

Characterization of promising smart nanoparticles that release drugs in response to illness-related signals: a review

Noor Hadi Aysa^{1,*} , Lena Fadhil Aljibouri¹ , Rafah S. Almuttairi¹ 

¹College of Pharmacy, University of Babylon, Hillah, Iraq

*Corresponding author: Noor Hadi Aysa, College of Pharmacy, University of Babylon, Hillah, Iraq

Tel.: +964-(0)7814491772

E-mail: phar.noor.hadi@uobabylon.edu.iq

Abstract

Smart nanoparticles with the capability to release drugs on demand and in response to specific illness signals, represent a promising avenue in the field of drug delivery. Their synthesis and characterization process involves the careful design of nanopolymeric structures, incorporating stimuli-responsive elements. The responsiveness of these nanoparticles to specific illness signals is evaluated through *in vitro* studies that simulate physiological conditions. The potential of these nanoparticles is explored in the context of personalized medicine, where tailored drug delivery systems respond to individual patient needs. The characterization of these smart nanoparticles showcases their potential as a novel and effective approach for on-demand drug release in response to illness signals. The findings contribute to the advancement of precision medicine and the development of innovative drug delivery systems with enhanced therapeutic efficacy and reduced side-effects.

KEYWORDS

smart nanoparticles; drug release; personalized medicine; drug delivery systems; innovation

How to cite: Aysa N. H., Aljibouri L. F., Almuttairi R. S. Characterization of promising smart nanoparticles that release drugs in response to illness-related signals: a review. *Rev. Clin. Pharmacol. Pharmacokinet. Int. Ed.* 38 (Sup2): 189-192 (2024).
<https://doi.org/10.61873/HYIS8690>

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2024 by the authors.
Licensee PHARMAKON-Press, Athens, Greece.
This is an open access article published under the terms and conditions of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) (CC BY) license.

1. INTRODUCTION

Smart nanoparticles offer a promising approach in personalized medicine by targeting specific triggers and by reducing side-effects. They can overcome challenges in chemotherapeutic drug delivery and treat tumours directly by enhancing the drug's solubility and effectiveness. Despite challenges in manufacturing, toxicity assessment, and regulatory approval, the future looks promising. The criteria for selecting biocompatible and biodegradable polymers are essential for drug delivery systems due to their sustainability, effectiveness, and potential for modification. These polymers can naturally break down in the body, thereby reducing environmental impact and improving therapeutic outcomes. Common polymers include collagen, alginate, chitosan, hyaluronic acid, and poly(vinyl alcohol). Some approved polymers can generate nanostructures and act as nanocarriers. Their

adaptability lowers environmental impact and allows for their use *via* multiple administration routes. Polymers are fundamental in drug conveyance frameworks, with regular hydrogels offering biocompatibility, biodegradability, and bioactivity. Manufactured hydrogels, such as poly(acrylic corrosive), offer tunable properties and can be changed for explicit functionalities. Polymeric nanoparticles and shrewd nanoparticles, such as poly lactic-co-glycolic acid copolymers, offer adaptability in surface functionalization and potential for designated helpful impacts on growths [1-5].

2. INCORPORATION OF SPECIFIC MOLECULES OR SIGNALING MECHANISMS

Smart nanoparticles are crucial for controlled drug delivery due to their ability to respond to external factors like pH, redox compounds, light, and temperature. Redox-responsive linkages and functionalization methods enhance their responsiveness to external influences [6,7].

3. CHARACTERIZATION TECHNIQUES

Analysing the physical and chemical properties of smart nanoparticles for drug delivery is essential for understanding their behavior and potential applications. Spectroscopy and microscopy are used in order to characterize their physical properties, while thermal analysis methods are used so as to investigate their thermal behavior and stability. These analytical techniques provide valuable insights into structure-function relationships and optimize their performance for personalized medicine applications [8].

4. DRUG RELEASE MECHANISMS EMPLOYED BY SMART NANOPOLYMERS

Smart nanoparticles for drug delivery have gained attention due to their capacity to react to different stimuli and release medications at specific sites in the body. Stimuli-responsive release involves materials responding to triggers such as light, temperature, pH, and enzyme concentration. Enzyme-based degradation involves polymers breaking down in response to specific enzymes found in pathological conditions. Targeted therapy strategies involve functionalized polymer nanocomposites targeting cancer cells with abnormal properties. These mechanisms enable precise drug delivery at specific times and locations while reduc-

ing side-effects and increasing effectiveness [8,9].

5. APPLICATIONS IN PERSONALIZED MEDICINE

Smart nanoparticles offer a range of advantages in personalized medicine, such as precise drug delivery with improved effectiveness and reduced side-effects. Smart nanoparticles have potential in tissue engineering, wound healing, biosensing, cancer therapy, and personalized medicine. They can respond to specific biological signals and achieve targeted drug delivery with enhanced efficacy, making them invaluable tools in revolutionizing disease treatment and prevention [9].

6. APPLICATIONS IN DISEASE TREATMENT AND PREVENTION

Smart nanoparticles are revolutionizing personalized medicine by enabling precise drug delivery, reducing side-effects, and enhancing effectiveness. They can be used in tissue engineering, wound healing, biosensing, tissue regeneration, and cancer therapies, potentially improving patient compliance and bioavailability [6].

7. CHALLENGES ASSOCIATED WITH SMART NANOPOLYMERS

The use of smart nanoparticles for drug delivery presents with a number of difficulties, including toxicity and regulatory issues. Although responsive polymeric nanocarriers and smart nanoparticles are promising drug delivery methods, there are substantial obstacles to their practical use. Regulatory factors like toxicity evaluations and established manufacturing processes need to be taken into account in order to guarantee safe clinical use. To guarantee safe clinical use, biocompatibility and non-cytotoxicity must also be taken into consideration [7].

8. POTENTIAL FUTURE APPLICATIONS

Smart nanoparticles have the potential to transform cancer treatments, personalized medicine, and targeted drug delivery methods. They can help create safer and more efficient treatments, improve circulation half-life, reduce internalization, prevent denaturation, and deliver target agents in a precise manner. Additionally, they offer improved specificity and efficacy in treating and preventing diseases. Future trends include the further devel-

opment of biocompatible materials, the designing of reversible systems using low-energy light sources, the further characterization of *in vivo* biological conditions, the enhancement of stability, and the combining of independent photo-induced reactions into one unified system [8,10].

Table 1. Overview of reactive oxygen species (ROS)-responsive groups in drug delivery systems and of their activity and oxidation reaction mechanism. Abbreviations used: i.m., intramuscular; i.p., intraperitoneal; i.v., intravenous; NP, nanoparticle

Group	Chemical oxidation reaction	Mechanism of activity	Systems	Administration
selenium		hydrophobic to hydrophilic phase transition	micelle	<i>in vitro</i>
diselenide		Structural cleavage	micelle	--
thioether		hydrophobic to hydrophilic phase transition	nanocomplex, micellar NP, polymersome, hydrogel, microsphere	i.v., i.m.
vinylthioether		Structural cleavage	micelle	<i>in vitro</i>
poly(thioetal)		Structural cleavage	fibrous patch, polyplex, microsphere, NP	transdermal, oral, i.v.
tellurium		hydrophobic to hydrophilic phase transition	micelle	
arylboronic acid/esters		Structural cleavage	polyplex, NP, microparticle, micelle	i.p., i.v.
polyoxalate		Structural cleavage	microparticle, NP	i.m.
poly(L-proline)		Structural cleavage	polymeric scaffolds	<i>in vitro</i>
poly(L-methionine)		hydrophobic to hydrophilic phase transition	vesicle	<i>in vitro</i>

9. CONCLUSION

Smart nanoparticles are revolutionizing drug delivery by improving targeting effectiveness, reducing side effects, and improving patient

adherence. Despite challenges like the lack of standardized manufacturing methods and a clear connection between pre-clinical and clinical studies, they hold significant promise for personalized medicine.

ACKNOWLEDGEMENTS

This work was supported by the College of Pharmacy of the University of Babylon. Professor Hussam Al-Humadi is acknowledged for helping us with the revision of the manuscript and valuable discussions.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Trehan K., Saini M., Thakur S.: Stimuli-responsive material in controlled release of drug. In: Malviya R., Sundram S. (editors): *Engineered Biomaterials: Synthesis and Applications*. Singapore: Springer (2023). DOI: [10.1007/978-981-99-6698-1_18](https://doi.org/10.1007/978-981-99-6698-1_18)
2. Filippov S.K., Khusnutdinov R.R., Inham W., Liu C., Nikitin D.O., Semina I.I., *et al.*: Hybrid nanoparticles for haloperidol encapsulation: *quid est optimum?* *Polymers (Basel)* 13(23): 4189 (2021). DOI: [10.3390/polym13234189](https://doi.org/10.3390/polym13234189) PMID: [34883693](https://pubmed.ncbi.nlm.nih.gov/34883693/)
3. Liu D., Yang F., Xiong F., Gu N.: The smart drug delivery system and its clinical potential. *Theranostics* 6(9): 1306-1323 (2016). DOI: [10.7150/thno.14858](https://doi.org/10.7150/thno.14858) PMID: [27375781](https://pubmed.ncbi.nlm.nih.gov/27375781/)
4. Dahiya S., Dahiya R.: Smart drug delivery systems and their clinical potential. In: Vyas S.P., Agrawal U., Sharma R. (editors): *Smart Polymeric Nano-Constructs in Drug Delivery: Concept, Design and Therapeutic Applications*. London: Academic Press, 401-436 (2023). DOI: [10.1016/B978-0-323-91248-8.00007-6](https://doi.org/10.1016/B978-0-323-91248-8.00007-6)
5. Bennet D., Kim S.: Polymer nanoparticles for smart drug delivery. In: Sezer A.D. (editor): *Application of Nanotechnology in Drug Delivery*. London: *InTech*, 257-310 (2014). DOI: [10.5772/58422](https://doi.org/10.5772/58422)
6. Kim Y.A., Jeong J.O., Park J.S.: Preparation and characterization of ionic conductive poly(acrylic acid)-based silicone hydrogels for smart drug delivery system. *Polymers (Basel)* 13(3): 406 (2021). DOI: [10.3390/polym13030406](https://doi.org/10.3390/polym13030406) PMID: [33514046](https://pubmed.ncbi.nlm.nih.gov/33514046/)
7. Cheng R., Meng F., Deng C., Klok H.A., Zhong Z.: Dual and multi-stimuli responsive polymeric nanoparticles for programmed site-specific drug delivery. *Biomaterials* 34(14): 3647-3657 (2013). DOI: [10.1016/j.biomaterials.2013.01.084](https://doi.org/10.1016/j.biomaterials.2013.01.084) PMID: [23415642](https://pubmed.ncbi.nlm.nih.gov/23415642/)
8. Tewari A.K., Upadhyay S.C., Kumar M., Pathak K., Kaushik D., Verma R., *et al.*: Insights on development aspects of polymeric nanocarriers: the translation from bench to clinic. *Polymers (Basel)* 14(17): 3545 (2022). DOI: [10.3390/polym14173545](https://doi.org/10.3390/polym14173545) PMID: [36080620](https://pubmed.ncbi.nlm.nih.gov/36080620/)
9. Thang N.H., Chien T.B., Cuong D.X.: Polymer-based hydrogels applied in drug delivery: an overview. *Gels* 9(7): 523 (2023). DOI: [10.3390/gels9070523](https://doi.org/10.3390/gels9070523) PMID: [37504402](https://pubmed.ncbi.nlm.nih.gov/37504402/)
10. Thananukul K., Kaewsaneha C., Opaprakasit P., Lebaz N., Errachid A., Elaissari A.: Smart gating porous particles as new carriers for drug delivery. *Adv. Drug Deliv. Rev.* 174: 425-446 (2021). DOI: [10.1016/j.addr.2021.04.023](https://doi.org/10.1016/j.addr.2021.04.023) PMID: [33930490](https://pubmed.ncbi.nlm.nih.gov/33930490/)