**RECENT LITERATURE IN HYDROXYAPATITE SYNTHESIS**

**ABSTRACT:**

Keywords*: Hydroxyapatite,biomedical,calcium,bones,nano size*

Due to its chemical similarity to human bone and teeth and its widespread use in biomedical applications, hydroxyapatite (HAp) is the most popular calcium phosphate ceramic. Using chemical precursors, particularly calcium and phosphorus, hydroxyapatite can be created utilising a variety of techniques, including dry, wet, thermal, or a combination of these techniques. HAp can also be obtained from natural sources, such as the HAp-rich scales and bones of animals, as an alternative to chemical manufacture.Several synthesising techniques produce crystals with various morphologies, sizes, and phase crystallinities. Because of the human bone, the goal of creating a nano-sized HAp has garnered a lot of attention.The clinical performance of HAp in the nano size range is superior than that of HAp in the micron size range.

**INTRODUCTION:**

Wound healing occurs in four distinct and highly programmed stages in the human body as a normal biological process: hemostasis, inflammation, proliferation, and remodeling [1]. Bone fractures are a common injury; the healing process is complex and involves both mechanical and biological aspects [2]. Bone is one of a few tissues that can heal without forming a fibrous scar. The bone injury or wounds can be caused by a variety of reasons, including falling from a height, trauma, motor vehicle accidents, direct blows, and repetitive forces such as those caused by running that can cause stress fractures on the foot, ankle, tibia, or hip, and other types of accidents. Bone healing is a complex restorative process that can be divided into primary (direct) and secondary (indirect) healing.

The Haversian canals, blood vessels, and lamellar bone directly remodeling each other can result in direct bone healing. Direct bone healing is feasible when the fracture ends are compressed together and rigid fixation is employed to reduce interfragmentary strain [3]. Secondary bone healing occurs when the fractured bones' ends are close enough to heal, not perfectly opposed, or when the fracture site moves. This movement is typical with cast immobilization or the insertion of an intramedullary nail or rod. Secondary bone healing includes the classic stages of injury, hemorrhage, inflammation, and "scar" formation. The "scar" in bone is a soft callus made of cartilage that then mineralizes and remodels so that, unlike skin, the tissue can eventually become normal tissue (without any permanent scarring).

Globally, in 2019, there were 178 million (95% UI 162–196) new fractures (an increase of 33·4% [30·1–37·0] since 1990), 455 million (428–484) prevalent cases of acute or long-term symptoms of a fracture (an increase of 70·1% [67·5–72·5] since 1990) [4]. Up to 10% of all fractures may experience failed or delayed healing, which can be brought on by a variety of conditions like an infection, a tumor, or a disrupted vascular supply [5]. Vascular injury and fractures are linked to greater mortality and poorer prognoses, particularly when there is quick and significant blood loss into the pelvic or femoral soft tissue compartments [6].

The increased rate of accidental bone fractures in the elderly population has been linked to their decreased mobility and strength [7]. The fractures have profound impacts on physical function or activity. These effects build up over time through a cycle of impairment, whereby a fracture causes longer-term physical function losses, such as muscle loss, activity avoidance, and decreased physical capacity, increasing the risk of fracture and raising the possibility of additional physical limitations [8].

To reduce the risk of physical impairment and to heal bone wounds, several factors are considered such as cells, growth factors/morphogenic signals, and scaffold materials to provide mechanical support and facilitate the growth of new tissues [9]. Among the factors of bone regeneration, a bone scaffold is a three-dimensional matrix that enables the stimulation and growth of osteoinducible cells on its surface [10].

Currently, bone grafts is the typical medication for skeletal fractures, or to replace and regenerate lost bone, as endorsed by the large number of bone graft procedures performed.

**MATERIALS REQUIRED:**

Sea Shell

Electrospinning Machine

Distilled Water

Phosphoric Acid

Polyethylene glycol

Chloroform

**METHODOLOGY**

There are numerous methods for synthesising synthetic HAp, which have been divided into dry, wet, and high-temperature methods[11]. In addition to producing distinct crystalline phases of calcium phosphate other than pure crystalline HAp, each of these processes produces varied sizes, morphologies, and yields. Hence, the bioactivity, mechanical, and biological qualities are greatly influenced by the features of HAp. It is intriguing to create a synthesis process that can control the morphology, crystallinity, size, and chemical composition of HAp since, according to Cox [12]], these features dictate the biological applicability of the HAp. In order to draw conclusions about the distinctions and complexity of each approach in the synthesis of synthetic HAp, the study of each synthesis method is evaluated.

**Synthesis from Dry Method**

Dry HAp synthesis can be divided into two categories: solid-state synthesis and mechanochemical synthesis. The precursor chemicals (calcium and phosphate), which are in a dry form, are combined in the dry process to create the HAp. The majority of dry procedures don't require exact and controlled conditions, according to Sadat-Shojai et al. [10]. They can thus be used to produce powders in large quantities [10].

**Synthesis from Solid State Method**

A solid-state reaction is described as the heating-induced breakdown of a mixed solid reactant to provide new solids and gases [13]. The solid-state approach is regarded as a straightforward process that involves milling and calcining chemical precursors including calcium and phosphate to produce HAp. The mechanism of this approach, according to Cox [12], involves the solid diffusion of the ion from chemical precursors (calcium and phosphate), which is followed by a high-temperature process to start the reaction.

**Synthesis from Mechanochemical method**

A process known as mechanochemistry uses friction, shear, or compression during grinding and milling to cause a chemical reaction [12]. Ball-milling or planetary mills are typically used in mechanochemical methods at particular speeds or frequencies.During a mechanochemical reaction, strong impact compression [13] and an increase in local temperature [14] both contribute to the chemical reaction and the diffusion process [15]. The mechanochemical process is typically carried out in a sealed tank constructed of materials such as stainless steel, agate, zirconia, etc. to overcome the restriction in controlling the air and moisture-sensitive ingredient

**Synthesis from Wet Method**

The use of an aqueous solution in the synthesis of HAp is referred to as the wet technique. Chemical precipitation, hydrolysis, and hydrothermal procedures are a few of the wet techniques typically employed for HAp extraction. The morphology and mean size of the powder can be manipulated using wet approaches. Wet techniques offer drawbacks in addition to their benefits, one of which is the HAp's low crystallinity due to low processing temperatures.

**Synthesis from High temperature method**

A high-temperature approach that uses high heat to break down the ingredients can also be utilised to synthesise HAp. The high-temperature approach includes two distinct processes: combustion and pyrolysis. The combustion and pyrolysis processes were hardly ever used to create HAp across all synthesis techniques. Its weak control on the processing parameter and the creation of secondary aggregates is the source of this.

**Synthesis from Pyrolysis method**

A precursor chemical is sprayed into a hot zone of the electric furnace using the pyrolysis approach . According to Sadat- Shojai et al. , pyrolysis products were applied as post-treatments to produce a high crystalline product. In contrast to the combustion approach, the pyrolysis synthesis does not require mixing fuel with reactants and may be simply scaled up to produce HAp particles continuously. It should be noted that the pyrolysis technique falls under the broad classification of aerosol methods (also known as gas-phase techniques), in which gas-to-particle or liquid-to-to particle conversions take place during an aerosol decomposition process.

Conclusion

Therefore, it can be concluded that various methods can be used for synthesising synthetic HAp. Each method requires several processing parameters such as pH, temperature, the molar ratio of chemicals, etc. in order to produce the pure HAp phase. It can also be concluded that a balanced molar ratio of calcium and phosphate precursors must be used in order to produce the stoichiometric HAp. pH, as another parameter, also plays an important role in some of the methods used for synthesising HAp. Furthermore, the morphology of the HAp particle has recently been controlled by the application of organic modifiers like CTAB and EDTA. As a result, a HAp particle with a consistent size and shape can be produced. The method for creating synthetic HAp also offers a number of strategies that aid in producing distinct HAp characteristics, including shape, size, and phase. Even though there are many different ways to make HAp nanoparticles, only a few of them are effective or economical. This is primarily caused by the variety of materials required for synthesis, challenging and expensive procedures, severe aggregation and agglomeration, wide particle size distribution, and numerous phase impurities that typically exist in crystal structure. As a result, there are other options, such getting HAp from a natural source, that could solve the issue of making synthetic HAp. The HAp-containing animal scale and bone can serve as a suitable source of HAp since they include all the beneficial trace elements needed to improve the biological effects of HAp.

Bibliography:

[1]. Guo, S., and L. A. DiPietro. “Factors Affecting Wound Healing.” *PubMed Central (PMC)*, Mar. 2010, [www.ncbi.nlm.nih.gov/pmc/articles/PMC2903966](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2903966).

[2]. Ghiasi, Mohammad S., et al. “Bone Fracture Healing in Mechanobiological Modeling: A Review of Principles and Methods.” *PubMed Central (PMC)*, Mar. 2017, <https://doi.org/10.1016/j.bonr.2017.03.002>.

[3]. Marsell, R., & Einhorn, T. A. (2011). The biology of fracture healing. Injury, 42(6), 551–555. https://doi.org/10.1016/j.injury.2011.03.031

[4]. Wu, Ai-Min, et al. “Global, Regional, and National Burden of Bone Fractures in 204 Countries and Territories, 1990–2019: A Systematic Analysis From the Global Burden of Disease Study 2019.” *The Lancet Healthy Longevity*, vol. 2, no. 9, Elsevier BV, Sept. 2021, pp. e580–92. *Crossref*, <https://doi.org/10.1016/s2666-7568(21)00172-0>.

[5]. Sheen JR, Garla VV. Fracture Healing Overview. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551678/>

[6]. Gilbert, F., et al. “Clinical Implications of Fracture-associated Vascular Damage in Extremity and Pelvic Trauma - BMC Musculoskeletal Disorders.” BioMed Central, 20 Nov. 2018, bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/s12891-018-2333-y.

[7]. Medicine Staff, Institute of, and Division of Health Promotion and Disease Prevention Staff. *The Second Fifty Years: Promoting Health and Preventing Disability*. Edited by Robert L. Berg and J. S. Cassells, 1992. *Bowker*, <https://doi.org/10.1604/978030904681710.17226/1578>.

[8]. Kerr, C., et al. “The Importance of Physical Function to People with Osteoporosis.” Osteoporosis International, vol. 28, no. 5, Springer Science and Business Media LLC, 6 Mar. 2017, pp. 1597–1607. Crossref, doi:10.1007/s00198-017-3911-9.

[9]. Polo-Corrales, Liliana, et al. “Scaffold Design for Bone Regeneration.” PubMed Central (PMC), <https://doi.org/10.1166/jnn.2014.9127>.

[10]. Ghassemi, Toktam, et al. “Current Concepts in Scaffolding for Bone Tissue Engineering.” PubMed Central (PMC), [www.ncbi.nlm.nih.gov/pmc/articles/PMC5867363](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5867363).

[11]. M. Sadat-Shojai, M.T. Khorasani, E. Dinpanah-Khoshdargi, A. Jamshidi, Acta

Biomater. 9 (2013) 7591–7621.

[12]. S.C. Cox, K.K. Mallick, R.I. Walton, Comparison of techniques for the synthesis

of hydroxyapatite, Bioinspired, Biomim. Nanobiomaterials. 4 (2014) 37–47.

[13]. M. Rahaman, M.N. Rahaman, Ceramic Processing, Taylor & Francis, 2006.