Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pharmacy and Pharmacology

Journal homepage: https://www.ijpp.org.in/

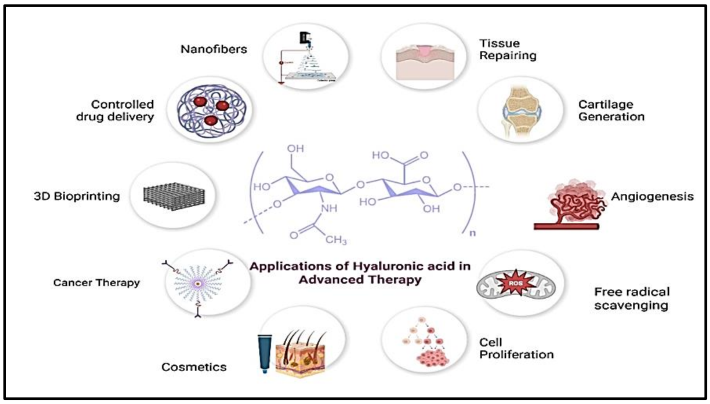
Editorial

Applications of Hyaluronic acid and its derivatives in advanced drug delivery systems: A future direction

Surya Kanta Swain[1]*, Apala Chakraborty[1]

[1]Amity Institute of Pharmacy, Amity University Kolkata, West Bengal, India.

Abstract



Hyaluronic acid (HA) is an indigenous biocompatible anionic hydrophilic polymer that has recently been applied to various advanced technologies. From nanotechnology to 3D bioprinting, this polymer shows huge potential as it has unique physicochemical properties and can promote various essential biological processes, including cell signaling, tissue regeneration, and repair.

Received: 14-05-2025; **Accepted:** 08-06-2025; **Available Online**: 19-06-2025

1. Introduction

Hyaluronic acid (HA), a biocompatible anionic hydrophilic endogenous biopolymer, is extremely renowned for its unique molecular weight-specific vaso-elastic properties for its application on various cosmeceutical, pharmaceutical, and medical devices.[1] Apart from its extremely high hydrophilicity and rheological properties, this polymer, depending on its molecular weight, shows various biochemical advantages during therapies. Though the molecular weight of HA is as high as 1000 kDa, in the presence of hyaluronidase enzyme the polymer gets cleaved. It produces much less molecular weight fragments which produce activities such as cellular quiescence (>500 kDa), anti-angiogenesis and immunomodulatory (> 500 kDa), wound healing (<250 kDa), endothelial cell proliferation and migration (<100 kDa), angiogenesis and free-radical scavenging (<10 Kda).[2]

*Corresponding author: Surya Kanta Swain
Email: sswain@kol.amity.edu

https://doi.org/10.18231/j.ijpp.2025.011

2. HA Modifications for Improved Functionality and Applications

HA modification through cross-linking and engineering helps to improve cell targeting and conjugation. The bio-conjugation of HA also enhances the mechanical, rheological, and swelling properties of the polymer, and improves the protection against enzymatic degradation allowing longer residence time at the site of action. Chemical modification of hydroxyl and carboxyl groups can enhance its properties such that modification of hydroxyl groups like etherification and esterification can improve the stability and functionality of the biopolymer, while carboxyl group modifications, including amidation and esterification, improve the drug conjugation and crosslinking with the drug delivery system.[3]

3. Applications for HA

3.1 Nanofiber

HA-based nanostructures, such as nanofibers and nano micelles, are some of the latest innovations that have not only improved the delivery of therapeutic agents for various skin conditions but also improved the efficacy of wound healing and tissue repair by promoting cell proliferation.[4]

3.2 Hydrogels

HA-hydrogels are extensively utilized in biomedical applications as they are biocompatible, and biodegradable, and for their ability to mimic extracellular matrix. The desired mechanical properties and controlled drug release profiles can be achieved for these types of hydrogels through various cross-linking strategies making them suitable for targeted therapies in conditions like osteoarthritis and cancer.[5]

3.3. 3D bio-printing

HA-based bioinks are in extensive use for the fabrication of tissue-engineered constructs. Application of HA bioink in tissue-engineered cartilage generation has been successfully conducted and showed improved functionality and matrix deposition. Some modifications such as gelatin methacrylate cross-linking have been shown to improve mechanical stability and much more robust printing during complex tissue fabrication.[6]

3.4 Cancer therapy

Being an indigenous biocomponent, HA has an affinity towards CD44 receptors that are overexpressed in tumor cells. These unique characteristics of HA further improve the targeted drug delivery of cancer therapeutics in the tumor cells. In the recent past, camptothecin and curcumin have been successfully targeted by HA-based nano-drug delivery systems to cancer cells with maximum therapeutic efficacy and minimum systemic toxicity. HA-coated chitosan nanoparticles have also promised outcomes in ROS-mediated apoptosis of tumor cells.[7]

4. Conclusion

HA stands as a promising biopolymer in biomedical innovation and with its multifaceted properties the polymer can bring many advancements in the field of regenerative medicine, targeted drug delivery, and diagnostic applications opening the path for various therapeutic possibilities.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Kim H, Shin M, Han S, Kwon W, Hahn SK. Hyaluronic acid derivatives for translational medicines. *Bio macromolecules*. 2019;20(8):2889–903.
2. Buckley C, Murphy EJ, Montgomery TR, Major I. Hyaluronic acid: A review of the drug delivery capabilities of this naturally occurring polysaccharide. *Polymers (Basel).* 2022;14(17):3442.
3. Vasi AM, Popa MI, Butnaru M, Dodi G, Verestiuc L. Chemical functionalization of hyaluronic acid for drug delivery applications. *Mater Sci Eng C*. 2014;38:177–85.
4. Sharma S, Sudhakara P, Singh J, Ilyas RA, Asyraf MRM, Razman MR. Critical review of biodegradable and bioactive polymer composites for bone tissue engineering and drug delivery applications. *Polymers (Basel).* 2021;13(16):2623.
5. Xu Q, Torres JE, Hakim M, Babiak PM, Pal P, Battistoni CM. Collagen- and hyaluronic acid-based hydrogels and their biomedical applications. *Mater Sci Eng R Rep.* 2021;146:100641.
6. Bupphathong S, Quiroz C, Huang W, Chung PF, Tao HY, Lin CH. Gelatin methacrylate hydrogel for tissue engineering applications—a review on material modifications. *Pharmaceuticals (Basel).* 2022;15(2):171.
7. Mattheolabakis G, Milane L, Singh A, Amiji MM. Hyaluronic acid targeting of CD44 for cancer therapy: from receptor biology to nanomedicine. *J Drug Target*. 2015;23(7–8):605–18.

Cite this article: Swain SK, Chakraborty A. Applications of Hyaluronic acid and its derivatives in advanced drug delivery system: A future direction. *Indian J Pharmacy and Pharmacology*. 2025;12(2):65-66.