Reviewer 1

First of all, I would like to congratulate the authors of this manuscript for their accomplishment. It has been a privilege to read and evaluate it. I believe that the manuscript has great merit. Concise and appropriate writing, good methodological development, clear and comprehensive explanations. The manuscript really deserves a lot of attention in the publication process. However, one highly worrying thing that I observed was that the p-value of the heterogeneity of the studies was "0.64" in the abstract and "0.53" in the results section. This makes me wonder if it would not be necessary for the authors to analyze subgroups in order to improve their knowledge of possible subvariables that are involved in their analyses not only by the differents values, as well as, because they are over than 0.05.

We appreciate the reviewer's comments. You pointed out that the content in the abstract and results sections refers to the same concept, specifically regarding the assessment of heterogeneity in the study. We mistakenly wrote incorrect result data during the editing process, and we sincerely apologize for any confusion this may have caused. To further investigate the heterogeneity, we conducted a subgroup analysis. The results indicate that different disease types and treatment durations significantly affect efficacy (as shown in Table 2). The subgroup analysis revealed notable differences in treatment responses among various types of rheumatic immune diseases. This suggests that personalized treatment plans may enhance therapeutic outcomes, allowing for targeted therapies based on individual patient characteristics.

It would be important to explain how the reviewers evaluated the articles, that is, whether they evaluated only the title, abstract, or full reading. It would be important to demonstrate how many articles were found in each database.

Thank you for your valuable suggestions. We will make appropriate modifications to the original content. According to our search strategy, we identified a total of 173 relevant articles, including 113 in Chinese and 60 in English. These articles were sourced from the following databases: China National Knowledge Infrastructure (CNKI): 80 articles; Wanfang Data: 45 articles; China Biomedical Literature Database (CBM): 20 articles; PubMed: 15 articles; Embase: 10 articles; Cochrane Library: 3 articles. During the literature screening process, two researchers independently evaluated the titles, abstracts, and full texts of the articles. In the preliminary screening phase, we excluded 142 articles, leaving 31 articles for full-text reading. After careful review of the full texts and based on the inclusion and exclusion criteria, we further excluded 19 articles, ultimately including 11 articles for the meta-analysis. The process of literature selection is shown in Figure 1.

Furthermore, i believe that there is a need to improve and expand a little more the discussion of the article. In this case, I would suggest that the authors of the manuscript provide a discussion regarding possible adverse effects of the use of combined therapy with Tripterygium wilfordii and Western medicine. I also think it is pertinent to highlight the access to this medication that the

general public has and its costs. I also think it would be pertinent to consider the following. I think it would be important to mention a counterpoint, demonstrating that the use of this formulation is not consensual, with some literature not obtaining convincing results on this and, of course, explaining the possible reason for this occurrence. It would also be very important to explain why the dose was repeated between studies and whether a possible variation in dose could provide different results.

Thank you for your valuable feedback! We have added relevant content to the manuscript. This study employed a systematic review and meta-analysis approach to comprehensively analyze the efficacy and safety of Tripterygium wilfordii glycosides tablets combined with Western medicine in the treatment of rheumatic immune diseases. Although the results indicate that this combined treatment has advantages in overall efficacy and adverse reactions, it is also necessary to conduct an in-depth discussion on its potential adverse effects. The concomitant use of Tripterygium wilfordii and Western medicine may lead to side effects, including but not limited to liver function impairment, gastrointestinal reactions, and immune system suppression. Therefore, close monitoring of patients should be conducted during clinical application to timely identify and manage potential adverse reactions.

Additionally, regarding the public accessibility and cost of Tripterygium wilfordii glycosides tablets, although this medication is widely used in China, its availability may be influenced by regional factors and health insurance coverage, and the economic burden on patients should also be considered. The price of this medication is relatively low, typically ranging from 500 to 1500 RMB; however, the financial status and affordability of patients remain important factors.

Moreover, opinions in the literature on the efficacy of Tripterygium wilfordii glycosides combined with Western medicine are not consistent. Some studies have not observed significant efficacy, which may be related to differences in study design, patient characteristics, and treatment protocols. Certain studies may have failed to include an adequate sample size or lacked a randomized controlled design, thus affecting the reliability of the results. This further emphasizes the need for high-quality research to establish more consistent conclusions. Finally, we note that, despite the majority of studies in this research using similar dosages, variations in dosages across different studies may lead to discrepancies in outcomes. Future research should investigate the effects of different dosages on efficacy to determine the optimal treatment regimen.

Reviewer 2

Introduction: Strengths: The introduction is informative and provides a detailed overview of rheumatic immune diseases, the limitations of current treatments, and the potential advantages of Tripterygium wilfordii glycosides tablets (TGT). It makes a strong case for the study's importance. Weaknesses: The introduction is somewhat lengthy and repetitive in sections. For instance, the discussion on the shortcomings of Western medicine could be condensed, focusing more on the rationale for combining TGT with Western therapies.

We thank the reviewer for their affirmation of our article and valuable suggestions. We agree that the introduction contained some redundancy and has been condensed according to the recommendations. Tripterygium wilfordii, a traditional Chinese medicine with potent immunosuppressive and anti-inflammatory effects, has been widely used in the treatment of immune-related diseases. Tripterygium glycosides tablets (TGT) demonstrate promising potential in modulating immune responses by regulating cytokines, T cell subsets, and B cell activities. Therefore, the combination of TGT with Western medicine can serve as a complementary approach in the treatment of rheumatic immune diseases.

Methods: Strengths: The methods section is comprehensive, explaining the search strategy, inclusion/exclusion criteria, and statistical methods. The use of PRISMA guidelines enhances the credibility. Weaknesses: While the methods are well-detailed, the section could be more concise in certain areas, particularly regarding the inclusion and exclusion criteria. Some of the details about databases could be presented in a more straightforward manner.

We sincerely appreciate the reviewer’ s affirmation and suggestions regarding the methods section. In accordance with your recommendations, we have simplified the description of the inclusion and exclusion criteria while making the database search strategy more straightforward and clear. The revised methods section improves conciseness while retaining essential details, ensuring that readers can quickly grasp key information.

Inclusion criteria: Randomized controlled trials (RCTs) involving patients with rheumatic immune diseases, with the intervention being the combination of Tripterygium glycosides tablets and Western medicine (such as non-steroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs, and biologics). The control group should receive treatment with Western medicine alone. The study outcomes must include at least one efficacy indicator (such as overall response rate, visual analog scale (VAS) score, and incidence of adverse reactions).

Exclusion criteria: Observational studies, retrospective analyses, case-control studies, patients with non-rheumatic immune diseases, and studies that did not use Tripterygium glycosides tablets in combination with Western medicine. Additionally, studies that were published repeatedly, had incomplete data, or were of low quality were also excluded.

Results: Strengths: The results are clearly presented, with relevant statistical data, including relative risk and confidence intervals. The use of forest plots is appropriate for visualizing the meta-analysis findings. The inclusion of information on heterogeneity strengthens the results' interpretation. Weaknesses: The results section could benefit from additional interpretation of findings. While the data is presented well, the implications of heterogeneity (or lack thereof) and specific differences between studies should be expanded. The discussion around adverse effects could also be more detailed, particularly regarding the long-term safety of TGT.

We thank the reviewer for their affirmation and suggestions regarding the results section. We will further explain the heterogeneity of the study and its implications, while also providing a more detailed discussion on the long-term safety of adverse reactions.

Most adverse reactions showed minor differences; however, these data suggest that the combination of TGT and Western medicine may have advantages in reducing certain adverse reactions. Regarding the long-term safety of TGT, although current studies indicate a low incidence of adverse reactions, a complete evaluation of TGT's long-term safety has not yet been achieved due to the short duration of these studies. Future research should include longer follow-up periods to provide more reliable safety data on the long-term use of TGT.

Discussion: Strengths: The discussion section effectively places the findings within the broader context of existing literature. The positive effects of TGT in combination with Western medicine are supported by the data presented. The consideration of potential biases and limitations adds depth to the analysis. Weaknesses: The discussion could benefit from a more critical analysis of the limitations. While biases are mentioned, the potential impact of these on the study's conclusions is not sufficiently explored. Additionally, more emphasis could be placed on the clinical applicability of the findings, especially given the limitations of the studies included in the meta-analysis.

We appreciate the reviewer’ s affirmation and valuable suggestions regarding the discussion section. We have conducted a more in-depth analysis of the limitations of the study and the impact of potential biases, and we have increased the discussion on the clinical applicability of the research findings. In response to your feedback, we have supplemented detailed explanations on these aspects.

Conclusion: Strengths: The conclusion is concise and effectively summarizes the study's findings, with a call for further high-quality research. The emphasis on the need for more studies to validate the findings adds a balanced perspective. Weaknesses: The conclusion could be enhanced by providing more specific recommendations for future research, particularly regarding dosage, treatment duration, or patient subgroups that might benefit most from the combined therapy.

We appreciate the reviewer’s affirmation and suggestions regarding the conclusion section. We have provided more specific recommendations for future research. To this end, we have added discussions on dosage, treatment duration, and patient subgroups in the conclusion to guide future clinical research and practice.Future studies should focus on the impact of different dosages of Tripterygium glycosides tablets on treatment efficacy and safety, particularly in identifying the optimal dosage to maximize therapeutic effects while minimizing adverse reactions. The duration of treatment is also a critical factor; extending the follow-up period will aid in a more comprehensive evaluation of the long-term safety and efficacy of this combination therapy. Therefore, future research should also target different

subgroups of rheumatic immune diseases to explore which patient populations may benefit most from this combined therapy and develop personalized treatment plans.

Tables and Figures: Strengths: The tables and figures (especially the forest plots and bias graphs) are appropriate and aid in the interpretation of the study's findings. They effectively summarize complex data. Weaknesses: Some tables, particularly the one comparing adverse reactions, could benefit from more detailed captions to enhance interpretability without needing to refer back to the text.

We appreciate the reviewer’s affirmation and suggestions regarding the conclusion section. We have made detailed modifications to the title. Table 3. Comparison of Adverse Reactions Associated with Tripterygium Wilfordii Glycosides Tablets Combined with Western Medicine versus Western Medicine Alone

Overall Strengths: The paper is well-structured and follows a logical flow from introduction to conclusion. The statistical analysis is robust, with a clear explanation of the methods used. The study addresses an important issue in the treatment of rheumatic immune diseases, with a focus on a novel treatment combination. Overall Weaknesses: The language could be more concise in certain sections to improve clarity and readability.

We appreciate the reviewer’s affirmation and suggestions regarding the conclusion section. We have revised most parts of the manuscript to provide more concise descriptions, thereby enhancing clarity and readability.

The limitations, particularly regarding study quality and heterogeneity, need to be more critically addressed. The conclusion, while strong, could provide more actionable insights for clinical practice and future research. Recommendations for Improvement: Conciseness: Reduce repetitive elements in the introduction and methods sections to improve readability. Interpretation: Expand on the clinical implications of the findings, particularly regarding long-term safety and specific patient populations. Limitations: Provide a more critical discussion of the study's limitations and how they might affect the interpretation of the results. Language and Style: Use more straightforward language, especially when describing methodological details.

We thank the reviewer for the detailed feedback on our manuscript. We identified redundancy in the introduction and methods sections and have simplified these parts based on your suggestions to enhance readability. Additionally, we have included a critical discussion of the study's limitations and expanded on the clinical applicability of the findings, particularly regarding long-term safety and specific patient populations. The specific modifications are as follows:

1. Conciseness: We have streamlined the introduction and methods sections by removing unnecessary repetitions, making the manuscript more concise and readable.

2. Clinical Applicability: In the discussion section, we have added a discussion on the clinical value of the study findings, particularly regarding their potential impact on long-term safety and

specific patient populations.

3. Study Limitations: We further explored the limitations present in the study, such as the quality of the included studies and issues of heterogeneity, and analyzed how these limitations may affect the interpretation of the results.

4. Language and Style: We employed clearer and more straightforward language in the methods section to improve readability.