**Bioactive glass**

The main characteristic of the bioactive glasses or bioglasses is the formation of a hydroxycarbonate apatite layer on their surface in aqueous solutions. This layer has the same composition and structure as the mineral phase of bone. Bioactive glasses have been used for the repair and reconstruction of diseased and damaged hard tissue such as bone, as well as soft tissue such as ligament. The use of bioactive glasses in tissue engineering allows control of a range of chemical properties and the rate of bonding to different tissues. These aspects make bioactive glasses different from other bioactive ceramics and glass-ceramics.

Depending on manufacturing process, bioactive glass can be divided mainly into two groups: sol-gel bioactive glasses and melt-derived bioactive glasses. Sol-gel glasses are made by a chemically based process at much lower temperatures than the melt-derived processing methods. Many researches have shown that gel-derived glasses in the system of Na2O-CaO-SiO2 are bioactive even up to 85 mole percent SiO2. The wide range of bioactive oxide compositions makes it possible to tailor the reactivity of the glasses to various applications. Also, sol-gel processing offers the potential advantages of ease of powder production, high purity of the material, and better control of bioactivity through changes in processing parameters. Compared with the sol-gel process, melt-derived process requires much higher working temperatures with a maximum SiO2 content of 60 mol. % and large amounts of alkali and/or alkaline earth oxides. However, melting is a simple and low cost technique and is much less time consuming than sol-gel processing. For production of a large amount of bioactive glasses the melting process is very suitable and reliable.

The oldest bioactive glass composition, namely 45S5 which was introduced in 1971 by Hench, consists of a silicate network Na2O-CaO-P2O5-SiO2. This Bioglass® was produced by a melt-derived process with a maximum SiO2 content of 60 mol. %. Other bioactive glass powders in the ternary system CaO-P2O5-SiO2 were produced by the sol-gel technique; these are more bioactive and resorb faster than melt-derived glasses of the same components due to the greater specific surface area that result from their nanometer textural porosity, the small changes in bioglass composition can determine if they are bioinert, resorbable or bioactive. This work is summarized in the ternary SiO2-Na2O-CaO diagram with a constant 6wt.% P2O5 content as shown in fig (3).

![Fig(3)Compositional dependence of bone bonding and soft tissue bonding of bioactive glasses and glass ceramics.](image-url)
Region A represents the bioactive glasses that have a constant 6 wt% of P\textsubscript{2}O\textsubscript{5} and bond to bone and soft tissue, inside the dashed line where Ib > 8 (45S5 Bioglass\textregistered, Ceravital\textregistered). Region B represents nearly bioinert glasses; Region C bioresorbable glasses. (A/W glass-ceramic has higher P\textsubscript{2}O\textsubscript{5} content); Region D finally shows non-glass-forming compositions.

**Surface reaction kinetics of bioactive glass**

The basis of the bone bonding properties of a bioactive glass is its chemical reactivity in body fluids. These surface chemical reactions result in the formation of a hydroxycarbonate apatite layer to which bone can bond. Hench and Andersson (1993a) described the three general processes that occur on immersion of a bioactive glass in an aqueous solution: leaching, dissolution and precipitation. Leaching is characterized by release, i.e. the exchange of alkali and alkaline earth ions in the glasses with H\textsuperscript{+} and H\textsubscript{3}O\textsuperscript{+} ions in the solution. This process is easy because these cations are network modifiers and thus only weakly bonded to the glass network. Network dissolution occurs concurrently by the breakdown of -Si-O-Si-O-Si- bonds through the action of hydroxyl (OH-) ions. Breakdown of the network occurs locally and releases silica into the solution in the form of silicic acid (Si(OH)\textsubscript{4}). Then, polycondensation of silanols occurs, resulting in a silica-rich gel on the surface. In the precipitation process, calcium and phosphate ions released from the glass together with those from solution form a calcium phosphate-rich (CaP-rich) layer on top of the Si-rich layer. By crystallization, the CaP-rich layer finally forms the hydroxycarbonate apatite layer. Generally, there are five reaction stages on the surface.

More detailed reaction processes have been described extensively by Hench and others. The chemical reactions are summarized as follows:

Stage 1) Rapid exchange of Na\textsuperscript{+} or K\textsuperscript{+} with H\textsuperscript{+} or H\textsubscript{3}O\textsuperscript{+} from solution:

\[
\text{Si-O-Na}^+ + \text{H}^+ + \text{OH}^- \xrightarrow[\text{network modifiers}]{} \text{Si-OH}^+ + \text{Na}^+ \text{(solution)} + \text{OH}^-
\]

Stage 2) Loss of soluble silica in form of Si(OH)\textsubscript{4} to the solution resulting from breakage of Si-O-Si bonds and formation of Si-OH (silanols) at the glass solution interface:

\[
\text{Si-O-Si} + \text{H}_2\text{O} \xrightarrow[\text{polycondensation}]{} \text{Si-OH} + \text{OH-Si}
\]

Stage 3) Condensation and repolymerization of a SiO\textsubscript{2}-rich layer on the surface depleted in alkalis and alkaline earth cations:

\[
\begin{align*}
\text{O} & \quad \text{O} & \quad \text{O} & \quad \text{O} \\
\text{\text{O--Si--OH + HO--Si--O} & \xrightarrow[\text{crystallization}]{} & \text{Si-O-Si-O + H}_2\text{O} & \\
\text{O} & \quad \text{O} & \quad \text{O} & \quad \text{O}
\end{align*}
\]
Stage 4) Migration of Ca\(^{2+}\) and PO\(_{4}^{3-}\) groups to the surface through the SiO\(_{2}\)-rich layer forming a CaOP\(_2\)O\(_2\)-rich film on top of the SiO\(_2\)-rich layer, followed by growth of the amorphous CaO-P\(_2\)O\(_5\)-rich film by incorporation of soluble calcium ions and phosphates from solution.

Stage 5) Crystallization of the amorphous CaO-P\(_2\)O\(_5\) film by incorporation of OH\(^-\), CO\(_3^{2-}\), or F\(^-\) anions from the solution to form a mixed hydroxyl, carbonate, fluorapatite layer.

Stage 6) Adsorption of biological moieties in the SiO\(_2\)-hydroxycarbonate apatite layer.

Stage 7) Action of macrophages.

Stage 8) Attachment of stem cells.

Stage 9) Differentiation of stem cells.

Stage 10) Generation of matrix.

Stage 11) Mineralization of matrix.

Different oxide systems have been studied in order to understand the effect of changes in composition on glass bioactivity. Studies on partial substitutions of CaO by CaF\(_2\) or SiO\(_2\) by B\(_2\)O\(_3\). The fluoride additions were found to reduce the rate of dissolution and degradation of the glass. Substitutions of MgO for CaO or K\(_2\)O for Na\(_2\)O only slightly affected the bone bonding ability of glasses. B\(_2\)O\(_3\) and Al\(_2\)O\(_3\) have the ability to improve the chemical durability of glass, thus, research on developing boron oxide and alumina containing bioactive glass is of interest. The presence of boron in the glass network improved the bioactivity performance, increase the degradation rate as well as the compressive strength and flexural strength. Zn-substituted bio-glasses create a template for osteoblast proliferation and differentiation that could be encouraged by the interaction between the Zn and inorganic phosphate at the surface of the bioactive glass. Addition of Zn is beneficial for cell attachment.

**Textural properties influencing bioactive behavior:**

It was reported that textural properties (pore size, pore volume, pore structure) of biomaterials may have complex influences on the development of the apatite layer. Increasing the specific surface area and pore volume of bioactive glasses may greatly accelerate the apatite formation and therefore enhance the bioactive behavior.