



A Review on Bionanogels

Prof Preetam L.Nikam¹ Prajakta Ahire² Yash Dhavan³ Dhanashri Bhoi⁴ Shivani Aware⁵ Ajay Birhade⁶
SND College of Pharmacy, Babulgaon, Yeola, Maharashtra

(Received: 14 April 2024

Revised: 1 May 2024

Accepted: 18 June 2024)

KEYWORDS

Nanotechnology, bio
nanogel, controlled
release, drug
delivery
Nanogels, Protein
drug.

ABSTRACT:

The use of nanogels as nanoscopic drug carriers has garnered significant interest, especially for the delivery of bioactive mediators at specific sites or under time constraints. Many different types of nanogel preparations have been made possible by a broad range of polymer systems and the straightforward alteration of their physico-chemical characteristics. Nanogels have exceptional stability, drug loading capacity, biologic consistency, good penetration ability, and environmental stimulus responsiveness. Nanogels have demonstrated great promise in a number of areas, such as gene transfer, chemotherapy medication delivery, diagnostics, organ targeting, and more. This review primarily focuses on various forms of nanogels, production techniques, such as drug loading techniques, various biodegradation mechanisms, and primary mechanisms of drug release from nanogels. Additionally, a quick discussion and examples of recent uses for nanogels are provided.

1. Introduction Of Bionanogels

Bionanogels are a unique class of nanomaterials that consist of a three dimensional network of polymer chains, nanosized particles, and water. These gels have gained significant attention in various fields, including drug delivery, tissue engineering, biosensors, and diagnostic imaging. The combination of their nanoscale size and unique properties makes them highly versatile and suitable for a wide range of applications.

1.1 Nanotechnology

Nanotechnology has been widely used in the construction of innovative drug delivery systems because it offers suitable methods for the time-

controlled, time-specific delivery of bioactive substances. Drug delivery can benefit from the nanoscale size in a few ways, including increased drug dissolution rate for poorly soluble drugs, increased drug accumulation in tumors, improved therapeutic agent stability against chemical and enzymatic degradation, and decreased cytotoxic side effects in cancer therapy. Various nanoscaled delivery systems, including liposomes, polymeric micelles, materials formed from sol-gel, and others, have been described to tackle these difficulties [1-3]. Hydrogel is another substance that has shown promise in the creation of nanocarrier systems. Hydrogels are made up of three-dimensional polymeric networks with a high water absorption capacity.

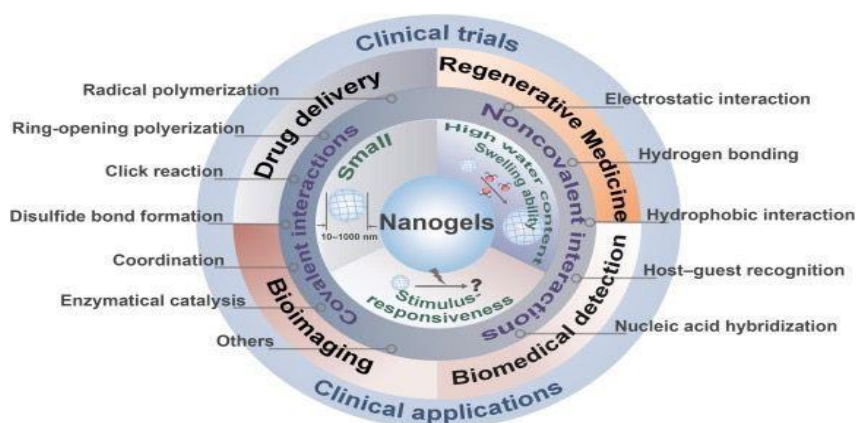


Fig.1 clinical trials

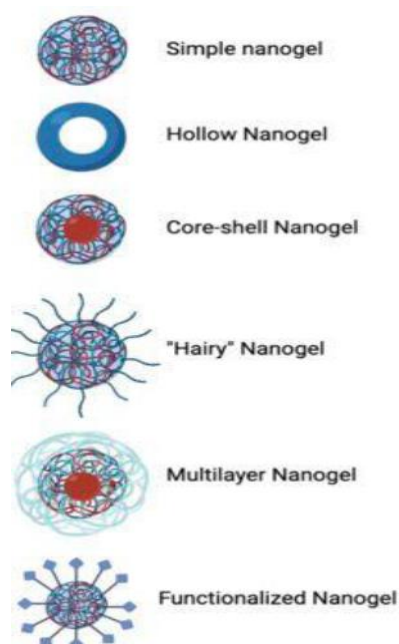


Fig:2

The term "nanogels" refers to particles that are nanoscale and created by cross-linked polymer

networks that swell quickly when a solvent is absorbed. The term "nanogel"polymer, such as poly(ethylene glycol) (PEG) and cross-linked polyethyleneimine (PEI); [PEG-cl-PEI] In summary, nanogels are cross-linked polymer systems that are three-dimensional and sub-micron in size. Because nanogel is composed of hydrogel particulate elements with a nanoscale size range, it has characteristics of both hydrogels and nanoparticles. From a materials perspective, polymer, lipid, and inorganic nanoparticles are the most frequent types of nanoparticles. This classification places nanogels in the same category as polymer nanoparticles. One can categorize nanogels into many categories.

1.2 Structure and Properties Of Bionanogels

Bionanogels are typically formed through the physical or chemical crosslinking of biopolymers or synthetic polymers. Physical crosslinking occurs through non covalent interactions such as hydrogen bonding, electrostatic interactions, van der Waals forces, or hydrophobic interactions. In contrast, chemical crosslinking involves the formation of covalent bonds between polymer chains.

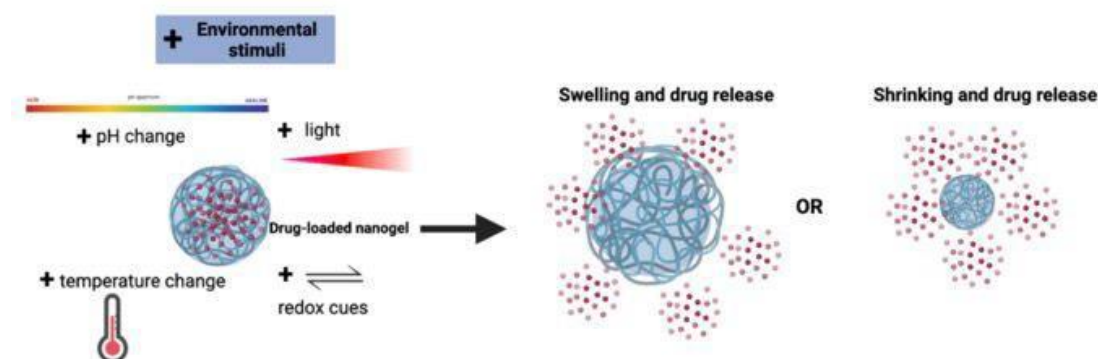


Fig:3: Structure of Bionanogels.

The properties of bionanogels can be tailored by adjusting various parameters, including the polymer composition, crosslinking density, particle size, and surface characteristics. These modifications allow for control over gel stability, drug loading and release, mechanical strength, and biological interactions.

1.3 Application Of Bionanogels

1.3.1 Drug Delivery

Bionanogels offer several advantages for drug delivery applications. Their high water content and porous structure enable the entrapment and encapsulation of drugs, providing protection against degradation and promoting sustained or controlled release. Drug-loaded bionanogels can be designed to respond to stimuli such as temperature, pH, or enzymatic activity, allowing for



site-specific drug delivery and enhanced therapeutic efficacy

1.3.2 Tissue Engineering

Bionanogels are promising materials for tissue engineering due to their ability to mimic the

extracellular matrix (ECM) found in natural tissues. They can provide mechanical support, promote cell adhesion and proliferation, and deliver bioactive molecules to guide tissue regeneration.

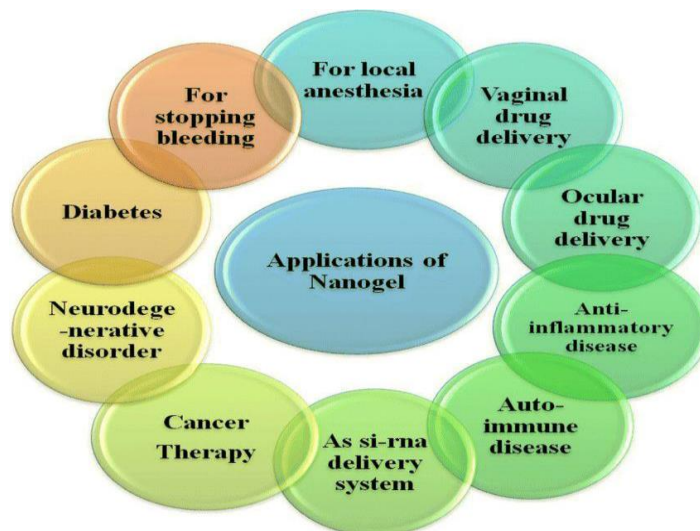


Fig:4: Application of Bionanogels

1.3.3 Biosensors And Diagnostic Imaging

The unique properties of bionanogels make them suitable for biosensing applications. By incorporating specific molecules onto their surfaces, bionanogels can selectively bind to target molecules, enabling the

detection and quantification of various analytes. Additionally, bionanogels can be functionalized with imaging agents, such as fluorescent dyes or contrast agents, to enhance the visualization and detection of diseases or cellular processes.

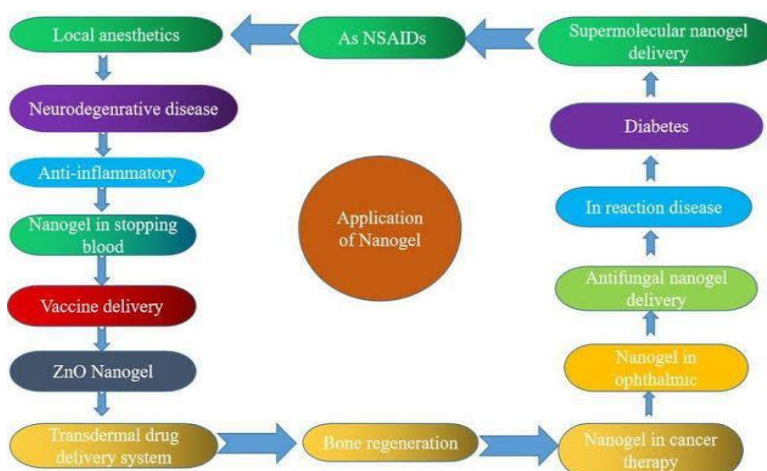


Fig:6: Application of Bionanogels



1.4 Advantage

- Both hydrophilic and hydrophobic drugs can be formulated in nanogels without any leakage of medication from the solution.
- Administration of nanogels can be through various routes such as parentals mucosal and topical.
- Nanogels can be controlled for sustained drug release from the formulation by adding a polymeric networks. Polymeric networks also contain the particles size of the formulation.
- Can be use in cosmetics as it absorbed much deeper into the skin.
- Can be used to deliver medicines as it is readily adsorbed.
- Increase solubility of highly lipophilic drugs.
- Tunable physical and chemical properties.

1.5 Disadvantage

- Many times, there is very substantial interaction between the drug or active agent and the polymer, which reduces the hydrophilic nature of the nanogels, causing the structure to be wrecked entrapping of the drug molecule.
- Restrained drug loading competency of nanogels and suboptimum standardization of drug discharge.
- Unpropitious effect can be seen in the formulation of nanogels due to the presence of surface active agents or monomers.
- Being used to deliver medicine could mean nanoparticles could damage our cells as they can easily be absorbed.
- Nanoparticles could accumulate in organism over time and we are unaware of the long term effect of this.
- Lack of proper knowledge about the effect of nanoparticles on biochemical pathways and processes in human body.
- Elimination and metabolism vary with different types of materials used in nanoparticles synthesis.

- There is not a large amount of information on the health and safety aspects of exposure to the materials.

1.6 Conclusion

Nanogels have draw extensive research interest for applications in targeted drug delivery, diagnosis, biosensing, and separation of biological substance. Nanogels have been helpful and providing better action of potency drug due to their small particle size, as the less the particles size more than the surface area and hence, more the action. Nanogels exhibits the features of both the hydrogel and nanoparticles that makes them a unique carrier system in that the hydrogel properties allow nanogels to accommodate enormous quantity of water and hence increase their drug loading capacities, impart tissues-like properties, and make them flexible while the nanometric size of these particles allow them to enter deeper tissues, escape invasion by the reticuloendothelial system, provide site-specific delivery, etc.

References

1. Qiu L, Qiao M, Chen Q et al. Enhanced effect of pH-sensitive mixed copolymer micelles for overcoming multidrug resistance of doxorubicin. *Biomaterials*, 35(37), 9877-9887 (2014).
2. Kono K, Takashima M, Yuba E et al. Multifunctional liposomes having target specificity, temperature-triggered release, and near-infrared fluorescence imaging for tumor-specific chemotherapy. *Journal of Controlled Release*, 216, 69-77 (2015).
3. Catauro M, Bollino F, Papale F. Synthesis of SiO₂ system via sol-gel process: Biocompatibility tests with a fibroblast strain and release kinetics. *Journal of Biomedical Materials Research Part A*, 102(6), 1677-1680 (2014).
4. Xue S, Pei D, Jiang W, Mu Y, Wan X. A simple and fast formation of biodegradable poly (urethane-urea) hydrogel with high water content and good mechanical property. *Polymer*, 99, 340-348 (2016).
5. Kabanov AV, Vinogradov SV. Nanogels as pharmaceutical carriers. *Multifunctional Pharmaceutical Nanocarriers*, 67-80 (2008).
6. Chintan D, Gayatri P. Application of Nanohydrogels in Drug Delivery Systems: Recent Patents Review.



- Recent Patents on Nanotechnology, 9(1), 17-25 (2015).
7. Khalili ST, Mohsenifar A, Beyki M et al. Encapsulation of Thyme essential oils in chitosan-benzoic acid nanogel with enhanced antimicrobial activity against *Aspergillus flavus*. *LWT-Food Science and Technology*, 60(1), 502-508 (2015).
 8. Akram M, Hussain R. Nanohydrogels: History, Development, and Applications in Drug Delivery. *Nanocellulose and Nanohydrogel Matrices: Biotechnological and Biomedical Applications*, 297-330 (2017).
 9. Hamidi M, Azadi A, Rafiei P. Hydrogel nanoparticles in drug delivery. *Advanced drug delivery reviews*, 60(15), 1638-1649 (2008).
 10. Pehlivanoglu H, Demirci M, Toker OS, Konar N, Karasu S, Sagdic O. Oleogels, a promising structured oil for decreasing saturated fatty acid concentrations: Production and food-based applications. *Critical Reviews in Food Science and Nutrition*, 58(8), 1330-1341 (2018).
 11. Davidovich-Pinhas M. Oleogels: a promising tool for delivery of hydrophobic bioactive molecules. (Ed.^(Eds) (Future Science, 2016)
 12. Hamidi M, Rafiei P, Azadi A, Mohammadi-Samani S. Encapsulation of valproate loaded hydrogel nanoparticles in intact human erythrocytes: a novel nano-cell composite for drug delivery. *Journal of pharmaceutical sciences*, 100(5), 1702-1711 (2011).
 13. Oh JK, Siegwart DJ, Matyjaszewski K. Synthesis and biodegradation of nanogels as delivery carriers for carbohydrate drugs. *Biomacromolecules*, 8(11), 3326-3331 (2007).
 14. Bae Y, Jang W-D, Nishiyama N, Fukushima S, Kataoka K. Multifunctional polymeric micelles with folate-mediated cancer cell targeting and pH-triggered drug releasing
 15. An Z, Qiu Q, Liu G. Synthesis of architecturally well-defined nanogels via RAFT polymerization for potential bioapplications. *Chemical Communications*, 47(46), 12424-12440 (2011).
 16. Raemdonck K, Demeester J, De Smedt S. Advanced nanogel engineering for drug delivery. *Soft Matter*, 5(4), 707-715 (2009).
 17. Stuart MAC, Huck WT, Genzer J et al. Emerging applications of stimuli-responsive polymer materials. *Nature materials*, 9(2), 101 (2010).
 18. Qiao Z-Y, Zhang R, Du F-S, Liang D-H, Li Z-C. Multi-responsive nanogels containing motifs of ortho ester, oligo (ethylene glycol) and disulfide linkage as carriers of hydrophobic anti-cancer drugs. *Journal of controlled release*, 152(1), 57-66 (2011).
 19. Chacko RT, Ventura J, Zhuang J, Thayumanavan S. Polymer nanogels: a versatile nanoscopic drug delivery platform. *Advanced drug delivery reviews*, 64(9), 836-851 (2012).
 20. Napier ME, DeSimone JM. Nanoparticle drug delivery platform. *Journal of Macromolecular Science, Part C: Polymer Reviews*, 47(3), 321-327 (2007).
 21. Oh JK, Drumright R, Siegwart DJ, Matyjaszewski K. The development of microgels/nanogels for drug delivery applications. *Progress in Polymer Science*, 33(4), 448-477 (2008).
 22. Kabanov AV, Vinogradov SV. Nanogels as pharmaceutical carriers: finite networks of infinite capabilities. *Angewandte Chemie International Edition*, 48(30), 5418-5429 (2009).
 23. Motornov M, Roiter Y, Tokarev I, Minko S. Stimuli-responsive nanoparticles, nanogels and capsules for integrated multifunctional intelligent systems. *Progress in polymer science*, 35(1-2), 174-211 (2010).
 24. Zha L, Banik B, Alexis F. Stimulus responsive nanogels for drug delivery. *Soft Matter*, 7(13), 5908-5916 (2011).
 25. Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. *Nature materials*, 12(11), 991 (2013).
 26. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. *Nature reviews Drug discovery*, 13(11), 813 (2014).
 27. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. *Journal of advanced research*, 6(2), 105-121 (2015).
 28. Assadpour E, Mahdi Jafari S. A systematic review on nanoencapsulation of food bioactive ingredients and nutraceuticals by various nanocarriers. *Critical reviews in food science and nutrition*, 1-23 (2018).
 29. Abaee A, Mohammadian M, Jafari SM. Whey and soy protein-based hydrogels and nano-hydrogels as bioactive delivery systems. *Trends in Food Science & Technology*, 70, 69-81 (2017).
 30. Mokhtari S, Jafari SM, Assadpour E. Development of a nutraceutical nano-delivery system through



- emulsification/internal gelation of alginate. *Food chemistry*, 229, 286-295 (2017).
31. Karaca AC, Erdem IG, Ak MM. Effects of polyols on gelation kinetics, gel hardness, and drying properties of alginates subjected to internal gelation. *LWT*, 92, 297-303 (2018).
32. Kunjachan S, Jose S, Lammers T. Understanding the mechanism of ionic gelation for synthesis of chitosan nanoparticles using qualitative techniques. *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm*, 4(2) (2014).
33. Fàbregas A, Miñarro M, García-Montoya E et al. Impact of physical parameters on particle size and reaction yield when using the ionic gelation method to obtain cationic polymeric chitosan-tripolyphosphate nanoparticles. *International journal of pharmaceutics*, 446(1-2), 199-204 (2013).
34. Fan W, Yan W, Xu Z, Ni H. Formation mechanism of monodisperse, low molecular weight chitosan nanoparticles by ionic gelation technique. *Colloids and Surfaces B: Biointerfaces*, 90, 21-27 (2012).
35. Akiyoshi K, Kang E-C, Kurumada S, Sunamoto J, Principi T, Winnik FM. Controlled association of amphiphilic polymers in water: thermosensitive nanoparticles formed by self-assembly of hydrophobically modified pullulans and poly (N isopropylacrylamides). *Macromolecules*, 33(9), 3244-3249 (2000).
36. Sultana F, Manirujjaman M, Imran-Ul-Haque MA, Sharmin S. An overview of nanogel drug delivery system. *J Appl Pharm Sci*, 3(8), 95-105 (2013).
37. Ferreira SA, Coutinho PJ, Gama FM. Synthesis and character nanogels made of pullulan. *Materials*, 4(4), 601-620 (2011).
38. Rekha M, Sharma CP. Pullulan as a promising biomaterial for biomedical applications: a perspective. *Trends in Biomaterials and Artificial Organs*, 20(2), 116 121 (2007).
39. Park S-J, Na K. Self-organized Nanogels of Polysaccharide Derivatives in Anti- Cancer Drug Delivery. *Journal of Pharmaceutical Investigation*, 40(4), 201-212 (2010).
40. Cooperstein MA, Canavan HEJB. Assessment of cytotoxicity of (N-isopropylacrylamide) and poly (N-isopropyl acrylamide)-coated surfaces. 8(1), 19 (2013).