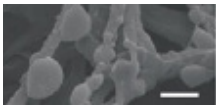


A winning synergy : a biodegradable nanocomposite hydrogel for drug

Engineering an advanced material for biomedical applications requires dealing with antagonistic requirements: it must exhibit resistance to fracture AND biodegradability, remain highly hydrated AND carry hydrophobic active substances... Moreover, the creativity of chemists is hidered by the compliance to the biocompatibility rules required by food and drug agencies, unavoidable bottleneck in the process of validating and launching a safe and efficient product. The « Multiple Scale Mechanics of Soft Solids » team at INSP has recently been part of such a projet involving several labs of Sorbonne University and gahering chemists, cell biologists, dermatologists and consensed matter physicists. The consortium has achieved and optimized the synthesis of a nanocomposite patch suitable for the controlled drug delivery to treat chronic skin wound, taking advantage of the synergy between a collagen matrix and nanoparticles of polyesters loaded with active substances.

Chronic skin wounds affecting in particular diabetic patients are usually treated by occlusive, alginate-based wound dressing. The biopolymer extracted from see weeds forms a network in presence of calcium ions. The hydrogel prenvents the wound from infection but plays no active healing role. Therefore, there is a need for drug-loaded wound dressings stimulating healing. Most drugs, like the spironolactone studied by our colleagues at Centre de Recherche des Cordeliers, are hydrophobic molecules poorly soluble in the dressing patches which must remain hydrophilic in order to absorb physiological fluids exsudated from the wound.
The LCMCP team relied on composite patches based on a gel of collagen (a protein, main constituent of skin, tendons, bones...) and hydrophobic polymer particles enabling the encapsulation of a large amount of lipophilic drug and its subsequent, controlled release over a month. The use of polyesters aready approved by FDA is is likely to speed-up validdation and future applications of these materials.

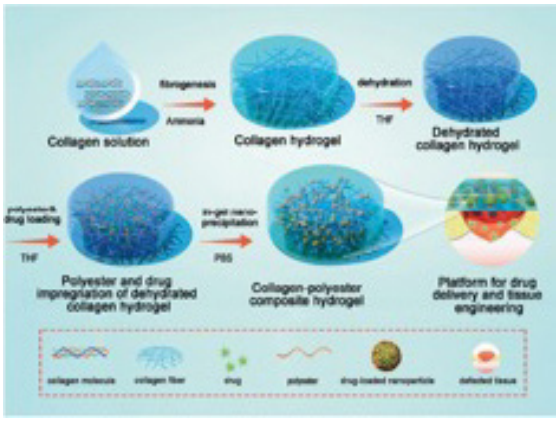
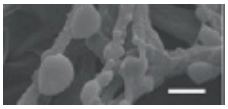


Figure
(Schematic diagram of fabrication of collagen-polyester composite hydrogels based on in situ nanoprecipitation process, which has promising applications in drug delivery and tissue engineering.)



Structure of collagen composites observed by SEM images exhibiting
the formation of polyesters nanoparticles along the collagen fibers.
Scale bar = 2µm

Since patches are expected to remain several days on the wound bed, one must ensure that they exhibit sufficient mechanical resistance. A collagen hydrogel consists of a network of micrometric fibrils swollen by an aqueous solvent. It is a typical «soft matter» system, at odd with usual «structural» materials (metals, concrete, ...). The INSP team has contributed with its expertise in the field of structural resistance of soft gels in physiological environment (see e.g. T. Baumberger, & O. Ronsin (2020). Environmental control of crack propagation in polymer hydrogels. Mechanics of Soft Materials, 2(1), 1-38) and characterized the mechanical properties of the patches.

A good surprize was that the composite structure, obtained by in situ precipitation of nanoparticles of the drug-loaded polyester, not only favored the controled release of spirolactone but also provided a mechanical strengthening of the gel with respect to rupture under traction. As far as applications are concerned, the multidisciplinary consortium gathered around our chemist colleagues has achieved the synthesis and characterisation of smart and fully biocompatible material class.

It can be taylored to adapt to several hydrophobic drugs and can be easily shaped to comply to any body part. In vivo studies are in progress. More basic physic studies are required to decypher the mechanism of strengthening by nanoparticles in theses fibrillar gels.

Reference

"Nanostructured Dense Collagen-Polyester Composite Hydrogels as Amphiphilic Platforms for Drug Delivery"
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