

Review report

Final title: **Astaxanthin as a potential therapeutic agent for knee osteoarthritis: A comprehensive review of mechanisms and clinical evidence**

Title at submission: Astaxanthin as a potential therapeutic agent for knee osteoarthritis: A comprehensive review of mechanisms and clinical evidence

Submission date: 20-Sep-24

Revised submission: 21-Dec-24

Accepted: 21-Dec-24

Reviewer A: Iftekhar Hussain Bandhan, ORCID: [0000-0002-3800-6155](https://orcid.org/0000-0002-3800-6155)

Overview

This manuscript is very well-written and interesting. Previously, we have seen many pre-clinical studies based on the mechanism of action that gave hope for effective drug therapy for knee OA; however, almost all of them failed to show adequate efficacy in the clinical trials. As mechanical loading plays a key role in the development of knee OA, only therapeutic exercises and lifestyle modifications have shown good efficacy in previous studies. So, I think astaxanthin should go for well-controlled clinical trials to prove its actual efficacy.

1. Comment	Are the table(s) and figure(s) clear and appropriate to address the objective(s) or research question(s)? = No Overall, the tables were appropriate, I am only suggesting a minor correction: Table 2: In the "Astaxanthin Effects" column, either use a bullet (make separate lines) or a comma between each mechanism.
Response	The table no. 2 is corrected according to the instruction.
2. Comment	Is the discussion section critical and comprehensive about the main message of the manuscript? = No I did not find any writing in the discussion section. Overall, the result section looks too elaborate. It should be brief, and the elaborated part might be moved to the "discussion" section.
Response	This comprehensive review article does not include a conventional results and discussion section. Instead, the research team has incorporated a discussion that provides an overview of the key findings and highlights the limitations of the review. Expanding beyond this would risk disrupting the coherence of the article and compromising its readability.
3. Comment	Mechanical factors (e.g., obesity, excessive bending, poor muscle strength), anatomic factors (e.g., joint shape), genetic factors, and inflammation play roles in the development of knee OA. Those pathogenic mechanisms were not mentioned in this manuscript. Those should be mentioned at least in the "introduction". Result > Comparative Analysis with Existing Treatments: Please avoid repeating the mechanism of action of astaxanthin.
Response	The introduction part has been revised according to the suggestions. The "Comparative Analysis with Existing Treatments" was revised according to the suggestions.

Editor: M Mostafa Zaman, ORCID: [0000-0002-1736-1342](https://orcid.org/0000-0002-1736-1342)

4. Comment	Please provide the names of the authors' departments on the title page. Double-check the instructions for the authors to meet all the requirements, e.g., ORCIDs, acknowledgements and BSMMUJ's style for the author contributions.
Response	The author affiliation has been updated according to the BSMMUJ's style.
5. Comment	Add a Discussion section. Compensate words from other sections so that the article remains reader-friendly.
Response	This comprehensive review article does not feature a traditional results and discussion section. However, to address the suggestion of adding a Discussion section, the research team has integrated a focused discussion that presents an overview of the key findings and acknowledges the limitations of the review. To maintain the article's coherence and reader-friendliness, adjustments were made by compensating words from other sections rather than expanding the overall content.