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A Brief Review on Bioactive Compounds from *Pseuduvaria* Species

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Abstract: The *Pseuduvaria* species belong to the family Annonaceae which is rich in bioactive compounds. They are commonly found in Malaysia, Thailand, Burma and Indonesia and in the northeastern part of Queensland, Australia. Currently, there are about 52*Pseuduvaria* species that were classified and documented but only a few were investigated chemically and biologically. This paper will briefly describe the bioactive compounds from the *Pseuduvaria* species based on previous studies.

Keywords: *Pseuduvaria* species, Annonaceae, bioactive compounds.

1. INTRODUCTION

Plants produce chemical constituents called 'phytochemicals' with protective and disease preventive properties. The term 'phytochemicals' are chemical substances that are generated naturally in plants that demonstrate various biological activities such as antioxidant, antibacterial, antifungal, anti-inflammatory, anti malarial and anticancer activities [1].

These phytochemicals include alkaloids, isoflavones, flavanoids and lycopene which are clinically proven to be of valuable therapeutic importance which may assist in the treatment of many diseases such as cancer, cardiovascular disease, degenerative diseases and HIV infection [2]. Vegetables, fruits, herbs and seeds are some of the plants that contain phytochemicals which are rich in phenolic compounds such as flavanoids, phenolic acids, anthraquinones and coumarins [3].

Over the years, there have been significant findings and evidence that naturally-occurring compounds derived from higher plants have the potential to be developed as modern therapeutic drugs.Approximately, about 25% of the drugs used in the world today originate from higher plants and among them were taxol, morphine, quinine caffeine, atropine, and reserpine [4].

1.1. The Annonaceae Family

The family Annonaceae is one of the largest family of the flowering plants from magnolia order (Magnoliales) which consists of approximately 128 genera and over 2,220 species [5]. There are about 51 genera and 950 species of the Annonaceous plants in Asia and Australia, 40 genera and 450 species in Africa, and 38 genera and 740 species in the American continent [6]. In Malaysia, there are 38 genera, 198 native and 5 cultivated species including 17 varieties of Annonaceae plants and they are abundantly found in the lowland forests mostly below 2,000 feet [7].

The members of the Annonaceae family are made up of small trees, shrubs and woody climbers that be found mainly in the tropical and subtropical regions [8]. The plants from Annonaceae family have been known to be rich in alkaloids especially the isoquinoline alkaloids where they are found mainly in most parts of the plants [9]. Most of the species from Annonaceae were used in folk medicine and many of the compounds isolated have exhibited potent biological activities such as cytotoxic, antitumor, antimalarial, antibacterial, antifungal, antiplatelet aggregation and immunosuppressive activities [10]. Traditionally, the plants of Annonacea (*mempisang*) have been used by the local healers to treat symptoms of fever and stomachache. And recently, they were claims that the plants can be also used in the treatment of cancer.

1.2. Genus Pseuduvaria

Pseuduvaria is a rainforest plant species that belongs to the family Annonaceae. Plants in this genus are in the major group of flowering plants (Angiosperms) that are made up of shrubs and trees usually found in the rainforest population [11]. It was reported that the *Pseuduvaria* species originated from Sundaland in the late Miocene and later migrated to the other part of the region [12].

The *Pseuduvaria* species are commonly found in Malaysia, Thailand, Burma, and Indonesia and in the northeastern part of Queensland, Australia (Fig. **1**). Currently, there are about 52 *Pseuduvaria* species that were classified and documented (Fig. **2**) but only a few have been investigated chemically and biologically.

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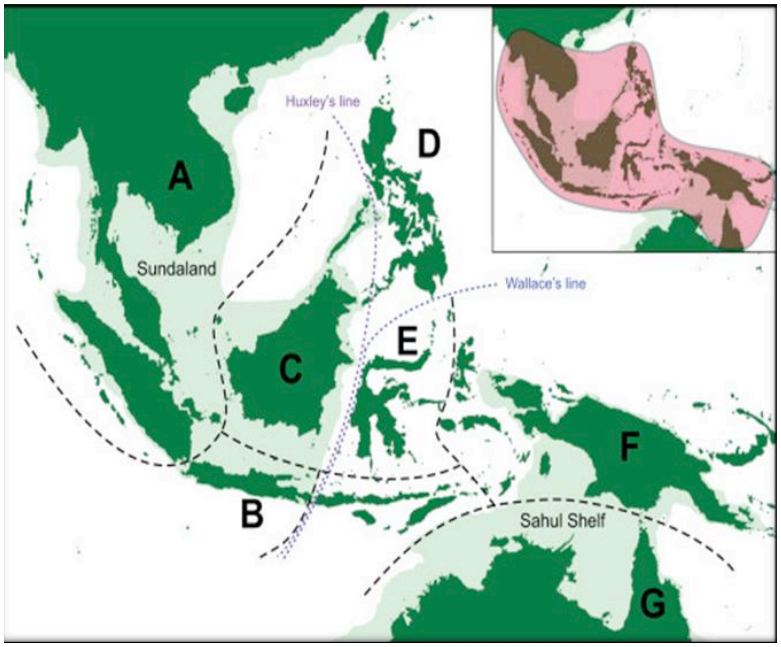


Fig. (1). Distribution of *Pseuduvaria* species in South East Asia (indicated in pink color) [12].

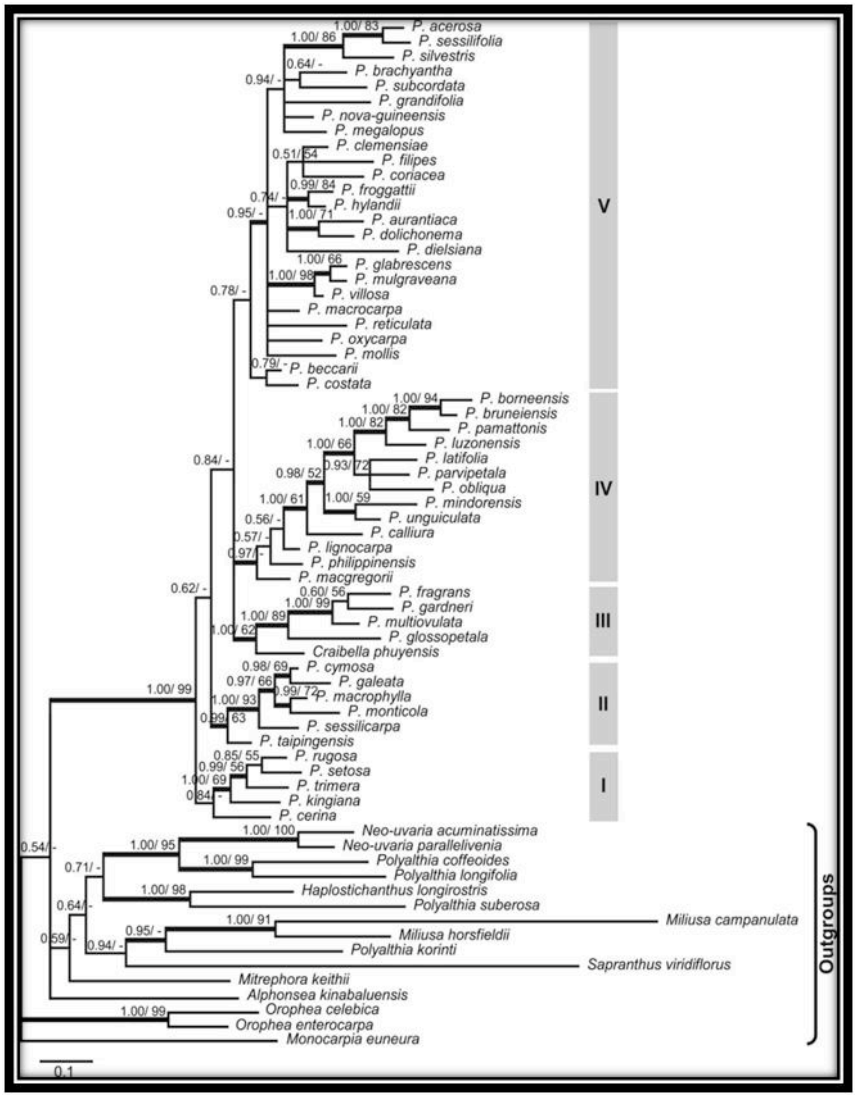


Fig. (2). Chronogram of *Pseuduvaria* species [13].

Fig. (3). The leaves, fruit and flower of Pseuduvaria species.

The *Pseuduvaria* genus was formerly known as *Orophearugosa*, *Mitrephorarugosa*and *Uvariarugosa*due to their close resemblances and similar morphological characteristics [13]. They are known to contain both alkaloid and non-alkaloid compounds, including essential oils. Some of the *Pseuduvaria*species are traditionally used in treating cough, fever and stomach ailments.

1.3. Morphological Description

The trees are 5-7 m high with slender and dark colored young twigs. The leaves are simple and alternate, membraneous and papery with lanceolate shape (spear shaped). The fruits are small which look like a bunch of berries consist of a group of fleshy carpels that is attached on a torus (Fig. **3**).

The bark is fibrous and aromatic, smooth and grey to brown in color. The flowers are bisexual and influorescences which are arranged in axillary fascicles solitary, paired or clustered and they are characterized by a cyclic perianth of three trimerous whorls, an androecium of several stamens and a gynoecium of free carpels on a flat or conical receptacle [14].

2. BIOACTIVE COMPOUNDS FROM *PSEUDUV-ARIA*SPECIES

2.1. *Pseuduvaria Macrophylla*

M. Othman *et al.* (2009) studied the antimicrobial and antioxidant activities of the crude extracts (hexane, ethyl acetate and ethanol) of *Pseuduvaria macrophylla*. The antimicrobial activity was evaluated by agar-based pour plate disc diffusion (PPDD) and broth -based turbidometric (TB) assay [15].

The investigation revealed that the crude extracts of *Pseuduvariamacrophylla* showed antimicrobial activity against two gram negative strains, (*Escherichia coli* and *Citrobacterfreundii*) and four gram positive strains (*Staphyllococcusaureus, Staphyllococcus epidermis*, *Bacillus cereus and Bacillus subtilis*) in a dose depending manner.

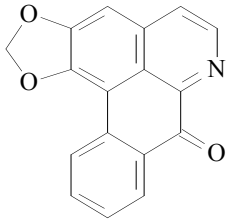
In the antioxidant test, all crude extracts showed high antioxidant activities in the β-carotene bleaching (BCB) assay test comparable to trolox and quercetin, but in Ferric Reducing Antioxidant Properties (FRAP) test, only the ethanol extract was active than the hexane and ethyl acetate extracts. However, the chemical compounds responsible for the bioactivities, have yet to be isolated.

2.2. Pseuduvariasetosa

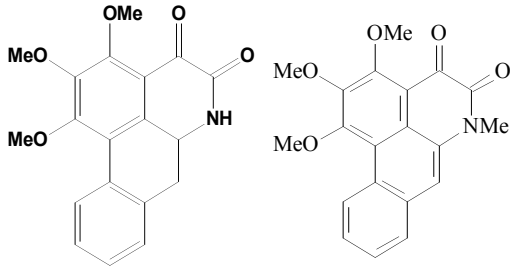
Biological activities of the four oxoaporphine alkaloids, N-methylouregidione, ouregidione, liriodenine and oxostephanine, isolated from the aerial part of *Pseuduvariasetosa*showed *in vitro*antituberculosis activity against *Mycobacterium tuberculosis* with MIC values of 100, 12.5 and 25 g/ml, respectively [16]. These results have demonstrated that aporphine alkaloids can be developed as potential anti-tubercular agents in chemotherapy [17]. In the same study, liriodenine isolated from *Pseuduvaria setosa* displayed antimalarial activity against *Plasmodium falciparum* (K1, multidrug-resistant) with 50% inhibitory concentration (IC_{50}) of 2.8 ug/ml.

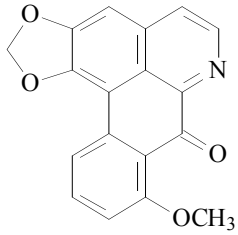
In the cytotoxicity study of *Pseduvaria setosa*, liriodenine and oxostephanineshowed strong cytotoxic activity against epidermoid carcinoma (KB) and breast cancer (BC) cell lines, whereas ouregidione was moderately active against BC cells. Both N-methylouregidioneand ouregidione were active against small cell lung cancer (NCI-H187) cell line and were able to stimulate lymphocyte proliferation with stimulation indices (SI) of more than 1.

In another study on bioactivity, ethanol crude extracts from *Pseuduvaria setosa* was found to stimulate lymphocyte proliferation in *in vitro* immunostimulating activity test. The isolated pure compounds: kaurenoic acid, β-sitosterol, quebrachitoland ouregidione were capable to enhance IL-12 secretion from J774A [18].

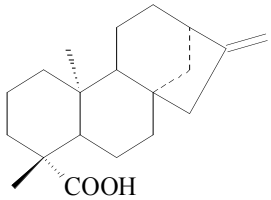


Liriodenine

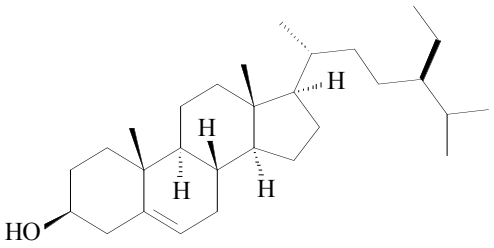


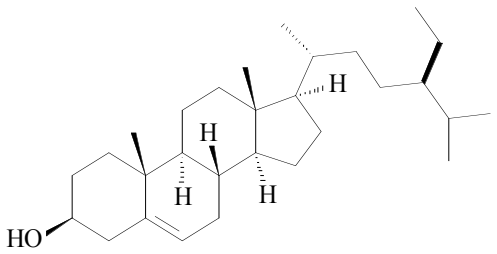


OuregidioneN-methylouregidioneoxostephanine



kaurenoic acid

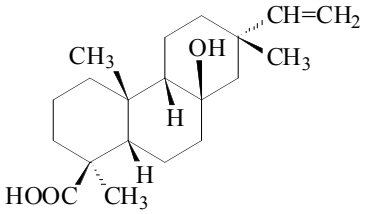


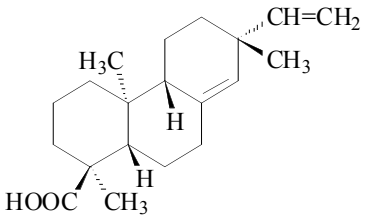


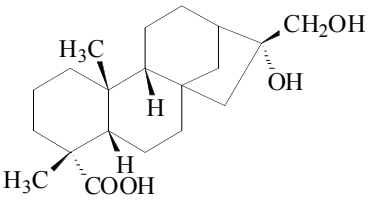
β-sitosterolquebrachitol

2.3. *Pseuduvaria Indochenesis*

Diterpenes, ent-8α-hydroxypimar-15-en-18-oic, ent-pimaric acid, and ent-16α,17-dihydrokauran-19-oic acid isolated from *Pseuduvariaindochenesis* was found to inhibit DNA topoisomerase activity [19].





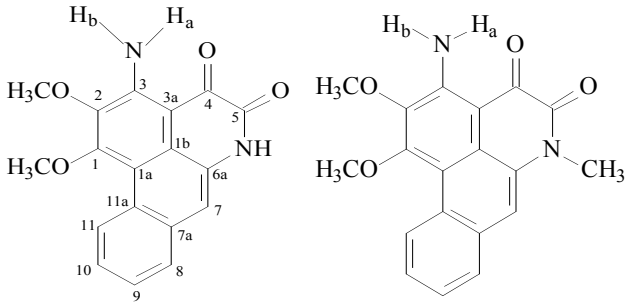


ent-8α-hydroxypimar-15-en-18-oicent-pimaric acident-16α,17-dihydrokauran-19-oic acid.

2.4. *Pseuduvaria Rugosa*

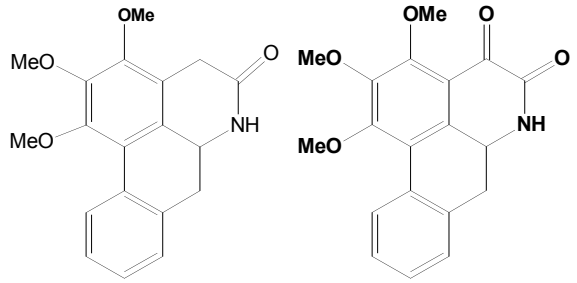
The two new oxoaporphine alkaloids with the amino group at C-3, *Pseuduvarine* A and *Pseuduvarine* B isolated from the methanol extract showed significant activity and selectivity in the cytotoxic test against three cancer cell lines namely human breast adenocarcinoma (MCF7), human liver carcinoma cells (HepG2) and human promyelocyctic leukemia cells (HL-60).

Pseuduvarine A and *Pseuduvarine* B showed significant and potent cytotoxicity and selectivity towards the tested cells with *Pseuduvarine* A being the most toxic against breast cells (MC7) at IC_{50} value of 0.9 µM and *Pseuduvarine* B being the most toxic and selective on human promyelocytic leukemia (HL-60) cell lines (IC_{50} 12.4µM).



***Pseuduvarine* A** ***Pseuduvarine* B**

In a another study of antiproliferative effect, 1,2,3-trimethoxy-5-oxonoraporphine and ouregidione induced cytotoxicity with HL-60, U937 and K562 cells [20].



1,2,3-trimethoxy-5-oxonoraporphine ouregidione

3. CONCLUSION

It can be concluded that compounds isolated from the *Pseuduvaria* species, mainly of oxoaporphine alkaloids and diterpenes exhibited interesting biological activities such as cytotoxictiy, antiproliferative, antimicrobial, anti-tuberculosis, anti-malarial activities and inhibition of DNA topoisomerase. Out of 52 species, only four species were studied chemically and biologically. It is hope that more studies can be carried out on other *Pseuduvaria* species to discover and investigate the pharmacological properties of the plants.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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