

Biomimetic colchicine nanoparticles for anti-atherosclerosis therapy

Xiuwen Zhang, Zi Sophia Gu

School of Chemical Engineering, University of New South Wales
Sydney, NSW, 2052, Australia

xiuwen.zhang@student.unsw.edu.au

zi.gul@unsw.edu.au

Atherosclerosis is a chronic cardiovascular disease caused by plaque development in arteries and remains a leading cause of morbidity and mortality.¹ In general, Atherosclerosis is initiated by the deposition of low-density lipoprotein (LDL) and followed by dysfunction and activation of vascular endothelial cells expressing cell adhesion molecules and chemokines, which continuously promotes the monocytes recruitment into the subendothelial space and differentiation into macrophages to form foam cells by internalizing oxidized LDL.^{2,3} Pathology analyses indicated that complicated interactions between vascular cells and immune cells promote atherosclerotic plaque development.⁴ Colchicine, an ancient herbal drug derived from *Colchicum autumnale*, was found as an effective anti-inflammatory agent, and used in cardiovascular disease in several clinical trials.⁵ However, the narrow therapeutic window and severe side effects at high dosages limit its therapeutic application.⁶ Nanoparticle-based drug delivery system is promising to help handle this issue through the targeted carrying of colchicine to specific plaque lesions, thus achieving high therapeutic efficiency while low toxicity. Herein, we established an inorganic nanoparticle system with layered double hydroxide (LDH) to load colchicine molecules and we also applied platelet membrane coating outside the nanosystem to endow targeted ability by taking advantage of the high affinity of platelets to the inflamed endothelium.⁷ We demonstrated that platelet membrane-coated colchicine nanoparticles effectively attenuated LPS-induced endothelial cell inflammation by reducing the intracellular ROS level, cell adhesion molecule expression, and monocyte capture without affecting cell viability. Ongoing in vivo tests can provide double verification of our nanosystem in atherosclerosis therapeutics.

References:

- ¹ Song, P.; et al. *Lancet Glob. health* **2020**, *8*, e721-e729.
- ² Gistera, A.; Hansson, G.K. *Nat. Rev. Nephrol.* **2017**, *13*, 368-380.
- ³ Zhu, Y.; et al. *Biomolecules* **2018**, *8*, 80.
- ⁴ Kong, P.; et al. *Signal Transduct. Target Ther.* **2022**, *7*, 131.
- ⁵ Zhang, F.; et al. *Acta Pharmacologica Sinica* **2022**, *43*, 2173-2190.
- ⁶ Finkelstein, Y.; et al. *Clinical Toxicology* **2010**, *48*, 407-414.