

Claudia González,<sup>1</sup> Marquiza Sablón,<sup>1</sup> Alicia Díaz,<sup>2</sup> Chryslaine Rodríguez<sup>1</sup>

<sup>1</sup> Neurochemistry Department, Cuban Neuroscience Center e-mail: claugc2309@gmail.com

<sup>2</sup> Laboratory of Bioinorganic, Faculty of Chemistry, University of Havana

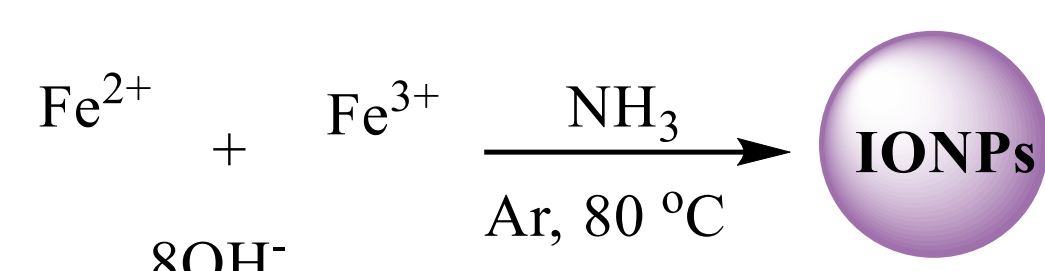
## Introduction

An early aggregation of amyloid plaques ( $\beta$ A) in the brain, principally composed of beta amyloid peptides, characterizes Alzheimer's disease (AD). Magnetic Resonance Imaging (MRI) helps visualize these structures with greater sensitivity and sharpness (resolutions). Still, it is necessary to contrast agents functionalized with compounds related to  $\beta$ A. The Cuban Neuroscience Center has developed a new family of naphthalene derivatives compounds called Amylovis<sup>®</sup>, to be used to diagnose AD through MRI. The use of contrast agents allows obtaining images with greater clarity. The most used contrast agents today in the clinic are based on metal oxide nanoparticles. The goal of this work is to synthesize, by coprecipitation method, iron oxide nanoparticles (IONPs) coated at first with (3-aminopropyl) triethoxysilane (APTES) and later with dicarboxylic polyethyleneglycol (PEGdiCOOH600), to be conjugated to Amylovis<sup>®</sup>, through the Steglich reaction. The values of the diameters of the IONPs@APTES@PEGdiCOOH600-Amylovis<sup>®</sup>, obtained by DLS, justify its use as a contrast agent.

## Experimental Section

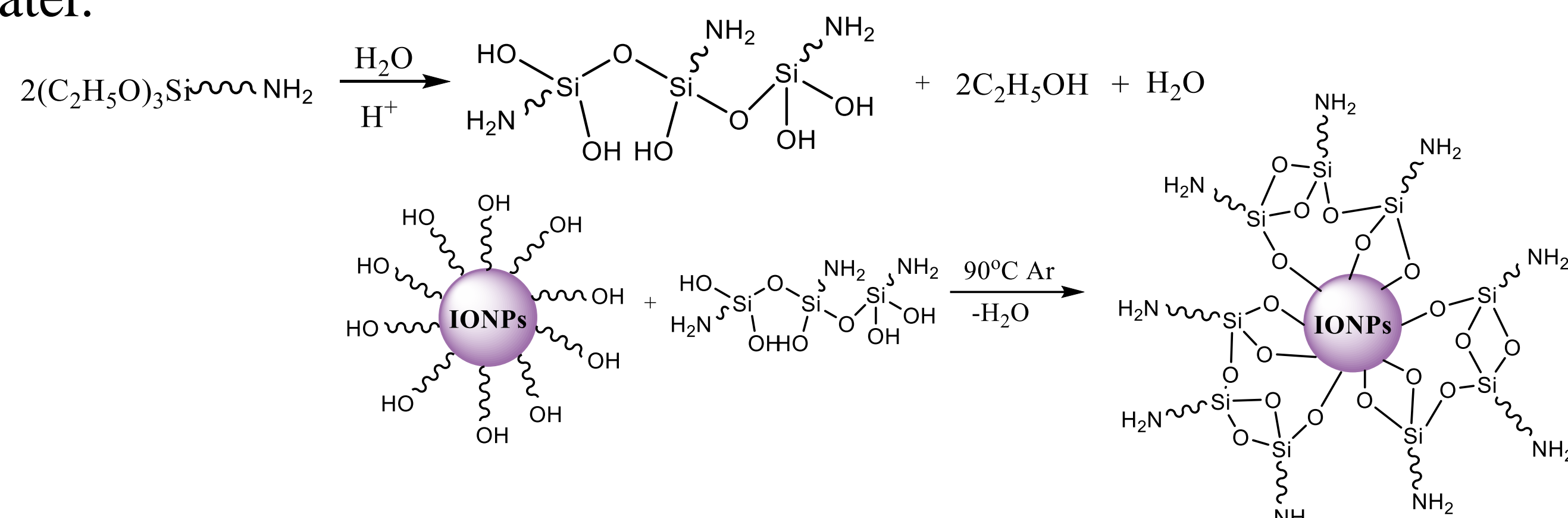
### Synthesis of IONPs by coprecipitation method

The IONPs were synthesized by coprecipitation, using  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$  and  $\text{Fe}_2(\text{SO}_4)_3$  as starting salts in a mixture of  $\text{H}_2\text{SO}_4$  (1M) and distilled water.



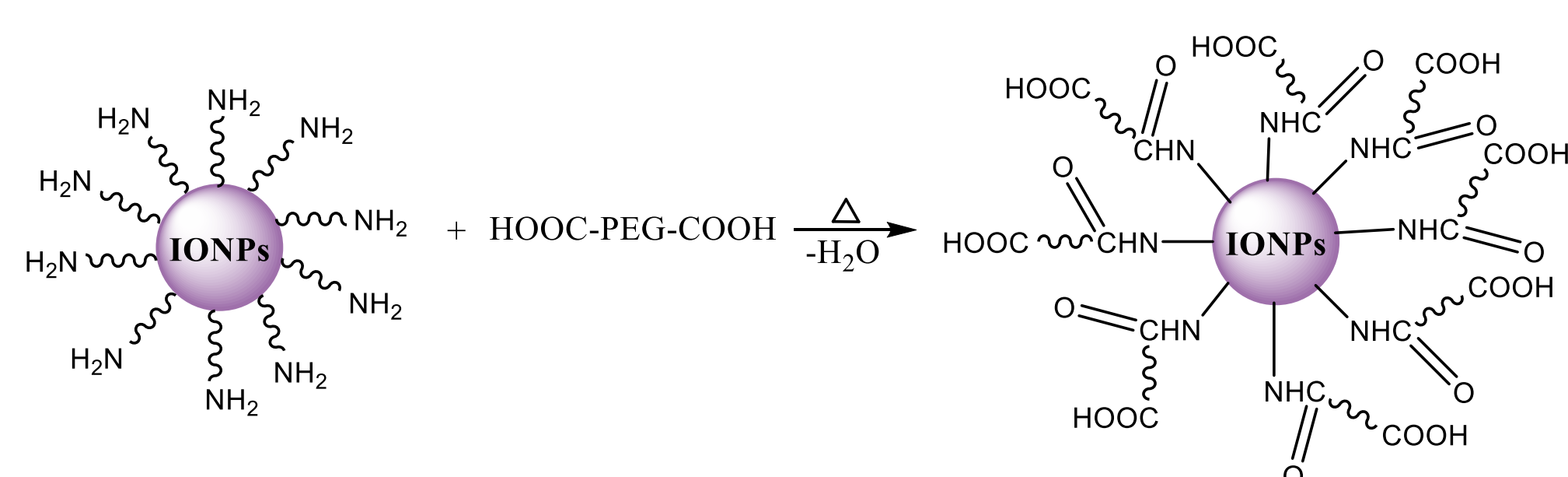
### Superficial modification of IONPs with APTES

For the superficial modification of the nanoparticles with APTES, the APTES is first hydrolyzed and then added to the IONPs dispersed in water.



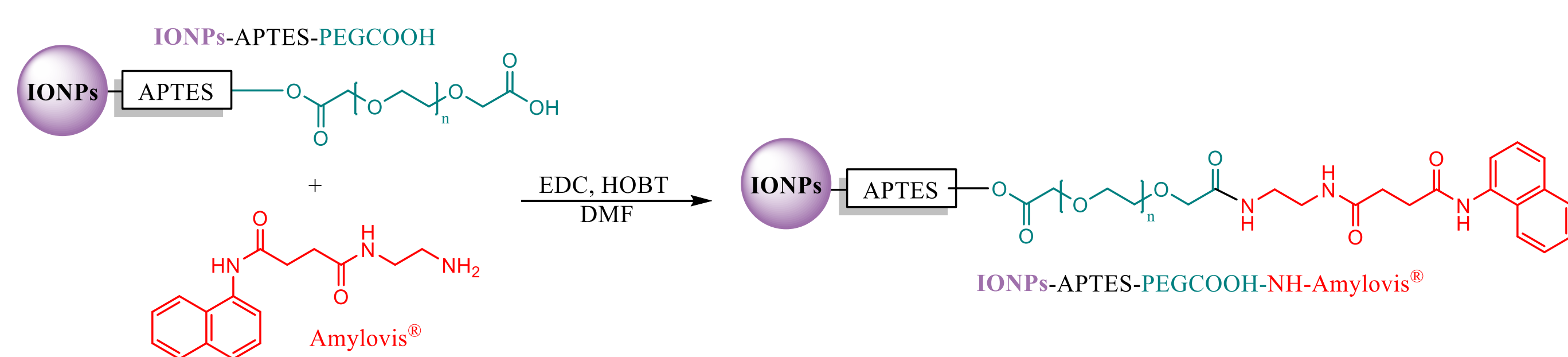
### Coating of APTES functionalized IONPs with dicarboxylic PEG

To synthesize diacid PEG functionalized IONPs-APTES, the amino-silane coated magnetite particles were mixed with the diacid PEG solution in a ratio of 1:2 and stirred under Ar atmosphere.



### Conjugation of Amylovis<sup>®</sup> to IONPs-APTES-PEG

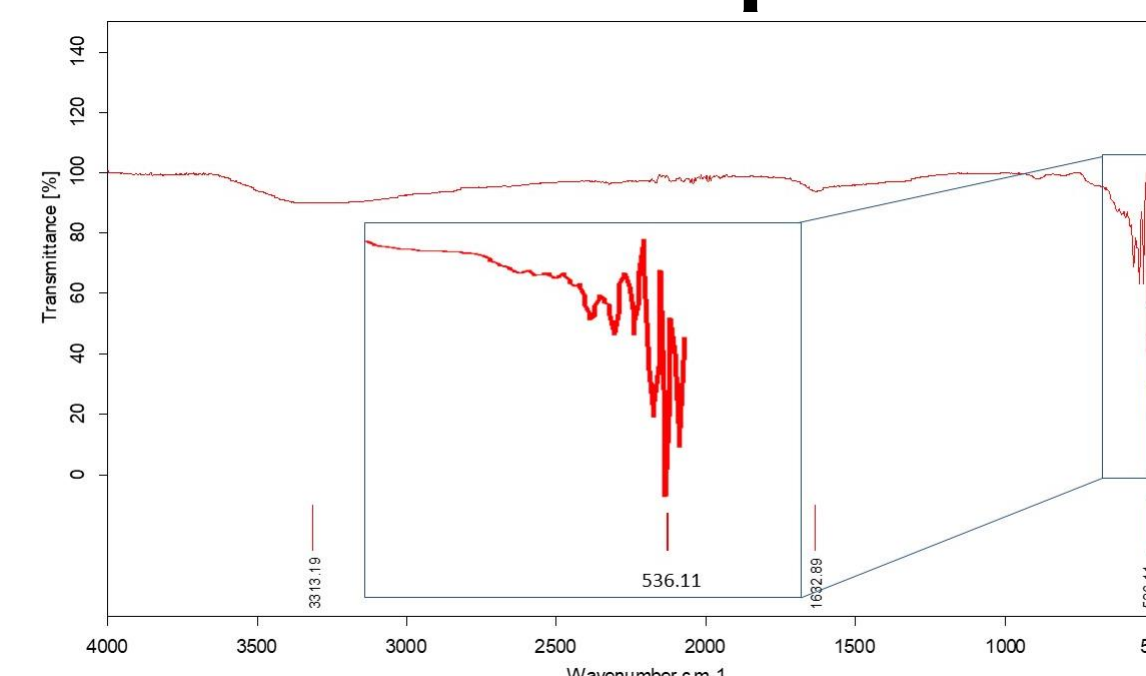
The conjugation reaction with Amylovis<sup>®</sup> was carried out by the Steglich reaction conditions. The aqueous dispersion of IONPs-APTES-PEG was diluted in DMF and the water was removed by rotary evaporation. To this solution, Amylovis<sup>®</sup>, HOBT and EDC previously dissolved in DMF was added consecutively.



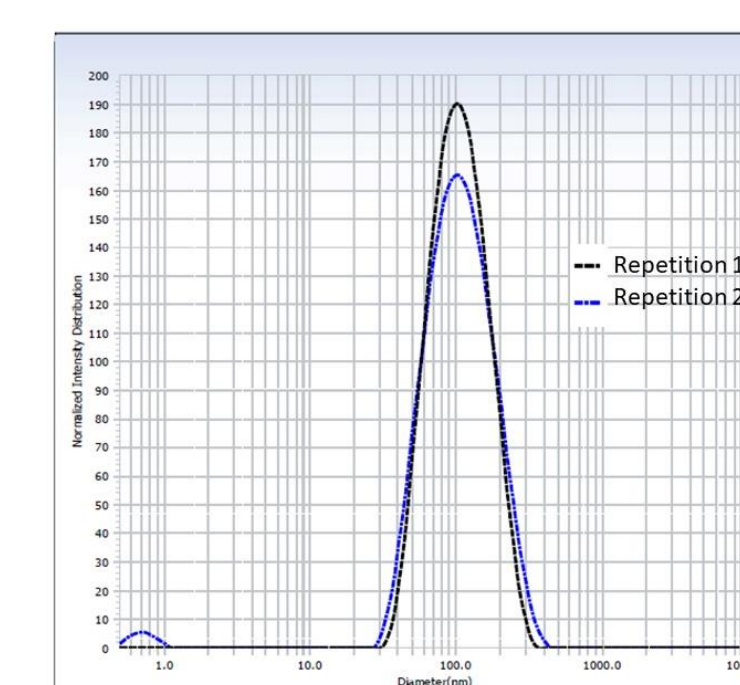
## Results and Discussion

### Synthesis of IONPs

#### FT-IR spectra



#### DLS



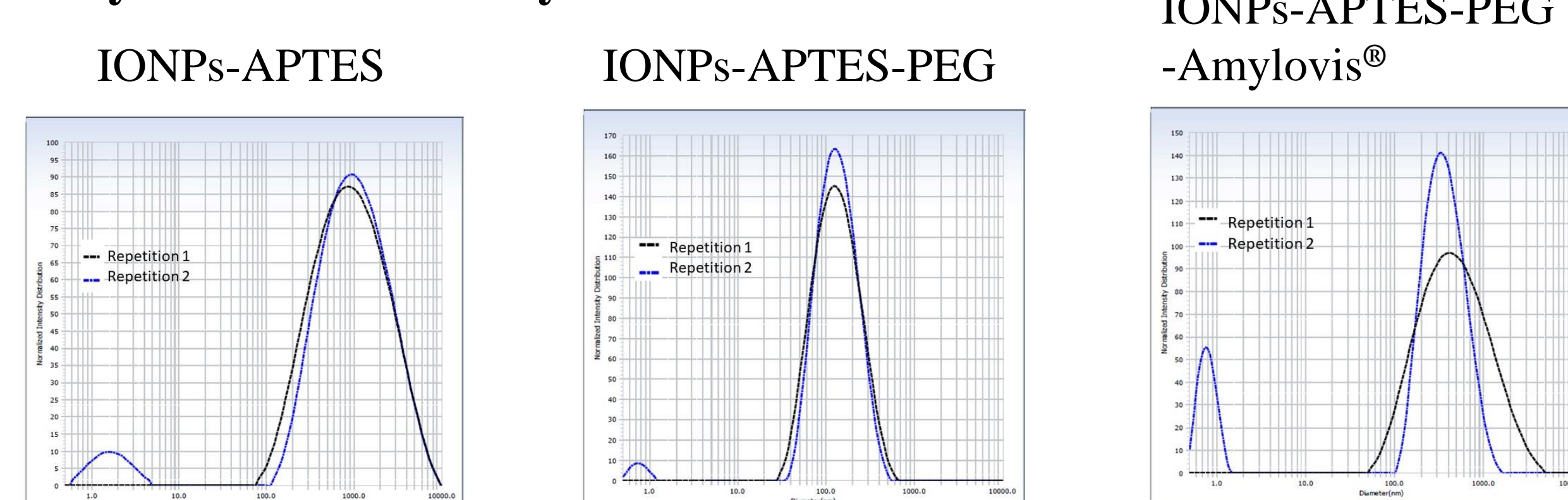
Average Hydrodynamic Diameter: 94.9 nm

Polydispersity Index: 0.16

In the FT-IR spectrum of the IONPs, three characteristic bands are observed towards 536, 1632 and 3313  $\text{cm}^{-1}$ . The first signal represents the Fe-O valence vibration, which suggests the presence of magnetite. The second signal corresponds to  $\delta\text{H-O-H}$  and the third signal, which appears as a broad band, to  $\nu\text{O-H}$ . In this way, the presence of water in the analyzed sample is corroborated, something that is characteristic of nanoparticles synthesized in aqueous medium.

### Superficial modification of IONPs

#### Hydrodynamic diameter by DLS



NPs	Average Hydrodynamic Diameter (nm)	Polydispersity Index
IONPs-APTES	812.6	0.33
IONPs-APTES-PEG	114.7	0.21
IONPs-APTES-PEG-Amylovis <sup>®</sup>	354.2	0.32

## Conclusions

According to the FT-IR results, it is possible to obtain IONPs by the coprecipitation method. The Steglich reaction allows obtaining IONPs conjugated to Amylovis<sup>®</sup>. Moreover, the nanoparticles obtained have adequate hydrodynamic diameter values to be used as a potential contrast agent for MRI.

## References

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