

Dear Lavina Araujo, Susana Maia, Nayara Souza, Paulo Silva, Vicente Saboia:

Your submission Effects of incorporating natural substances into sodium alginate in the cultivation of human dental pulp stem cells: a systematic review with meta-analysis to Brazilian Dental Science, has been revised and according to reviewers' comments, there are questions to be addressed and/or points to be clarified/corrected. Please answer the reviewers considerations point-by-point in a separate document and also please make all the corrections in the text highlighted in yellow.

Deadline: 30 days

Thank you for considering Brazilian Dental Science for publishing your research.
We are looking forward the revised version of you manuscript.

Sincerely,

Reviewer A:
Recommendation: Revisions Required

Questionnaire

Does the manuscript contain new and significant information to justify publication?*

Yes

Does the Abstract (Summary) clearly and accurately describe the content of the article?

Yes

Is the problem significant and concisely stated?

Yes

Are the methods or research design described comprehensively? Is the statistical analysis adequate?

No

Are the interpretations and conclusions justified by the results?

Yes

Is adequate reference made to other work in the field?

Yes

Is the language acceptable?

Yes

Manuscript Structure

Length of article is:*

Adequate

Number of tables is:

Adequate

Number of figures is:

Adequate

Please state any conflict(s) of interest that you have in relation to the review of this paper (state “none” if this is not applicable).

None.

Rating

Interest*

Good

Quality

Good

Originality

Good

Overall

Good

Recommendation

Major Revision

Would you be willing to review a revision of this manuscript?

Yes

Comments

Comments to the Author

Dear Authors,
Thanks for submitting your work. After reading the manuscript, some points must be considered:

In the PICOT structure, "T" is considered "time", and should be adjusted to PICOS, where "S" refers to the type of study.

The Embase database was used, but there is no reference to the use of Emtree descriptors (Embase Subject Headings). Why were they not considered?

Were the terms from the Health Sciences Descriptors (DeCS) also not used?

Additional databases for "gray literature" should be performed to improve the systematic review. Was "gray literature" not considered?

Articles not available should not be considered as an exclusion criterion. If full texts were not found, the ResearchGate network could be used to contact the corresponding authors, a bibliographic request could be made to the library database (COMUT) or an email could be sent to the corresponding authors to obtain the texts.

How was the calibration performed between the reviewers? It is important to indicate the value of the Kappa concordance test.

Was data extraction performed by two reviewers independently?

Reviewer H:
Recommendation: Revisions Required

Questionnaire

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none

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Average

Overall

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Recommendation

Minor Revision

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Comments

Comments to the Author

1-Risk of bias (how it was done vs what it implies):

Tool used: JBI experimental checklist, 11 items listed.

Findings: Authors note no randomization or blinding in the included studies, some lacked sample-size justification and protocol/statistics details, yet all were labeled “low risk of bias.” That’s internally inconsistent; absence of randomization/blinding is a genuine risk for performance/detection bias, even in vitro.

Grading thresholds: Text says “1–3 yes = high risk; 4–5 = moderate; 6–8 = low.” With an 11-item list, this scheme leaves 9–11 “yes” unclassified and sets a low bar for “low risk.” I’d recommend revising the categorization.

2- Meta-analysis (statistics & interpretation):

Publication bias: Authors report Egger’s $p < 0.001$ and funnel asymmetry with only 3 studies. With $k \approx 3$, funnel plots and Egger tests are generally not interpretable; I would not make strong claims either way from this test. (Still: the field is small, so true small-study effects or reporting bias remain plausible.)

3- GRADE assessment: Labeled “Moderate certainty,” downgraded only for publication bias (“highly suspicious”). Given the acknowledged lack of randomization/blinding and tiny k with imprecision around design details, I’d argue for at least one more downgrade (\rightarrow Low) for risk of bias/indirectness.

4- Reporting & editorial issues (worth fixing before submission):

- Internal consistency: Study called “Porreli/Porrelli” in different places; fix spelling.

- Typos: “publication biasa,” “papila,” “Disco” (likely “disc”). Clean these.

- Risk-of-bias thresholds: Re-specify categories to match the 11-item list; don't label everything "low risk" when randomization/blinding are absent.
 - Meta-methods clarity: State which timepoint per study was pooled, confirm independence of replicates, and provide means/SD/SE and exact n per group for all included contrasts.
 - Publication bias claim: With $k=3$, drop funnel/Egger claims from the abstract and move to limitations as "not assessable."
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