some aspects of the plant.

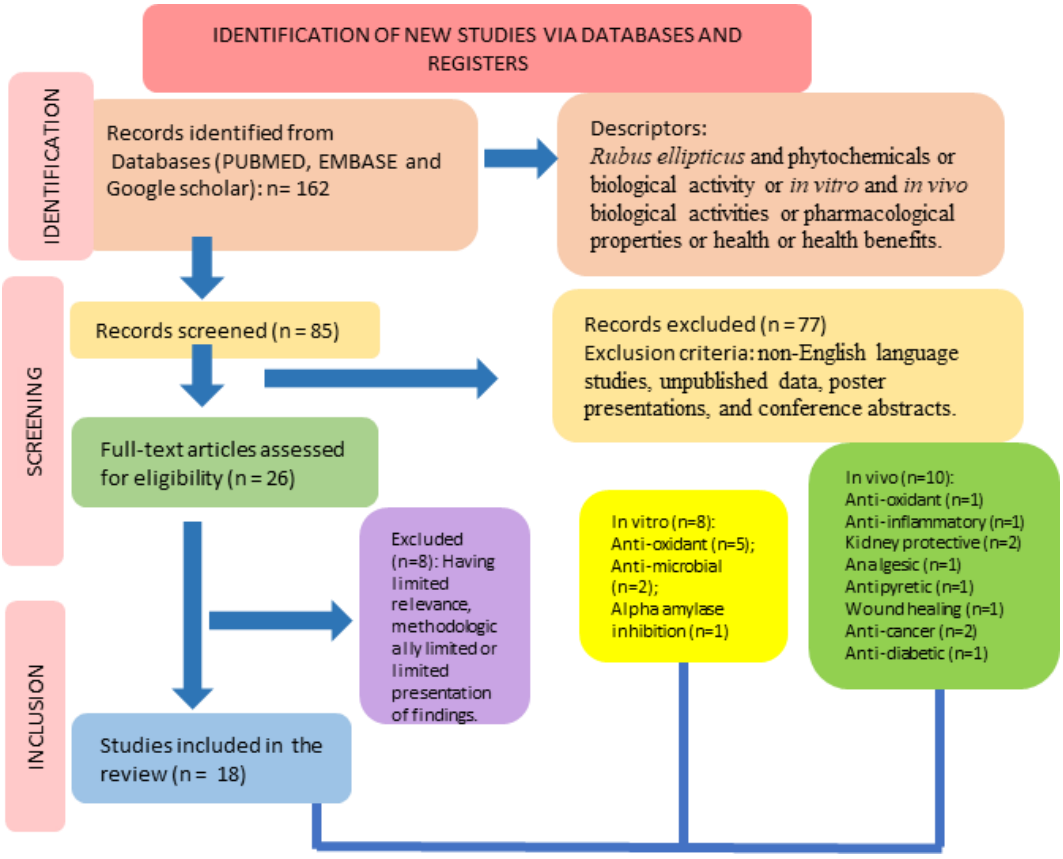


Figure 1. Flow diagram showing the study selection

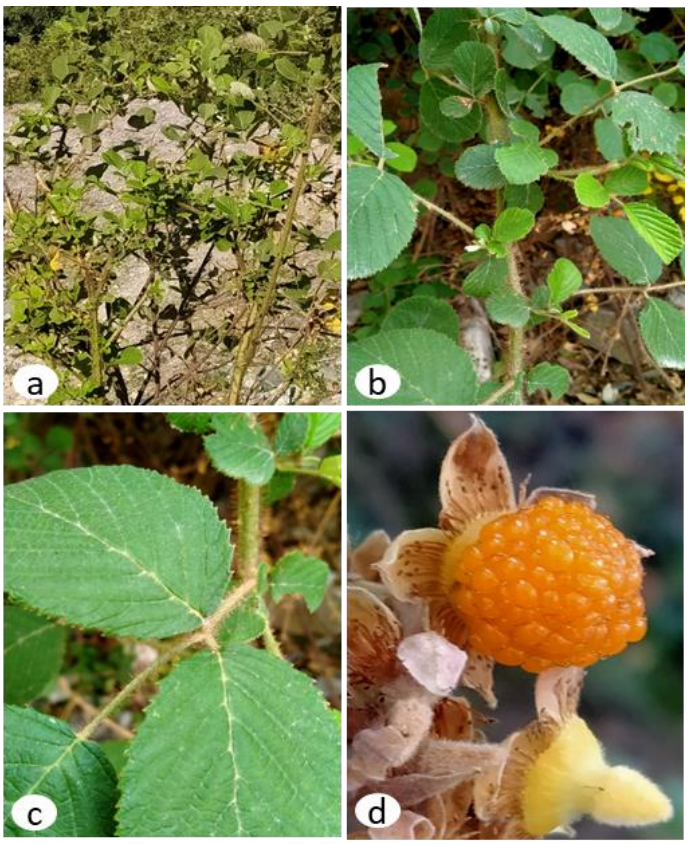
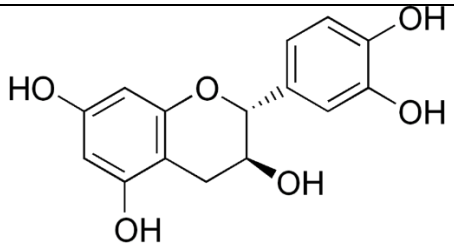
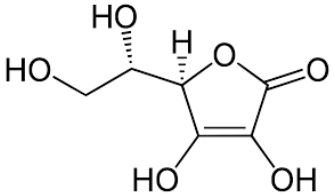
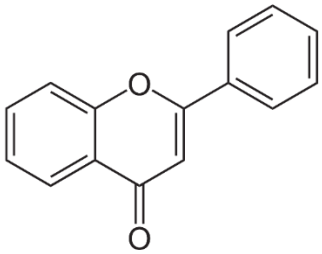
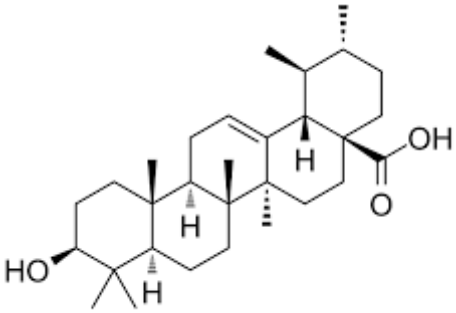
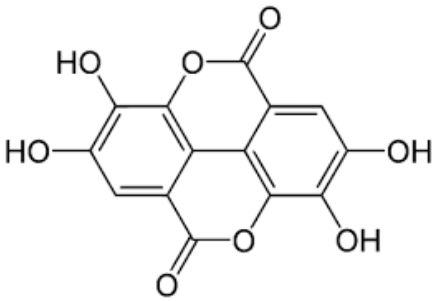


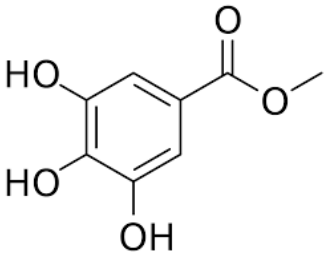
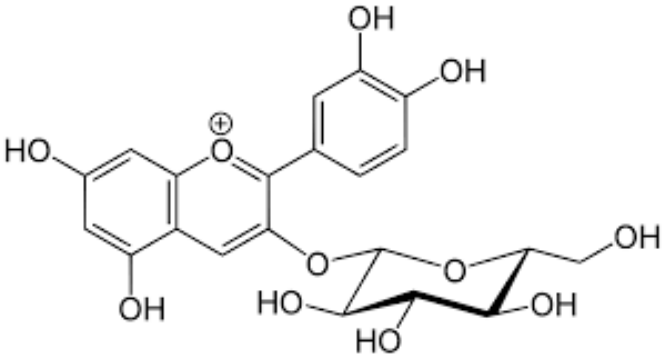
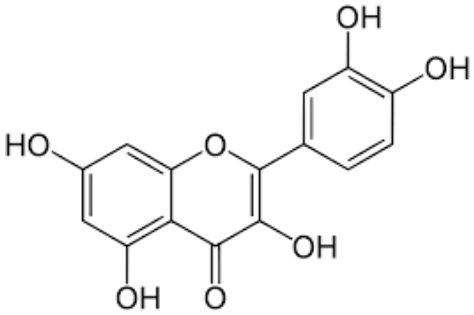
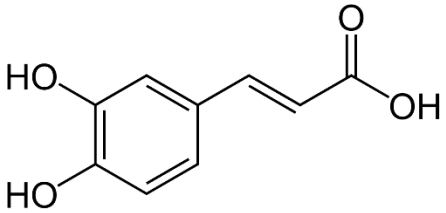
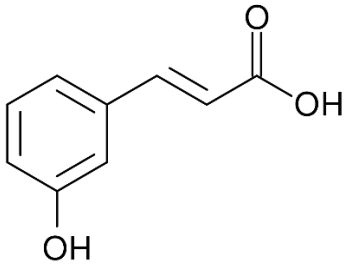
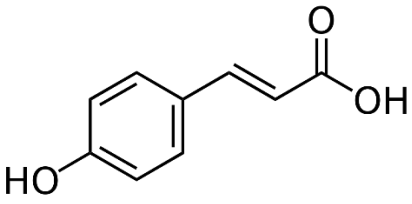
Figure 2. *R. ellipticus* plant. a) shrub; b) detail of the leaf and prickly stem; c) leaf; d) fruit.

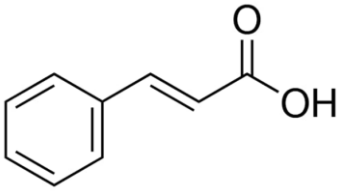
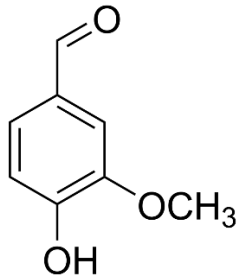
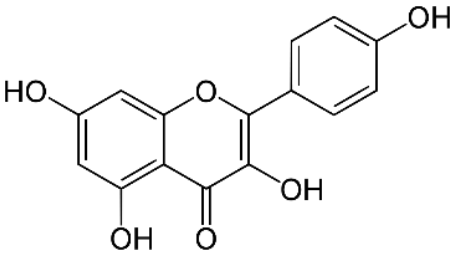
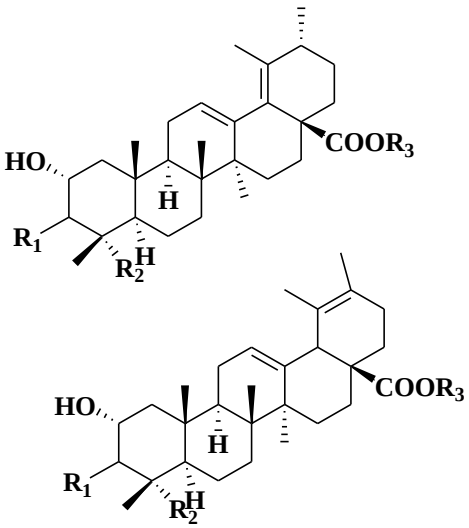
4. Phytochemical Profile

R. ellipticus contains various phytoconstituents like catechin, ascorbic acid,flavonoids, ursolic acid, ellagic acid, glycosides,terpenoids,saponins and others.Table 1 shows the main bioactive compound isolated from *R. ellipticus.*

Table 1. Main bioactive compounds of *R. ellipticus*

Main Components	Structures of main components	Activity	References
Catechin		Antioxidant, anti-cancer, anti-diabetic, anti-lipidemic	[18,21-22]
Ascorbic acid		Antioxidant, anti-cancer, anti-diabetic, anti-lipidemic	[23-24]
Flavonoids		Anti-inflammatory, antioxidant, anticancer, anti-diabetic, anti-lipidemic	[25-26]
Ursolic acid		Anti-inflammatory, antioxidant, anticancer	[27]
Ellagic acid		Anti-inflammatory, antioxidant, anticancer	[28-29]

Methyl gallate		Anti-inflammatory, antioxidant, neuroprotective	[30]
Anthocyanin		Anti-inflammatory, antioxidant	[31]
Quercetin		Anti-inflammatory, antioxidant	[32-33]
Caffeic acid		Anti-inflammatory, antioxidant	[23]
m-Coumaric acid		Antioxidant, anticancer	[18,34-35]
p-Coumaric acid			

trans-Cinnamic acid		Antioxidant, anti-inflammatory, anticancer	[18, 35-36]
Vanillin		Antioxidant, anticancer	[18, 37]
Kaempferol		Anti-inflammatory, antioxidant Anticancer; Neuroprotection	[10, 38]
Triterpenoid Saponins		inhibitory activities against α-glucosidase	[39]

5. Biological and Pharmacological Effects of *R. ellipticus*.

5.1 Antioxidant Activity

Khanal et al. [49] produced silver nanoparticles using aqueous root extracts of *R. ellipticus* and observed 2, 2-diphenyl-1-picrylhydrazyl radical scavenging activity.Saini et al [41] found that extracts of *R. ellipticus* can exhibit free radical scavenging activities (2, 2-Diphenyl-1-picrylhydrazyl, 2, 2′-Azinobis-3-ethylbenzothiazoline-6-sulphonic acid, superoxide, and linoleate hydroperoxide radicals) and ferric reducing effects mainly in the acetone and acidic acetone extracts. Acetone and methanol extracts showed potent antiproliferative activity against human cervical cancer cells (C33A) with an EC50 of inhibition at 5.04 and 4.9 mg/ml fruit concentration, respectively, while showing no cytotoxicity to normal PBMCs cells. Therefore, the present study concluded that the yellow Himalayan raspberry is a potent source of phytochemicals having super antioxidant and potent antiproliferative activities [41].

A study showed that the extract of the leaves of *R. ellipticus* present relevant *in vitro* antioxidant actions in terms of radical scavenging ability or hydrogen donating using the 2,2-diphenyl-1-

picrylhydrazyl. The results also demonstrated the extract is safe in acute oral and dermal toxicity up to a dose of 2 g/kg [43].

Other study showed [40] that petroleum ether, aqueous and ethanolic, extracts of *R. ellipticus* fruits exhibits significant free radical scavenging and reducing properties suggesting that these fruits could be pharmaceutically exploited. Table 2 shows several studies performed with different parts of *R. ellipticus*.

5.2 Anti-inflammatory, Analgesic, and *Antipyretic Activity*

George et al. [15] evaluated the effects of the methanolic extract of *R. ellipticus* (200 and 400 mg/kg) and observed significant anti-inflammatory, analgesic antipyretic actions. Both doses significantly diminished the ear and paw edema compared to indomethacin, diminished the writhing response, and augmented the latency period of analgesia compared to aspirin and morphine. The authors also observed a significant reduction of rectal temperatures of rats compared to paracetamol. These results suggest that this plant can be used against inflammatory conditions. Moreover, they showed that methanolic leaf extract at up to 2000 mg/kg b. wt did not show acute toxicity.

Figure 3 highlights the antioxidant and anti-inflammatory effects of *R. ellipticus* and gives ideas of its actions against different oxidative and inflammatory diseases and disorders.

5.3 Antiproliferative Activity

Saini et al. [41] found that extracts of *R. ellipticus* can show potent antiproliferative effects against human cervical cancer cells with an effective concentration of 50 of inhibition (5.04 and 4. 9 mg/mL of fruit concentration, respectively) while producing no cytotoxicity to normal blood cells. George et al. [43] showed that treatment with 250mg/kg of *R. ellipticus* leaf extract prolonged the life span of animals with Ehrlich ascites carcinoma in 46.76% and reduced the volume of Dalton's lymphoma ascites solid tumors, suggesting that this plant can be effective for treating skin diseases and wounds. Figure 4 highlights the roles of *R. ellipticus* in suppressing cancer cell growth and decreasing tumor progression.

Table 2. *In vitro* and *in vivo* biological activities of *R. ellipticus.*

Ref.	Properties	Plant part used or compounds	Type of extract	Assay	Results
[40]	Antioxidant	Dried fruits	Petroleum ether, ethanol, and water extract (extracts were dissolved in ethanol at a concentration of 50–200 mg/mL)	DPPH free radical scavenging activity	All extracts showed significant antioxidant actions compared to the standard antioxidants AA and BHA.
[41]		Fresh ripe fruit	Methanol; acid methanol; acetone and acid acetone extracts	DPPH scavenging activity, ABTS and Superoxide scavenging activity, ferric reducing power	The antioxidant action was highest in acetone extract, and intermediate in acidic methanol and acidic acetone.
[42]		Leaf	Water, methanol, Hexane, and ethyl acetate extracts	DPPH, ABTS free radical scavenging activity and total reducing power	Methanol extract showed higher reducing power and free radical scavenging in DPPH and ABTS methods.

[43]		Leaf	Methanol, ether, acetone, water extracts	Liver of Swiss albino male mice were evaluated for DPPH, Superoxide, Nitric oxide, Super Oxide Dismutase, Catalase, and Glutathione Peroxidase	Leaf methanol extract, showed higher *in vitro* antioxidant activity.
[44]		Ripened fruits	Methanol extract	Scavenging capacity towards hydroxyl ion radicals, nitric oxide and DPPH, and reductive potential were tested.	The extract showed significant scavenging capacity towards DPPH, superoxide (hydroxyl ion radicals and nitric oxide (NO). Strong reducing capacity was also observed for Fe^{2+} chelation and lipid peroxidation.
[45]		Leaf	Methanol extract	Scavenging capacity towards DPPH	Methanol extract showed most active scavenging actions with half maximal inhibitory concentration values (33.41and 47.28 µg/ml, respectively).
[15]	Anti-inflammatory	Leaf	Methanol extract	Anti-inflammatory effects were evaluated with the use of carrageenan induced paw edema in Wistar rats and croton oil to induce ear edema in mice.	The extracts (200 and 400 mg/kg) resulted in significant anti-inflammatory effects and led to the reduction of paw and ear edema compared to indomethacin.
[41]	Antimicrobial	Fresh ripe fruit	Methanol; acid methanol; acetone and acid acetone extracts	Identification of zone of inhibition for each of the test bacteria (*E.coli* MTCC739, *Bacillus* subtilis MTCC441, and *S.* aureus MTCC 96).	No inhibition zone was found by any of the fruit extracts against the tested bacterial species.

[9]		Air dried fruit and root	Petroleum ether, chloroform, ethyl acetate, acetone, methanolic, ethanolic and water extracts	Ten bacterial strains were used (*Escherichia coli, Klebsiella pneumoniae, Enterobacter gergoviae, salmonella entericatyphim, shigella flexneri, Staphyloccus aureus, staphyloccus epidermidis, streptococcus pyogenes,* and *Bacillus cereus*)	The ethanolic fruit extracts of produced significant activity against *Escherichia coli* (MTCC 443), *Escherichia coli* (MTCC 729), and *Streptococcus pyogenes* (MTCC 1925)
[41]	Anticancer	Fresh ripe fruit	methanol; acid methanol; acetone and acid acetone extracts (cells were cultured with extract concentration of 0.667, 1.66, 3.33, 5.0 and 6.67 mg/mL)	Cervical cancer cell lines (C33A and HeLa cell lines).	The extracts exhibited a potent antiproliferative action against C33A cells (40–60 %), but no inhibition action was observed against HeLa cells.
[43]		Leaf	Methanol, ether, acetone, water extracts	Dalton's lymphoma ascite cells were introduced subcutaneously into the limb of Swiss albino mice for solid tumor development.	Treatment with 250mg/kg prolonged the life span of mice affected by Ehrlich ascite carcinoma (46.76%) and decreased the volume of Dalton's lymphoma ascite solid tumors (2.56 cm^3).
[43]	Wound healing	Leaf	Methanol, ether, acetone, water extracts	Excision was done on the shaved dorsal side Swiss albino male mice (1.5 cm in diameter and 0.2 cm depth). In the infected model, *S. aureus* suspension was swab-bed on the wounded area.	In the treated groups, significant wound healing was seen in incision, excision, and wounds infected by *S. aureus* wound models.

[46]	Antidiabetic	Fruit	Ethanolic and aqueous extracts	Diabetic Wistar rats and Diabetic Swiss albino mice (induced by alloxan)	All the extracts showed significant anti-diabetic effects, however, the effects produced by ethanolic extract were maximum.
[15]	Analgesic	Leaf	Methanol extract	Analgesic effects were evaluated with the use of acetic acid induced writhing and Eddy's hot plate mediated pain Swiss albino mice models.	The extracts (200 and 400 mg/kg) resulted in significant analgesic effects. There was also reduction of the writhing responses and augmented the latency period significantly in analgesic activity compared to aspirin or morphine.
[15]	Antipyretic	Leaf	Methanol extract	Antipyretic effects were investigated by yeast induced pyrexia in Wistar rats.	The extracts (200 and 400 mg/kg) resulted in significant antipyretic effects. The rectal temperature of the animals was decreased significantly compared to paracetamol.
[45]	α-amylase inhibition test	Leaf	Methanol extract	Alpha-amylase inhibitory effects	Methanol extract was effective toward α-amylase inhibition with IC_{50} values of 269.94 µg/ml.
[47]	Nephroprotection	Fruit	Ethanolic and aqueous extract	Gentamicin and cisplatin induced nephrotoxicity in Wistar rats.	Both aqueous and ethanolic extracts significantly protect kidney from cisplatin and gentamicin induced damage (normalization of serum creatinine, uric acid, urea, and blood nitrogen.

[48]		Fruit	Ethanolic and aqueous extract	Acetaminophen induced nephrotoxicity in male albino rats.	All the extracts showed nephroprotective activity as evidenced by histopathological and biochemical observations against APAP induced renal damage in rats

ABTS: 2,2′-Azinobis-3-ethylbenzothiazoline-6-sulphonic acid; AA: ascorbicacid; BHA: butylated hydroxyanisole; *DPPH:* 1,1-Diphenyl-2-picrylhydrazyl; *S. aureus: Staphylococcus aureus;* TCA: trichloroacetic acid

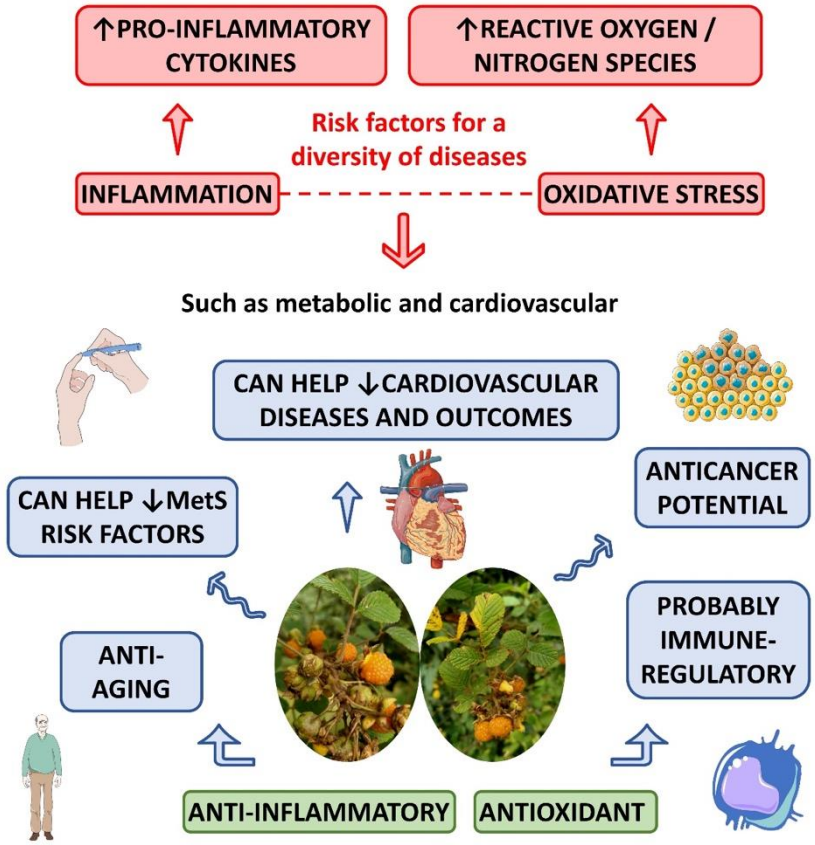


Figure 3. Antioxidant and anti-inflammatory effects of *R. ellipticus* and its probable actions against different oxidative and inflammatory diseases and disorders.↑, increase; ↓, decrease.

5.4 Anti-microbial Activity

Silver nanoparticles using aqueous root extracts of *R. ellipticus* (Khanal et al., 2022) produced inhibition zones against *Escherichia coli*, *Enterococcus faecalis*, *Staphylococcus aureus*), and Klebsiella pneumoniae suggesting that root extract based nanoparticles are promising for biomedical practices [49]. Panda et al. [50] found that the extract of the leaves of *R. ellipticus* showed anti *Escherichia coli, Staphylococcus aureus* and *Candida albicans*. Moreover, they also observed anthelmintic and antiviral activities. The study performed by Latha et al. [51] showed that methanolic extract of *R. ellipticus* exert significant antibacterial activity against gram-negative and gram-positive strains (*Staphylococcus aureus, Micrococcus luteus* and *methicillin-resistant Staphylococcus aureus*). Moreover, it can also show significant antifungal activity (*Aspergillus flavus, Aspergillus niger Trichophyton*

mentagrophytes, and *Trichophyton rubrum*). These results suggest that *R. ellipticus* leaves could be used in pharmaceutical and food applications.

Figure 5 revises the microbial classes against which *R. ellipticus* exerts anti-actions.

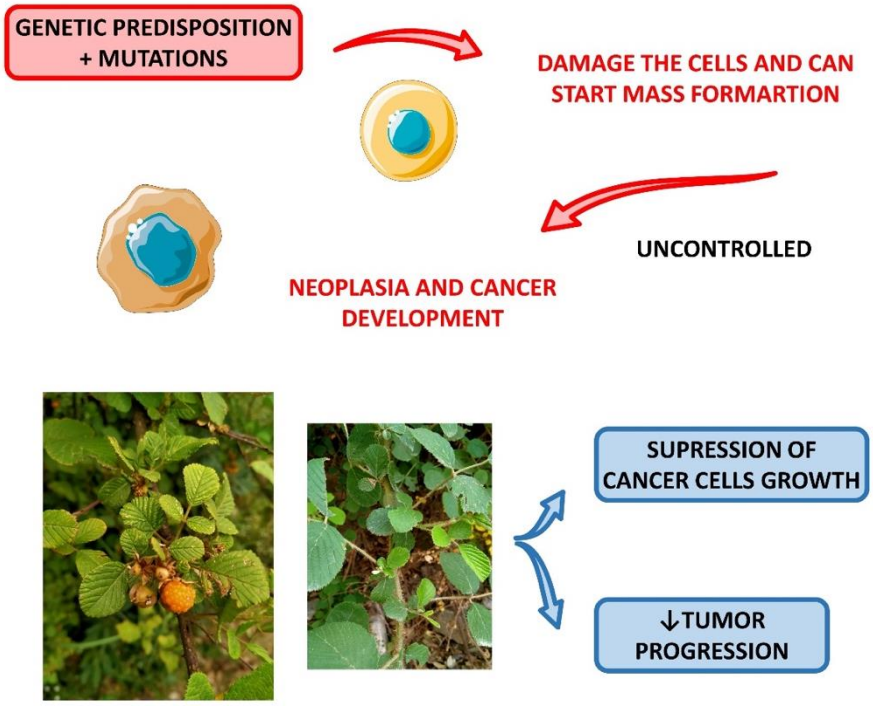


Figure 4. Roles of *R. ellipticus* in suppressing cancer cells growth and decreasing tumor progression.

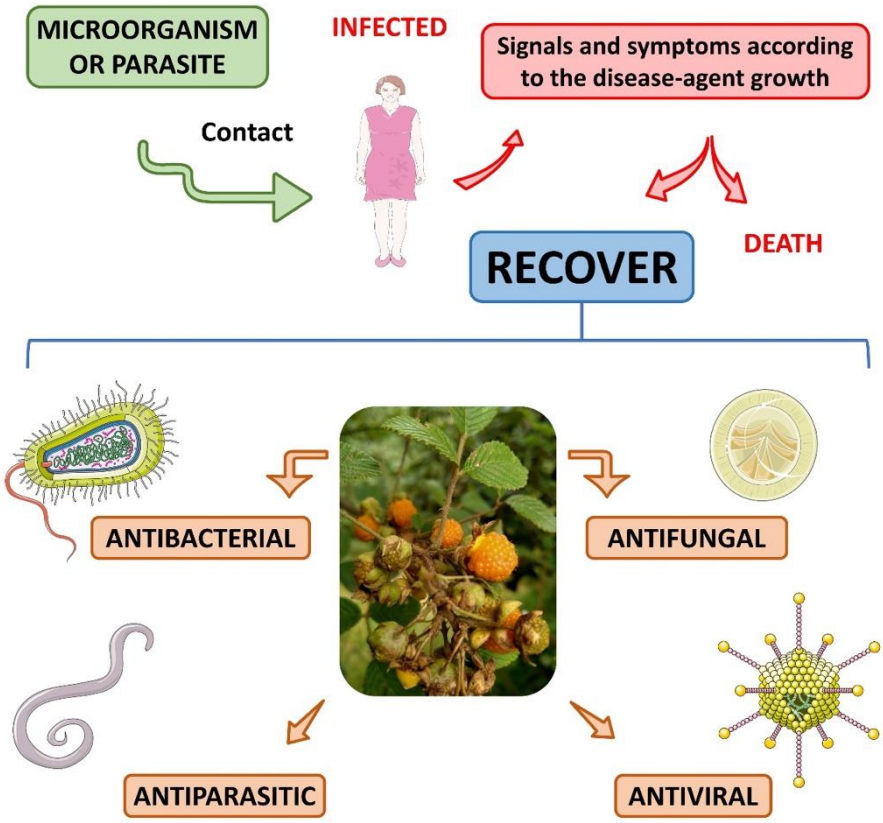


Figure 5. Microbial classes against which *R. ellipticus* exerts anti-actions.

5.5 Anti-diabetic Activity

A study evaluated the effects of *R.ellipticus* fruit on glucose tolerance test diabetic rats and found that ethanolic, ether, and aqueous extracts of the fruits and showed that all the extracts could significantly produce anti-diabetic effects. Furthermore, the authors showed that the plant extracts up to a dose of 2000 mg/kgdid not produce neurological and behavioral symptoms in acute use [46].

5.6 Wound Healing Activity

George et al. [43] demonstrated significant wound healing actions of *R. ellipticus* leaf extract in excision, incision, and in infected wound induced by *Staphylococcus aureus*. A complete epithelialization was observed during the 13th and the 19th day.

4. Conclusion

Some studies have shown that *R. ellipticus* is a fruit with several beneficial potentials for human health, and exhibits anti-oxidant, anti-inflammatory, anti-diabetic, anti-microbial, analgesic, antipyretic, wound-healing, and anti-proliferative actions. For these reasons, the consumption of this fruit could reduce oxidative stress and anti-inflammatory processes and, consequently, reduce diabetes and metabolic-related diseases such as cardiovascular diseases and cancer. *R. ellipticus* also has huge economic importance due to its nutritional value and can be used in the food, cosmetics, and pharmaceutical industries.

Conflict of Interests

The authors declare no conflict of interests or funding support.

ORCID
Rakesh Kumar Joshi:0000-0002-6930-5190
Lucas Fornari Laurindo:0000-0003-3159-0982
Preeti Rawat:0000-0002-1106-2915
Ricardo de Alvares Goulart:0000-0002-1989-3457
Sandra M. Barbalho:0000-0002-5035-876X

References

[1] A. Lippert and B. Renner (2022). Herb-drug interaction in inflammatory diseases: review of phytomedicine and herbal supplements, *J. Clin. Med*. **11**, 1567.

[2] T.B. Agbabiaka, N.H. Spencer, S. Khanom and C. Goodman (2018). Prevalence of drug-herb and drug-supplement interactions in older adults: a cross-sectional survey, *Br. J. Gen. Pract*. **68**, e711-e717.

[3] A. Djuv, O.G. Nilsen and A. Steinsbekk (2013). The co-use of conventional drugs and herbs among patients in Norwegian general practice: a cross-sectional study, *BMC Complement. Altern. Med*. **13**, 295.

[4] A. Garcia-Alvarez, B. Egan, S. de Klein, L. Dima, F. M. Maggi, M. Isoniemi and L. Serra-Majem (2014). Usage of plant food supplements across six European countries: findings from the Plant LIBRA a consumer survey, *PLoS One*. **9**, e92265. doi:10.1371/journal.pone.0092265

[5] P.L. Lakatos, Z. Czegledi, G. David, Z. Kispal, L.S. Kiss, K. Palatka and L. Lakatos (2010). Association of adherence to therapy and complementary and alternative medicine use with demographic factors and disease phenotype in patients with inflammatory bowel disease, *J. Crohns Colitis.* **4**, 283-290.

[6] J. Peklar, M.C. Henman, M. Kos, K. Richardson and R.A. Kenny (2014). Concurrent use of drugs and supplements in a community-Dwelling population aged 50 years or more: Potential benefits and risks, *Drugs Aging*.**31**, 527-540.

[7] S.K.J. Urumarudappa, C. Tungphatthong, J. Jaipaew, N. Pornputtapong, D. Pakdeesattayapong, S. Vimolmangkang and S. Sukrong (2022). Development of a DNA barcode library of plants in the Thai Herbal Pharmacopoeia and Monographs for authentication of herbal products, *Sci. Rep*. **12**, 9624.

[8] R. Lalla, M. Cheek, M. Nxumalo and J.J. Renteria (2018).First assessment of naturalised Rubus ellipticus Sm. populations in South Africa-A potential invasion risk, *S. Afr. J. Bot.***114**, 111-116.

[9] S.Saklani, S.Chandra, P.P. Badoni and S. Dogra (2012). Antimicrobial activity, nutritional profile and phytochemical screening of wild edible fruit of Rubus ellipticus,*Int. J. Med. Arom. Plants.***2**, 269-274.

[10] S.M. Barbalho, R. Direito, L.F. Laurindo, L.T. Marton, E.L. Guiguer, R.A. Goulart, R.J. Tofano, A.C.A.Carvalho, U.A.P. Flato, V.A. Capelluppi Tofano, C.R.P. Detregiachi, P.C.S. Bueno, R.S.J. Girio and A.C. Araújo (2022). Ginkgo biloba in the ageing process: A narrative Review, *Antioxidantsm.* **11**, doi:10.3390/antiox11030525

[11] A.V. Patel, J. Rojas-Vera and C.G. Dacke (2004).Therapeutic constituents and actions of Rubus species,*Curr. Med. Chem*.**11**,1501-1512.

[12] B.K. Pradhanand H.K. Badola (2008). Ethnomedicinal plant use by Lepcha tribe of Dzongu valley, bordering Khangchendzonga Biosphere Reserve, in North Sikkim, India,*J. Ethnobiol. Ethnomed*. **4**, 22.

[13] Y. Uprety, R.C. Poudel, H. Asselin and E. Boon (2011). Plant biodiversity and ethnobotany inside the projected impact area of the Upper Seti Hydropower Project, Western Nepal, *Environ. Dev. Sustain*. **13**, 463-492.

[14] J. Dhatwalia, A. Kumari, A. Chauhan, K. Mansi, S. Thakur, R.V. Saini and R. Kumar (2022). *Rubus ellipticus* Sm. fruit extract mediated Zinc Oxide Nanoparticles: A green approach for dye degradation and biomedical applications, *Materials (Basel).* **15**, doi:10.3390/ma15103470

[15] B.P. George, P. Thangaraj and S. Saravanan (2013). Anti-inflammatory, analgesic and antipyretic activities of *Rubus ellipticus* smith. leaf methanol extract, *Int. J. Pharm. Pharm. Sci*. **5**, 220-224.

[16] K. Muniyandi, E. George, S. Sathyanarayanan, B.P. George, H. Abrahamse, S.Thamburaj and H. Wellness (2019). Phenolics, tannins, flavonoids and anthocyanins contents influenced antioxidant and anticancer activities of Rubus fruits from Western Ghats, India, *Food Sci.Hum. Wellness.* **8**, 73-81.

[17] Y. Pandey and S.S Bhatt (2016). Overview of Himalayan yellow raspberry (*Rubus ellipticus* Smith.): A nutraceutical plant, *J. Appl. Nat. Sci*.**8**, 494-499.

[18] P. Kewlani, L. Singh, T. Belwal and I.D Bhatt (2022). Optimization of ultrasonic-assisted extraction for bioactive compounds in *Rubus ellipticus* fruits: An important source for nutraceutical and functional foods, *Sustain. Chem. Pharm*. **25**, 100603.

[19] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P. Ioannidis and D. Moher (2009). The Prisma statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, *PloSMed*. **6**, e1000100. doi:10.1371/journal.pmed.1000100.

[20] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C. Mulrow and D. Moher (2021). The Prisma 2020 statement: an updated guideline for reporting systematic reviews, *BMJ*. **372**, n71. doi:10.1136/bmj.n71.

[21] A. Armenia, F.S.Wahyuni, A. Almahdy, R. Abdillah, P.G. Aquista, D.P. Putri and M. Zikra (2022). Blood pressure and blood sugar-lowering effects of purified gambir on diabetic hypertensive Wistar Kyoto rats, *J. Complement. Integr. Med*. **19**, 627-636.

[22] N. Bodin-Thomazo, F. Malloggi, N. Pantoustier, P. Perrin, P. Guenoun and V. Rosilio (2022). Formation and stabilization of multiple w/o/w emulsions encapsulating catechin, by mechanical and microfluidic methods using a single pH-sensitive copolymer: Effect of copolymer/drug interaction, *Int. J. Pharm*.**25**, 622, 121871.

[23] M. Joshi and B. Prabhakar (2020). Phytoconstituents and pharmaco-therapeutic benefits of pitaya: A wonder fruit, *J. Food Biochem*. **44**, e13260.

[24] Z. Namkhah, D. Ashtary-Larky, F. Naeini, C.C.T. Clark and O. Asbaghi (2021). Does vitamin C supplementation exert profitable effects on serum lipid profile in patients with type 2 diabetes? A systematic review and dose-response meta-analysis, *Pharmacol. Res*. **169**, 105665.

[25] P.Li,X.Yao, Q. Zhou, X.Meng,T.Zhou andQ.Gu, (2022). Citrus peel flavonoid extracts: health-beneficial bioactivities and regulation of intestinal microecology *in vitro*, *Front Nutr*. **9**, 888745.

[26] F. Rubab (2022). Gastroprotective effects of caragana ambigua stocks on ethanol-induced gastric ulcer in rats supported by LC-MS/MS characterization of formononetin and biochanin A, *J.Sci. Food Agric*. **102**, 7030-7038,12064.

[27] R. Saini, K. Dangwal, H. Singh and V. Garg (2014).Antioxidant and antiproliferative activities of phenolics isolated from fruits of Himalayan yellow raspberry (*Rubus ellipticus*), *J. Food Sci. Technol*.**51**, 3369–3375.

[28] A. Ullah, S.Munir, S.L. Badshah, N. Khan, L.Ghani, B.G.Poulson, A.H.Emwas and M. Jaremko (2020). Important flavonoids and their role as a therapeutic agent, *Molecules.* **25**, 5243.

[29] F. Xie, L. Xu, H. Zhu, Y. Chen, Y. Li, L. Nong, Y. Zeng and S. Cen (2022). The potential antipyretic mechanism of ellagic acid with brain metabolomics using rats with yeast-induced fever, *Molecules.* **27,** 2465.

[30] P. Liu, W. Wang, Q. Li, X. Hu,B. Xu, C. Wu, L. Bai, L. Ping, Z. Lan and L.Chen (2021). Methyl gallate improves Hyperuricemia nephropathy mice through inhibiting NLRP3 Pathway, *Front Pharmacol*. **12**, 759040.

[31] C. Saenjum, T. Pattananandecha and K. Nakagawa, (2021). Antioxidative and anti-inflammatory phytochemicals and related stable paramagnetic species in different parts of dragon fruit, *Molecules.* **26**, 3565.

[32] D.D. Castro-Enríquez, B. Montaño-Leyva, C.L.D. Toro-Sánchez, J.E. Juárez-Onofre,E. Carvajal-Millán, G.A. Lopez-Ahumada, C.G.Barreras-Urbina, J.A.Tapia-Hernandez and F.J.Rodríguez-Félix, (2020). Effect of ultrafiltration of Pitaya extract (*Stenocereus thurberi*) on its phytochemical content, antioxidant capacity, and UPLC-DAD-MS profile, *Molecules.* **25**, 281.

[33] B.Salehi, J. Sharifi-Rad, F. Cappellini, Ž. Reiner, D. Zorzan, M. Imran, B. Sener, M. Kilic, M. El-Shazly, N.M.Fahmy, E. Al-Sayed, M. Martorell, C. Tonelli, K. Petroni, A.O. Docea, D. Calina and A. Maroyi (2020). The therapeutic potential of anthocyanins: current approaches based on their molecular mechanism of action, *Front Pharmacol*.**11**, 1300.

[34] V. Buza (2022). Biological activities and chemical profile of gentiana asclepiadea and inula helenium ethanolic extracts, *Molecules.* **27**, 3560.

[35] S.M. Iqbal (2022). Nephroprotective potential of a standardized extract of bambusa arundinacea: *in vitro* and *in vivo* studies, *ACS Omega* .**7**, 18159-18167.

[36] S.Khatuaand K. Acharya (2022). Exploring the chemical composition and bioactivity of ethanol extract from russula pseudocyanoxantha (agaricomycetes), a novel mushroom of tribal preference in India, *Int. J. Med. Mushrooms.* **24**, 73-83.

[37] H. Chen, N.L. Li, Q. Gu and G.M. Zhang (2022). Cervical cancer cell proliferation inhibition by vanillin oxime through HIF-1α expression inhibition, ERK1/2 and Akt protein down-regulation, *Acta Biochim.Pol.***69**, 79-84.

[38] G.A.de Souza, S.V.de Marqui,J.N.Matias, E.L. Guiguer and S.M.Barbalho (2020). Effects of Ginkgo biloba on Diseases Related to Oxidative Stress, *Planta Med*. **86**, 376-386.

[39] W.Li, H. Fu, H. Bai, T. Sasaki, H. Kato and K. Koike, (2009). Triterpenoid saponins from *Rubus ellipticus* var. obcordatus, *J. Nat. Prod*. **72**, 1755–1760

[40] U.S. Sharma and A. Kumar, (2011). In vitro antioxidant activity of Rubus ellipticus fruits, *J. Adv. Pharm. Technol. Res.***2**, 47-50.

[41] R. Saini, K. Dangwal, H. Singh andV.Garg (2014). Antioxidant and antiproliferative activities of phenolics isolated from fruits of Himalayan yellow raspberry (*Rubus ellipticus*), *J. Food Sci. Technol*. **51**, 3369-3375.

[42] M. Sharma, G. Neerajani, A. Kumar and D. Basak (2014). Evaluation of total phenolic content and antioxidant properties of different leaf extract of *Rubus ellipticus*, *Ethiopian Int. J. Mulitidiscip. Res*. **2**, 14-17.

[43] B.P. George, T. Parimelazhagan, Y.T. Kumarand T. Sajeesh (2015). Antitumor and wound healing properties of *Rubus ellipticus* smith, *J. Acupunct. Meridian Stud.***8**, 134-141.

[44] R.C. Poulin, J.M. Sasikumar, C.E. Meseret and P. Selvakumar (2015). In vitro analysis of antioxidant capacity of Indian yellow raspberry (*Rubus ellipticus* Smith.), *Int. Food Res. J.***22**, 1338-1346.

[45] B. Subba, S. Gaire and K.R. Sharma (2019). Analysis of phytoconstituents, antioxidant and ά-amylase inhibitory activities of Persea americana MILL, Rhododendron arboretum SM. *Rubus ellipticus* SM. From Arghakhanchi District Nepal, *Asian J. Pharm. Clin. Res.***12**, 301.

[46] U . Sharma and A. Kumar (2011). Anti-diabetic effect of Rubus ellipticus fruit extracts in alloxan induced diabetic rats, *J. Diabetol.***2**, 4.

[47] U.S. Sharma and A. Kumar (2011). Naphro-protective evaluation of Rubus ellipticus (Smith) fruits extracts against cisplatin and gentamicin induced renal-toxicity in rats, *J. Pharm. Res.***4**, 285-287.

[48] U.S. Sharma and A.J. Kumar (2010). Therapeutic efficacy of *Rubus ellipticus* (Smith) fruits extracts in acute acetaminophen induced nephrotoxicity in rats, *Pharmacologyonline.* **3**, 514-524.

[49] L.N. Khanal, K.R. Sharma, H. Paudyal, K. Parajuli, B. Dahal, G.C. Ganga, Y.R. Pokharel and S.K. Kalauni (2022). Green synthesis of silver nanoparticles from root extracts of *Rubus ellipticus* Sm. and comparison of antioxidant and antibacterial activity, *J. Nanomater*. **1**, 1-11.

[50] S.K. Panda, L. Padhi, P. Leyssen, M. Liu, J. Neyts and W. Luyten (2017). Antimicrobial, anthelmintic and antiviral activity of plants traditionally used for treating infectious disease in the similipal biosphere reserve, Odisha, India, *Front. Pharmacol*. **8**, 658.

[51] R. Latha, T. Sarkar and S. Jansy (2015). Evaluation of antimicrobial efficiency and alpha-glucosidase inhibition of *Rubus ellipticus* Smith leaf extracts and its phytochemical analysis, *Asian J. Pharm. Clin.Res.***8**, 423-426.