International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Dynamic Hydrogels for Smart Controlled Release: Mitigating Burst Release and Long-Term Cargo Delivery: A REVIEW

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A B S T R A C T :

Hydrogels have emerged as one of the most promising biomaterials in controlled and sustained drug delivery systems. However, conventional hydrogels often suffer from uncontrolled burst release and lack environmental responsiveness. Dynamic or smart hydrogels, composed of reversible and stimuli-sensitive crosslinking networks, overcome these limitations. This review discusses the chemistry, mechanisms, and biomedical applications of dynamic hydrogels for mitigating burst release and ensuring long-term cargo delivery. The integration of reversible covalent and supramolecular interactions allows self-healing, adaptability, and precise release control. These systems demonstrate potential for smart therapeutic delivery in oncology, tissue regeneration, and responsive drug administration.

Keywords: Dynamic hydrogels, Controlled release, Smart drug delivery, Burst release, Self-healing materials

1. Introduction

Controlled drug delivery aims to maintain therapeutic drug concentrations for prolonged periods while minimizing side effects. Hydrogels—three-dimensional polymeric networks—are especially suitable due to their biocompatibility, flexibility, and ability to retain large amounts of water. However, conventional hydrogels often exhibit an undesirable burst release, leading to poor dose control. Dynamic hydrogels have been developed to address this issue by introducing reversible covalent or supramolecular bonds, enabling stimuli-responsive behavior, self-healing, and tunable degradation rates.

2. Dynamic Crosslinking Mechanisms

Dynamic hydrogels rely on reversible linkages that form and dissociate under mild physiological conditions. Common dynamic covalent bonds include imine (Schiff base), disulfide, Diels–Alder, and boronate ester linkages. These interactions provide flexibility and control over the hydrogel's structural integrity. Non-covalent interactions—such as host–guest inclusion, hydrogen bonding, and ionic pairing—also contribute to dynamic network formation. Boronate ester-based hydrogels, in particular, exhibit glucose- and pH-responsive behavior useful for insulin or anticancer drug delivery.

3. Mechanisms of Controlled Drug Release

Drug release from hydrogels depends on diffusion, swelling, degradation, or environmental triggers. Dynamic hydrogels mitigate burst release by regulating diffusion through reversible crosslink rearrangement. This allows for sustained release following zero-order or diffusion-controlled kinetics. Environmental stimuli like pH or glucose can further modulate the rate, offering personalized and site-specific delivery.

4. Biomedical Applications

Dynamic hydrogels have found applications across multiple therapeutic domains. In oncology, they enable localized, long-term chemotherapy with minimized systemic toxicity. In diabetes management, glucose-sensitive hydrogels regulate insulin release according to glucose levels. Additionally, these systems are applied in wound healing, tissue engineering, and gene delivery, where adaptability and self-healing are crucial for maintaining function.

5. Advantages Over Conventional Hydrogels

Dynamic hydrogels outperform conventional systems in several aspects: (i) reduced burst release, (ii) improved mechanical strength, (iii) self-healing ability, and (iv) responsiveness to environmental stimuli. Their reversible bonding provides adaptability and stability under physiological stress, allowing reliable long-term drug administration.

6. Challenges and Future Perspectives

Despite significant progress, challenges remain in scaling up production, achieving precise control over responsiveness, and ensuring consistent biocompatibility. Further research is needed to optimize mechanical–dynamic balance and evaluate in vivo performance. Integrating nanotechnology, bio-orthogonal chemistry, and 3D bioprinting could enable next-generation multi-responsive, hybrid hydrogel systems for personalized medicine.

7. Conclusion

Dynamic hydrogels represent an advanced platform for smart and sustainable drug delivery. Their reversible and adaptive structures effectively mitigate burst release, extend therapeutic duration, and respond to physiological cues. Ongoing innovations in polymer chemistry and materials design will likely expand their applications, moving closer to clinical and commercial translation.

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