BONE-G ACTIVE

Meta Bioengineering

BONE-G ACTIVE is a biocompatible bone graft material designed to support growth and repair in the defected bone tissue where it is implanted and is intended to temporarily fill a bone injury caused by traumatic, pathological or surgical intervention until bone formation and regeneration.

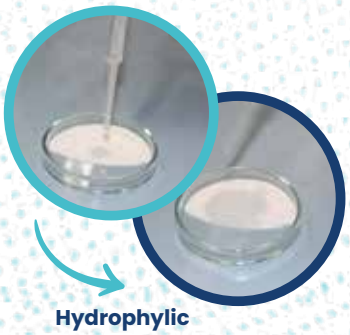
BONE-G ACTIVE products are used at Trauma, Orthopaedic, Spine and Dental Surgery.

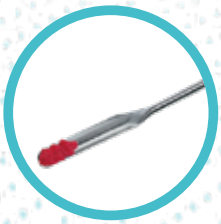
1 Fully Synthetic and Hydrophylic Structure

BONE-G ACTIVE contains oxide forms of natural four elements in the bone (SiO_2, CaO, Na_2O, P_2O_5) and has no tissue of human or animal origin. It can be mixed with patient's blood, patient's bone or saline solution.

2 Physical Structure

BONE-G ACTIVE has granular structure and can be offered in different sizes and volumes upon request.





3 Safe and Sterile

BONE-G ACTIVE is fabricated in the modern laboratory of ISO Class 7 clean rooms that is certified with a quality management system (ISO 13485:2016).

BONE-G ACTIVE is sterilized with EtOH and has CE-marked as a Class III Medical Device according to Directive 93/42/EEC.

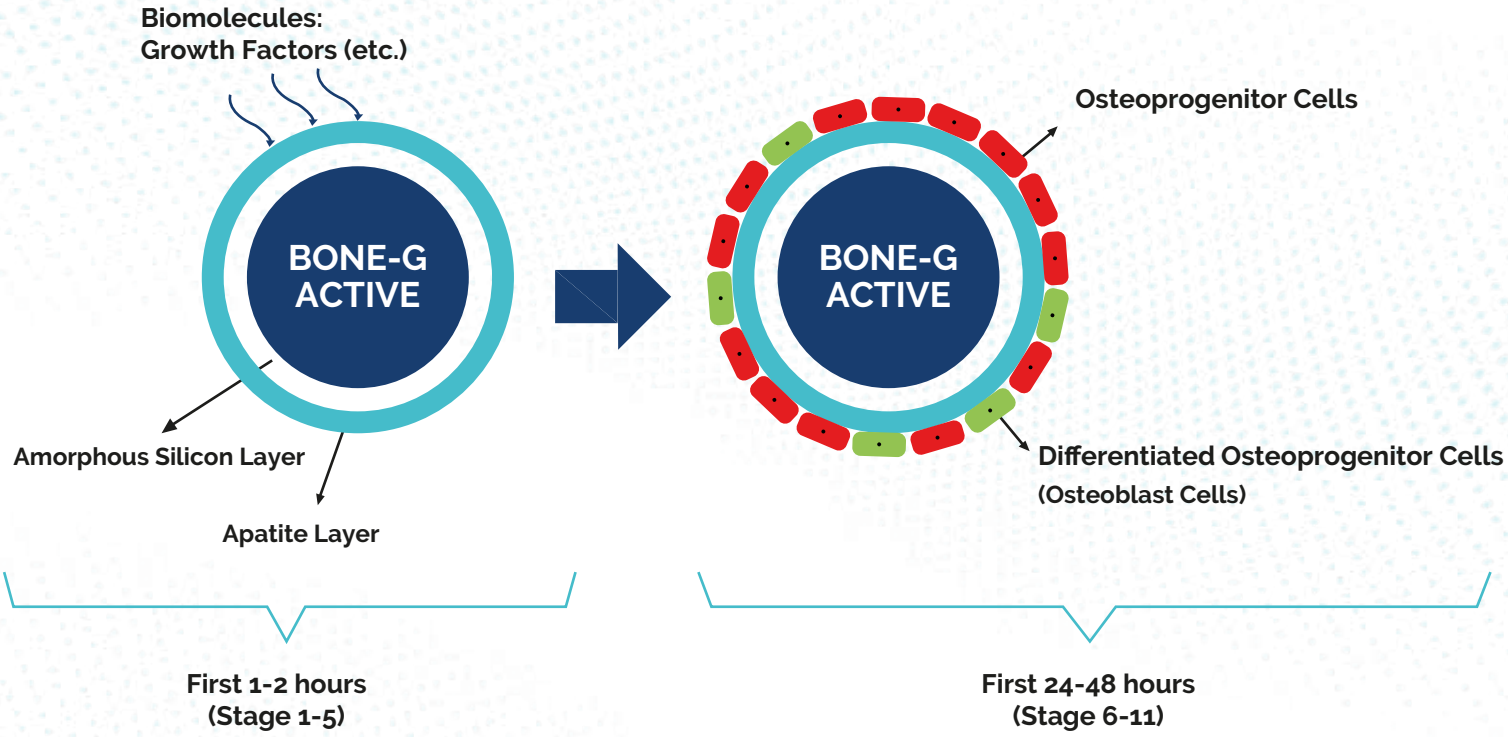
BONE-G ACTIVE was tested with biocompatibility tests (*in vitro* and *in vivo*), bioactivity tests, chemical tests, bioburden and sterility tests.

4 Bioactivity Reaction, Osteoconduction and Osteostimulation

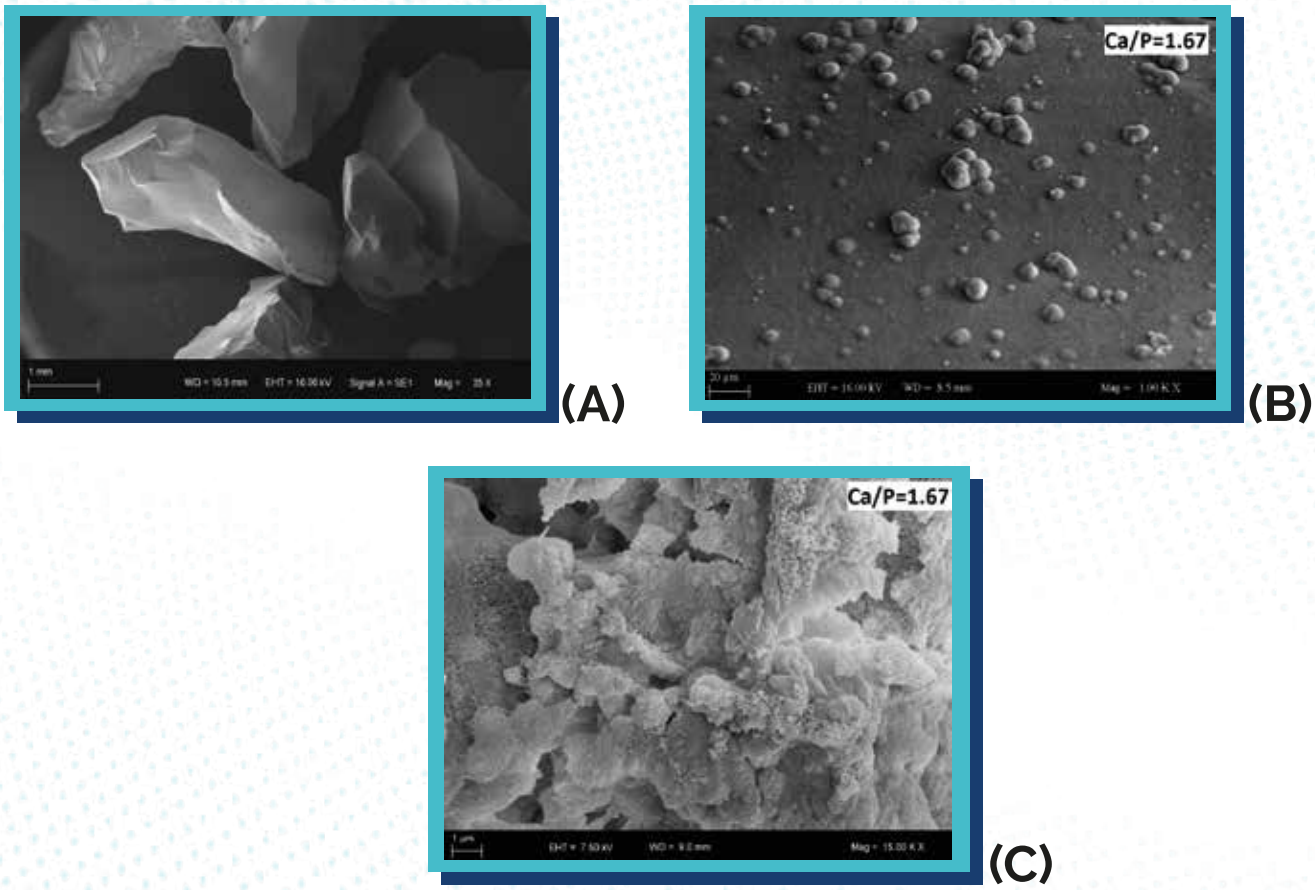
BONE-G ACTIVE has the property to form on its surface a calcium phosphate layer (bioactivity), which is substantially equivalent in composition and structure to the hydroxyapatite from the mineral phase of human bone.

- There is a sequence of 11 reaction stages that occur at the surface of BONE-G ACTIVE branded product. The effect of the surface reactions is rapid release of soluble ionic species from the BONE-G ACTIVE into the interfacial solution (Biological solutions). A high surface area hydrated silica and polycrystalline hydroxyl-carbonate apatite (HCA) bilayer is formed on the BONE-G ACTIVE surface within hours (Stages 1-5). The reaction layers enhance adsorption and desorption of growth factors produced by the cells[1,4].

- Attachment of osteoprogenitor stem cells and synchronized proliferation and differentiation of the cells towards the mature osteoblast phenotype rapidly occurs on the surface of BONE-G ACTIVE. Osteoprogenitor cells colonize the surface of BONE-G ACTIVE within 24–48 hours, and begin production of various growth factors which stimulate cell division, mitosis, and production of extracellular matrix proteins. Mineralization of the matrix follows soon thereafter and mature osteocytes, encased in a collagen-HCA matrix, are the final product by 6–12 days *in vitro* and *in vivo* (Stage 6-11) [1,4].



References:
[1] C. Y. Kim, A. E. Clark and L. L. Hench, "Early Stages of Calcium-Phosphate Layer Formation in Bioglass," Jour-nal of Non-Crystalline Solids, Vol. 113, No. 2-3, pp. 195-202, 1989.
[2] I. D. Xynos, M. V. J. Hukkanen, J. J. Batten, I. D. Buttery, L. L. Hench and J. M. Polak, "Bioglass® 45S5 Stimulates Osteoblast Turnover and Enhances Bone Formation in Vitro: Implications and Applications for Bone Tissue Engineering," Calcified Tissue International, Vol. 67, No. 4, pp. 321-329, 2000.
[3] B. D. Ratner, A. S. Hoffman, F. J. Schoen, and J. E. Lemons, "Biomaterials science: an introduction to materials in medicine", Elsevier, ISBN: 978-0-12-374626-9, 2004.
[4] L.L. Hench," Chronology of Bioactive Glass Development and Clinical Applications", New Journal of Glass and Ceramics, Vol.3, No.2, pp. 67-73, 2013.



SEM Images (A: Before SBF incubation-at 35X magnification-, B: After 28 Day SBF incubation-at 1KX magnification-, C: After 28 Day SBF incubation-at 15KX magnification-)

SEM image at 35X magnification shows that BONE-G ACTIVE has granular structure and has a flat surface (dense, nonporous surface-reactive ceramics) before *in vitro* Simulated Body Fluid (SBF) incubation. When the SEM images at 1KX and 15KX magnifications were examined, it was observed that BONE-G ACTIVE sample has Ca-P precipitation and Hydroxyapatite (HA; Ca/P molar ratio= 1.67) accumulation on their surface at the end of 28 Day SBF incubation. In addition, amorphous Ca-P precipitation, which is shown at 15KX magnifications, facilitate migration and attachment of bone cells and some biomolecules such as grown factors etc. The presence of surface HA formation on BONE-G ACTIVE promotes attachment directly by chemical bonding with the bone which is called bioactive fixation [1-4].

References:
[1] I. Rehman, L. L. Hench, W. Bonfield, and R. Smith, "Analysis of surface layers on bioactive glasses," Biomaterials, vol. 15, no. 10, pp. 865–870, 1994.
[2] B. D. Ratner, A. S. Hoffman, F. J. Schoen, and J. E. Lemons, "Biomaterials science: an introduction to materials in medicine", Elsevier, ISBN: 978-0-12-374626-9, 2004.
[3] L. C. Gerhardt, and A. R. Boccaccini, "Bioactive glass and glass-ceramic scaffolds for bone tissue engineering", Materials (Basel)., vol. 3, no. 7, pp. 3867–3910, 2010.
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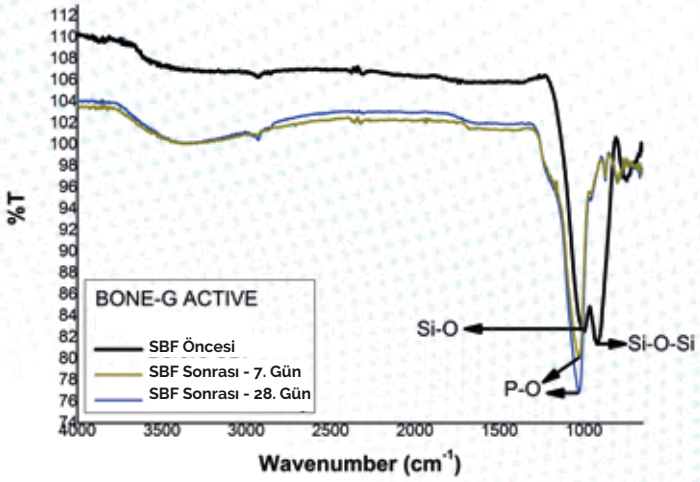
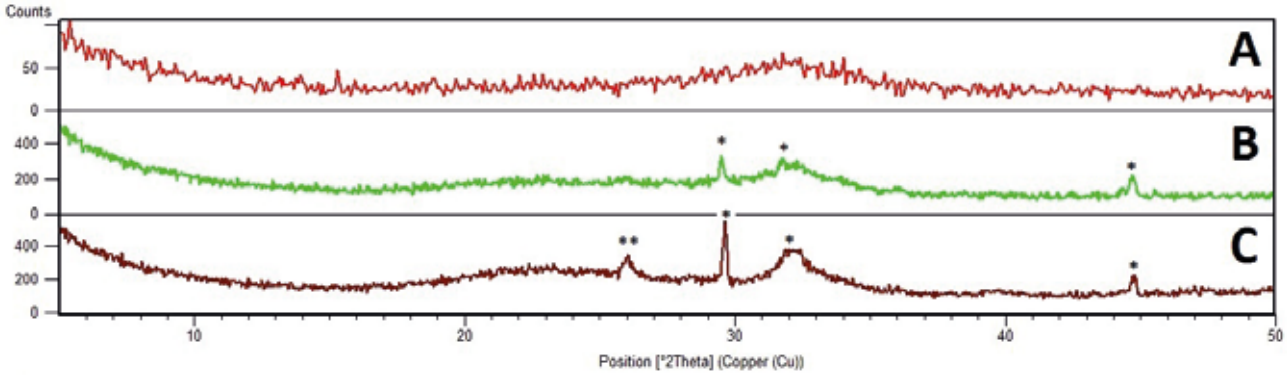


FT-IR graphs of Bone-G Active (Spectrum Black: Before SBF incubation, Spectrum Green: After 7 Day SBF incubation, Spectrum Blue: After 28 Day SBF incubation)

When the FT-IR graphs are examined, BONE-G ACTIVE has two specific peaks; the bands at 930 cm^{-1} and the band at 1070 cm^{-1} present Si-O-Si and Si-O, respectively (Spectrum Black). After SBF incubation of BONE-G ACTIVE branded product, the band at 1090 cm^{-1} is attributed to the P-O which indicates the presence of hydroxyapatite (Spectrum Green and Spectrum Blue). Furthermore, P-O peak intensity increased depending on the increase of SBF incubation time [1,2,3,4].



XRD Graphs of Bone-G Active (XRD pattern A: Before SBF incubation, XRD pattern B: After 7 Day SBF incubation, XRD pattern C: After 28 Day SBF incubation)

BONE-G ACTIVE has amorphous structure which is proven by XRD pattern A. On the other hand, at the end of 7 Day SBF incubation of BONE-G ACTIVE, XRD pattern B demonstrates two specific peaks at 2θ=29˚ and 32˚ with JCPDS (Joint committee on Powder Diffraction Standards) Card No.090432, hydroxyapatite; "*" and also the peak at 2θ=44˚ with ICSD (Inorganic Crystal Structure Database) Ref No.010740566, hydroxyapatite; "*". Additionally, at the end of 28 Day SBF incubation of BONE-G ACTIVE, more intense peaks at 2θ=29˚, 32˚ and the peak at 2θ=26˚ (JCPDS Card No.090432, hydroxyapatite; "**") were observed in the XRD pattern C. These results indicate that BONE-G ACTIVE branded product has bioactivity properties which are associated with chemical bonding with the bone and these results also show that as time increases, the binding will increase [1,2,3,4].

References:
[1]A. R. Boccaccini, Q. Chen, L. Lefebvre, L. Gremillard, J. Chevalier, "Sintering, crystallisation and biodegradation behaviour of Bioglass®-derived glass-ceramics, Faraday Discuss, 136, pp. 27-44, 2007.
[2]A. C. Özarslan, and S. Yücel, "Fabrication and characterization of strontium incorporated 3-D bioactive glass scaffolds for bone tissue from biosilica", Material Science and Engineering C, 68, 350-357, 2016.
[3]B. Karakuzu-İkizler, P. Terzioğlu, B. S. Oduncu-Tekerek, and S. Yücel, "Effect of selenium incorporation on the structure and in vitro bioactivity of 45S5 bioglass," Journal of the Australian Ceramic Society, pp. 1–13, 2019.
[4]B, Karakuzu-Ikizler, P. Terzioğlu, Y. Basaran-Elalmis, B. S. Tekerek, and S. Yücel, "Role of magnesium and aluminum substitution on the structural properties and bioactivity of bioglasses synthesized from biogenic silica," Bioactive Materials, vol. 5, no. 1, pp. 66–73, 2020.

Product Name	Reference Code	Particle Size (mm)	Volume (cc)
BONE-G ACTIVE	BGA1.3/10	1-3	10
	BGA1.3/5	1-3	5
	BGA05.1/5	0.5-1	5
	BGA05.1/4	0.5-1	4
	BGA05.1/3	0.5-1	3
	BGA05.1/2	0.5-1	2
	BGA05.1/1	0.5-1	1
	BGA025.05/5	0.25-0.5	5
	BGA025.05/4	0.25-0.5	4
	BGA025.05/3	0.25-0.5	3
	BGA025.05/2	0.25-0.5	2
	BGA025.05/1	0.25-0.5	1

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Notes:

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