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Colloidal nanomedicines with prolonged release based on interactions involving aromatic groups

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Polymeric drug delivery systems in the form of nanoparticles (NPs) are advantageous for controlled administration of drugs into the body, helping to achieve desired target tissues, prolonging drug release and providing stable drug concentration in blood [1]. Among the different drugs, it deserves special attention the vast number of active molecules accomplishing these four requisites: possessing aromatic residues, bearing ionizable groups, showing low molecular weight (≤ 500 Da), and being water-soluble [2]. Unfortunately, following traditional nanoencapsulation strategies, these drugs are hardly encapsulated [3-5]. Interestingly, this kind of drugs should potentially undergo aromatic-aromatic interactions with aromatic excipients such as aromatic polymers [4, 5].

In this investigation, colloidal nanomedicines containing the aromatic drug chloroquine and the polymer poly(sodium 4-styrenesulfonate) have been theoretical designed and experimental synthesized, following the simple mixture of two aqueous solutions. Theoretical calculations show higher binding energy between both the aromatic polymer and chloroquine, and a higher tendency to release water from their hydration spheres, as compared to the binding between the drug and the aliphatic polymer poly(sodium vinyl sulfonate). Molecular dynamics simulations show the tendency of formation of stable 10 nm structures, even combining short polymer chains, highly diluted reactants, and short reaction time (in the range of μs). Rapid mixing experiments in a stopped flow equipment show nanoparticle formation in the range of tenths of seconds. Experimental studies in the range of minutes, evidence spheroidal nanoparticles with almost quantitative association efficiency, 48.6 % of drug loading, size of 170 – 410 nm, low polydispersity (PdI = 0.25 – 0.47), and negative zeta potential (-18 – -45 mV). They provide drug release for 30 days, and are stable to NaCl exposure, pH gradient, several temperature values, and long-term storage. Furthermore, we demonstrate that the increasing in the reaction volume of reactants allowing scale up. Our studies demonstrated that these highly loaded drug nanoparticles are based on the occurrence of site-specific short-range interactions between the drug and the aromatic excipient such as π-stacking. In the absence of the aromatic group in the polymer, weak interactions and unstable formulations are evidenced, both theoretically and experimentally. These theoretical and experimental studies promote the efficiently production of drug / polyelectrolyte formulations with therapeutical applications. The selected components could be considered as potential medicines or as model components to design, develop, characterize and scale up medicines comprising other combinations of drugs and polymers.

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References

[1] Begines B. et al. (2020), doi.org/10.3390/nano10071403
[2] Tomar V. et al. (2019), doi.org/10.1016/B978-0-12-809633-8.20157-X
[3] Jin X. et al. (2019), doi.org/10.1093/nsr/nwz018
[4] Villamizar-Sarmiento M.G. et al. (2019), doi.org/10.1021/acs.molpharmaceut.9b00097
[5] Villamizar-Sarmiento M.G., et al. (2021), doi.org/10.1016/j.ejpb.2021.05.023