Universidad Autónoma de Baja California

“System of fluorescent nanogels functionalized with glucosamine capable of crossing the BBB”

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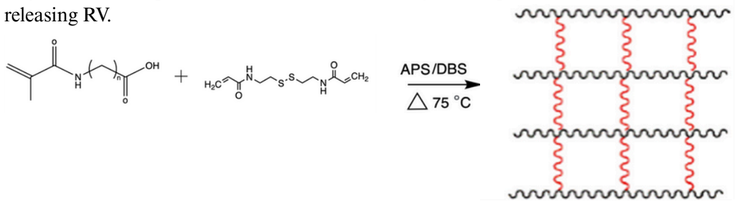
BACKGROUND

With the diproportionate growth of the elderly population, the need for treatments prevent cognivite and neurodegenerative condition associated with aging is also increasing. Nutrauceutical options that have shown proven efficacy in protecting against oxidative damage. However, their therapeutic use is limited due to their low bioavalibility and limited access to the brain, primarily because of they have poor permiability across the Blood- Brain Barrier (BBB). And important example is Resveratrol (RV).

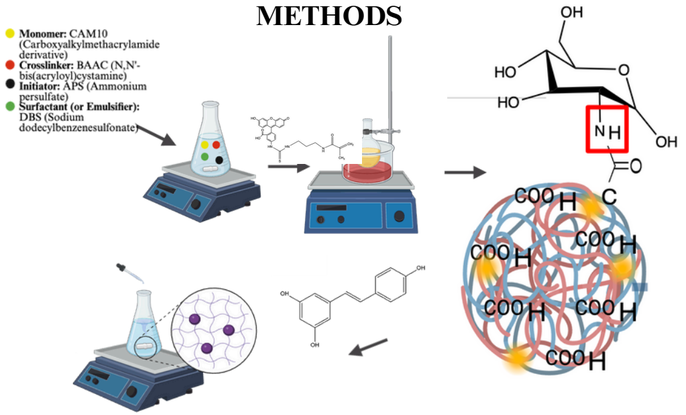
In this study, we propose the use of CAM nanogels (NG) loaded with RV and functionalized glucosamine (GLSM), aiming to contribute to the development of advanced of drug delivery system targeted to the brain.

Object: To develop a GLSM-funtionalized NG system capable of crossing the BBB and releasing RV.



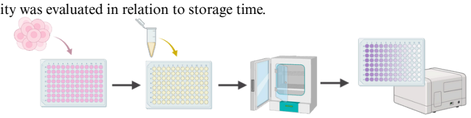
- Carboxyalkylmethacrylamide (CAM10) monomer was synthesized from 11-undecanoic acid via Schotten-Baumann reaction. A flouorescent monomer (Fluorescein metacrylamide) was also synthesized for NG labebeling. Both monomers wer structurally characterized by FT-IR spectroscopy.
- NG and fluorescent NG (NGF) were prepared by emulsion polymerization using CAM10 and a crosslinked with N,N’-bis(acriloil)cystamine (BAAC). Resulting NG were characterized by FT-IR, ^{1}H NMR, dynamic light scattering (DLS), and zeta potential.
- Surface funtionalization was performed using glucosamine (GLSM) via amidation reactions. The success of functionalization was confirmed by FT-IR, ^{1}H NMR, DLS, zeta potential and thermogravimetric analysis (TGA).

METHODS



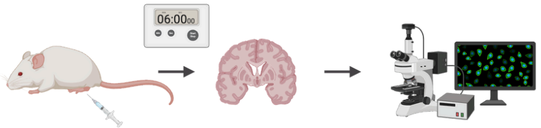
In vitro assays

- Redox-triggered degradation of NG was evaluated under different glutation (GSH) concentrations and exposure times.
- RV loading experiments were performed to determine encapsulation efficiency, folowed by release assays under simulated neuronal conditions to assess release kinetics and mechanisms.
- NG stability was evaluated in relation to storage time.

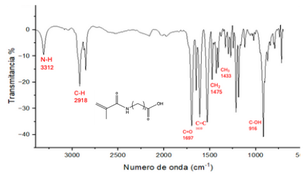


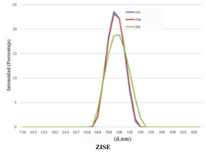
In vivo assays

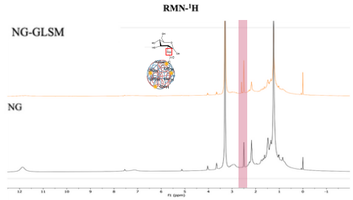
- NG’s brain uptake was assessed in CD1 mice through histological and fluorescence microscopy analyses.

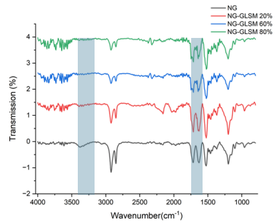


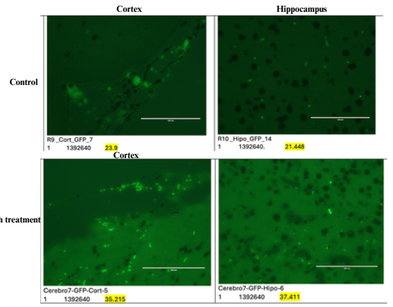
RESULTS AND DISCUSSION

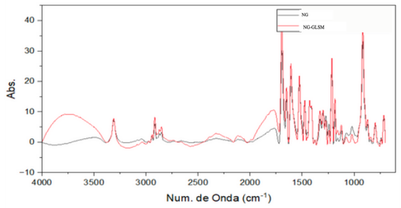


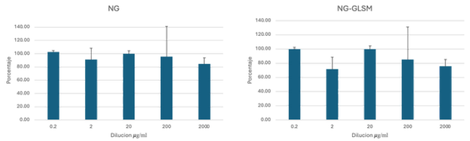


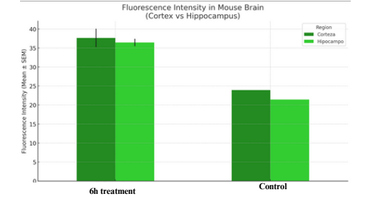












Conclusion and future work

The successful functionalization of the NGs with GLSM significantly improved their colloidal stability over time in aqueous media, maintaining homogeneity and preventing aggregation. *In vivo* fluorescence imaging revealed higher signal intensity in the cortex and hippocampus 6 hours post-administration, suggesting enhanced interaction with brain tissue.

In addition, *in vitro* release studies under redox conditions demonstrated that GLSM-functionalized NGs respond to glutathione exposure by releasing resveratrol (RV) in a controlled and concentration-dependent manner, consistent with the expected degradation of disulfide-crosslinked networks.

These findings highlight the potential of GLSM as a biocompatible functional ligand that contributes to brain-targeted delivery and redox-responsive release.

Based on these promising results, future work will involve functionalization with transferrin (TF), aiming to further improve nanogel penetration across the blood-brain barrier and enhance site-specific therapeutic delivery to the central nervous system.

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