

Effects of metal cations on poly(methyl methacrylate)s solubility: a combined analysis by ATR-FTIR spectroscopy and computational approaches

F. Cilurzo¹, C. Gennari¹, F. Selmin¹, G. Vistoli¹

¹Università degli Studi di Milano-Dipartimento di Scienze Farmaceutiche "P. Pratesi"

Purpose.

Poly(methacrylic acid-methyl methacrylate)s, namely Eudragit[®]L and Eudragit[®]S, are pH-dependent polymers containing carboxylic groups which ionise and form salts (PMMs) in neutral to weak alkaline conditions. Despite their wide use in tablet coating, the interactions of PMMs with polyelectrolytes present in biorelevant media and luminal fluids have been scantily investigated. This work aims to elucidate possible interactions and their extent between dissociated PMMs and ions with different electronegativity, namely Ca⁺⁺, Zn⁺⁺ and Mn⁺⁺.

Methods.

The interactions between polymers and metal ions were analyzed by ATR-FTIR spectroscopy and *in silico* combining molecular dynamic simulations in water to explore the conformational profile of several oligomers with different Mw, taken as model of the polymers, with *ab initio* and semi-empirical calculations in gas phase to evaluate their complexes with metal ions.

Results.

The computational results were in good agreement with the experimental data in terms of spatial disposition of the bications with respect to PMMs as well as interaction strength. The carboxylate groups of PMMs coordinated to Ca⁺⁺ and Mn⁺⁺ as bidentate form and Zn⁺⁺ as unidentate ligand.

The extent of interactions was strongly dependent on ion electronegativity and the trend was fulfilled also by cross-linked complexes, but here the distribution of the energies was markedly different allowing the recognition of two clusters since Zn⁺⁺ and Mn⁺⁺ cross-linked complexes appeared vastly more stable than Ca⁺⁺ complexes. These different features are consistent with the precipitation of PMMs from 4% w/v solutions when MnCl₂ and ZnCl₂ were added. Globally, the reliability of computed PM6 semi-empirical energies suggests that the here reported study can be conveniently applied to larger sets of representative oligomers to realize a sort of virtual screening for the polymer solubility with metal ions.

Conclusion.

The investigated interactions between metal ions and fully deprotonated or partially protonated PMMs, suggested that the possible concomitant assumption of food supplements containing metal ions could affect the time required to crack the polymeric coating and, consequently, disintegrate the dosage form due to physical cross-linking.