

ABSTRACT

Treatments based on polymer therapeutics offer numerous advantages when compared to conventional treatments and other nanomedicine approaches. These include passive tumor accumulation and the ability to cross specific biological barriers. Furthermore, polymer conjugation of drugs offers additional advantages such as improved pharmacokinetics, multivalency, co-delivery of drugs at the desired ratio, and specific release/activation at the required site of action via the application of polymer-drug linkers that respond to physiological stimuli. One of the most important types of polymers suitable for drug delivery belong to polypeptide polyelectrolytes, mainly due to their biocompatibility and synthetic plasticity of side chain modification.

The merging of polyelectrolyte science with other branches of chemistry seems very promising; however, it still remains in an embryonic state. While the control of polyelectrolyte self-assembly remains a complicated task, research in this area may provide more advanced biocompatible systems with unique profiles of action and new materials with yet unknown properties. The combination of polyelectrolytes with supramolecular moieties represents an especially interesting research topic, with the potential to derive more complicated architectures.

This thesis is focused on the development of supramolecular-polyelectrolyte-based drug delivery systems with high degree of control over physicochemical properties, focusing mainly on shape and size. Several families of star-polyglutamates with cores of different hydrophobicity have been studied in depth in order to determine how the core structure and polyelectrolyte chain length affect self-assembly mechanism.

Once these correlations were defined, the most promising candidates were selected for preparation of two drug delivery systems consisting of either spherical or rod-like particles. Finally, conjugation of several drugs (fasudil and dinaciclib) as single agents or in combination through different responsive linkers were also performed; physicochemical properties and *in vitro* activity of the conjugates were studied in depth and *in vivo* experiments with selected conjugates are currently ongoing in a preclinically relevant orthotopic Triple Negative Metastatic Breast Cancer Model.