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To: Jutti Levita, Sri Adi Sumiwi, Oktavia, Anas Subarnas, Marline Abdassah Dear Dr Jutti Levita.

I am happy to inform you regarding your submission to International Journal of Pharmacy and Pharmaceutical Sciences, "A Study to Predict • Anti-inflammatory Activity of Eugenol, Myristicin, and Limonene of Cinnamomum sintoc" that it has been recommended for publication after peer review.

I acknowledge you receipt of registration fee by NEFT for IJPPS 7356.

Your article is now accepted for publication and your article is scheduled to be published in Vol 7 Issue 12, December 2015.

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Discovering COX inhibitors in Volatile Oil of Cinnamomum sintoc L.

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Abstract

Objective: In this work we predicted anti-inflammatory activity of volatile oil of C. sintoc L.

Methods: Molecular docking was performed to predict the binding modes of eugenol, myristicin, and limonene chemical constituents of *C. sintoc* L. with COX enzymes, using AutoDock 4.2. COX enzymes were obtained from Protein Data Bank (PDB); COX-1 (PDB code: 2AYL) and COX-2 (PDB code: 3PGH). Flurbiprofen and celecoxib were used as standards. Further assay was carried out on lipopolysaccharide (LPS)-induced fibroblast cells reacted with 800; 400; 200; 100; 50; 25 and 12.5 ul of *C. sintoc* L. bark essential oils. The absorbance of the product was measured using microplate reader at 450 nm. Acetosal was used as the standard drug.

Results: Eugenol and myristicin could be categorized as non-selective inhibitors of COX-2, while limonene is categorized as preferential COX-2 inhibitor. The essential oils of *C. sintoc* L. bark reduced PGE2 production on LPS-induced fibroblast cells. The inhibitory activity of *C. sintoc* L. was weaker than acetosal.

Conclusion: Bioactive compounds in essential oil of *C. sintoc* L. bark show inhibition on PGE2 production on LPS-induced human fibroblastcells, and could be categorized as COX inhibitors

Keywords: anti-inflammatory, *Cinnamomum sintoc*, cyclooxygenase, eugenol, limonene, myristicin

INTRODUCTION

Selective inhibition of cyclooxygenase-2 (COX-2) enzyme is a target of anti-inflammatory drugs, due to their property to reduce the side effect of anti-inflammatory non-steroid (AINS). Anti-inflammatory activity of essential oils of *Cinnamomum sintoc* L. (*C. sintoc* L.) bark, belonging to Lauraceae family, had been proven *in vivo* (65.35% oedema-decrease on carrageenan-induced rats at 0.1 ml/200 g of rat body weight) [1]. Other species, *C. tamala*, from the same family proved anti-inflammatory activity [2].

Leem et al (2011) declared that eugenol has anti-inflammatory activity by inhibition of COX-2 by 58.15% (IC₅₀ = 8.85 mg/ml in vitro), while in vivo assay on carrageenan-induced mice gave 0.17 g/kg of bodyweight [3]. Ozaky and colleagues (1989) concluded that myristicin