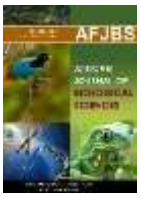
African Journal of Biological Sciences



Review Article

THE USE OF EXTRACT COMBINATION OF BLOOD CLAM SHELL (Anadara granosa) AND GREEN CLAM SHELL (Perna viridis) IN WOUND HEALING POST TOOTH EXTRACTION OF Rattus norvegicus

Combination Extract of Blood Clam Shell (Anadara Granosa) and Green Clam Shell (Perna Viridis) in Wound Healing

M. Hendra Chandha[1], Rasmidar samad[2], Eva Fauziah[3], Harun Achmad[4], Sri Ramadany[5], Asrina Zohraeni Thamrin[6]
[1]Department of Oral Surgery, Faculty of Dentistry, Hasanuddin University, Makassar, Indonesia
[2]Department of Community Dental Health, Faculty of Dentistry, Hasanuddin University, Makassar, Indonesia
[3]Department of Pediatric Dentistry, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia
[4]Department of Pediatric Dentistry, Faculty of Dentistry, Hasanuddin University, Makassar Indonesia
[5]Department of Public Health, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
[6]College Student of Education Program for Dentists Specializing in Pediatric Dentistry at Hasanuddin University,

ORCHID ID M. Hendra Chandha : 0000-0001-6291 9766
ORCHID ID Rasmidar Samad : 0000-0002-1384-6967
ORCHID ID Eva Fauziah : 0000-0002-8785-5874
ORCHID ID Harun Achmad: 0000-0003-3124-2064
ORCHID ID Sri Ramadany: 0000-0002-5160-9890
ORCHID ID Asrina Zohraeni Thamrin : 0000-0001-8452-3471

Correspondence Author: Prof. DR. Harun Achmad
Email: harunachmader@gmail.com
Perintis Kemerdekaan street KM. 10 Makassar, 90245, South Sulawesi, Indonesia

Article History
Volume 6, Issue 13, 2024
Received: 18June 2024
Accepted: 02July 2024
doi:10.48047/AFJBS.6.14.2024. 395-405

ABSTRACT

Introduction: *Efforts have been focused on wound management in order to develop novel healing and therapeutic techniques after tooth extraction. Calcium carbonate, which is also present inside the shells, makes up 95–99% of the bulk of blood clams. Previous research has shown that hydroxyapatite and tricalcium phosphate, which are useful in a variety of dental specialties, may be shaped from blood clam shells. Green clam shells contain about 95% CaCO3 and include mineral components that are similar to those found in bones, making them suitable for biomedical uses.*

research targets: *examine the efficacy of green and blood clam shells as a material to quicken publish-extraction wound recovery in rats (Rattus norvegicus) used in experiments.*

methods: *This study used a systematic review methodology. References have been accumulated from internet databases over the last 5 years, including portals for Pubmed, science Direct, Cochrane, and Wiley internet Library. A aggregate of blood clam (Anadara granosa) and green mussel (Perna viridis) shell extracts had been used to hurry wound healing after enamel extraction, according to journal papers that served as the basis for this systematic review.*

results: *A total of 275 journals, acquired from four sources and obtained in accordance with the inclusion standards. As many as 6 decided on journals and data synthesis changed into completed.*

discussion: *By analyzing the regeneration of alveolar bone and surrounding tissue, blood clam shells and green mussel shells have been shown to be efficient as materials that could hasten the healing of post-extraction wounds.*

conclusion: *Blood clam and green mussel shells have been processed to provide hydroxyapatite as a uncooked material, and this substance has been successfully used to hasten the healing of wounds that have passed through extraction.*

keywords: *Hydroxyapatite, Blood Clams, green Mussels, Tissue Regeneration, tooth Extraction*

Introduction

Indonesia was predicted to have 249 million citizens in 2013, placing it fourth on the list of countries by population behind China, India, and the United States. According to current research, there was an increase in oral health problems between 2007 and 2013 in Indonesia, where they are highly prevalent. Dental and oral health problems, like dental caries and periodontal disease, have the potential to exacerbate acute or long-term medical disorders and reduce a person's quality of life. Both young and old persons have a reduced quality of life in terms of oral health when dental caries and tooth loss occur but are not treated.[1] In contrast to periodontal disease, which is a collection of inflammatory conditions in the tissue supporting the teeth that are brought on by bacteria, dental caries is a chemical injury to the tooth surface (enamel and dentin) brought on by dental plaque and induced by variations in saliva acidity.[2,3]

Tooth loss is one of the most crucial indicators of oral health in a community and one of the factors that is most frequently included in study. Analyzing the number of missing teeth in a population might reveal whether or not that population practices good oral hygiene and has access to adequate dental and oral care.[4]

The majority of operations frequently carried out in developing nations still include tooth extraction. A huge public health issue facing the entire world is tooth loss. The most frequent causes of tooth extraction continue to be dental caries and periodontal disease, both of which are avoidable.[5]

The process of extracting a tooth will leave the patient with an open tooth socket wound that will pain. Following tooth extraction, wounds will go through a healing phase until the wound is entirely closed and the tissue is restored to normal.[6] The majority of wound healing occurs in new extraction sockets, just like it does when teeth are extracted because they are damaged or have cavities. In order to create innovative healing methods and therapeutic philosophies following tooth extraction, several efforts have been concentrated on wound care.[7]

Numerous studies on the preparation of bone graft, paste, and scaffold in the field of tissue engineering have been conducted. These materials must be biocompatible and biodegradable to provide optimal function for tissue regeneration.[8]

Due to its chemical closeness to human hard tissue and exceptional qualities like osteoconductivity, bioactivity, biocompatibility, non-toxicity, and anti-inflammatory characteristics, hydroxyapatite (HAp) has generated a lot of attention as a biomaterial in dentistry. A variety of chemical synthesis techniques can be used to produce HAp, a bioactive ceramic material that can enhance tooth remineralization. HAp is made from materials that include calcium and phosphorus.[9]

A species of shellfish called the blood clam (Anadara granosa) has enormous potential for development as a source of the minerals and protein required for human consumption. 66,70% and 95-99% of the total mass of this species' shell is made up of calcium carbonate. In addition to being employed as active ingredients in fertilizers, biodiesel production catalysts, bone tissue regeneration, and bioabsorption to remove heavy metal ions, calcium carbonate has a number of polymorphism properties that can be exploited for other purposes.[10]

On the other hand, one of the natural marine species, namely the shell of the green mussel (Perna viridis) has been widely recorded as having superior quality and having a pure calcium carbonate aragonite polymorph composition. About 95% of the constituents in green mussel shells include oxides like SiO2, MgO, and SO3, as well as organic materials. In addition, green mussel products do not contain heavy metals like mercury (Hg) or arsenic (As), which is obviously practical for human needs in dentistry and other biomedical fields. Green mussel shells also have mineral components that are almost identical to bones with a high Calcium Carbon (CaC) content.[11]

As a result, the purpose of this study was to determine if the combined use of blood clam (Anadara granosa) and green mussel (Perna viridis) shell extracts could speed the healing of wounds following tooth extraction.

Methods

This study uses a systematic review method. References were gathered from internet databases over the last five years, including portals for Pubmed, Science Direct, Cochrane, and Wiley internet Library. This systematic review was conducted based on journal publications that discussed the efficacy of a mixture of blood clam (Anadara granosa) and green mussel (Perna viridis) shell extracts in healing wounds following tooth extraction.

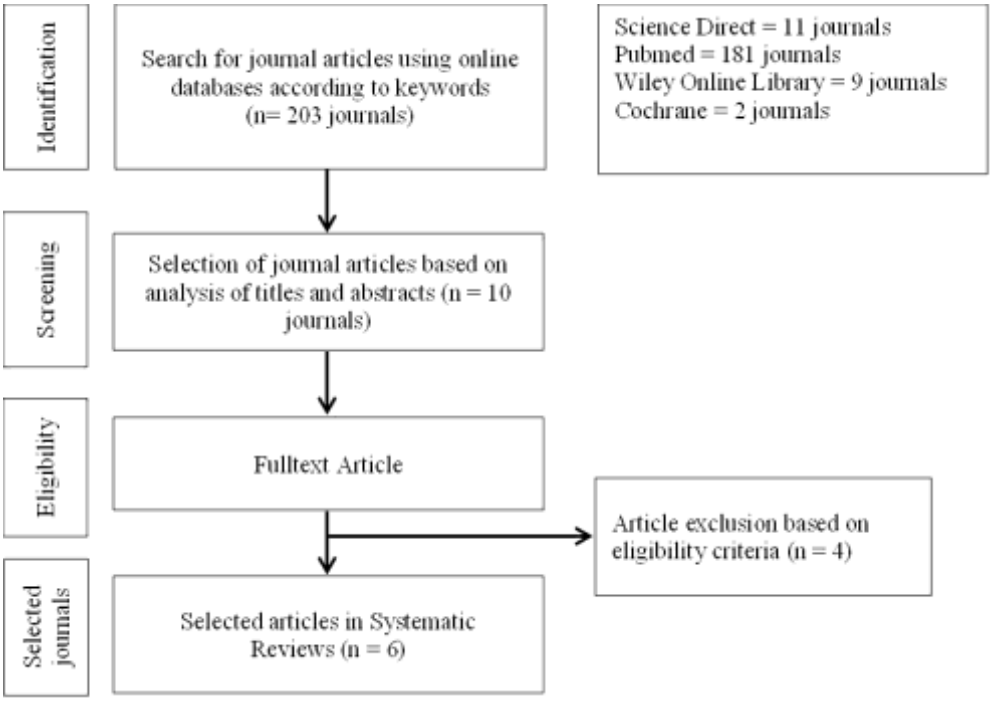


Figure 1. *Journal Article Search Flowchart*

Research Standards

A. Criteria for Inclusion

1. Articles released in the period 2017–2023.

2. Articles written in English.

3. Scientific publications with online access

4. A study examining the use of a mixture of blood clam shell extract (Anadara granosa) and green mussel shell extract (Perna viridis) to promote wound healing after tooth extraction.

Exclusion standard

B. Criteria for Exclusion

1. Articles cited in case studies, literature reviews, systematic reviews, and editorials.

2. Articles that aren't available for free.

Table 1. *Synthesis table*

Number	***Author***	***Title***	***Conclusion***
1.	*Mediarman GN, Sumardianto, Riyadi PH, Rianingsih L, and Purnamayati L. 2021*[12]	*CaO powder's antibacterial properties come from the calcination of green shells (Perna Viridis), scallops (Placuna Placenta), and blood clams (Anadara granosa).*	*These three shells could stop the growth of both gram-negative and gram-positive bacteria, however blood clam CaO powder exhibited the strongest antibacterial effect with an inhibition zone value of 15, 22 mm. The habitat, the type of shellfish, the liming temperature, and the size of the powder particle all have an impact on the inhibitory zone's dimensions.*
2.	*Solanki H., and Kumari B. 2021*[13]	*Compounds with anti-inflammatory properties found in the hydrolysate of Perna viridis L., an Indian marine green mussel.*	*This research involves producing the most potent and versatile bioactive compounds with anti-inflammatory capabilities that may be employed as future medications. The most active portion of the raw shellfish hydrolysate will be extracted, identified, and used commercially in the same project.*

3.	*Rima Parwati Sari, Hansen Kurniawan. 2019*[14]	*The ability of Anadara granosa shell-Stichopus to hasten the production of woven bone fourteen days after tooth extraction*	*A combination of shells from Anadara granosa are used to create scaffold granules and Stichopus hermanni can hasten the creation of woven bone on the fourteenth day following tooth extraction to stop alveolar bone degradation (socket preservation). On the fourteenth day following tooth extraction, the concentration of Stichopus hermanni 0,8% was most effective in speeding the production of woven bone.*
4.	*Rima Parwati Sari, Hansen Kurniawan, Syamsulina Revianti, Sri Agus Sudjarwo, Retno Pudji Rahayu, Widyasri Prananingrum, and Aisah Faiz Bachmid. 2017*[15]	*The effects of Anadara granosa shell-Stichopus hermanni on bFGF expression and blood vessel counts during Wistar rats' repair of bone defects*	*In order to efficiently boost bFGF expression and the number of blood vessels in mending bone injury in Wistar rats, Anadara granosa and Stichopus hermanni shells were combined.*
5.	*Rahayu R P, Sari R P, Revianti S, Andriani D, Prananingrum W, and Sudjarwo S A. 2020* [16]	*The reduction of osteoclasts during socket healing is caused by Anadara granosa Shell's Stichopus hermanni Scaffoid's expression of CD44 and IL-10.*	*The scaffold of the AGSH combination, where the highest effective concentration of S. hermanni was 0,8%, was effective for boosting CD44 and IL-10 expression to inhibit osteoclasts in post-tooth extraction socket healing.*
6.	*Dian Widya Damaiyanti, Rima Parwati Sari, Chaterina Diyah Nanik Kusuwardhani, A. Retno Pudji Rahayu, and Sri Agus Sudiarwo. 2021*[17]	*The Impact of a Shell-Stichopus Hermanni Scaffold from Anadara Granosa on Blood Vessel Counts Following Tooth Extraction*	*The number of blood vessels after tooth extraction is effectively increased by the scaffold made of Anadara granosa shells and 0.8% Stichopus hermani.*

Result

A total of 275 journals were obtained according to the inclusion criteria which were sourced from 4 databases, namely 12 science direct journals, 240 pubmed journals, 16 wiley online library journals and 7 cochrane journals. After analyzing the title and abstract, 10 journals were obtained. After performing due diligence by reading the entire contents of the journals that passed the eligibility test, 4 journals were eliminated because their titles did not correspond to this study's. The remaining 6 journals were then chosen, and data synthesis was completed.

When a tooth cannot be repaired or maintained in the oral cavity under circumstances that are acceptable to maintain health, function, and/or aesthetics, the dentist will frequently employ the tooth extraction approach.[11] The removal of a tooth from its socket is done through the dental process of tooth extraction. An ideal tooth extraction would not be painful, cause little damage to the surrounding tissue, allow the extraction wound to heal correctly, and not result in any complications afterward.[12]

Wounds resulting from tooth extraction need proper treatment such as administering antiseptic agents so as not to cause various post-extraction complications.[15] Following the surgical treatment, the patient should receive the necessary advice on how to manage and control the postoperative side effects that are typical.[16]

After tooth extraction, wound healing is a crucial component. It is characterized as a challenging and dynamic process to replace lost and damaged cellular components and tissue layers. Hemostasis, inflammation, proliferation, and remodeling are the four crucial stages of proper socket wound healing (Figure 2). Radiation, chemotherapy, anti-resorptive medications, smoking, and general health issues like uncontrolled diabetes can all have an impact on these four phases. As demonstrated in alveolar osteitis, any interference with wound healing can lead to excessive bleeding or a lack of blood clot formation.[17,18]

Blood clam shells (Figure 3) are one of the seashell wastes that can be found along the ocean coasts and in several seafood industries. [25] More than 98,7% of the minerals are found in calcium carbonate and carbon, which make up the mineral composition of blood clam shells. It contains about 1,3% of Mg2+, Na+, P3-, K+, Fe2+, Cu+, and Ni2+. Blood clam shells contain high calcium carbonate and with a higher density in particle size.[26] This substance can be utilized as a bone healing material and is a rich source of calcium. Calcium carbonate tested negatively for genotoxicity in vitro because it is water insoluble.[27] It is commonly used in both medicine and dentistry to create bones and dentures due to the significant amount of hydroxide and calcium phosphate it contains.[2]

Based on the XRF test results of gel materials from blood cockle shells and green cockle shells as follows:

***Table 1**. Oxide Content in Blood Mussel (Anadara granosa) Gel*

Parameter	***Satuan***	***Hasil***
CaO	*m/m%*	*73.82*
P_2O_5	*m/m%*	*20.90*
SrO	*m/m%*	*3.87*
Nb_2O_5	*m/m%*	*0.54*
MoO_3	*m/m%*	*0.31*
Sb_2O_3	*m/m%*	*0.219*
SnO_2	*m/m%*	*0.171*
In_2O_3	*m/m%*	*0.167*

The table above shows the highest value for the CaO compound content contained in the

blood cockle (Anadara granosa) gel of 73.82% and the P2O5 content of 20.90%. The high levels of CaO and P2O5 in blood cockles are also in line with research by Mediarman et al. (2021)[12] as a component of the shell.

***Table 1.1** Element Content in Blood Mussel (Anadara granosa) Gel*

Parameter	***Satuan***	***Hasil***
Ca	*m/m%*	*80.12*
Px	*m/m%*	*12.62*
Sr	*m/m%*	*5.48*
Nb	*m/m%*	*0.65*
Mo	*m/m%*	*0.35*
Sb	*m/m%*	*0.306*
In	*m/m%*	*0.239*
Sn	*m/m%*	*0.231*

The table above shows the highest value for the Ca element content contained in blood cockle (Anadara granosa) gel of 80.12%, while the lowest value for the Sn element content contained in blood cockle (Anadara granosa) gel is 0.231%. The gel form also increases Ca levels because purification from other substances reduces levels of impurities other than Ca, but there is a significant decrease in phosphorus levels even though it is still the second dominant element after Ca.

***Table 2**. Compound Content in Green Mussel Gel (Perna viridis)*

Parameter	***Satuan***	***Hasil***
CaO	*m/m%*	*64.67*
P_2O_5	*m/m%*	*27.11*
SiO_2	*m/m%*	*7.24*
CI	*m/m%*	*9.37*
Nb_2O_5	*m/m%*	*0.352*
MoO_3	*m/m%*	*0.227*
Sb_2O_3	*m/m%*	*0.171*
In_2O_3	*m/m%*	*0.126*
SnO_2	*m/m%*	*0.102*

The table above shows the highest value for the CaO compound content contained in green mussel gel (Perna Viridis) of 64.67%, while the lowest value for the SnO2 compound content contained in green mussel gel (Perna Viridis) is 0.102%. High CaO levels in green mussels are also in line with research by Mediarman et al. (2021) and Revankar et al. (2021)[35] with dominant CaO levels. CaO levels are also in line with levels of the Ca element as a constituent in both studies, thus becoming the basis for the connection between oxide content and Ca elements. The Ca element levels in green mussel shell gel can be seen in Table 2.1.

***Table 2.1** Element Content in Green Mussel Gel (Perna viridis)*

Parameter	***Satuan***	***Hasil***
Ca	*m/m%*	*77.02*
Px	*m/m%*	*17.05*
Si	*m/m%*	*4.57*
Nb	*m/m%*	*0.47*

Mo	*m/m%*	*0.29*
Sb	*m/m%*	*0.261*
In	*m/m%*	*0.197*
Sn	*m/m%*	*0.153*

The table above shows the highest value for the Ca element content contained in green mussel gel (Perna Viridis) of 77.02%, while the lowest value for the Sn element content contained in green mussel gel (Perna Viridis) is 0.153%. Ca levels increased significantly in gel form and there was an increase in phosphorus content from powder to gel form.

The green clam (Perna viridis), a significant bivalve mollusc, is useful in biomedical studies. Many key chemicals have been isolated and described from green mussels, and the majority of them have noteworthy biological action against malaria parasites, the treatment of osteoporosis, osteoarthritis, and rheumatoid arthritis, tuberculosis, and diabetes. Further scale research and investigations continue to be developed to discover new potentials for green mussels with the ultimate goal of producing new types of treatment.[32,33]

One of the natural marine species, namely green mussel shells (Figure 4) has been widely noted to have superior quality and has a pure calcium carbonate aragonite polymorph composition. In addition, calcium carbonate ($CaCO_3$) in green mussel shells can be used as an antibacterial through a calcination process. Gram positive and gram negative bacteria can both be treated with calcium oxide powder (CaO), which is created during the calcination process.[11,12,34]

Discussion

The XRF method is carried out by identifying and calculating the characteristics of x-rays that occur from the photoelectric effect. The photoelectric effect occurs because the electrons in the target (sample) atoms are exposed to high-energy rays (gamma radiation, x-rays). The content of each element in each shellfish is of course different based on the shellfish's habitat, therefore when an XRF test is carried out the content of CaO and other elements is different. A study conducted by Mediarman et al. (2021) and Revankar et al. (2021) proves that CaO is included in the inorganic antibacterial category where generally this antibacterial comes from metal materials, such as Cu, Zn, Au, Ag, Ca, and other metal elements. Several previous studies stated that CaO has a fairly high antibacterial effect compared to MgO and ZnO against Escherichia coli bacteria. The antibacterial mechanism is the interaction with the tisol, amino and carboxylic protein groups found in microbial cell walls. CaO causes loss of cell structural integrity which results in changes in cell morphology, so that bacterial cells die.[12,35]

Stichopus hermanni, which was recovered from the shells of Anadara granosa and Stichopus hermanni, was shown to be the most efficient granula scaffold at a concentration of 0.8% in a study by Sari RP et al.[14]

The sintering time of bone graft calcium compounds made from blood clam shells (Anadara granosa) had an effect on fibroblast cell proliferation in socket healing, according to a study by Yonatasya et al. For a calcium-based bone transplant, a 12-hour sintering period can more efficiently boost fibroblast cell proliferation.[18,19]

According to Widyastuti et al.'s research, the Anadara granosa shell graft used in this study, which had been processed at high temperature and reduced to a powder with a size of 150 m by SEM test and examination, may be used as osteoconduction and vascularization.[20]

According to Alharissy's study, according to M et al., this study demonstrated equal dimensions changes in extraction sockets treated with scallop shells or TCP bone replacements. The retrieved bone tissue's three-dimensionality was reduced as a result of healing over the nine months that followed socket treatment. The buccal and palatal bone walls both experience similar decreases. After 9 months, examination revealed a decrease in cross-sectional area that was nearly

same in both treatment modalities.[21]

The scaffold from the combination of AGSH to increase CD44 and IL-10 expression to suppress osteoclasts in socket repair after tooth extraction was the most efficient concentration of S. hermanni, according to research by Sari RP et al in 2021.[16]

Widyastuti, Rubianto, and Soetjipto's 2018 study found that by elevating FGF-2 and VEGF, AG shell transplantation may hasten the angiogenesis process in the mandible..[31]

Research conducted by Kurniawan E, et al[36] *on three shellfish was influenced by several factors. CaO powder has the alkaline nature of CaO, making CaO have a high level of alkalinity, so it can be used as an inhibitor of bacterial growth. The influence of alkali on antimicrobial activity by hydration of CaO is considered to be an important one of the basic antibacterial mechanisms. Moreover, due to the bactericidal activity of CaO powder greater than NaOH solution at the same pH, not only because of the antibacterial mechanism of CaO alkalinity but also the action of active oxygen resulting from CaO.*[12]

Conclusion

Of the 6 articles reviewed, it was stated that the CaO content was very high in blood clams (Anadara granosa) and green clams (Perna viridis). Among the 6 articles, there were 4 articles which stated that combined AGSH shell transplantation could accelerate wound healing after extraction. Blood clam and green mussel shells have been processed to provide hydroxyapatite as a uncooked material, and this substance has been successfully used to hasten the healing of wounds that have passed through extraction.

Availability of Data

The corresponding author will provide the datasets produced during and/or analyzed during the current work upon reasonable request.

Interest Conflicts

The authors declare that there are no conflicts of interest with regard to the publication of this work.

References

1. *Malik NA, Rosalien R, Khalissya N, Badruddin IA, Maharani DA. Perceived need and utilization of dental health care services in Indonesia: A secondary analysis using the national socioeconomic data. Makara Journal of Health Research 2020; 24(2): 121.*

2. *Ketut I H, Asriyani A, Roosa VF. Overview of Periodontal Disease Based on Age and Gender in Visitors to the Tikala Baru Health Center Dental Polyclinic in Manado City in 2017. JIGIM. 2020. 3(1); 20-26*

3. *Achmad H, Ramadhany YF. Effectiveness of Chitosan Tooth Paste from White Shrimp (Litopenaeusvannamei) to Reduce Number of Streptococcus Mutans in the Case of Early Childhood Caries. Journal of International Dental and Medical Research. 2017; 10 (2): 358-363.*

4. *Passarelli PC, Pagnoni S, Piccirillo GB, et al. Reasons for Tooth Extractions and Related Risk Factors in Adult Patients: A Cohort Study. International Journal of Environmental Research and Public Health 2020; 17(7): 2575.*

5. *Taiwo AO, Ibikunle AA, Braimah RO, Sulaiman OA, Gbotolorun OM. Tooth extraction: Pattern and etiology from extreme Northwestern Nigeria. European Journal of Dentistry 2017; 11(3): 335.*

6. *Santoso AH, Kintawati S, Sugiaman VK. Effect of Resorbable Collagen Plug (RCP) on Extraction Wound Healing. e-GiGi 2022; 10(1): 82.*

7. *Cho YD, Kim KH, Lee YM, Ku Y, Seol YJ. Periodontal Wound Healing and Tissue Regeneration: A Narrative Review. Pharmaceuticals 2021; 14(5):456.*

8. *Basi DL, Hughes PJ, Thumbigere-Math V, et al. Matrix metalloproteinase-9 expression in alveolar extraction sockets of Zoledronic acid-treated rats. Journal of Oral Maxillofacial Surgery 2011; 69(11): 2699.*

9. *George P, Hamid ZA, Zakaria ZAB, Perimal E, Bharatham H. A Short Review on Cockle Shells as Biomaterials in the Context of Bone Scaffold Fabrication. Sains Malaysiana 2019; 48(7):1539.*

10. *Nugroho JJ, Natsir N, Trilaksana AC, Rovani CA, Atlanta MM. The Increase of Tooth Enamel Surface Hardness After Application Blood Cockle Shells (Anadara Granosa) Paste as Remineralization Agent. International Journal of Applied Pharmaceutics. 2019; 11(4): 26.*

11. *Pramudi G, Sulmartiwi L, Mashitah E, Patmawati, Amin MNG. Characterization of nano calcium powder from blood cockle (Anadara sp.) shell produced by using different hydrochloric acid concentration. IOP Conference Series: Earth and Environmental Science 2020; 441: 1.*

12. *G N Mediarman et al. Potentials of CaO powder result of calcination from green shells (Perna viridis), scallops (Placuna placenta), and blood clams (Anadara granosa) as antibacterial agent. 2021. IOP Conf. Series: Earth and Environmental Science;1-7. doi:10.1088/1755-1315/890/1/012043*

13. *Sari RP, Kusumawardani CDN, Damaiyanti DW, Rahayu ARP, Sudjarwo SA. The Effectivity of Scaffold From Anadara Granosa Shell-Stichopus Hermanni on Blood Vessel Counts After Tooth Extraction. ODONTO Dental Journal 2021. Vol.8(2): 12.*

14. *Sari, RP, Kurniawan, H. Effectiveness of Anadara granosa shell- Stichopus hermanni granules at accelerating woven bone formation fourteen days after tooth extraction. Dental Journal (Majalah Kedokteran Gigi). 2019. Vol.52(4);177-182.*

15. *Alvarenga AF, Picinini LS, Ferreira AP, de Oliveira RG. Tooth Extraction: A Systematic Revision. Journal of Dental Sciences 2020; 5(2): 1.*

16. *Sari, RP et al. The Effect of Anadara granosa Shell's–Stichopus hermanni Scaffold on CD44 and IL-10 Expression to Decrease Osteoclasts in Socket Healing. European Journal of Dentistry. 2021. Vol. 15;228–235*

17. *Taiwo AO, Ibikunle AA, Braimah RO, Sulaiman OA, Gbotolorun OM. Tooth extraction: Pattern and etiology from extreme Northwestern Nigeria. European Journal of Dentistry 2017; 11(3): 335.*

18. *Broers DLM, Dubois L, de Lange J, Su N, de Jongh A. Reasons for Tooth Removal in Adults: A Systematic Review. International Dental Journal 2022; 72(1): 52.*

19. *Yonatasya, FD, Prananingrum, W, Ashrin, MN. The Effect of Calcium Compounds Bone Graft Synthesized from Blood Cockle Shells (Anadara granosa) with Sintering Time Variation in Fibroblast Proliferation on Socket Healing Process. 2019. 13(1);34-43.)*

20. *Widyastuti, Rubianto, M, Soetjipto. Induction of Angiogenesis Process in Mandible Using Anadara granosa Shell Graft (Experimental Laboratory Study on Rattus norvegicus). IOP Conf. Series: Earth and Environmental Science. 2019:1-7. doi:10.1088/1755-1315/217/1/0120330.*

21. *Alharissy, M, AbouSulaiman, A, Manadili, A, Dayoub, S. Radiographic Alternations in Alveolar Bone Dimensions Following Socket Preservation using Two Bone Substitutes. Journal of International Dental and Medical Research. 2018; 11(3): 906-910*

22. *Kurniawati A, Saputra DR, Cholid Z, Putra HK. Cacao Seed (Theobroma Cacao L.) Extract*

Gel Effect On The Neutrofil Number After Tooth Extraction. ODONTO Dental Journal 2020; 7(1): 60.

23. *Goswami A, Ghorui T, Bandyopadhyay R, Sarkar A, Ray A. A General Overview of Post Extraction Complications-Prevention, Management and Importance of Post Extraction Advices. Fortune Journal of Health Sciences 2020; 3(3): 136.*

24. *Alrayyes Y, Aloraini S, Alkhalaf A, Aljasser R. Soft-Tissue Healing Assessment after Extraction and Socket Preservation Using Platelet-Rich Fibrin (PRF) in Smokers: A Single-Blinded, Randomized, Controlled Clinical Trial. Diagnostics 2022; 12(10): 2403.*

25. *Politis C, Schoenaers J, Jacobs R, Agbaje JO. Wound Healing Problems in the Mouth. Frontiers Physiology 2016; 7: 507.*

26. *Saputra DR. Minor Oral Surgery and Dental Extraction Procedures Management of Patients with Antithrombotic Drugs Administration. dentika Dental Journal 2020; 23(1):2.*

27. *Yahya BH, Chaushu G, Hamzani Y. Evaluation of Wound Healing Following Surgical Extractions Using the IPR Scale. International Dental Journal 2020; 71: 134.*

28. *Jaji AZ, et al. Synthesis, characterization, and cytocompatibility of potential cockle shell aragonite nanocrystals for osteoporosis therapy and hormonal delivery. Nanotechnology, Science and Applications 2017; 10: 23-33.*

29. *Kurniawan AA, Imam DNA, Hirawan H. The Effect of Addition of Nano hydroxyapatite Powder of Anadara granosa Shells on Surface Roughness of Heatcured Acrylic Resin. Denta Jurnal Kedokteran Gigi 2020; 14(2): 83.*

30. *Yonatasya FD, Prananingrum W, Ashrin MN. Effect of Bone Graft of Calcium Compounds Resulted from Synthesis of Blood Clams (Anadara granosa) Shells with Sintering Time Variations on Fibroblast Cell Proliferation in the Socket Healing Process. Denta Journal of Dentistry 2019; 13(1): 37.*

31. *Widyastuti, Rubianto M, Soetjipto. Induction of Angiogenesis Process in Mandible Using Anadara granosa Shell Graft (Experimental Laboratory Study on Rattus norvegicus). IOP Conf. Series: Earth and Environmental Science. 2018;217*

32. *Kumari B, Solanki H. Anti-inflammatory Compounds from the Hydrolysate of Indian Marine Green Mussel (Perna viridis L). International Journal of Plant and Environment 2021; 7(2): 172.*

33. *Park YK. Repression of pro inflammatory gene expression by lipid extract of Nostoccommune var sphaeroides Kutzing, a blue-green alga, via inhibition of nuclear factor-kappaBin RAW 264.7 macrophages. Nutr Res 2008; 28(2): 83-91.*

34. *Djais AI, Mappangara S, Gani A, Achmad H, Endang S, Tjokro J, Raja N. South Sulawesi Milkfish (Chanos Chanos) Scale Waste as a New Anti-inflammatory Material in Socket Preservation. Open Access Maced J Med Sci [Internet]. 2022 Apr. 10 [cited 2023 Jun. 20];10(D):221-8.*

35. *Revankar VD, Saranyan R, Chakravarthy Y, Manivannan E, Rajmohan M. Remineralising Potential of Marine Skeletal Species-Perna viridis Powder Extract on Human Teeth Enamel: An In-vitro Study. J Clin Diagnostic Res. 2021;15(2):13-16. doi:10.7860/jcdr/2021/46096.14482.*

36. *Kurniawan E, Asril A dan Ningsih J R.Sintesis dan Karakterisasi Kalsium Oksida dari Limbah Cangkang Bekicot (Achatina fulica). 2019. Jamb.J.Chem. 1(2), 50-4.*