**Polysulfide as Active ‘Stealth’ Polymers with Additional Anti-Inflammatory Activity**

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**Abstract**: Since 40 years, poly (ethylene glycol) (PEG) has been the gold standard in biomaterials and drug delivery, because of its combination of chemical and biological inertness. However, the possibility of its breakdown under oxidative conditions and the demonstrated development of anti-PEG antibodies highlight the necessity to develop carriers based on materials with increased stability in a challenging biological environment. Here, we describe the synthesis of polysulfide via anionic ring-opening polymerization. In vitro, the synthesized polymer was characterized by low toxicity and a level of complement activation (in human plasma) and macrophage uptake slightly lower than PEG and poly (2-methyl-2-oxazoline) (PMOX), of a similar size. Importantly, and differently from PEG, on activated macrophages, the synthesized polymer showed a strong and dose-dependent ROS scavenging activity, which resulted in the corresponding reduction of cytokine production. Therefore, the results from these studies show that polysulfide is highly biocompatible and are potential candidates to be used as an alternative to PEG for various applications in nanomedicine.

**Keywords**: PEG, low toxicity, ROS scavenging, biocompatible

**Conference Title**: ICPP 2019 : International Conference on Pharmacy and Pharmacology

**Conference Location**: London, United Kingdom

**Conference Dates**: September 25-26, 2019