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The Use of Marine Biota in Bone Tissue Regeneration: A Systematic Review

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ABSTRACT
This systematic review tries to determine the use of the various types of marine biota in bone tissue regeneration. There were 637 articles gathered from PubMed, Wiley, and google scholar databases. Title selection obtained 172 reports and 69 duplications. Abstract selection resulted in 34 articles. The full-text selection was done afterward and produced 11 articles, which were finally analyzed by the authors. The research was done by 11 groups of researchers who came from 10 different countries. The countries were Spain, Tunisia, India, Brazil, Poland, Singapore, England, China, Malaysia, and South Africa. Marine biota that were used in the studies were shark teeth, pearl, fish skin, seaweed, sponge, cockle shell, and deep-sea fish head. The activated marker that appeared in the bone formation process by the stimulation of the material was alkaline phosphatase, collagen 1-a-1, osteopontin, osteocalcin, and runx2. Various types of marine biota dan are used in bone tissue regeneration through osteoblastic stimulation with the activity of bone formation markers, such as Alkaline phosphatase, collagen 1-a-1, osteocalcin, runx2, as well as other markers.

Keywords: Bone regeneration, Bone remodeling, Marine biota, Osteoblast.

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INTRODUCTION

Utilization of marine biota, both animals and plants of the middle sea, is widely applied in efforts to regenerate bones. Various types of marine animals and plants have been studied as a material that can help in the process of bone formation through multiple mechanisms that involve osteoblast stimulation, including osteoblast formation markers.[1]

METHODS

This systematic review was compiled based on PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyzes) guidelines.[2] This guide is used in reporting evaluations of interventions in the health sector. In addition to the preparation guidelines in writing this review using a manual, questions can lead the discussion to the focus of a more specific analysis, namely the PICO question.[3] PICO questions consist of population, intervention, control, and Outcome. The PICO question in this review is to regenerate bones, what marine life can be used to stimulate bone formation, and what markers appear in the process. The population and intervention of this review are marine animals or plants throughout the world. The comparison or control of this review is a type of marine animal or plant that can stimulate the growth of bone cells with the appearance of bone formation stimulants. In comparison, the Outcome of this review is data on types of marine animals and plants that can be used in bone regeneration efforts based on each published article's results.

Data search was performed using the PubMed, Wiley, and Google Scholar databases. His search refers to articles in English as one of the inclusion criteria. This data search was performed to identify articles published in medical and dental journals in the past five years. Besides, the article must have a focus on the use of marine animals or plants in bone regeneration efforts. The MeSH keywords used are "marine material" and "bone regeneration." Search restrictions refer to the English language, publication period, and type of published article. The types of articles published include original research articles. A manual search of published articles is done through a database. A total of 637 articles were obtained in a data search through the PubMed, Wiley, and Google Scholar databases. The title selection produced 172 articles with 69 duplications. Then abstract selection provides 34 items, followed by full-text selection and 11 articles, which are finally analyzed by the two authors.

There are several inclusion criteria for preparing this systematic review. The inclusion criteria are the language used in writing the article, the time of publication, the article's focus, the type of article, and the subject of the article. The language used in the article is English. The time of publication is the last five years. The focus of the article is the use of marine animals or plants in bone regeneration. In comparison, the type of article can be in the form of an original research article.

Keywords are used by two participating authors (DM and EM) who assist in the article selection process based on the abstract and full-text analysis. Separately, the two authors selected the article based on the specified inclusion criteria. Then, all abstracts and full text are downloaded and evaluated independently. Eligibility criteria are used to identify articles that will be used for this systematic review. Data were selected by the two authors (DM and EM) based on year of publication, type of marine biota, and activated markers in the process of stimulating bone regeneration. All full text that meets the inclusion criteria is read separately by the two authors and evaluated to formulate this systematic review.

RESULT

Six hundred and thirty-seven articles were obtained from database searches that included PubMed, Wiley, and Google Scholar. The three databases' searching data resulted in 637 articles, which were the first selected based on duplications and titles. The title selection produced 172 articles with 69 duplications. Then abstract selection provides 34 articles, followed by full-text selection and 11 articles, which are finally analyzed by the two authors. Below is the flow of selection of articles in this systematic review (figure 1).

The study was conducted by 11 groups of researchers from 10 different countries based on the collected articles. These countries are Spain, Tunisia, India, Brazil, Poland, Singapore, the United Kingdom, China, Malaysia, and South Africa. The marine life used is shark teeth, pearls, fish skins, seaweed, sponges, seashells, and deep-sea fish heads. Markers that are activated and appear in returning home with stimulus materials include alkaline phosphatase, collagen 1-a-1, osteopontin, osteocalcin, Runt-related transcription factor 2 (RUNX2), and other markers (Table 1).

Alvarez et al. in his research used sharks to determine the content of hydroxyapatite, apatite-CaF, fluorapatite that can be used in bone regeneration in mice.[4] Rym Ben, et al. conducted research on sea oysters and obtained results in the form of osteocalcin, runx2, osteopontin, collagen 1-a-1 in bone formation occurs.[5] JR Parisi also founds hydroxyapatite in his research on the marine sponge.[6] The study conducted by Bellaaj-Zouari et al. in 2012 also found that P. radiata pearl oysters gave rise to phenotypes related to differences in environmental and ecological conditions throughout the Tunisian bay and focused on differences in character from the thickness of the shell layers.[7] Jeevithan Elango, et al. in 2016 conducted research on shark skin and found that the material can stimulate osteoblast formation through collagen 1-a-1 activity.[8]

Gildácio Pereira Chaves Filho et al. in 2017 researched seaweed *Caulerpa prolifera* and obtained ALP as a marker of osteoblast formation.[9] Research on seaweed was also conducted by Pamela J. Walsh et al., who got fucoxanthin.[10] Jakub Hadzik et al. in 2016 in Poland conducted a study on fish skin. They held a histological analysis showing the formation of new bone in the whole group after eight weeks.[11] Research on fish skin was also carried out by Chau Sang Lau et al., and it was found that there was mineral deposition by cells MC3T3-E1.[12] Siti Hajar Saharudin, et al. in Malaysia in 2018 conducted a study on shellfish wrinkles and obtained mineral deposition in the form of phosphorus, chlorine, calcium, and sodium.[13]

CONCLUSION

Various types of marine biota can be useful in bone regeneration, through the mechanism of osteoblast stimulation with the activity of bone formation markers, such as alkaline phosphatase, collagen 1-a-1, osteocalcin, runx2, and other markers. Further research needs to be done to increase the variety of scientific knowledge about the ability of various marine biota in stimulating bone regeneration.

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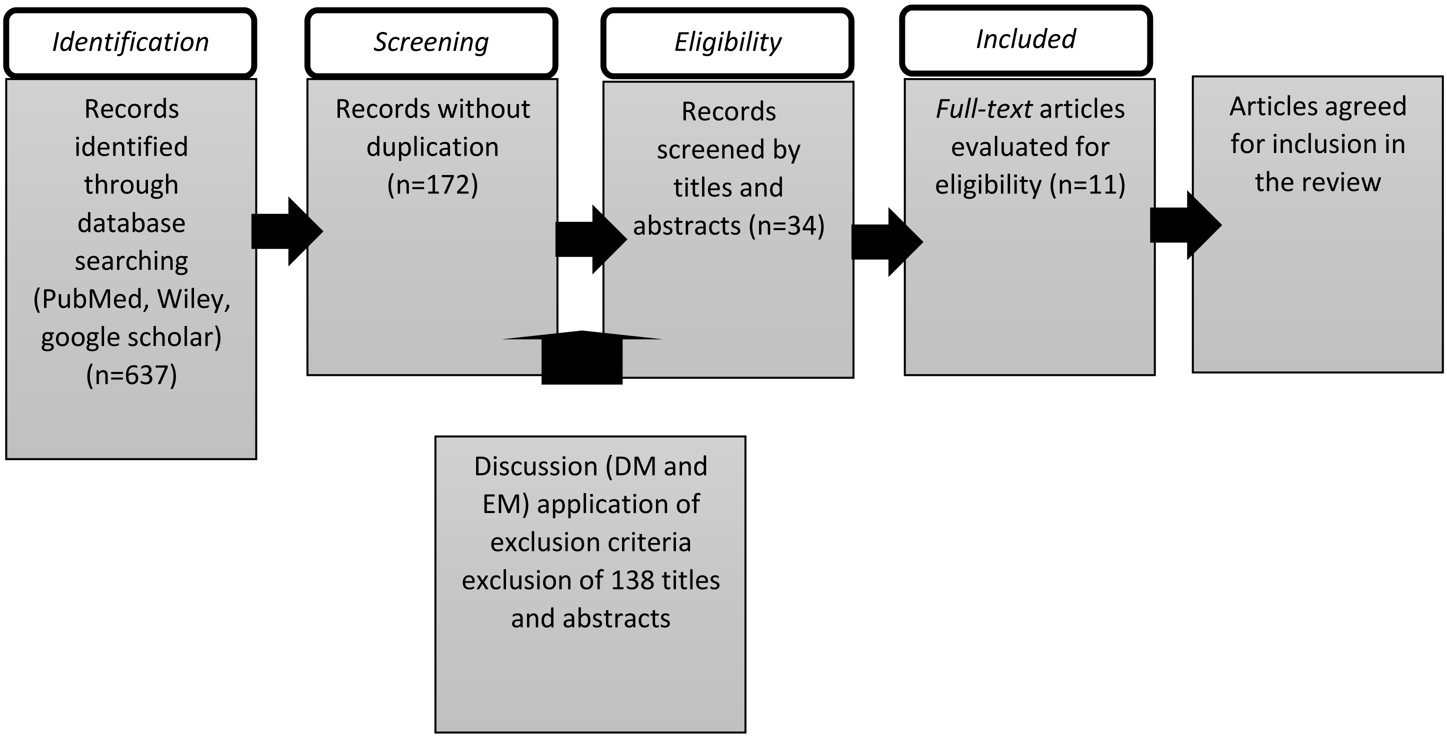

Figure 1. Article selection flow chart

Table 1. Descriptive data from the 11 included studies that reported on the use of marine biota in bone tissue regeneration.

No.	Author	Geographic region	Source	Result
1	Miriam Lopez-Alvarez (2016)	Spain	Shark teeth	Hydroxyapatite, apatite-CaF, fluorapatite
2	Rym Ben Ammar (2019)	Tunisia	Tunisian Pinctada radiate pearl	*Marker:* osteocalcin, runx2, osteopontin, collagen 1-a-1
3	Jeevithan Elango (2016)	India	Shark catfish skin	Collagen 1-a-1
4	Gildácio Pereira Chaves Filho (2017)	Brazil	*Caulerpa prolifera* seaweed	ALP
5	Jakub Hadzik (2016)	Poland	Silver carp skin	Histological analysis showed the new bone formation in all groups after eight weeks
6	Chau Sang Lau (2019)	Singapore	Tilapia Skin	Mineral deposition by MC3T3-E1 cells
7	Pamela J. Walsh (2019)	England	Brown Seaweed	Fucoxanthin
8	Junde Chen (2019)	China	Red Stingray (*Dasyatis akajei*) Skin	Collagen type 1 (acid-soluble collagen (ASC) dan pepsin-soluble collagen (PSC))
9	J.R. Parisi (2018)	Brazil	Marine Sponges (Spongin)	Hydroxyapatite
10	Siti Hajar Saharudin (2018)	Malaysia	Cockle Shell Waste	Mineral deposition: phosphorus, chlorine, calcium, and sodium
11	Jasmin Swart (2018)	South Africa	Monkfish Lophius vomerinus	Octacalcium Phosphate