

PHYTOCHEMISTRY OF PHALERIA MACROCARPA (THYMELACEAE), MEDICINAL AND THERAPEUTIC POTENTIAL

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Keywords: *Phaleria macrocarpa*; Phytochemistry, Ethnopharmacology; Therapeutic properties; Toxicology

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Summary

The utilization of medicinal plants has been at the forefront worldwide. Diverse plants have been utilized for years to conserve and add flavor to foods, prevent ailments like epidemics and treat health-related disorders. This might be due to the therapeutic and curative characteristics associated with the plants which are mainly observed as the secondary metabolites in various parts of the plants. These ideas of healing and therapeutical usage have been transferred over the years within and amidst human

communities in different parts of the world. The phytochemicals produced during secondary metabolism are mostly responsible for their biological importance. Recently, the use of diverse medicine-rich plants has greatly increased. *Phaleria macrocarpa* (Scheff.) Boerl is one of the medicinal plants used for therapeutic purposes. This plant is also called Mahkota Dewa; it is indigenous to Malaysia and Indonesia. The extracts from different parts of *P. macrocarpa* have been reported to possess diverse therapeutic properties including anti-diabetic, anti-cancer, anti-inflammatory, anti-hyperlipidemic, anti-fungal, anti-bacterial, vaso-relaxant, antioxidant, and others. Besides, this plant is endowed with different phytochemicals such as gallic acids, phalerin, icariside-C, mahkoside, mangiferin, dodecanoic acid, des-acetyl flavicordin-A, palmitic acid, ethyl stearate, flavicordin-A, flavicordin-D, flavicordin-A glucoside, lignans, saponins, alkaloids, and others. Hence, this chapter presents an up-to-date review of the occurrence, botanical descriptions, phytochemistry, therapeutic properties, and toxicological studies of *P. macrocarpa*.

1. Introduction

Human beings depend wholly on nature for their day-to-day survival as it happens to be the source of their foods, shelters, fertilizers, clothing, fragrances, flavors, means of transportation, and medicines. A larger percentage of the world population especially in the developing countries predominantly relies on medicinal plants in their healthcare system because herbal medicine has a long history of usage (Mamatha et al., 2020). Other than this, several developed countries including UK, Australia, North America, and other European countries have widely embraced the utilization of herbal medicines as complementary and alternative medicines (CAMs) (Ekor, 2014). Till today, the use of medicinal plants remains the most important parameter in fighting different infectious diseases and ailments including inflammation, cancer, diabetes, cardiovascular diseases, hypertension, and others. The importance of using medicinal plants can be ascribed to their distinct advantages that include low toxicity, easy accessibility, low cost, and reduced or no adverse effects when consumed with accurate doses (Alara et al., 2018a; Andriani et al., 2016). Thus, the use of herbal medicines play the main role in pharmaceuticals; thereby increases the demand for medicinal plants in the global market (Ekor, 2014). Even though, there are numerous species of medicinal plants; smaller portions are utilized in traditional treatments. Although several species are enlisted as medicinal plants, only a smaller species have been commercially utilized in traditional medicine. These traditional medicines are much more prominent and considered as the alternative to modern medicine.

Plant, animal and mineral products are being used as the major sources of medicines (Othman et al., 2014). Additionally, a lot of the medicinal plants have been reported to possess secondary metabolites such as terpenoids, alkaloids, acetogenins, and phenolics (Alara et al., 2018b; Alara et al., 2019; Othman et al., 2014). The secondary metabolites indicate properties that can be presented based on the taxonomy, ecology, biochemical diversity, and differentiation. The wider diversities of secondary metabolites all through the plant kingdom have been showing rich biogenic resources in developing innovative remedies and discovering novel drugs (Othman et al., 2014). Until now, natural products and their derivatives contributed to over 50% of clinically used drugs in the world. Not less than 25% of the total medicinal plants are from higher plants. In the past

years, potent drugs have been achieved from different flowering plants (Gurib-Fakim, 2006).

As previously reported, the Thymelaeaceae is a global family belonging to flowering plants; this family comprises about 898 species and 50 genera (Rogers, 2009). Thymelaeaceae are broadly spread in both hemispheres (Othman et al., 2014). About 89 species and 9 genera of the Thymelaeaceae plants are from China. The larger number of Thymelaeaceae genera are (Kubitzki and Bayer, 2003):

- *Daphne* with 95 species,
- *Gnidia* with about 160 species,
- *Pimelea* (110),
- *Struthiola* (35),
- *Wikstroemia* (70),
- *Daphnopsis* (65),
- *Thymelaea* (30),
- *Lachnaea* (30),
- *Gonystylus* (25),
- *Phaleria* (30).

Thymelaeaceae family is mainly of small trees or shrubs, rarely herbs, deciduous, or evergreen. Furthermore, some of these species possess medicinal properties while some are toxic (Othman et al., 2014). *Phaleria macrocarpa* (Scheff.) Boerl is part of the plants belonging to the family Thymelaeaceae. *P. macrocarpa* was first presented as *Drimyspermum macrocarpum* by Scheffer; this was done relative to the fruiting specimens obtained through Teysmann nearly Doré in western New Guinea (Angiosperm Phylogeny Group, 2003). *P. macrocarpa* is commonly called 'Mahkota Dewa'; also to known to be God's Crown (Alara et al., 2016). Locally, it is called 'Simalakama' in Depok (West Java) and Sumatra (Malay), and 'Makuto rajo', 'Makuta Dewa', 'Makuto mewa' or 'Makuto ratu' in Java (Othman et al., 2014). Generally, *P. macrocarpa* is utilized as herbal medicine in East Asia. The extracts from this plant are utilized in treating diverse ailments including cancer, *Diabetes mellitus*, allergies, liver and heart diseases, blood diseases, kidney failure, stroke, and high blood pressure (Alara et al., 2016; Fariza et al., 2012; Mamatha et al., 2020; Parhizkar et al., 2015; Sugiwati, 2006). Besides, extracts from *P. macrocarpa* are employed to treat different skin diseases such as acne. Due to the various important and ethnopharmacological properties of *P. macrocarpa*, this book chapter focuses on outlining and discussing the phytochemistry, medicinal and therapeutic properties of this important plant.

2. Occurrence, Ethnopharmacology and Botanical Description

2.1. Occurrence of *P. macrocarpa*

P. macrocarpa (Scheff.) Boerl otherwise called Mahkota Dewa is a plant in the family of Thymelaeaceae. This plant is associated with tropical regions like Malaysia and Indonesia; it is originated from Papua (Alara et al., 2016; Othman et al., 2014). Moreover, this plant is called 'pau' or God's crown. *P. macrocarpa* has been identified to be a medicinal plant for ages. It is grown all through the year and can reach a height of about 1-18 m and 1 m long straight root; it has white wood with brownish-green

bark. Likewise, it can grow at altitudes of about 10-1200 m above sea level with around 10-20 years of productive age. Its leaves are tapering and green with the width and length fall within 3-5 cm and 7-10 cm, respectively. The pit is poisonous, white and round; the color of its flowers varies from green to maroon (making a compound between 2 and 4) (Altaf et al., 2013). As illustrated in Figure 1, *P. macrocarpa* is a complete tree having leaves, flowers, fruits, and stems. The diameter of its fruit is about 3 cm and eclipse in shape; the color of this fruit is red after it has fully ripe, and green when unripe. Its seeds are anatropous, ovoid and brown, they are arranged as 1-2 seedlings in each fruit (Hendra et al., 2011). Even though the extracts from *P. macrocarpa* are being utilized in both processed and unprocessed forms; nevertheless, the unprocessed form can sometimes be toxic or poisonous (Yosie et al., 2011).

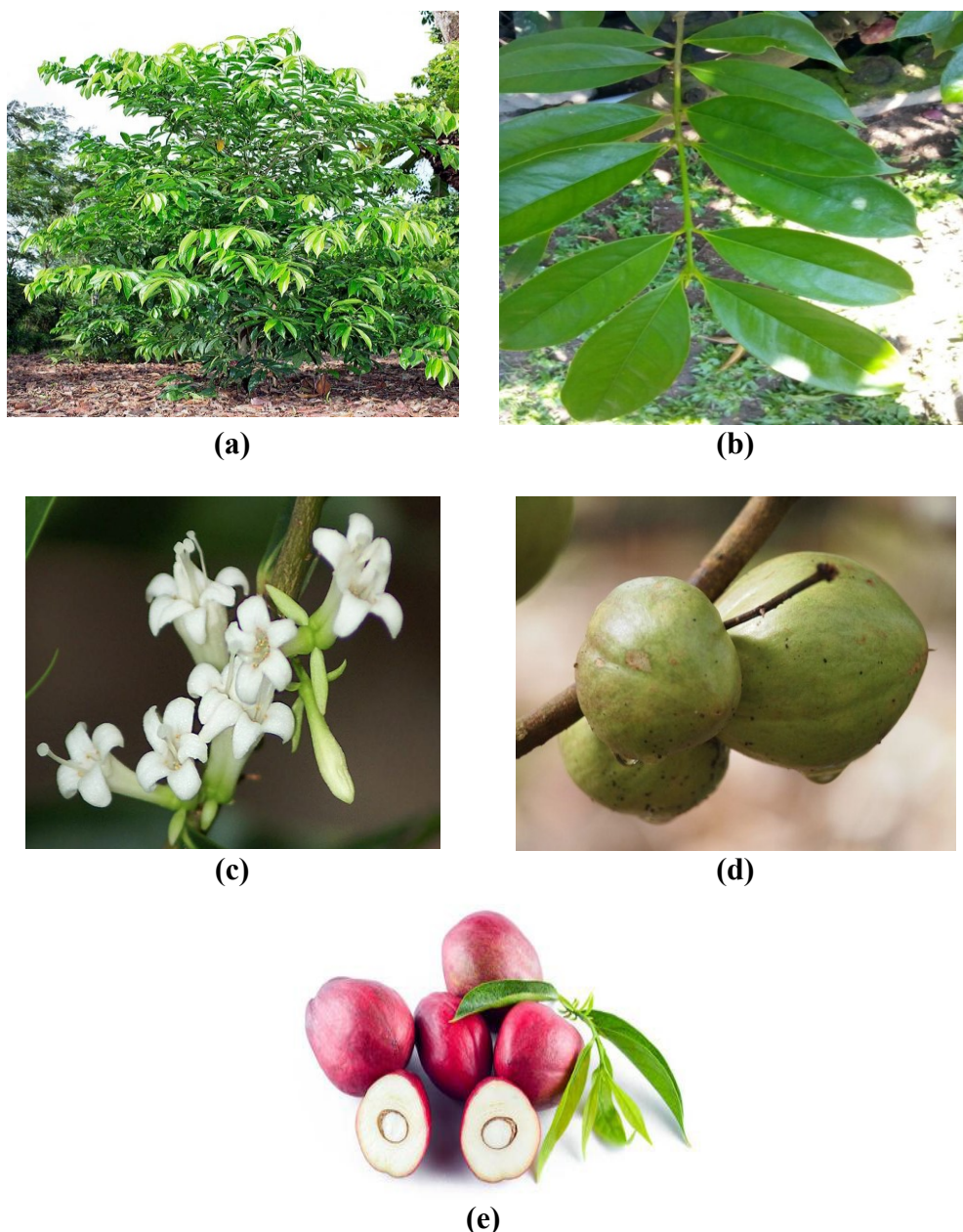


Figure 1a. The tree (a), the leaves (b) the flowers (c), the unripe fruits (d), and ripe fruits showing the seeds of *P. macrocarpa* (e).

2.2. Taxonomy of *P. macrocarpa*

The taxonomy of *P. macrocarpa* is illustrated in Figure 1b.

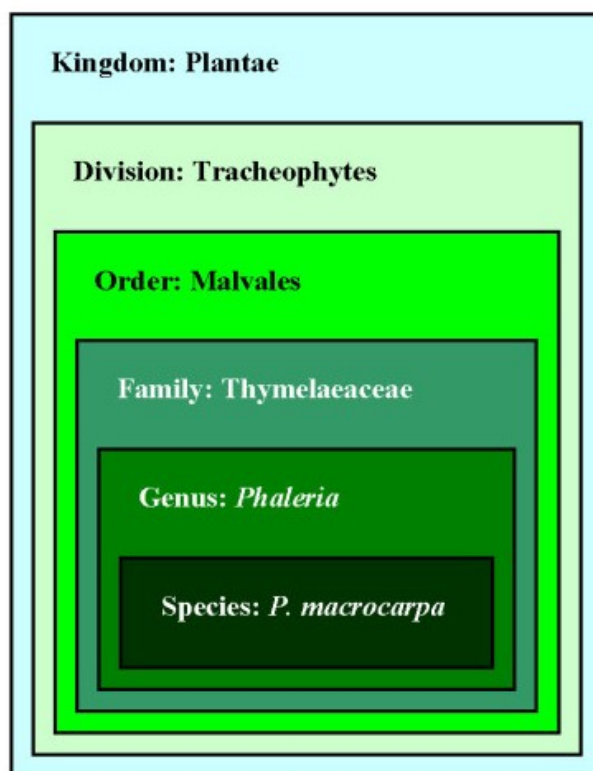


Figure 1b. Taxonomy of *P. macrocarpa*

2.3. Ethnopharmacology and Traditional Uses of *P. macrocarpa* Parts

For ages, *P. macrocarpa* has been known for its medicinal properties. This plant has been known as a medicinal plant since antiquity. Locally, the fruits are being utilized to treat diverse ailments including *Diabetes mellitus*, impotency, hypertension, hemorrhoids, cancer, rheumatism, kidney disorder, heart and liver diseases, dysentery, blood diseases, stroke, acne, migraine, kidney disorders, and several skin infections (Alara et al., 2016; Mamatha et al., 2020; Othman et al., 2014; Parhizkar et al., 2015; Ramdani et al., 2017; Yanti and Radji, 2015). Moreover, *P. macrocarpa* fruit extract is being drunk locally as a herbal tea either only or mixed with other plants of higher medicinal values to cure ailments including *Diabetes mellitus*, hypertension and cancer (Hendra et al., 2011a).

Given the ethnopharmacological importance of *P. macrocarpa*, boiled fruit extract using water as a solvent is being employed in treating or alleviating diverse disease symptoms. This plant is mostly employed as an alternative in therapeutic healing within the low-income Malaysians and Indonesia health system (Mamatha et al., 2020). All parts of *P. macrocarpa* including leaves, stem, seeds, and fruits have been widely utilized in traditional medicine; it is known to possess diverse therapeutic properties. The pharmacological and biological properties of the leaves, stems, seeds, and fruits

have been extensively reported in different studies (Alara et al., 2016; Mamatha et al., 2020; Othman et al., 2014; Parhizkar et al., 2015; Ramdani et al., 2017; Yanti and Radji, 2015). The extracts from leaves comprise phytochemicals that can alleviate allergies, impotence, tumors, diabetes, and blood diseases; extracts from the stem are employed to treat bone cancer; the extracts from seeds (eggshells) are utilized as an antidote for cervix cancer, breast cancer, heart diseases, and lung ailments; and the extract from fruits can treat gout, cancer, high blood pressure, diabetes, liver and skin diseases (Alara et al., 2016). Biologically, the extracts from different parts of *P. macrocarpa* have been reported in different studies to possess properties including anti-hyperglycemia, anti-tumor, anti-inflammation, anti-hypertensive, anti-diarrheal, anti-viral, antioxidant, anti-bacterial, vaso-relaxant, antidiabetic, and anti-fungal (Alara et al., 2019; Altaf et al., 2013; Azmir et al., 2014; Endra et al., 2009; Fariza et al., 2012; Lay et al., 2014; Rahmawati et al., 2006; Sugiwati, 2006; Yanti and Radji, 2015). Some of the ethnopharmacological properties of different parts of *P. macrocarpa* are summarized in Table 1 (Alara et al., 2019; Altaf et al., 2013; Azmir et al., 2014; Endra et al., 2009; Fariza et al., 2012; Lay et al., 2014; Mamatha et al., 2020; Rahmawati et al., 2006; Sugiwati, 2006; Yanti and Radji, 2015).

S/N	Parts of <i>P. macrocarpa</i>	Properties
1.	Leaves, mesocarp, pericarp, seeds	Antibacterial
2.	Fruits, fruit pericarp, fruit powder	Antidiabetic
3.	Mesocarp, pericarp, seeds	Anti-fungal
4.	Fruits, leaves	Anti-hypertensive
5.	Fruits	Anti-inflammatory
6.	Pericarp, various parts of old and young fruits	Antioxidant
7.	Fruits, fruit pulps, leaves, mesocarp, pericarp, seeds	Cytotoxic
8.	Fruits	Vasorelaxant

Table 1. Ethnopharmacological properties of different parts of *P. macrocarpa* (Alara et al., 2019; Altaf et al., 2013; Azmir et al., 2014; Endra et al., 2009; Fariza et al., 2012; Lay et al., 2014; Mamatha et al., 2020; Rahmawati et al., 2006; Sugiwati, 2006; Yanti and Radji, 2015)

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Biographical Sketches

O. R. Alara received the Bachelor of Technology from Ladoke Akintola University of Technology (LAUTECH), Nigeria in 2009; an MSc degree from Universiti Malaysia Pahang in 2016; and a PhD degree from Universiti Malaysia Pahang in 2019 (All degrees are obtained in Chemical Engineering). She has worked as an assistant regulatory officer in National Agency for Food, Drug and Control (NAFDAC) in Nigeria, Research Assistant, Research Officer, and Postdoctoral Fellow in Universiti Malaysia Pahang. She has received several scholarships during her academic pursuits including two competitive scholarships from the United State of America (Ogbomoso Sons and Daughters in North America Scholarship) and Oyo State Scholarship from Nigeria (these scholarships catered for her first-degree

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N.H. Abdurahman is an award-winning professor of Chemical Engineering. Prof. Abdurahman is an outstanding mentor, he has graduated 17 PhD, 14 masters, and 85 undergraduate students. He had served as an external examiner for over 70 theses. Another contribution he made to the body of knowledge is that he published over 300 research articles, 14 books, 10 book chapters, over 50 conferences, and over 50 research exhibitions. His research publications have received over 5000 citations in Google Scholar with an h-index of 36. He is a professional in his endeavours. He has been excellent in administration and leadership; he had previously been appointed as the deputy dean for research and innovations for 2 consecutive terms (8 years) in the faculty. Currently, he is the Head of the Separation Processes cluster. Moreover, Prof. Abdurahman is internationally recognised for his significant achievement in the body of knowledge. He is always at his best and a role model to many. He is an outstanding teacher, researcher, consultant, inventor, and award-winning professional with a great passion for changing and advancing the body of knowledge. Besides, he is one of the best brains in Chemical Engineering, Environmental Engineering, Petroleum Engineering, and Circular Economy.

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