Rational development of a novel hydrogel as a pH-sensitive controlled release system for nifedipine

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This work depicts the rational development (in-silico design, synthesis, characterization and in-vitro evaluation) of polyvinyl alcohol hydrogels (PVAH) cross-linked with maleic acid (MA) and linked to ?-cyclodextrin molecules (? -CDPVAHMA) as systems for the controlled and sustained release of nifedipine (NFD). Through computational studies, the structural blocks (PVA chain + dicarboxylic acid + ?-CD) of 20 different hydrogels were evaluated to test their interaction energies (?E) with NFD. According to the DE obtained, the hydrogel cross-linked with maleic acid was selected. To characterize the intermolecular interactions between NFD and ?-CDPVAHMA, molecular dynamics simulation studies were carried out. Experimentally, three hydrogel formulations with different proportions of ?-CD (2.43%, 3.61% and 4.76%) were synthesized and characterized. Both loading and release of NFD from the hydrogels were evaluated at acid and basic pH. The computational and experimental results show that ?-CDs linked to the hydrogels were able to form 1:1 inclusion complexes with NFD molecules. Finally, ?-CDPVAHMA-3 demonstrated to be the best pH-sensitive release platform for nifedipine. Its effectiveness could significantly reduce the adverse effects caused by the anticipated release of NFD in the stomach of patients.

Crosslinking

Cyclodextrin

Drug release

Interaction energy

Molecular simulation

Nifedipine

Swelling

Thermogravimetric analysis

Carboxylic acids

Crosslinking

Cyclodextrins

Drug products

Hydrogels

Molecular dynamics

Molecules

pH sensors

Pyridine

Swelling

Synthesis (chemical)

Targeted drug delivery

Thermogravimetric analysis

Computational studies

Controlled release systems

Drug release

Interaction energies

Intermolecular interactions

Molecular dynamics simulations

Molecular simulations

Nifedipine

Controlled drug delivery