

# Poly(2-oxazoline)s: From a Potential Alternative for the "Gold Standard" Poly(ethylene oxide) to Tailor-Made Linear Poly(ethylene imine)s

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Poly(2-oxazoline)s (POx), which were already discovered in the 1960s, have been discussed as potential alternatives for poly(ethylene oxide) (PEG) as stealth polymers within the last few years.<sup>[1]</sup> They can easily be synthesized using the living cationic ring-opening polymerization (CROP) of 2-substituted 2-oxazolines, thus offering the advantage of a straightforward control of the degree of polymerization and the polymer architecture with low polydispersity index (PDI) values.<sup>[2]</sup> In a direct comparative study, PEGs and poly(2-ethyl-2-oxazoline)s (PEtOx) with pharmaceutically relevant molar mass were tested regarding cytotoxicity and hemocompatibility under standardized conditions.<sup>[3]</sup> Both types of polymers showed comparable properties in the therapeutically relevant dose range demonstrating the potential of PEtOx as an adequate candidate to substitute PEG with regard to biological compatibility. Furthermore, the acidic<sup>[4]</sup> and basic<sup>[5]</sup> hydrolysis of POx results in the formation of another pharmaceutical relevant polymer, linear poly(ethylene imine)s (LPEI). The living character of the POx polymerization technique allows the synthesis of defined LPEIs. In addition, various end groups in the LPEI backbone can be introduced during synthesis, such as hydroxyl-, primary amino-, and azido groups.<sup>[6]</sup> Nowadays, microwave irradiation is frequently used as alternative heating source accelerating not only organic reactions but also a wide range of polymerizations.<sup>[7]</sup> Exemplarily, the polymerization time of 2-oxazolines can be reduced to several minutes allowing a high-throughput approach for the synthesis of POx. In a similar manner it was shown that the acidic hydrolysis can be accelerated, which enables the production of LPEI in about 1 hour under optimal conditions.

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