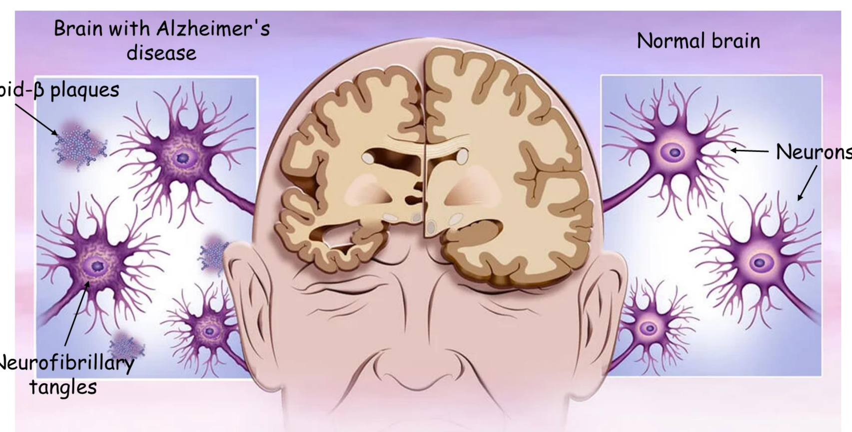
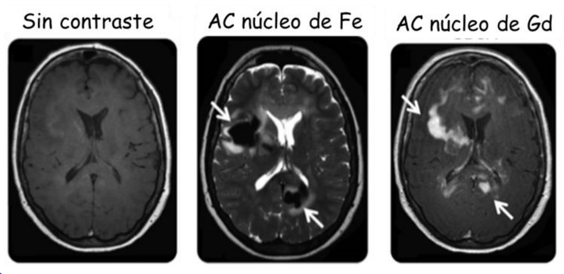
Design of nanostructured systems for detection of Alzheimer´s disease, an experimental and theoretical approach

Claudia González,[1] Marquiza Sablón,[1] Alicia Díaz,[2] Chryslaine Rodríguez [1]
[1] Neurochemistry Department, Cuban Neuroscience Center e-mail: claugc2309@gmail.com
[2] Laboratory of Bioinorganic, Faculty of Chemistry , University of Havana

Introduction

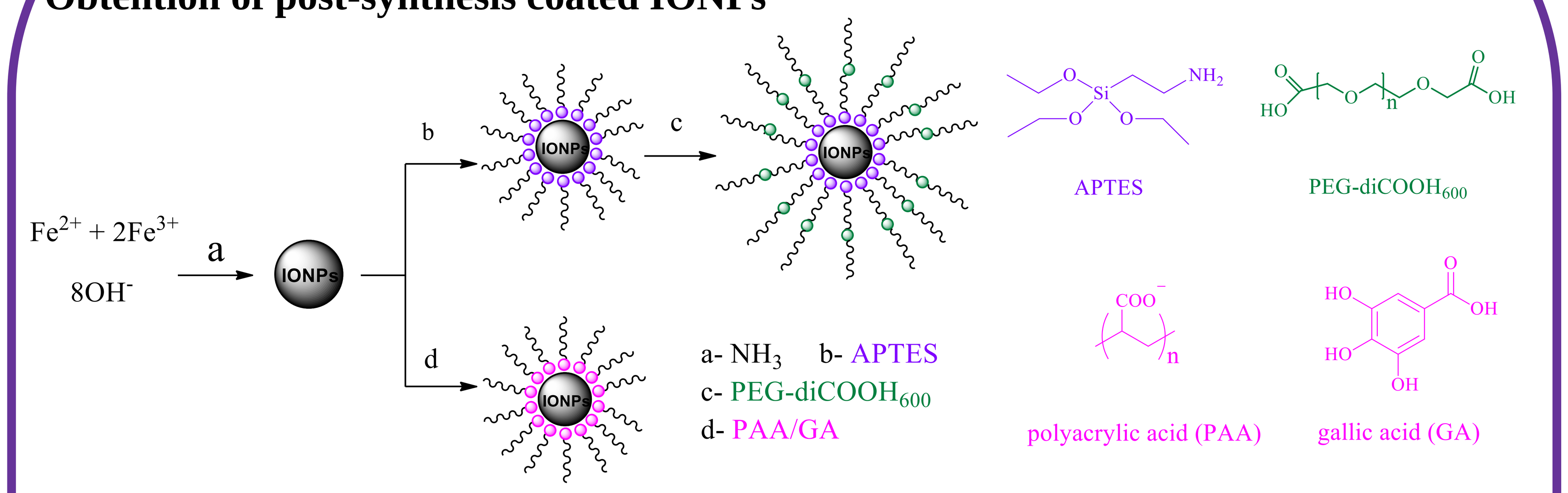
Magnetic Resonance Imaging (MRI) → Contrast Agents (CA) → Metallic core functionalized with molecules related to Aβ-plaques → Nanoparticles → Mn / Fe / Gd



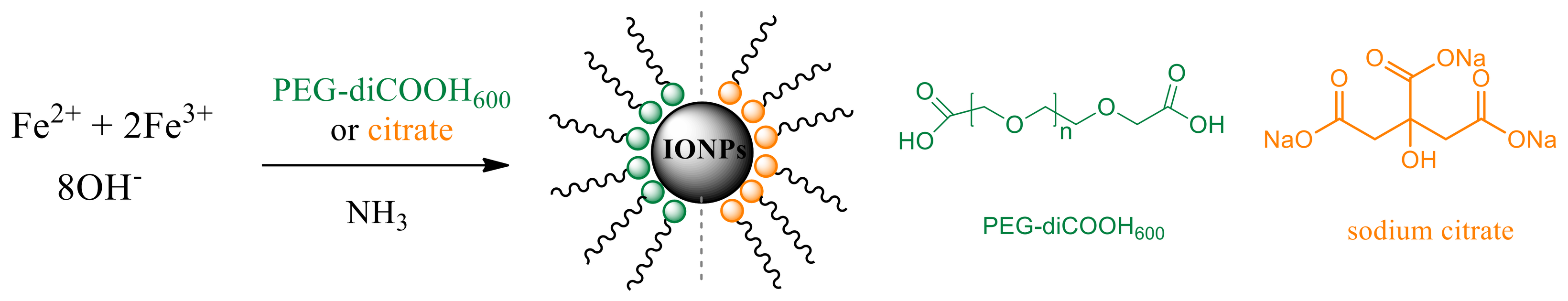


Experimental Section

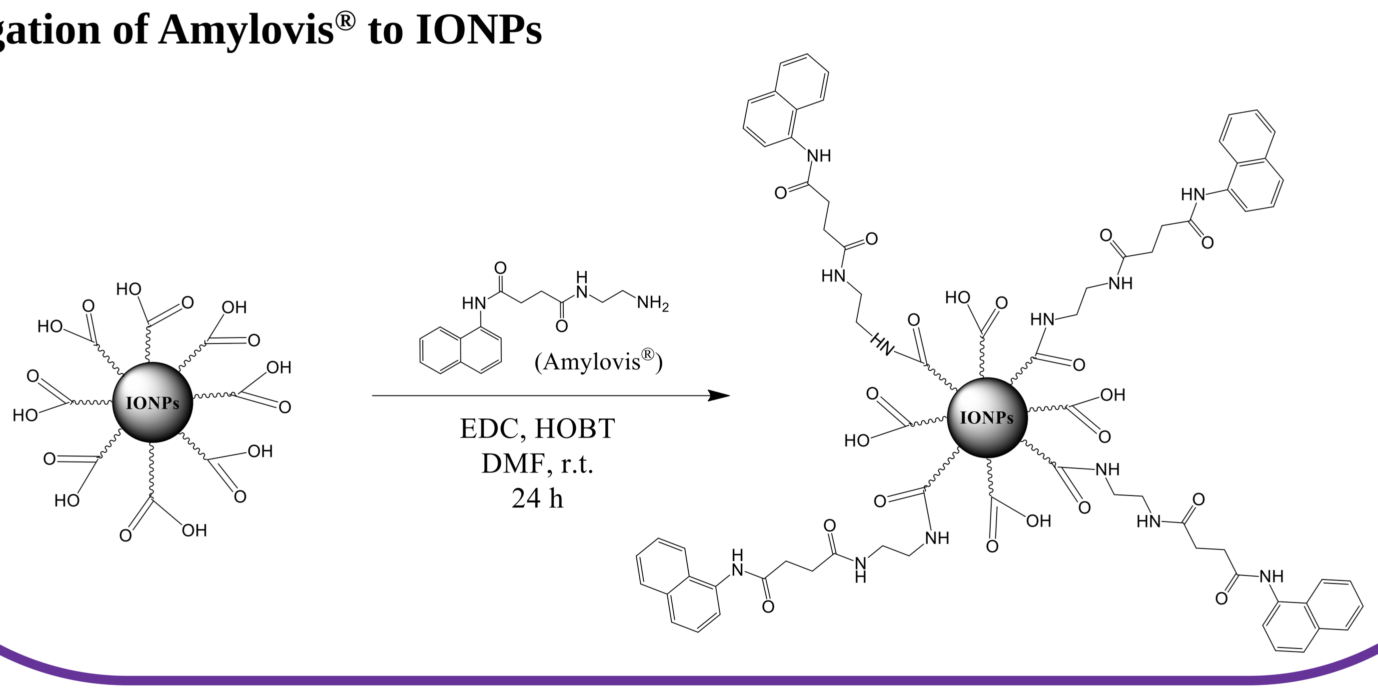
Obtention of post-synthesis coated IONPs



Obtention of *in situ* coated IONPs



Conjugation of Amylovis® to IONPs



Conclusions

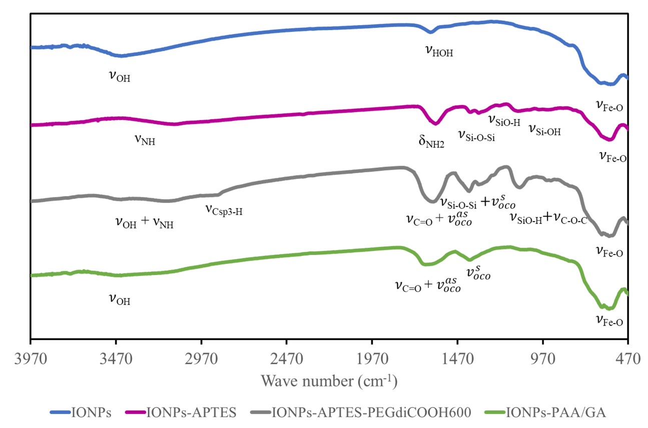
1. Using the coprecipitation method it was possible to obtain IONPs with the different coatings, which was verified by FT-IR.
2. The carbodiimide method allowed the conjugation of Amylovis® to nanoparticles that have free carboxylate groups.
3. IONPs@PAA/GA-Amylovis present physical-chemical properties suitable for their possible use as contrast agents for MRI.
4. The *in silico* evaluation by molecular docking shows that the conjugation of Amylovis® to the nanosystems does not affect its affinity for the βA_{1-42} peptide.

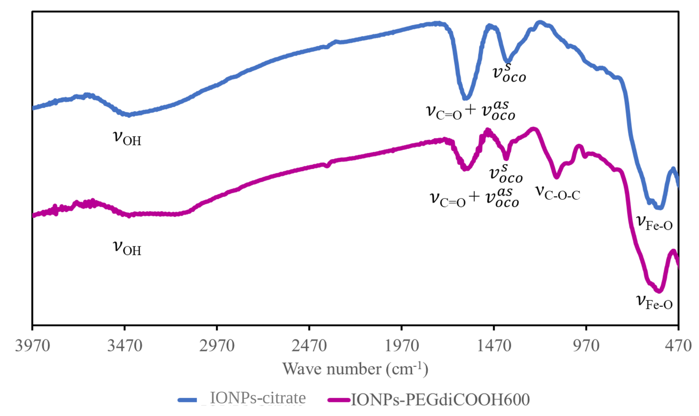
References

1. Sablón-Carrazana M, Fernández I, Bencomo A, et al. Zheng J, *ed. PLoS One.* 2015; 10(9): 135
2. Sosa-Acosta J., Silva JA, et al. *Colloids Surf, A Physicochem Eng Asp.* 2018; 545: 167-178.
3. Feng B, Hong RY, Wang LS, et al. *Colloids Surf, A Physicochem Eng Asp.* 2008; 328(1-3): 52-59.
4. Stanicki D, Boutry S, Laurent S, et al. *J Mater Chem B.* 2014; 2(4): 387-397.
5. Fahmy H, Abd T, Ali O, et al. *J of Biochem and Molecular Toxicology.* 2021; 35(3): 22671.
6. Iriarte-Mesa C, et al. *Colloids and Surfaces B: Biointerfaces.* 2019; 181: 470-479.
7. Lowry G, Hill R, Harper S, Rale A, et al. *Environ. Sci.: Nano.* 2016, 3, 953-956

Results and Discussion

Characterization of functionalized IONPs

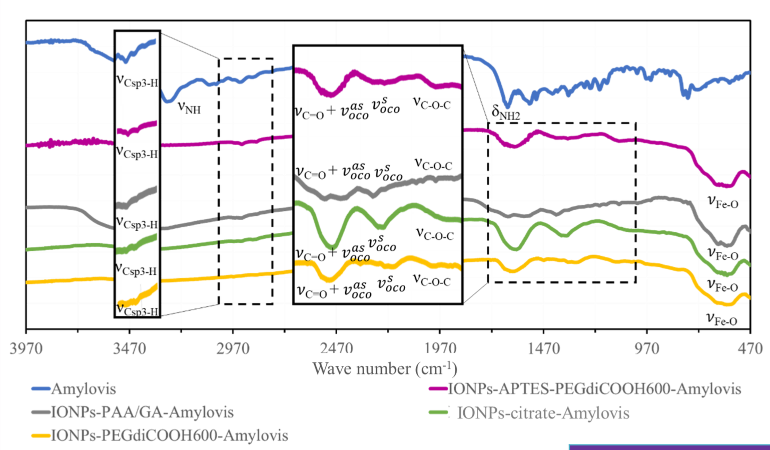


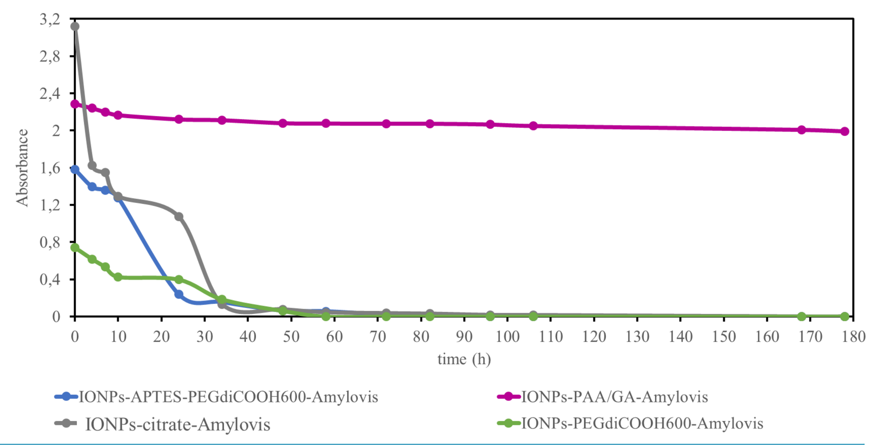


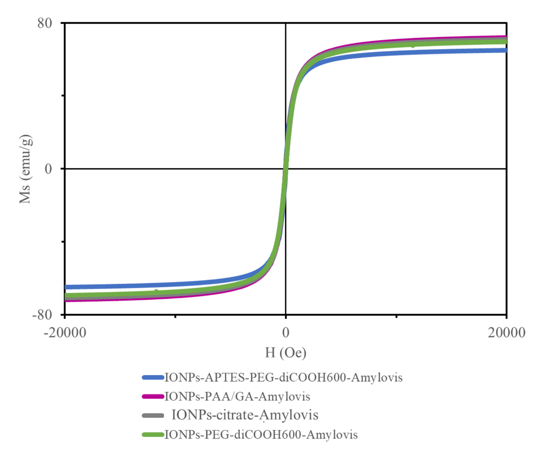
Nanoparticles	Hydrodynamic diameter (nm)	ζ Pot (mV)
IONPs	94	-21
IONPs@APTES	352	-15
IONPs@APTES-PEG-diCOOH$_{600}$	132	-18
IONPs@PAA/GA	75	-54
IONPs@citrate	89	-25
IONPs@PEGdiCOOH$_{600}$	112	-19

- The functionalization of IONPs with different coatings was confirmed by FT-IR.
- The analysis of the DLS profiles allows the hydrodynamic diameters to be determined and the Pot ζ values, measured by ELS, are a quantitative value that can be used as a stability parameter.

Characterization of IONPs conjugated to Amylovis®



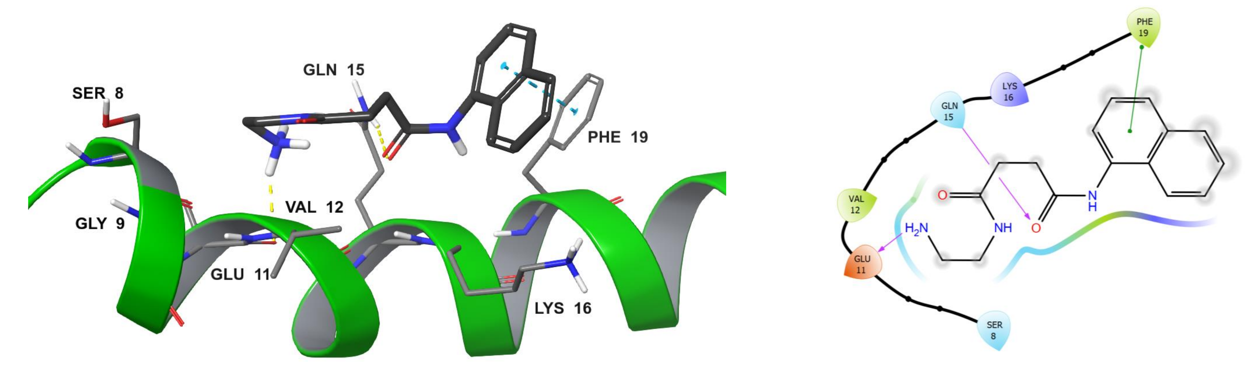




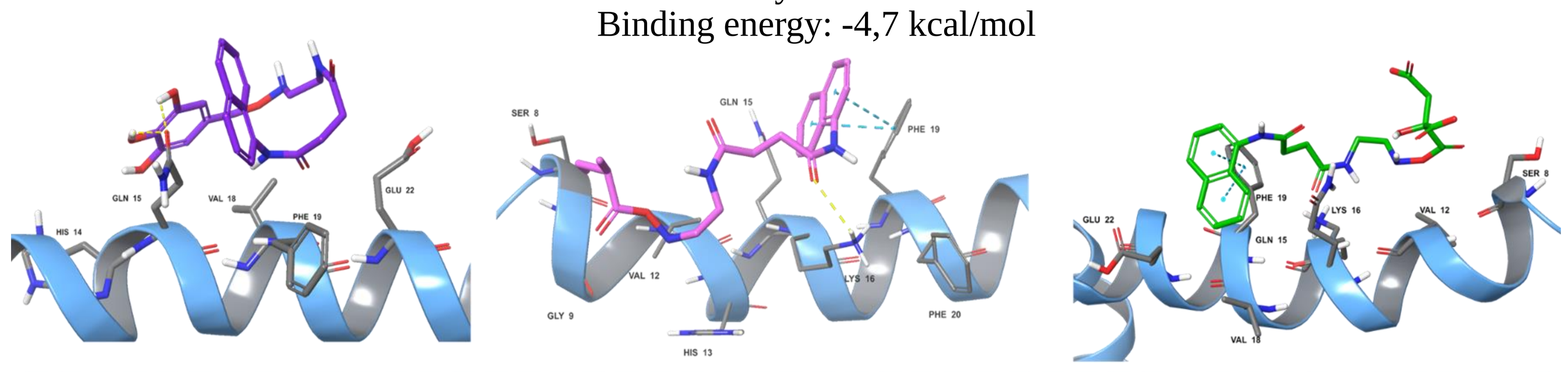
Nanoparticles	Hydrodynamic diameter (nm)	ζ Pot (mV)	Ms (300 K, emu/g)
IONPs@APTES-PEG-diCOOH$_{600}$-Amylovis	329	-12	65,09
IONPs@PAA/GA-Amylovis	170	-48	72,85
IONPs@citrate-Amylovis	229	-16	71,94
IONPs@PEG-diCOOH$_{600}$-Amylovis	272	-16	69,56

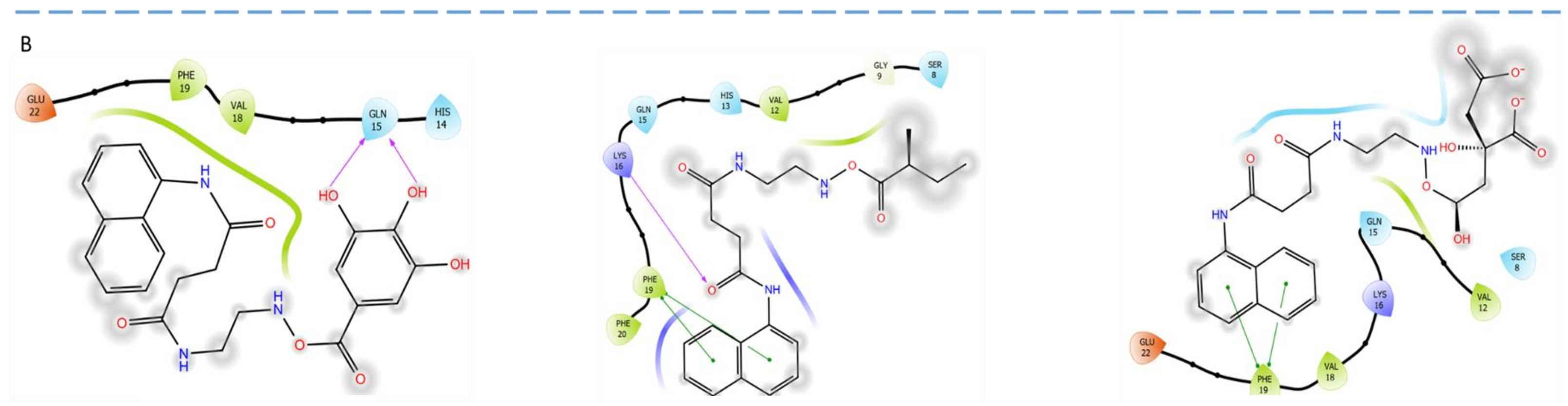
- Through the analysis of the DLS profiles, it was obtained that the only system capable of crossing the BBB was that of IONPs@PAA/GA-Amylovis.
- The temporal stability of the nanoparticles determined by UV-Vis and Pot ζ shows that the most stable system is that of IONPs@PAA/GA-Amylovis.

In silico evaluation of the affinity of the coatings for the βA_{1-42} peptide



Amylovis®
Binding energy: -4,7 kcal/mol





GA-Amylovis
Binding energy: -4,5 kcal/mol

PAA-Amylovis
Binding energy: -4,8 kcal/mol

citrate-Amylovis
Binding energy: -4,8 kcal/mol

- The in silico evaluation by molecular docking shows that the conjugation of Amylovis® to the nanosystems does not affect its affinity for the βA_{1-42} peptide.

The 9th International Electronic Conference on Medicinal Chemistry
01–30 November 2023 | Online