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Traditional Medicinal Values of *Rubus ellipticus* with Biological Activities Observed from its Crude Extract: A Review

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ABSTRACT

This review article on *Rubus ellipticus* mainly systematically summarizes classification, morphology, distribution, traditional uses, phytochemical constituents and biological activities. *Rubus ellipticus* is commonly known as Yellow Himalayan Raspberry and has been used as a traditional medicine to cure for fever, diarrhoea, gastralgia, skin infection, joint pain, wound healing, diabetes, anti-fertility agent, analgesic, antiepileptic, as renal tonic, ulceretc. Its phytochemicals analysis have revealed the presence of phenolic compounds, flavonoids, terpenoids and steroids. The crude extract shows biological activities such as antimicrobial, antioxidant, anti-inflammatory, wound healing, anti-diabetic, anticancer, antiulcerogenic etc.

Key words: *Rubus, Flavonoids, Antimicrobial, Antioxidant, Phytochemicals.*

Introduction

Plants are one of the major kingdom of natural living system on the earth which consists of leaves, stems, bark, roots, flowers, fruits, seeds etc. These may be in the form of trees, shrubs, herbs, climbers or creepers and have broad spectrum of uses in pharmaceuticals, food, textile and agriculture industries. Moreover, these maintain atmospheric oxygen level, water quality and carbon sequestration (Fernando, 2012; Usman *et al*., 2014). These are also known to produce essential foods like carbohydrates, fats, proteins, minerals salts, organic acids, vitamins etc. which are required for human health care (Fernando, 2012). All over the World, ~3,00,000 plant species are present but only 21,000 plant species are known to have the high potential ability of Unani, Ayurveda and Siddha traditional medicines. According to World Health Organization more than 80% of the earth's population depends on the natural plant products as traditional medicines for their primary healthcare needs (Prakash *et al*., 2020; 2020a).

Medicinal plants are very important for the pharmaceutical industry, considering that they are a resource for the development of drugs such as

phytomedi-cines and phytopharmaceutics, and also as prototypes for the synthesis of new drugs (Cechinel and Yunes, 1998; Halvorsen *et al*., 2002; Yadav *et al.,* 2022; Elisabetskiand Souza, 2004; Barreiro and Bolzani, 2009; Cragg et al. 2012; Slatnar *et al.,* 2012; Mujeeb *et al*., 2014; Anand *et al.,* 2019; Suntar, 2020). In recent years, there have been significant scientific advances involving chemical and pharmacological studies of medicinal plants, focusing on new compounds with therapeutic properties (Bendazzoli, 2000; Cechinel, 2002). The demands for medicinal plants are increasing all over the world due to the growing recognition that the medicinal plants have fewer side effects and are lesser toxic as compare to synthetic medicines pharmacologically active, cost effective and easier to use for human diseases (Niero *et al.,* 2003). The plants particularly fruit berries are also gaining more attention to the researchers as they contain the best dietary sources of bioactive compounds (Heinrich, 2000; Koehn and Carter, 2005; De Souza, 2014).

The main objective of the present review is to report traditional medicinal values of *R. ellipticus* and comparison of those medicinal values with suitable biological activity in support of traditional uses from the crude/phytochemicals isolated from its various parts.

Classification, morphology and distribution

Classification

R. ellipticus is commonly known as Yellow Himalayan Raspberry (Maciel *et al.,* 2002, Badhani, 2015) or Cheeseberry and scientifically it is placed in Kingdom: Plantae, Divison: Magnoliphyta, Class: Magnoliopsida, Order: Rosales, Family: Rosaceae, Sub-family: Rosoideae, Genus: *Rubus,* Species: *ellipticus,* Binomial Name: *Rubus ellipticus* Smith.

Morphology

R.ellipticus is a stout, weakly climbing, evergreen thorny shrub 1-3 m tall.Branchlets are pubescent and purplish brown or brownish with sparse, curved prickles and dense, purplish brown bristles or glandular hairs. Leaves are pinnate, digitate or pedate, with 3-7 dentate leaflets (Tutin *et al.,* 1968). Flow ering occurs during March to April, and the fruiting period is from April to May, when it produces aggregate golden-yellow fruits (Lu and Boufford, 2003). It is native from southern Asia and Southeast Asia, including southwestern India, China, Bhutan, Myanmar, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, and Vietnam (Lu *et al.,* 2003; Ringmichon *et al.,* 2013; Maity *et al.,* 2004).

Distribution

The genus *Rubus* includes over 750 species which is grows on slopes, in mountain valleys, sparse forests, andon roadsides at elevations between 300 and 2,600 m, where annual precipitation levels range from 2,000 to 6,500 mm (Corner and Beaman, 1996; Stratton, 1996; Graham and Woodhead, 2011). It is widely distributed across the globe from North Temperate Zone to the tropics (Southern hemisphere) (Heinrich, 2000; Koehn and Carter, 2005). It is native

Table 1. The traditional medicinal values of *R.ellipticus'*sdifferent parts

S. No.	Plant/ Parts	To treat	References
1.	Whole plant	Reduce typhoidic fevers and act as an astringent.	Patel *et al.,* 2004
2.	Roots	Fever, diarrhea, gastric problems, wounds healing, antipyretics, fractured bones, headache, urinary tract infection.	(Ringmichon *et al.,* 2013; Patel *et al.,* 2004; Kirtikar and Basu, 2001)
3.	Fruits	Fever, dysentery, gastralgia, wound healing, diabetes sore throats, colds, antifertility, antimicrobial, analgesic, epilepsy, ulcer, constipation.	(Tutin *et al.,* 1968; Maity *et al.,* 2004; Vadivelan *et al.,* 2009; Pandey and Bhatt, 2016; Dovydaitis, 2017)
4.	Shoots	Stomach ache, diabetes, colic pains, hypothermia.	(Rojas *et al.,* 2002; Hazarika and Pongener, 2018)
5.	Bark	Stomach ache, kidney tonic, renal tonic, cough, cold, blood disorders, and anti-diuretic, vaginal discharge, diabetes, andanti-diuretic.	(Patel *et al.,* 2004; Pandey and Bhatt, 2016; Wangchuk *et al.,* 2017)
6.	Aerial Parts	Hypothermia.	Patel *et al.,* 2004
7.	Leaves	Fever, dysentery, stomach pain, diabetes, wound healing, ulcer and anti-ferility.	(Sharma *et al.,* 1983; Erdemoglu *et al.,* 2003; Latha *et al.,* 2015)

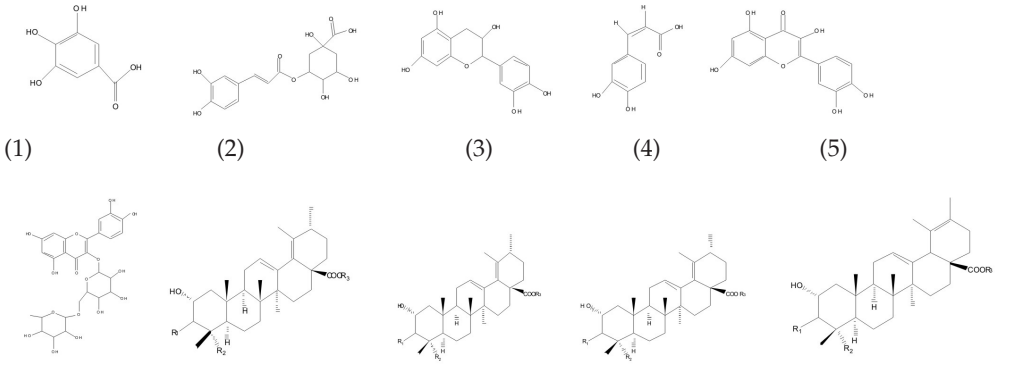
to tropical and subtropical India (Nagata, 1995; Flynn and Lorence, 1998).

Traditional medicinal uses

In ancient Indian (Ayurveda), Greek, Chinese and American system, raspberry had been used for the treatment forwounds and diarrhea (Heywood and Moore, 1978; Castleman, 1991; Moon, 1991; Kim, 1996; Moerman, 1998; Otaizaand Arzola, 2001; Rojas Vera *et al.,* 2002; Latha *et al.,* 2015; Sasikumar *et al.,* 2015). Traditionally different parts of plant are used to treat fever, diarrhoea, gastralgia, skin infection, joint pain, wound healing, diabetes, anti-fertility agent, analgesic, antiepileptic, as renal tonic, ulcer etc. (Table 1).

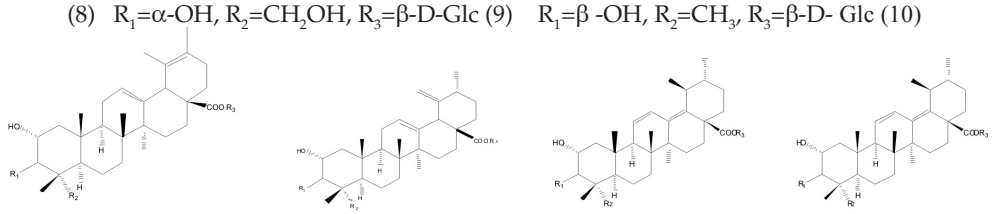
Phytochemical constituents

At least nineteen chemical constituents (Table 2) have been identified from different parts of *R. ellipticus* that includes **04** phenolic compounds **(1-4)**,

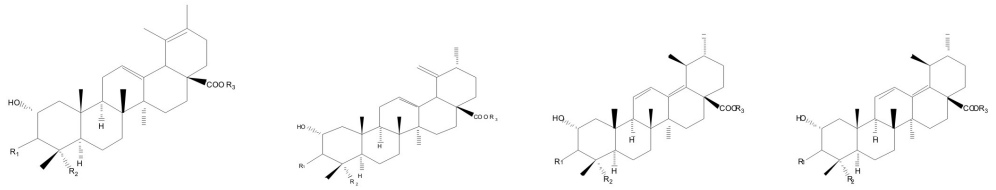


(1) (2) (3) (4) (5)

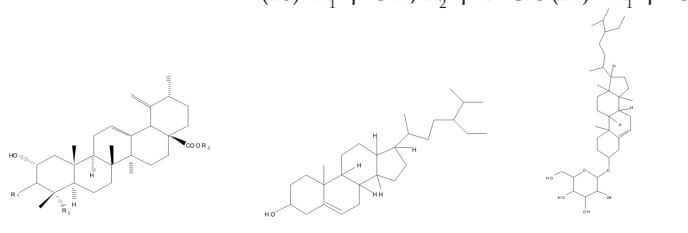
(6) R_1=β-OH, R_2=CH_3, R_3=β-D-Glc (7) R_1=α-OH, R_2=CH_3, R_3=β-D-Glc
(8) R_1=α-OH, R_2=CH_2OH, R_3=β-D-Glc (9) R_1=β -OH, R_2=CH_3, R_3=β-D- Glc (10)



R_1=β-OH, R_2=CH_3, R_3=α-D-Glc (11) R_1=β -OH, R_2=CH_3, R_3=β-D-Glc
(12) R_1=α-OH, R_2=CH_2OH, R_3=β-D-Glc (13) R_1=β-OH, R_2=CH_2OH, R_3=β-D-Glc(14)



R=β-D-Glc (15) R_1=H, R_2=OH, R_3=α-OH, R_4=CH_3, R_5= CHO, R_6= β-D-Glc
(16) R_1=β-OH, R_2=β-D-Glc (17) R_1=β -OH, R_2=H(18)



R_1=α-OH, R_2=CH_3, R_3=β-D-Glc(19) (20) (21)

Fig. 1. Structures of identified phytochemicals from *R. ellipticus*

Table 2. Chemical constituents and Biological activities of *R. ellipticus*

S. No.	Chemical Constituents	Plant Part Used	Solvent Used	Biological Activities	Reference
	Phenols				
1.	Gallic acid (**1**)	Fruits; Roots	Methanol	———–	Vadivelan *et al.*, 2009; Badhani *et al.*, 2015
2.	Chlorogenic acid (**2**)	Fruits	Methanol and Hydroalcohol (4:1)	———–	Badhani *et al.*, 2015
3.	Catechin (**3**)				
4.	Caffeic acid (**4**)				
	Flavonoids				
5.	Quercetin (**5**)	Fruits	Methanol	———–	Sasikumar *et al.*, 2015
6.	Rutin (**6**)	Roots	Methanol	———–	Vadivelan *et al.*, 2009
	Triterpenoid				
7.	Rubusides A (**7**)	Roots	Methanol	———–	Wei *et al.*, 2009
8.	Rubusides B (**8**)				
9.	Rubusides C (**9**)				
10.	Rubusides D (**10**)				
11.	Rubusides E (**11**)				
12.	Rubusides F (**12**)				
13.	Rubusides G (**13**)				
14.	Rubusides H (**14**)				
15.	Rubusides I (**15**)				
16.	Rubusides J (**16**)				
17.	Sericoside (**17**)	Roots	Methanol	———–	Wei *et al.*, 2009
18.	Sericic acid (**18**)	Roots	Methanol	———–	Wei *et al.*, 2009
19.	Alpinoside (**19**)	Roots	Methanol	———–	Wei *et al.*, 2009

———– Not Reported

02 flavonoids **(5** and **6)**,**13** triterpenoids **(7-19)**. The soxhlet type apparatus has been employed for extraction of these constituents with suitable solvents such as ethanol, methanol, hydroalcohol (4:1) etc. The structures of isolated constituents have been shown in Figure 1.

Phenols

Compounds (**1-4**) have been reported from the roots and fruits of the *R. ellipticus.* By using solvent methanol compound (**1**) has been identified from the both roots and fruits of the plant where as compounds (**2-4**) have been reported from the fruits by using methanol and hydroalcohol (4:1) as a solvent (Vadivelan *et al.*, 2009; Badhani *et al.*, 2015; Sasikumar *et al.*, 2015).

Flavonoids

Flavonoids fulfill many functions of plants such as plant pigment for coloration, producing red, blue or yellow pigmentation (Galeotti *et al.*, 2008). From fruits and roots, two flavonoid compounds **(5** and **6)** have been identified. Dried fruits extracted with methanol by soxhlet extraction method and compound **(5)** has been reported while compound (**6**) has been reported from roots by using methanol as a solvent (Vadivelan *et al.*, 2009; Sasikumar *et al.*, 2015).

Triterpenoids

Triterpenoids are a class of chemical compounds that consists of three terpene units and have a molecular formula $C_{30}H_{48}$. Thirteen compounds (**7-19**) have been identified from the roots of plant by using methanol as a solvent (Wei *et al.*, 2009).

Biological activities

Ninteen compounds has been isolated from the various parts of *R. ellipticus* so far but no biological activities has been reported on any isolated compound (Table 2). However, a wide range of biological activities has been carried out on crude extracted from various parts of *R. ellipticus* such as antimicrobial, antioxidant, anti-inflammatory, wound healing, anti-diabetic, anticancer, and antiulcerogenic (Table 3).

Antimicrobial Activity

The extracts prepared by using hexane, ethyl acetate and methanol from the leaves of *R. ellipticus* showed

Table 3. Biological Activities of crude extracted from various parts of *R. ellipticus*

Plant part Used	Solvent used	Srains/ Test animals	Doses and control	Result	Reference
Antimicrobial Activity					
Leaves	Hexane, ethyl acetate and methanol	**Bacteria:** **Gram positive:***Staphylococcus aureus*, *Micrococcus luteus, Bacillus subtilis, Enterococcus faecalis*,*Staphylococcus epidermis* and methicillin resistant *Staphylococcus aureus.* **Gram negative:** *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*, *Salmonella typhimurium*, *Shigellaflexneri* and *Proteus vulgaris*. **Fungi:** *Aspergillus flavus*, *Trichophytonmentagrophytes*, *Trichophyton rubrum*, *Aspergillus niger*, *Scopulariopsis* and *Curvularia lunata*	250 µg/ml, 500 µg/ml and 1000 µg/ml and Streptomycin (10 µg/ml) for bacteria, fluconazole (30 µg/ml) for fungi.	Methanol extracts shown Effective result against all bacterial and fungal stain.	Latha *et al.*, 2015
Leaves	Ethanol	**Bacteria:** *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa* and *E. coli* **Fungi:** *Candida krusei* and *Trichoderma lignorum*	40 mg/ml and Ampicillin (100 µg/ml) for bacteria, Clotrimazole (10 µg/ml) for fungi.	Ethanol extracts given significant activity against selective strain.	Prasanthand Chandran, 2017
Fruit	Petroleum ether, chloroform, ethyl acetate, acetone, ethanol and water	**Bacteria:** *Bacillus cereus, Escherichia coli, Enterobactergergoviae, Kelbi,Klebsiella pneumonia, Salmonella entericatyphm, Shigella flexneri, Staphyloccus aureus, Staphyloccus epidermidis, Streptococcus pyogenes* **Fungi:** *Candida albicans, Aspergillusflavus, Aspergillusparasiticus*	10 mg/ml, 50 mg/ml and erythromycin (10 mg/ml) for bacteria, ketoconazole (10 mg/ml) forfungi.	Ethanol extracts shown significant activity against *Escherichia coli, Staphyloccus aureus* and all fungal strain.	Saklani *et al.*, 2012
Antioxidant Activity					
Leaves	Methanol	Mice	50 mg/kg,100 mg/kg,150 mg/kg and butylatedhydroxytoluene (10 mg/kg)	Effectively reduced DPPH, nitric oxide and Superoxide radical scavenging.	George *et al.*, 2015
Leaves	Methanol	Leaves	40 µg/ml, 80µg /ml, 160µg/ml, 320 µg/ml, 640 µg/ml, 1000 µg/ml and EDTA 10 µg/ml	Methanolic extract of the plant reveled good result of DPPH assay.	Subba *et al.*, 2019
Fruit	Methanol	Leaves	50 µg/ml, 100 µg/ml, 200 µg/ml, 400 µg/ml and EDTA 50 µg/ml	Shown good result of DPPH assay.	Ahmad *et al.*, 2015
Fruit	Methanol	Leaves	25 µg/ml, 50 µg/ml,100 µg/ml, 200 µg/ml, 500 µg/ml, 1000 µg/ml and ascorbic acid 10µg/ml	Reveled significantly results free radical scavenging and reducing power properties by polyphenolic compounds.	Sasikumar *et al.*, 2015
Fruit	Petroleum ether, Ethanol and water	Leaves	50 µg/ml, 100 µg/ml, 200 µg/ml and ascorbic acid 10 µg/ml	Ethanolic extracts shown significant free radical scavenging and reducing power	Sharma and Kumar, 2011

Plant part Used	Solvent used	Srains/ Test animals	Doses and control	Result	Reference
				properties as compare to petroleum ether and water.	
Roots	Petrolium ether, Chloroform, Ethylacetate, n-butanol, Methanol and water	Leaves	50 mg/kg, 100 mg/kg,150 mg/kg and Ascorbic acid (10 mg/kg)	Methanol extracts shown strongest radical scavenging activity while ethylacetate extracts shown lowest radical scavenging activity.	Stratton, 1996
Anti-inflammatory Activity					
Roots	Ethanol	Rat	125 g/kg, 250 g/kg, 500 g/kg and Indomethacin 10 mg/kg	Significantly reduce the edema swelling of the rats.	Vadivelan *et al.,* 2009
Wound healing Activity					
Leaves	Methanol	Mice	50 mg/kg, 100 mg/kg, 150 mg/kg, 200 mg/kg and betadine 10 mg/kg	Shown significant wound healing property.	George *et al.,* 2015
Anti-diabetic Activity					
Leaves	Methanol	Leaves	200 µg/ml, 400 µg/ml, 600 µg/ml, 800 µg/ml, 1000 µg/ml and acarbose (50 µl/ml)	Methanol extracts shown strongest inhibition of the enzyme and effectively reduced the glucose level during α-glucosidase inhibition assay as compared to ethyl acetate and hexane.	Latha *et al.,* 2015
Anticancer Activity					
Leaves	Methanol	Mice	50 mg/ml, 100 mg/ml, 200 mg/ml and cyclopho-sphamide (10mg/mL)	Reduced the ascites and solid tumors.	George *et al.,* 2015
Antiulcerogenic Activity					
Roots	Ethanol	Rat	125 g/kg, 250 g/kg, 500 g/kg and Omeprazole 2 mg/kg	Reduced ulcer area and reduced ulcerative lesions.	Vadivelan *et al.,* 2008

antimicrobial activity against the strains of *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Candida tropicalis*, *Penecilliu mmarneffi*, and *Trichophyton rubrum* by using well-diffusion method (Latha *et al.,* 2015). Saklani *et al.* in (2012) have reported that ethanolic fruits extract shown good activity against selected bacteria strain: *Bacillus cereus, E. coli, Enterobacter gergoviae, Klebsiella pneumonia, Salmonella entericatyphm, Shigella flexneri, S. aureus, Staphy loccus epidermidis, Streptococcus pyogenes* and fungal strain i.e. *C. albicans, Aspergillus flavus* and *Aspergillus parasiticus* by usind well-diffusion method (Saklani *et al.,* 2012). Ethanol leaves extracts of *R. ellipticus* shown significant activity against selective bacterial and fungal strain, i.e. *S.aureus*, *S. epidermidis*, *Pseudomonas aeruginosa*, *E. coli; Candida krusei*, *Tricho-*

derma lignorum (Prasanth and Chandran, 2017).

Antioxidant Activity

Methanolic leaves extracts of *R. ellipticus* shown in-vitro antioxidant activity by DPPH free radical scavenging (Subba *et al.,* 2019) while Ahmad *et al.* (2015) also reported the similar activity from its fruit (Ahmad *et al.,* 2015). Petroleum ether, ethanol and water have been used to extract the fruits of *R. ellipticus*. All the extracts i.e. petroleum ether, ethanol and water shown the antioxidant activity but ethanol extracts shown the best scavenging and reducing power activities as compared to petroleum etherand aqueous extracts (Sharma and Kumar, 2011) while methanol fruit extracts also given the similar *in-vitro* antioxidant activity (Sasikumar *et al.,* 2015).

George *et al.* (2015) reported that methanolic extracts shown in-vivo antioxidant activity by effectively reduced DPPH, nitric oxide and Superoxide radical scavenging while the methanolic roots extracts also given strongest Superoxide radical scavenging (Vadivelan *et al.,* 2009; George *et al.,* 2015).

Anti-inflammatory Activity

Flavonoids result into anti-inflammatory activity. Vadivelan and his coworkers have studied that ethanolic extracts of roots of *R. ellipticus* gave the high anti-inflammatory activity by reducing the edema swelling of the rats (Vadivelan *et al.,* 2009).

Wound healing Activity

This activity is shown by phenolic compounds. Leaves of *R. ellipticus* when extracted with methanol solvent have shown the wound healing activity (George *et al.,* 2015).

Anti-diabetic Activity

Phenolic compounds are also responsible for antidiabetic Activity. The dried powder of leaves of *R. ellipticus* has been extracted with methanol and it has been shown anti-diabetic activity by the inhibition of α-glucosidase (Latha *et al.,* 2015).

Anticancer Activity

Triterpenoids generally cause for anticancer activity. Methanolic leaves extract of *R. ellipticus* has shown the anticancer activity. It was carried out on mice and there were be reduction of ascites and solid tumor (George *et al.,* 2015).

Antiulcerogenic Activity

Ethanolic extracts of roots of *R. ellipticus* has been shown good antiulcerogenic activity by effectively reduced ulcer area and ulcerative lesions (Vadivelan *et al.,* 2008). This activity is exhibited by phenolic compounds.

Future Scope

Traditionally different parts of *R. ellipticus* (whole part, roots, fruits, shoots, bark, aerial parts, and leaves) have been used to treat fever, diarrhea, gastralgia, skin infection, joint pain, wound healing, diabetes, anti-fertility agent, analgesic, antiepileptic, as renal tonic, ulcer etc. To prove the consistency of traditional uses, biological activities of leaves, roots and fruit are yet to be verified in the area of Fever, diarrhea, gastric problems, diabetes, and wounds healing. Similarly, the bark, aerial parts, shoots and whole plant of *R. ellipticus* has been used traditionally stomach ache, kidney tonic, renal tonic, cough, cold, blood disorders, kidney tonic, anti-diuretic, vaginal discharge, and diabetes but no significant study has been carried out on it.

Nineteen chemical compounds have been identified from *R. ellipticus* as yet but till now no activity has been carried out on the any compound isolated from this plant.

Conclusion

The traditional medicinal values of *R. ellipticus* have been compared with suitable biological activity in their support from the crude/phytochemicals extracted from various parts of the plant with different solvents. So far, **19** chemical constituents have been identified in its crude, out of which **04** are phenolic compounds, **02** are flavonoids, and **13** are triterpenoids. The crude has shown biological activities likeeffective antimicrobial (both bacterial and fungal), antioxidant (mainly due to the presence of phenolic compounds, flavonoids and terpenoids), anticancer (due to flavonoids, terpenoids), anti-inflammatory (due to flavonoids), antidiabetic (due to phenols and triterpenoids), wound healing and antiulcerogenic activities (due to phenolic compounds).

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Conflict of Interest

The authors declare that they have read the policy and guidelines of the journal and there are no conflicts of interest.

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