**Permethylated amino acids-grafted chitosan as potential wound dressing materials with advanced properties**

María Ines Erreaa,c, Gabriel Lombardoa,b,c, Bruna C. Dormd, Andrés G. Salvaye, Eliane Trovattid, Ezequiel Rossia,c

*a Instituto Tecnológico de Buenos Aires (ITBA), CABA (1437), Argentina.*

*b YPF Tecnología S.A., Berisso (1923), Argentina*

*c Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina*

*d Universidad de Araraquara – UNIARA, Araraquara (14801-340), Brasil*

*e Universidad Nacional de Quilmes, Dpto. de Ciencia y Tecnología, Bernal (1876), Argentina*

*Email:* [*merrea@itba.edu.ar*](mailto:merrea@itba.edu.ar)

Chitosan is a polysaccharide derived from the partial deacetylation of natural chitin, the second most abundant natural polymer globally. It is a cost-effective raw material, as it is sourced from the waste of the fishing industry. Due to its well-established biocompatibility, chitosan is considered an ideal candidate for a wide range of biomedical applications. Among these, its application as a wound dressing stands out, due to its inherent angiogenic, angiostatic, and antimicrobial properties. On the other hand, various α-amino acids have been reported to have specific benefits for traumatic wound healing.

In this context, four natural α-amino acids: glycine, L-arginine, L-glutamic acid, and L-cysteine, were grafted onto native chitosan (DA = 30%) through amide bonds formed between the amino groups of chitosan and the carboxyl groups of the amino acids, activated by EDC. Besides, given that the most common and unavoidable challenge for wound healing materials is the prevention and control of bacterial infections, and considering the recognized antimicrobial activity of quaternary ammonium salts, the amino acid-grafted chitosans were subsequently permethylated, resulting in four novel derivatives, which were chemically characterized by *FT*-IR, conductometric titration, Z-potential, TGA and 1H-NMR. The thiol group content of the cysteine-grafted chitosan was assessed by Ellman’s test [1]. Antibacterial studies against *Staphylococcus aureus* (Gram +) and *Escherichia coli* (Gram -) were also carried out [2].

All the permethylated products were transparent hydrogels insoluble in water in the whole range of pH, with fixed positive charges. The viscoelastic properties of the materials were assessed by oscillatory rheological experiments. Besides, swelling studies were also performed. The swelling kinetics of the materials was remarkably fast, reaching equilibrium in less than a minute. They all had the following remarkable characteristics: i) high-water absorption capacity (32-44 g H2O per g of polymer), ii) viscoelastic behavior at low deformations, iii) flexibility when subjected to deformations and iv) stability over long time scales.

All the permethylated derivatives successfully inhibited 100% of the growth of *S. aureus*, one of the bacteria that most frequently causes complications from skin wound infections. Moreover, they also exhibited higher antimicrobial activity against *E. coli* compared to native chitosan.

Referencias:

[1] A.H. Krauland, D. Guggi, A. Bernkop-Schnürch. Journal of Controlled Release, 2004, 95(3), 547-555.

[2] ASTM, Standard Test Method for Determining the Antimicrobial Activity of Antimicrobial Agents Under Dynamic Contact Conditions, 2020.