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Literature Review

A Literature Review of Gelatin: Past, Present and Future in Drug Delivery

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Abstract

Hydrogels are liquid-absorbing polymer networks that can absorb any liquid, including biological fluids. The hydrogels are made up of natural polymers and their derivatives, as well as synthetic polymers. The crosslinking of either synthesised polymers starting from monomers or already established polymers creates the networks that make up hydrogels. Crosslinking can occur either physically, involving secondary intermolecular interactions, or chemically, involving the formation of a covalent connection between polymeric chains. Gelatins are protein polymers that are derived from natural sources. Gelatin is one of the most common biopolymers used to make hydrogels. Other than hydrogels, gelatin has a wide range of applications. Hydrogels, their properties and synthesis mechanisms, as well as their application in biomedicine and gelatin chemistry and application, are discussed in this review. Gelatin-based hydrogels could be used in drug delivery, bioink, transdermal therapy, wound healing, and tissue repair due to their nonimmunogenicity, nontoxicity, low cost, and great availability. On the condition that cost-effective, sustainable technologies for converting gelatin into valuable bioproducts exist or are developed, gelatin beneficiation can result in their sustainable conversion into high-value biomaterials.

Keywords: Characteristics; Gelatin; Drug Delivery

Overview of gelatin

Gelatin is a biopolymer that is natural, biocompatible, biodegradable, and multifunctional. Because of its particular mechanical and technological qualities, it is frequently employed in food, pharmaceutical, cosmetic, and medical applications [1].

Gelatin is currently utilised as a matrix for implants, device coatings, and as a stabiliser in vaccines against measles, mumps, rubella, Japanese encephalitis, rabies, diphtheria, and tetanus toxin in the medical and pharmaceutical areas. [1] It's also employed in drug delivery, intravenous infusions, hard and soft capsules, plasma expanders, wound dressings, tissue bioadhesives, hemostats, and sealants [2-5].

Since World War I, gelatin has been utilised for intravenous infusions.[5]It was first commercially made in 1685 in Holland [6]. The demand for gelatin in a variety of applications has risen steadily over the years, reaching roughly 326,000 tonnes per year globally [7]. The numerous properties of gelatin, as well as its capacity

to generate a thermoreversible gel, have made it a viable choice for tar.

Mechanical properties, swelling behaviour, thermal properties, and other physiochemical parameters are influenced by the collagen supply, the type of hydrolytic treatment utilised, the extraction process, the amount of thermal denaturation used, influence the crosslinking degree of gelatin [5,8-10]. The diversity of gelatin characteristics allows for the selection of the best circumstances for achieving desired drug-release profiles.

Gelatin sources

Gelatin is a water-soluble polypeptide generated by acid, alkaline, or enzymatic hydrolyzing collagen, the major protein component of the skin, bones, and connective tissue of animals, including fish and insects.

Type A gelatin is made from an acid treatment, such as hydrochloric acid or sulfuric acid, whereas type B gelatin is made from an alkaline treatment. Membrane filtration and/or vacuum evaporation are used to filter, deionize, and concentrate the solutions after both types of treatments.

To obtain purified gelatin; minerals, lipids, and albuminoids found in bones or skin are removed through chemical and physical treatment [9]. The most popular source is porcine skin-derived gelatin(46%), followed by bovine skin (29.4%), bone (23.1%), and other sources (1.5%) [10]. However, because to religious considerations (porcine-derived goods are outlawed in both Judaism and Islam, and Hindus do not consume bovine-derived products), as well as the global surge in vegetarianism, these sources face significant constraints and concerns among consumers.

Furthermore, the transmission of infectious vectors such as prions poses a health risk [11]. As a result, other gelatin sources, such as chicken, fish, vertebrates, and even recombinant gelatin, have been developed in the last decade.Because commercial synthesis of gelatin from poultry skin is currently hampered by low yields, it is not widely used as a gelatin source [12]. Gelatin from fish (particularly warm-water fish) has similar properties to porcine gelatin and hence might be used as a substitute.

Gelatin made from fish could also be a way to put some of the fishing industry's by-products to good use. Fish gelatin, on the other hand, has a different main amino acid sequence than pig and bovine skin gelatin.The lower melting temperature of fish gelatin (particularly from cold-water fish) can reduce its thermal stability and effectiveness at body temperature. The possibility of allergic reactions to fish gelatin is also a worry [13,14].

In order to circumvent the drawbacks of animal tissue-derived material, recombinant gelatins were created. This method enables the creation of gelatins with precise qualities to meet the needs of a particular application [15].

Characteristics of gelatin

Properties [2-4]

Gelatin has a white or slightly yellow look and is nearly tasteless and odourless. It comes in sheets, flakes, or powder form and is translucent and brittle. Gelatin may be dissolved in hot water, glycerol, and acetic acid, but it is insoluble in organic solvents like alcohol. To produce a gel, gelatin absorbs 5-10 times its weight in water.

Gelatin gel may be melted by reheating it, and it has a higher viscosity when stressed (thixotropic). On the Bloom scale of gel strength, commercial gelatin will have a gel strength of 90 to 300 grammes Bloom. When gelatin is hydrolyzed, collagen protein fibrils of roughly 300,000 Da are broken down into smaller peptides. Peptides will have extensive molecular weight ranges related with physical and chemical processes of denaturation, depending on the process of hydrolysis.

Composition [6,7]

Gelatin has 98-99% protein when dry, however it lacks tryptophan and is lacking in isoleucine, threonine, and methionine, making it a nutritionally incomplete protein. Hydrolyzed collagen has the same amino acid profile as collagen.

Glycine (Gly) 26-34%, proline (Pro) 10-18%, and hydroxyproline (Hyp) 7-15% are the most abundant amino acids in hydrolyzed collagen, accounting for about half of the total amino acid content. Alanine (Ala) contributes 8-11%, arginine (Arg) contributes 8-9%, aspartic acid (Asp) contributes 6-7%, and glutamic acid (Glu) contributes 10-12%.

Gelatin as a drug delivery carrier

Significant attempts have been made to modify formulations in order to improve drug stability over a long period of time. A drug's

therapeutic impact is most effective in the body when its blood concentration is above the minimum effective level but below the harmful level. However, because each medicine has its unique biological half-life, it can only be kept at an effective concentration for a limited amount of time. Increasing the drug's dose is one answer to this problem [15,16].

It's crucial, though, not to get too close to the harmful response zone. Another option is to take the medicine numerous times over a period of time, which is less convenient for the patient. As a result, extensive efforts are being made to generate dosage forms that extend a protein's biological activity in the body or aid in targeting it to a specific region. Incorporating the medicine into a suitable matrix is one technique to achieve these objectives [16].

When compared to traditional dosage forms, drug controlled-release carriers offer a number of benefits, including improved efficacy, the ability to maintain the desired drug concentration in the blood for an extended period of time without reaching toxic levels or falling below the effective level, reduced toxicity, and improved patient compliance and convenience [16,17].

Despite these benefits, if the controlled medication delivery system is not properly built, the patient may suffer injury. As a result, the ideal drug delivery system must be biocompatible with no harmful degradable products, mechanically strong with the capacity to load large amounts of medicine without fear of inadvertent release, simple to build and sterilise, quick to put and remove, and comfortable to use for the patient [17].

Controlling the release of active chemicals from medication delivery devices into the environment can be accomplished through a number of mechanisms [17-19]:

i) diffusion; ii) swelling followed by diffusion (mostly in hydrogels); iii) diffusion and degradation (erodible systems); iv) hydrolysis of the covalent bond if the drug is covalently bound to the biodegradable polymer (pendant chain systems); v) osmotic pressure; and vi) externally or self-regulated systems.

Polymeric carriers that physically entrap molecules of interest must be protected to avoid rapid immune system detection and subsequent clearance from the body. Drug carriers physicochemical qualities, such as size, hydrophilicity, and zeta potential, have a huge impact on their recognition and phagocytosis by macrophages.

The suppression of nonspecific interactions with the body, such as opsonization of blood components and complement activation, would lower drug carrier blood clearance. A hydrophilic polymer, such as gelatin, can be coated on drug delivery carriers to decrease opsonization while also improving water solubility [18]. Furthermore, utilising a biodegradable polymer as a drug carrier would protect the drug from gastric acid corrosion and enzyme disassembly, keeping the medication's efficient functioning in the body [19].

Gelatin has been extensively investigated as a drug delivery carrier for many classes of drugs due to its characteristics as a natural biomaterial and a long history of safe application in a variety of medicinal and pharmaceutical applications Inflammatory medications, antineoplastic chemicals, antibacterial agents and recently nucleic acid and hydrophobic materials were reported in the literature [20-28]. The characteristics of gelatin can be tweaked to increase drug loading efficiency [29]. By utilising an alkaline or acidic treatment, the isoelectric point of gelatin can be modified to match the electrostatic characteristics of the drug molecule [30].

Furthermore, gelatin's hydrophilic nature makes it easier for bodily fluids to penetrate the particles, increasing the diffusion-mediated release of bioactive compounds [31]. The gelatin source, molecular weight, and degree of crosslinking can all be tweaked to improve drug release characteristics.

Furthermore, the drug profile release can be customised for a wide range of tissue engineering [32,33], cancer therapy [24,25], and therapeutic angiogenesis [34,35] applications by modifying gelatin to other types of carriers and adding synthetic or natural polymers.

Conclusion

Hydrogels are a type of polymer that is insoluble, crosslinked, hydrophilic, and three-dimensional, with the potential to absorb a large amount of liquid. Hydrogels can be classified based on their source, crosslinking, quantity of polymers, environmental sensitivity, and other factors, the majority of which have been discussed in this work.

Bibliography

1. Burke CJ., *et al*. "Formulation, stability, and delivery of live attenuated vaccines for human use". *Critical Reviews™ in Therapeutic Drug Carrier Systems* 16 (1999): 1-83.

2. Karim AA and Bhat R. "Fish gelatin: properties, challenges, and prospects as an alternative to mammalian gelatins". *Food Hydrocolloids* 23 (2009): 563-576.

3. Pollack SV. "Silicone, fibrel, and collagen implantation for facial lines and wrinkles". *Journal of Dermatologic Surgery and Oncology* 16 (1990): 957-961.

4. Rao KP. "Recent developments of collagenbased materials for medical applications and drug delivery systems". *Journal of Biomaterials Science, Polymer* 7 (1995): 623-645.

5. Saddler JM and Horsey PJ. "The new generation gelatins. A review of their history, manufacture and properties". *Anesthesia* 42 (1987): 998-1004.

6. Roy BC., *et al*. "Extraction and characterization of gelatin from bovine heart". *Food Bioscience* 20 (2017): 116-124.

7. Karim AA and Bhat R. "Gelatin alternatives for the food industry: recent developments, challenges and prospects". *Trends in Food Science and Technology* 19.12 (2008): 644-656.

8. Asghar A and Henrickson RL. "Chemical, biochemical, functional, and nutritional characteristics of collagen in food systems". *Advances in Food Research* 28 (1982): 231-372.

9. Farrugia CA., *et al*. "Comparison of the molecular weight distribution of gelatin fractions by sizeexclusion chromatography and light scattering". *Pharmacy and Pharmacology Communications* 4 (1998): 559-562.

10. Courts A. "The N-terminal amino acid residues of gelatin. 2. Thermal degradation". *Biochemical Journal* 58 (1954): 74.

11. Wilesmith JW., *et al*. "Bovine spongiform encephalopathy: epidemiological studies on the origin". *Veterinary Record* 128 (1991): 199-203.

12. Schrieber R and Gareis H." Gelatine handbook". Wiley-VCH GmbH and Co Weinhem (2007).

13. Aas K. "Studies of hypersensitivity to fish. A clinical study". *International Archives of Allergy and Immunology* 29 (1966): 346.

14. Sakaguch M., *et al*. "IgE antibody to fish gelatin (type I collagen) in patients with fish allergy". *The Journal of Allergy and Clinical Immunology* 106 (2000): 579-584.

15. Olsen D., *et al*. "Recombinant collagen and gelatin for drug delivery". *Advanced Drug Delivery Reviews* 55 (2003): 1547-1567.

16. Foox M and Zilberman M. "Drug delivery from gelatin-based systems". *Expert Opinion on Drug Delivery* 12.9 (2015): 1547-1563.

17. Uhrich KE., *et al*. "Polymeric systems for controlled drug release". *Chemical Review* 99 (1999): 3181-3198.

18. Knop K., *et al*. "Poly (ethylene glycol) in drug delivery: pros and cons as well as potential alternatives". *Angewandte Chemie* 49 (2010): 6288-6308.

19. Meng ZX., *et al*. "Preparation and characterization of electrospun PLGA/gelatin nanofibers as a potential drug delivery system". *Colloids and Surfaces B: Biointerfaces* 84 (2011): 97-102.

20. Lee EJ., *et al*. "Studies on the characteristics of drugloaded gelatin nanoparticles prepared by nanoprecipitation". *Bioprocess and Biosystems Engineering* 35 (2012): 297-307.

21. Rajan M and Raj V. "Formation and characterization of chitosan-polylacticacid-polyethylene glycol-gelatin nanoparticles: a novel biosystem for controlled drug delivery". *Carbohydrate Polymer* 98 (2013): 951-958.

22. Kumar R., *et al*. "In-vitro and in-vivo study of indomethacin loaded gelatin nanoparticles". *Journal of Biomed Nanotechnology* 7 (2011): 325-333.

23. Narayanan D., *et al*. "Poly- (ethylene glycol) modified gelatin nanoparticles for sustained delivery of the antiinflammatory drug Ibuprofen-Sodium: an in vitro and in vivo analysis". *Nanomedicine* 9 (2013): 818-828.

24. Madan J., *et al*. "Sterically stabilized gelatin microassemblies of noscapine enhance cytotoxicity, apoptosis and drug delivery in lung cancer cells". *Colloids and Surfaces B: Biointerfaces* 107 (2013): 235-244.

25. Lee SJ., *et al*. "Biocompatible gelatin nanoparticles for tumor-targeted delivery of polymerized siRNA in tumor-bearing mice". *Journal of Control Release* 172 (2013): 358-366.

26. Li WM., *et al*. "In situ doxorubicin--CaP shell formation on amphiphilic gelatin--iron oxide core as a multifunctional drug delivery system with improved cytocompatibility, pHresponsive

drug release and MR imaging". *Acta Biomaterials* 9 (2013): 5360-5368.

27. Wang J., *et al*. "The combined effects of size and surface chemistry on the accumulation of boronic acid-rich protein nanoparticles in tumors". *Biomaterials* 35 (2014): 866-878.

28. Bonner DK., *et al*. "Crosslinked linear polyethylenimine enhances delivery of DNA to the cytoplasm". *Journal of Control Release* 167 (2013): 101-107.

29. Santoro M., *et al*. "Gelatin carriers for drug and cell delivery in tissue engineering". *Journal of Control Release* 190 (2014): 210-218.

30. Tabata Y and Ikada Y. "Protein release from gelatin matrices". *Advanced Drug Delivery Reviews* 31 (1998): 287-301.

31. Lu Z., *et al*. "Paclitaxel-loaded gelatin nanoparticles for intravesical bladder cancer therapy". *Clinical Cancer Research* 10 (2004): 7677-7684.

32. Wang H., *et al*. "Combined delivery of BMP-2 and bFGF from nanostructured colloidal gelatin gels and its effect on bone regeneration in vivo". *Journal of Control Release* 166 (2013): 172-181.

33. Kim YH., *et al*. "Enhancement of bone regeneration by dual release of a macrophage recruitment agent and platelet-rich plasma from gelatin hydrogels". *Biomaterials* 35 (2014): 214-224.

34. Kimura Y and Tabata Y. "Controlled release of stromal-cell-derived factor-1 from gelatin hydrogels enhances angiogenesis". *Journal of Biomaterials Science, Polymer* 21 (2010): 37-51.

35. Saito T and Tabata Y. "Preparation of gelatin hydrogels incorporating low-molecular-weight heparin for antifibrotic therapy". *Acta Biomaterials* 8 (2012): 646-652.

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