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Secondary metabolites in *Uvaria hamiltonii* Hook. f. & Thoms. (Annonaceae) and their pharmacological properties: A review

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ABSTRACT

Uvaria hamiltonii, commonly known as "Eastern Uvaria", "Lakankoli" or "Latkan", is one of the valuable medicinal plants of Annonaceae family. It is native to India, Bangladesh, Myanmar, Nepal, Bhutan, Cambodia, Thailand, Vietnam Nepal, Bhutan, Bangladesh and Burma. Different parts of the plant are reported to contain a number of alkaloids, steroids, flavonoids and terpenoids, which are responsible for antibacterial, anticancer and á-glucosidase inhibitory and various other pharmacological properties.This paper presents a comprehensive overview of traditional uses, current knowledge on the phytochemistry and biological activities of *U. hamiltonii,* which may open up avenues for its utilization in traditional and modern medicine in future.

1. Introduction

Natural products and traditional medicines have always been in the forefront of all cultures and civilisations despite the predominance of modern medicine. The therapeutic properties of medicinal plants are attributed to the presence of various secondary metabolites such as alkaloids, flavonoids, steroids, phenolics, saponins, tannins, terpenoids, iridoids and cardiac glycosides. They are potential sources of phytochemicals for drug formulation and the examples are: quinine from *Cinchona*, insulin from roots of *Dahlia*, morphine from poppy and digoxin from *Digitalis* (Padmavathi, 2013). WHO endorses and promotes the application of herbal drugs in national health care programmes of the states as they are cost-effective, eco-friendly and without minimal or no side effects in comparison to synthetic drugs (Singh & Singh, 1981).

2. Botany, distribution and traditional uses of *U. hamiltonii*

The family Annonaceae is comprised of 108 accepted genera and about 2400 species globally (Chatrou *et al.*, 2012). The species of the family are used in the tropics in traditional medicines for the treatment of various illness (Frausin, 2014). *Uvaria hamiltonii* Hook. f. & Thoms., a rare woody climber of the family Annonaceae is well-known for its anti-cancerous properties. Taxonomically, *Uvaria hamiltonii* belongs to the family Annonaceae, order Magnoliales, subclass Magnoliidae, class Magnoliopsida and phylum Tracheophyta (Mabberley, 2008). The plant is known by several vernacular names such as Latkan in West Bengal, Zawl-thei in Mizoram, Taipak in Tripura and Lakankoli/ Lakhankoli in Odisha (POWO, 2022) (https://www.flowersofindia.net).

Uvaria hamiltonii Hook. f. & Thoms. is a large scandent shrub with rusty tomentose branches and the leaves are simple, elliptic to oblong, obovate, tomentose beneath. The flowers are deep red or scarlet, bisexual, solitary or 2-3 fascicles; flower stalks are woolly; sepals 3, petals 6; stamens many. Carpels are many, about 10, orange, tomentose; style short, thick; seeds many, flat and shining (Saxena & Brahmam, 1994) (Fig. 1 a & b).

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Fig. 1. (a) *Uvaria hamiltonii* plant (b) Flower of *Uvaria hamiltonii*

Turner (2015) has described the range of distribution of the species in the world. It is native to South Asian countries like Nepal, Thailand, Vietnam, Bhutan, India, Bangladesh and Burma. In India, it is reported to occur wild in Uttar Pradesh, Bihar, Mizoram, Sikkim, West Bengal, Assam, Meghalaya, Tripura, Odisha and Andhra Pradesh.

Though no published report on the mode of propagation of *U. hamiltonii* is available, as per the field observation by the authors and local inhabitants, it multiplies by seeds. In Odisha, the species mostly grow wild along streams and rivers and the seeds are dispersed by water and get established at suitable habitats. Majority of the ripe fruits are consumed by the local tribals and frugivorous birds and the fallen seeds in stream water perish and do not germinate, resulting in rarity of the species in forests.

In traditional medicine, the extracts of different parts of this plant are being used for treatment of diabetes mellitus, malaria, gonorrhea, jaundice, bronchitis and minor infections (Asha *et al*., 2003; Rahmatullah *et al*., 2010).

3. Phytochemical constituents

The phytochemical analysis of different parts of *U. hamiltonii* carried out by previous workers revealed the presence of alkaloids, steroids, flavonoids, terpenoids and carbohydrates. List of phytochemicals found in the plant is provided in Table 1. Besides, a total of five aristolactams have been isolated from the stem bark of *U. hamiltonii* by Hasan *et al*. (2001). While four of these were isolated from the dichloromethane extract, the fifth alkaloid was obtained from the methanolic extract. Two flavanones, hamiltones A and B, an aurone, hamiltrone, a chalcone, hamilcone and a tetrahydroxanthene, hamilxanthene have been isolated from *U. hamiltonii* extracts guided initially by fractionation based on DNA strand-scission and/or 9KB cytotoxicity assays (Huang *et al*., 1998). Further, Huong *et al.* (2022) analysed the leaf essential oil of *U. hamiltonii* and identified germacrene D (22.9%), â-caryophyllene (21.1%), bicyclogermacrene (11.2%) and caryophyllene oxide (8.6%) as the main constituents. Two known steroids, stigmasterol and 6-hydroxystigmasta-4, 22-dien-3-one and two unusual polyketides, *cis*-4-hydroxymellein and *trans*-4-hydroxymellein were isolated from the stem bark of *Uvaria hamiltonii* (Asha *et al*., 2004). They elucidated the structures of the compounds by high-resolution 2D-NMR techniques and confirmed the same by comparison with previously reported values.

Barman *et al*. (2021) identified specialized metabolites contributing to colour and scent volatiles in *Uvaria hamiltonii* flowers. Among the 34 compounds identified, they found sesquiterpenoids as the dominant constituents in the floral volatiles. The anthocyanin pigment responsible for the flower colour was also explored and it was revealed that a single anthocyanin compound, cyanidin-3-O-glucoside, was principally responsible for petal colour.

4. Pharmacological properties

Different plant parts of *U. hamiltonii* have been investigated for their pharmacological properties and biological activities as presented in Table 1. The bioactivities of different plant parts are described below, which may facilitate exploration of the species for various pharmaceutical applications.

Table 1

Chemical compounds with medicinal value isolated from plant parts of *U. hamiltonii*

Pharmacological Activity	Plant parts used	Solvent used	Specific compounds involved	Figures	References
Anticancer	Leaf and stem	Ethanol	Hamiltone, Hamiltrone, Hamilcone and Hamilxanthene	Fig.2. (a, b, c, e)	Huang *et al*., 1998
á-glucosidase inhibitory	Leaf	Ethyl acetate	Grandifloracin, Kaempferol and Benzoic acid	Fig.2. (d, f, g)	Meesakul *et al*., 2020
Antibacterial	Stem bark	Petroleum ether Dichloromethane Methanol	Piperolactum C	-	Asha *et al*., 2003
Anti-oxidant	Flower	Methanolic extract Aqueous extract	Anthocyanins	-	Barman *et al*., 2021

4.1. Anticancer activities

Huang *et al.* (1998) isolated compounds from the combined leaf and stem ethanolic extracts of *U. hamiltonii*, guided initially by fractionation based on DNA strand-scission or 9KB cytotoxicity assays.They found that two flavanones namely, hamiltones A & B and an aurone called hamiltronewere inactive in the 9KB cytotoxicity assay, while a chalcone, hamilcone and a tetrahydroxanthene, hamilxanthene exhibited weak cytotoxic activity. It was suggested that these compounds can be useful in cancer chemotherapy.

4.2. á-glucosidase inhibitory activities

A preliminary screening of á-glucosidase inhibitory activity of this plant indicated that ethylacetate extract of leaves have promising á-glucosidase inhibitory activities with an IC_{50}value of 78.4 µg/mLand compounds like grandifloracin, kaempferol and benzoic acid have potent á-glucosidase inhibitory activity (Meesakul *et al*.,2020).

4.3. Antibacterial activities

The antibacterial activity of *U. hamiltonii* has been assessed with standard antibiotic kanamycin by Asha *et al.* (2003). The work discussed aboutchemical compounds namely piperolactum C, goniopedaline, 6b-hydroxystigmasta-4,22-dien-3-one and a mixture of cis-and trans-4-hydroxymelleins obtained from *U. hamiltonii* stem bark, which are responsible for antibacterial properties. The leaf essential oil of *U. hamiltonii* demonstrated notable antimicrobial activity against *Enterococcus faecalis* ATCC299212 with minimum inhibitory concentration (MIC) value of 7.99 µg/mL and *Bacillus cereus* ATCC14579 (MIC 5.67 µg/mL) (Huong *et al*., 2022)

4.4. Antioxidant capacity

Total phenolic content was evaluated and antioxidant capacities of *U. hamiltonii* flowers were studied by Barman *et al.* (2021) with the help of DPPH, FRAP and ABTS assays. The total phenolic content and the antioxidant capacity were found to be higher in methanolic extract as compared to aqueous, petroleum ether and ethyl acetate extracts.

The structures of medicinally potent chemical compounds reported in this plant are depicted in Fig. 2.

5. Conclusion

U. hamiltonii is a unique source of various types of chemical compounds with diverse bioactivities. Since very less works have been performed on its biological activity, intensive investigation is necessary to identify and isolate other bioactive compounds from the plant which may help in drug formulations. The present review focuses on the antibacterial, anticancerous, á-glucosidase inhibitory and antioxidant activity of this plant.

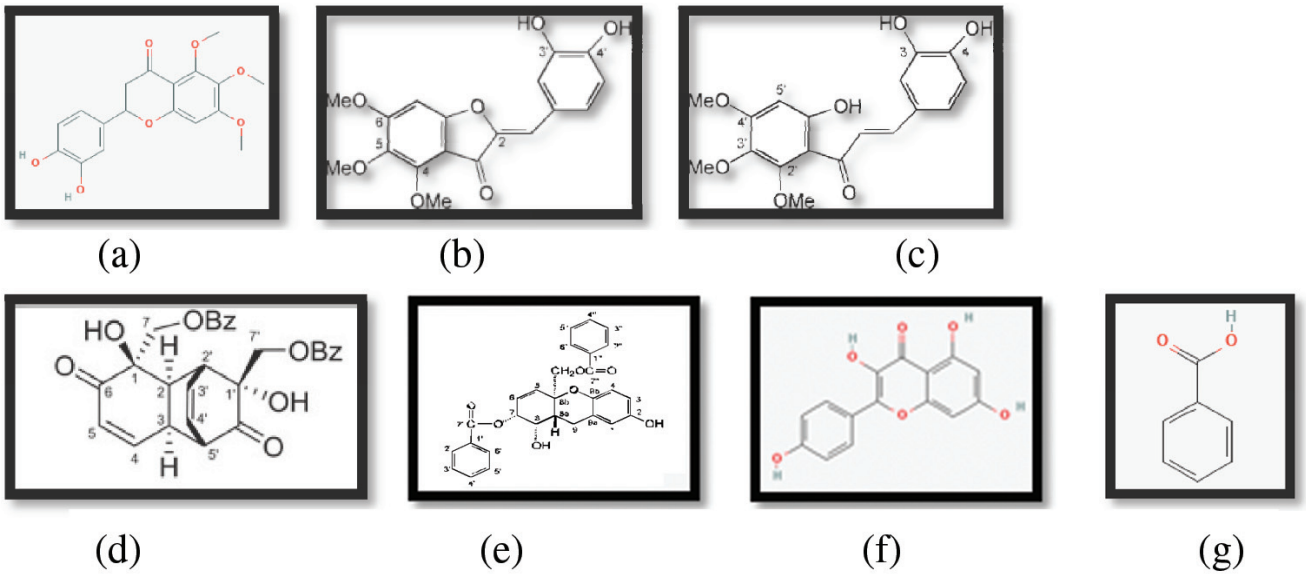

Fig. 2. Structures of compounds isolated from *Uvaria hamiltonii*: (a) Hamiltone (b) Hamiltrone (c) Hamilcone (d) Grandifloracin(e) Hamilxanthene (f) Kaempferol (g) Benzoic acid (Source: Huang *et al*., 1998; Asha, *et al*., 2003; Meesakul *et al*., 2020)

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