Dear Editor,

Please find our manuscript entitled ***‘Uncovering key anti-inflammatory constituents and mechanism of Wuwei Xiaodu Decoction by a combined strategy of phytochemistry, AIDD, network pharmacology, and in vitro and in vivo assay’*** for publication in the ***Journal of Ethnopharmacology***. The work has not been under consideration for publication elsewhere and all authors listed have approved the submission.

Chronic inflammatory responses exert detrimental effects on organismal homeostasis. Wuwei Xiaodu Decoction (WXD), a classical traditional Chinese medicine formula, has demonstrated therapeutic potential in managing chronic inflammatory disorders. Although modern pharmacological studies have confirmed its efficacy, the bioactive constituents and molecular mechanisms underlying WXD's anti-inflammatory actions remain incompletely characterized. Therefore, in order to better guide the clinical application of WXD in treating inflammatory diseases, we systematically investigated the basis and mechanism of the anti-inflammatory efficacy of WXD. With this study, we successfully

1. identified WXD-PE (petroleum ether extract) and WXD-EA (ethyl acetate extract) fractions as the most potent anti-inflammatory fractions by ELISA assay;
2. predicted potential anti-inflammatory targets and pathways with AI-based drug design platforms;
3. found that both fractions significantly suppressed pro-inflammatory mediators (NO, TNF-α, IL-6, IL-1β) and downregulated COX-2, iNOS expression through modulating MAPK and STAT3 signaling pathways;
4. demonstrated that both fractions could significantly alleviate DNCB-induced acanthosis, lymphocyte and neutrophil infiltration, and excessive collagen deposition in model mouse skin.

We think that this work is useful in guiding the clinical application of WXD. Therefore, we wish to publish it in the **‘*Journal of Ethnopharmacology*’**.

Yours Sincerely

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**Suggested Editor**

Dr. Guangbo Ge

Affiliation: Shanghai University of Traditional Chinese Medicine

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Research Focus: Natural product drug discovery

Rationale: As an Associate Editor of the Journal of Ethnopharmacology, Prof. Ge’s expertise in ethnopharmacology ensures rigorous evaluation of traditional medicine mechanisms and modern pharmacological evidence.

**Suggested Reviewers**

Dr. Qinshi Zhao

Kunming Institute of Botany, Chinese Academy of Sciences

Email: qinshizhao@mail.kib.ac.cn

Rationale: Dr. Zhao’s pioneering work in phytochemistry and drug innovation aligns with this study’s integration of traditional knowledge and AI-driven discovery.

Prof. Haiyu Xu

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Rationale: Prof. Xu’s expertise in multi-target evaluation systems strengthens methodological validity for complex TCM studies.

Dr. Aijun Hou

Affiliation: Fudan University

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Rationale: Dr. Hou’s experience in bioactive constituent validation offers critical insights into phytochemical claims.

Prof. Lihong Hu

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Rationale: Dr. Hu’s work on resource-efficient strategies provides unique perspectives for assessing innovation.

**Declaration**

No conflicts of interest between the authors and the suggested editor and reviewers.