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## **HEDYCHIUM: A COMPREHENSIVE EXPLORATION OF ITS PHYTOCHEMICAL AND MEDICINAL SIGNIFICANCE**

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### **ABSTRACT**

Plants in the Zingiberaceae family, including the genus *Hedychium*, have been extensively studied for their phytochemistry and pharmacological properties. Numerous bioactive compounds have been isolated from these plants, demonstrating significant pharmacological effects. *Hedychium* species are commonly used in folk medicine across various countries. *Hedychium* genus is recognized for its significant medicinal properties, which are utilized in various folk remedies worldwide. These plants are employed to address a range of health issues such as allergies, cancer, diabetes, inflammation, rheumatism, and skin ailments. Additionally, they serve as analgesics, antimicrobials, anti-helminthics, antioxidants, and insect repellents. Numerous studies have been conducted to investigate the efficacy and mechanisms of these plants, focusing on their essential oils, extracts, and pure secondary metabolites. Among these species, *Hedychium coronarium* and *Hedychium spicatum* are the most extensively researched. This review highlights the potential of *Hedychium* plants as a source of natural medicinal products, its phyto-constituents and pharmacological properties. Due to unauthorized harvesting and uncontrolled use of its rhizome extract in producing different kinds of drugs, the original population of this species has vanished. It's necessary to reintroduce this plant into its native environment for its conservation.

**Keywords: Zingiberaceae, volatile oil, myrcene, limonene, p-cymene, pharmacological properties**

## INTRODUCTION

The Indian Himalayan Region (IHR) is a vast storehouse of plant diversity, originated from its wide range of altitudes and diverse geographic areas. It has been identified as the most abundant reserve of medicinal and aromatic plants. The wide range of plant species in the IHR thrives due to its diverse landscape characteristics, providing numerous habitats [1]. Covering an area of around 591,000 km<sup>2</sup>, the IHR includes five different biogeographic areas with altitude ranging from 200 to 8000 m [2]. Among the various geographical regions, the Western Himalayas are renowned for their abundant variety of medicinal and aromatic plants.

The Indian Himalayan region provides habitat to about 18,440 plants species. Among these, there are 8,000 angiosperms, 44 gymnosperms, and 6,001 pteridophytes, 736 bryophytes, 1,159 lichens, and 6,900 fungi species. The majority of plant types found in the IHR region are utilized by the local residents for various purposes such as medicine, sustenance, energy, animal feed, and construction material. Among all the vascular plant species, there are 1,748 species recognized for their medicinal properties [3].

India contributes approximately 45,000 plant species to global biodiversity, although the actual figure could be closer to 60,000 since many regions of India remain unexplored botanically. Among these,

around 15,000-18,000 species are seed-bearing plants. The diverse climatic conditions across India, ranging from alpine in the Himalayas to tropical wet in the south and arid in Rajasthan, have contributed a rich and diverse flora in the Indian subcontinent. In order to encourage the utilization of Indian herbal remedies, it's essential to assess the therapeutic benefits of these drugs in accordance with WHO guidelines [4].

Zingiberaceae family, is considered as the largest family in the order Zingiberales, having 53 genera and over 1200 species [5]. By examining morphological characteristics such as the number of locules and placentation in the ovary, the development of staminodia, modifications of the fertile anther, and the orientation of rhizome-shoot-leaf, researchers have identified four tribes within the Zingiberaceae: Alpinieae, Globbeae, Hedychieae, and Zingibereae [6]. Important genera belongs to Zingiberaceae family are *Alpinia*, *Curcuma*, *Globba*, *Zingiber*, *Amomum*, *Renealmia*, *Boesenbergia*, *Hedychium*, *Riedelia*, *Aframomum*, *Hornstedtia*, *Meisteria*.

One of the important genera of Zingiberaceae family is *Hedychium* comprises of 80 species distributed globally [7]. Among these, 29 species are found in the tropical and sub-tropical regions of China, while 40 species are present in Indonesia [8,

9]. The essential oils extracted from the leaves, flowers, and rhizomes of these plants are well-documented for their medicinal properties [9]. These oils have been traditionally used in treating various ailments such as asthma, bronchitis, gastric issues, and as anti-emetics, particularly among the hill tribes of Uttarakhand. Additionally, they are utilized for treating eye diseases in Nagaland [10, 11, 12]. Apart from their medicinal uses, *Hedychium* species are also cultivated for their fragrant essences and their aerial stems are valuable raw materials for paper manufacturing. Furthermore, some species are cultivated for their edible flowers [7].

## PHYTOCHEMICAL CONSTITUENTS

### Volatile oil

Essential oils are widely utilized in a variety of products such as soaps, cosmetics, toiletries, medicines, perfumes, and food [13]. These natural oils are found in different parts of plants including flowers, leaves, barks, roots, seeds, fruits, rhizomes, and exudates like gums or oleoresins. They are stored in various structures within the plant such as oil cells, ducts, glandular hairs, modified parenchymal cells, resin canals,

vittae (oil tubes), lysigenous cavities, schizogenous passages, or gum canals [13, 14]. Among the Zingiberaceae family, particularly in the genus *Hedychium*, rhizomes are a significant source of these volatile oils. The primary components of volatile oils found in all examined samples of *Hedychium* species include: myrcene, limonene, p-cymene, camphene, and  $\gamma$ -terpinene [15].

Medeiros and his co-workers in 2003 [16] analyzed the volatile oils in the leaves and flowers of *H. gardnerianum* using GC-MS. They also extracted volatile oils from *H. coronarium* flowers using enfleurage method in which whale's fat-palm oil (1:1) was used as the solvent [14]. This method yielded oils with a scent closest to that of fresh flowers. The chemical components identified in these oils included ethyl hexadecanoate, tetradecanol, benzyl alcohol,  $\alpha$ -farnesene, and linalool. Additionally, the volatile oils from the rhizomes of various *Hedychium* species (*H. ellipticum*, *H. aurantiacum*, *H. spicatum*, and *H. coronarium* from India) were analyzed using GC-MS [17].

Table 1: Phytochemical Content of *Hedyhcium* Species with proven activities

Sources	Extract /Compound	Activity	References
<i>H. gardnerianum</i> (Rhizome); <i>H. longipetalum</i> ; X.Hu and N.Liu (rhizome)	Hedyforrestin B (1)	Antitumor Anti-inflammatory	[18, 19]
<i>H. gardnerianum</i> rhizome; <i>H. coronarium</i> rhizome; <i>H. longipetalum</i> rhizome	Hedyforrestin C (2)	Antitumor      Anti- inflammatory	[18, 19, 20]
<i>H. longipetalum</i> rhizome	Hedylongnoid A (3)	Anti-inflammatory	[19]
<i>H. longipetalum</i> rhizome	Hedylongnoid B (4)	Anti-inflammatory	[19]
<i>H. longipetalum</i> rhizome	Hedylongnoid C (5)	Anti-inflammatory	[19]
<i>H. gardnerianum</i> rhizome; <i>H. spicatum</i> rhizome; <i>H. longipetalum</i> rhizome	Yunnancoronarin A (6)	Antitumor      Anti- inflammatory	[18, 19, 21]
<i>H. coronarium</i> rhizome	Coronararin D (7)	Antitumor Antibacterial Antifungal	[22, 23, 24]
<i>H. coronarium</i> rhizome	Coronararin D ethyl ether (8)	Antitumor	[23]
<i>H. coronarium</i> rhizome <i>H. coronarium</i> rhizome	Coronararin B (9) Chloroform extract	Antitumor Cytotoxic against Cloned Chinese hamster V-79 cell	[23, 25, 26]
<i>H. coronarium</i> rhizome	Coronararin D acetate (10)	Antitumor	[25]
<i>H. coronarium</i> rhizome	Isocoronarin D (11)	Antitumor	[23,25, 27]
<i>H. coronarium</i> rhizome <i>H. coronarium</i> (Leaves and pseudo stem)	Benzoyl eugenol (12) Ethanol extract composition	Antitumor Antidiabetic	[27, 28]
<i>H. coronarium</i> rhizome	Ethoxycoronarin D (13)	Antitumor	[27]
<i>H. coronarium</i> rhizome	Methoxy-coronarin D (14) Hexane, Chloroform, Methanol extract	Antitumor Anti-inflammatory	[27, 29]
<i>H. coronarium</i> (aerial part)	Hedychiumin (15)	Antitumor	[30]
<i>H. coronarium</i> (aerial part)	Calcaratarin A (16)	Antitumor	[30]

<i>H. gardnerianum</i> rhizome; <i>H. coronarium</i> aerial part	Coronarin A (17)	Antitumor	[18, 30]
<i>H. spicatum</i> rhizome	9-Hydroxy hedychenone (18)	Antitumor	[21]
<i>H. spicatum</i> rhizome <i>H. spicatum</i> rhizome	Hedychilactone B (19) Essential oil	Antitumor Anthelmintic	[21, 31]
<i>H. spicatum</i> rhizome <i>H. spicatum</i> root	Hedychilactone C (20) Hydroalcoholic extract	Antitumor Antihistaminic; Mast cell stabilizer Bronchodilator	[21, 31]
<i>H. spicatum</i> rhizome	Hedychilactone D (21)	Antitumor	[21]
<i>H. spicatum</i> rhizome <i>H. spicatum</i>	Chrysin (22) Essential oil	Antitumor Pediculicidal	[21, 32]
<i>H. spicatum</i> rhizome	Teptochrysin (23)	Antitumor	[21]
<i>H. forrestii</i> rhizome	Hedychin C (24)	Antitumor	[33]
<i>H. gardnerianum</i> rhizome	Coronarin E (25)	Antitumor	[18]
<i>H. gardnerianum</i> rhizome	Villosin (26)	Antitumor	[18]
<i>H. gardnerianum</i> rhizome <i>H. gardnerianum</i> Leaves	Yunnancoronarin B (27) Essential oil	Antitumor Antioxidant	[18, 34]
<i>H. gardnerianum</i> rhizome	1-Hydroxyxanthone (28)	Anti-depressant	[35, 36]
<i>H. gardnerianum</i> rhizome	Salicylic acid (29)	Anti-hemorrhagic	[35, 37, 38]

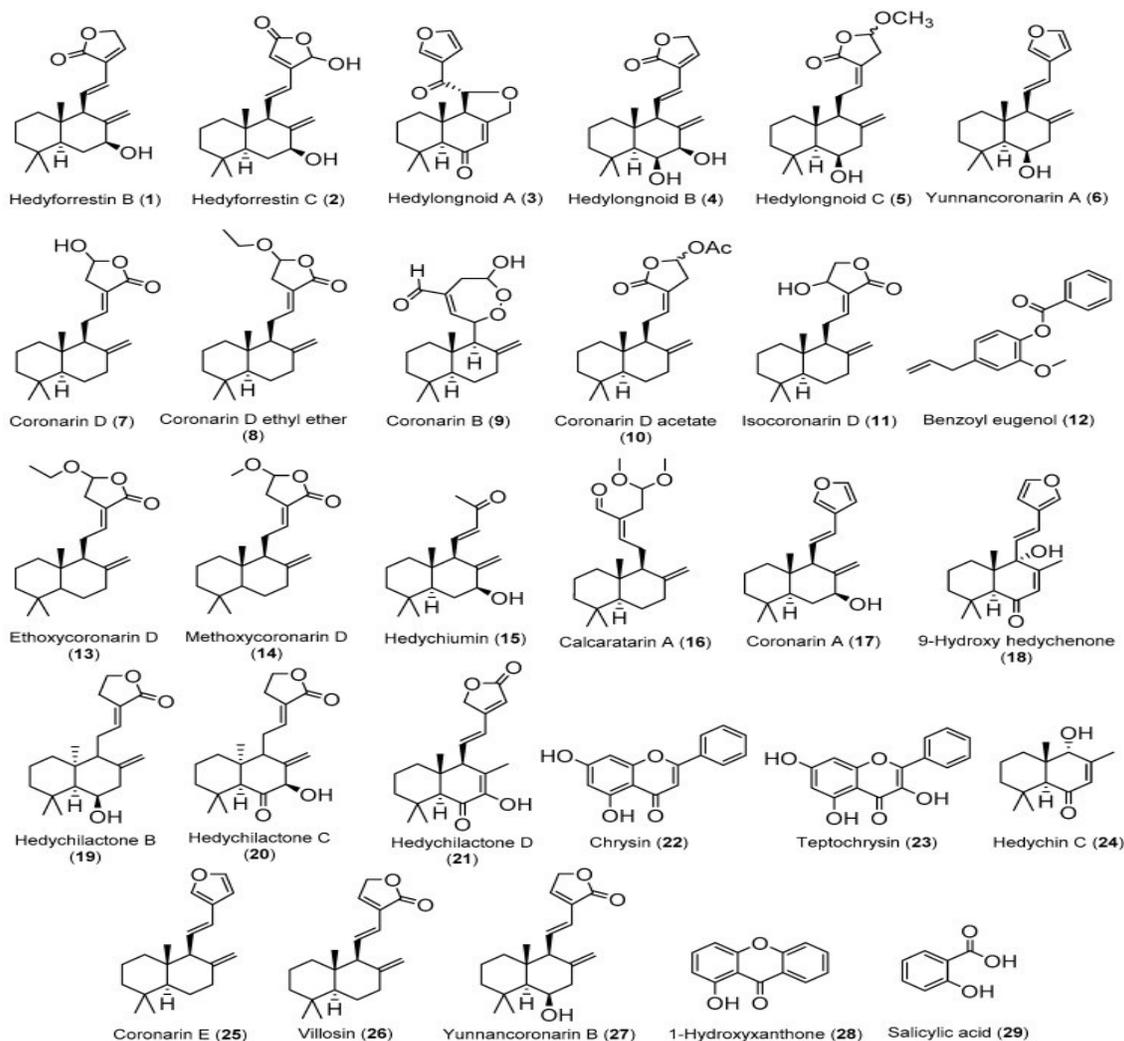


Figure1: Chemical structure of the compounds referred on Table 1

## PHARMACOLOGICAL PROPERTIES

### Antimicrobial Activity

Essential oils of *H. aurantiacum*, *H. ellipticum*, and *H. coronarium* demonstrated broad-spectrum antimicrobial activity. Inhibition zones were observed against *Staphylococcus aureus*, *Shigella flexneri*, *Pasteurella multocida*, *Escherichia coli*, and *Salmonella enterica* [17]. *H. spicatum*

extracts exhibited inhibitory activity against both Gram-positive and Gram-negative bacteria [39]. Methanolic extract of *H. coronarium* showed strong inhibition against *S. enterica* and *S. aureus* (MIC 0.05 mg/mL) but no activity against *E. coli* and *Vibrio parahaemolyticus* [40].

*H. coronarium* Koenig leaves oil exhibited activity against *Candida glabrata*,

*Malassezia furfur*, and *Candida albicans*. Rhizome oil showed strongest activity against *C. glabrata*, followed by *C. albicans* and *M. furfur*. Methanol and aqueous extracts (leaves and rhizome) demonstrated weak or no activity [40]. *H. gardnerianum* leaves essential oils displayed antimicrobial activity against *S. aureus* and *S. epidermidis* but not with *P. aeruginosa* [16]. *H. spicatum* rhizome essential oils exhibited fungitoxic activity against *Aspergillus flavus* with MIC 2.5  $\mu\text{L}/\text{mL}$  and MFC 6.0  $\mu\text{L}/\text{mL}$  [42].

### Antioxidant activity

The antioxidant capacity of *H. coronarium* Koenig rhizome extract was  $89.6 \pm 11.6\%$ , whereas its methanolic extract in DPPH scavenging activity, showed  $90.1 \pm 7.2\%$

reducing power [40]. Methanolic leaf extracts showed the highest radical scavenging activity (98.1%), followed by aqueous leaf extracts (97.8%), methanolic rhizome extracts (95.5%), and aqueous rhizome extracts showed 92.9% inhibition [41].

The antioxidant activity of methanolic extracts of *H. spicatum* Buch. Ham. Ex. D. Don rhizome from some regions of India were considered and the results revealed IC<sub>50</sub> values ranging from 0.549-1.059 mM AAE per 100 g dry weight [43]. While the essential oils exhibited IC<sub>50</sub> values of  $21.67 \pm 0.22 \mu\text{L}/\text{mL}$  in DPPH assay [42], indicating their potential as antioxidant sources.

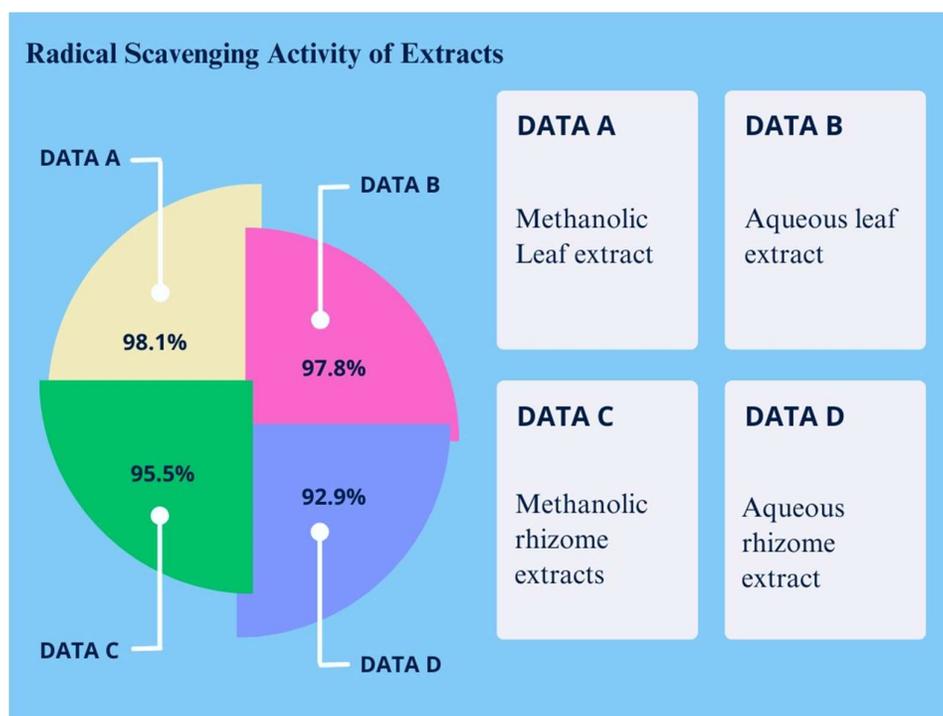


Figure 2: Radical scavenging activity of methanolic and aqueous extracts

**Antidiabetic activity**

Deficiency in insulin secretion, or insulin action leads to chronic hyperglycemia, which is the primary characteristic of diabetes mellitus [44]. Anti-diabetic drugs are used in the treatment of this condition to regulate blood glucose levels [45].

An in vivo study was conducted by Tse and his co-workers in 2019 [46] to test aqueous extract of *H. coronarium* could lower blood sugar in animal models with induced-type 2 diabetes mellitus (T2DM). The study used Wistar rats with diabetes induced by a chemical streptozotocin (STZ) and C57BKS<sup>db/db</sup> mice (which have a mutation causing high blood sugar, pancreatic beta cell atrophy, low insulin, and obesity). After giving a daily dose of the extract for 28 days (8.928 mg/kg for the rats and 17.71 mg/kg for the mice), their blood sugar management improved significantly compared to the group given only distilled water (control group).

In another in vivo study, after 14 days of treatment with an oral dose of 0.3 mL of essential oil from *H. spicatum* rhizomes, blood sugar and urea levels went down in rats, in which diabetes was induced by intraperitoneal injection of a solution of alloxan monohydrate (150 mg/kg). These results were found similar to the group of rats which were treated with the drug glibenclamide. Additionally, after the treatment period, it was found that the Islets

of Langerhans returned to their normal shape [47].

**Tranquilizing activity**

It has been reported that the essential oil from *H. spicatum* rhizomes have a mild and short-lived tranquilizing effect. It reduced conditioned avoidance response and performance on the rota-rod test, and enhance both phenobarbitone-induced hypnosis and morphine analgesia in rats [48].

**Anthelmintic activity**

*H. spicatum* rhizomes were tested for anthelmintic property on adult Indian earthworms (*Pheretima posthuma*). The duration until paralysis and death for each worm was measured. These results were compared to those obtained with the standard treatment (piperazine citrate). The methanol extract of *H. spicatum* displayed dose-dependent anthelmintic activity, while the aqueous extract was ineffective. Overall, the methanol extract showed greater anthelmintic property than the standard drug i.e., piperazine citrate [49].

**Hepatoprotective activity**

Significant hepatoprotective activity is demonstrated by ethyl acetate and alcohol extracts of dried rhizomes. They effectively reduced enzyme levels, such as serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT), in albino rats intoxicated with carbon tetrachloride (CCl<sub>4</sub>).

The results were comparable to those of marketed products [50].

Another study showed that liver antioxidants (superoxide dismutase, glutathione peroxidase, and catalase) were replenished by treatment of hydroalcoholic extract of *H. spicatum* rhizomes and significantly prevented the increase of serum biomarkers (aspartate transferase, alanine aminotransferase, alkaline phosphatase, and others) following hepatotoxicity induced by both chloroform and paracetamol in a rat model [51].

#### **Cytotoxicity activity**

Labdane-type diterpenes from *H. coronarium* were tested for cytotoxicity on some cancer cell lines using MTT assays. Isocoronarin D (C-14 epimers) demonstrated the highest activity against most cancer cell lines (except S102), with an IC<sub>50</sub> of 4 µg/mL [25]. Other compounds isolated from the hexane extract of *H. coronarium* were evaluated against the A-549, SK-N-SH, MCF-7 and HeLa cancer cell lines using the SRB (sulforhodamine B) assay, revealing significant differences in their anticancer effects. Compounds like 4-hydroxy-3-methoxy ethyl cinnamate, 4-hydroxy-3-methoxycinnamaldehyde, hedychenone, coronarin C, and coronarin D revealed potent cytotoxicity against the A-549 cell line, with LC<sub>50</sub> values ranging from 1.26 - 8.0 µM. Two other compounds (6-oxo-7,11,13-labdatrien-17-al-16,15-olide

and 7,17-dihydroxy-6-oxo-7,11,13-labdatrien-16,15-olide) showed average cytotoxicity [25].

Isolates from *H. spicatum* were tested against various cell lines using the MTT assay. 7-hydroxy hedychinal displayed strong activity, while spicatanic acid showed moderate activity. Additionally, the cytotoxicity test of the isolates from CHCl<sub>3</sub> extracts of *H. spicatum* were tested against different cell lines. Hedychilactone-D showed significant activity on several lines (Colo-205, A-431, MCF-7, CHO cell lines) whereas 9-hydroxy-hedychenone exhibited moderate to potent activity against Colo-205, A-431 and CHO cell lines [21].

#### **Anti-inflammatory activity**

To examine the inflammatory activity, inhibitory effect on the pro-inflammatory cytokines production is used as a parameter. Kiem and his associates in 2011 [20] evaluated isolates from *H. coronarium* as anti-inflammatory agents. Their findings indicated that IL-6 and IL-12 production LPS-stimulated BMDCs was potently inhibited by hedyforrestin C. Coronarin G, coronarin H, and hedyforrestin C from *H. coronarium* showed inhibition activity against TNF-α, IL-6, and IL-12 in LPS-stimulated [52, 53]. 2 g/100 g body weight dose of *H. spicatum* ethanolic extract demonstrated 55.54% inhibition of carrageenan-induced edema in Wistar rats, exhibiting anti-inflammatory activity [54].

### Analgetic activity

The methanolic extract of *H. coronarium* demonstrated a significant analgesic effect. At doses of 100, 200, and 400 mg/kg body weight, pain threshold in tail immersion method was notably increased by it in a dose dependent manner in acetic acid-induced writhing test. At 400 mg/kg body weight, the extract exhibited maximum of 73.12% writhing inhibition, comparable to the standard drug sodium diclofenac (25 mg/kg body weight) that showed 75.78% inhibition of writhing [55].

### Larvicidal activity

The essential oils from *H. coronarium* leaves and rhizomes showed significant larvicidal activity against *Aedes aegypti* (L.). The leaves oil had LC50 values of 111 ppm (2 hours) and 90 ppm (24 hours), while the rhizome oil had LC50 values of 86 ppm (2 hours) and 47 ppm (24 hours). It has been noted that  $\alpha$ -pinene,  $\beta$ -pinene, and 1,8-cineole exhibited larvicidal effects (LC50 values of 15.4, 12.1, and 57.2 ppm, respectively) on *A. aegypti* larvae. *H. coronarium* essential oil presents a potential source of natural origin for new biodegradable larvicides [41].

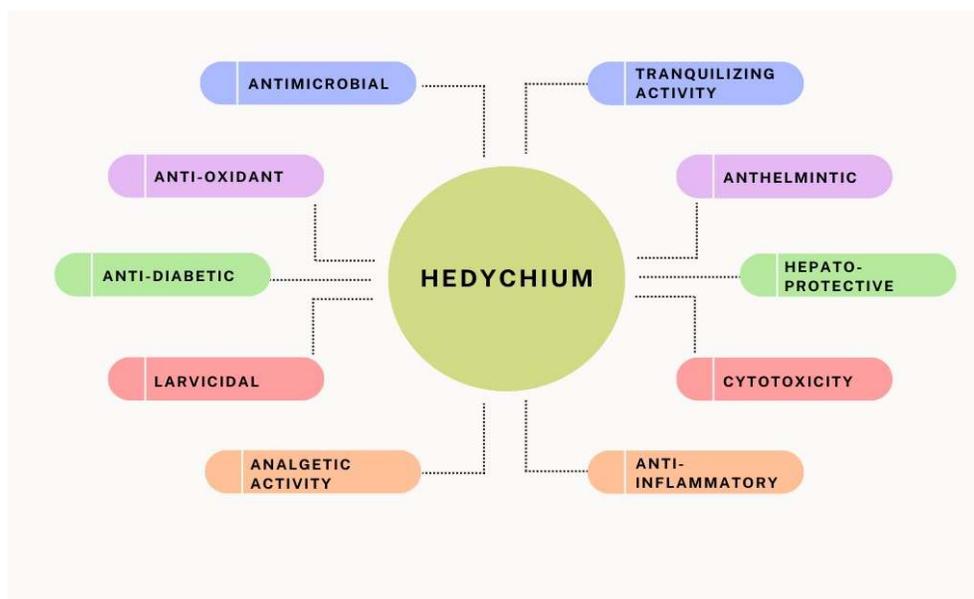


Figure 3: Biological activities of *Hedychium* species

### CONCLUSION

*Hedychium* genus is recognized for its significant medicinal properties, which are utilized in various folk remedies worldwide. These plants are employed to address a range of health issues such as allergies, cancer, diabetes, inflammation, rheumatism,

and skin ailments. Additionally, they serve as analgesics, antimicrobials, anti-helminthics, antioxidants, and insect repellents. Numerous studies have investigated the pharmacological effects of *Hedychium* species, focusing on their essential oils, extracts, and individual

compounds. Recent literature confirms the diverse pharmaceutical activities of these plants, including anti-acetylcholinesterase, antidiabetic, anti-inflammatory, antimicrobial, antioxidant, antitumor, and hepatoprotective properties, along with potential insecticidal effects. The available scientific knowledge about the *Hedychium* genus is still inadequate. However, findings from prior research on selected *Hedychium* plants suggest that other plants within the *Hedychium* genus may offer potential for exploration as natural product resources. Because of unauthorized harvesting and uncontrolled use of its rhizome extract in producing different kinds of drugs, the original population of this species has vanished. It's necessary to reintroduce this plant into its native environment.

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