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LETTER

Further Insights into the Mechanisms and Clinical Implications of Run-Mu-Ling Granules in Dry Eye Disease [Letter]

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Dear editor

We have read with great interest the article by Luo et al[1] titled "Run-Mu-Ling Granules Mitigate Ocular Surface Inflammatory Injury Associated with Dry Eye by Suppressing the NLRP3/GSDMD-Mediated Pyroptosis Pathway", published in Journal of Inflammation Research. The study provides valuable insights into the potential therapeutic effects of Run-Mu-Ling Granules (RMLG) in treating dry eye disease (DED) through modulation of the NLRP3/GSDMD-mediated pyroptosis pathway.

Appreciation of the Study

The authors are commended for their comprehensive investigation into RMLG's effects in both in vivo and in vitro models. The study makes a solid case for the use of traditional Chinese medicine in managing ocular surface inflammation, providing a novel mechanistic perspective involving pyroptosis inhibition.

Discussion and Suggestions

1. Dose-Response Relationship: The study shows that MCC950 effectively inhibits NLRP3, but the dose-response relationship of both MCC950 and RMLG remains unclear. Exploring this relationship in greater detail could help optimize treatment dosages and minimize potential side effects.
2. Validation of Pyroptosis Markers: While the study highlights NLRP3/GSDMD-mediated pyroptosis, further validation using quantitative methods such as real-time PCR or flow cytometry could strengthen the findings. This would allow for more precise measurement of pyroptosis-related markers in ocular tissues.
3. In Vivo Evidence of Pyroptosis: The animal data show improved inflammation, but there is limited direct evidence linking this to pyroptosis inhibition. Additional histological analysis, such as electron microscopy, could offer clearer insights into the mechanisms of action in vivo.
4. Translational Potential: The scopolamine-induced dry eye model may not fully replicate the complexity of human dry eye, particularly in cases with autoimmune components like Sjögren's syndrome. It would be helpful to discuss how these findings could be translated to human patients with different underlying causes of DED.
5. Other Inflammatory Pathways: While NLRP3 inhibition is promising, dry eye disease involves multiple inflammatory pathways (eg, NF-κB, MAPK). Investigating whether RMLG modulates these pathways as well could provide a more comprehensive understanding of its anti-inflammatory effects.
6. Long-Term Efficacy and Safety: The study primarily focuses on short-term outcomes. Long-term studies are needed to assess both the durability of RMLG's therapeutic effects and its safety profile in chronic use.

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Conclusion

Luo et al's study significantly advances our understanding of RMLG's role in treating dry eye disease through modulation of pyroptosis. Addressing the points above, especially regarding the dose-response, pyroptosis validation, and the broader inflammatory network, would further strengthen the study's clinical relevance.

Disclosure

The authors report no conflicts of interest in this communication.

Reference

1. Luo D, Ji HJ, Yan XQ, et al. Run-Mu-Ling Granules Mitigate Ocular Surface Inflammatory Injury Associated with Dry Eye by Suppressing the NLRP3/GSDMD-Mediated Pyroptosis Pathway. *J Inflamm Res*. 2024;17:10770–10774. doi:10.2147/JIR.S496231

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