

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

In this manuscript, the authors describe the molecular mechanisms of Biyu decoction in the treatment for psoriasis. The title is informative, the abstract is complete. In the introduction section, there are poor information about basic characteristics of Psoriasis including the age of presentation, risk factor and pathogenesis, and the correct therapeutic approach.

Response:

The basic cutaneous manifestations of psoriasis, pathogenesis, and conventional treatments have been described in the Introduction section ([Page 5, Line 96-110](#)). In response to your suggestions, the role of age, gender, genetics, and other factors in the pathogenesis of psoriasis has been added in the Introduction section.

Changes in the text: [Page 5, Line 91-93](#).

Additionally, for line 94 to line 114 there are no references and more than one should be included. Especially for this sentence "BYT comprises Zicao, Diyu, Cebaiye, and Gancao, which have definite curative effects on psoriasis. The therapeutic effects of BYT on PSO have been verified clinically" Reference must be included and additionally also if the therapeutic effect were proved by a or more randomized clinical trials.

Response:

We supplemented the description of TCM for psoriasis and the effectiveness of TCM in the treatment of psoriasis and added literature support for the components of BYT and the source of its formula (Xiaoyin Jiedu Decoction) in the treatment of psoriasis.

Changes in the text: [Page 5-6, Lines 111-118, Lines 124-126](#).

The material and methods section is complex but complete. In the discussion, there are just a few references and many topics are discussed that should be supported by evidence. In the text, the strength and limits of the study are missing and should be included.

Response:

Based on your suggestion, we have added some necessary literature support in the Discussion section. At the end of the discussion, the strengths and limitations of the study are described.

Changes in the text: [Page 17, lines 430-445](#).

"Our results confirm that BYT can treat PSO through multi-component, multi-target, and multi-channel synergy and provide a basis for further in-depth clinical research of BYT treatment for PSO" this study was not done in vitro or in vivo so in my opinion, it is not able to confirm. This study may represent a start for further and more complex research. Minor English revisions are needed.

Response:

The sentences were revised to make the Conclusion more meaningful and scientific.

Changes in the text: Page 17–18, lines 456–457.

In addition, the research team is conducting experimental validation of BYT in human and animal models. This paper is a preliminary exploration of BYT for further in-depth experiments and provides theoretical support for it. Due to the limitation of the length of the article, some experimental results are attached at the back for the reviewers and editors to consult. (These are internal data of the experimental group. The relevant experiments have not been completed, and the pictures are only for reviewers' reference)

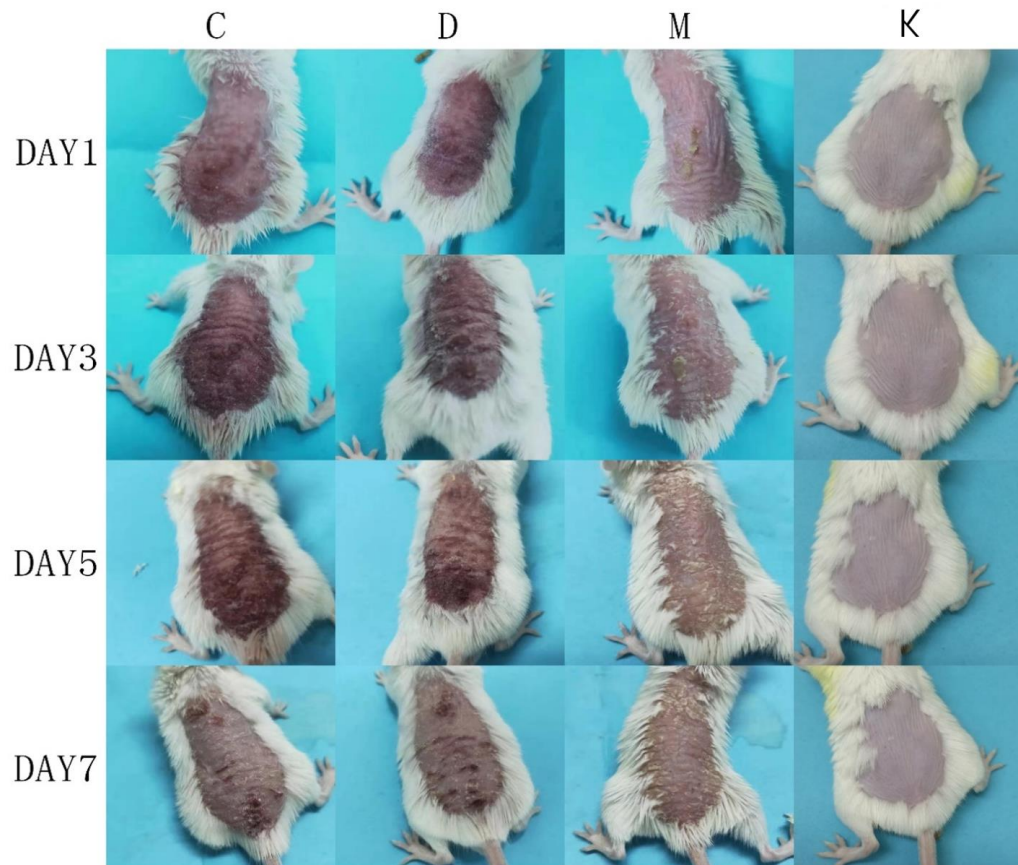


Figure 1: C: BYT gavage group; D: BYT external use group; M: model group; K: blank control group. Except for the control group, 5% Imiquimod (IMQ) was locally administered at the back skin of mice for 7 consecutive days. After 6 hours of daily IMQ administration, mice in group C were given BYT by gavage, and mice in group D underwent external application of BYT concentrate. On the 7th day of administration, the severity of back psoriasis skin lesions in groups C and D was lower than that in the model group.

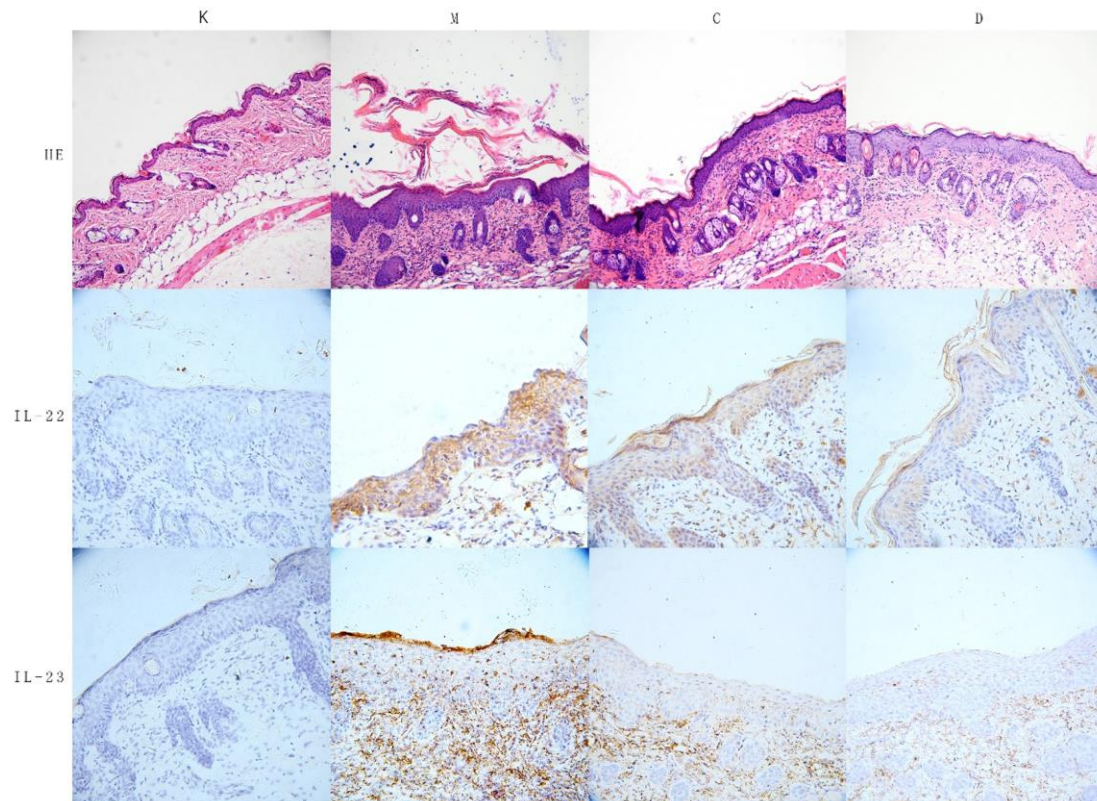


Figure 2: C: BYT gavage group; D: BYT external use group; M: model group; K: blank control group. The mice were sacrificed on the 7th day of administration; the back skin samples of the four study groups were stained. HE staining showed that after treatment in groups C and D, the epidermis became thinner, and the infiltration of inflammatory cells was significantly improved, which was statistically significant compared with the model group ($P < 0.05$). Immunohistochemistry showed that normal mice did not express or had low expression of IL-22 and IL-23. In psoriatic skin lesions, IL-22 was mainly expressed in the lymphocytes infiltrating all layers of the epidermis and dermis, and IL-23 was highly expressed in the dermis. In the stratum corneum and superficial dermis, the cumulative optical density was significantly higher than that in normal mice; after treatment, the positive cells decreased, and the cumulative optical density was significantly different from that in the model group ($P < 0.05$).

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: "I would like to thank authors for conducting this study "Molecular mechanisms of Biyu decoction as treatment for psoriasis: a network pharmacology and molecular docking study" Overall: However, the manuscript is good and it will add valuable information. Abstract Abstract is written well. However. It's too lengthy. Please make abstract in less than 300 words Introduction Too short.

Response:

The abstract has been shortened according to the reviewer's comments.

Changes in the text: Page 3-4, Line 34-36, Line 68-71.

Please add information about psoriasis in China.

Response:

In the Introduction section, we have added more description about the incidence of psoriasis in China and the popularity and superiority of traditional Chinese medicine for treatment of psoriasis.

Changes in the text: Page 5, lines 90–91; page 5–6, lines 111–118.

Methods Please included the duration of data obtaining in methods .

Response:

Details of the time for data acquisition times have been included in the "Drug and gene data" section of the Methods.

Changes in the text: Page 7, line 144.

Results No comments. It was written good Discussion. Please add “strengths and limitations” of your study in the discussion section, and write each one of them in a separate paragraph.

Response:

Based on your comments, we have described the strengths and limitations of this study in a separate paragraph at the end of the Discussion section.

Changes in the text: Page 17, lines 430–445.

Conclusion If you could add recommendations for further, it will be good. Please add them."

Response:

According to your suggestion, we have highlighted the future research direction and experimental ideas in the conclusion section.

Changes in the text: Page 17–18, lines 458–460.

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: "Molecular mechanisms of Biyu decoction as treatment for psoriasis: a network pharmacology and molecular docking study", by Wang et al., is computational work exploring the interactions among chemical components of a traditional medicine with potential genes in psoriasis. Psoriasis is an autoimmune disorder that remains to benefit from an accepted therapeutic regime and hence at best managed symptomatically currently in clinical practice. Therefore the present work by the authors is an interesting theoretical attempt to address the potential drugs like benefits of a traditional decoction. Few suggestions for the authors to address are:

1. The title of the study is rather vague since the molecular mechanisms are not

investigated and only gene targets from the available data sources are curated and their binding under defined conditions are explored using computational tools. Hence, it will be good to modify the title to reflect the work undertaken.

Response:

First, thank you very much for your suggestion. In this study, based on network pharmacology, the reactivity between drugs and biological targets was verified by computer molecular docking [1]. After screening out the target genes, the possible biological pathways for BYT action in psoriasis were explored through KEGG and GO enrichment analysis.

We retrieved relevant literature, which supported this propositional model [2-3], and no other suitable propositional reference was found. Therefore, we have not yet changed the title. If you still find it inappropriate, we can make further adjustments based on your comments at any time.

Reference:

- [1] Xin Wang , Zi-Yi Wang , Jia-Hui Zheng , Shao Li . TCM network pharmacology: A new trend towards combining computational, experimental and clinical approaches. Chin J Nat Med. 2021 Jan;19(1):1-11. doi: 10.1016/S1875-5364(21)60001-8.
- [2] Jinlong Zhao, Fangzheng Lin, Guihong Liang, Yanhong Han, Nanjun Xu, Jianke Pan, Minghui Luo, Weiyi Yang, and Lingfeng Zeng. Exploration of the Molecular Mechanism of Polygonati Rhizoma in the Treatment of Osteoporosis Based on Network Pharmacology and Molecular Docking. Front Endocrinol (Lausanne). 2021; 12: 815891. doi: 10.3389/fendo.2021.815891
- [3] Boran Zhang, Wenchao Dan , Ganlin Zhang , Xiaomin Wang. Molecular Mechanism of Gleditsiae Spina for the Treatment of High-Grade Serous Ovarian Cancer Based on Network Pharmacology and Pharmacological Experiments. Biomed Res Int. 2022 Mar 8;2022:5988310. doi: 10.1155/2022/5988310.

2. Introduction section is too brief and does not adequately provide the background of the proposed work.

Response:

The introduction of psoriasis and the relevant background of Chinese medicine have been improved, and the relevant literature has been cited.

Changes in the text: Page 5, lines 90–93; Page 5–6, lines 111–126.

3. Authors have not established the use of BYT as traditional treatment and no experimental evidence is provided to the effect.

Response:

The research team is conducting experimental validation of BYT in human and animal models. This paper is a preliminary exploration of BYT for further in-depth experiments and provides theoretical support for it. Due to the limitation of the length of the article, some experimental results are attached at the back for the reviewers and editors to consult. **(These are internal data of the experimental group. The relevant experiments have not been completed, and the pictures are only for the reviewers' reference)**

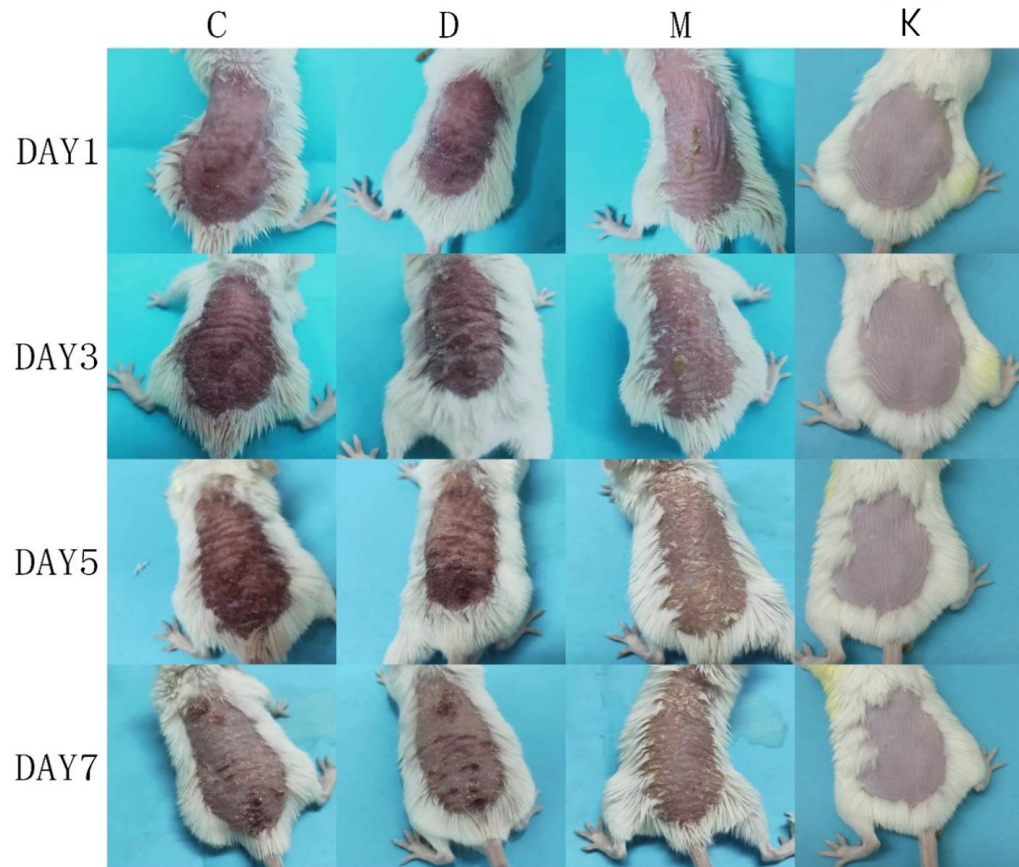


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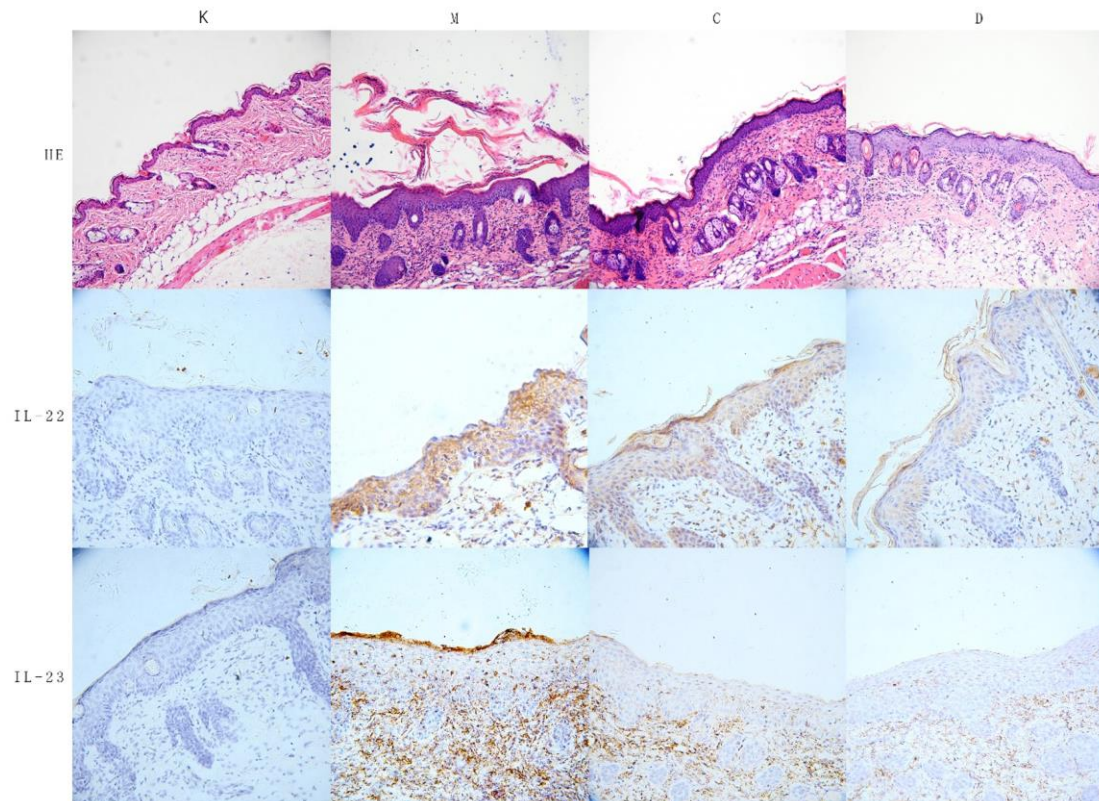


Figure 2: C: BYT gavage group; D: BYT external use group; M: model group; K: blank control group. The mice were sacrificed on the 7th day of administration; the back skin samples of the four study groups were stained. HE staining showed that after treatment in groups C and D, the epidermis became thinner and the infiltration of inflammatory cells was significantly improved, which was statistically significant compared with the model group ($P<0.05$). Immunohistochemistry showed that normal mice did not express or had low expression of IL-22 and IL-23. In psoriatic skin lesions, IL-22 was mainly expressed in the lymphocytes infiltrating all layers of the epidermis and dermis, and IL-23 was highly expressed in the dermis. In the stratum corneum and superficial dermis, the cumulative optical density was significantly higher than that in normal mice; after treatment, the positive cells decreased, and the cumulative optical density was significantly different from that in the model group ($P<0.05$).

4. The authors have also not established the use of BYT in clinics but have alluded in the Introduction section that it has verified clinically.

Response:

Professor Jin Qifeng, a national famous senior Chinese medicine doctor from the Department of Dermatology, Dongzhimen Hospital, Beijing University of Traditional Chinese Medicine, has unique experience in the treatment of psoriasis and founded the traditional Chinese medicine compound "xiaoyinjiedu decoction" (the source of BYT). For decades, a lot of clinical application experience has been accumulated, and excellent efficacy evaluation has been obtained.

However, broader adoption of traditional Chinese medicine is hindered by many limitations, such as delayed molecular research and difficulty in internationalization. Previous researches

were mostly published in Chinese journals, and relevant English literatures are scanty. Some English literatures have been marked in the text, and here is a list of some Chinese articles previously published by the research team for the reviewers' reference.

Reference:

[1]张润田,陈曦,霍春波,段行武,陈兵,李玲玲.消银解毒颗粒对 Jurkat 细胞异常增殖模型的影响[J].中医杂志,2017,58(12):1049-1052.DOI:10.13288/j.11-2166/r.2017.12.016.

Zhang RT, Chen X, Huo CB, Duan XW, Chen B, Li LL. Effect of Xiaoyin Jiedu granules on model of jurkat cell abnormal proliferation[J]. Journal of Traditional Chinese Medicine 2017,58(12):1049-1052. DOI:10.13288/j.11-2166/r.2017.12.016.

[2]陈曦,霍春波,陈广山,张云璧,段行武,张润田,李玲玲.消银解毒方颗粒对 Jurkat T 细胞内 JAK1/STAT3 信号通路作用机制的研究[J].北京中医药大学学报,2017,40(02):119-124.

Chen X, Huo CB, Chen GS, Zhang YB, Duan XW, Zhang RT, Li LL. Effect of Xiaoyin Jiedu Fang on JAK1/STAT3 signaling pathway in Jurkat T cells[J]. Journal of Beijing University of Traditional Chinese Medicine. 2017,40(02):119-124.

[3]霍春波. 消银解毒颗粒对 Jurkat T 细胞 JAK/STAT 信号转导通路的影响[D].北京中医药大学,2016. DOI:10.26973/d.cnki.gbjzu.2016.000030.

Huo CB. Effect of Xiaoyin Jiedu Granule on JAK / STAT signal transduction pathway of Jurkat T cells[D]. Beijing University of traditional Chinese Medicine, 2016. DOI:10.26973/d.cnki.gbjzu.2016.000030.

[4]李玲玲,孙少馨,徐杰,董玢,金秋硕,瞿幸,段行武.消银解毒免煎颗粒治疗寻常型银屑病 40 例临床观察[J].中医杂志,2014,55(10):850-853. DOI:10.13288/j.11-2166/r.2014.10.012.

Li LL, Sun SS, Xu J, Dong F, Jin QS, Qu X, Duan XW. Clinial Observation on Xiaoyin Jiedu Granules for 40 cases of Psoriasis Vulgaris[J]. Journal of Traditional Chinese Medicine. 2014,55(10):850-853. DOI:10.13288/j.11-2166/r.2014.10.012.

[5]孙少馨. 消银解毒颗粒治疗寻常型银屑病临床研究[D].北京中医药大学,2013.

Sun SS. Clinical study on Xiaoyin Jiedu Granule in the treatment of psoriasis vulgaris[D]. Beijing University of traditional Chinese Medicine,2013.

5. Discussion section does not elaborate the importance of such analyses since these interactions are mapped computationally under defiend set of conditions which of course is not the case in cellular environment.

Response:

Network pharmacology is based on the theory of systems biology, combined with pharmacology, bioinformatics, network analysis, and other disciplines, to study the relationship between TCM components, targets, and diseases from a holistic perspective, which can be used to systematically reflect the mechanism of action of TCM compounds. Screening a large number of molecular targets can pave the way for the next experiment and can guide the synthesis of new drugs [1].

Through experiments, the research team has previously confirmed the effectiveness of BYT components in psoriasis (see answer 4). Currently, we are conducting follow-up experiments based on the ideas provided by the results of this study (see Answer 3). Preliminary experiments also show that this data-based calculation can reflect the interaction between drugs and diseases to a certain extent, but further experimental verification is needed.

Reference:

[1] Michael Maes, Nikita G Nikiforov, Kitiporn Plaimas , Apichat Suratanee , Daniela Frizon Alfieri , Edna Maria Vissoci Reiche. New Drug Targets to Prevent Death Due to Stroke: A Review Based on Results of Protein-Protein Interaction Network, Enrichment, and Annotation Analyses. *Int J Mol Sci.* 2021 Nov 9;22(22):12108. doi:10.3390/ijms222212108.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Firstly, thank you for opportunity to review very interested article. I don't feel qualified to judge about the English language and style due to not native language. 1. The title reflect the main subject about Biyu decoction treatment for psoriasis, title was clear and easy to understand. 2. The abstract summarize and reflect the work described in the manuscript. 3. The key words reflect the focus of the manuscript. 4. The manuscript adequately describe the background, present status, and significance of the study. The authors explain nature of Psoriasis disease and standard treatment. However, the Biyu decoction (BYT) was a main treatment of study, so that I suggested the authors to more explain about that. 5. The manuscript describe methods in adequate detail, study subjects were clear. 6. The research objectives achieved by the experiments used in this study. 7. The manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly, and logically. 8. Tables and figures sufficient, good quality and appropriately illustrative of the paper contents. 9. The manuscript meet the requirements of biostatistics. 10. The manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections.

Response:

Thank you for your affirmation. In response to your suggestion, the background of BYT and TCM treatment of psoriasis has been explained in more detail in the Introduction section.

Changes in the text: Page 5–6, lines 111–126.

Reviewer #5:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

1. Was the local average connectivity-based method considered for the PPI network?

Response:

The PPI network was constructed with the local average connectivity-based method (LAC) in mind.

All 110 drug-disease-associated genes were included in the construction of the PPI-protein interaction network in this study, and six criteria, including LAC, were used to evaluate the core gene screening. Nodes with scores above the median for each item were retained to obtain the core network.

2. How was the molecular docking scored? Was Root Mean Square Deviation considered?

Response:

The docking score of Autodock Vina is represented by Affinity (Table 3). The smaller the value, the stronger the binding force, that is, the tighter the binding. The Root Mean Square Deviation (RMSD) was also taken into consideration. In the docking calculation by Vina software, the combination with too large RMSD value was not included in the final result.

Therefore, the final and selected combination revealed a stable interaction on RMSD.

3. How is molecular docking linked to the clinical activity / drug response?

Response:

Based on molecular docking, we found that MAPK8/Kaempferol and STAT3/licochalcone A had lower binding energies (-8.7 kcal/mol and -6.6 kcal/mol, respectively), indicating better binding activity. Both MAPK8 and STAT3 are important pathways in the pathogenesis of psoriasis [1,2].

These results suggest that these drug molecules may directly bind to the corresponding core targets with high and stable affinity and provide evidence for the key roles of these core targets in the treatment of psoriasis. The docking results confirm the accuracy of the PPI network analysis results in identifying the core targets. Therefore, in future research, these screened compounds can be considered for clinical or experimental application.

This part is also discussed in the text.

Changes in the text: Page 16, lines 397–403.

Reference:

[1]Sun W,Gao Y,Yu X,Yuan Y,Yi J,Zhang Z,Cheng Y,Li Y,Peng X,Cha X.'Psoriasis 1' reduces psoriasis-like skin inflammation by inhibiting theVDR-mediated nuclear NF-κ B and STAT signaling pathways[J].Mol Med Rep,2018,18(3):2733-2743.

[2] Chuang SY,Chen CY,Yang SC,Alalaiwe A,Lin CH,Fang JY,2,4-Dimethoxy-6-Methylbenzene-1,3-diol, a Benzenoid From Antrodia cinnamomea, Mitigates Psoriasiform Inflammation by Suppressing MAPK/NF-κ B Phosphorylation and GDAP1L1/Drp1 Translocation[J].Front Immunol,2021,12:664425.

4. Does PPI network activity guarantee the desired clinical response?

Response:

In this study, when the PPI network was constructed, all genes in the PPI network were enriched by GO and KEGG pathways. The enrichment results show the molecular mechanisms of genes included in the PPI network that are involved in the disease process of psoriasis, suggesting that we may receive better treatment outcomes by focusing on the intervening genes. This reflects the clinical significance of the PPI network.

For example, the genes of the PPI network in this study were abundantly enriched in the Th17 cell differentiation and TNF signaling pathways, which are also the core concerns of psoriasis.

5. Is the interaction between core genes and hub genes taken into consideration?

Response:

We have considered the interaction between core genes and hub genes in our study.

In the present study, we chose to screen core genes in a more stringent manner than hub genes. Specifically, hub genes refer to genes with high connectivity (i.e. degree centrality, DC) in the PPI network. When screening core genes in this study, in addition to DC, five measures were considered: local average connectivity (LAC), betweenness centrality (BC), closeness centrality (CC), eigenvector centrality (EC), and network centrality (NC).

Taken together, this study evaluates the interaction between core and hub genes in each dimension. See *Page 8, Line 171-181, Page 11, Line 255-266*, in the text for details, please review.

6. What are the study limitations?

Response:

We have added the study strengths and limitations at the end of the Discussion section.

Changes in the text: Page 17, lines 430–445.

7. "Biyu decoction is useful in psoriasis treatment through multi-component, multi-target, and multi-channel synergy". Is the statement valid (based on the molecular mechanisms alone without a animal model / human study)?

Response:

We have supplemented the background of traditional Chinese medicine related to this research.

Changes in the text: Page 5–6, lines 111–126.

Professor Jin Qifeng, a national famous senior Chinese medicine doctor from the Department of Dermatology, Dongzhimen Hospital, Beijing University of Traditional Chinese Medicine, has unique experience in the treatment of psoriasis and founded the traditional Chinese medicine compound "xiaoyinjiedu decoction" (the source of BYT). For decades, a lot of clinical application experience has been accumulated, and excellent efficacy evaluation has been obtained.

However, broader adoption of traditional Chinese medicine is hindered by various limitations, such as delayed molecular research and difficulty in internationalization. Previous researches were mostly published in Chinese journals, and English literatures are scanty. Some English literatures have been marked in the text, and below is a list of some Chinese articles previously published by the research team for the reviewers' reference.

Also, the research team is conducting experimental validation of BYT in human and animal models. This paper is a preliminary exploration of BYT for further in-depth experiments and provides theoretical support for it. Due to the limitation of the length of the article, some experimental results are attached at the back for the reviewers and editors to consult. **(These are internal data of the experimental group. The relevant experiments have not been completed, and the pictures are only for reviewers' reference)**

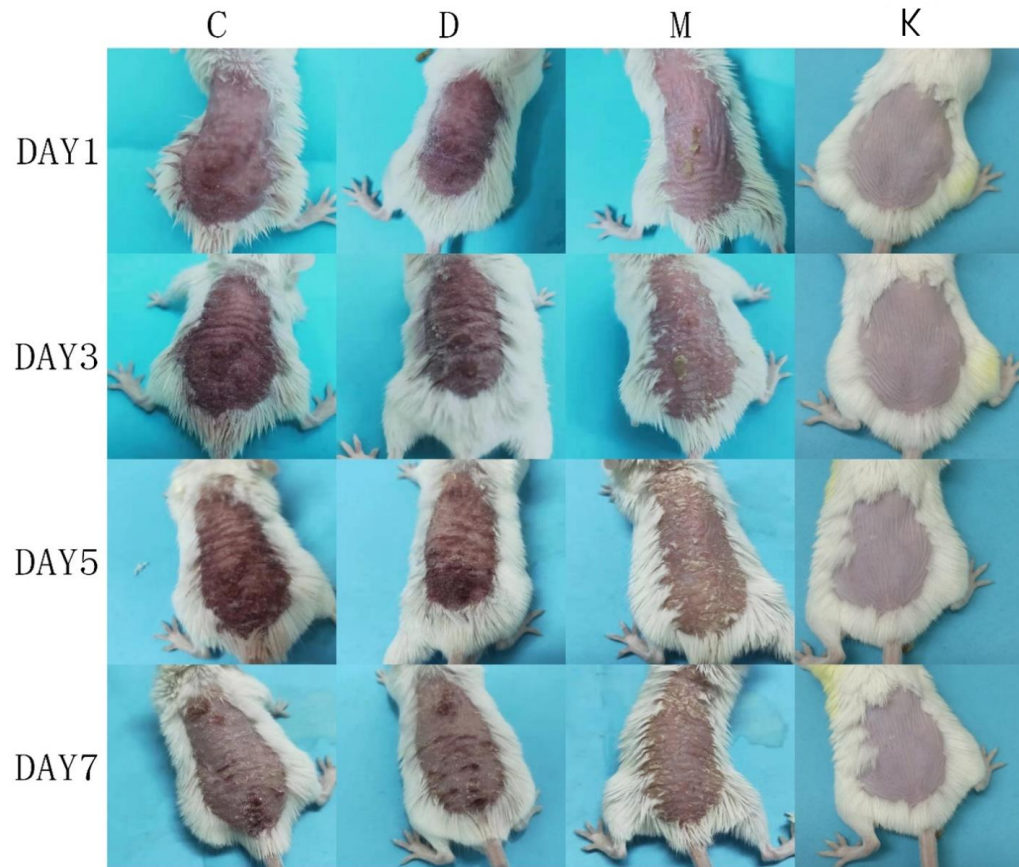


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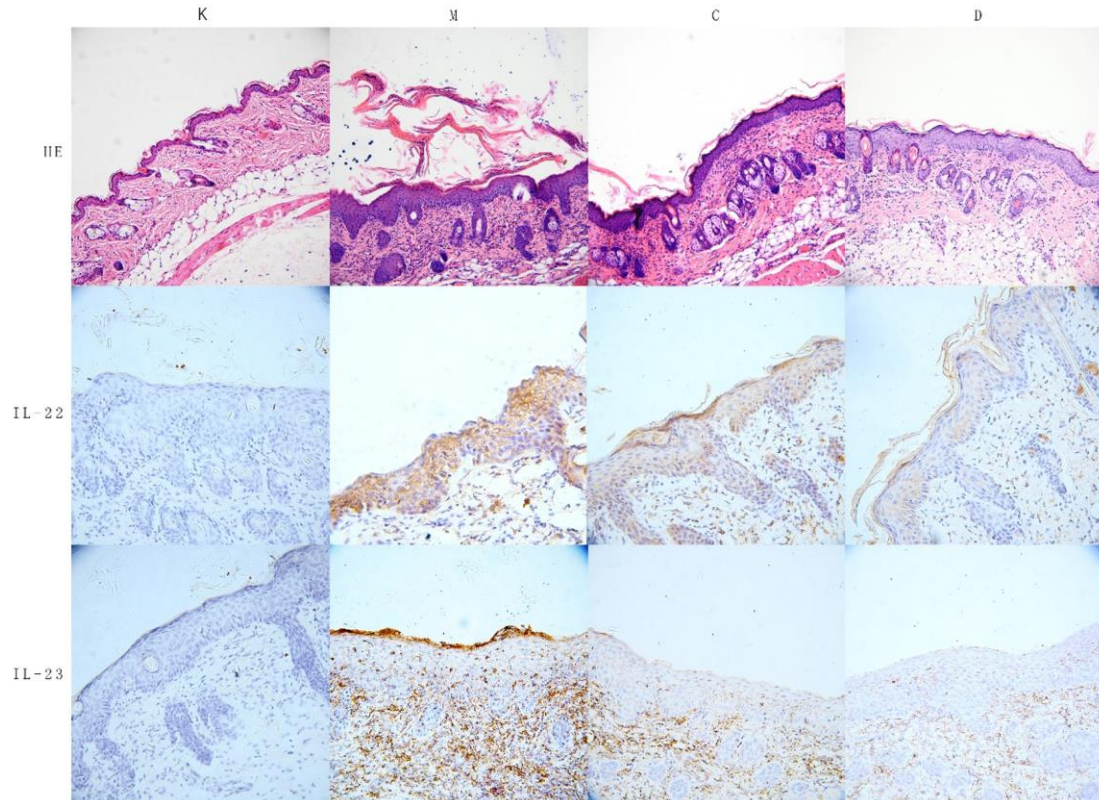


Figure 2: C: BYT gavage group; D: BYT external use group; M: model group; K: blank control group. The mice were sacrificed on the 7th day of administration; the back skin samples of the four study groups were stained. HE staining showed that after treatment in groups C and D, the epidermis became thinner, and the infiltration of inflammatory cells was significantly improved, which was statistically significant compared with the model group ($P<0.05$). Immunohistochemistry showed that normal mice did not express or had low expression of IL-22 and IL-23. In psoriatic skin lesions, IL-22 was mainly expressed in the lymphocytes infiltrating all layers of the epidermis and dermis, and IL-23 was highly expressed in the dermis. In the stratum corneum and superficial dermis, the cumulative optical density was significantly higher than that in normal mice; after treatment, the positive cells decreased, and the cumulative optical density was significantly different from that in the model group ($P<0.05$).

Reference:

- [1]张润田,陈曦,霍春波,段行武,陈兵,李玲玲.消银解毒颗粒对 Jurkat 细胞异常增殖模型的影响[J].中医杂志,2017,58(12):1049-1052.DOI:10.13288/j.11-2166/r.2017.12.016.
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- [2]陈曦,霍春波,陈广山,张云璧,段行武,张润田,李玲玲.消银解毒方颗粒对 Jurkat T 细胞内 JAK1/STAT3 信号通路作用机制的研究[J].北京中医药大学学报,2017,40(02):119-124.
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[3]霍春波. 消银解毒颗粒对 Jurkat T 细胞 JAK/STAT 信号转导通路的影响[D].北京中医药大学,2016. DOI:10.26973/d.cnki.gbjzu.2016.000030.

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[4]李玲玲,孙少馨,徐杰,董玢,金秋硕,瞿幸,段行武.消银解毒免煎颗粒治疗寻常型银屑病40例临床观察[J].中医杂志,2014,55(10):850-853. DOI:10.13288/j.11-2166/r.2014.10.012.

Li LL, Sun SS, Xu J, Dong F, Jin QS, Qu X, Duan XW. Clinial Observation on Xiaoyin Jiedu Granules for 40 cases of Psoriasis Vulgaris[J]. Journal of Traditional Chinese Medicine. 2014,55(10):850-853. DOI:10.13288/j.11-2166/r.2014.10.012.

[5]孙少馨. 消银解毒颗粒治疗寻常型银屑病临床研究[D].北京中医药大学,2013.

Sun SS. Clinical study on Xiaoyin Jiedu Granule in the treatment of psoriasis vulgaris[D]. Beijing University of traditional Chinese Medicine,2013.

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

This manuscript is a network pharmacology study about Biyu decoction as treatment for psoriasis, which is interesting and of some significance to the clinical field. However, some issues have to be addressed. The writing language needs to be further refined. Some of the discussions in the paper need to be supported by data and literature, and the wording should be scientifically rigorous. The number of total references is few and a bit outdated, maybe a little more related references could also be cited. The figures need further arranged and the resolution of the images needs to improve.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response:

1. Reasonable consideration has been given to the wording, and the manuscript has been checked again for language by a professional editing service.
2. References have been reasonably added and updated in the Discussion to make the arguments more meaningful.
3. The original image has been uploaded in the PowerPoint file.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights.

Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response:

1. The original image file has been placed in the PowerPoint file.
2. All data and pictures in this study were originally prepared by the author, and the pictures and table formats have been edited according to the journal requirements.
3. The project initiation documents of the funded projects have been uploaded as needed.