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Review

Hedychium spicatum: a systematic review on traditional uses, phytochemistry, pharmacology and future prospectus

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Abstract

Objectives *Hedychium spicatum* Buch. Ham. ex D.Don. (Family Zingiberaceae) is a rhizomatous herb, used in medicines, food, cosmetics and perfumery industries. Traditionally, it is widely used in treating inflammation, pain, asthma, foul breath, vomiting, diarrhoea, bronchitis, hiccough and blood diseases. This study systematically reviewed traditional and folk uses, pharmacological properties, bioactive compounds and market potential of *H. spicatum*. Research gaps and potential of future research have also been discussed.

Key findings Available literature indicates that research on this species is largely focused on phytochemical and pharmacological studies; however, propagation and modern interventions for high productivity have been contravened. These studies demonstrated that the rhizome of the species exhibited many valuable and medicinally important compounds, such as labdane terpenes, hedychinone and polyphenols. Many of the traditional uses of the species have been validated through the findings of pharmacological studies and biological properties of the extracts and pure compounds. Phytochemical constituents and related pharmacological activities have provided some suggestive scientific evidences for the various ethnomedicinal uses of the species in the treatment, control and management of diseases and for new drug discovery.

Summary Literature reveals that the species is lacking in exact scientific basis of the beneficial properties. Although, some other distinct biological properties identified in this species also opened new door way for its new applications. Therefore, the mentioned phytochemical constituents such as phenolic and flavonoids compounds; and related pharmacological activities such as antimicrobial, anti-inflammatory and antioxidant activity of the species have provided some suggestive scientific evidences for its potential in pharmaceutical, food and aromatic industries.

Research Highlights

- Traditional and folk uses of species as well as pharmacological properties, bioactive compounds and propagation of *H. spicatum* is reviewed.
- Different solvent extracts, isolated compounds and essential oils of the rhizome possess number of pharmacological properties such as anti-inflammatory, analgestic, anti-asthmatic, antidiabetic, cytotoxic, antimicrobial and anthelmintic activity.
- Although, some distinct biological properties identified in this species also opened new avenue for its new applications.
- A systematic approach for variety improvement, conservation and sustainable utilisation has been summarised.

Introduction

Therapeutic potential of medicinal plants has gained wide popularity all across the globe. This popularity can be judged from the fact that over 80% of the populations of developing countries relies on traditional medicine, 85% of the traditional medicine involves the use of plant extract,[1] and 70% of modern medicines are derived from medicinal plants.[2] Considering the effective use of medicinal plants and their parts singly or in combination with others for treating various human ailments, these medicinal plants have remained subject of enormous curiosity in the pharmaceutical and food industries.[3] Among others, family Zingiberaceae consisting of 52 genera and over 1500 species is known for its medicinal, cosmetics, fragrance and food value.[4] In India, this family represented by 22 genera and about 170 species.[4,5] Of these, major commercially cultivated species include *Zingiber officinale* (ginger), *Curcuma longa* (turmeric), *Amomum subulatum* (large cardamom), *Elettaria cardamomum* (small cardamom) and *Alpinia galanga* (Thai galangal). The genus *Hedychium*, which consists of over 80 species worldwide and reported to be used medicinally for various ailments, is yet to go in commercial cultivation.[6] The taxonomy of the genus *Hedychium* has remained controversial since the middle of the nineteenth century, and around 115 names of the genus have been published; however, very few were found to be authenticated and biologically valid.[7,8]

Hedychium spicatum Buch. Ham. ex D.Don. commonly known as 'spiked ginger lily', 'Van haldi' or 'Kapoorkachari' is considered as one of the important species for its medicinal and food value.[9,10] The species is native to south-eastern Asian countries in temperate and subtropical areas found within an altitude of 1000–2800 m asl.[11] It is being used in the traditional as well as in modern medicine, cosmetic and perfumery industries.[9–12] The overexploitation from wild for essential oil has put the species in the vulnerable[13] and rare categories.[14]

Over the last 4–5 decades, different research groups have explored this species in various aspects and validated many traditional uses through the use of laboratory animals and a range of *in-vitro* pharmacological approaches. Phytochemical research has expanded the knowledge about the metabolites present in the plant and revealed their potential to interact with biological systems; however, the mechanisms of action as well as the compounds involved in such activities remain mostly unknown or partially known. This review will provide baseline information on the subject, which can be further utilised for the development of better therapeutic agents and health products from *H. spicatum*. Although, review reports are available on the species, but those are largely in the form of compilation of existing information in specific area of research and are lacking with analysis of the results and trends for future research. It is, therefore, anticipated that the collection of comprehensive and up-to-date information and their critical analysis will be useful in creating new avenues for discovery of novel agents for curing various health ailments. To date, there are four reviews published on the *H. spicatum*. The first review published in 2010 was an overview of traditional uses, essential oil composition and trade value of the species.[15] This review listed, around 18 essential oil compounds and few other chemical constituents. The second review published in 2011 was focused on pharmacological activity of the species.[16] In this review, a limited number of compounds were listed without any other detailed description. In addition, pharmacognosy work carried out in the species has been covered in this review, and pharmacological properties of the species have been also discussed. The third review published in 2011 highlighted major oil constituents and 4–5 major pharmacological properties.[17] In forth review, Badola (2010) summarised ethnopharmacological importance and conservation status of the species.[14] As the species has been studied extensively for its phytochemistry and pharmacological activities, there is a need to analysed and discuss the complete scientific data available for this ethnomedicinally important species in the form of a systematic knowledge product. The main objective of this was to discuss in detail ethnomedicinal uses, phytochemistry, and *in-vitro* and *in-vivo* pharmacological activities studied with various extracts, fractions or isolated phytochemicals by different research groups. This paper, thus, systematically analysed available information w.r.t. traditional and folk uses, pharmacological properties, bioactive compounds, propagation and market trade of *H. spicatum*. Based on the in-depth review of each aspect, gap in research has also been highlighted. Also, a systematic approach for variety improvement, conservation and sustainable utilisation of *H. spicatum* has been developed.

Methodology

Literature survey was conducted for information collection. Scientific search engines, such as Google Scholar, ScienceDirect, PubMed, Mendeley, Scopus, SpringerLink and JSTOR, were used to retrieve information published in journals, conference papers, books, scientific reports of international, regional and national organisations and research thesis to carry out using a systematic and comprehensive literature search. Preset searching keywords, such as '*Hedychium spicatum*', 'Kapoor kachari', 'Kapur-Kachari' and 'Van haldi', were used to explore the relevant papers. The first 100 results from each search engine were retrieved, and literatures directly relevant to the species were

collected. Some reputed libraries of the Himalayan region were also consulted for enhancing the scientific database of the species. The results were then cross-referenced to generate maximum number of publications available in the species, and a total number of 137 publications were used in this review (during the time span of 1930–2017). All the papers were arranged and categorised in different thematic areas (i.e. pharmacology; phytochemical analysis; antimicrobial and anthelmintic properties; molecular genetics and phylogeny; propagation, tissue culture and cultivation; and distribution, review and others). Chemicals structures of some of the most important compounds present in essential oil were prepared with the help of the software 'Instant JChem' (version 6.2.1, Chem-Axon) with ChemDraw-like edit layout.

Botany, Morphology and Occurrence

The plant is a leafy herb, up to 2 m tall, having a camphoraceous horizontal rhizome, sessile leaves, broadly lanceolate, 30–60 cm long with long clasping sheaths and up to 10 cm wide (Figure 1). Flowers are fragrant with pale yellow colour, up to 5 cm long corolla tube with pink base, enclosing white staminoides and red anthers. The flowers are hermaphrodite.[9,11] The fruits are globose capsule, and three valves are reflected exposing numerous small seeds embedded in a red aril upon ripening. Flowering occurs in June to October and fruiting in October to November.[12] In the Himalayan region, the species is distributed in Jammu and Kashmir to Arunachal Pradesh including Nepal, Bhutan and also in Myanmar, North Thailand and some part of China.[18] The species is also reported from the hills of Thiruvananthpuram district of Kerala in south India (Figure 2).[19] It prefers sandy to sandy clay soil with high moisture content, acidic in nature and a low content of organic carbon.[20]

The *Hedychium* genus is diploid with basic chromosome number of x = 9, 10, 11, 12, 14 and 17.[21,22] The chromosome number in *H. spicatum* has been found to be 34 (n = 17).[23] Genome size (total genomic DNA content) of *H. spicatum* has been estimated as small as 2.94 pg (2C) or 2875.32 Mbp (2C) using a flow cytometer.[23] Histological studies of the species revealed that the rhizome consists of a delicate parenchyma. Most of the cells are loaded with starch grains, and a few contain a yellowish resin and essential oil. The epidermis is composed of several rows of compressed, nearly empty, reddish-brown cells.[24]

Folk and Traditional Medicinal Uses

The Indian medicinal system (Ayurveda) described the species is useful in the treatment of swelling, asthma, fever, and pain,[25] which mean that 'Shati' (*H. spicatum*) is also known as Palashi, Shatgrantha Subratha, Gandhmulika, Gandharika, Gandhvadhu and Prathupalashika in Sanskrit language.[25,26] It has pungent, light, bitter, strong, heating properties and used in grime of mouth, swelling, cough, asthma, pain and hiccough.[9,16,25] *H. spicatum* is being used in different parts of the Indian subcontinent since ancient time and having different names in different parts of world. In Ayurvedic, literature species possess 'Rasa' (tastes) such as 'Katu' (pungent – stimulatory for digestion), 'Tikta' (Bitter – tends to fairly dry) and 'Kashaya' (astringent – effect on digestion); 'Guna' (properties) such as 'Laghu' (light – purification of body channels and developing vigour and joy of the body) and 'Teekshna' (penetrating – fast in action and helps in evacuation of the body); 'Veerya' (potency) such as 'Ushna' (heating);

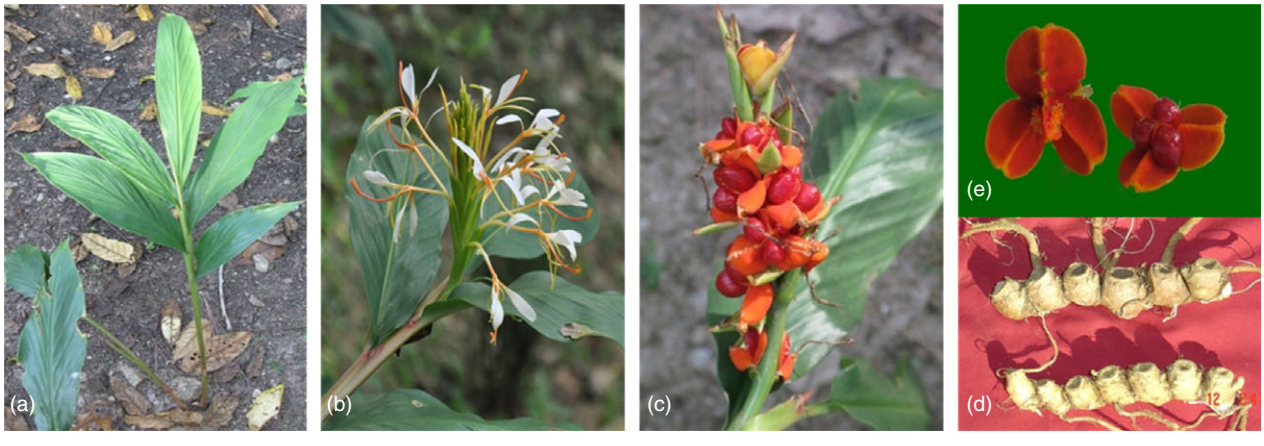

Figure 1 Different growth stages of *Hedychium spicatum* (a) a growing plant in its natural condition; (b) inflorescence of the species with pale yellow flowers with pink base; (c) mature spike showing the ripened seeds; (d) rhizome of the species; and (e) numerous small seeds embedded in a red aril. [Colour figure can be viewed at wileyonlinelibrary.com]

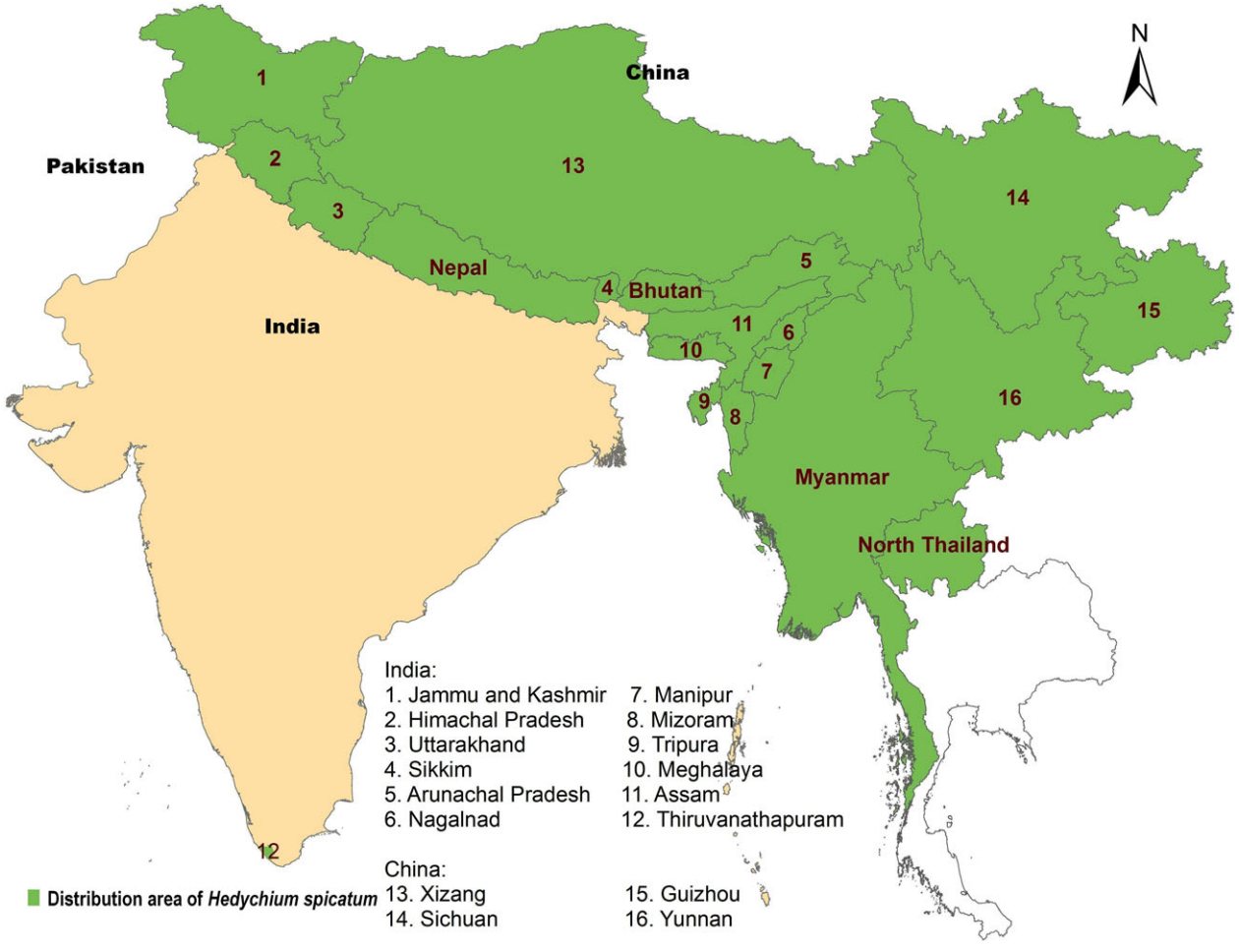

Figure 2 Broad distribution range of *Hedychium spicatum* across the world (map not to the scale). [Colour figure can be viewed at wileyonlinelibrary.com]

'Rogaghnata' (disease-curing properties) such as 'Sandhishotha' (swelling), 'Shoola' (pain), 'Dantashoola' (toothache), 'Mukhadurgandha' (halitosis), 'Vrana' (wound healing), 'Apatantraka' (apoplectic convulsions), 'Amavata' (rheumatoid arthritis), 'Aruchi' (tastelessness), 'Agnimandhya' (poor digestion), 'Adhamana' (flatulence), 'Udarashoola' (colic pain), 'Atisara' (diarrhoea), 'Arsha' (piles), 'Raktavikara' (blood disorder), 'Pratishyaya' (allergic rhinitis), 'Kasa' (cough), 'Shwasa' (respiratory disorder) and 'Hikka' (hiccup).[16,25] Also, in Tibetan medicine system, this species is widely used in many formulations such as PADMA-28, which was revived in Poland and now used against chronic inflammatory diseases, peripheral vascular occlusive disease and revealed promising results in intermittent claudication, atherosclerosis and chronic active hepatitis.[27]

Hedychium spicatum is traditionally used to cure various diseases through various preparations in different parts of India (Table 1). The therapeutic properties of the species are generally considered due to the presence of essential oil in the rhizomes. The rhizomes powder is used as an antimicrobial agent and as a poultice for various acnes and pains. The species is also an ingredient of some traditional Chinese medicine (TCM), Tibetan medicine and Unani medicinal system.[14] The powder as well as decoction of the rhizome is carminative, digestive and emmenagogue. A small cup of the rhizome decoction twice in a day is considered expectorant, stimulant, stomachic, tonic and vasodilator. One spoonful powder of rhizomes thrice a day is useful in the treatment of liver complaints and treating fever, vomiting, diarrhoea, inflammation, pain and snake bite. It is also used in the treatment of indigestion and poor circulation due to thickening of the blood.[14] The rhizome powder 3–4 g two times in a day is used in asthma, foul breath, bronchitis, hiccough, vomiting, tridosha and blood diseases. Rhizome powder is laxative to the bowel, and the rhizome decoction is tonic to the brain.[14] Also, the fruit of this species may be cooked and eaten with lentils in savoury

dishes.[28,29] Crushed dried rhizomes, both the bruised and the dried, are very aromatic with a fragrant, somewhat pungent smell similar to orris root but more powerful. The essential oil has a scent somewhat like hyacinths and highly perfumed for a considerable period. The dried rhizomes are also burnt as incense.[14]

In Tibetan medicine, the rhizome which has an acrid taste is given as two spoonful powder twice a day for heating potency. The species is widely used and shared in 19.43% of 175 known herbal formulations in Tibetan medicines.[14] In Indian medicines, the species finds place in 233 formulations and therapeutic index of its uses is 10.3%.[14] 'Abir', a fragrant coloured powder marketed for religious ceremonies, is prepared from its dried rhizomes.[18] In Andhra Pradesh, the dried rhizome is used in the treatment of asthma.[30] In the hills of Uttarakhand, rhizomes are boiled and eaten with salt, and the roasted powder is given for asthma, and decoction of rhizome with deodar sawdust for tuberculosis.[31,32] Powder of the species is used orally for body pain and inflammation; however, small pieces of fresh roots cooked in burning flame and chewed with one glass of hot milk for the treatment of asthma and internal injury.[15,33] The rhizome is also chewed by the local inhabitants of Uttarakhand to remove the bad smell from their teeth or mouth. The paste of fresh rhizome is given orally with hot water to the cattle and other domestic animals in case of stomach disorder.[33] However, in Manipur, the rhizome is cooked to prepare chutney.[14] In Himachal Pradesh, leaves are used in making mats for the home, combined with wheat straw, enhancing the durability of the product.[14]

Pharmacological Studies

This species is widely known as 'Kapur-kachari' in Ayurvedic preparations. The rhizomes are stomachic carminative, stimulant and tonic and are used in the treatment of dyspepsia, asthma and bronchitis.[34] Different biological and pharmacological properties of the species have been summarised in Table 2 and discussed below.

Table 1 Traditional uses of *Hedychium spicatum* in different parts of India

S.N	Plant part	Geographic Region	Dose/mode of administration	Used in	Reference
1	Rhizome powder	Whole India	–	Antimicrobial agent, laxative to brain	[14]
2	Rhizome poultice	Whole India	–	Various acnes and pains	[14]
3	Rhizome powder and decoction	Whole India	A small cup twice a day	Expectorent, stomachic, stimulant, tonic, vasodilator, carminative, expectorant and emmenogogue	[14,15]
4	Rhizome powder	Whole India	One spoonful powder three times in a day	Liver complains, fever, vomiting, diarrhoea, pain and inflammation, indigestion, poor circulation of blood due to thickness of blood	[14,15]
5	Rhizome powder	Whole India	4–5 mg three times in a day	Asthma, foul breaths, bronchitis, hiccough and vomiting,	[14,15]
6	Decoction of rhizome	Whole India	With deodar sawdust	Tuberculosis	[32]
7	Rhizome decoction	Whole India	–	Tonic to brain	[14]
8	Fruits	Whole India	With lentils	Food	[28,29]
9	Dried and crushed rhizome	Whole India	Burnt	Incense	[14]
10	Fresh rhizome	Whole India	Isolated oil	Scent	[14]
11	Rhizome powder	Whole India	Abir	Dye	[11]
12	Rhizome paste	Whole India	–	Hair loss	
13	Rhizome powder	Tibet	Paste	Heating impotency of female	[14]
14	Fresh rhizome	Hills of Uttarakhand	Boiled with salt	Food	[31]
15	Roasted powder	Hills of Uttarakhand	–	Asthma	[14,32]
16	Rhizome powder	Andhra Pradesh	–	Asthma	[14,30]
17	Root powder and small pieces	Hills of Uttarakhand	With milk	Chewed for asthma and internal injury	[33]
18	Fresh rhizome	Manipur	Cooked for making Chutney	Food	[14]

Anti-inflammatory activity

Alcoholic extract of the species possesses significant anti-inflammatory activity against carrageenan-induced hind-paw oedema in rat and mice. Hexane soluble extract showed the maximum activity of 42.16% in mice (200 mg/kg) and 27.2% in rats (100 mg/kg) compared to 37% of indomethacin (2 mg/kg) in mice and 27.2% of phenylbutazone (30 mg/kg) in rats.[35] The hexane and the benzene fractions of *Hedychium* inhibited the granuloma formation by 8 and 5%, respectively, at a dose of 200 mg/kg. Phenylbutazone (30 mg/kg) in the same experiment inhibited the granuloma formation by 25%. The ED_{50} value of the hexane extract in the phenylquinone writhing test was 284.53, and benzene extract was 93.28.[35] In other experiment, alcoholic extract of plant suspended in Tween-80 was orally administrated in Mice and Rats. In carrageenan-induced hind-paw oedema test, the alcoholic extract (30 mg/kg) significantly reduced the oedema volume. The percentage inhibition of oedema volume was 64.2%, while it reduced up to 49.1% in acetyl salicylic acid in a dose of 300 mg/kg.[36] The anti-inflammatory activity of the species was reported to be localised mainly due to furanoid diterpene compound 'Hedychinone', but a similar compound 7-hydroxy-hedychinone did not show any activity in mice as well as in rats.[36–38]

In another study, single dose of aqueous and ethanolic extracts (200 mg/kg) and indomethacin (10 mg/kg), 60 min before carrageenan administration in 18-h fasted rats, was administrated orally. The volume of rat hind paw up to the ankle joint was measured plethysmographically by the mercury displacement method just after administration of 0.1 ml of 1% carrageenan (0 h) was recorded in a successive interval of 1 h, 2 h and 3 h and revealed a significant decrease in paw volume against carrageenan-induced inflammation from 1 h onwards to 3 h of the study period (% decrease in inflammation aqueous extract – 11.00–28.10%; ethanolic extract – 8.79–25.62%; indomethacin – 16.49–41.32%, respectively).[39]

Analgesic activity

Analgesic activity of the species was demonstrated in acetic acid-induced writhing movements in mice and Randall–Selitto assay in rats. The ED_{50} of the hexane fraction in the phenylquinone writhing test was 284.53 ± 2.06 mg/kg while that of benzene extract was 93.28 ± 3.17 mg/kg.[35] In other studies, using hot plate test method, the reaction time in control mice was 7.66 s, and extract (30, 100 and 300 mg/kg) did not prolonged the reaction time to thermal stimuli suggested lack of activity in morphine type of analgesia. While in acetic acid-induced writhing movement and Randall–Sellitt assay, methods were used to test the peripherical analgesic activity of the extract. Effect of single oral dose at 30 and 100 mg/kg did not increase pain threshold as 1 h as compared to control value (60.83 g). However, extract (300 mg/kg) and aspirin (300 mg/kg) significantly decreased the pain threshold. Also, acetic acid-induced writhing count was 57.33, and administration of extract (300 mg/kg) and acetylsalicylic acid (300 mg/kg) significantly inhibited the writhing movements by 34.32 and 70.35, respectively. Thus, it concluded the peripheral analgesic activity of the plant.[36]

Anti-asthmatic and anti-allergic activities

Studies reported that 10 mg of powdered rhizome daily dose in 25 patients was found useful in recurrent paroxysmal attacks of dyspnoea (bronchial asthma) and relieved completely in 4 weeks time. Bronchi disappeared completely in 36% patients, the mean R/R was reduced by 25%, the vital capacity increased by 20%, and the mean absolute count decreased by 55.6%.[40] In an another clinical study of patients of tropical pulmonary eosinophilia, which were treated with the powder of *H. spicatum* in the dose of 6 g b.i.d. reported to reduce the eosionophil count by 60.54% after 4 weeks of treatment.[26] Different doses (100, 200 and 400 mg/kg) of aqueous and ethanolic extracts of *H. spicatum* administered orally to Guiana pigs (once daily for 7 days) indicated dose-dependent protection against histamine-induced bronchospasm in terms of increase in preconvulsive dyspnoea time from 39.2 to 75.1% and 25.8 to 65.1%, respectively, while chlorpheniramine maleate (2 mg/kg) showed an increase by 71.3% ($P < 0.001$). The result indicated comparable effects of both the extracts with CPM, a known H_1 blocker.[39]

Ulcer protection activity

Rats were fed with the extracts daily for 6 days, and after 7 day, rats were sacrificed. Results revealed dose-dependent protection against histamine-induced bronchospasm by increasing preconvulsive dysponea time from 39.2 to 75.1% ($P < 0.05$ to $P < 0.001$) and 25.8 to 65.1% ($P < 0.1$ to $P < 0.001$), respectively, while chlorpheniramine maleate (2 mg/kg) showed an increase by 71.3% ($P < 0.001$).[35] In another study, both aqueous and ethanolic extracts (200 mg/kg) when administered orally, once daily, to GP for 7 days showed protection against histamine-induced gastric ulcer (H1 mediated) in GP, and the result showed comparable effects of aquous (75% protection) and ethanolic extract (62.5% protection), while chlorpheniramine maleate (2 mg/kg) was able to protect 87.5% protection against gastric ulcers.[39]

Blood pressure-lowering activity

Extracts of the rhizome showed blood pressure-lowering activity in the benzene and hexane extracts of the species.[35] For instance, benzene extract when administered to cats at doses of 10 and 25 mg/kg intravenous, it was observed that the lower dose of benzene extract raised the blood pressure by 24 mm Hg in 7 min, and at the higher dose (25 mg/kg), the blood pressure was lowered by 50 mm Hg in 30 min. However, the hexane extract lowered the blood pressure by 80 mm Hg for 16 min at 10 mg/kg and more at 25 mg/kg dose followed by hyptotension lasting more than 30 min. However, no change was found in the response to adrenaline, acetylcoline, histamine and isoprenaline activity by both the extracts.[35]

Hepatoprotective properties

The ethyl acetate and alcohol extracts of dried rhizomes were shown significant hepatoprotective activity, lowering the enzymes such as serum glutamate oxaloacetate transaminase (SGOT) and Serum Glutamate Pyruvate Transaminase (SGPT) in albino rats intoxicated with Carbon tetrachloride (CCl_4) and also were comparable to marketed product.[41] In another study, the diterpene isolated from methanol extract of *H. spicatum* was subjected to *in-vitro* hepatoprotective activity using paracetamol-induced hepatotoxicity in primary rat hepatocytes by determining the change in hepatocytes viability and other parameters such as glutamic transaminase, glutamic pyruvic transaminase and total protein. The isolated diterpene showed significant protective effect by restoring altered parameters in the selected *in-vitro* model.[42] Another study demonstrated that hydroalcoholic extract of rhizomes of *H. spicatum* treatment restored depletion of liver antioxidants (superoxide dismutase, glutathione peroxidase and catalase) and prevents serum biomarkers (aspartate transferase, alanine aminotransferase, alkaline phosphatase and many others) significantly after both chloroform and paracetamol-induced hepatotoxicity in rat model.[43] The protective activity observed with hydroalcoholic extract of rhizomes (500 mg/kg, p.o.) was comparable to that of silymarin (100 mg/kg, p.o.).

Anticancer and cytotoxic properties

Labdane diterpenes isolated from the rhizomes of the species showed cytotoxicity against the THP-1 (human acute monocytic leukaemia), HL-60 (human promyelocytic leukaemia), A-375 (human malignant melanoma), A-549 (human lung carcinoma) colon cancer (Colo-205), skin cancer (A-431), breast cancer (MCF-7), lung cancer (A-549) and Chinese hamster ovary cells (CHO cell lines) cancerous cell lines.[44,45] More recently, volatile compounds in the essential oil of the rhizomes rich in 1,8-cineol, eudesmol, cubenol, spathulenol and α-cadinol exhibited *in-vitro* cytotoxic activities against human cancer cell lines, such as the lung (A549), colon (DLD-1,SW620), breast (MCF-7, MDA-MB-231), head and neck (FaDu), and cervix (HeLa). Different essential oil samples exhibited different level of cytotoxic properties.[46]

Antihyperglycaemic activity

Pretreatment of rats with hexane extract significantly reduced the sharp rise in blood glucose level for the first 30 min of poststarch feeding. To explore the mechanism of action of antihyperglycaemic activity, *in-vitro* rat intestinal α-glucosidase inhibitory potential of this extract was carried out using q-nitrophenyl-α-D-glucopyranoside as substrate. It was found that hexane extract displayed 21.2% inhibition of the enzyme at primary screening concentration (100 μg/ml). Some isolated compounds such as spicatanol and hedychenone showed antihyperglycaemic activity by inhibiting intestinal α-glucosidase due to the presence of α, β-unsaturated γ-lactone and furan ring.[47]

Nootropic effects and memory restorative activity

Study on n-butanol fraction of rhizomes has revealed some nootropic effects in experimental mice.[48] The elevated plus maze and double-unit mirrored chamber test were used to assess the nootrophic effects of n-butanol fraction of the rhizomes. Results have confirmed the memory restorative activity, which highlighted the use of species for treatment of dementia during Alzheimer's disease. Preliminary results indicated the presence of saponins in the n-butanol extract using HPTLC.[48]

Hair growth promoting activity

The hair growth promotion activity of hexane extract (33%) and pentadecane (30%) showed good reduction in hair growth time, where as minoxidil, a positive control, showed an excellent activity (47%) in the standard method, but it had other side effects. Even though the plant is being used in the preparation of hair oils, so far no reports on the compounds are responsible for hair growth promotion activity.[49]

Toxicity studies

Toxicity studies of the species have not much been carried out. Only a published report stated that the hexane as well as benzene extracts had a weak CNS-depressant effect as

Table 2 Pharmacological and medicinal properties of the species

S.N.	Pharmacological properties	Responsible compounds /extract	Model	Method	Description	Reference
1	Anti-inflammatory activity	Hexane and benzene extract	Mice and rats	Carrageenan-induced oedema and cotton pellet test	Reduced 42.16% in mice (200 mg/kg) and 27.2% in rats (100 mg/kg) compared to 37% of indomethacin (2 mg/kg) in mice and 27.2% of phenylbutazone (30 mg/kg) in rats. Also, inhibited the granuloma formation by 8 and 5%, respectively, (200 mg/kg s compared to 25% in phenylbutazone (30 mg/kg).	[35]
2	Anti-inflammatory activity	Ethanolic extract	Mice and rats	Carrageenan-induced hind-paw oedema test	Ethanolic extract (300 mg/kg) significantly reduced the oedema volume (64.2%) as compare to 49.1% in acetyl salicylic acid (300 mg/kg).	[36]
3	Anti-inflammatory activity	Aqueous and ethanolic extracts	Rat	Hind paw up to the ankle joint measured plethysmographically by mercury displacement method	Percentage decrease in inflammation in aqueous extract was as 11.00 to 28.10%; ethanolic extract – 8.79–25.62%; indomethacin - 16.49–41.32%, respectively.	[37]
4	Analgesic activity	Hexane and benzene extract	Mice	Writhing movements assay	The ED_{50} of the hexane fraction in the phenylquinone writhing test was 284.53 mg/kg while that of benzene extract was 93.28 mg/kg.	[35]
5	Analgesic activity	Ethanolic extract	Mice and rats	Writhing movement and Randall–Sellitto assay	Extract (300 mg/kg) and aspirin (300 mg/kg) significantly increased the pain threshold. Acetic acid-induced writhing count was 57.33, and administration of extract (300 mg/kg) and acetylsalicylic acid (300 mg/kg) acid significantly inhibited the writhing movements by 34.32 and 70.35, respectively.	[36]
6	Ulcerogenic activity	Hexane and benzene extract	Rats	Reduction in ulcerogenic index	Hexane extract had an ulcerogenic index of 0.08 while benzene extract had an index of 0.02. Phenylbutazone (30 mg/kg) gave an ulcerogenic index of 0.3.	[35]
7	Ulcer protection activity	Aqueous and ethanolic extracts	Guinea pigs	Protection against histamine-induced gastric ulcer	Protection against histamine-induced gastric ulcer (H1 mediated) in aquous (75% protection) and ethanolic extract (62.5% protection) while chlorpheniramine maleate, (2 mg/kg) was able to protect 87.5% protection against gastric ulcers.	[39]
8	Toxicity	Hexane and benzene extract	Mice and rats	Acute toxicity	Weak CNS-depressant effect and decreased locomotor activity at high doses 600 mg/kg as compared to the control. The lethal dose (LD_{50}) of both the extracts was more than 1000 mg/kg after 24 h with no mortality	[35]

Table 2 (*Continued*)

S.N.	Pharmacological properties	Responsible compounds /extract	Model	Method	Description	Reference
9	Toxicity	Ethanolic extract	Mice and rats	Acute toxicity	Graded dose of the extract (2.5 to 10 g/kg) did not produce any acute toxicity and death during 72 h of observation.	[37]
10	Toxicity	Hexane and benzene extract	Mice and rats	Acute toxicity	No harmful effects were observed after acute toxicity study even with 10 times of the effective dose (2 g/kg) of the extracts.	[39]
11	Anti-asthmatic activity	Aqueous and ethanolic extracts	Humans	Recovery from recurrent paroxysmal attacks of bronchial asthma	Recurrent paroxysmal attacks of bronchial asthma completely relieved after 4 weeks, and bronchi disappeared completely in patients. The mean R/R was reduced by 25%, the vital capacity increased by 20%, and the mean absolute count decreased by 55.6%.	[40]
12	Anti-asthmatic activity	Rhizome powder	Humans	Reduction in eosionophil count	A dose of 6 gm b.i.d. reduced the eosionophil count by 60.54% after 4 weeks of treatment.	[26]
13	Anti-asthmatic and anti-allergic activity	Aqueous and ethanolic extracts	Guinea pigs	Protection against histamine-induced bronchospasm by preconvulsive dyspnoea	Dose-dependent protection against histamine-induced bronchospasm by increasing Preconvulsive dyspnoea time from 39.2 to 75.1% ($P < 0.05$ to $P < 0.001$) and 25.8 to 65.1% ($P < 0.1$ to $P < 0.001$), respectively, while chlorpheniramine maleate (2 mg/kg) showed an increase by 71.3% ($P < 0.001$).	[39]
14	Blood pressure-lowering activity	Benzene and hexane extracts	Cats	Reduction in blood pressure	Hexane extract lowered the blood pressure by 80 mm Hg for 16 min (10 mg/kg) and sharp decrease in blood pressure lasting more than 30 min by 25 mg/kg dose.	[35]
16	Anti-asthmatic activity	Ethyl acetate and alcohol extracts	Albino rats	Enzymatic assays	Exhibited hepatoprotective activity by lowering Serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) enzymes intoxicated with chloroform.	[41]
17	Hepatoprotective properties	Methanol extract	Rats	*In-vitro* activity against paracetamol-induced hepatotoxicity	In paracetamol-induced hepatotoxicity in primary rat hepatocytes, isolated diterpene showed significant protective effect by restoring altered parameters in the selected *in-vitro* model.	[42]

Table 2 (*Continued*)

S.N.	Pharmacological properties	Responsible compounds /extract	Model	Method	Description	Reference
18	Hepatoprotective properties	Hydroalcoholic extract	Rats	Recovery of serum antioxidant enzymes and biomarkers	Restored depletion of liver antioxidants (superoxide dismutase, glutathione peroxidase and catalase) and prevents serum biomarkers (aspartate transferase, alanine aminotransferase, alkaline phosphatase, etc.) after chloroform and paracetamol-induced hepatotoxicity (500 mg/kg, p.o.) which was comparable to silymarin (100 mg/kg, p.o.).	[43]
19	Anticancer and cytotoxic properties	Labdane diterpenes	*In-vitro* cells	Cytotoxic activity against cancer cell lines	Isolated labdane diterpenes showed cytotoxicity against the THP-1 (human acute monocytic leukaemia), HL-60 (human promyelocytic leukaemia), A-375 (human malignant melanoma), A-549 (human lung carcinoma) colon cancer (Colo-205), skin cancer (A-431), breast cancer (MCF-7), lung cancer (A-549) and Chinese hamster ovary cells (CHO cell lines) cell lines.	[44,45]
20	Anticancer and cytotoxic properties	Volatile compounds	*In-vitro* cells	Cytotoxic activity against cancer cell lines	1,8-cineole, eudesmol, cubenol, spathulenol and a-cadinol exhibited cytotoxic activities against human cancer cell lines that is the lung (A549), colon (DLD-1,SW620), breast (MCF-7, MDA-MB-231), head and neck (FaDu) and cervix (HeLa).	[46]
21	Antihyperglycaemic activity	Hexane extract and spicatanol and hedychenone	Rats	Protection against Histamine induced gastric ulcers	Significantly reduced the sharp rise in blood glucose level for the first 30 min of poststarch feeding. Hexane extract (100 μg/ml) displayed 21.2% inhibition of the enzyme. Spicatanol and hedychenone also inhibited intestinal α-glucosidase.	[47]
22	Nootropic effects memory restorative activity	n-Butanol fraction	Mice	Maze and double-unit mirrored chamber test	n-Butanol fraction exhibited the memory restorative activity, thus, can be used for treatment of dementia during Alzheimer's disease.	[48]
23	Tranquillising activity	Essential oil	Rats	Reduction in secondary conditioned avoidance response (SCR)	80% blockade in secondary conditioned avoidance response (SCR) and 40% inhibition in conditioned avoidance response which was compared to chloromazine.	[50]
24	Hair growth promoting activity	Hexane extract and pentadecane	Rats	Reduction in hair growth time	Reduction in hair growth time by hexane extract (33%) and Pentadecane (30%), where as minoxidil, a positive control showed an excellent activity (47%) in the standard method but it had other side effects.	[49]

Table 2 (*Continued*)

S.N.	Pharmacological properties	Responsible compounds /extract	Model	Method	Description	Reference
25	Antioxidant activity	Essential oil	*In-vitro*	Radical scavenging activity	Strong antioxidant activities such as radical scavenging by ABTS, DPPH and FRAP assays, metal ion chelating and reducing properties.	[10,51–54]
26	Antioxidant activity	Solvent extracts	*In-vitro*	Radical scavenging activity	Methanolic extract of rhizome has also shown antioxidant properties using ABTS, DPPH and FRAP assays, which was attributed to the presence of phenolic compounds.	[9,55,56]
27	Anthelmintic properties	Essential oil	Earthworm, tapeworm, hookworm and nodular worms	Inhibitory activity against Earthworm, tapeworm, hookworm and nodular worms	Higher anthelmintic activity of extract was reported than piperazine phosphate against earthworm and tapeworm.	[67]
28	Anthelmintic properties	Ethanolic extracts	*In-vitro*	Inhibitory activity against *Pheretima posthuma*	Death time was 146 min in extract and 124.83 min in albendazole at 25 mg/mL, while it was 137.5 min for extracts and 95.5 min for albendazole at 50 mg/ml.	[68]
29	Anthelmintic properties	Methanolic extracts	*In-vitro*	Inhibitory activity against *Pheretima posthuma*	Time taken for *Pheretima posthuma* for paralysis and death was comparable with standard that is piperazine citrate.	[88]
30	Fungitoxic property	Essential oil	*In-vitro*	Inhibitory activity against Various fungal strains	Fungitoxic property of essential oil has also been reported.	[65]
31	Antibacterial properties	Various solvent extracts	*In-vitro*	*Inhibitory activity against Salmonella typhi, Escherichia coli, Streptococcus aureus* and others	Inhibitory activity against Gram (+) and Gram (–) bacterium strain, including *Salmonella typhi, Escherichia coli* and a strain of methicelin- and vaneomycin-resistant *Streptococcus aureus*	[61,63,76]
32	Antibacterial properties	Essential oil	*In-vitro*	Inhibitory activity against *Salmonella enterica enterica*.	Showed some antibacterial activity, by producing inhibition zones of 9–16 mm in diameter and found to be effective against *Salmonella enterica enterica*.	[51,60]
33	Antifungal properties	Various solvent extracts	*In-vitro*	Inhibitory activity against *Candida albicans* and *C. glabrata*.	Inhibitory activity against many fungal strains such as *Candida albicans* and *C. glabrata*.	[63,76]
34	Antifungal properties	Essential oil	*In-vitro*	Inhibitory activity against *Aspergillus flavus* and *F. verticillioide*	Totally inhibited the growth of pregerminated spores of *Aspergillus* that produce two major classes of mycotoxins, aflatoxin and fumonisin	[66]
35	Pediculicidal activity	Essential oil	*In-vitro* assays	Inhibitory activity against *Pediculus humanus capitis*, *Pthirus pubis* and *Pediculus humanus humanus*	At 5, 2 and 1% concentration, the essential oil showed more significant activity than 1% permethrin-based product	[70]

evidenced by decreased locomotor activity as compared to the control group, and it manifests only at high doses 600 mg/kg or more. The lethal dose (LD_{50}) of both the extracts was more than 1000 mg/kg after 24 h, and there was no mortality even at this dose.[35] Also, in an acute toxicity experiments conducted by Tandan *et al.* (1997), graded dose of the methanolic extract (2.5 to 10 g/kg) did not produce any acute toxicity and death during 72 h of observation in rats.[36] Recently, no harmful effects were observed in the rhizome extracts of this plant after acute toxicity study even with 10 times of the effective dose of the extracts, indicating the safety status of its rhizomes.[39] Thus, mice tolerated very high dose of extract without producing, and harmful effect suggested that the extract possessed high level of safety.

Tranquillising activity

The therapeutic activity of the rhizomes of the species was initially assumed due to the presence of essential oil, which showed mild tranquillising activity of short duration on central nervous system. Studies of the essential oil of *H. spicatum* rhizomes showed 80% blockade in secondary conditioned avoidance response (SCR) and 40% inhibition in conditioned avoidance response as compared to chlorpromazine in rats.[50]

Antioxidant and radical scavenging properties

Essential oil obtained from rhizomes of *H. spicatum* has also shown strong antioxidant activities such as radical scavenging, metal ion chelating and reducing properties.[51,52] Methanolic extract of rhizome has also shown antioxidant properties, which was correlated with the presence of phenolic compounds.[10,53–55] A variation was recorded in antioxidant activity in essential oil and methanolic extract collected from different localities of Himalaya.[10,51,52] Other nonphenolic antioxidant compounds are also reported in its rhizomes such as xanthophylls, α-carotene, β-carotene and DL-α-tachopherol etc.[56,57]

Antimicrobial activity

Essential oil of the rhizomes possesses strong activity against a wide range of bacteria and fungus species.[51,58–64] Essential oil showed some antibacterial activity, by producing inhibition zones of 9–16 mm in diameter and found to be effective against *Salmonella enterica enterica*.[51] Extract of various solvents showed inhibitory activity against Gram (+) and Gram (−) bacterium strain, including a strain of methicelin- and vaneomycin-resistant *Streptococcus aureus* and fungal strains.[63] Fungitoxic property of essential oil has also been reported.[65] Essential oil of the species totally inhibited the growth of pregerminated spores of *A. flavus* and *F. verticillioides* that produce two major classes of mycotoxins, aflatoxin and fumonisin.[66] Interestingly, plethora of studies is available on *in-vitro* activity of crude solvent extract, but none of these are focused on isolated compound or solvent fraction of the species.

Anthelmintic and pediculicidal activity

Anthelmintic properties are also reported in the essential oil of the species. Higher anthelmintic activity was reported in extract of the species than piperazine phosphate against earthworm and tapeworm, but the activity against hookworm and nodular worm was lower than hexylresorcinol.[67] Also, at 25 mg/ml concentration of extract, death time of tapeworm was observed as 146 ± 2.83 min in extract and 124.83 ± 6.99 min in albendazole, while at 50 mg/ml concentration, activity against the worms was 137.5 ± 9.75 min for extracts and 95.5 ± 4.84 min for albendazole.[68] The anthelmintic activity of rhizomes of *H. spicatum* against adult Indian earthworms, *Pheretima posthuma,* was evaluated. The time taken for each worm for paralysis and death was determined. The results were compared with the standard, that is piperazine citrate. Methanol extract of produced dose-dependent anthelmintic activity where as aqueous extract was not all effective. Methanol extract showed better anthelmintic activity when compared with the standard drug piperazine citrate.[16,69] The rhizome of the species also has insect repelling activity, and essential oil of the species showed strong pediculicidal activity, which is required for the treatment of head lice infection. At 5, 2 and 1% concentration, the essential oil showed more significant activity than 1% permethrin-based product.[70]

Phytochemical Studies

Rhizomes of *Hedychium* harbour various nutritionally and medicinally important compounds extracted in essential oil and solvent extract. Aromatic rootstock contains essential oil, saccharin, albumin, starch and mucilage. The essential oil obtained from the rhizome of the species founds as 0.06 to 6.12%[71] and 1,8-cineole (27–75%) exhibited as a major component. α- and β-Pinene, linalool, 10-epi-γ-eudesmol and β-slinene were also reported from the essential oil of the rhizome in significant quality. Besides, (E)-caryophyllene, (-)spathulenol, 1-epi-cubenol, 4-terpineol, 4-thujanol, borneol, camphene, camphor, caryophyllene oxide, cubebene, elemol, germacrene d-4-ol, hedycaryol, limonene, sabinene, spathulenol, terpine-4-ol, α-cadinol, α-eudesmol, α-humulene, α-selinene, α-terpinene, α-terpineol, α-thujene, β-caryophyllene, β-cadinene, β-eudesmol, β-farnesene, β-himachalene, β-myrcene,

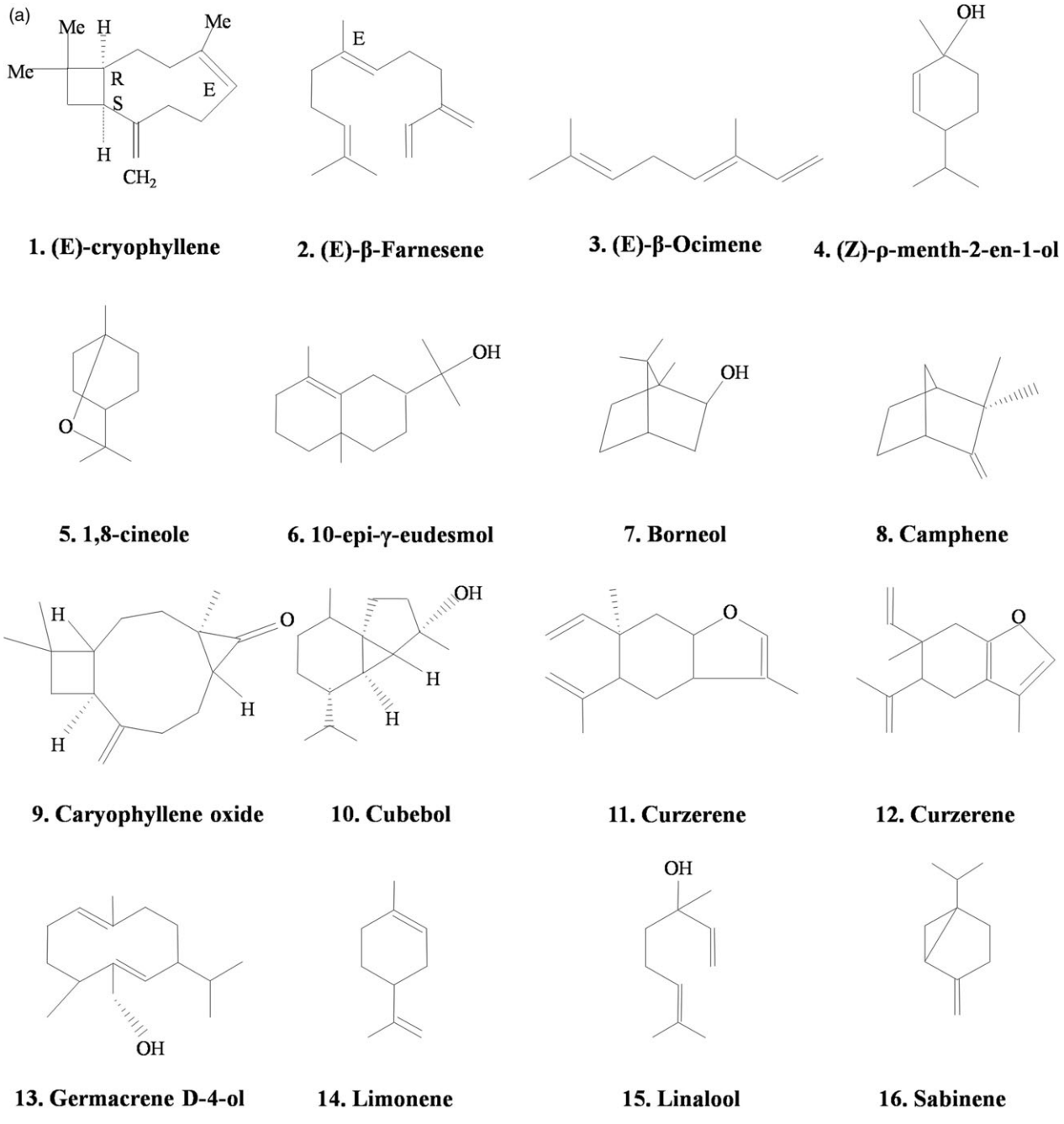

Figure 3 (a, b) Structure of selected chemical compounds present in the essential oil of *Hedychium spicatum*.

β-phellandrene, γ-muurolene, p-cymene and δ-cadinene have also been reported in the essential oil of the species (Figure 3).[46,51,52,60,70–78] Variation in the essential oil components such as sabinene, trans-m-mentha-2,8-dienes, *p*-cymene, 1,8-cineole and terpine-4-ol in different species of *Hedychium* genus, that is *H. coronarium*, *H. aurantiacum*, *H. ellipticu*m and *H. spicatum* from Uttarakhand Himalaya and *H. venustum*, *H. coronarium*, *H. flavescens* and *H. spicatum* from south India, has been reported.[51,76,80] The essential oil obtained from leaves of the species showed higher amount of β-pinene (about 40%) as compared to rhizome essential oil, but 1,8-Cineole (11.9%) was found in lesser quantity.[77] A comparative composition of essential oil of rhizomes in different studies has been presented in Table 3. The essential oil of *H. spicatum* obtained from different

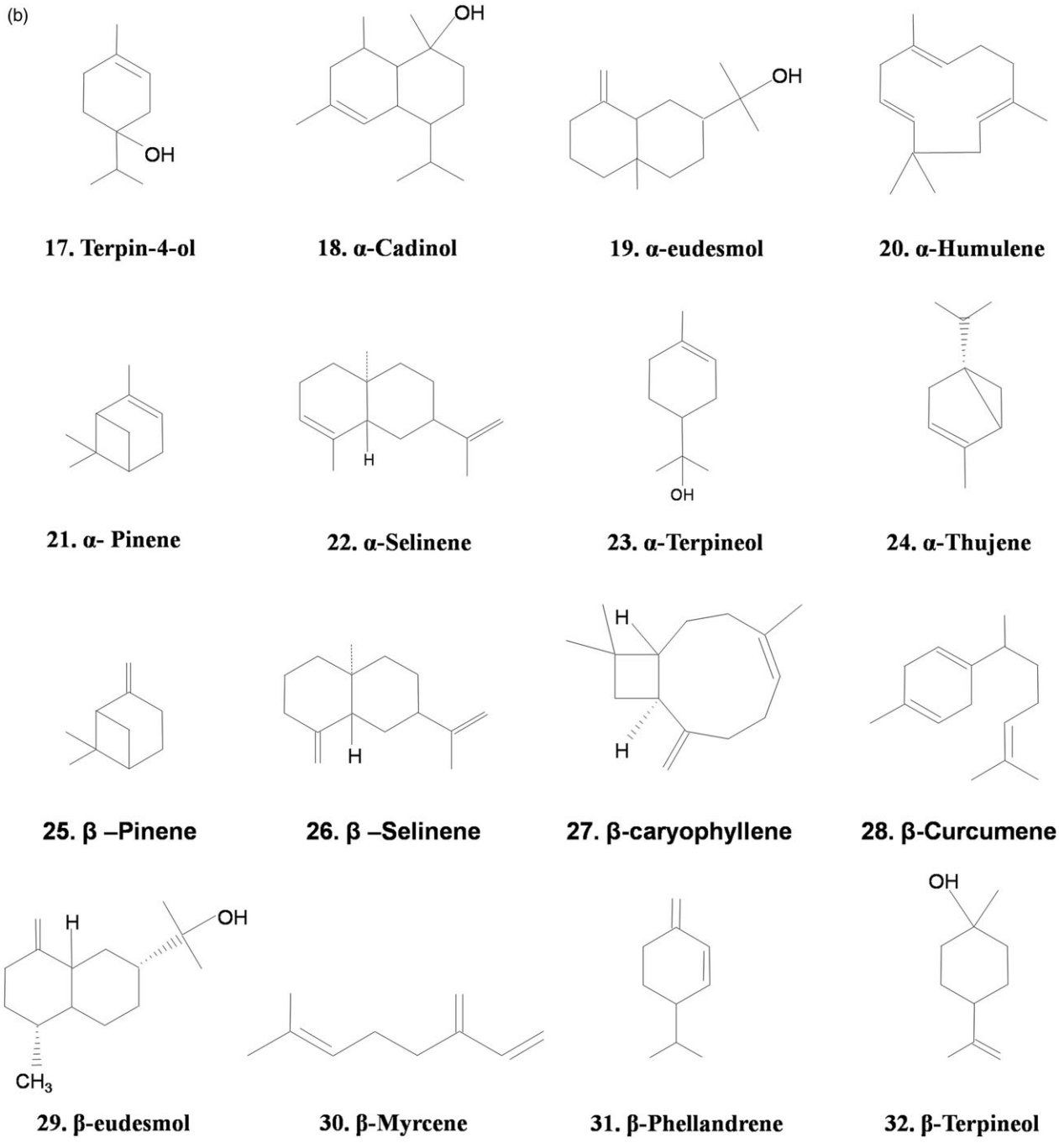

Figure 3 Continued.

locations of Himalayan region has shown great variation in its components especially in 1,8-cineole, terpine-4-ol and 10-epi-γ-eudesmol, eudesmol, cubenol, spathulenol and α-cadinol,[46,51,52,78] thus, influenced its antioxidant properties,[51,52] antimicrobial properties[51,76] and cytotoxic properties.[46] Essential oil samples of *H. spicatum* rhizomes were carried out and found to be active against various human cancer cell lines.[46] These location-specific and genotypic variations can be important for superior germplasm selection. Essential oil from *H. spicatum* inhibited the growth of pregerminated spores of *Aspergillus flavus* and *Fusarium verticillioides* two of the most important fungal species responsible for mycotoxin contamination of several food crops.[66]

Table 3 Composition of essential oil in *Hedychium spicatum* revealed by different authors in different part of the world

SN	Compounds name	Garg *et al.*,[a] (1977) [72]	Dixit *et al.*,[a] (1977) [73]	Nigam *et al.*,[a] (1979) [74]	Bottini *et al.*,[a] (1987) [75]	Sabulal *et al.*,[a,b] (2007) [76]	Joshi *et al.*,[a] (2008) [51]	Verma *et al.*,[a] (2010) [77]	Prakash *et al.*,[a] (2010) [60]	Raina and Negi,[a] (2015) [78]	Koundal *et al.*,[c] (2015) [52]	Semwal *et al.*,[a] (2015) [79]	Mishra *et al.*,[a] (2016) [46]
1	α-Pinene	1.44	1.40	4.50	–	–	1.80–3.70	0.70	1.10	0.10–4.40	0.90–1.5	9.12	0.00–0.53
2	α-Thujene	–	–	–	–	–	0.10–5.80	–	–	–	–	–	–
3	Camphene	–	–	–	–	0.30	0.10–0.40	–	–	0.10–1.20	0.00–0.10	–	–
4	Sabinene	–	–	–	–	0.10	0.00–13.00	–	–	0.10–1.30	0.00–0.40	–	–
5	β-Pinene	1.41	1.40	–	–	1.30	4.00–5.90	1.60	1.40	0.50–3.20	2.20–3.80	9.24	0.13–0.67
6	Myrcene	–	–	–	–	0.10	–	–	–	0.60–2.50	0.00–0.20	–	–
7	β-Myrcene	–	–	–	–	–	0.30–8.70	0.10	–	–	–	–	–
8	α-Phellandrene	–	–	–	–	0.10	–	–	–	–	–	–	–
9	δ-2-Carene	–	–	–	–	0.10	–	–	–	–	–	–	–
10	σ^3-Carene	–	1.40	1.80	–	–	–	–	–	–	–	–	–
11	α-Terpinene	–	–	–	–	0.10	–	–	–	–	–	–	–
12	p-Cymene	0.48	5.00	9.60	–	0.10	0.00–0.70	0.10	–	0.30–1.10	–	–	–
13	β-Terpineol	–	–	1.80	–	–	–	–	–	–	–	–	–
14	Limonene	–	1.30	170	–	0.50	0.00–0.20	0.40	–	–	–	6.42	0.08–0.60
15	1,8-Cineole	56.25	37.20	27.10	29.70	44.30	4.30–45.70	64.00	17.60	15.50–58.20	50.10–72.10	30.84	5.00–25.78
16	(E) -β-Ocimene	–	–	–	–	–	–	0.10	–	–	–	–	–
17	β-Phelllendrene	–	4.50	7.00	–	–	–	0.30	–	–	–	–	–
18	4-Thujeol	–	–	–	–	–	–	–	–	–	–	–	0.00–0.10
19	Cis-linalool oxide	–	–	–	–	0.20	–	–	–	–	–	–	–
20	γ-terpinene	–	–	–	–	0.10	–	–	–	–	–	4.30	–
21	*trans* -Linalool oxide	–	–	–	–	0.20	–	–	–	–	–	–	–
22	Terpinolene	0.17	–	–	–	–	–	–	–	–	–	–	–
23	Linalool	6.75	18.00	16.60	4.40	25.60	0.60–6.40	0.50	2.60	0.80–10.60	0.80–2.80	5.29	0.40–4.05
24	(Z)-ρ-menth-2-en-1-ol	–	–	–	–	–	–	0.70	–	–	–	–	–
25	Camphor	–	–	–	–	0.40	–	–	–	–	–	2.16	–
26	Borneol	0.31	–	–	–	–	0.00–0.60	0.10	0.10	0.40–2.70	–	1.53	–
27	δ-Terpineol	–	–	–	–	0.30	–	–	–	–	–	–	–
28	Terpin-4-ol	–	–	–	0.70	1.30	0.90–16.50	0.10	0.20	0.70–15.20	–	–	–
29	4-Terpineol	–	–	–	–	–	–	–	–	–	0.50–1.00	–	0.17–0.51
30	α-Terpineol	1.56	–	6.50	1.00	1.90	0.10–1.70	0.20	–	0.30–2.30	1.40–1.80	1.48	0.35–0.87
31	Copaene	–	–	–	–	–	–	–	–	–	–	–	0.03–0.59
32	α-Cubebene	–	–	–	–	–	–	–	0.10	–	–	–	0.00–0.10
33	Furfuryl hexanoate	–	–	–	–	–	–	–	0.10	–	–	–	–
34	β-Cadinene	–	–	–	–	–	–	–	–	–	–	–	1.74–6.77
35	β-Elemene	–	–	–	–	–	–	–	0.20	–	–	–	–
36	α-Gurjunene	–	–	–	–	–	–	–	–	–	–	4.51	–
37	α-(Z)-Bergamotene	–	–	–	–	0.70	–	–	0.10	–	–	–	–

Table 3 (*Continued*)

SN	Compounds name	Garg *et al.*,[a] (1977) [72]	Dixit *et al.*,[a] (1977) [73]	Nigam *et al.*,[a] (1979) [74]	Bottini *et al.*,[a] (1987) [75]	Sabulal *et al.*,[a,b] (2007) [76]	Joshi *et al.*,[a] (2008) [51]	Verma *et al.*,[a] (2010) [77]	Prakash *et al.*,[a] (2010) [60]	Raina and Negi,[a] (2015) [78]	Koundal *et al.*,[c] (2015) [52]	Semwal *et al.*,[a] (2015) [79]	Mishra *et al.*,[a] (2016) [46]
38	(Z)-Caryophyllene	–	–	–	–	–	–	–	0.10	–	–	–	–
39	β-Caryophyllene	0.12	24.10	3.50	–	0.20	–	0.10	1.50	0.40–1.40	0.20–0.70	–	0.57–1.46
40	α-Humulene	–	–	–	–	0.30	0.00–0.50	0.20	2.00	0.30–2.60	0.30–1.20	–	–
41	α-Himachalene	–	–	–	–	–	–	–	0.10	–	–	–	–
42	allo-aromadendrene	–	–	–	–	0.10	–	–	–	–	–	–	–
43	9-epi-β-caryophyllene	–	–	–	–	0.10	–	–	–	–	–	–	–
44	Dehydroaromadendrane	–	–	–	–	–	–	–	1.00	–	–	–	–
45	γ-Muurolene	–	–	–	–	–	–	0.10	1.50	–	0.00–0.60	–	–
46	β-Curcumene	–	–	–	–	–	0.60–1.10	–	–	–	–	–	–
47	β-Selinene	–	–	–	–	–	1.30–6.80	2.30	–	0.90–8.60	–	–	–
48	*epi*-Cubebol	–	–	–	–	0.20	–	–	–	–	–	–	–
49	α-Selinene	–	–	–	–	–	0.10–1.40	–	3.20	0.8–9.50	–	–	–
50	Curzerene	–	–	–	–	–	0.20–1.20	–	–	–	–	–	–
51	δ-Selinene	–	–	–	–	–	–	4.40	–	–	–	–	–
52	α-Muurolene	–	–	–	–	0.20	–	–	–	1.50	–	–	0.41–1.19
53	τ-Elemene	–	–	–	–	–	–	–	–	–	–	–	0.00–0.57
54	Cubenol	–	–	–	–	–	–	–	–	–	–	–	1.65–8.85
55	γ-Cadinene	0.73	–	–	–	0.30	–	–	5.40	–	0.30–1.70	–	–
56	Cubebol	–	–	–	–	–	0.00–0.80	–	–	–	–	–	–
57	β-Farnesene	–	–	–	–	–	0.00–2.00	–	0.10	0.70–3.90	0.50–2.80	–	0.06–0.40
58	β-Himachalene	–	–	–	–	0.10	–	–	–	–	–	–	–
59	δ-Cadinene	–	–	–	–	0.90	–	–	7.50	–	0.90–5.90	–	–
60	Elemol	–	–	–	–	–	–	–	–	0.70–16.60	1.30–4.10	3.31	–
61	(+)–Elemol	–	4.20	–	8.50	–	–	–	–	–	–	–	–
62	*trans*-Nerolidol (furanoid)	–	–	–	–	–	–	–	–	–	–	–	0.00–0.93
63	Hedycaryol	–	–	–	–	2.60	–	–	–	–	–	–	1.10–22.38
64	Germacrene D	–	–	–	–	–	–	–	–	–	–	–	0.00–0.38
65	cis-sesquisabinene hydrate	–	–	–	–	0.70	–	–	–	–	–	–	–
66	(–)Spathulenol	–	–	–	–	–	–	–	–	–	–	–	1.67–13.83
67	Germacrene D-4-ol	–	–	–	–	–	0.00–2.00	1.50	6.80	0.40–2.10	0.40–0.60	–	0.47–3.51
68	(E) –Nerolidol	–	–	–	–	0.30	–	–	0.60	–	–	–	–
69	Spathulenol	–	–	–	–	0.60	–	–	–	0.60–3.50	–	–	–
70	Caryophyllene oxide	–	0.50	–	–	0.50	–	1.30	–	1.40–3.20	0.00–0.50	–	0.04–0.23
71	Aromadendrene	–	–	–	–	–	–	–	–	–	–	–	0.00–0.18
72	Humulene epoxide II	–	–	–	–	–	–	–	–	0.70–3.10	–	–	–
73	10-epi-γ-eudesmol	–	–	–	5.10	–	1.20–12.40	3.00	9.70	0.20–13.90	1.00–5.70	–	–
74	γ-Eudesmol	–	–	–	–	–	–	–	–	1.60–6.20	–	–	–

Table 3 (*Continued*)

SN	Compounds name	Garg *et al.*,[a] (1977) [72]	Dixit *et al.*,[a] (1977) [73]	Nigam *et al.*,[a] (1979) [74]	Bottini *et al.*,[a] (1987) [75]	Sabulal *et al.*,[a,b] (2007) [76]	Joshi *et al.*,[a] (2008) [51]	Verma *et al.*,[a] (2010) [77]	Prakash *et al.*,[a] (2010) [60]	Raina and Negi,[a] (2015) [78]	Koundal *et al.*,[c] (2015) [52]	Semwal *et al.*,[a] (2015) [79]	Mishra *et al.*,[a] (2016) [46]
75	Hinesol	–	–	–	–	–	–	–	–	–	0.90–2.30	–	–
76	1-epi-Cubenol	–	–	–	–	0.50	–	–	6.90	–	–	–	–
77	τ-Eudesmol	–	–	–	–	–	–	–	–	–	–	–	0.00–12.35
78	*epi*-α-Cadinol	–	–	–	–	–	–	1.10	–	–	–	–	–
79	Eremoligenol	–	–	–	–	1.30	–	–	–	–	–	–	–
80	α-Cadinol	–	–	–	5.30	2.30	1.20-3.30	2.40	–	4.50–11.20	–	–	–
81	β-Eudesmol	–	–	–	12.60	2.20	–	2.20	–	2.70–10.80	5.70–14.70	14.5	0.00–26.57
82	α-eudesmol	–	–	–	4.80	2.30	–	–	17	–	–	2.97	0.24–1.29
83	τ-Muurolene	–	–	–	–	–	–	–	–	–	–	–	0.00–0.98
84	τ-Muurollol	–	–	–	–	4.40	–	–	–	–	–	–	0.00–6.63
85	α-Copaene	–	–	–	–	–	–	–	0.50	–	–	–	–
86	Agarospirol	–	–	–	–	0.90	–	–	–	–	–	–	–
87	8-epi-β-bisabolol	–	–	–	–	0.50	–	–	–	–	–	–	–
88	Oplopanone	–	–	–	–	–	–	–	0.10	–	–	–	–

[a]Population collected from Utttarakhand State of India (west Himalaya). [b]Populations collected from Kerala State of India (south India). [c]Populations collected from Himachal Pradesh State of India (west Himalaya).

Rhizome of the species possesses starch, resins, organic acids, ethyl esters of para-methoxy-cinnamic acid, d-sabinene sesquiterpenes.[12,24,81] Plethora of literature is available on chemical studies of this species (Table 4). Furanoid diterpene such as hedychenone and 7-hydroxyhedychenone was isolated from rhizome of the species, which is considered as one of the major active molecules in the species.[37,82] Sharma *et al.* (1975) found some terpinoids such as β-sitosterol in the benzene fraction of the rhizome.[83] Some labdane diterpenes and other diterpones that is 9-hydroxy-hedychenone, chrysin, hedychilactone B, hedychilactone C, hedychilactone D, teptochrysin, yunnacoronarin A, 18-spicatanol, 6-oxo-7,11,13-labdatrien-16,15-olide, 7-hydroxyhedychenone, hedychenone, spicatanol methyl ether, 4-methoxy ethyl cinnamate, 7-hydroxy hydichinal, 8 (12)-drimene, coronarin-E, ethyl cinnamate, spicatanoic acid and yunnacoranarin-D have been isolated from rhizomes of the species (Table 4).[44,45,47] Recently, some more sesquiterpenes, such as 5,6-dehydro-α-eudesmal, γ-eudesmal, 3-hydroxy-γ-eudesmal, anhuienosol, 1,2-dehydrocarrissonol, 4,15-epoxy-eudesmol, eudesma-4(15)-ene-β-11diol, crytomeridiol, β-eudesmol, 3-hydroxy-β-eudesmol, mucrolidin, oplapanone, α-terpineol, elemol, dehydrocarissone, σ^7-β-eudesmol, opladiol, hydroxy-cryptomeridiol, β-caryophyllene oxide, coniferaldehyde and ethylferulate, have been isolated from the rhizome of the species.[84] Other compounds investigated in the species are phenolic content, xanthophylls, α-carotene, β-carotene, DL-α-tocopherol, *p*-methoxy-cinnamic acid, pentadecane and ethyl *p*-methoxycinnamate.[49,56,81] Among these, many important secondary metabolites such as, phenolic content, xanthophylls, α-carotene, β-carotene, DL-α-tocopherol and γ-tocopherol have been quantified in the species, which showed variation among different growing conditions, spatial or geographical distribution and seasons.[56,57,85,86] Recently, it has been reported that the accumulation of phenolic compounds in natural populations of the species is affected by genetic diversity pattern.[86] These variations provide opportunities for verity development for quality traits and standardisation of cultivation practices.

Two furanoid diterpenes, hedychenone and 7-hydroxyhedychenone isolated from the hexane fraction were tested for reduction in carrageenan-induced oedema, and hedychenone (2 mg/kg) had significant activity (38.65 and 20.4%), but 7-hydroxyhedychenone had no activity in mice as well as in rats.[35] β-Sitosterol isolated from the rhizome of the *H. spicatum* exhibited strong *in-vitro* anthelmintic activity against *Pheretima posthuma*. Molecular docking studies revealed that β-sitosterol binds very efficiently within the active pockets of tubulin, even better than the orientation of standard drug piperazine citrate.[69] Stigmasterol-β-D-glucoside also revealed anthelmintic activity against *Pheretima posthuma* in similar manner.[88]

Table 4 Phytochemical diversity in the *Hedychium spicatum*

S.N.	Active constituents	Nature of compound	Reference
1	Hedychenone	Furanoid diterpene	[37]
2	7-Hydroxyhedychenone	Furanoid diterpene	[78]
3	9-Hydroxy-hedychenone	Furanoid diterpene	[44]
4	Chrysin	Flavonoid	[44]
5	Hedychilactone B	Labdane diterpene	[44]
6	Hedychilactone C	Labdane diterpene	[44]
7	Hedychilactone D	Labdane diterpene	[44]
8	Teptochrysin	Flavonoid	[44]
9	Yunnacoronarin A	Labdane diterpene	[44]
10	18-spicatanol	Labdane diterpene	[45]
11	6-Oxo-7,11,13-labdatrien-16,15-olide	Labdane diterpene	[45]
12	Spicatanol methyl ether	Labdane diterpene	[45]
13	4-Methoxy ethyl cinnamate	Phenolic compounds	[47]
14	7-Hydroxy hydichinal	Labdane diterpines	[47]
15	8(12) drimene	Labdane diterpene	[47]
16	Coronarin-E	Labdane diterpene	[44,47]
17	Ethyl cinnamate	Phenolic compounds	[47,80]
18	Spicatanoic acid	Labdane diterpene	[47]
19	Yunnacoranarin-D	Labdane diterpene	[47]
20	Ethyl-*trans-p*-methoxy cinnamate	Phenolic compound	[84]
21	Phenolic content	Phenolic compound	[9,47]
22	Xanthophylls	Carotenoids	[47]
23	α-Carotene	Carotenoids	[47]
24	β-Carotene	Carotenoids	[47]
25	DL-α-tocopherol	Methylated phenol	[47,84]
26	γ-Tocopherol	Methylated phenol	[84]
27	*p*-Methoxy cinnamic acid	Phenolic compound	[77]
28	Pentadecane	Alkane hydrocarbon	[49]
29	Ethyl *p*-methoxycinnamate	Phenolic compound	[49]
30	β -Sitosterol	Phytosterols	[79,82]
31	Lupeol	Triterpenoid	[82]
32	Stigmasterol- D-glucoside	Phytosterols	[82]
33	β -Sitosterol-D-glucoside	Phytosterols	[82]
34	Ethylferulate	Sesquiterpene	[80]
35	5,6-Dehydro-α-eudesmal	Sesquiterpene	[80]
36	γ-Eudesmal	Sesquiterpene	[80]
37	3-Hydroxy-γ-eudesmal	Sesquiterpene	[80]
38	Anhuienosol	Sesquiterpene	[80]
39	1,2-Dehydrocarrissonol	Sesquiterpene	[80]
40	4,15-Epoxy-eudesmol	Sesquiterpene	[80]
41	Eudesma-4(15)-ene-β-11diol	Sesquiterpene	[80]
42	Crytomeridiol	Sesquiterpene	[80]
43	β-Eudesmol	Sesquiterpene	[80]
44	3-Hydroxy-β-eudesmol	Sesquiterpene	[80]
45	Mucrolidin	Sesquiterpene	[80]
46	Oplapanone	Sesquiterpene	[80]
47	α-Terpineol	Sesquiterpene	[80]
48	Elemol	Sesquiterpene	[80]
49	Dehydrocarissone	Sesquiterpene	[80]
50	Δ^7-β-Eudesmol	Sesquiterpene	[80]
51	Opladiol	Sesquiterpene	[80]
52	Hydroxy-cryptomeridiol	Sesquiterpene	[80]
53	β-caryophyllene oxide	Sesquiterpene	[80]
54	Coniferaldehyde	Sesquiterpene	[80]

Isolated compounds from the species have been well-characterised for cytotoxicological studies with respect to their growth inhibitory properties against the A-549, SK-N-SH, MCF-7 and HeLa cancer cell lines. Results from a study revealed that structural differences in the labdane diterpenes significantly affected the anticancer activity. IC_{50} values of *in-vitro* cytotoxicity were observed between 7.69 and 49.29 μg/ml for labdane diterpenes, and between 20.36 and 54.21 μg/ml for isoflavanoids against Colo-205 (colon cancer), A-431 (skin cancer), MCF-7 (breast cancer), A-549 (lung cancer) and CHO (Chinese hamster ovary cells) cell lines. 7-Hydroxy,6-oxo-7,11,13-labdatrien-16,15-olide exhibited significant activity on Colo-205, A-431 and MCF-7 and CHO cell lines and moderate activity on A-549 cell lines. 9-hydroxy,15,16-epoxy-7,11,13(16)14-labdatetraen-6-one also shown moderate activity Colo-205, A-431 and significant activity on CHO cell lines.[44] In another study, other labdane diterpenes isolated from the species, such as 7-hydroxy hedichinal-exhibited potent activity and spicatanoic acid, showed moderate activities on the tested cell lines with the IC_{50} value ranging from 14.14 μg/ml to 36.56 μg/ml. The furan moiety and hydroxyl group at C-7 position are markedly affected the activity profile of the labdane diterpenes class compounds. It is interesting that yunnacoronarin-D, the structural analogue of 7-hydroxy hedichinal, showed weak activity, and this may be due to lack of hydroxyl group at C-7 position.[45] Hedychenone, a labdane diterpenoid, showed potent *in-vitro* cytotoxic activity against cancerous cells. Structure–activity relationship studies indicated that furanoid ring has a greater impact on cytotoxicity than that of the decalone nucleus. However, dimerisation through C-8 significantly enhanced the cytotoxic activity of the hedychenone.[87] Sesquiterpenes isolated from the species, namely, anhuienosol, were the most cytotoxic against HeLa cells with IC_{50} value of 0.30 μg/ml, followed by 5,6-dehydro-α-eudesmal and 1,2-dehydrocarrissonol, at 1.80 μg/ml. The hydroxyl group at C-1 significantly enhanced the cytotoxicity of anhuienosol against HeLa cell lines, which suggested that the relative hydrophilicity of this part of the molecule contributes to the activity and presence of the aldehyde group at C-4, and hydroxyl group at C-3 does not influenced the toxicities of the molecules.[84]

However, spicatanol, spicatanol methyl ether and hedychenone displayed most potent α-glucosidase inhibitory activity (IC_{50}, 34.1 μM). This reveals that the presence of α,β-unsaturated γ-lactone and furan ring in labdane diterpenes is required for α-glucosidase inhibition. The presence of –OH group at C-16 in lactone ring strongly increases enzyme inhibitory potential as against –OMe group.[47]

GC-MS analysis of fatty acid content obtained by headspace solid-phase microextraction of rhizome revealed the presence of linoleic acid (18:2ω6), α-linolenic acid (18:3ω3), oleic acid (18:1ω9), palmitic acid (16:0), stearic acid (18:0), α-linolenic acid (18:3ω6), eicosanoic acid (20:0), eicosenoic acid (20:1) and eicosadienoic acid (20:2), etc. Among these linoleic acid (18:2ω6), α-linolenic acid (18:3ω3) and oleic acid (18:1ω9) were found higher in wild plant material as compared to cultivated conditions.[57] Similarly, variation in γ-tocopherol, α- tocopherol, hedychenone, ethyl-trans-*p*-methoxy cinnamate, ethyl cinnamate, d-sabinene and mineral content exhibited variation in wild and cultivated conditions.[56,57]

Propagation, Variety Improvement and Market Demand

For extraction of active constituents, a large scale availability of quality material can be ensured by effective propagation methods. Propagation methods of the species at the commercial level have not been developed. Some tissue culture-based and small-scale nursery-based protocols are available which can be further scaled up for commercial level. Reports revealed that seed germination percentage enhanced using various hormonal concentrations and soil types in the field.[89] In an another study, Bisht *et al.* (2015) observed that in laboratory conditions, scarification of seeds and dark conditions during germination favours quick and uniform seed germination of this species as compared to light conditions.[90] Rana *et al.* (2004)[91] developed cultivation methods for propagation of the species in hilly regions. Some other authors reported that the maximum economic yield of rhizomes is obtained in the beds prepared on slope in comparison with beds prepared in plain, rows and furrows. However, best results are obtained in the bed prepared in slope and supplemented with forest litter.[92] Yield of the plant is influenced by plant distance in fields, and a higher plant-to-plant spacing (40 cm × 40 cm) provides more biomass and yield.[93] Bisht *et al.* (2015)[94] observed that the incubation of seeds in indole-acetic acid (100 μg/ml) for 24 h showed highest germination (95.83%) with mean germination time (84.00 days). On the contrary, nontreated seeds exhibited only 37.50–60.42% germination. Imbibitions by the seeds were fast in first 2 h, and then, it increased gradually up to 24 h, thus, confirming that 24 h is sufficient to imbibe the plant growth regulators (PGRs). PGRs are also found useful in reducing time for initiation of germination, time for maximum germination, mean germination time and germination rate. Furthermore, Giri and Tamta (2012) found that various presowing treatments, gibberellic acid (GA_3) and potassium nitrate (KNO_3) were significantly effective treatments regarding *in-vitro* seed germination of this species.[95] Similarly, incubation of seeds in indole-acetic acid (100 μg/ml) for 24 h showed highest germination of

95.83 ± 3.6% with mean germination time of 84.00 ± 7.0 days. On the contrary, nontreated seeds exhibited only 37.50–60.42% germination.[96] An another study showed maximum seed germination percentage (42.14 ± 26.42%) in garden soil with litter and farmyard manure (2 : 1 : 1, respectively) with higher plant height (8.35 ± 1.60 cm), leaf length (8.44 ± 0.99 cm), leaf width (3.73 ± 0.33 cm) and biomass parameters.[97] Also in another study, germination percentage was achieved up to 32.33% for different concentrations of IBA and IAA concentrations during 2004 and 2005, and higher concentration of IAA, IBA and NAA produced plant with higher height.[98]

Koul *et al.* (2005) established multiple shoots from preexisting buds of the rhizome using MS medium supplemented with BAP and IAA[99] and successfully transferred to the field with 99% rooting and 80–85% field survival. Shoot elongation and higher shooting percentage were also reported in MS medium supplemented with 5.0 mM kinetin and 1.0 mM IAA.[32] Direct somatic embryos were developed by Giri and Tanta (2013) on cotyledon explants of zygotic embryos on MS supplemented with a high concentration of NAA (20.0 μM).[100] Induction of high frequency shoot multiplication (83.33%), number of shoots per explant (3.86 shoots) and average number of shoots per flask (19.33 shoots) were reported in selected cytokines combinations when seed raised shoot tips of the species were taken as explants.[101] *In-vitro* rooting was observed using lower concentration of indole-3-butyric acid (2.5 μM). Well rooted and healthy plantlets were obtained after 2 months of hardening and were then transferred to the field (1990 m) with 90.0% survival.[101] However, reports are limited on the effect of different propagation methods and treatment on quality of produce which ultimately determines the quality of product or formulation.

The genomic sequence information is very limited for this species, and only 28 nucleotide sequences are available in NCBI database (as on dated 20/12/2016); thus, sequence-specific markers are not easily available. Hence, marker-assisted selection (MAS) and breeding for quality improvement are not possible in the species. The cultivar of the species 'Himkachari' has been released by CSIR-IHBT, Palampur, (Himachal Pradesh, India), in 2006. The crop was harvested after 2 years of growth in the field and has a good average yield of fresh rhizomes and essential oil on a dry weight basis.[102] Still, the species is harvested from the wild thus causing vulnerability in its wild stock. Considering this, the species has been prioritised by Government of India and Government of Uttarakhand state for cultivation and conservation.[103,104] Market value of the species varies among the different parts of the country ranging from Rs. 25 to 40 per kg.[105] It is estimated that in India, annual demand of the species is approximately 400 tons per year.[106] Trade and economics of the species are highly influenced by adulterants of the herb. *Kaempferia galangal, Zingiber officinale* and *Curcuma zedoria* are mostly used as adulterants along with *H. spicatum*.[107] *H. spicatum* has a good market potential in India as demand is increasing rapidly.

Rhizomes of the species are marketed from different Himalayan regions.[24] Large traders often employ local agents to collect raw material from villagers, who are lured economically for *in situ* harvesting. In Himachal Pradesh, the species is mentioned under export permit after 1993 by the State Forest Department with Rs. 70 per quintal royalties. In Sikkim, by 2001, the state government has completely banned the harvesting of herbs from the wild due to fast depletion in the wild.[14] Overexploitation of the species for its valuable medicinal properties by pharmaceutical, essential oil and other industries indicates the severe threat to its existence. *H. spicatum* has become a vulnerable oil-bearing plant due to reduction in its populations by more than 20% in last 10 years.[12,99,108] Therefore, there is an urgent need to develop agrotechniques of the species so that demand of the species can be fulfilled, and pressure in its natural habitat can be reduced.

Future Prospective and Conclusion

The species is used for the treatment of inflammation, pain, asthma, foul breath, fever, vomiting, diarrhoea, bronchitis, hiccough, vomiting and diseases of blood, some of which (e.g. anti-inflammatory, analgestic, anti-asthmatic, etc.) are validated pharmacological and clinical assays. However, recent research on *H. spicatum* largely focused on assessing the antidiabetic, cytotoxic, antimicrobial, anthelmintic activity, which sometime seems irrelevant to its traditional uses. The labdane terpene, hedychinone, polyphenols and terpenoids appear to be the major constituents in the species. Although contemporary research involving in the species is promising, it is too preliminary and sometimes too general to be used to explain and support some of the ethnomedicinal uses. In addition, some of the pharmacological activities assessed so far, for example, antimicrobial, antioxidant, cytotoxic and antiproliferative, were routine screenings lacking molecular mechanisms of the pharmacological effects of the species.

The pharmacological and medicinal studies of *H. spicatum* highlight the immense potential of this plant for the treatment of various ailments. All the marketed products of the species are available in the form of polyherbal formulations. Therefore, it is difficult to attribute a particular phytochemical of an herb for a specific property. Also, plant extracts are a complex mixture of phytochemicals; therefore, a particular pharmacological property may be due to synergistic effect of existing constituents of the species. All

such issues can be addressed by adopting a system biology approach, wherein a very large number of components at the level of genome, transcriptome, proteome and metabolome, as well as physiological parameters, bioactivity, etc. can be studied to infer correlations to understand the mechanism of action. A key technology in the system biology is metaboliomics, which allows for the identification and quantification of metabolites of the cell.[109] Adverse effects of the species in different conditions have not been determined; however, this is desirable for drug safety, for both polyherbal formulations and single phytochemical-based drug. Generally, it has been hypothesised that a particular compound-rich fraction/extract of the species may be responsible for a particular activity,[35,44,45,47] but actual and reasonable action mechanism has not been understood and needs to be addressed immediately. Similarly, statistical significant difference and relationships among phytochemicals with any activity have not been mentioned, as a result, efficacy of the drug for a particular property can not been estimated.

Effectiveness of medicinal plants dependents upon amount of active constituents present in the species, which may be highly influenced by different factors such as, growing conditions, seasons, climatic conditions, sun light exposure, altitude, along with genetic make-up etc.[10,56,85,86,110–114] Therefore, selection of elite plants is essentially required, which contain higher phytochemical content and good pharmacological activity for obtaining maximum benefits. Elite individuals/genotypes can be selected on the basis of high quantity of active ingredient, which may be further confirmed through molecular studies. Marker-assisted selection for high-yielding varieties/genotypes is another popular technique that can be used. Thereafter, elites may be propagated through micropropagation or conventional methods. Tissue culture has some advantages over conventional methods. It provides clonally uniform genotypes for constant supply of plants for commercial production of active principles. It also helps stabilise any seasonality and geographical changes on active principles. It will create a sound platform for conservation strategies of species under natural conditions, as well as creating opportunities for generating income. Controlled growth system for cultivation also made it feasible to contemplate manipulation of phenotypic variation in the context of medicinally important phytochemicals and uniform supply of the raw material. It also increases productivity and reduces the level of undesired compounds, thus, increasing uniformity and predictability of the extract.[113]

This species has a great prospect for future due to its increasing demand. Sustainable multiplication of the species may be adopted if a suitable cultivation/agrotechnique could be developed. This can be achieved by plant breeding, which essentially requires identification of the genetic variation of traits and knowledge of the impact of environmental parameters on its expression. Variation in antioxidant properties, essential oil composition, phenolic content and other phytochemical composition in different population and geographic location provides baseline data for future breeding programmes for variety improvement and suitable conditions for cultivation.[9,42,46,52] Variation in these constituents can be used for breeding programmes as the success of any breeding programme depends on identifying the genetic variation in traits and knowledge of the impact of environmental parameters on its expression.[61,114] A great variation was also observed in certain phytochemicals such as total phenolic compounds and antioxidant activity in plant material collected from different sites of Uttarakhand, Himalaya and different development stages.[10,86] These studies might be more relevant in relation to genetic make-up of the species which showed a high variability among the populations. Moderate genetic differentiation and high genetic diversity have been detected among populations of the species using isozyme markers.[115] Similarly, genetic diversity analysis by RAPD markers showed a high genetic diversity among the populations.[116] It assured future research for development of high-yielding varieties. Due to limited availability of sequence information in NCBI database, specific and functional genetic markers are not easy to develop for diversity characterisation, marker-assisted selection and genetic mapping.

H. spicatum is gaining attention of researchers due to its high market demand, and there has been an acceleration of publications of the species since 2006 (Figure 4a). The literature available on the species indicate that research has focused on phytochemical (~32.8%); followed by pharmacological studies (~25.5%); antimicrobial, and insecticidal activity (~15.3%); and propagation/tissue culture (~12.4%); distribution and other reviews (~7.3%); and molecular biology or modern technological interventions for its varietal improvement (~6.6%) (Figure 4b). Interestingly, traditional medicinal uses of the species were validated by determining pharmacological properties earlier (in 1980s and 1990s), and modern research (after 2000) is largely focused on routine screening of some generalised pharmacological properties. Modern biotechnological tools may be adopted for elite population/genotype selection, which may be used for further breeding programmes. Next-generation sequencing (NGS)-based RNA-seq/ transcriptome analysis may provide deeper insight for biosynthesis of active metabolites, which can be utilised for quality improvement by pathway engineering, transgenic development and genetic mapping in such nonreference crop species. These modern biotechnological tools provide opportunities to understand the regulatory mechanism of key genes

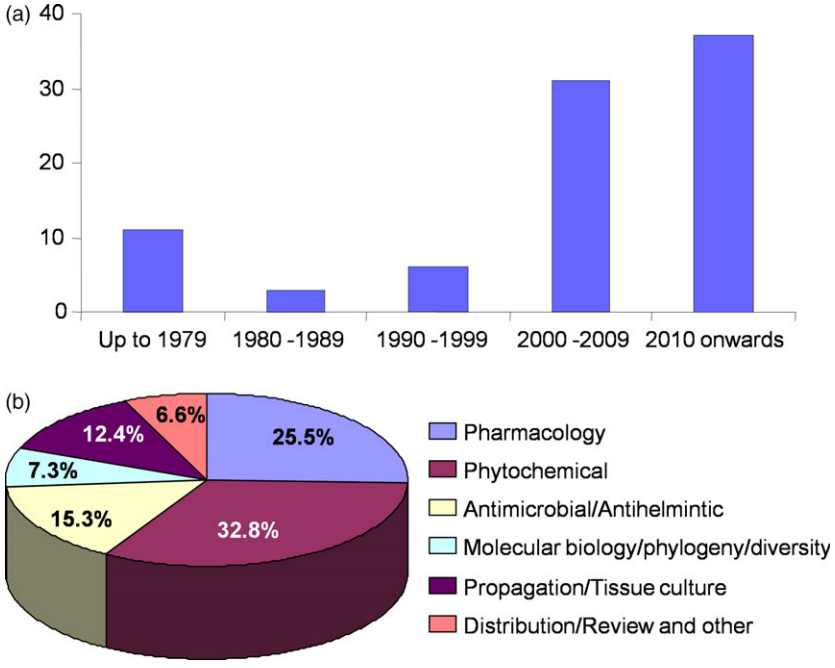

Figure 4 Publication in *Hedychium spicatum* (a) trend of research output (publications) during different time periods up to 2015; and (b) categorisation of research papers available in the species into different subject area. [Colour figure can be viewed at wileyonlinelibrary.com]

responsible for biosynthesis of active molecules in this species. So, pathway engineering may be a suitable tool for maximising the level of important compounds. On the other hand, different environmental conditions may alter species phenology, chemical composition, change in physiological and biochemical responses, level of enzymes, gene expression, metabolites, etc., which may result altered pharmacological effects. Recently researches have applied different stresses during the cultivation of medicinal plants for stimulating accumulation of pharmaceutical products and essential oils.[117] Thus, optimisation of a suitable agrotechnique will have additional benefits for quality planting material with higher productivity.

This review has revealed *H. spicatum* as a highly important medicinal plant exhibiting valuable pharmacological properties. Literature reveals that the species is lacking in exact scientific basis of the beneficial properties. Although, these distinct biological properties identified in this species also opened new door way for its new applications. The mentioned phytochemical constituents such as phenolic and flavonoids compounds; and related pharmacological activities such as antimicrobial, anti-inflammatory and antioxidant activity have provided some suggestive scientific evidence for the various ethnomedicinal uses of the species in the treatment, control and management of infections diseases, diarrhoea and spoilage of its food products. Therefore, thorough studies to explain its medicinal properties are urgently needed. It would be worthwhile embarking on intensive scientific experimentation and investigations on advanced cultivation technologies, genetic inheritance of traits, phytochemical investigation, bioactivity and pharmacology so as real potential of species can be harnessed.

Declarations

Conflict of interest

The authors declare no conflict of interest.

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