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Review

Rivea hypocrateriformis (Desr.) Choisy: A Review of its Ethno-medicinal uses, Phytochemistry and Biological activities

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Abstract: *Rivea hypocrateriformis* (Desr.) Choisy is a robust woody climbing shrub of the genus *Rivea* which is found in India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar and Thailand. *R. hypocrateriformis* is a promising medicinal herb with enormous helpful and wellbeing advancing impacts. *R. hypocrateriformis* has been utilized as a customary medication for a long time to treat rheumatic pain, fever, urogenital problem, snake bite, cough, piles, malaria, and skin disease. Apart from the traditional uses its leaves and young shoots are cooked and eaten as a vegetable and for preparation of bread with millet flour. This review comprehensively summarizes the up-to-date information on the botanical characterization, distribution, traditional uses, phytochemistry, pharmacology and toxicity study of *R. hypocrateriformis*. Phytochemical investigation has been revealed that alkaloids, glycosides, coumarins, flavonoids, xanthones, stilbenes, and other organic compounds are contained in *R. hypocrateriformis*. Crude extracts and isolated compounds have exhibited numerous pharmacological activities such as anovulatory effect, antifertility activity, antiarthritic, antimicrobial, anticancer, antioxidant, hepatoprotective, antilithiatic, antimitotic. *R. hypocrateriformis* is a promising restorative spice with monstrous remedial and wellbeing advancing impacts. Along these lines, further investigations on the bioactive mixtures and systems of *R. hypocrateriformis* are justified. Extra clinical and toxicological examinations are expected to assess its wellbeing.

Keywords: *Rivea hypocrateriformis* (Desr.) Choisy; Traditional medicines; Phytochemistry; Biological activity; Pharmacology

1. Introduction

The family Convolvulaceae is a fairly large and homogeneous group comprising about 50 genera and nearly 1,700 species [1-3]. *Rivea hypocrateriformis* (Desr.) Choisy is a robust woody climbing shrub belonging to the family Convolvulaceae and is found in subtropical forests of India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar and Thailand [4]. The different parts of the plant are utilized for the treatment of different sorts of sicknesses, for example, malaria, cancer, mental disorders and to relieve pain. Evan though the plant is known for a large number of biological activities such as anti-oxidant, anti-implantation, antimicrobial, pregnancy irruption, as anticancer and as an antiarthritic [5-8]. Indigenous populaces of Tharparkar of Pakistan utilize this plant for the treatment

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of malaria fever and pain. Indians utilize these plants as hallucinogenic medication while Pakistani utilize this plant as psychoactive medication plant like different types of a similar family, for example, *Rive corymbosa* Hall and *Ipomea violacea* L. found in Mexico [9].

Argyreia bona-nox Sweet, *Argyreia uniflora* Sweet, *Convolvulus hypocrateriformis* Desr., *Lettsomia uniflora* Roxb., *Modesta coriacea* Rafin., *Rivea bona-nox* Choisy, *Rivea fragrans* Nimmo are the synonyms of *R. hypocrateriformis*. Taxonomical classification of *R.* hypocrateriformis is Kingdom: Plantae; Phylum: Tracheophyta; Class: Magnoliopsida; Subclass: Asteridae; Order: Solanales; Family: Convolvulaceae; Genus: *Rivea* [10]. It is likewise known by a variety of names, such as "Midnapore Creeper" in English, "Thor-ki-bel" or "Phang" in Hindi, "Sanjvel" in Marathi "Budthi Kiray" or "Musuttai" in Tamil, and "Niruboddi" in Telugu [11,12]. Customarily, its bark, roots, and leaves are utilized for the treatment of different diseases and issues [13]. Other than its customary uses, leaves and youthful shoots - cooked and eaten as a vegetable. The leaves are bubbled along with toppings and arranged dishes, for example, bhaji [14,15] or jowari flour which is then made into bread [14].The plant has high nutrient A substance (almost 2.34 retinal reciprocals), holding 75 - 98% of this in any event, when cooked [16,17]. The leaves are a decent useful food. They contain a scope of dynamic mixtures and have gentle cell reinforcement potential. The plant is acceptable wellspring of energy and micronutrients and can be utilized as nutritious verdant vegetable in everyday life and explicitly in conditions, for example, when experiencing conditions like hack, skin sickness, and asthma [18].

It is also used as an ingredient in ayurvedic formulation "Parnasapancaka" used for the treatment of asthma [19]. Till date there is no review available on the R. *hypocrateriformis.* Therefore, the present review aimed at providing a more comprehensive analysis on the ethnomedicinal uses, phytochemistry, and biological activities. Furthermore, this study would highlight areas for future research on potential bioactivities of *R. hypocrateriformis*.

2. Research Methodology

The research methodology adopted for the selection of articles for this review is stipulated as flow chart in Figure 1.

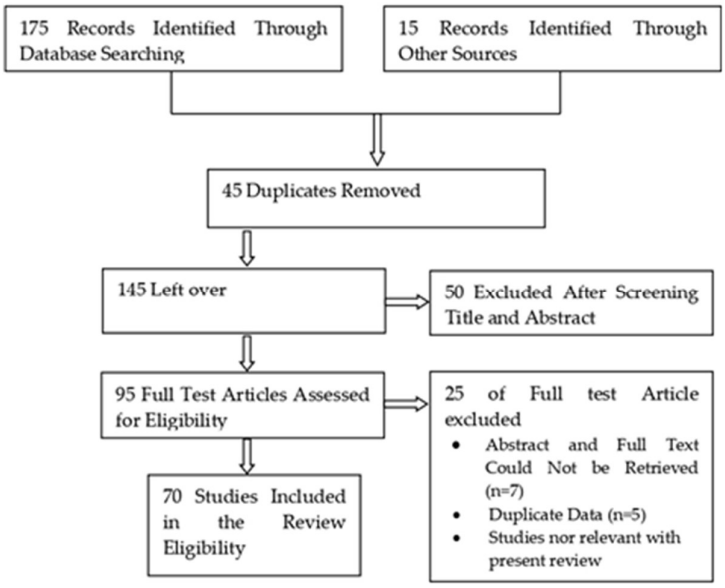

Figure 1. Flow diagram of research methodology.

3. Botanical Description

3.1. Habitat

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Midnapore Creeper is a robust woody climbing shrub, found in dry subtropical forests of India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar and Thailand. In India it is found in Assam, Bihar, Maharashtra, Rajasthan, and Tamil Nadu [20] (Figure 2).

Figure 2. Natural distribution of *R. hypocrateriformis* in the India. The shaded area represents its natural habitat.

3.2. Morphological and Microscopical Characteristics

Morphological characterization of *R. hypocrateriformis* plant and its parts (Figure 3a-d) describes that its flowers are creamy white, typical morning glory form, flat-faced, 6-9 cm long. Flowers usually solitary, occasionally subspicate. Sepals unequal, ovate, blunt apically, 10-12 mm long, densely short villose. Leaves are rounded-heart-shaped, blunt apically, densely appressed velvet-hairy below. Fruit indehiscent or tardily dehiscent, dry-baccate, 2 cm long. Seeds are brown, hairless, smooth, glabrous, slightly trigonous, surrounded by dry white pulp. Transverse sections of the leaf showed that the upper and lower epidermis comprise of single-layered polygonal cells that cover the adhesive fingernail skin; vein islet and vein termination 9–11 and 13–15, individually [21,22].


(a) (b)

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(c)

(d)

Figure 3. *R. hypocrateriformis* (a) Whole plant; (b) Leaf; (c) Fruit; (d) Flower.

3.3. Ethnomedicinal Uses

R. hypocrateriformis, an ordinary ayurvedic plant, is utilized by various local populace bunches in different manners due to the different helpful employments of its bark, roots, organic products, leaves and blossoms (Table 1).

Table 1. Ethnomedicinal Uses of *R. hypocrateriformis*.

Plant Part used	Method of Administration	Uses	References
Whole plant and root	The plant juice/paste is orally taken	Treatment of snake bite	[23-25]
Whole plant	Powder	Piles and Heart disease	[26]
Leaves	Cooked	Indigestion	[27]
Whole plant	Powder	Constipation	[28]
Leaves	Paste	Diarrhoea	[29-31]
Whole Plant	Powder	Diuretic	[32]
Whole Plant	Powder	Laxative	[32]
Stem	Powder	Cough and Headache	[27]
Leaves	Juice with Cow's milk	Rheumatic pain	[33]
Leaves	Juice	Skin disease of hair scalp	[33]
Whole plant and Root	Plant juice/paste is orally taken	Snake bite	[23,24,34]
Root	Decoction	Fever	[35]
Leaf	Powder	Urogenital problem (Hematuria)	[36]
Leaf	Powder	Blood purifier	[37]
Root	Paste	Cough, swelling and headache, poisonous animals bite	[23-25]
Leaf	Internal Use	Stomach wounds	[39]
Leaf	Internal use (Cooked)	Stomach upset and Indigestion	[40,41]
Root	Powder	After Parturition	[16]

Apart from these ethnomedicinal uses its leaves and young shoots are eaten as a vegetable and roots are given after parturition. Cooked leaves of this plant are utilized as vegetable curry by the tribals of India. Leaves of this plant are used as vegetable by some hill dwelling Kandha tribes of Odisha [42]. Ayurvedic physicians use *R. hypocrateriformis* to prevent fertility in women. Leaves and young shoots are eaten as a vegetable and roots are given after parturition. Cooked leaves of this plant are utilized as vegetable curry by the tribals of India. This plant had maximum vitamin A activity and has the capacity of maximum (75-98%) retention of β-carotene upon processing [43,44].

3.4. Physiochemical and Nutritional Analysis

Loganayaki et al. studied the extractive value of leaf, stem and flower parts of *R. hypocrateriformis* with three different solvents chloroform, methanol and acetone respectively. Flower part of this plant exhibited higher extractive value 13.3%, followed by flower methanol extract 12.5%, flower chloroform extract 11.5%, leaf methanol extract

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8.6%, Stem methanol extract 7.43 %, leaf acetone extract 5.9%, leaf chloroform extract 2.9%, stem acetone extract 1.87%, stem chloroform extract 0.7% [45]. Nutritional analysis of *R. hypocrateriformis* reported that its leaves contains Carbohydrate (%) 57.63, Fat (%) 2.66, Protein (%) 19.27, Energy 331.54 kcals/100 g, Moisture content (%) 6.25, Calcium (%) 0.99, Magnesium (%) 0.34, Phosphorous (%) 0.32, Zinc (%) 0.011 [18].

Loganayaki et al. studied the total phenolic content determination of different parts (leaves, stem and flower) of *R. hypocrateriformis* in different solvent. Quantitative parameters of different parts were depicted in Table 2. Higher total phenolic content was reported in the flower acetone extract and flower methanolic [45].

Table 2. Quantitative phytochemical content in *R. hypocrateriformis.*

Plant Part	Extract/Fraction	Total Phenolic Content	Total Flavonoid Content	References
Aerial	Polyphenolic	0.170 µg TAE/mg fraction	0.193 µg QAE/mg fraction	[17]
	Chloroform	1.1 g GAE/100 gm	---	
Leaves	Acetone	2.1 g GAE/100 gm	---	
	Methanolic	1.1 g GAE/100 gm	---	
	Chloroform	0.9 g GAE/100 gm	---	
Stem	Acetone	1.5 g GAE/100 gm	---	
	Methanolic	1.2 g GAE/100 gm	---	[45]
	Chloroform	1.6 g GAE/100 gm	---	
Flower	Acetone	4.2 g GAE/100 gm	---	
	Methanolic	3.5 g GAE/100 gm	---	

TAE: Tannic acid equivalent; QAE: Quercetin equivalent; GAE: Gallic acid equivalent.

4. Phytochemistry

The qualitative phytochemical screening of different parts of *R. hypocrateriformis* showed the relatively presence alkaloids, flavonoids, tannins, saponins, phenolic compounds, glycosides, steroids, carbohydrates, phytosterols, and amino acids [18, 46-50]. These phytochemicals have shown a wide variety of pharmacological effects. FTIR analysis of whole plant of *R. hypocrateriformis* revealed the presence of various functional groups viz. phenol, alkanes, nitrocompounds (oxime and lactams), ethers, aromatic compounds, and halogen derivatives (chloro and bromo compounds) [36].

4.1. Alkaloids

Three pyrrolizidine alkaloids macrophylline (1), meteloidine (2) and Symlandine (3) as well as three tropane alkaloids cochlearine (4), darlingine (5) tigloidine (6) and one more alkaloidal compound serratanidine (7) were found in the root of *R. hypocrateriformis* [51]. Two other alkaloids were found in the aerial part of *R. hypocrateriformis* namely hypocretine 1(8i) and hypocretine 2 (8ii) [17]. The presence of aminopyrimidine pyrimethanil (9) was reported in the root of *R. hypocrateriformis* [51]. These alkaloids are shown in Figure 4.

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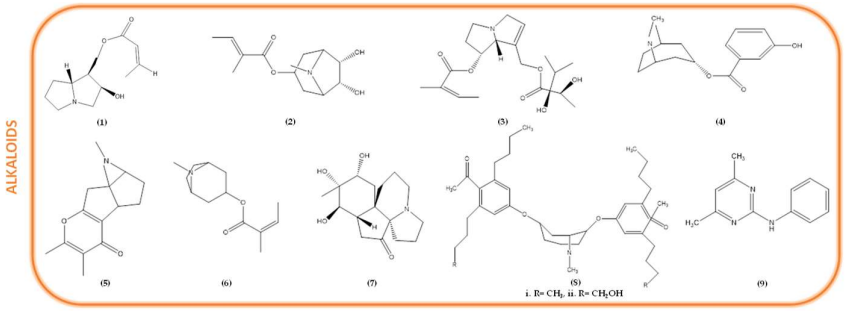

Figure 4. Alkaloids from the *R. hypocrateriformis*.

4.2. Glycosides

Four glycosides bergenin (10), norbergenin (11), rivebergenin A (12i) and rivebergenin B (12ii) were reported from the stem of *R. hypocrateriformis* [52]. One aromatic glycoside lucuminic acid (13), one cardiac glycoside oleandrose (14) were found in the root of *R. hypocrateriformis* [51]. Their structures are shown in Figure 5.

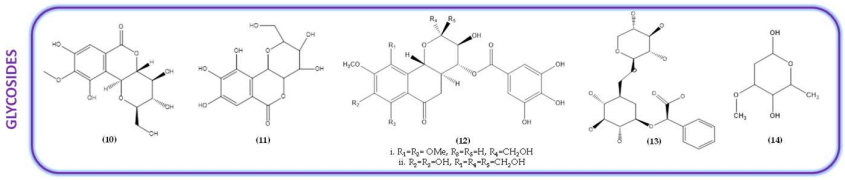

Figure 5. Glycosides from the *R. hypocrateriformis*.

4.3. Flavonoids

Godipurge et al. reported the presence of quercetin (15) in polyphenolic fraction of aerial part [17] (Figure 6). Two flavonoid *C*-glycosides 3'-deoxymaysin (16) and 6-*C*-Glucopyranosylpilloin (17), one flavonoid *O*-glycoside peruvianoside II (18) and one prenylated flavonoid morusin (19) were found in the root of *R. hypocrateriformis* [51] (Figure 6).

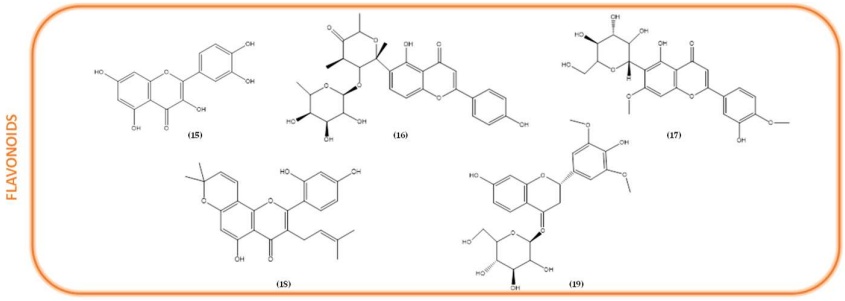

Figure 6. Flavonoids from the *R. hypocrateriformis*.

4.4. Xanthones

Xanthone derivative dulciol B (20) mangostenone B (21) were reported in root of *R. hypocrateriformis* [51] (Figure 7).

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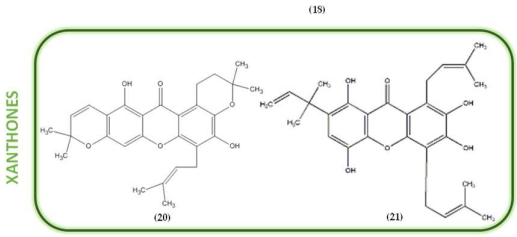

Figure 7. Xanthones from the *R. hypocrateriformis.*

4.5. Stilbenes

Blestriarene B (22) and α-viniferin (23) was reported in the root of *R. hypocrateriformis* [51] (Figure 8).

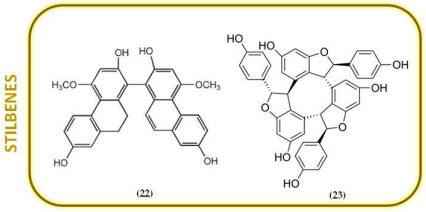

Figure 8. Stilbenes from the *R. hypocrateriformis.*

4.6. Coumarins

Tomentolide A (24) and calophyllolide (25) was reported in the root extract [51] while desmethylbergenin hemihydrates (26) was found in the whole plant of *R. hypocrateriformis* [51] (Figure 9).

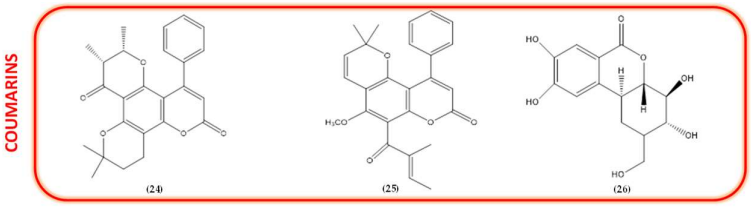

Figure 9. Coumarins from the *R. hypocrateriformis.*

4.7. Sterols and fatty acid derivatives

Sphingosine (27) and 3S,7S-dimethyl-tridecan-2S-ol (28) were found in root of *R. hypocrateriformis* [51] (Figure 10).

One long-chain fatty aldehyde pentadecanal (29), two fatty acids 2-hexyl-decanoic acid (30) and 1-palmitoyl lysophosphatidic acid (31) and 2,4-undecadienal (32) were found in the root of *R. hypocrateriformis* [51] (Figure 10).

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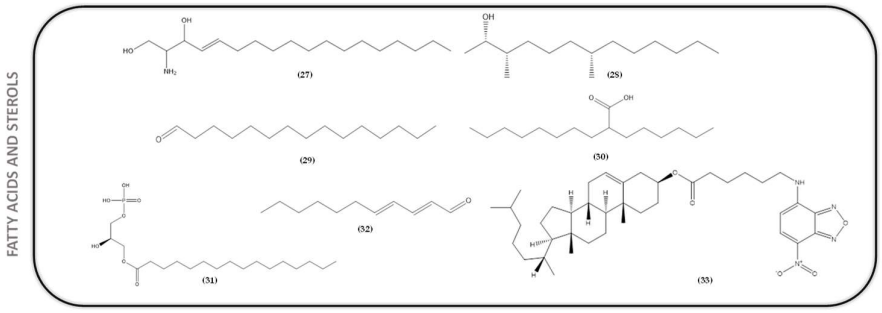

Figure 10. Fatty acids and sterol derivatives from the *R. hypocrateriformis.*

4.8. Other compounds

Other compounds have been also reported (Figure 11). N-acetylmuramoyl-alanine (33) belongs to the class of organic compounds known as acylaminosugars. These are organic compounds containing a sugar linked to a chain through N-acyl group. Two tripeptides His-His-Lys (34) and Asp-Arg-Asp (35), one bipeptide Glu-His (36) and one amino cyclitol streptidine (37) and one volatile compound methyl jasmonate (38) were reported in the root of *R. hypocrateriformis* [51].

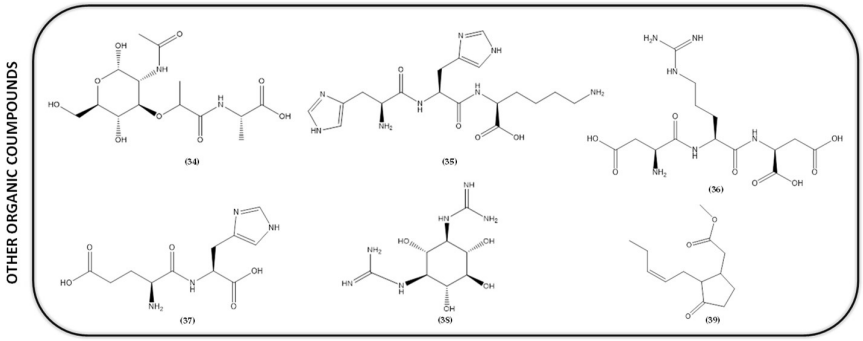

Figure 11. Other organic compounds from the *R. hypocrateriformis.*

5. Biological activities

Extracts from *R. hypocrateriformis* possess a broad spectrum of pharmacological activities. Past research affirmed that presence of phenolic acids and flavonoids is liable for its cancer prevention agent potential [53-55]. Past research uncovered that phenolic compounds are profoundly dynamic cell reinforcements, and such cancer prevention agent rich botanicals offer promising potential in the administration of degenerative illnesses. Phenolic compounds are auxiliary metabolites blended in plants because of ecological anxieties like assaults from microbes and bugs, UV radiation, and wounds [56]. These phytochemicals can kill hydroxyl extremists [57], superoxide anion revolutionaries [58], lipid peroxyl revolutionaries [59] and even to chelate metals, other than to assume an indispensable part in the steadiness of food items, just as in the protection components of natural frameworks [60]. These atoms likewise forestall oxidative misfortunes and have cytoprotective, mitigating, and adaptogen properties. The numerous pharmacological activities have been also reported, by the extracts and isolated bioactive compounds from *R. hypocrateriformis* including antiarthritic, anticancer, anti-inflammatory, antimicrobial, anovulatory, antioxidant, hepatoprotective, antifertility, antimitotic, antiproliferative, antilithiatic activity. Simultaneously, several *in vitro* and *in vivo* studies on pharmacological profile of *R. hypocrateriformis* are under way. Scientific exploration has revealed that

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different types of *R. hypocrateriformis* extracts possess multiple bioactive attributes (Table 3).

Table 3. Biological activities of *R. hypocraterformis.*

Part used	Extract/Fraction	Dose tested / Route of administration	Animals/ Cell lines	Experimental models	Results	Ref
			Antiarthritic			
Leaves	Methanolic	250 and 500 mg/kg, p.o.	Wistar albino Rat	Complete Freund's adjuvant (CFA) induced arthritis	Extract showed significant anti-arthritic activity	[61]
			Antimicrobial			
Aerial	Au, Ag and Au-Ag alloy NPs	25-100 µg/mL	KP, SA, BS, PA, EC, CA, TR, and CI	Agar Well diffusion method	Green synthesized AgNPs displayed very good antimicrobial Potential compared to AuNPs	[62]
Aerial part fruit	Pet. Ether, chloroform, ethanol and aqueous extract	10000, 5000, 2500, 1250 and 0.625 µg/mL	SA, BS, EC, PA, PV, AN, CA, Af	Agar disk diffusion method	Ethanolic and aqueous extract showed higher antimicrobial potential than other extracts	[48]
			Anticancer			
Aerial	Au, Ag and Au-Ag alloy NPs	1-100 µg/mL	MCF7, Sf9, Vero	MTT assay	Significant cytotoxicity on tested cancer cells in concentration dependent manner	[17]
Aerial part	Pet. Ether, chloroform, ethanol and aqueous	$4x10^3$ cells/ml	MCF-7, MCF-15, MOLT-4, HOP-62, prO	SRB assay	Chloroform and ethanolic extracts exhibited strong anticancer activity	[48]
			Anovulatory effect			
Aerial Part	Ethanolic	200 and 400 mg/kg	Wistar albino rat	*in-vivo* (Effect on duration of different phases of oestrous cycle)	Significant ↓in number of graafian follicles and corpora lutea and significant ↑ in number of atretic follicles	[49]
			Antioxidant			
Aerial	Polyphenolic fraction	---	*In vitro*	Hydroxyl radical scavenging assay	Extracted demonstrated significant antioxidant activity	**[17]**
Aerial	Au, Ag and Au-Ag alloy NPs	10-100 µg/ml	*In vitro*	DPPH assay	NPs were capable of scavenging DPPH radicals	**[62]**
Leaf	Aqueous	15.51, 62.5, 250 and 1000 µg/ml	*In vitro*	DPPH assay	Aqueous extract showed highest DPPH radical scavenging activity	**[18]**
Leaf, Stem and Fruit	Chloroform, acetone and Methanol		*In vitro*	DPPH, ABTS and FRAP assay	Antioxidant activity was highest in MeAA extracts and while	**[45]**

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					intermediate in MeAM and MeA extracts.	
Antifertility activity						
Aerial part	Pet. Ether, chloroform, ethanol and aqueous	200 and 400 mg/kg	Albino Wistar rats	*In-vivo* (antiimplantation effect)	ethanol extract found significant antiimplantation and interruption of early pregnancy	[49]
Whole plant	95% ethanolic extract	200 and 400 mg/kg	Albino Wistar rats	*In-vivo* (antiimplantation effect)	Extract dose 400 mg/kg showed significant antiimplantation potential	[7]
Hepatoprotective						
Aerial	Polyphenolic fraction	300 and 600 mg/kg	Wistar albino rat	Paracetamol induced hepatotoxicity	↓ALT, ↓AST, ↓ALP, ↓TB	[17]
Antimitotic activity						
Aerial part	Pet. Ether, chloroform, ethanol and aqueous	10 mg/ml	*in-vitro*	*Allium cepa* root inhibition	Chloroform and ethanol extracts showed Significant antimitotic activity	[48]
Antiproliferative activity						
Aerial part	Pet. Ether, chloroform, ethanol and aqueous	--	*In-vitro*	Yeast *Saccharomyces cerevisiae* model	Chloroform and ethanol extracts showed Significant antiproliferative activity	[48]
Antilithiatic activity						
Leaves	Ethanolic	**2.5 ml OF 0.2 g/ml solution**	*In-vitro*	---	Extract showed significant inhibition of calcium and phosphate accumulation	[37]
Antiinflammatory activity						
Leaves	Ethanolic	**200 and 400 mg/kg**	Wistar albino rat	Carrageenan induced paw edema	Ethanol extracts showed Significant antiinflammatory activity	[63]
Analgesic activity						
Leaves	Ethanolic	**200 and 400 mg/kg**	Wistar albino rat	Radiant Heat Tail Flick method	Ethanol extracts showed Significant analgesic activity	[63]

6. Toxicity Study

The toxicity study of PPFRH indicated, there was no adverse effect on mortality detected in Swiss albino mice and Wistar albino rats that were administered up to 4000 mg/kg, orally. This was observed during 24 h period, and the extract was found to be safe at the given dose [17].

7. Conclusions

This survey sums up the wide pharmacological exercises of *R. hypocrateriformis* and its dynamic constituents dependent on customary writing and current proof. Some toxicological examinations on *R. hypocrateriformis* are additionally announced. Our investigation gives an exhaustive and inside and out assessment of *R. hypocrateriformis* and shows that it is a promising conventional medication that can be abused for its helpful and tonic advantages. Leaves of *R. hypocrateriformis* are a good source of energy and micronutrients. It possesses zinc, phosphorous, magnesium, and calcium along with protein, fat, and carbohydrate. It has the highest amount of energy content. The study revealed that the plant is good source of energy and micronutrient and can be used as nutritious leafy vegetable in daily life and specifically in conditions such as cough, skin disease, and asthma. Earlier study revealed that bergenin (10), a C-glycoside isolated from the *R. hypocrateriformis* exhibited hepatoprotective, antiarrhythmic, neuroprotective, antifungal, anti-inflammatory, immunomodulatory, anti-HIV, antifungal, antihepatotoxic, wound and ulcer healing potential. Calophyllolide (25) has been reported to exhibit some biological activity, including anti-inflammation, lower capillary vascular permeability, anti-cancer, anti-microbial, and anti-coagulant properties. Earlier researches also reported that stilbene trimers like α-Viniferin (23) exhibited AChE activity in a dose-dependent manner. Therefore, the further clinical studies are warranted these potential derivatives of *R. hypocrateriformis* for development of novel therapeutic approach. Earlier research reported that norbergenin (11), is the *O*-methyl derivative of bergenin (10) exhibited the neuroprotective potential on rat cortical neurons. Despite the fact that *R. hypocrateriformis* has been utilized broadly as a therapeutic spice and in a few tonics, quality norms have not yet been set up. The current logical techniques are not agreeable to control the nature of *R. hypocrateriformis*. The nature of *R. hypocrateriformis* is affected by the environment and picking time, and the classifications of dynamic segments contrast broadly among various territories and picking times; along these lines, quantitative distinguishing proof is fundamental for control the nature of restorative materials, which will likewise dispose of contaminated and assurance the remedial impact of *R. hypocrateriformis*. It is important that the current examinations on *R. hypocrateriformis* are lacking. The particular systems of activity and material premise of the adequacy are not extremely clear, and its clinical worth has not been totally investigated at this point. Along these lines, the deliberate examinations on *R. hypocrateriformis* ought to be attempted to represent its ethnomedicinal use.

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