Nanoscale Celecoxib Prodrugs: As efficient Anti-Inflammatory Principles

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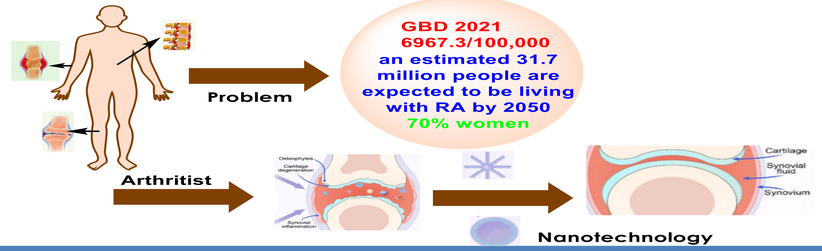
Rheumatoid Arthritis



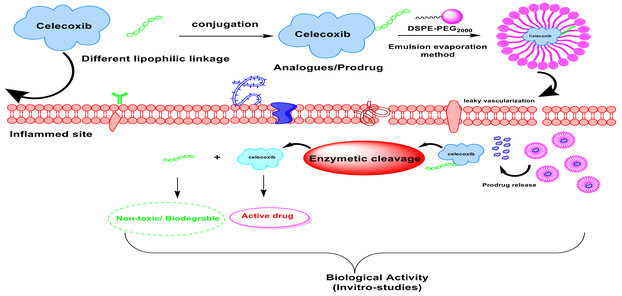
Abstract

Celecoxib Prodrugs were synthesized with 3 different biodegradable linkers, they were confirmed by different Spectroscopic techniques. Prodrug 1-3 were encapsulated into Nanoparticles via sole addition of DSPE-PEG_{2000}. Physicochemical characterization of these NPs were analyze. Further these Nps were subjected to In vitro studies and found active against cytokines like TNF-∞, MCP-1 and IL-β. In Vivo studies reveal Nps are potent but comparatively Least active than celecoxib

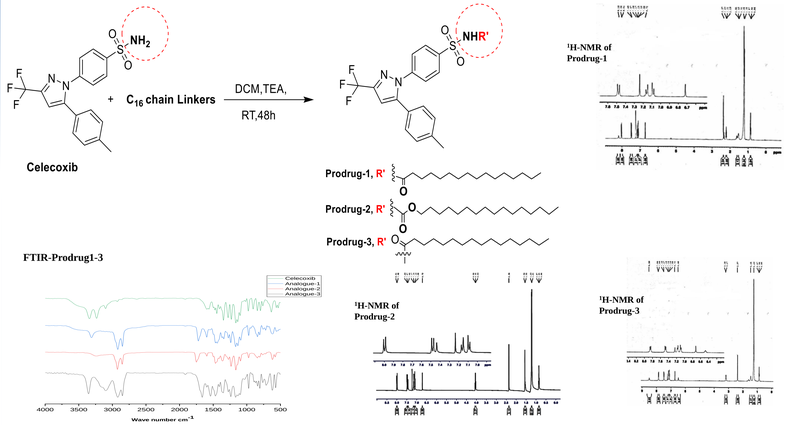
Introduction

- Celecoxib is a non-steroidal anti-inflammatory drug (NSAID) that selectively inhibits cyclooxygenase-2 (CoX-2) to alleviate inflammation.
- Despite its therapeutic benefits, it faces challenges, including low bioavailability, unfavorable pharmacokinetics, and potential cardiac toxicity.
- To enhance its efficacy, we have developed nanoparticles designed to improve hydrophobicity, biodegradability and stability profile.

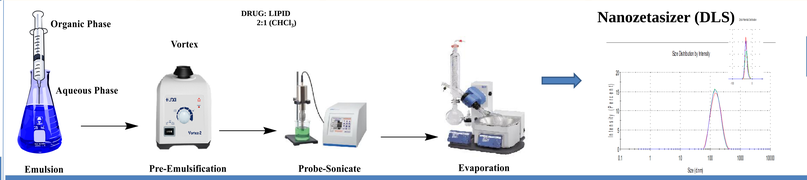
Graphical Abstract



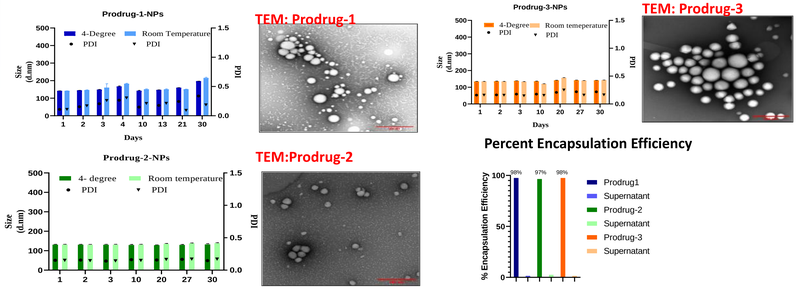
Synthesis and Characterization of Prodrugs (1-3)



Synthesis of Nanoparticles (Emulsion Evaporation)



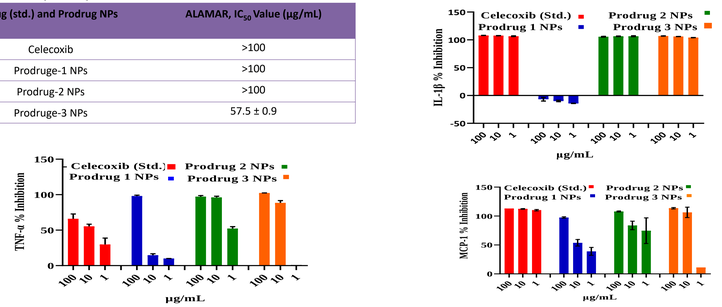
Physicochemical Characterization of Nanoparticles



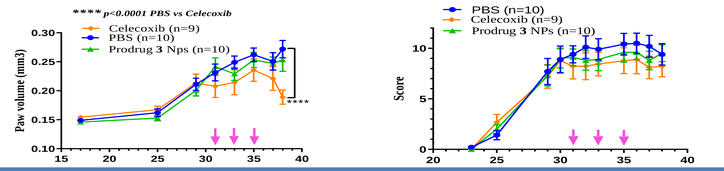
In Vitro Studies

Cytotoxicity Assay

Drug (std.) and Prodrug NPs	ALAMAR, IC_{50} Value (µg/mL)
Celecoxib	>100
Prodruge-1 NPs	>100
Prodrug-2 NPs	>100
Prodruge-3 NPs	57.5 ± 0.9



In Vivo Studies (Prodrug-3 NPs)



Conclusion

We have successfully synthesized prodrugs of celecoxib with different biodegradable linkages using the C16 chain (1-3). Furthermore, we have synthesized nanoparticles with DSPE-PEG2000, which have an average size of 150 nm and a zeta potential of -32.5 mV. The encapsulation efficiency has been found to be 99%. In in vitro studies, these nanoparticles have shown activity against inflammatory cytokines. In in vivo studies, Prodrug-3 Nps have exhibited some activity against CIA mice, but they are not as effective as the free drug.

Future Prospects

- We are set to validate prodrugs 1 and 2 against CIA model mice.
- We plan to effectively design prodrugs that ensure sustained and controlled release in biological media with a detailed pharmacokinetics profile.

References

Saleem, R., Rehman, M. U., Hussain, S., Arif, A., Malik, H. N., Naqvi, F., & Jabeen, A. (2023). Nanoscale celecoxib prodrugs: As efficient anti-inflammatory principles. *Journal of Drug Delivery Science and Technology*, *90*, 105089.

Acknowledgment

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