



HAL
open science

pH-sensitive polymethacrylate derivatives Eudragit E100 & L100 nanoparticles preparation in aqueous medium

Fabrice Ofridam, E. Gagnière, Nouredine Lebaz, Denis Mangin, Abdelhamid Elaïssari

► To cite this version:

Fabrice Ofridam, E. Gagnière, Nouredine Lebaz, Denis Mangin, Abdelhamid Elaïssari. pH-sensitive polymethacrylate derivatives Eudragit E100 & L100 nanoparticles preparation in aqueous medium. 21st International Symposium on Industrial Crystallization, Aug 2021, Postdam, Germany. hal-03334747

HAL Id: hal-03334747

<https://hal.science/hal-03334747>

Submitted on 9 Nov 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

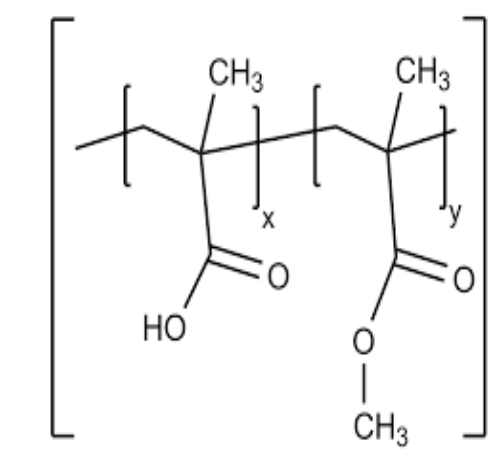
Introduction & Context

- Polymers in general and polymethacrylate derivatives are largely used in numerous applications including drug encapsulation and in controlled oral drug delivery [1].
- pH-sensitive polymers are macromolecules that contain potential ionizable groups or hydrolyzable compounds and which react to pH variation by undergoing structural and property changes such as surface activity, chain structure, conformation, solubility and configuration [2].
- The use of pH-sensitive polymers to prepare pH-sensitive capsules or particles has not been widely reported probably due to the few potential applications of pH sensitive environment.
- Various pH-sensitive carriers have been reported but the literature is free from any deep characterization of the used polymers.

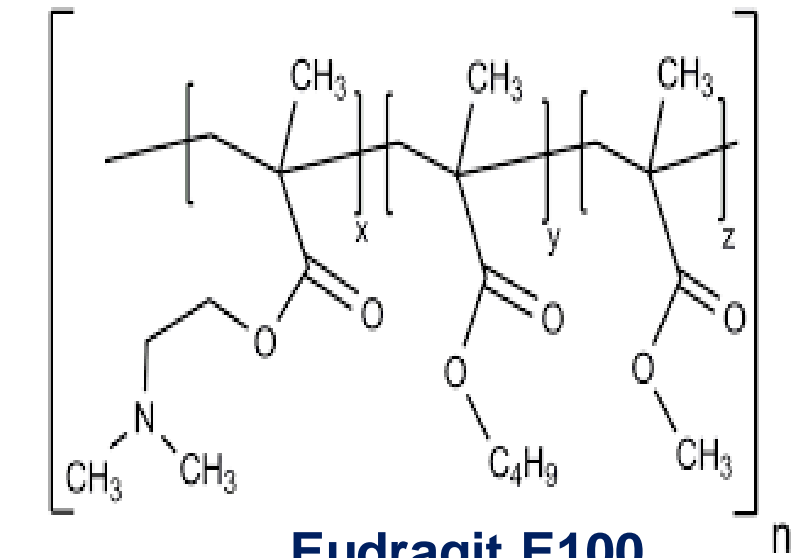
Objectives

- Investigation of the effect of different physicochemical parameters such as pH, salinity, polymer concentration, buffer concentration, and incubation time on the solubility and precipitation of two oppositely charged polymethyl methacrylate derivatives.
- Investigation of the effect of added secondary polymer or surfactant on the precipitation of both polymers
- Effect on size, size distribution, zeta potential and morphology of the particles.

Materials

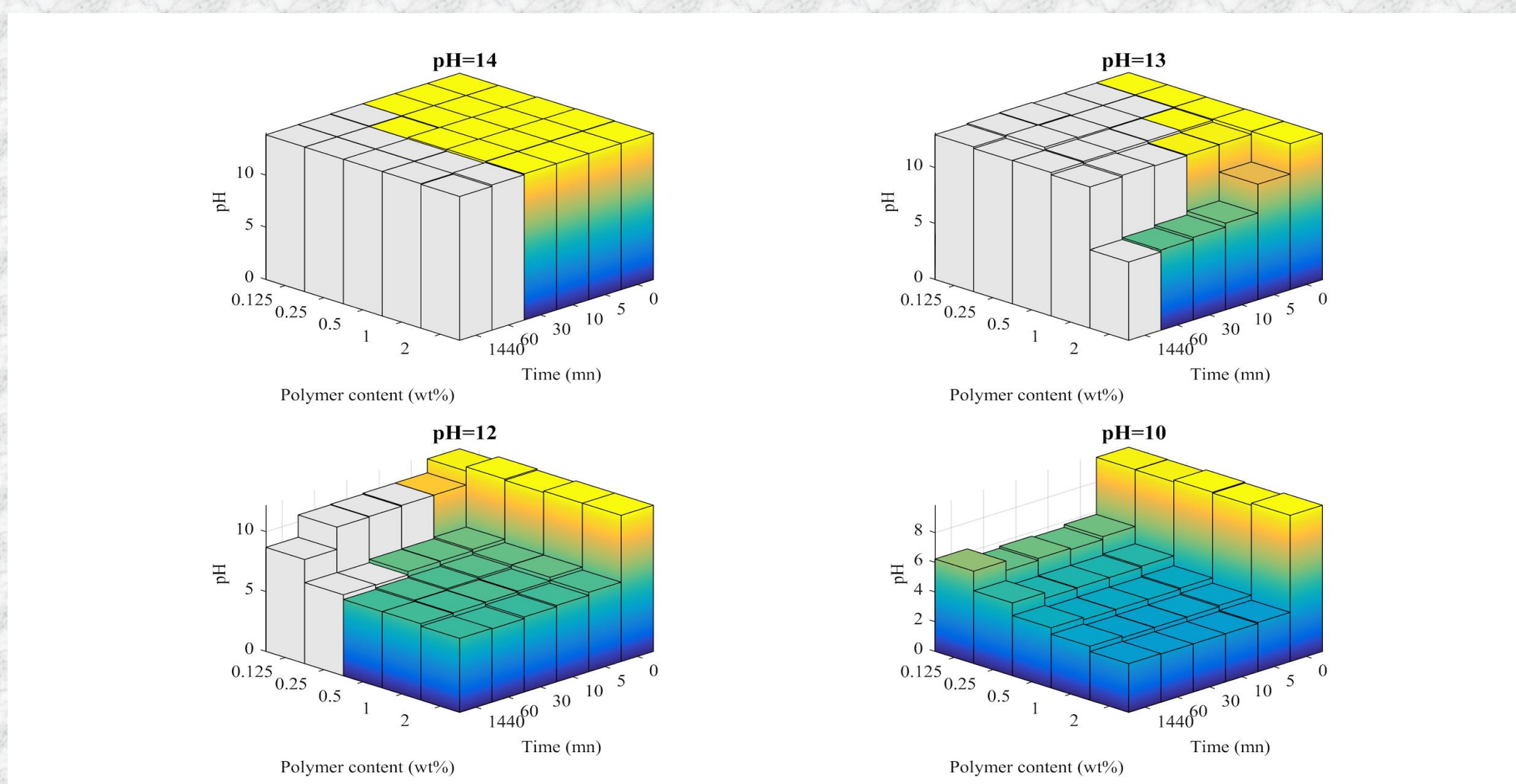


Eudragit L100
Copolymer of methacrylic acid and methyl methacrylate in a ratio 1:1; MW=125000 g/mol

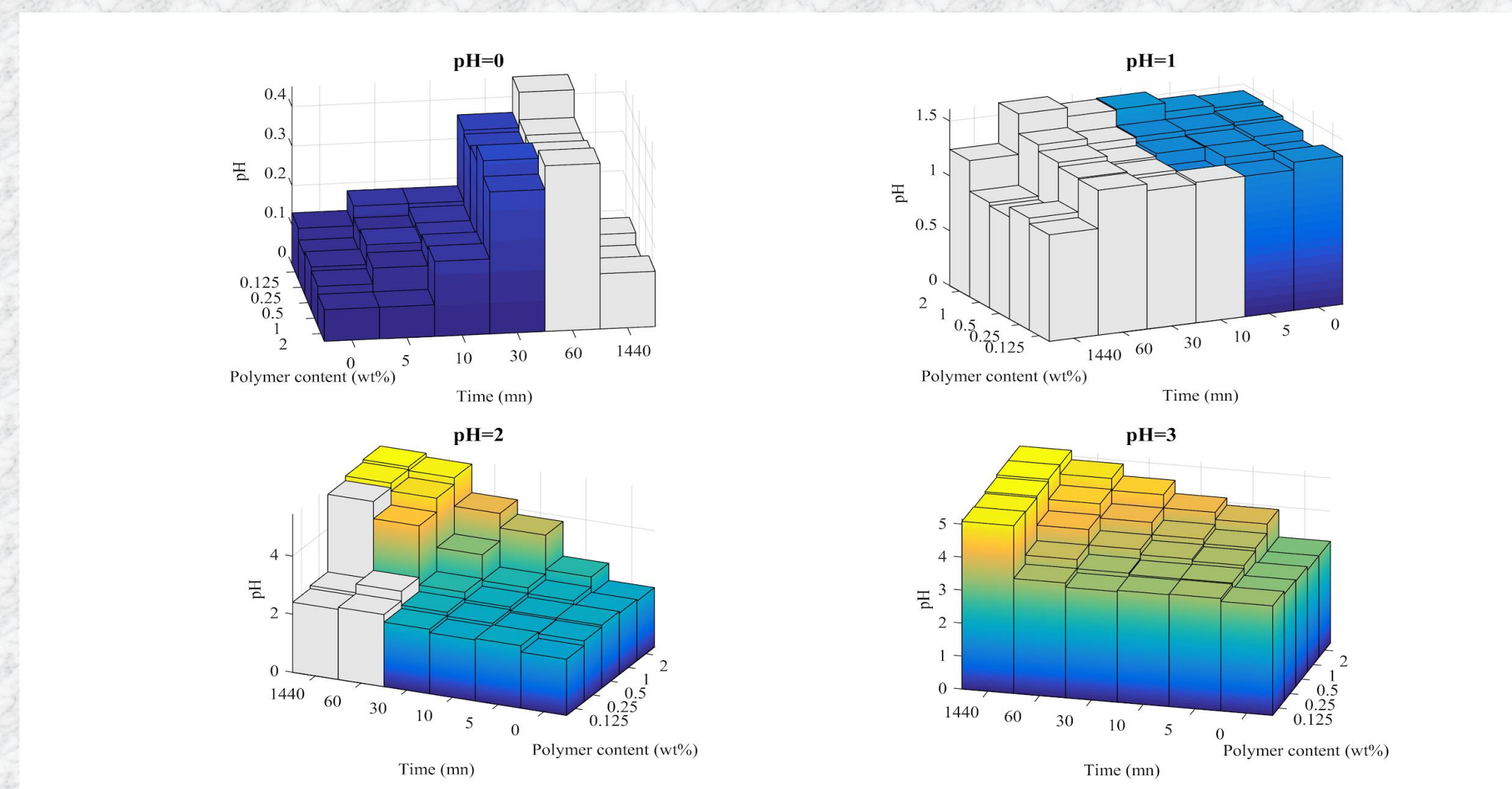


Eudragit E100
Copolymer of dimethyl aminoethyl methacrylate, butyl methacrylate, and methyl methacrylate tri-copolymer with a ratio of 2:1:1; MW=47000 g/mol

Solubilization domains



Solubilization of Eudragit L100 in NaOH medium as a function of polymer amount and time [3]



Solubilization of Eudragit E100 in HCl medium as a function of polymer amount and time [3]

- ✓ Grey bars on the 3D graphics refer to solubilized samples.
- ✓ L100 and E100 Eudragit polymers act respectively as polyacid and poly base
- ✓ In addition to the initial pH of the medium, the solubility conditions of the two investigated polymers are closely related to the polymer content and its incubation time.

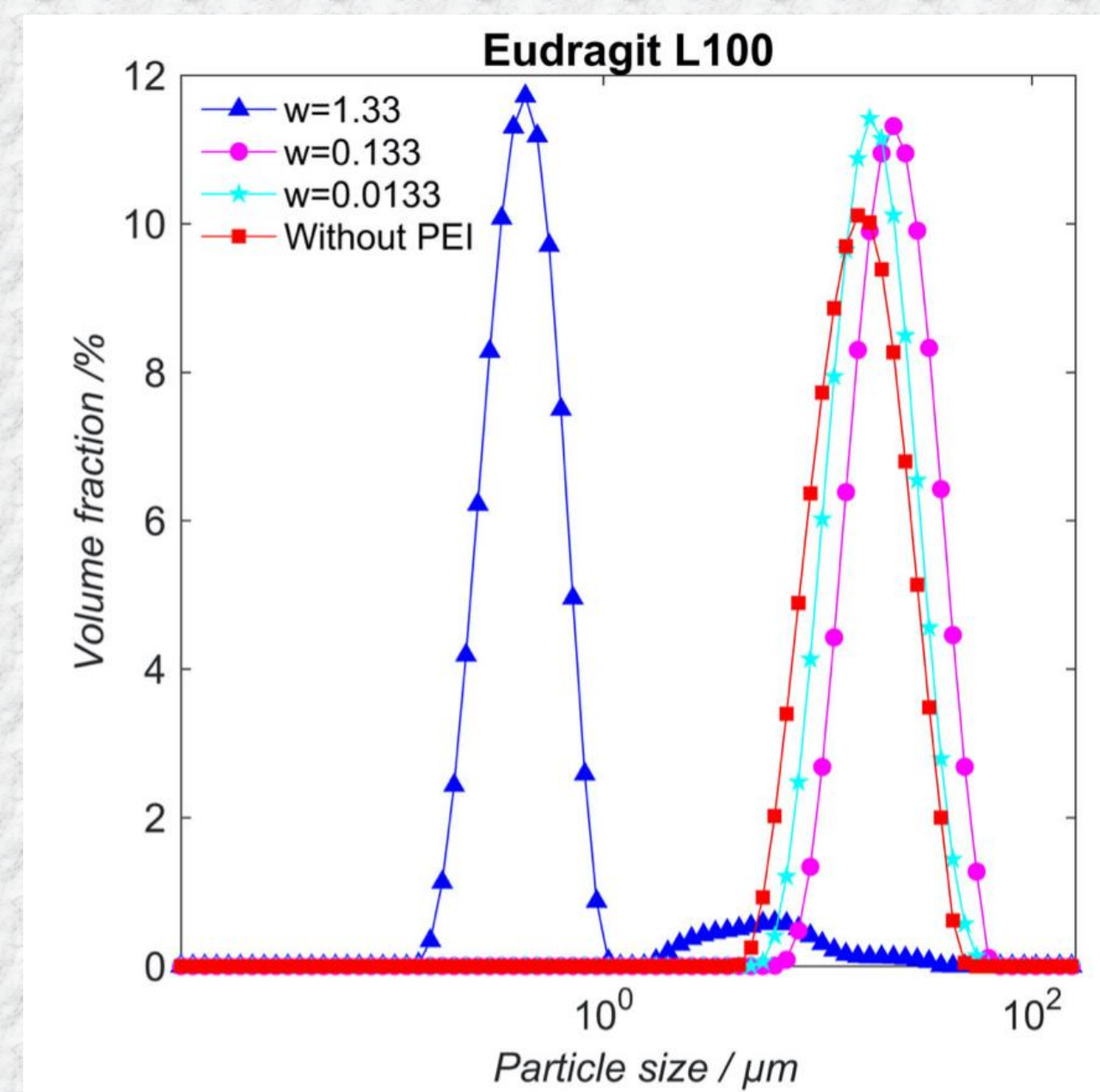
☛ Solubilization studies in buffer solutions confirms that Eudragit L100 was soluble above pH = 6.50 and Eudragit E100 up to pH = 5.20

☛ By pH titration, it was found that Eudragit L100 contains around 4.8 nmol/mol of carboxylic groups and Eudragit E100 contains around 8.5 nmol/mol of ammonium groups.

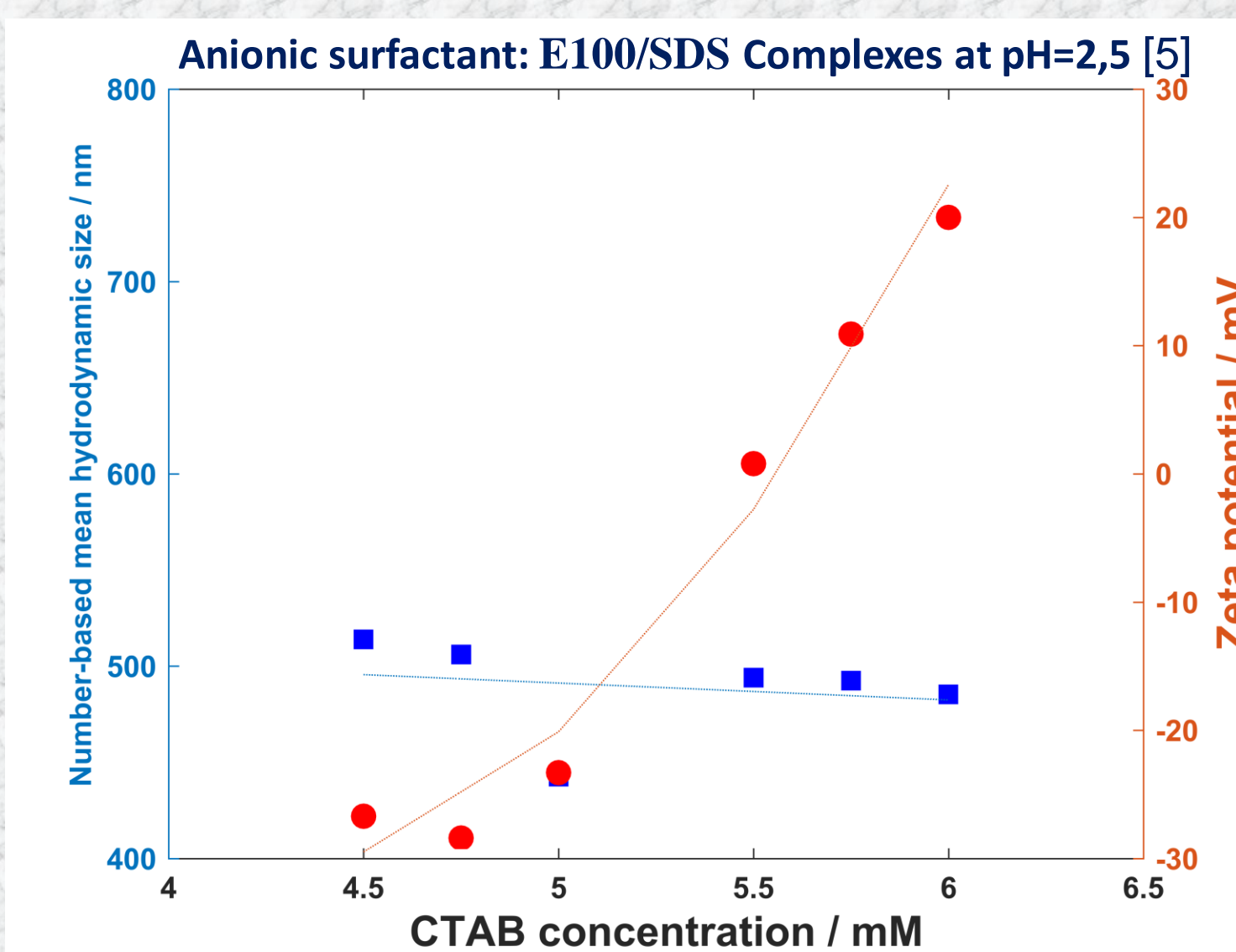
Polymers precipitation: Particle preparation and characterization

- Precipitated particles were micrometric in size with mean size between 30 and 50 μm , and large size distributions.
- TEM images show that all obtained dispersions are spherical polymer-based particles and highly polydisperse, which agrees with diameters deduced from diffraction light analysis.
- Stabilization of submicronic Eudragit particles was made through complexation either as Polyelectrolytes complexes (PECs) or Polyelectrolyte-Surfactant complexes (PSCs)

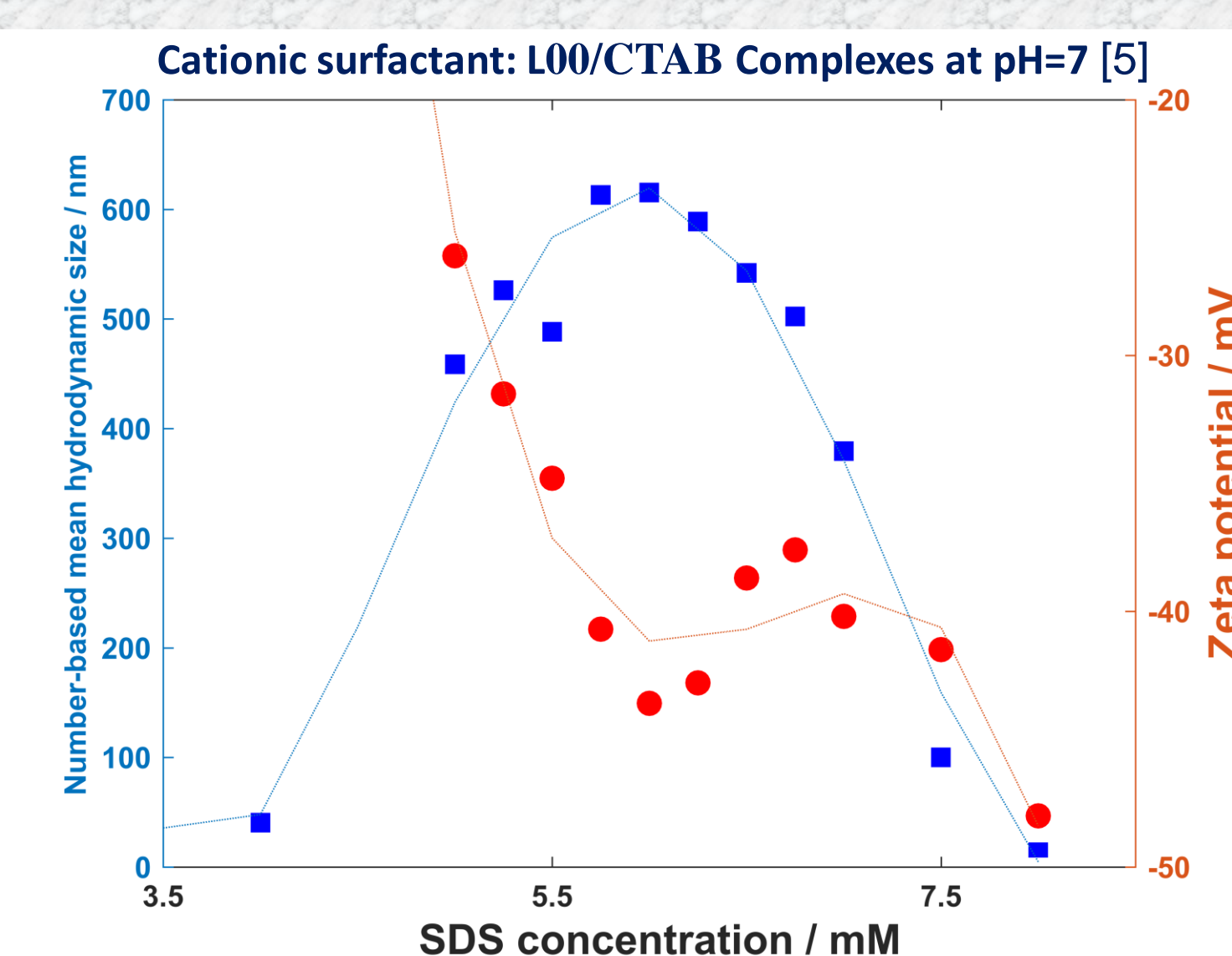
- Narrow size distribution around 200 nm was obtained when Eudragit L100 is precipitated in presence of polyethylenimine (PEI) with particles zeta potential found to be +45mV. No aggregation and no sedimentation occurred.
- Results suggest the formation of well defined spherical and monodisperse Eudragit particles stabilized by polyethylenimine.



Volume-based hydrodynamic particle size distribution of particle formed in presence of polyethylenimine (PEI) as a function of w ratio (mass ratio polyelectrolyte/Eudragit polymer) [4].



- Charges Screening between SDS 4 and 8 mM (SDS/E100 charge ratio between 0,4 and 0,8)
- Polymer precipitation as E100-SDS particles
- Solubilization of complexes in micellar regimen (> 8mM SDS)



- Charges Screening in micellar regimen between CTAB 4,5 and 6 mM (CTAB/L100 charge ratio between 0,3 and 0,4)
- Polymer precipitation as L100-CTAB particles
- Solubilization of complexes at high CTAB concentration (> 8mM SDS)

Conclusion & Perspectives

- Solubilization and precipitation domains of oppositely charged polyelectrolytes Eudragit L100 & E100 were clearly established
- Eudragit L100 & E100 micrometric particles were prepared in buffer solutions
- Stabilization of submicrometric Eudragit particles in aqueous solution was able through formation of PECs (200 nm spherical Eudragit L00-polyethylenimine particles) or PSCs (stable oppositely charged E100/SDS & L100/CTAB complexes dispersions).
- Eudragit particles preparation by acidification or basification in confined systems (using the two microemulsions process) and based on results obtained in aqueous solutions was not successful.
- It would be interesting to study the encapsulation efficiency of complexes prepared in aqueous solutions and their ability as potential nanocarriers.
- A better understanding of confined systems is needed at this point to continue the exploration of those systems for preparation of Eudragit L100 & E100 nanoparticles

References

- [1] Ch. N. Patra, R. Priya, S. Swain, G. Kumar Jena, K. C. Panigrahi, and D. Ghose, Jun. 2017, doi: 10.1016/j.fjps.2017.02.001.
- [2] G. Kocak, C. Tuncer, and V. Bütün, "2017, doi: 10.1039/C6PY01872F.
- [3] C. Sester, F. Ofridam, N. Lebaz, E. Gagnière, D. Mangin, and A. Elaissari, Oct. 2019, doi: 10.1002/pat.4780.
- [4] F. Ofridam, N. Lebaz, É. Gagnière, D. Mangin, and A. Elaissari, Feb. 2020, doi: 10.1002/pat.4856.
- [5] F. Ofridam, N. Lebaz, É. Gagnière, D. Mangin, and A. Elaissari, 2021, doi: 10.1002/pat.5093