Chapter 2

Objectives

Therapeutic ions like zinc, copper, and strontium are present as trace elements in almost every part of our bodily organs, including the skeletal and immune systems. Zinc, Copper, and Strontium due to their therapeutic properties, uphold the entire system wholesomely. But due to disease, pregnancy, injury, and some other complications (like aging), the consumption of such trace therapeutic ions increases multifold compared to their reproduction. As these therapeutic trace elements are inevitable in maintaining a healthy system, their scarcity also causes severe damage to the bodily system as a whole. Bone disease like osteoporosis, where bone strengths are significantly compromised, is one of the most serious concerns for aged people, especially for pregnant women in recent times. Bone is the natural composite of fibrous collagen (provides framework) and bone mineral (provides strengths). Cortical (dense and compact bones; outer layer) and trabecular bones (porous, surrounded by cortical bone) are the two most important types of bones. The trabecular bone is porous internal structure consisting of network of trabeculae (porous struts) enclosed with macropores. In osteoporosis, the reduction in total bone density occurs due to faster bone resorption than new bone formation, causing the trabeculae to become weaker and thinner. As a result, the overall bone strengths are significantly compromised, leading to an eventual failure of bones. However, the damage is severe, particularly at the trabecular area due to the scarcity of these therapeutic ions. These trace (Zinc, Copper, and Strontium) elements play a pivotal role to cure osteoporotic bones, and prevents from bone resorption of osteoclastic bones, thus regulates overall health of bones. Even, strontium has been used as supplements [SrRAN, strontium renalate, Protelos®) to increase bone density, cure osteoporosis, and prevent bone loss. Thus, controlled delivery of such ions from

bioactive glasses/ glass scaffolds could introduce therapeutic properties to the skeletal system to prevent osteoclastic bone resorption and stimulate bone remodeling.

This investigation, however, deals with the preparation and characterization of therapeutic ions (copper, zinc, and strontium) incorporated 1393 and 1393B3 bioactive glass derived scaffolds mimicking trabecular bones and their reliability for bone tissue regenerative applications. The therapeutic ions incorporated scaffolds were examined through a series of experiments to analyze their mechanochemical, physical, and biological performance in the physiological system. Also, an in vivo study of CuO derived 1393B3 glass scaffolds was executed to assess their bone regeneration potentials.

Therefore, the incorporation of therapeutic ions into our 1393/1393B3 glass derived scaffolds was on the purpose of augmentation of properties of the glass scaffolds as follows

- Enhanced biocompatible glass surface to improve the cell-scaffold interactions with optimal bioactivity and minimal cytotoxicity: In these investigations we have seen that scaffold materials exhibit excellent biological compatibility and an optimal bioactivity in all materials (Chapter 4 to Chapter 7). However, the therapeutics ions incorporated scaffolds were appeared to be better (except a few) in biological performance than the parent glass system in the time and dose (material concentration) dependent compatibility study.

- Introduction of the therapeutic ions to stimulate the osteogenic potential of the materials: Herein, we observed a significantly enhanced osteogenic differentiation of the stromal cells in our zinc incorporated glass materials in comparison to the pure glass system (Chapter 4). Moreover, the in vivo investigation (Chapter 7)

suggests an enhanced bone healing potential for the CuO incorporated 1393B3 (CBBGs) than its pure (BG) form. However, a more detailed study comprising advanced techniques is needed to understand better the bone formation phenomenon in the 1393/ 1393B3 glass-driven biomaterials accompanied by these therapeutic ions.

- Augmentation of scaffolds' structural stability in physiological fluid: The structural stability of the scaffolds is important to ensure mechanical support in the physiological fluid. We, therefore, have examined the mechanical strengths both in dry and wet (in SBF; except CuO-based 1393 system) conditions to assess the variation in strengths and mechanical stability in the physiological fluid. We have seen an enhanced mechanical strength in almost all the metallic ions incorporated scaffold than the basal system. Although a further enhancement in strengths was desirable, still the strengths were comparable to the trabecular bones' maximum value reported.