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Mini Review

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A Critical Overview on the Extraction of Bioactive Compounds from *Phaleria macrocarpa* (Thymelaceae)

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Abstract

Medicinal importance of many plants has drawn the attention of researchers to focus on unveiling their therapeutic molecules. Approximately, 25% of the commonly used medicines contain compounds isolated from plants. The World Health Organization has highlighted that many plants in the world have been discovered to possess high medicinal value. The presence of large amounts of polysaccharides, polyphenols, hydrosable tannins and other secondary metabolites makes these plants to be medicinal. Moreover, the plants may contain simple phenolic compounds, phenolic acids, coumarin, flavonoids, stilbenes, hydrosable and condensed tannins, lignin and lignans. The phenolic compounds and flavonoids in particular, are ubiquitous in plants and therefore, represent an important component of a normal human diet. Hence, this review tends to elucidate the extraction of bioactive compounds from Mahkota Dewa (*Phaleria macrocarpa*) and the extraction methods.

Keywords: Maceration; Microwave-assisted extraction; Subcritical water extraction; Supercritical-fluid extraction; *Phaleria macrocarpa*

Introduction

Mahkota Dewa illustrates in Figure 1 scientifically known as *Phaleria macrocarpa* is one of the important medicinal plants. This plant is commonly known as God's crown [1], it originates from Papua Island located in the far east of the Indonesian archipelago, Indonesia and grows in tropical areas. *Phaleria macrocarpa* that belongs to Thymelaceae family has been traditionally used as an indispensable medicinal plant for centuries in Malaysia and Indonesia [2]. The *Phaleria macrocarpa* trees are thick, evergreen and grow in a tropical region up to 1,200 meters above sea level. The tree height ranges from 1 to 18 metres. The leaves are green and tapering with length and width ranging from 7-10 cm and 3-5 cm respectively. The flowers are either in green or maroon. The eclipse shaped fruits change from green to red when ripening. The diameter of the fruit is 3 cm and its grows on the trunks and branches of trees, and each fruit has 1 to 2 brown, ovoid and anatropous seeds [3].

The four major parts of *Phaleria macrocarpa* that are mostly enriched in medicine are: the stems, the leaves, the egg shell of the seeds and the fruits. The stems has been used in treating bone cancer [4], the leaves has been used for impotence, blood diseases, allergies, diabetes mellitus and tumor treatments [5,6]. Likewise, the egg shell of seeds are used for breast cancer, cervix cancer, lung diseases, liver and heart diseases treatments [7] and the fruits consisting of alkaloid, saponin, flavonoid and polyphenol and has been used as antioxidants [3].

Phaleria macrocarpa has a long history of ethnopharmacological usage. Due to the antihistamine [6], anti-oxidation [8] and antitumor effects in the plant, the stems, leaves, and fruits have been used as medicine. Empirically, *Phaleria macrocarpa* can be used to treat cancer [5], impotence, haemorrhoids, *Diabetes mellitus* [6], allergies, liver and heart diseases, kidney disorders, blood diseases, rheumatism, high blood pressure, stroke, migraine, various skin diseases, acne and so on [6,9,10].

Phaleria macrocarpa fruits can prevent arteriosclerosis and reduced cholesterol level in Japanese quails and in primary culture of rat hepatocytes [11,12]. Likewise, studies has been conducted on *in-vivo* and *in-vitro* hypercholesterolemia model to determine the effects of *Phaleria macrocarpa* fruit on blood lipid profile (total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein) as well as LDL receptor, PCSK9 protein and mRNA expression [13]. Meanwhile, the work performed by Press [14] on DLBS1245, a *Phaleria macrocarpa* standardized extract of fresh fruit, revealed the anticancer activities of this plant. In the study as further, DLBS1425 showed an inhibition of proliferation on breast cancer cells, MDAMB-231 and MCF-7 cells. In addition, DLBS1425 also acts as an anti-inflammation and anti-angiogenesis [14]. *Phaleria macrocarpa* fruits and seeds had shown the existence of important biological activities in the extract in term of anti-microbial, anti-inflammatory and its antioxidant activity [8,15].

Phaleria macrocarpa has shown a potential value as an alternative medicine for improving the sexual strength in male adult Spraque Dawley rats by increasing the level of testosterone and libido behaviour which has suggested that *Phaleria macrocarpa* can be used in man's fertility improvement [16]. *Phaleria macrocarpa* (Scheff.) Boerl has been studied to posses antidiabetic activity that inhibit alfaglukosidase

Figure 1: *Phaleria macrocarpa* tree.

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enzyme and effect on mice induced sterptozotosin sugar level. The leaf and fruit *Phaleria macrocarpa* (Scheff.) Boerl have ACE inhibitors activity with IC50 values in the leaves was 189.13 µg/mLin PEE, 157.74 µg/mL in EEA and 101.52 µg/mL ME. While the IC50 values in the fruit was 161.7 µg/mL in PEE, 139.11 µg/mL in the EEA and 122.38 µg/mL in ME [17].

This review entails the theoreotial overview of extraction of bioactive compounds from *Phaleria macrocarpa* and the extraction methods that has been used [18].

Results

Table 1 and Figure 2 show the bioactive compounds that had been extracted from *Phaleria macrocarpa* which have medicinal values and their percentages respectively [19-23]. Table 2 reviews different methods of extraction and solvents that has been used in the extraction of bioactive compounds from *Phaleria macrocarpa* [24-29].

Discussion

Table 1 shows different bioactive compounds isolated from *Phaleria macrocarpa* which include phenolic compounds [30] (luteonin, apigenin, tangeritin, quercetin, kaemferol, myricetin, isorhamnetin, pachypodol, hesteretin, naringenin, eriodictyol, catechins and epicatechins, genistein, daidzein, glycitein, cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin, aurones, xanthones, and condensed tannins); terpenes (isoprenoids) compounds [28] (29-norcucurbitacin, deacethyl fevicordin A, fevicordin A glucoside, and fevicordin D glucoside); alkaloid compounds [31] and benzophenone compounds (Makoside A [10], 4,5-dihydroxy-4´-metoxybenzophenone-3-O-glucoside [3], 4´-6-dihydroxy-4- metoxybenzophenone-2-O glucoside [1], 3,4,5-trihydroxyl-4´-methoxybenzophenone-3-O-β-D-glucoside [22], Phalerin [19], dodecanoic acid, palmitic acid, ethyl stearate, sucrose, vasorelaxant icariside C3, and mangiferin [10,22]).

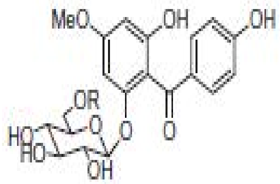
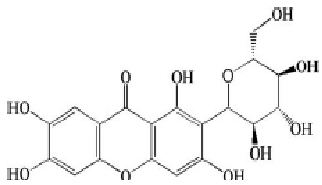
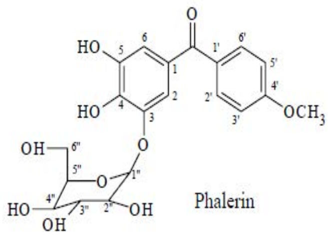
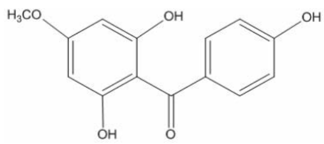
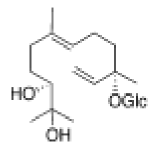
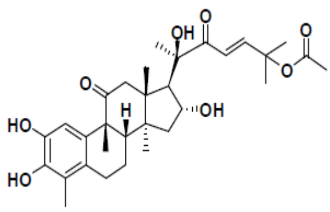
Part of *Phaleria macrocarpa*	Bioactive compounds present	Chemical Structure	References
Nut shell, fruit	2,4́,6-trihydroxy-4-methoxy-benzophenone-2-O-β-ᴅ-glucoside (Mahkoside A) 2,4́,6-trihydroxy-4-methoxy-6"-acetyl-benzophenone-2-O-β-ᴅ-glucoside (Mahkoside B).		[10,21,23]
Fruit	Magniferin		[21,22]
Leaf	4,5-dihydroxy,4´-methoxybenzophenone-3-0-β- ᴅ -glucoside (Phalerin)		[20,24]
Leaf	2,6,4'-trihydroxy-4-methoxybenzophenone		[23]
Fruit	icariside C_3		[19]
Seed	fevicordin A		[24]

Table 1: Bioactive compounds in *Phaleria macrocarpa* and their chemical structures.

Part of *Phaleria macrocarpa*	Methods of Extraction	Solvent	Bioactive compound/Extraction Yield	References
Nut shell	Refluxing	ethanol	Mahkoside A (206 mg) Mahkoside B (17 mg)	[18]
Fruit	Subcritical water Sohlex Room temperature Heat of reflux Supercritical carbondioxide extraction	Water Methanol Ethanol Water Methanol Ethanol Water Methanol Ethanol water CO_2	Magniferin 21.7 mg/g 24.6 mg/g 12.1 mg/g 18.7 mg/g 23.4 mg/g 7.4 mg/g 15.1 mg/g 25.0 mg/g 13.2 mg/g 18.6 mg/g 0 mg/g	[20]
Fruit	Boiling	Water	13%	[13]
Seed	Solvent	n-hexane	55.32 g/100 g of dry sample	[2]
Seed	Supercritical carbon dioxide Solvent	CO_2 n-hexane	52.9 g per 100 g of dry sample 10.9 ml/g	[25]
Fruit	Solvent	Methanol	0.3234 μmol DPPH/mg dry basis	[3]
Fruit	Liquid-liquid	Ethyl acetate	1736.989 μg/L of E2.2 compound	[26]
Bark	Maceration	Ethyl acetate n-hexane ethanol	IC50=10.15 g/mL IC50=13.35 g/mL IC50=12.92 g/mL	[7]
Fruit	Maceration	ethanol		[27]
Leaf	Maceration	methanol	61.2 g	[22]
Leaf	Maceration	Ethyl acetate	25 g	[23]
Fruit	Maceration	Methanol Hexane Chloroform Ethyl acetate	47.2 g 2.1 g 3.1 g 12.2 g	[28]
Fruit	Boiling	Water	13%	[16]
Fruit	Maceration	$CHCl_3$ Methanol	15.4 g 96.0 g	[19]
Fruit	Conversional	Methanol	42 g	[29]
Seed	Maceration	Methanol	10 g	[8]
Fruit	Sohlex	Petroleum ether Methanol Water	3.06% 18.5% 6.08%	[5]

Table 2: Methods of extraction, solvents used and the yield of *Phaleria macrocarpa*.

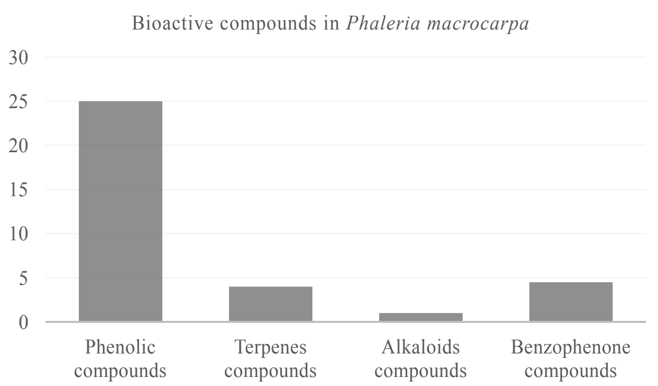


Figure 2: Bioactive compounds in *Phaleria macrocarpa*.

Furthermore, different extraction techniques used in the isolation of *Phaleria macrocarpa* bioactive compounds include the solvent extraction, pressurized liquid extraction, subcritical water extraction, supercritical extraction, microwave-assisted extraction, ultrasonic-assisted extraction, enzyme-assisted extraction and instant controlled pressure drop-assisted extraction as shown in Table 2. Likewise, different solvents been used are water, ethanol, methanol, ethyl acetate, dichloromethane, hexane, chloroform and carbon(IV)oxide. These gave different extraction yields. From the study conducted so far, it can be clearly seen that methanol gave the highest yields as obtainable in Table 2. However, the yield from methanol had been considered as highly toxic and can therefore not be considered as generally recognised as safe (GRAS) solvent [20]. The methanol extract of *Phaleria macrocarpa* seeds exhibited the highest yields of total flavoid content, total phenolics and flavonoid contents [8].

Conclusion

In the extraction of bioactive compounds from *Phaleria macrocarpa*, the choice of extraction method is an essential factor in order to achieve quality and higher yields. During the preparation of *Phaleria macrocarpa*, the process such as grinding and drying can affected the efficiency and phytochemical constituents of the final extracts. In conclusion, there is no specific extraction methods that is the ideal method but each extraction procedures has its own uniqueness. However, the most suitable methods are microwave-assisted, hydrodistillation, maceration, supercritical fluid extraction and subcritical water extraction but supercritical fluid extraction gives the highest yield of extracts.

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