chemistry proceedings

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Proceeding Paper

Phytochemistry of *Uvaria narum*: A Multifaceted Perspective and Ethnopharmacological Potential †

Javesh Patil [1,*], Aayushi Tatiya [2,*], Raju Wadekar [3,*], Tejasweeni Girase [2] and Kiran Patel [2]

[1] Department of Pharamacognosy and Phytochemistry, PSG Vidya Prasarak Mandal's College of Pharmacy, Tal-Shahada, Dist-Nandurbar, Shahada 425409, India
[2] Department of Quality Assurance, PSG Vidya Prasarak Mandal's College of Pharmacy,Tal-Shahada, Dist-Nandurbar, Shahada 425409, India;
[3] Department of Pharmacognosy and Phytochemistry, Shri Vile Parle Kelavani Mandal's Institute of Pharmacy, Dhule 424001, India
* Correspondence: javesh4u@gmail.com (J.P.); aayushitatiya@gmail.com (A.T.); rajuwadekar@svkm.ac.in (R.W.); Tel.: +91-992-344-1004 (J.P.); +91-969-108-1450 (A.T.); +91-942-153-2297 (R.W.)
† Presented 26th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2022. Available online: https://ecsoc-26.sciforum.net/.

Abstract: The Blooming ethnomedicinal plant *Uvaria narum* (Dunal) Wall is mostly found in the deep forests of the Western Ghats and belongs to the Annonaceae family. *Uvaria narum* is a spreading, pubescent shrub with large, dark bluish-green leaves. Phytochemistry and pharmacognostic studies have revealed that the plant possesses variety of phytochemicals that are remarkable and beneficial to humans. The Plant possesses a number of beneficial properties, such as antioxidant activity exhibited by the presence of Polyphenols and tannins, antifungal activity brought on by the benzoic acid moiety, and tumor-fighting abilities contributed by terpenoid and alkaloids. The presence of phytoconsituents in plants has been attributed to various medicinal properties in plants like anticancer activities. The plant may also be considered against ageing and other diseases caused by free radicals. In vitro cytotoxicity is due to terpenoid, phytosterols, and flavonoids, whereas the liver is protected by flavonoids. The chemical profile of plant shows that Acetogenins including Stereoisomers are important constituents of the root bark. Eczema, itching, varicose veins, haemorrhoids, jaundice, inflammation, and fever are the main ailments for which this herb is used.

Keywords: *Uvaria narum*; benzoic acid; terpenoid; acetogenins; tumor-fighting

Citation: Patil, J.; Tatiya, A.; Wadekar, R.; Girase, T.; Patel, K. Phytochemistry of *Uvaria narum*: A Multifaceted Perspective and Ethnopharmacological Potential. *Chem. Proc.* **2022**, *4*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s): Julio A. Seijas

Published: 15 November 2022

1. Introduction

India, which is aptly known as the Botanical Garden of the World, is the country that produces the most medicinal plants. Several medicinal herbs have been used by the indigenous system of medicine for thousands of years. India has a valuable heritage of herbal remedies for various ailments [1]. About 120 genera and more than 2000 species make up the enormous plant family known as the Annonaceae. It is a highly uniform family in terms of habitat and anatomy. This family is valuable economically because it produces edible fruits and oils [2]. Approximately 210 species of the Annonaceae have been identified, and they are widely distributed in tropical and subtropical wet forests in Africa, Madagascar, continental Asia, Malaysia, northern Australia, and Melanesia. Some Uvaria species are known to possess biologically valuable compounds, which have a number of therapeutic characteristics, and are often evergreen [3]. Uvaria is a genus of flowering plants in the soursop family, Annonaceae. Because several species in this genus produce edible fruits that resemble grapes, the name Uvaria is derived from the Latin word uva, which means grape. These are spectacular bushes with sparsely haired branchlets. It has huge, woody stems and is a climbing shrub. Uvaria is a sizable straggling shrub

with dark bluish green leaves that is woody and stellately hairy [1]. This article seeks to give a thorough overview of *Uvaria narum*'s botanical characteristics, phytochemistry, ethnopharmacology, and ethnomedical applications.

2. Plant Description

2.1. General Details

Binomial Name: *Uvaria narum* (Dunal) Wall
Family: Annonaceae
Common Name: Narumpanal, Pulikkan
Habit: Shrub or Woody climber
Flowering Class: Dicot
Part Used: Seeds, Aerial parts, Roots, Leaves.

2.2. Taxonomical Classification

Kingdom: Plantae
Order: Magnoliales
Family: Annonaceae
Phylum: Magnoliophyta
Class: Magnoliatae
Genus: Uvaria

2.3. Vernacular Names

English: South Indian *Uvaria*
Indian Languages: Saplivel
Malayalam: Narumpanal, Kureel, Kooril, Koorilvalli
Tamil: Puliccan,
Sanskrit: Nilavalli, Valeesha-khota
Kannada: Bugadee balli, Bugadee hoo, Guavaara
Marathi: Kala-apakara.

2.4. Distribution

2.4.1. Global Distribution

Uvaria narum is found in South India and Sri Lanka.

2.4.2. Indian Distribution

Uvaria narum is particularly found in southern India. Mainly found in the forest of western Ghats from S. Kanara to Travancore, hills of salem. It is occasionally distributed in the Southern dry mixed deciduous forests at low altitudes.

The plant is specifically seen in Maharashtra State (Kolhapur, Satara, Raigad Districts); Karnataka State (Coorg, Chikmagalur, North and South Kanara, Mysore Districts); Kerala State (All districts); Tamil Nadu State (Madurai, Salem, Namakkal, Nilgiri, Tiruvannamalai, Vellore, Viluppuram, Dharmapuri, Tirunelveli Districts).

2.5. Morphology

2.5.1. Leaves

Leaves are simple alternate Lanceolate -oblong to eliptic about 10–16 × 2.5–6 cm across, apex acuminate, assymetrical, dark green, base rounded, oblong pointed or long-pointed, stalks short less than 6 mm and leaves hairless on both sides. Crushed leaves smell like cinnamon.

2.5.2. Flowers

Flowers bisexual, usually solitary, extra axillary, leaf opposed, pedicels slender about 1–1.2 cm tomentose: sepals 8 × 5 mm, broadly ovate, basally connate; outer petals slightly larger and wider than the inner petals, petals fleshy with outer 2 × 1.5 cm and inner 2 × 1 cm, obovate, apex incurved, golden-brown; Stamens have anthers concealed by the overlapping connectives; carpel's numerous, 5 mm, oblong, scarlet-red, tomentose.

2.5.3. Seeds

Those are around 4–6 in a row, compressed or ovoid, chestnut brown, sub orbicular, and have the extremities of the carpels that are plano-convex and the middle ones that are compressed and nearly flat.

2.5.4. Reproduction

Uvaria species flowers are complete bisexual, i.e., with the functional male(androecium) and female(gynoecium) including stamens, carpels ovary. Pollination is entomophillous i.e., by insects. The plant is rarely unisexual.

2.5.5. Flowering/Fruiting

The season of flowering is November to December and fruiting is December to April.

2.5.6. Soil Requirement

Sandy loam soil with loose structure, good drainage is needed [1,4].

3. Phytochemistry

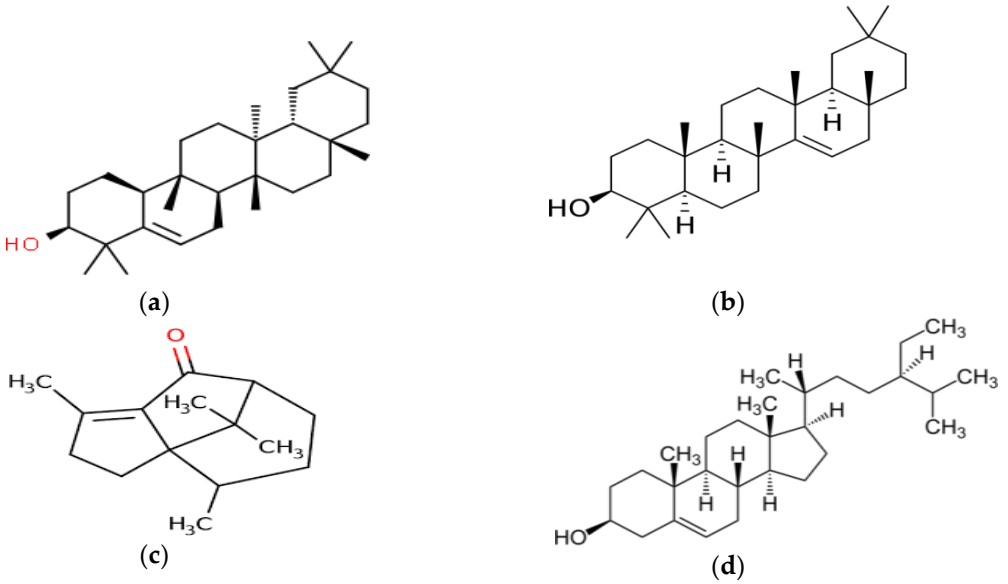
Investigations into the phytochemistry of plants identified various types of compounds with a variety of structural characteristics, and these compounds are still a rich source of novel natural products. *Uvaria narum* (Annonaceae) was one of the less chemically studied species in this intriguing group, according to a chemical literature review. Oils and fatty acids are discovered to be abundant in a number of Annonaceae species. Before 1982, fatty acids with abnormally high molecular weight that were insecticidal were found in the seeds of Annonaceae species. These substances appear to have later been classified as Lipids and Fatty Acids as a new class of natural goods known as tetrahydrofuranoid Acetogenins. It has been discovered that certain Annonaceae plants, including *Uvaria narum*, contain polyphenolic chemicals. Many species of the Annonaceae family include phenolic acids, including caffeic acid, p-hydroxy benzoic acid, p-coumaric acid, vanillic acid, etc. The leaves of several members contain common flavonoids including quercetin, quercitrin, rutin, etc.

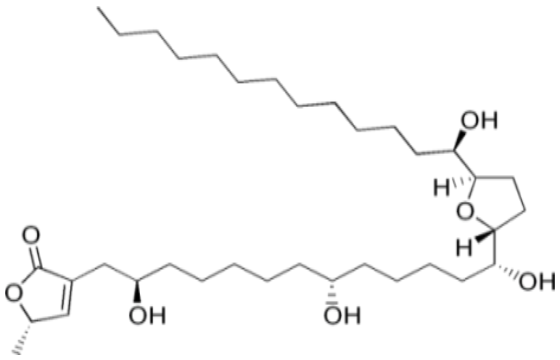
Due to the presence of essential oils, many Annonaceae are aromatic.These oils typically contain monoterpenes, sesquiterpenes, or aromatic chemicals that are well-known.There are species of *Uvaria* from specific Annonaceae genera that elaborate aromatic chemicals. In numerous *Uvaria* species, benzylbenzoate or its derivatives are frequently found. It seems that the potential to use benzyl or benzoyl groups to substitute various kinds of secondary metabolites is a recurring topic in the chemistry of *Uvaria*.Through research on various *Uvaria* species, a new class of secondary metabolites known as poly-oxygenated cyclohexene derivatives combined with benzoyl esters has been discovered. They belong to a tiny family of secondary metabolites found in plants, and the curiosity about these peculiar substances has led to inquiries on their biogenesis [2].

Most Annonaceae alkaloids have an isoquinoline-derived structure, and they can be divided into simple isoquinolines, benzyltetrahydroisoquinolines, bisbenzylisoquinolines, and bisbenzyltetrahydroisoquinolines, protoberberines, tetrahydroprotoberberines, oxoaporphines, phenanthrenes and other miscellaneous isoquinoline type alkaloid.

Acetogenins, including stereoisomer Glutinone, Glutinol, Taraxerol, Beta-Sitosterol, Benzyl benzoate 15.2%, and Patchoulenone, are typically found in this plant. Benzoic acid ester, 2-E-(2- oxo-cyclopent-3-en-1-ylidene) ethyl benzoate, tetratriacontanol, tritriacontane, and -sitosterol isolate from leaves, as well as novel acetogenins such as Squamocin-28-one, Panalicin, and *Uvaria* micin-I, II, and III,isolated from bark. By using mass spectrometry and capillary gas chromatography, the leaf oils of certain Annonaceae genera were examined. The three main substances were found to be -phellandrene (20.1%), -gurjunene (21.9%), and bicycloelemene (9.6%). Selinene (12.3%), bicyclogermacrene (10.9%), caryophyllene oxide (10.4%), and bicycloelemene (5.6%) were all present in high concentrations in the oil. The primary components of *Uvaria* were bicycloelemene (18.3%), germacrene D (30.2%), bicyclogermacrene (26.4%), and -bisabolene (7.7%), whereas -elemene (54.0%) was the component of *Uvaria* dac oil with the highest single abundance. The majority of the other chemicals, myrcene (3.8%) and limonene (3.8%), were all found in concentrations less than 5%.By using GC/MS to examine the root bark essential oil, roughly 52 components—22 of which were identified—were found to be present. The two main chemical components of the oil were discovered to be bornyl acetate (15.2%) and patchoulenone (8.1%), a tricyclic sesquiterpene ketone [1].

The crude leaf aqueous extracts of *Uvaria narum* revealed the presence of alkaloid carbohydrate, coumarins, flavonoids, phenols, proteins, quinones, sterols, and terpenoides, according to the preliminary phytochemical screening [5].Similar studies were done using a leaf extract that was dissolved in methanol and contained phenols, saponins, glycosides, and steroids.Carbohydrate, Coumarins, Phenols, Phytosterols, Proteins, Sterols, and Terpenoids were discovered in the Chloform extract. Glycosides, Phenols, Phytosterols, Proteins, Terpenoids, Alkaloid, and Carbohydrate were found in the acetone extract of *Uvaria narum* leaf. Steroids are recognised to be crucial for their cardiotonic effects in *Uvaria narum*, as well as having insecticidal and antibacterial characteristics [6–9].





(**e**)

Figure 1. The structures of some of the Phytochemicals found in *Uvaria narum* (**a**) Glutinol; (**b**) Taraxerol; (**c**) Patchoulenone; (**d**) Beta Sitosterol; (**e**) Acetogenins [10].

4. Ethnopharmacology

The various therapeutic activities proved by many researchers are as mentioned below.

4.1. Antioxidant Activity

When compared to previous studies, the plant *U. narum* whole root extract's 523.70 uM (Fe)/gm root powder level of antioxidant activity is promising. As antioxidant activities are directly proportional to phenolic compounds in plants, this activity may be attributed to the 0.8% of phenols present in the total root powder. Therefore, the plant *U. narum*'s entire root extracts could be used medicinally as a potential free radical scavenger. The plant may also be utilized as a defense against diseases like ageing and others brought on by free radicals [1,11].

4.2. Antibacterial Activity

Antibacterial activity of the sample was analyzed by standard tube dilution procedures with some modifications. In terms of antibacterial activity, the plant showed inhibitory properties against both Gram positive and Gram negative bacteria namely, *Staphylococcus aureus*, *Escherichia coli*, *Bacillus* spp. and *Lactobacillus* ferment. Herbs frequently have antibacterial properties, especially when utilized as drugs to treat skin conditions. Therefore, given that the plant has been used as a medicine to treat skin conditions, it is not surprising that it possesses antibacterial action against a diverse variety of bacterial species. As a result, the plant may be used to treat skin conditions like eczema and others brought on by bacterial infections [11–13].

4.3. Hepatoprotective Activity

Significant hepatoprotective action is demonstrated in the ethanolic extract of *U. narum* leaves against CCl4-induced liver damage in rats. This might be because of the presence of identified phytoconstituents, particularly flavonoids with antioxidant properties. Number of plants is being used for treatment of hepatic disorders, *Uvaria narum* is one of the potential plant for the liver disease like jaundice. The Hepatoprotective activity of extract was found by carbon tetrachloride induced liver toxicity, paracetamol induced liver toxicity and Thiocetamide induced Liver Toxicity by using chemicals like carbon tetrachloride. The hepatoprotective potential of leaves of *Uvaria narum* (Annonaceae) by noting elevationin hepatic biomarkers like SGPT, SGOT, ALP, bilirubin & other biochemical parameters like Cholesterol, triglycerides, urea & tissue LPO, and decrease in total protein, albumin, glucose & tissue GSH, CAT, SOD in CCl_4 induced liver toxicity [14,15].

4.4. Antitumor Activity

Plants have strong immune-modulating and antioxidant characteristics that promote anticancer action. It was discovered that taxol and podophyllotoxin were effective in treating refractory ovarian, breast, and other malignancies. A good source of potential cytotoxic alkaloids and antraquinones is the seed oil of *Uvaria narum*. The phytoconstituents terpenoid and alkaloid found in *Uvaria narum* contribute to the antitumor action [1].

4.5. In Vitro Cytotoxicity

Using the trypan blue exclusion method, the cytotoxic effects of each extract on Ehrlich's ascites carcinoma (EAC), Dalton's lymphoma ascites (DLA), and normal rat spleen cells were assessed. Extracts of PE, CHL, acetone (ACT), and methanol (MeOH) demonstrated a strong toxic effect on these cells. The aqueous extract, however, proved non-toxic. Petroleum ether extract chemicals, which are toxic to cancer cell lines but less deadly to healthy spleen cells, serve as an example of differential cytotoxicity. In the phytochemical screening and TLC analysis of Petroleum extract, terpenoid and phytosterol are determined to be two of the major phyto-constituents. The cytotoxic effect of the PE extract is therefore anticipated to be connected to its Terpenoidal concentration. The cytotoxicity demonstrated by PE extract was selective, being more toxic to cancer cells than normal spleen cells (IC50 for DLA was 19 ± 0.57 and that for EAC cells was 38 ± 0.74 g/mL, while over 100 g/mL). CHL, ACT, and MeOH extracts have demonstrated the potential for cytotoxicity, and they have cytotoxic effects on cancer cells that are comparable to those of normal cells. This suggests that U. narum leaf is an important source of physiologically significant cytotoxic phytoconstituents [16].

4.6. Antidiabetic Activity

The earlier trend in diabetes treatment involved oral administration or injections, which necessitated careful examination of natural products, particularly *Uvaria narum*, by attempting to identify phytochemicals and chemical constituents as well as conducting clinical trials on natural products and their analogues in drug discovery studies. Ac-cording to review of many literary works, diabetes can be treated with plant leaves. *Uvaria narum's* methanolic extract substantially reduced the activity of glucosidase and amylase. Acarbose was used as the reference medication to quantify these inhibitory effects. Additionally, the cell saw no cytotoxic effects from *Uvaria narum*. Amylase and glucosidase activities were effectively inhibited by the *Uvaria narum* extract in a good percentage. UN extract inhibited amylase activity by 71.31%, while the control medication acarbose inhibited it by 88.54%. In addition, the extract inhibited—glucosidase activity by 79.11% whereas acarbose inhibited it by 87.35%. Additionally, IC50 values were found. Furthermore, after being exposed to the extract, 75.49% of 3T3-L1 cells took up glucose and 70.67% of them expressed GLUT4 [17].

4.7. Antifungal Activity

In traditional and ethnomedicalpractises, *Uvaria narum* has been used to treat gastrointestinal issues, jaundice, fever, and skin ailments. The acetone extract of *U. narum*'s different leaf extracts showed extremely good antifungal activity in preliminary antifungal testing. By using bioactivity-guided fractionation, the active ingredient in the acetone extract of *U. narum* leaves was identified. It was then characterized as a novel compound called 2-E-(2″-oxo-5″-acetoxy cyclopent-3″-en-1″-ylidene) ethyl benzoate using NMR, IR, and mass spectroscopic methods. The viable isolation has shown excellent effectiveness against the fungus *Colletotrichum gloeosporioides* [18]. *Uvaria narum*, were tested against two important plant fungal pathogens, *Fusarium moniliforme*, and *Corynespora cassiicola*. The leaves of *Uvaria narum* were subjected to sequential soxhelet extraction in four solvents, i.e., Petroleum Ether (PE), Chloroform (Chl), Acetone (Ac) and Methanol (Me). The extracts thus obtained were subjected to antifungal tests by Poison Food Technique The sequentially extracted PE extract and the chloroform extract derived thereafter inhibited

the fungus growth by 65% and about 49% in case of *Fusarium* and 70% and 45% in case of *Corynespora* [19].

4.8. Antihelmintic Activity

The acetogenins were tested in concentrations of 0.05%, 0.15%, 0.25%, 0.75%, and 1.25%, and the crude extract was tested in concentrations of 0.1%, 0.3%, 0.5%, and 2.5%. The same ethanol/water mixture (30% ethanol) in which drug solutions were prepared, mebendazole was employed as the standard drug. At every concentration, it exhibited a very notable inhibitory effect, and when compared to the control, it exhibits almost 0.5% inhibition. This demonstrated the effectiveness of *U. narum's* antihelmintic activity [13].

4.9. Antiproliferative Activity

To measure antiproliferative activity, MTT test was utilized. *Uvaria narum* seed oil showed a dose-dependent reduction in cell viability in Vero (normal monkey kidney cells), HCT-15 (human colorectal adenocarcinoma cells), HepG2 (hepatocellular carcinoma cells), and HeLa cells (human cervical carcinoma cells) in culture exposed to it at various concentrations, indicating that it has anti-proliferative potential. The viability of all cells was shown to be lowered depending on the amount of oils and all cells were susceptible to UNSO. The needed UNSO concentration in HeLa cells to cause a 50% reduction in cell viability (IC50 value) was discovered to be greater than 100 ± 2.35 g/mL. However, the IC50 values with HepG2, HCT-15, and Vero cells after exposure to UNSO were 50.30 ± 1.45, 40.0 ± 1.94, and 48.05 ± 2.43 g/mL, respectively [20].

5. Ethnomedicinal Applications

Uvaria narum is mostly used to treat patients with skin conditions like dermatitis, pityriasis, and constipation. It is also used to treat fever, jaundice, haemorrhoids, varicose veins, and irritation and itching. In rheumatic swellings, jaundice, biliousness, and fevers, leaves are advised. Root is used to cure typhoid, jaundice, fever, and biliousness. Women are given a decoction of the root bark to manage fits during birth. It is also used for skin conditions, eczema, children's gastrointestinal troubles, and rheumatism.Oil Reduces liver burning when extracted from the root. *Uvaria narum* whole root extract may be used medicinally as a potential free radical scavenger. The plant may also be utilized as a defense against diseases like ageing and others brought on by free radicals. For gastrointestinal disorders, Uvaria's aerial portions are employed [1,21].

6. Conclusions

The above review about *Uvaria narum* shows that, it is significant because of its therapeutic benefits and extensive phytochemical profile. The plant displayed a good amount of phenols, tannins, antioxidants. The chemical composition of the plant also reveals that stereoisomers and acetogenins are significant components of the root bark. Additionally discovered in isolation are glutinone, glutinol, beta-sitosterol, taraxerol, and benzyl benzoate. According to research that has been written about a variety of plants, the existence of these phytoconstituents in plants has been linked to various medical qualities in plants like anticancer, antioxidant, anthelmintic, antiproliferative, hepatoprotective, antitumor and antibacterial activities.. As a result, it is used to treat rheumatic infections as well as eczema, biliousness, jaundice, and gastrointestinal issues.

Author Contributions: Conceptualization, J.P. and R.W.; formal analysis, A.T. and R.W.; investigation, A.T and T.G.; resources, A.T. and K.P.; writing—original draft preparation, J.P.; writing—review and editing, A.T.; visualization, J.P. and R.W.; supervision, J.P. All authors have read and agreed to the published version of the manuscript.

Funding: This review received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: We would like to convey our obligation to Management and Principal, P.S.G.V.P. Mandal's College of Pharmacy, Shahada, Dist. Nandurbar, for furnishing all the essential facilities to accomplish the literature review endeavor.

Conflicts of Interest: The authors declare no conflict of interest.

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