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Review Article

Rivea hypocrateriformis (Desr.) Choisy: An Overview of Its Ethnomedicinal Uses, Phytochemistry, and Biological Activities and Prospective Research Directions

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Rivea hypocrateriformis (Desr.) Choisy is a robust woody climbing shrub of the genus *Rivea* which is widely distributed in India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar, and Thailand. *R. hypocrateriformis* is a promising medicinal herb with a wide range of beneficial and health-promoting properties. Since the ancient times, it has been used as a traditional medicine to treat rheumatic pain, fever, urogenital problems, snake bites, cough, piles, malaria, and skin diseases. Aside from these traditional uses, its leaves and young shoots are also cooked and eaten as a vegetable and used for the preparation of bread with millet flour. This study extensively analyzes the available information on R. hypocrateriformis botanical characterization, distribution, traditional applications, phytochemistry, pharmacology, and toxicological properties. Phytochemical investigations of the plant has revealed the presence of highly valuable secondary metabolites including alkaloids, glycosides, coumarins, flavonoids, xanthones, stilbenes, and other organic compounds. Its crude extracts and isolated compounds have revealed anovulatory, antifertility, antiarthritic, antimicrobial, anticancer, antioxidant hepatoprotective, antilithiatic, and antimitotic potentials. This review of literature clearly identifies *R. hypocrateriformis* as a potent medicinal plant with remarkable healing and health-promoting properties. Further research directions into the bioactive extracts, clinical, and toxicological evaluations to assess the beneficial health-promoting properties of this promising herb are also discussed.

1. Introduction

Medicinal plants are among the vital sources of secondary metabolites used for the management of various diseases since the establishment of the human era [1]. Even today, it is among the most useful sources for the discovery and development of novel drugs against various diseases [2, 3]. Especially, plants which are traditionally used by indigenous people to treat various diseases are more useful as their safety and efficacy are already established [4]. The discovery and clinical approval of numerous drugs using a knowledge-driven ethnomedicinal approach signify the role of medicinal plants and traditional knowledge in the discovery of novel drugs [5, 6]. Further, the development of novel and highly sensitive isolation and identification techniques and the discovery of novel molecules from these plants are easier and more cost-effective. *Convolvulaceae* is a vast and homogeneous plant family of approximately 50 genera and nearly 1,700 species [7–9]. *Rivea hypocrateriformis* (Desr.) Choisy is a woody climbing shrub belonging to the *Convolvulaceae* family and is widely distributed in India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar, and Thailand [9]. Its bark, stems, and leaves are traditionally used to cure a range of ailments including malaria, cancer, mental disorders, and analgesia. For instance, the indigenous people of Pakistan's Tharparkar region use this plant for the treatment of malaria and to relieve pain. The plant is reported for a wide range of biological potentials including antioxidant, anti-implantation, antimicrobial, pregnancy irruption, anticancer and antiarthritic properties [10, 11]. It is also used as a vital ingredient in the ayurvedic formulation "Rasa panchaka" used for the treatment of asthma [12]. Moreover, similar to other varieties of a related genus, such as *Rivea corymbosa* Hall and *Ipomea violacea* L. found in Mexico, this plant is also used as a hallucinogenic drug in India and as a psychoactive medicine in Pakistan [13].

Besides, young shoots and leaves of the plant are also cooked and consumed as a vegetable. The leaves are bubbled along with toppings and arranged dishes, for example, *bhaji* or *jowari* flour which was then used to prepare bread [14]. It is a rich source of micronutrients, in particular vitamin A [15, 16]. As far as we know, there is no review paper available on *R. hypocrateriformis* that was accessible in January 2022. The review paper is aimed at providing a more comprehensive analysis of the ethnomedicinal uses, phytochemistry, and biological activities. Furthermore, this review also focuses on filling some of the gaps among the currently performed studies and proposes some areas for future research on potential bioactivities of *R. hypocrateriformis*.

2. Methods

Publications were retrieved from PubMed, Google Scholar, and ScienceDirect. The strategy was using different combinations of keywords "Traditional medicines, Phytochemistry, Biological activity, Pharmacology" associated with "*Rivea hypocrateriformis*" and its synonyms. *Argyreia bona-nox* Sweet, *Argyreia uniflora* Sweet, *Convolvulus hypocrateriformis* Desr., *Lettsomia uniflora* Roxb., *Modesta coriacea* Rafin., *Rivea bona-nox* Choisy, and *Rivea fragrans* Nimmo are the synonyms of *R. hypocrateriformis*. The detailed research methodology adopted for the selection of articles for this review is stipulated as a flowchart in Figure 1.

3. Botanical Description

3.1. Taxonomical Classification and Habitat. The taxonomical classification of *R. hypocrateriformis* is Kingdom: *Plantae*; Phylum: *Tracheophyta*; Class: *Magnoliopsida*; Subclass: *Asteridae*; Order: *Solanales*; Family: *Convolvulaceae*; Genus: *Rivea* [9] 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 [17]. *R. hypocrateriformis* is a woody climbing shrub found in subtropical forests of India, Nepal, Sri Lanka, Pakistan, Bangladesh, Myanmar, and Thailand. In India, it is mainly found in Assam, Bihar, Maharashtra, Rajasthan, and Tamil Nadu (Figure 2).

R. hypocrateriformis (Desr.) Choisy is a woody climbing shrub belonging to the family *Convolvulaceae*.

3.2. Morphological and Microscopical Characteristics. Morphological characterization of *R. hypocrateriformis* plant and its parts are presented in Figures 3(a)–3(d). Its flowers, usually solitary, are creamy white, typical morning glory form, flat-faced, and 6–9 cm long. Sepals unequal, ovate, blunt apically, 10–12 mm long with dense short villoses. Leaves are round-heart-shaped, blunt apically, densely appressed velvet-hairy below. Fruit are indehiscent or tardily dehiscent, dry-baccate of 2 cm long. Seeds are brown, smooth, glabrous, slightly trigonous, and surrounded by a 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 [18, 19].

4. Ethnomedicinal Uses

R. hypocrateriformis is a common ayurvedic herb, used in different ways by various local population groups due to the various beneficial uses of its bark, roots, leaves, and blossoms. Ayurvedic physicians traditionally use *R. hypocrateriformis* preparations to prevent fertility in women [20, 21]. The various ethnomedicinal usages of this herbal medicine are summarized in Table 1.

5. Phytochemistry

R. hypocrateriformis is extensively reported for the presence of important metabolites. For instance, Loganayaki et al. reported the extractive value of leaf, stem, and flower parts of the plant using polarity-directed solvent systems including chloroform, methanol, and acetone. Flowers exhibited a higher extractive value of 13.3%, followed by the flower-methanol extract 12.5%, flower-chloroform extract 11.5%, leaf-methanol extract 8.6%, stem-methanol extract 7.43%, leaf-acetone extract 5.9%, leaf-chloroform extract 2.9%,

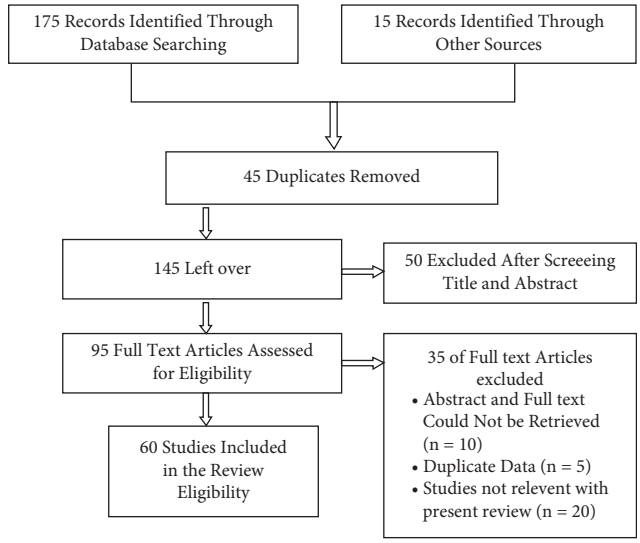


Figure 1: Flow diagram of research methodology.

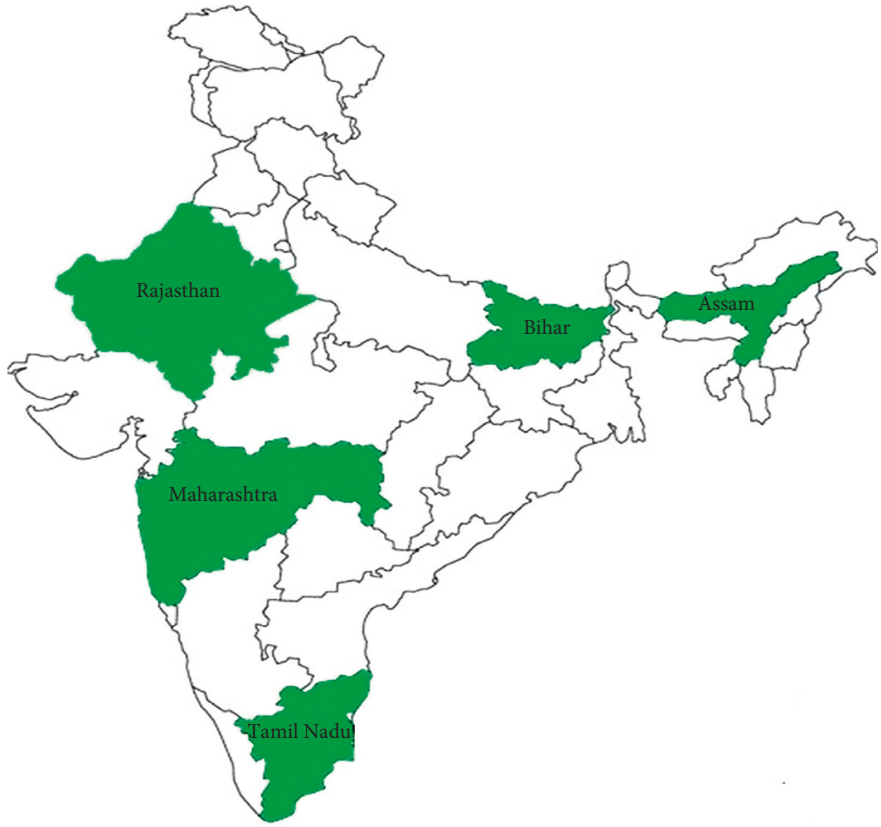
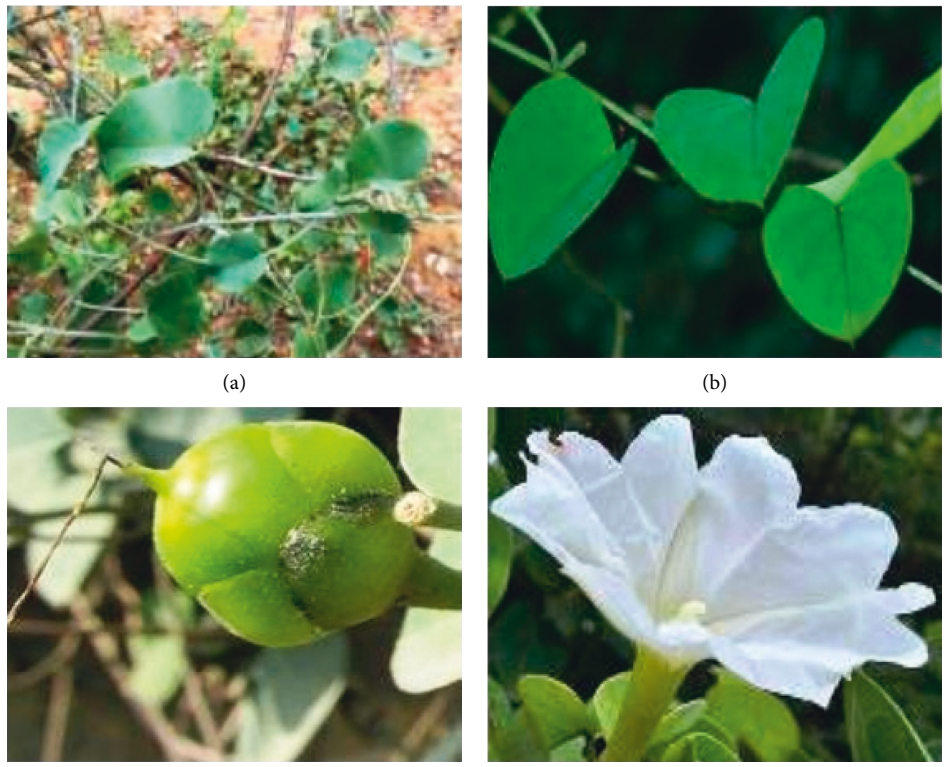


Figure 2: Natural distribution of *R. hypocrateriformis* in the India. The shaded area represents its natural habitat.

stem-acetone extract 1.87%, and stem-chloroform extract 0.7%. The same group of researchers also reported *R. hypocrateriformis* as a rich source of phenolic compounds as observed in the different extracts from leaves, stems, and flowers obtained using organic solvents. The highest total phenolic content was quantified in the flower-acetone extract and flower-methanolic extracts [39] as summarized in Table 2. These quantitative results are in agreement with recent the study [40] (Table 2). Furthermore, qualitative phytochemical screening of different parts of *R. hypocrateriformis* revealed the presence of alkaloids, flavonoids, tannins, saponins, glycosides, steroids, carbohydrates, phytosterols, and amino acid derivatives.



(a) (b) (c) (d)

Figure 3: *R. hypocrateriformis*. (a) whole plant; (b) leaf; (c) fruit; (d) flower.

Table 1: Ethnomedicinal uses of *R. hypocrateriformis*.

Plant part used	Method of administration	Usage	References
Whole plant and root	The plant juice/paste is orally taken	Treatment of snake bite	[22–24]
Whole plant	Powder	Piles and heart disease	[25]
Leaves	Cooked	Indigestion	[26]
Whole plant	Powder	Constipation	[27]
Leaves	Paste	Diarrhoea	[28,29]
Whole plant	Powder	Diuretic	[30]
Whole plant	Powder	Laxative	[30]
Stem	Powder	Cough and headache	[26]
Leaves	Juice with cow's milk	Rheumatic pain	[31]
Leaves	Juice	Skin disease of hair scalp	[31]
Whole plant and root	Plant juice/paste taken orally	Snake bite treatment	[23,24,32]
Root	Decoction	Fever	[33]
Leaves	Powder	Urogenital problem (hematuria)	[34]
Leaves	Powder	Blood purifier	[35]
Root	Paste	Cough, swelling and headache, poisonous animals bite	[22–24]
Leaves	Internal use	Stomach wounds	[36]
Leaves	Internal use (cooked)	Stomach upset and indigestion	[37,38]
Root	Powder	After parturition	[16]

5.1. Alkaloids. Three pyrrolizidine alkaloids, namely, macrophylline (1), meteloidine (2), and symlandine (3) as well as four tropane alkaloids, namely, cochlearine (4), darlingine (5), tigloidine (6), and serratanidine (7) were found in the root of *R. hypocrateriformis* [41]. Two other alkaloids were quantified in the aerial parts of the plant, namely, hypocretine 1(8i) and hypocretine 2 (8ii) [40]. The presence of aminopyrimidine pyrimethanil (9) was also reported from the roots of *R. hypocrateriformis* [41].

5.2. Glycosides. Four glycosides, namely, bergenin (10), norbergenin (11), rivebergenin A (12i), and rivebergenin B (12ii) are reported from the stem of *R. hypocrateriformis*. An

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

Plant part	Extract/fraction	Total phenolic content	Total flavonoid content	Extractive value (%*w*/*w*)	References
Aerial	Polyphenolic	0.170 μg TAE/mg fraction	0.193 μg QAE/mg fraction	—	[40]
Leaves	Chloroform	1.1 g GAE/100 g	—	2.9	
	Acetone	2.1 g GAE/100 g	—	5.9	
	Methanolic	1.1 g GAE/100 g	—	8.6	
Stem	Chloroform	0.9 g GAE/100 g	—	0.7	
	Acetone	1.5 g GAE/100 g	—	1.87	[39]
	Methanolic	1.2 g GAE/100 g	—	7.43	
Flower	Chloroform	1.6 g GAE/100 g	—	11.5	
	Acetone	4.2 g GAE/100 g	—		
	Methanolic	3.5 g GAE/100 g	—	12.5	

TAE: tannic acid equivalent; QAE: quercetin equivalent; GAE: gallic acid equivalent.

aromatic glycoside lucuminic acid (13) and a cardiac glycoside oleandrose (14) were reported from the roots of *R. hypocrateriformis* [41].

5.3. Flavonoids. Godipurge et al. reported the presence of multifunctional compound quercetin (15) in a polyphenolic fraction of the aerial part [40]. Flavonoids including *C*-glycosides 3′-deoxymaysin (16), 6-*C*-glucopyranosylpilloin (17), *O*-glycoside peruvianoside II (18), and a prenylated flavonoid morusin (19) were identified in the roots of *R. hypocrateriformis* [41].

5.4. Xanthones. Several xanthone derivatives including dulciol B (20) and mangostenone B (21) are also reported from the roots of *R. hypocrateriformis* [41].

5.5. Stilbenes. The occurrence of blestriarene B (22) and α-viniferin (23) was reported from the roots of *R. hypocrateriformis* [41].

5.6. Coumarins. Various coumarins including tomentolide A (24) and calophyllolide (25) were reported from the root extract of the plant. Likewise, desmethylbergenin hemihydrate (26) was reported from the whole plant of *R. hypocrateriformis* [41].

5.7. Sterols and Fatty Acid Derivatives. Sterols and fatty acids including sphingosine (27) and 3S, 7S-dimethyl-tridecan-2S-ol (28) were found in the root of *R. hypocrateriformis* [41]. A long-chain fatty aldehyde pentadecanal (29), two fatty acids, namely, 2-hexyl-decanoic acid (30) and 1-palmitoyl lysophosphatidic acid (31), and 2,4-undecadienal (32) were reported from the roots of *R. hypocrateriformis* [41].

5.8. Miscellaneous Compounds. Various other compounds are also reported from the plant. Among these, *N*-acetylmuramoyl-alanine (33) belongs to the class of organic compounds known as acylamino sugars. 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 an amino cyclitol streptidine (37), and a volatile compound methyl jasmonate (38) were reported from the roots of *R. hypocrateriformis* [41]. Structures of these bioactive phytoconstituents reported in the *R. hypocrateriformis* plant are presented in Figure 4.

6. Pharmacological Studies

Crude extracts from medicinal plants are extensively studied for various pharmacological properties [3, 42–44]. *R. hypocrateriformis* is also reported for various pharmacological potentials which might be attributed to the presence of various phytochemicals (Table 3). Many studies have shown that the presence of phenolic acids and flavonoids may be linked to cancer-prevention action [2, 48–51]. The identified phytochemicals offer protection against oxidative stress by scavenging radicals [52, 53].

Various identified phytochemicals from the plant might be implicated in the therapeutic properties of the crude extracts as they are reported for protective properties in various diseases [54, 55]. For instance, bergenin is reported to exhibit hepatoprotective, antiarrhythmic, neuroprotective, antifungal, anti-inflammatory, immunomodulatory, anti-HIV, antifungal, antihepatotoxic, wound, and ulcer healing potentials [56, 57]. Norbergenin, an *O*-methyl derivative of bergenin, is also reported to have antioxidant [58, 59] and gastroprotective [60] potentials. Likewise, calophyllolide has been reported to exhibit some biological activities including anti-inflammatory, vasodilatory, anticancer, antimicrobial, and anticoagulant properties [61]. Further, stilbene trimers including α-viniferin are reported to exhibit AChE potentials in a dose-dependent manner [62].

These findings suggest that clinical studies into the pharmacological potentials of *R. hypocrateriformis* and its derivatives could be warranted for the discovery of new potential therapeutic entities. Simultaneous *in vitro* and *in vivo* experiments on the pharmacological profile of *R. hypocrateriformis* and its derivatives might help evaluate their modes of action.

7. Toxicological Studies

The toxicological properties of the plant were reported in various studies. In a toxicological study performed on the

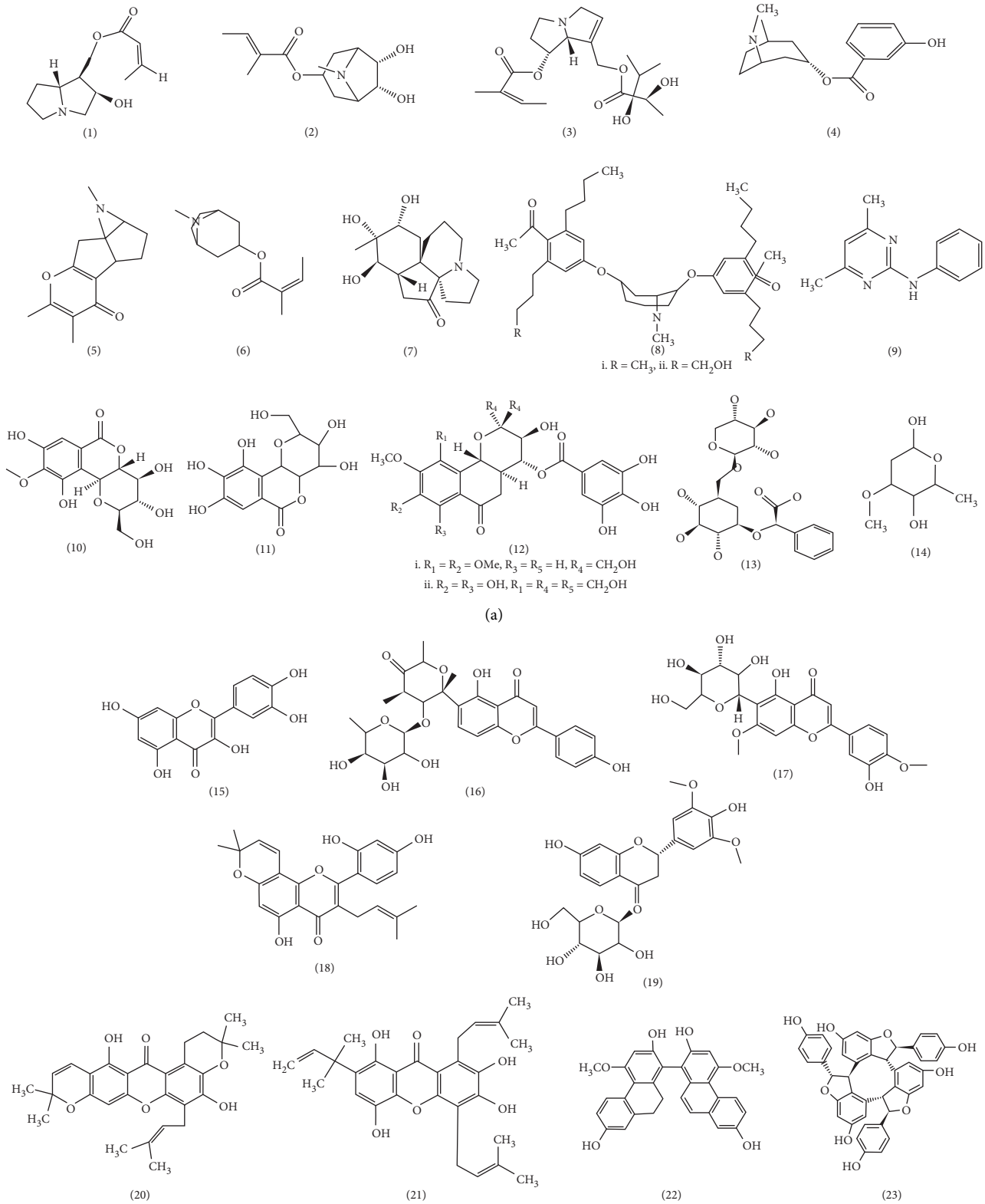


Figure 4: Continued.

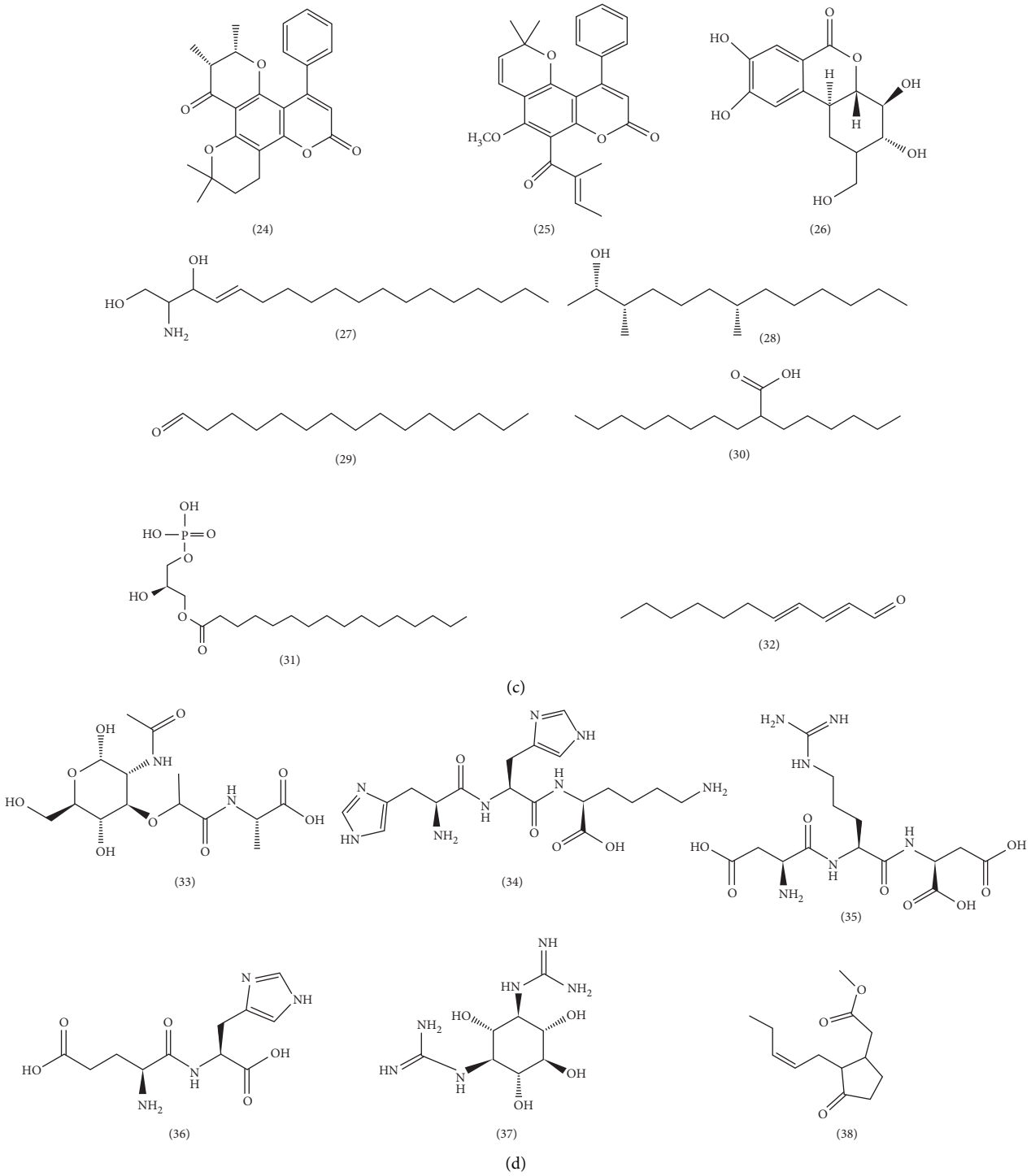


Figure 4: (a) Structure of some isolated alkaloids and glycosides from different parts of *R. hypocrateriformis*. (1) Macrophylline, (2) meteloidine, (3) symlandine, (4) cochlearine, (5) darlingine, (6) tigloidine, (7) serratanidine, (8) (i) hypocretine 1 and (ii) hypocretine 2, (9) pyrimethanil, (10) bergenin, (11) norbergenin, (12) (i) rivebergenin A and (ii) rivebergenin B, (13) lucuminic acid, (14) oleandrose. (b) Structure of some isolated flavonoids, xanthones, and stilbenes from different parts of *R. hypocrateriformis*. (15) Quercetin, (16) 3′-deoxymaysin, (17) 6-C-glucopyranosylpilloin, (18) peruvianoside II, (19) morusin, (20) dulciol B, (21) mangostenone B, (22) blestriarene B, and (23) α-viniferin. (c) Structure of some coumarins, fatty acids, and sterols from different parts of *R. hypocrateriformis*. (24) Tomentolide A, (25) calophyllolide, (26) desmethylbergenin hemihydrate, (27) sphingosine, (28) 3S, 7S-dimethyl-tridecan-2S-ol, (29) pentadecanal, (30) 2-hexyl-decanoic acid, (31) 1-palmitoyl lysophosphatidic acid, and (32) 2, 4-undecadienal. (d) Structure of some isolated other organic compounds from different parts of *R. hypocrateriformis*. (33) N-acetylmuramoyl-alanine, (34) his-his-lys, (35) asp-arg-asp, (36) glu-his, (37) streptidine, and (38) jasmonate.

Table 3: Biological activities of *R. hypocrateriformis*.

Part used	Extract/fraction	Dose tested/route of administration	Study model	Experimental models	Results	References
Antiarthritic activity						
Leaves	Methanolic	250 and 500 mg/kg, p.o.	Albino Wistar rats	Complete Freund's adjuvant (CFA)-induced arthritis	Extract showed significant anti-arthritic activity	[45]
Antimicrobial activity						
Aerial part	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	[40]
Aerial part	Pet. ether, chloroform, ethanol, and aqueous extract	10000, 5000, 2500, 1250 and 0.625 μg/mL	SA, BS, EC, PA, PV, AN, CA, and AF	Agar disk diffusion method	Ethanolic and aqueous extract showed higher antimicrobial potential than other extracts	[46]
Anticancer activity						
Aerial part	Au, Ag, and Au–Ag alloy NPs	1–100 μg/mL	MCF7, Sf9, Vero	MTT assay	Significant cytotoxicity on tested cancer cells in a concentration-dependent manner	[40]
Aerial part	Pet. ether, chloroform, ethanol, and aqueous	4×10^3 cells/ml	MCF-7, MCF-15, MOLT-4, HOP-62, prO	SRB assay	Chloroform and ethanolic extracts exhibited strong anticancer activity	[46]
Anovulatory effect						
Aerial part	Ethanol	200 and 400 mg/kg	Wistar albino rat	*In vivo* (effect on duration of different phases of the oestrous cycle)	Significant decrease in number of Graafian follicles and corpora lutea and significant increase in number of atretic follicles	[20]
Antioxidant activity						
Aerial part	Polyphenolic fraction	—	*In vitro*	Hydroxyl radical scavenging assay	Extracted demonstrated significant antioxidant activity	[40]
Aerial part	Au, Ag, and Au–Ag alloy NPs	10–100 μg/ml	*In vitro*	DPPH assay	NPs were capable of scavenging DPPH radicals	[40]
Leaf	Aqueous	15.51, 62.5, 250 and 1000 μg/ml	*In vitro*	DPPH assay	Aqueous extract showed highest DPPH radical scavenging activity	[15]
Leaf, stem, and fruit	Chloroform, acetone, and methanol		*In vitro*	DPPH, ABTS, and FRAP assay	Antioxidant activity was the highest in MeAA extracts, while it was intermediate in MeAM and MeA extracts.	[39]
Antifertility activity						
Aerial part	Pet. ether, chloroform, ethanol, and aqueous	200 and 400 mg/kg	Albino Wistar rats	*In vivo* (anti-implantation effect)	Ethanol extract found significant anti-implantation and interruption of early pregnancy	[20]
Whole plant	95% ethanolic extract	200 and 400 mg/kg	Albino Wistar rats	*In vivo* (anti-implantation effect)	Extract dose 400 mg/kg showed significant anti-implantation potential	[47]
Hepatoprotective activity						
Aerial part	Polyphenolic fraction	300 and 600 mg/kg	Albino Wistar rats	Paracetamol-induced hepatotoxicity	Decreased ALT, AST, ALP, and TB	[40]
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	[46]

Table 3: Continued.

Part used	Extract/fraction	Dose tested/route of administration	Study model	Experimental models	Results	References
Antiproliferative activity						
Aerial part	Pet. ether, chloroform, ethanol, and aqueous	—	*In vitro*	Yeast *Saccharomyces cerevisiae* model	Chloroform and ethanol extracts showed significant antiproliferative activity	[46]
Antilithiatic activity						
Leaves	Ethanolic	2.5 ml of 0.2 g/ml solution	*In vitro*	—	Extract showed significant inhibition of calcium and phosphate accumulation	[35]
Anti-inflammatory activity						
Leaves	Ethanolic	200 and 400 mg/kg	Albino Wistar rats	Carrageenan-induced paw edema	Ethanol extracts showed significant anti-inflammatory activity	[31]
Analgesic activity						
Leaves	Ethanolic	200 and 400 mg/kg	Albino Wistar rats	Radiant heat tail flick method	Ethanol extracts showed significant analgesic activity	[31]

polyphenolic fraction of *R. hypocrateriformis*, no adverse effects or mortality were observed in the Swiss albino mice and Wistar albino rats at 4,000 mg kg^{-1} p/o dose. This was observed during 24 h period, and the extract was found to be safe at the given dose [40]. However, further detailed studies are required on different fractions and/or extracts for their toxicological effects on individual organs. Here, it should also be emphasized that the nature of *R. hypocrateriformis* can be affected by the environment and the picking time [19]. It is critical to implement authentication methods to monitor the nature and quality of the collected materials, remove the contaminated material, and ensure the biological activity associated with the resulting extracts for safety purposes, but also to ensure the reproducibility of the experiments [63, 64]. It is important to note that if the material authentication has not been done or is not sufficiently clear, its therapeutic significance is therefore meaningless. This critical prior authentication work is still conducted too infrequently and should be systematized for *R. hypocrateriformis* but also other medicinal herbs.

8. Conclusion

Based on the findings of the current study that sum up the traditional usages and pharmacological activities of its extracts and constituents, *R. hypocrateriformis* clearly appears as a promising medicinal herb with a wide range of beneficial and health-promoting properties. Nevertheless, it also appears that additional evidence from clinical studies as well as toxicological examinations are required. A particular effort should be made to put in place an adequate authentication method. Along these lines, the deliberate examinations on *R. hypocrateriformis* ought to be attempted to rationalize its ethnomedicinal uses and consider future pharmacological applications to take advantage of the properties of this herbal medicine.

Data Availability

The data used to support the findings of this study will be available on request from the corresponding author.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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