

## ENGINEERING OF INJECTABLE MULTIFUNCTIONAL POLYURETHANE-BASED HYDROGELS FOR THE ADVANCED TREATMENT OF HARD-TO-CLOSE WOUNDS

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To improve the hard-to-close wound treatment effectiveness and minimize side-effects on not-target tissues, the design of smart drug carriers locally releasing their payload in a controlled way is attracting widespread interest. The work was aimed at designing a multi-functional injectable delivery platform for wound treatment, overcoming the main limitations of traditional wound dressings, allowing shape-adaptability to defects through rapid post-injection gelation and controlled drug release kinetics. The aims were achieved by exploiting the versatile chemistry of polyurethane (PU) for the synthesis of multi-functional polymers and taking advantage of the alkaline characteristics of chronic wounds exudates when colonized by bacteria.

Specifically, PU amphiphilicity was ensured by selecting Poloxamer®407 as macrodiol; alkaline pH-responsiveness was introduced by plasma-treating PU powders to expose carboxyl groups (i.e.,  $5.3 \times 10^{18} \pm 0.6 \times 10^{18}$  units/g of polymer) while preserving PU molecular weight ( $M_n$ :  $29 \pm 1$  kDa) and hydrogel thermo-responsiveness (gelation within 7 minutes at 37 °C for 15% w/V concentrated systems). Hydrogel thermo-sensitivity was exploited to: (1) encapsulate drugs (e.g., Ibuprofen, 1 mg/mL) in the sol state, (2) tune hydrogel viscosity for its easy injection up to room temperature through G18 needles, (3) localize payload release, and (4) perfectly fill the wound cavity. On the other hand, hydrogel pH-responsiveness was explored to enhance drug release in the presence of alkaline exudate. Hydrogel was biocompatible according to ISO10993, and able to quickly change its internal pH (i.e.,  $\text{pH}_{\text{change\_5min}} = 3.76$  vs. 2) and release high drug amounts when incubated with alkaline buffer compared to an acid milieu (approx. 60% vs. 8% within 1 h).

### References

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