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Short Communication

Pimpinella pruatjan Molk: LC-MS/MS-QTFT Analysis of Bioactive Compounds from Decoction and Ethanol Extract of Aerial Parts

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Abstract

Pimpinella pruatjan Molk is native to Java and well known as aphrodisiac in traditional medicine. A water-boiled extract of the plant has been used in the treatment of erectile dysfunction (ED). No study has been found on the phytochemical constituents and identification of corresponding biological activities in water and polar extract. This study is aimed to identify phytoconstituents of a decoction and ethanol extract from the aerial parts of *P. pruatjan* Molk. Liquid chromatography-tandem mass spectroscopy (LC-MS/MS) was used to analyze and predict the bioactive compounds in both extracts. LC-MS/MS revealed both extracts contained two important compounds: Luteolin-7-O-β-D glucopyranoside and Undulatoside A. Luteolin and Luteolin glucoside are also found in *P.anisum* L. Lutein 7-O glucoside was found in water extract, while more bioactive compounds, including populnin, 3,5-O-dicaffeoylquinic acid, quercetin-3'-O glucoside, methylophiopogononeone-A, kaempferol-7-O-α-L-arabinofurano side, and 7-hydroxy-3,5,6,3',4'-pentamethoxyflavone, were found in ethanol extract. Accumulation of flavonoids, phenols, phenylpropanoids, alkaloids, and furanochromone in low quantities was observed in both extracts. This is the first report providing evidence justifying its use as a traditional medicine. Further investigation into the pharmacology mechanism of action is required.

Keywords: *Adaptogen, Apiaceae, luteolin-O-glycosides, methylophiopogonone-A, pimpinella, populnin, undulatoside A*

Introduction

Pimpinella and other genera in the Apiaceae family are known to possess pharmacological benefits.[1] Pimpinella is distributed in Europe, Africa, and Asia. Essential oils from this genus are common and have been well studied in some species. Besides essential oils, some bioactive compounds from this genus include flavonoids,[1,2] phenols, phenylpropanoids,[2] saponins,[2] furanochromones,[3] furanocoumarins,[3,4] coumarins,[5] polyacetylenes,[6] steroids, and diterpens.[2]

P. pruatjan Molk is native to the Dieng Plateau in Central Java and well known in traditional herbal therapy as an aphrodisiac plant and treatment for erectile dysfunction (ED) (Farmakope Indonesia). The plant is available as herbal tea or coffee, and the aerial parts are usually brewed in hot water. The main component of the essential oil from *P. pruatjan* Molk aerial part is (Z)—bisabolene. It also contains oxygenated monoterpenes, oxygenated sesquiterpenes, and sesquiterpenes.[7] Essential oil from the root contains thymol methyl ester, 2,5-dimethoxy-p-cymene, and 2-isopropenyl-5-methyl-benzene-1,4-diol.[8]

Unlike *P. anismum* L, an essential oil from the aerial part of *P. pruatjan* Molk does not exhibit antimicrobial activity,[7] whereas those found in the root do exhibit antimicrobial activity.[8] Although the utilization of P. pruatjan Molk in ethnomedicine has been known, however, the hydrophilic extract of this plant has not

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been well investigated in terms of both corresponding constituents and biological activity. This study is the first to report bioactive compounds from water (decoction) and ethanol extracts from aerial parts identified using Liquid chromatography-tandem mass spectroscopy- hybrid quadrupole time of flight (LCMS/MS-QTFT). Relevant pharmacology activities that correspond to the phytoconstituents were discussed.

Material and Methods

Plant materials

P. pruatjan Molk was collected from Dieng Plateau, Central Java, at about 2,000 m above sea level and 14°C of average annual temperature. The aerial part, consisting of stems, leaves, and flowers, was separated from the roots. Standard preparation of herbal material was performed, including cleaning, drying, and milling into fine powder. Aerial part was used in the current study.

Extraction

Fine powder of dried aerial parts was cognate with water by heating for 3 hours. The water extract was then filtered before being freeze-dried. Meanwhile, ethanol extract was obtained by macerating fine powder of dried aerial plant parts for 48 hours with the agitation of 300 rpm at room temperature, followed by filtration, and evaporating the remaining solvent with a rotary evaporator (Buchi, Switzerland) at 40°C. Both extracts were kept at 4°C until further analysis.

Liquid chromatography-tandem mass spectroscopy-hybrid quadrupole time of flight (LCMS/MS-QTFT)

LCMS/MS-QTFT with maunakea spectroscopic explorer (Waters, United Kingdom), operating mode equipped with positive and negative mode electrospray ionization sources (ESI) was used. The stationary phase was Cosmosil 5C18-MS-II (4.6 i.d. × 150 mm; Nacalai tesque). All eluents were provided in High-performance liquid chromatography (HPLC) analytical grade. Each extract (0.5 g) was dissolved in 10 mL methanol, homogenized, and filtered using a 0.22 µm Membrane Filter (GHP)-Hyrophilic (PTFE) filter before being injected at 10 µL/sample. Scientific Information System from Waters (TM) (UNIFI) library was used to identify the compounds. Intensity was expressed as a range from the values obtained in the two measurements.

Results and Discussion

Bioactive compounds in *P. pruatjan Molk*

LCMS/MS-QTFT revealed that water and ethanol extracts from the aerial part contained two main constituents, namely Luteolin-O-glycosides, Luteolin-7-O-(6”-O-Beta-D-Apiofuranosyl)-β-D-Glucopyranoside and Luteolin-7-O-D-Glucopyranoside [Figure 1]. Both extracts also contain Undulatoside A [Table 1].

Ethanol extract is more concentrated and enriched in constituents than water extract. Besides Luteolin-O-glucosides and Undulatoside A, ethanol extract contains a series of flavonoids, phenols, and phenylpropanoids, including populnin, 3,5-O-dicaffeoylquinic acid, quercetin-3’-O-glucoside, dihydroresveratrol, 7-hydroxy-3,5,6,3’,4’-pentamethoxyflavone, kaempferol-7-O-α-L-arabinofuranoside, methyl ophiopogonone A, and traces of alkaloids [Figure 2 and Table 1].

In this study, luteolin-O-glucoside was identified as the most prominent flavonoid in *P. pruatjan* Molk. This compound has also been reported in *P. anisum* L.[3] Moreover, water and ethanol extracts contained flavonoids and their derivatives, including those with sugar moieties [Table 1]. Ethanol extract contains more concentrated and diverse compounds when compared to water extract. Chromone glycoside in the form of undulatoside A was also dominant in both extracts, followed by phenylpropanoids. Undulatoside A has not been found in other Pimpinella species, and this study is the first to report high abundance in P. pruatjan Molk [Table 1]. Dichotomitin, a furanochromone, was found in ethanol extract in less abundance [Table 1]. Furanochromones, such as khelin, visnagin, visamminol, ammino, khellol, and pimolin, have been reported in P.monica Dalz.[3]

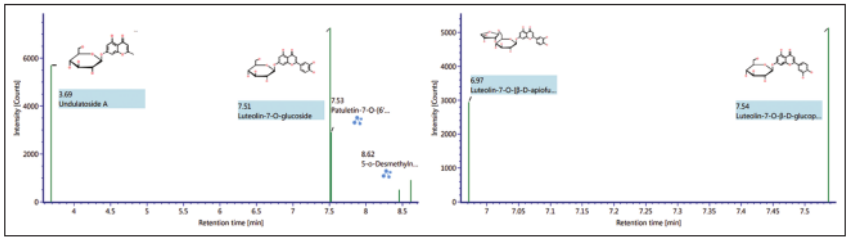

Figure 1: Chromatograms of water extract of *P. pruatjan* Molk

Table 1: Intensity response of LC MS analysis from the aerial parts of *P. pruatjan Molk*

Compounds Abundance components	Group	Water extract		Ethanol extract	
		Positive	Negative	Positive	Negative
Populin[9]	Phenol				102.393-110.575
Luteolin-7-O-β-D glucopyranoside[10]	Flavonoid	4.914-5.134		51.651-54.864	
Luteolin-7-O-[β-D-apiofuranosyl (1→6)] β-D-glucopyranoside[11]	Flavonoid	2.942-3.188		3.496-3.566	7.277-7.463
Luteolin-7-O-glucoside[12]	Flavonoid		7.265-7.311		
Undulatoside A[13]	Chromone glycoside		5.702-6.467		53.338-59.899
Dihydroresveratrol[14]	Phenylpropanoid				30.436-30.473
Dihydrooxyresveratrol[15]	Phenylpropanoid			2.956-3.274	1.591-1.656
3,5-O-Dicaffeoylquinic acid[16]	Phenylpropanoid				24.111-25.077
Quercetin-3′-O-glucoside[17]	Flavonoid				16.522-17.608
Kaempferol-7-O-α-L-arabinofuranoside[18]	Flavonoid			3.730-3.971	10.268-11.205
Methyl ophiopogonone A[19]	Flavonoid				10.106-10.368
7-Hydroxy-3,5,6,3',4'-pentamethoxyflavone[20]	Flavonoid				9.258-10.366
Less abundance components					
Ophiopogonanone A[21]	Flavonoid				7.055-7.516
Genistin[22]	Flavonoid			6.517-6.813	
Patuletin-7-O-[6″-(2-methylbutyryl)]-glucoside[23]	Flavonoid		2.891-2.987	3.632-5.494	
5-Hydroxy-7,8,2',3'-tetramethoxyflavone[24]	Flavonoid				5.598-6.453
Dichotomitin[25]	Furanochromone				4.510-4.586
6′-O-Galloyl-homoarbutin[26]	Phenypropanoid			3.685-4.175	3.350-3.764
6-Hydroxykaempferol-7-O-glucoside[27]	Flavonoid			3.533-3.994	
Dihydrokaempferol[28]	Flavonoid				650-695
3,4-Dihydroxyphenothyl-3-O-β-D-glucopyranoside[26]	Phenypropanoid			3.200-3.855	
Dendrocandin E[29]	Phenol			3.099-3303	
1-Ethyl-4,8-dimethoxy-β-carboline[30]	Alkaloid			2.253-2.305	
3′-O-Methylviolanone[31]	Flavonoid				1.653-1.783
Hordenine-O-α-L-rhamnopyranoside[32]	Alkaloid			1.451-1.585	
Hesperetin[33]	Flavonoid				1.276-1.368
5,7,8,4′-Tetrahydroxy flavone[34]	Flavonoid				1.367-1.506
Methyl caffeate[35]	Phenylpropanoid				1.321-1.469
Renifolin[36]	Flavonoid			812-947	
5-O-Desmethylnobiletin[37]	Flavonoid		890-895		
Supinine[38]	Alkaloid			772-885	
N-(2-Methylamino-benzoyl) tryptamine[39]	Alkaloid			803-867	
Kushenol S[40]	Flavonoid			695-774	
Areapillin[41]	Flavonoid				720-744
Chrysosplenetin B[42]	Flavonoid				698-853
Shogaol[43]	Phenylpropanoid				545-689
Neocomplanoside[44]	Flavonoid			498-548	
Isovitexin (Homovitexin)[45]	Flavonoid		512-518		
Apigenin-7-O-β-D-glucuronopyranoside[46]	Flavonoid			357-408	

Potency of pharmacology activity of phytoconstituents contained in *P.pruatjan Molk*

Luteolin 7-O-β-d-glucopyranoside shows an inhibitory effect to lactate dehydrogenase in humans by interacting with the enzyme's active site.[47] Luteolin, either aglycone or glycoside, has many biological activities, including: antimicrobial,[48] antioxidant,[49] anti-inflammatory activity,[50] anticancer,[51] monoamine oxidase inhibition,[52] inhibitory effects on lens aldose reductase,[53] and antiplatelet effects.[54] Luteolin also has multiple cardioprotective effects by enhancing contractility, upregulating autophagy, and preventing cardiac fibrosis[55] and anti–HIV-1 activity.[56]

Undulatoside A, a derivative of chromone or triterpene glycoside, possesses antimicrobial activities,[57] anti-inflammatory (inhibition of nitric oxide production),[58] and immunomodulatory activities.[59] One of the most abundant components found in ethanol extract is populnin (*Kaempferol-7-O*-b-*D-glucopyranoside),* a monoglucoside of kaempferol with antioxidant and anti-inflammatory activities.[60] Besides populnin,

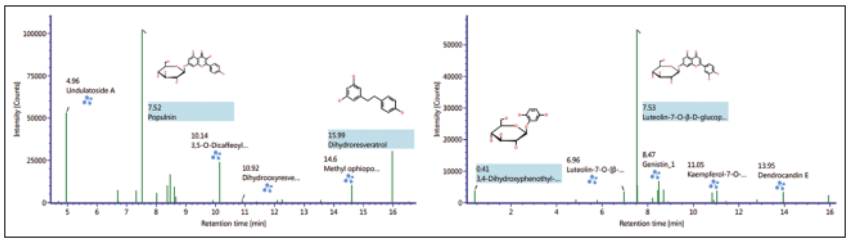

Figure 2: Chromatogram of ethanol extract of *P. pruatjan* Molk

ethanol extract also contains dihydroresveratrol and 3,5-O-dicaffeoylquinic acid. Dihydroresveratrol (dihydro-R) has anticancer activity[61] and an inhibitory effect to the pro-inflammatory response.[62,63]

Moreover, 3,5-O-dicaffeoylquinic acid possesses anti-inflammatory,[64] anticancer,[65,66] anti-obesity,[67] antioxidative stress,[68] and antiviral effects.[69] Quercetin-3-O-glucoside is a potent antioxidant and has the ability to inhibit local metastases in pancreatic cancer.[70] Methylophiopogonanone A is able to prevent myocardial apoptosis, repair cerebral ischemia or reperfusion injury,[71,72] and prevent obesity and dyslipidemia.[73]

Phytochemicals of *P. pruatjan Molk* involved in aphrodisiac properties

Soymida febrifuga, used to treat several diseases and as an aphrodisiac agent in India, contains Luteolin 7-O-glucoside.[74] *Avicennia officinalis* L leaf extract, traditionally used as an aphrodisiac plant in Vietnam, contains Luteolin 7-Oβ-D-glucopyranoside, 3'-methylluteolin 4'-O-β-Dglucopyranoside, and flavogadorinin.[75] Many flavonoids and their derivatives have shown an aphrodisiac effect,[76] such as chrysin and benzoflavone from an ethanolic leaf extract of *Passiflora incarnate*,[77] flavonol glycoside, icariin, and their derivatives from Epimedium,[78] rutin, catechin, apigenin, myricetin, and quercetin from *Ipomoea batatas*[79] and flavonoids from *Abutilon pannosum* stem bark.[80]

Oxidative stress has been known to increase the risk of ED.[81] Oxidative stress can also affect the development of pathophysiological dysfunctions such as anxiety, depression, diabetes mellitus, obesity, stroke, and aging-related diseases.[82,83] Flavonoids can increase antioxidant enzymes such as superoxide dismutase and catalase.[17,84] Antioxidant enzymes can decrease malondialdehyde level and consequently increase NO-cGMP level, resulting in erection.[85] Antioxidant compounds, such as natural flavonoids and phenols, may become a rational candidate for "antioxidant adaptogens" for the multifactorial risk of ED.

For the first time, this study reports two important bioactive compounds in water and ethanol extracts of P. pruatjan Molk's aerial part, namely Luteolin-7-O-glycosides and Undulatoside A. Ethanol extract contained a higher concentration and diversity of bioactive compounds, including populnin, dihydro-resveratrol, and 3,5-O-dicaffeoylquinic acid. This study constitutes the presence of unknown compounds and describes the plant's biological and pharmacological potencies a as therapeutic agent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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