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Pharmacological Activities of *Plectranthus scutellarioides* (L.) R.Br. Leaves Extract on Cyclooxygenase and Xanthine Oxidase Enzymes

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***Plectranthus scutellarioides* (L.) R.Br. (family Lamiaceae) has been widely used in West Java, Indonesia, to cure various diseases. People boiled the leaves of the plant in water and consumed the tea daily until the symptoms reduced. This work was conducted to study the pharmacological activity of *P. scutellarioides* (L.) R.Br. extract on cyclooxygenases (COXs) and xanthine oxidase (XO) enzymes. The plant was purchased from Manoko plantation in Lembang, West Java, Indonesia. The leaves were sundried, crushed, and soaked in ethanol for 3 × 24 h, prior to be used. The extraction was continued further using ethyl acetate and water. Inhibitory activity of the extract on COXs was performed by measuring the absorbance of reduced-tetramethyl-*p*-phenylendiamine (TMPD) at 590 nm, which correlates to the level of PGH_2 production, while its inhibitory on XO was measured at 290 nm. *P. scutellarioides* (L.) R.Br. leaves extracts (ethanolic, ethyl acetate, and water) showed inhibition on COX-1 and COX-2 enzymes (40.43% for COX-1 and 97.04% for COX-2), while on XO, the water extract showed the highest inhibition (IC_{50} water extract = 6 µg/ml; IC_{50} allopurinol = 0.15 µg/ml). This plant could be further proposed as XO and nonselective COX inhibitors.**

Key words: Anti-inflammatory, cyclooxygenase (COX), gout, non-steroidal anti-inflammatory drugs (NSAIDs), prostaglandin, prostaglandin H_2 (PGH_2), xanthine oxidase (XO).

INTRODUCTION

The inflammatory response protects the body against infection and injury but it could become disregulated with deleterious consequences to the host. It is now evident that endogenous biochemical pathways activated during defense reactions can counter-regulate inflammation and promote resolution. Hence, resolution is an active rather

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than a passive process, as once believed, which now promises novel approaches for the treatment of inflammation-associated diseases based on endogenous agonists of resolution (Serhan et al., 2007).

Plectranthus scutellarioides (L.) R.Br. which belongs to Lamiaceae or Labiatae family, is a native plant of Southeast Asia, including Indonesia. This plant could also be cultivated in tropical and temperate regions around the world (Hanelt et al., 2001; Acevedo-Rodriguez and Strong, 2012). *P. scutellarioides* (or *Coleus scutellarioides*) has been widely used in West Java, Indonesia, to cure various diseases (Roosita et al., 2008). People boiled the leaves of the plant in water and consumed the tea daily until the symptoms reduced.

Other species of the same family, known as *Plectranthus amboinicus* or Indian borage, exhibited antiplatelet aggregation ability, antibacterial activity, and antiproliferative effect against Caco-2, HCT-15, and MCF-7 cell lines (Bhatt et al., 2013).

Iranian researchers, Saghafi et al. (2013) reported that *Teucrium polium* extract in different regions is a rich source of antioxidant and showed inhibitory effect on xanthine oxidase.

Some drugs, such as the widely used cyclooxygenase-2 (COX-2) inhibitors, have been proven to be toxic (Gilroy et al., 1999; Bannenberg et al., 2005; Serhan et al., 2007), whereas others possess pro-resolving actions, such as glucocorticoids (Rossi and Sawatzky, 2007), cyclin-dependent kinase inhibitors (Rossi et al., 2006), and aspirin (Serhan, 2007). Non-steroidal anti-inflammatory drugs (NSAIDs) work by inhibiting both COX isoforms, thus the conversion of arachidonic acid into prostaglandin is disturbed (Katzung, 2007). All NSAIDs in clinical use have been shown to inhibit COX, leading to a marked reduction in PG synthesis. The inhibition by aspirin is due to irreversible acetylation of the cyclooxygenase component of COX. In contrast, NSAIDs like indomethacin or ibuprofen inhibit COX reversibly by competing with the substrate, arachidonic acid, for the active site of the enzyme (Vane et al., 1990). Aspirin is the most commonly non-steroidal anti-inflammatory drug, which low doses could be used to prevent and treat cardiovascular diseases. Recent studies showed that there is increasing evidence that aspirin initiates biosynthesis of novel anti-inflammatory mediators by means of interactions between endothelial cells and leukocytes. These mediators are classified as aspirin-triggered 15-epi-lipoxins (Chiang et al., 2004).

Xanthine oxidase (XO) is a member of group of enzymes known as molybdenum iron-sulphur flavin hydroxylases (Symons et al., 1989). It catalyses the oxidation of hypoxanthine to xanthine and then to uric acid, the final reactions in the metabolism of purine bases (Zarepour et al., 2010). Xanthine oxidase inhibitors (XOI) are much useful, since they possess lesser side effects compared to uricosuric and anti-inflammatory agents. Allopurinol is the only clinically available XOI, which also suffers from many side effects such as hypersensitivity syndrome, Steven's Johnson syndrome and renal toxicity. Thus, it is necessary to develop compounds with XOI activity with lesser side effects compared to allopurinol. Flavonoids and polyphenols have been reported to possess xanthine oxidase inhibitory activity. In addition, flavonoids also have anti-inflammatory and antitumor properties (Umamaheswari et al., 2013; Lio et al., 1985).

This work was aimed to study the pharmacological activity of *P. scutellarioides* (L.) R.Br. leaves extracts (ethanolic, ethyl acetate, and water) on cyclooxygenases (COXs) and xanthine oxidase (XO) enzymes.

MATERIALS AND METHODS

Plant

The fresh plant was purchased from Manoko plantation at Lembang, West Java, Indonesia, in November 2015. The specimen (No. 1011/11.CO2.2/PL/2015) was determined at Laboratory of Identification and Determination, School of Life Sciences and Technology, Bandung Institute of Technology, Indonesia, and confirmed as *P. scutellarioides* (L.) R.Br. (family Lamiaceae).

Preparation of extracts

The leaves were sundried in a glass-roofed room for 5 days, and then 1.2 kg of the dried leaves were crushed to powder and soaked in 1 L of 70 % ethanol for 3 × 24 h at room temperature. The extraction was continued sequentially using ethyl acetate and water. The extracts were filtered through Whatman No. 41, the solvent was vacuum-evaporated at 40 to 60°C, followed by freeze-drying process, prior to be further used.

Phytochemical screening

Phytochemical screening was performed according to standard method using specific reagents to detect secondary metabolites (alkaloids, flavonoids, polyphenols/tannins, terpenoids, quinones, and saponins) in *P. scutellarioides* (L.) R.Br. leaves extracts.

Thin layer chromatography (TLC) analysis

TLC was performed on silica GF_{254} plate using a mixture of *n*-butanol, acetic acid, and water (4:1:3) was used as eluent for ethanol and water extracts, whereas a mixture of toluene, ethyl acetate, and acetic acid (7:2:1) was used for ethyl acetate extract. The spots were observed using $AlCl_3$ as spray reagent.

Spectrophotometry analysis

Spectrophotometry analysis was performed to the ethanol extract (with and without $AlCl_3$) at 220 to 450 nm. Quercetin was used as standard.

High performance liquid chromatography (HPLC)

Reversed-phase HPLC was performed on LC-10AT VP (Shimadzu),