



Gold Nanoparticles as Scaffolds for the Multimerization of Iminosugars: New Multivalent Modulators of the Enzyme GCCase

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The enzyme β -glucocerebrosidase (GCCase) is a lysosomal glycosidase whose misfolding and dysfunction is involved in many pathological disorders, such as Gaucher Disease (a lysosomal storage disorder). A therapeutic strategy for restoring the GCCase activity is based on the use of Pharmacological Chaperones (PCs), molecules able of binding and stabilizing the tertiary structure of the enzyme [1].

Recent studies showed that *N*-alkylated 3,4,5-trihydropiperidines (red moiety **1** in Figure 1) are promising PCs for GCCase (1.25-fold recovery GCCase activity at 100 μ M) [2]. Moreover, the multimerization of **1** in a trimeric dendron has shown a significant enhancement in the PCs activity (1.25-fold recovery GCCase activity at 10 μ M) [2].

Gold nanoparticles (AuNPs) have already been used as scaffolds for the multimerization of iminosugars and sugars, leading to biocompatible and water dispersible systems and guaranteeing the possibility of the simultaneous grafting of different thiol-ending ligands in a controlled manner [3].

In my project, I employed for the first time AuNPs as scaffolds for the multimerization of dendronic *N*-alkylated 3,4,5-trihydropiperidine. After the synthesis and characterization, I performed preliminary *in vitro* tests demonstrating the binding affinity of the AuNPs towards GCCase and their ability of stabilizing the tertiary structure of GCCase against thermal denaturation.

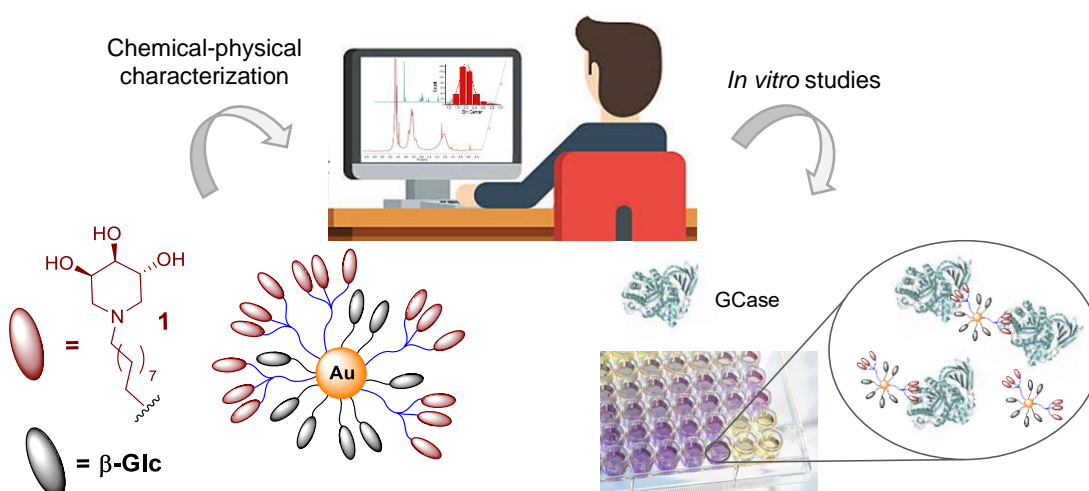


Figure 1: Graphical abstract.

[1] D. M. Pereira et al., *Chem. Sci.* **2018**, 9, 1740-1752

[2] M. Martinez-Bailén et al., *Pharmaceuticals* **2022**, 15, 823

[3] M. Marradi et al., *Chem. Soc. Rev.* **2013**, 42, 4728-4745.