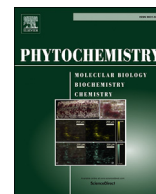




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Review

Medicinal uses, chemistry and pharmacology of *Dillenia* species (Dilleniaceae)

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ABSTRACT

The genus *Dillenia* is comprised of about 100 species of evergreen and deciduous trees or shrubs of disjunct distribution in the seasonal tropics of Madagascar through South and South East Asia, Malaysia, North Australia, and Fiji. Species from this genus have been widely used in medicinal folklore to treat cancers, wounds, jaundice, fever, cough, diabetes mellitus, and diarrhea as well as hair tonics. The plants of the genus also produce edible fruits and are cultivated as ornamental plants. Flavonoids, triterpenoids, and miscellaneous compounds have been identified in the genus. Their extracts and pure compounds have been reported for their antimicrobial, anti-inflammatory, cytotoxic, antidiabetes, antioxidant, antidiarrheal, and antiprotozoal activities. Mucilage from their fruits is used in drug formulations.

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1. Introduction

The genus *Dillenia* belongs to the Dilleniaceae family and contains approximately 100 known species (Lim, 2012). According to The Plant List (2013), as many as 175 scientific plant names from the genus *Dillenia* have been recorded with 58 accepted names (low and medium confidence levels) and 71 names of synonym species. The name *Dillenia* is derived from Joannes Jacobus Dillenius, a British botanist who dedicated his efforts in the field of taxonomy of this genus (Quattrocchi, 2012). *Dillenia* species are monoecious plants which produce attractive flowers and yellow fruits. *D. indica* is known for its lemon-flavored fruits that are used to make jellies and curries. These species are evergreen and deciduous trees or shrubs of disjunct distribution in the seasonal tropics of Madagascar through South and South East Asia, North Australia, and Fiji (Dickison, 1979; Horn, 2007; Kerrigan et al., 2011; Lim, 2012). They grow from sea level to an elevation of about 2000 m. The plants also grow in forests, and several species show an adaptation to temporary flooded situations. They are mostly trees that form large leaves and flowers in few-flowered inflorescences (Dickison, 1979). Their barks are unique in fine colors of red, grayish, and reddish brown that are used in furniture making (Hoogland, 1952). Several species of this genus produce sweetish-sour and astringent edible fruits (Hoogland, 1952; Jansen et al., 1992; Kerrigan et al., 2011; Lim, 2012; Saha and Sundriyal, 2012) and are cultivated as ornamental plants (Hoogland, 1952; Kerrigan et al., 2011).

Based on our extensive search regarding medicinal uses, chemical constituents, and biological activities of the species from the genus *Dillenia*, only very few species have been described thus far. Starting from 1962 to the present, 19 species of the genus *Dillenia* have been reported for their medicinal uses and their phytochemistry. These 19 species are *Dillenia andamanica* C.E.Parkinson, *D. aurea* Sm., *D. bracteata* Wight, *D. excelsa* (Jack) Martelli ex Gilg., *D. indica* L., *D. ovata* Wall. ex Hook.f. & Thomson, *D. papuana* Martelli, *D. parviflora* Griff., *D. pentagyna* Roxb., *D. philippinensis* Rolfe, *D. pulchella* (Jack) Gilg., *D. reticulata* King, *D. retusa* Thunb., *D. scabrella* (D.Don) Roxb. ex Wall., *D. eximia* Miq., *D. serrata* Thunb., *D. suffruticosa* (Griff.) Martelli, *D. sumatrana* Miq., and *D. triquetra* (Rottb.) Gilg. However, out of these, only 7 species have been evaluated for their biological activities. As part of our search for natural anti-inflammatory compounds, three triterpenes have been isolated from *D. serrata* and they performed pronounced inhibitory activity on the production of prostaglandin E₂, which is known as a predominant inflammatory mediator (Jalil et al., 2015). This review describes the current state of their medicinal properties, chemistry, and pharmacological aspects.

2. Medicinal uses of *Dillenia* species

Dillenia species have been widely used as medicinal plants by natives in South and Southeast Asian countries (Lim, 2012), including India, Nepal, Sri Lanka, Bangladesh, Laos, Thailand, Vietnam, Malaysia, Indonesia, Philippines, and Papua New Guinea. Table 1 lists the known medicinal uses of several *Dillenia* species.

Almost all parts of *Dillenia* plants are traditionally utilized for therapeutic purposes. The fresh and dried materials of different parts of *Dillenia* plants are processed as decoction, poultice, juice, and mucilage for the treatment of diarrhea, wounds, cancer, diabetes, fever, cough, rheumatism, urinary problems, skin-related diseases, and aches as well as hair tonics (Table 1). Different preparations of *D. excelsa*, *D. ovata*, and *D. parviflora* are traditionally used to cure diarrhea (Burkill, 1966; Srithi et al., 2009; Quattrocchi, 2012). Skin-related diseases such as leucoderma, skin itches, skin rash, and eczema can be treated using the leaf,

fruit, and stem bark of *D. andamanica*, *D. indica*, *D. ovata*, and *D. pentagyna* (Prasad et al., 2008; Quattrocchi, 2012; Boer et al., 2012; Bhat et al., 2014). In addition, the stem barks of *D. aurea* and *D. parviflora*, as well as the leaf of *D. suffruticosa*, in the form of paste or poultice are applied onto skin to heal wounds (Mat-Salleh and Latiff, 2002; Quattrocchi, 2012; Junsongduang et al., 2014). Juice and decoction of the fruit and stem bark, as well as the leaves of *D. indica*, *D. pentagyna*, and *D. suffruticosa*, are used daily to alleviate cancerous growth, in particular breast and gastric cancers (Ahmad and Holdsworth, 1995; Sharma et al., 2001; Prasad et al., 2008; Rosangkima et al., 2008b; Das et al., 2009; Dubey et al., 2009). Moreover, fruit juices of *D. indica* and *D. philippinensis* are given orally to cure fever and cough symptoms (Angami et al., 2006; Macahig et al., 2011; Quattrocchi, 2012). The mixed juice of fruit and calyx of *D. indica* and the powdered stem bark of *D. pentagyna* are administered daily for the treatment of diabetes (Dubey et al., 2009; Pavani et al., 2012; Ripunjoy et al., 2013). In pregnancy, the root of *D. indica* is often used to cause abortion (Quattrocchi, 2012), while the stem barks of *D. papuana* and *D. pentagyna* are used to assist body delivery at labor time as well as to avoid infection after delivery (Nick et al., 1994; Dubey et al., 2009). Preparations of *D. pentagyna* and *D. suffruticosa* in the form of paste or poultice are applied onto joint areas to alleviate rheumatism (Quattrocchi, 2012; Hanum and Hamzah, 1999). Furthermore, the juice and mucilage of *D. indica*, *D. pentagyna* and *D. philippinensis* fruits are used to treat hair loss as well as to clean hair and to remove dandruff (Saikia et al., 2006; Macahig et al., 2011; Rahman et al., 2011a). Their sweetish-sour edible fruits are consumed directly or juiced with sugar as a fresh and healthy drink. Meanwhile, the bark of the stem and root of some *Dillenia* plants are reported as a food poisoning neutralizer (Grosvenor et al., 1995b; Islam et al., 2014). Such usage suggested that *Dillenia* plants might contain chemical constituents with broad biological activities including antimicrobial, anti-inflammatory, anticancer, and antidiabetes.

3. Chemistry of *Dillenia* species

Current investigation of the chemical constituents of *Dillenia* species resulted in the isolation of two major classes of compounds that are flavonoids and triterpenoids. In addition to these classes, miscellaneous compounds including phytosteroids, a diterpene, a norisoprene, an ionone, phenolics, an anthraquinone, an alcohol, and ketones also enrich the diversity of phytochemistry in *Dillenia* plants. As many as 74 compounds are included in this review according to our search and this fact emerges future research opportunities as a noble challenge to discover new chemical constituents from the genus *Dillenia*.

3.1. Flavonoids

Flavonoids found in *Dillenia* species are divided into flavonols (1–18), dihydroflavonols (19–25), a flavan (26), flavan-3-ols (27–28), and flavanones (29–32) and a chromane (33) as minor flavonoids. Most of these flavonoids were isolated from the leaves of *Dillenia* plants, but some flavonoids were also reported from the stem bark. Five flavonoids (5, 16–17, 22, 27, 29 and 33) are reported as new compounds from *Dillenia* plants. Two flavonols (1 and 3) are frequently found in these species. Meanwhile, 4–8 are common feature methylated flavonols in *Dillenia* species. Only *D. triquetra* and *D. bracteata* have been reported to produce sulfated flavonols (9–11). The occurrence of flavonoid sulphates in the Dilleniaceae family is closely related to the derivatization of *O*-methylated aglycones (Gurni et al., 1981). Seven dihydroflavonols (19–25) were found in *D. indica*, *D. retusa* and *D. pentagyna* and they occurred as

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