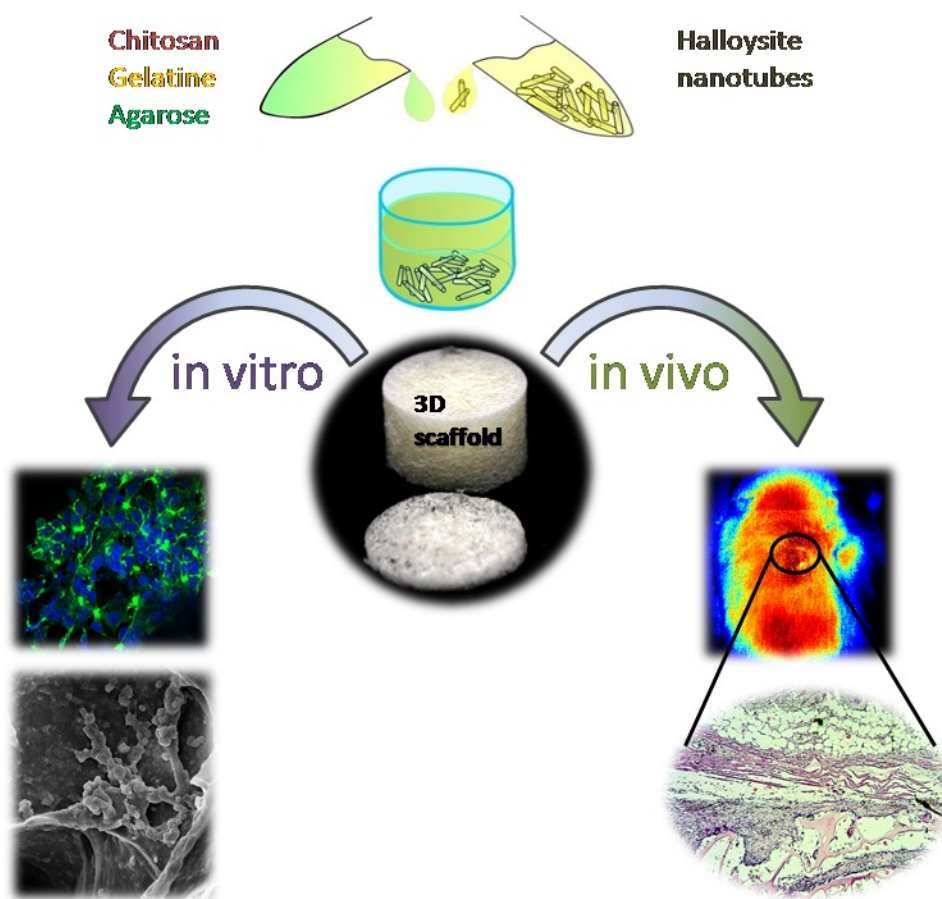


Clay nanotube-biopolymer composite scaffolds for tissue engineering

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A sketch demonstrating the fabrication and in vitro and in vivo testing of novel halloysite-doped biopolymer tissue engineering scaffold. Credit: Bionanotechnology Lab, Institute of Fundamental Medicine and Biology, KazanFederal University,

The fabrication of a prototype tissue with functional properties close to natural tissues is crucial for effective transplantation. Tissue engineering scaffolds are typically used as supports that allow cells to form tissue-like structures essentially required for the correct functioning of the cells under the conditions close to the three-dimensional tissue.

Scientists of the Bionanotechnology Lab at Kazan Federal University combined biopolymers chitosan and agarose (polysaccharides) and gelatine protein to produce tissue engineering scaffolds and demonstrated the enhancement of mechanical strength, higher [water uptake](#) and thermal properties in chitosan-gelatine-agarose hydrogels doped with halloysite.

Chitosan, a natural biodegradable and chemically versatile biopolymer, has been effectively used in antibacterial, antifungal, anti-tumour and immunostimulating formulations. To overcome the disadvantages of pure chitosan scaffolds such as mechanical fragility and low biological resistance, chitosan scaffolds are typically doped with other supporting compounds that allow for mechanical strengthening, thus yielding composite biologically resistant scaffolds.

Agarose is a galactose-based backbone polysaccharide isolated from red algae, with remarkable mechanical properties that are useful in the design of tissue engineering scaffolds.

Gelatine is formed from collagen by hydrolysis (breaking the triple-helix structure into single-strand molecules) and has a number of advantages over its precursor. It is less immunogenic compared with collagen and it retains informational signal sequences promoting cell adhesion, migration, differentiation and proliferation.

The surface irregularities of the [scaffold](#) pores result from insoluble nanosized components; these promote the best adhesion of the cells on

scaffold materials, while the nanoparticle fillers increase the composites' strength. Thus, researchers doped halloysite nanotubes into a chitosan-agarose-gelatine matrix to design the implantable 3-D cell scaffolds.

The resulting scaffolds demonstrate shape memory upon deformation and have the porous structure suitable for cell adhesion and proliferation, essential for artificial tissue fabrication. Macroscopic observations have confirmed that all the samples of scaffolds exhibit the sponge-like behaviour with the shape memory and shape reconstitution after deformation both in wet and dry states.

The swelling experiments indicated that the addition of halloysite can greatly improve the hydrophilicity and wetting of composite scaffolds. The incorporation of halloysite nanotubes into the scaffolds increases the water uptake and subsequently improves biocompatibility. The intrinsic properties of halloysite nanotubes can be used to improve the biocompatibility of scaffolds by the loading and sustained release of different bioactive compounds. This offers the prospect of scaffolds with defined properties for directed differentiation of cells on matrices due to gradual release of differentiation factors.

Experiments on two types of human cancer cells (A549 and Hep3B) show that in vitro [cell adhesion](#) and proliferation on the nanocomposites occur without changes in viability and cytoskeleton formation.

Further in vivo biocompatibility and biodegradability evaluation in rats has confirmed that the scaffolds promote the formation of novel blood vessels around the implantation sites. The scaffolds show excellent resorption within six weeks after implantation in rats. Neo-vascularization observed in newly formed connective tissue placed near the scaffold allows for the complete restoration of blood flow.

The results obtained indicate that the halloysite-doped scaffolds are

biocompatible as demonstrated both in vitro and in vivo. In addition, they confirm the great potential of chitosan-agarose-gelatine nanocomposite porous scaffolds doped with halloysite in [tissue engineering](#) with potential for sustained nanotube drug delivery.

More information: Ekaterina A. Naumenko et al, Clay nanotube–biopolymer composite scaffolds for tissue engineering, *Nanoscale* (2016). [DOI: 10.1039/C6NR00641H](https://doi.org/10.1039/C6NR00641H)

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