

Characterisation and in vitro validation of biopolymers for the treatment of iron overload

Iron metabolism is precisely regulated by a number of proteins that ensure its absorption, circulation, storage and recycling. When iron homeostasis is disrupted, various pathologies can occur, including iron deficiency anaemia and haemochromatosis resulting from iron overload. While haemochromatosis is a well-known chronic disease characterised by excessive iron levels, acute dysregulation of iron homeostasis has also been linked to a number of other pathologies, including sepsis stroke, acute kidney injury. Iron levels have even been proposed as an indicator of outcome in intensive care patients (Figure 1)

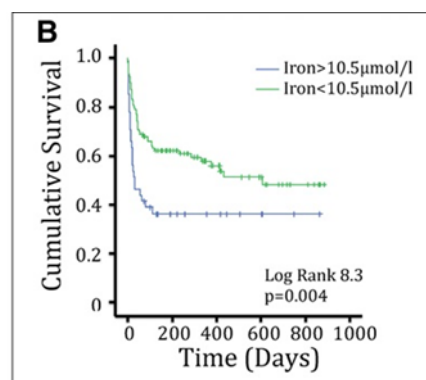


Figure 1: Survival and iron levels on admission of intensive care patient

ILM (François Lux, Fennec Team) has developed a biopolymer composed of chitosan functionalised by various chelates, including DOTAGA (M. Natuzzi et al., *Sci. Rep.*, 2021). Chitosan@DOTAGA has been associated with a haemodialysis system and has been approved by the French and Spanish authorities in clinical trials for the treatment of copper overload in Wilson's disease (NCT05917327). In parallel, ISA (Agnès Hagège, TechSep team) specialises in the development of analytical techniques to study chelation in biological media and to determine the size of nano-objects. A unique tool based on Taylor dispersion analysis coupled to ICP/MS has been developed to monitor the fate of nano-objects in media as complex as serum: biodegradation, association with proteins, etc. (L. Labied et al., *Anal. Chem.* 2021; L. Labied et al. *Anal. Chim. Acta*, 2021; A. Degaspero et al, *Talanta*, 2022).

Such chitosan-based biopolymers are currently being studied for the treatment of iron overload. A clinical trial in acute or chronic liver failure has been submitted to the French agency in October 2023. In this context, the characterisation of these biopolymers and the study of their iron chelation in competition with various biomolecules, including albumin, transferrin and small ligands such as citrate or haem, compared with traditional chelating agents such as deferiprone, is of prime importance. The use of such a coupling will enable unique characterisation of their chelation capacity, both in buffers and in biological fluids such as serum.

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Main ArchiFun theme involved:

- Host-pathogen interactions;
- Mechanisms of bacterial resistance and cancer onsets;
- Neurodegenerative and autoimmune diseases;
- Translational research in prevalent diseases;
- Physiology and ecology;
- Neurosciences and cognition.

