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PEER-REVIEW REPORT

Name of journal: *World Journal of Orthopedics*

Manuscript NO: 66851

Title: Antibiotic-free antimicrobial poly(methyl methacrylate) bone cements: A state-of-the-art review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05685534
Position: Peer Reviewer
Academic degree: PhD
Professional title: Chairman, Professor
Reviewer's Country/Territory: Egypt
Author's Country/Territory: United States

Manuscript submission date: 2021-04-07

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-07-23 08:47

Reviewer performed review: 2021-08-02 09:58

Review time: 10 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The exact mechanism responsible for the antimicrobial activity of Ag has not been established but there is consensus on possible reasons, such as inactivation of the bacterial cell (cell membrane and enzymes) by the Ag ions interfering with enzymes that interact with sulfur in the protein chains and/or generating reactive oxygen species[54], which kill the cells. ^ Please through light on the different theories of Ag antimicrobial effect Please mention the a literature based possible antimicrobial effects of bioactive glass However, results of bacterial adhesion tests showed that each of the AFAMBCs significantly reduced biofilm formation relative to the plain cement[58]. These results suggest that while the AFAMBCs have no antimicrobial activity against planktonic bacteria, they have good potential for use in cases where prevention of bacterial adhesion is needed (for example, in primary TJAs)[58]. Please explain how is the biofilm phenomenon could represent a challenge for the antimicrobial effect Please combine the antimicrobial effects of each modality with its clinical relevance related to PJI In vitro cytotoxicity/cytocompatibility please explain importance and factors affecting biocompatibility of the cement and factors affecting bio adherence and more evidences regarding the negative effects of antibiotics on cellular adhesion Other cement properties The number of studies in which other cement properties were determined varied widely, from < 5 (example properties: tensile modulus, tensile strength, fracture toughness, and radiopacity) to ~20 (property: compressive strength) (Table 1). Among these results, some are clear evidence that for an AFAMBC, its maximum polymerization temperature is lower (which is desirable), setting time is longer (which is not desirable), compressive strength is comparable, flexural modulus is

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comparable, and cell viability is higher (please mention the clinical relevance for each charchter) After 7-28 days of immersion of specimens of bioactive glass powder-loaded cement in simulated body fluid, at 37 oC, there was evidence of agglomerates on the specimen surface that were rich in calcium and phosphorus (HAP) (Ca/P ratio = 0.9 - 4.0)[60,62,63]. Please clarify the added value of Calcium and phosphate in improving substance bioactivity