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LETTER

Critical Response to Article "Integrated Network Pharmacology and Experimental Validation Approach to Investigate the Mechanisms of Stigmasterol in the Treatment of Rheumatoid Arthritis" [Letter]

Ratih Rinendyaputri, Novaria Sari Dewi Panjaitan

Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Cibinong Science Center, Cibinong - Bogor, West Java, Km. 46, Indonesia

Correspondence: Novaria Sari Dewi Panjaitan, Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Cibinong Science Center, Jl. Raya Bogor No. 490, Cibinong – Bogor, West Java, Km. 46, Indonesia, Email nova014@brin.go.id

Dear editor

We have read, reviewed and appreciated the work performed by Xie et al regarding the integrated network pharmacology and experimental approaches in order to investigate the mechanisms of Stigmasterol, the active components of *Sinomenium acutum* used in arthritis treatment.[1] Based on their results, 5 main differentially expressed genes involved in osteoclast differentiation, the major mediators of bone destruction, including NCF4, NFKB1, CYBA, IL-1β and NCF1 were determined to be targeted by the through protein–protein interaction (PPI) network. *Sinomenium acutum* (Thumb.) Rehd. et Wils. (Menispermaceae, SA) was known as a Chinese herbal medicine with various active chemical components, mainly alkaloid sinomenine.[2] The pharmacological profile of this herb includes immunosuppression, rheumatoid arthritis relief, anti-inflammatory, and protection against by lipopolysaccharide (LPS) induced hepatitis.[2] The study and drug design revealed in this article were found interesting and worth to be discussed further.

In this study, the target genes of *Sinomenium acutum* active components related to rheumatoid arthritis were screened by heatmap and volcano map of dataset in Batman-TCM website which then was imported into Cytoscape software. Here, a question could be raised that the in silico prediction should be confirmed firstly by an in vitro experiment. However, based on the network pharmacology analysis, the authors identified and defined the active compounds of *Sinomenium acutum*, including Stigmasterol, Sinactine and GammaSitosterol where Stigmasterol targets IL-1β, Sinactine targets NCF4, NCF1, and CYBA, and Gamma-Sitosterol targets NFKB1 based on the KEGG analysis performed. Even though the final results reported in this study were fascinating, the preliminary in vitro experiment is important enough to be skipped or excluded in order to define the bioactivity of a compound.[3,4] Therefore, further in vitro study could be considered for other bioactive compounds which were excluded in this particular study in order.

In addition, the promising effect or physiological outcome of Stigmasterol treatment was obtained from the treatment of high dosage Stigmasterol (STG-H) 200 mg/kg, which slightly still lower than the effect caused by Indomethacin. Indomethacin itself is a non-steroidal anti-inflammatory drug commonly used to treat inflammatory arthritis which has been well established as an inhibitor of AKR1C3.[5] However, the significant effect on arthritis index (AI) obtained from STG-H 200 mg/kg was still lower than the AI effect obtained from Indomethacin 1 mg/kg. This dosage gap could be a site where authors should pay attention to in their future study.

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Disclosure

All authors report no conflicts of interest in this communication.

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