We thank the Reviewers and Editors for their time and effort for reading and commenting on the manuscript. In the following, we respond to each comment in detail. Sections that have been changed in the manuscript are marked in blue.

Reviewer 2:

The manuscript entitled “Injectable Thermosensitive Chitosan-Collagen Hydrogel as a Delivery System for Marine Polysaccharide Fucoidan” by Julia Ohmes and et al. devoted to the creation of fucoidan delivery system, based on chitosan, collagen and β-glycerophosphate, investigation of its physicochemical parameters and the determination of the biocompatibility of obtained injectable thermosensitive hydrogel. This work is beneficial for researchers who focus on the investigation of fucoidans and their application.

The manuscript seems well written, and contents look important.

The part of the work devoted to the preparation and physicochemical characterization of the fucoidan delivery system represented in detail. Gelation time, gelation temperature, pH, appearance, swelling and internal microscopic structure were determined and well described.

The biocompatibility of obtained injectable thermosensitive hydrogel was assessing only by cell life/dead staining of MSC and OEC cells. To confirm the perspectiveness of the delivery system for fucoidan for the use in regenerative medicine, the additional experiments on biocompatibility of injectable thermosensitive hydrogel are needed.

We thank the Reviewer for the comments on the manuscript. In the following, we would like to answer specifically to the last comment which refers to the necessity of conducting further biocompatibility assays. The present manuscript provides a very first characterization of the developed hydrogel-based delivery system. To our knowledge, the combination of thermosensitive composite collagen-chitosan hydrogel with fucoidan was not described in the literature before. The goal of this paper is to provide a broad overview over many characteristics (different physicochemical parameters, appearance, biocompatibility) and thereby evaluate whether this hydrogel represents a potential delivery system for fucoidan for regenerative medicine. The biocompatibility was assessed using primary human MSC isolated from cancellous bone and primary human OEC which were isolated from peripheral blood. Two different cultivation techniques were tested: Seeding of cells on top of the hydrogels (2D) and encapsulation of cells inside the hydrogels (3D). The 3D cultivation is probably the more relevant one for bone tissue engineering applications. We found that MSC and OEC cultured on top of the hydrogel were vital to the largest extent. Encapsulated MSC were vital as well. However, encapsulated OEC struggled to elongate inside the hydrogel. Similar results were observed for co-encapsulation of MSC and OEC. Hence, in future studies, the mechanical properties of the hydrogel need to be improved in order to achieve an increased biocompatibility especially for OEC. To provide further information on the biocompatibility of the hydrogels, we performed DNA quantification.

The figure below shows preliminary data of DNA quantification from the hydrogel. Therefore, MSC were encapsulated inside the hydrogel with and without fucoidan and DNA content was quantified on day 1 and day 6. As shown below, the DNA content is not decreased in hydrogels which contain fucoidan. Also, DNA content is not decreased from day 1 to day 6, indicating the biocompatibility of the hydrogels. Before the conduction of in-depth biocompatibility assays we first would try to optimize the mechanical properties to ensure elongation of OEC.

