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The Potential of Biosilica Derived from Indonesian Marine Sponges as a Biomaterial in Bone Tissue Engineering Utilizing Mesenchymal Stem Cells

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Abstract. *Indonesia is renowned for possessing the highest marine biodiversity globally, encompassing approximately 850 species of sea sponges, particularly within the Coral Triangle region, including areas such as Raja Ampat (West Papua), Wakatobi (Southeast Sulawesi), the Thousand Islands (Java), and Weh Island (Aceh). Numerous species from the Demospongiae and Hexactinellida families are known to produce natural silica skeletons, referred to as biosilica, which hold potential as biomaterials. Sea sponges, classified as simple invertebrate organisms within the phylum Porifera, inhabit marine environments. A distinctive biological characteristic of sponges is their capacity to form biogenic silica skeletons, termed biosilica, through the process of biomineralization. This biosilica is distinguished from synthetic silica by its hierarchical nanoscale structure and elevated bioactivity. Over the past two decades, biosilica derived from sea sponges has garnered increasing attention in the field of biomaterials, particularly for its potential applications in tissue engineering, with a focus on bone regeneration.*

Keywords: *biosilica; sea sponge; biomaterial; tissue engineering*

Type of the Paper: Review Article

1. Introduction

The process of healing bone defects is complex and necessitates osteogenesis, which encompasses both osteoconduction and osteoinduction. To promote osteogenesis in the treatment of bone damage, it is crucial to utilize a material with osteoinductive properties. Biosilica, a component found in sponges, is one such material. The discovery of various bioactive compounds, including biosilica, suggests that sponges have potential as biomaterials for scaffolds. In tissue engineering, a biomaterial is necessary to act as a foundation for biological growth, similar to the extracellular matrix in body tissues [1]. Biomaterials provide a three-dimensional environment for cell development. In tissue engineering, biomaterials can be either synthetic or natural[2]. The choice of compounds for use as biomaterials in scaffolds is vital, as it influences the success of tissue engineering, much like the role of growth factors or bioreactors in the development of engineered tissue.[3]

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2. Discussion

Biosilica isolated from sponge animals serves as a source of calcium for bone cells, suggesting its potential application in bone tissue engineering. Biosilica induces the expression of the key mediator BMP (Bone Metallo Protein) 2, which is responsible for promoting the differentiation of bone-forming progenitor cells and inhibiting the function of osteoclasts, thereby presenting itself as a promising candidate for osteoporosis treatment [4]. Recently, silicon-substituted hydroxyapatite has been developed to enhance the bioactivity and mechanical properties of bone substitute materials. Enhanced bioactivity facilitates excellent integration of osteocyte cells by increasing the interaction between bone and implant[4,5].

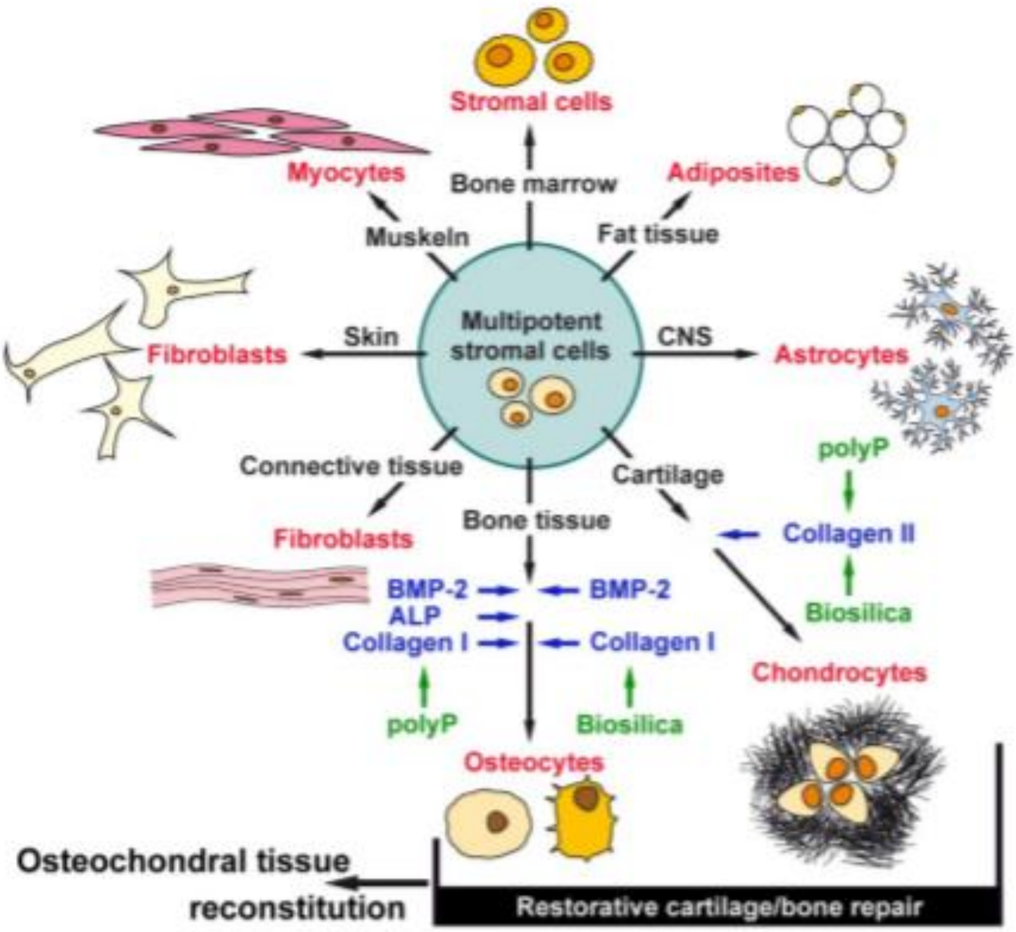

Figure 1. The Function of Biosilica Derived from Marine Sponges in Bone Tissue Regeneration (Bone Tissue Engineering), Adapted from: [4]

Two classes of sponges that contain biosilica, as noted by [6], are as follows: Class Demospongiae: Members of the class Demospongiae, within the phylum Porifera, are capable of inhabiting both marine and freshwater environments. Their spicules are fiber-shaped, forming structures of spongin or silica arranged into six rays. An example of Demospongiae is Spongilla sp., which resides in freshwater. Class Hexactinellida: Porifera in this class are commonly referred to as glass sponges (Hyalospongiae). These organisms are marine and possess spicules with six ray arms. Their bodies can attain lengths of nearly 1 meter and are found at depths ranging from 100 to 4,500 meters. An example of a poriferan from this class is Euplectella aspergillum.

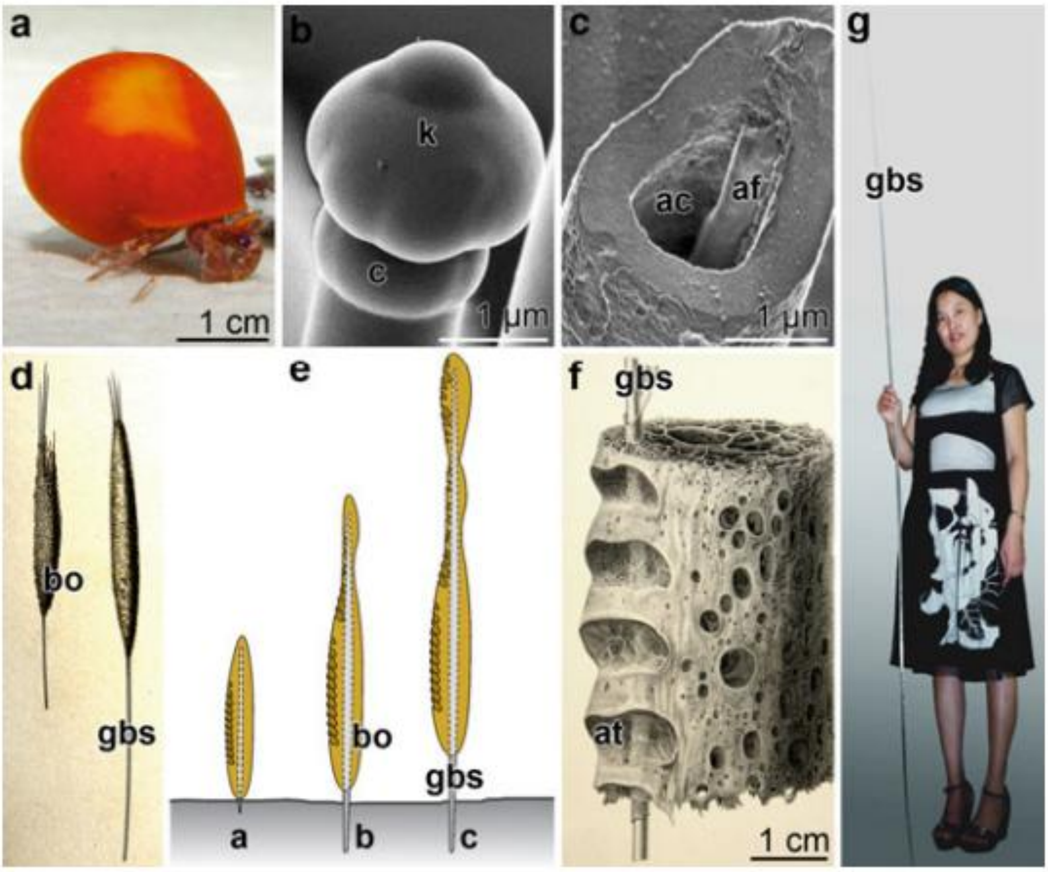

Figure 2. Physical structure of the sponge and sponge size compared to the size of an adult human body. S. domuncula specimen (a), spicule from S. domuncula (b); view of the swollen knob, Broken spicule (c), showing the central axial canal, Young specimens of M. chuni (d), Schematic representation of the growth phases of the sessile animal with its giant basal spicule (e), Part of the body (bo) with its atrial openings (at) (f). Giant basal spicule of M. chuni, representing the largest biosilica structure on earth (g).[7]

El Yacouby [3]investigated the potential of biosilica as a bone substitute material through the use of osteosarcoma cell line cultures (SaOS-2), concluding that silica in combination with Polylactidacid (PLA) can facilitate cell growth. Rutkovskiy[8] employed type 1 collagen, which was incorporated into human fetal osteoblast cells, and observed enhanced cell proliferation alongside increased expression of CBFA/RUNX2, osteocalcin, osteopontin, alkaline phosphatase, and histone.[9,10]

Biosilica is an enzymatically synthesized factor derived from over 100 phosphate residues that promote the mineralization process in osteogenic cells.[11] It is a naturally occurring polymer isolated from sponges (phylum: Porifera), where it contributes to the formation of spicules [12].

This inorganic polymer material also encompasses polyphosphate, which is present in all living organisms and is found in high concentrations in sponges [13]. Preliminary studies have demonstrated that biosilica, enzymatically formed from ortho-silicate by the enzyme silicatein, exhibits bone-forming inductive effects on osteosarcoma cells (SaOS-2).[14,15]

PolyP serves multiple functions, including acting as a storage substance, a chelator for metal cations, a phosphate donor for sugars and adenylate kinase, and an inducer of apoptosis. It is also integral to the mineralization process of bone tissue.[16,17] Furthermore, PolyP modulates gene expression in osteoblast-like cell lineages, such as MC3T3-E1 and SaOS-2 cells, as well as in hMSCs. This modulation enhances the expression of genes responsible for producing osteocalcin, osterix, bone sialoprotein, BMP-2, and tissue-nonspecific alkaline phosphatase, all of which are essential for bone formation [18,19].

Biosilica serves as an alternative to calcium within cellular structures and facilitates the proliferation and mineralization of osteogenic cells. The sponges under examination are those containing biosilica sourced from the Sangihe Islands [20], specifically: *Ircinia strobilina, Melophlus sarasinorum, Spechiospongia vagabunda, and Xetospongia testudinaria*.

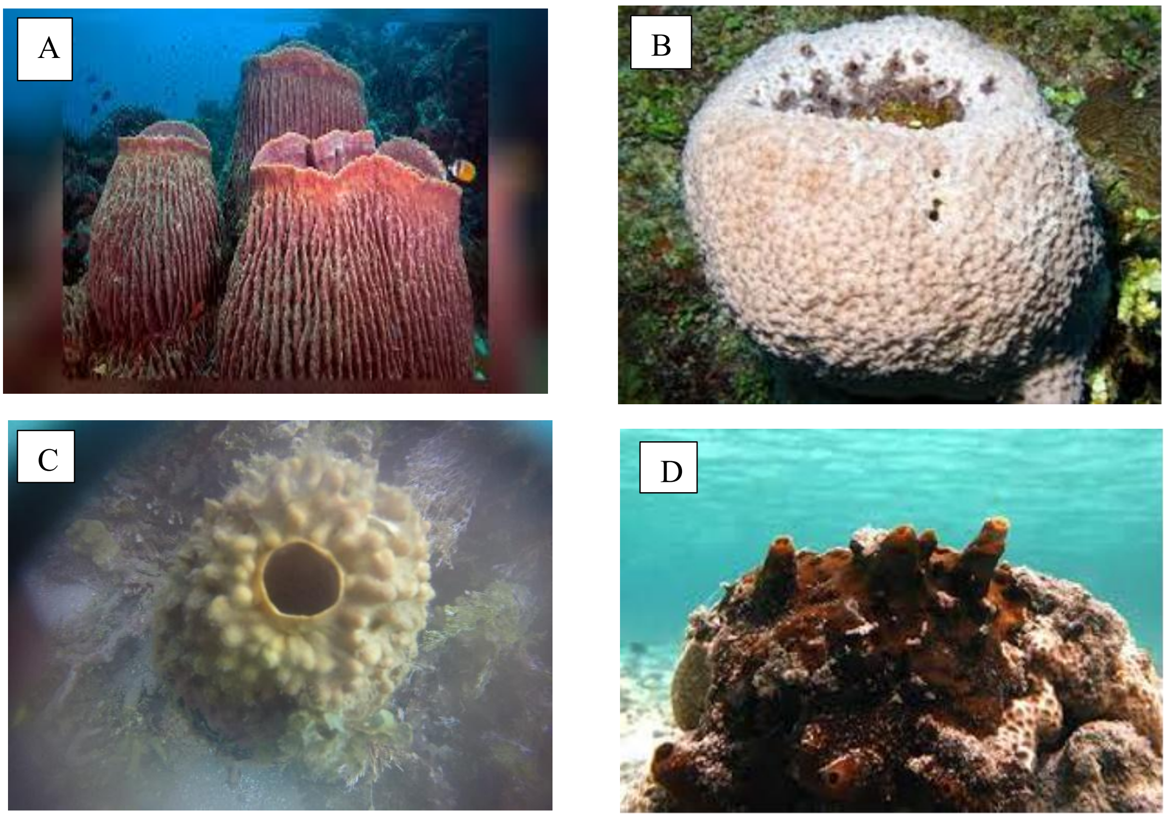

Figure 3. *Xestospongia testudinaria* (A), *Ircinia strobilina* (B), *Melophlus sarasinorum* (C), *Spechiospongia vagabunda* (D) [20]

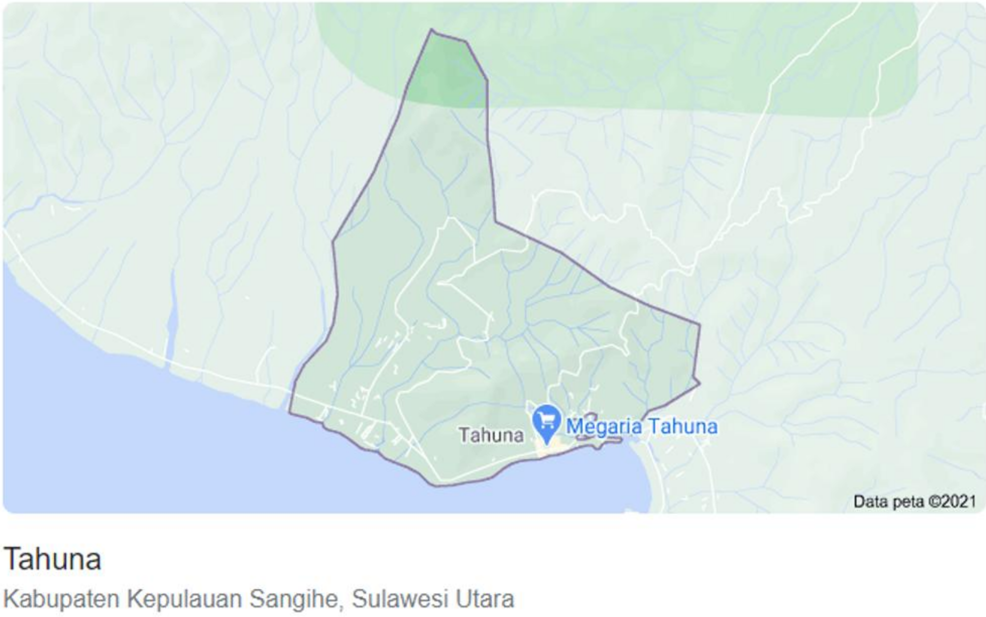

Figure 4. The map illustrates the original habitat of Indonesian sea sponges, specifically located in the Sangihe Islands, Tahuna.

Biosilica and sponge components can be readily adapted or combined with both synthetic and natural polymers, such as chitosan, gelatin, collagen, or polycaprolactone (PCL). These adaptations enhance mechanical strength and manage degradation, enabling customization for specific applications, including those involving bone, skin, and blood vessels. Certain marine sponge species produce secondary metabolites, such as alkaloids and terpenoids, which possess antibacterial and anti-inflammatory properties. Moreover, these metabolites exhibit antioxidant properties that aid in wound healing and promote cell growth and growth factors, such as vascular endothelial growth factor (VEGF) and bone morphogenetic protein (BMP) [21–23].

The organic and inorganic components of sea sponges demonstrate considerable biocompatibility, thereby preventing the elicitation of excessive immune responses. This structural composition fosters cell proliferation and viability, supports a tolerogenic immune response, and facilitates in vivo tissue integration. The sponge framework is characterized by high porosity and a natural morphology similar to the trabecular architecture of bone [8]. This feature is essential as it permits cell infiltration and vascularization, enhances cell-biomaterial interactions, and provides space for the growth of new tissue. Sea sponges synthesize biosilica (biogenic silica) through biomineralization. This biosilica possesses a porous and hierarchical structure that supports the diffusion of oxygen and nutrients; active silanol groups (Si–OH) that enhance cell adhesion and protein binding; and osteoinductive properties that promote the differentiation of stem cells into osteoblasts [24,25].

3. Conclusions

Biosilica sourced from Indonesian marine sponges presents considerable potential as a novel biomaterial in bone tissue engineering. Its unique architecture, high porosity, and biocompatibility, along with its ability to facilitate the adhesion, proliferation, and differentiation of mesenchymal stem cells (MSCs), position marine sponge biosilica as an excellent candidate for bone scaffold applications. Additionally, the high silica content inherent in this biosilica plays a crucial role in activating osteogenic pathways, thereby promoting osteogenesis. The use of biosilica from these natural Indonesian sources also provides the benefits of sustainability and local accessibility. In summary, Indonesian marine sponge biosilica holds a promising and impactful role in advancing biomaterials for mesenchymal stem cell-based bone regeneration applications.

Credit authorship contribution statement

Soraya: Writing original draft, review and editing. Anggraini: Conceptualization, writing, Review and supervision. Indra: Resources and editing. Ekavianty: Supervison.

Declaration of Competing Interest

The authors declare no conflict of interest.

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