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Alopecia Areata and its Effective Nano-gel

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Abstract

Alopecia Areata is an auto-immune disease signalized by chronic and scarring hair loss. Hair loss can take many forms from the loss of scalp spreading or complete loss of hairs, which can affect all sites covered with hairs. Traditional drug delivery systems that include lotions, ointments, patches and creams are associated with many barriers such as limited drug load performance and poor penetration. In addition, they can adhere to a slightly diffuse coefficient, so they need to be applied to the application leading to patient suffering. Proper delivery is essential for targeting hair follicle selection, maximizing therapeutic effects and minimizing unwanted side effects due to systemic absorption. Nano gels are promising and innovative biological systems as the disintegration of hydrogel nanoparticles formed from physically or chemically linked polymeric networks has been named as the next generation of drug delivery systems due to their potency of drugs, variability of injectable drugs, and response to external factors.

Keywords

Alopecia Areata, nano gel, auto-immune disease, hair follicles.

INTRODUCTION

Alopecia areata (AA) is a complex form of self-injury that affects the hair follicles, causing permanent hair loss (1). AA can manifest in a variety of patterns, from well- defined patches of scalp to the worst, irreversible, complete skin and complete body hair loss (2). The beginning of alopecia areata can occur at

any point of time; however, mostof the patients develop this disease before the age of forty, which means age starts between twenty-five and thirty-six years. Untimely onset of alopecia areata (ages five to ten years) mainly present a more serious form, like alopecia universalis and alopecia totalis (3). Alopecia totalis describes the complete removal of hair from the scalp, whereas alopecia universalis is the name given to those with complete head and body hair(4). Alopecia areata is associated with a number of related diseases including depression, anxiety and a number of independent diseases, such as hyperthyroidism, goiter, thyroiditis and hypothyroidism etc. (5).

Traditional drug delivery systems that include lotions, ointments, patches andcreams are associated with many barriers such as limited drug load performance and poor penetration. In addition, they can adhere to a slightly diffuse coefficient, so they need to be applied to the application leading to patient suffering. The novel methods of the delivery are a promising new treatment for hair disorders. Proper delivery is essential for targeting hair follicle selection, maximizing therapeutic effects and minimizing unwanted side effects due to system absorption (6). It is evident from the literature that the formation of topical Nano sized can promote drug delivery by attaching temporary disruption to a highly structured lipid bilayer framework.

NANOGELS

Nano gel has attracted a lot of attention as one of the various drug delivery systems especially the site-specific delivery and / or time management of bioactive agents due to its combination of hydrogel and nanoparticle components (7, 8). Nano gels are promising and innovative biological systems as the disintegration of hydrogel nanoparticles formed from physically or chemically linked polymeric networks has been named as the next generation of drug delivery systems due to their potency of drugs, variability of injectable drugs, similarity, adjustment, size, adjustment minimal, stability in the presence of serum, and response to external factors (9). These gels contain composite polymers that have a natural origin and are made with good water-holding properties. These polymers immerse the water in the surrounding environment and show a longer duration of extraction after inflammation. Due to the hydrophilic nature of Nano gels, they provide good water absorption and biomedical power to provide controlled, targeted and continuous drug release (10, 11).

CLASSIFICATION OF NANOGELS ACCORDING TO THEIR STRUCTURE

Nano gels are classified on the basis of their properties. The various types of Nano gels are simple Nano gels (artificial chaperons), Nano gels that include pH- or temperature sensitive Nano gels, core-linked-shell-Nano gels are also used to prepare reaction Nano gels,Combined hair Nano gels, multilayer Nano gels and active Nano gels (12).

1. Nano gels Respond To Stimuli

Encouraging gels are critical of their anti-inflammatory impact and with inside the manufacturing of anti-cancer treatments. Nano gels have proven a reversible impact of infection or a lower in polymer in reaction to numerous environmental elements inclusive of magnetic field, pH and temperature (13). Changes arise with inside the responsereaction that alters the lipophilic and hydrophobicity of Nano gels (14). As stated by Sahu *et al*., the earth conversion of Nano gel is achieved through double coating of pH- based polymers. Nano gels organized from decomposing polymers are bonded with different penetration enhancers (e.g., eucalyptus oil), whilst mixed with 5- Fluorouracil (5-FU) that has the ability to deal with pores and skin most cancers. In ex-vivo and in vitro studies, poly-lactideglycolic acid (PLGA)-chitosan is a double-enclosed Nano gel whilst mixed with a high-overall performance anticancer drug, has proven its chemical activity (15).

a) pH Responsive Nano gels: pH reactive polymers such as poly-acrylic acid andlatex cellulose acetate phthalate (CAP) contain invisible components that are responsible for dissolving of polymer at different pH conditions, stated by Al- kinani *et al.* These polymers are converted into a gel form, i.e., the weakest material into a weaker base. A high-density polymer, poly-acrylic acid convertsits transformation into a gel-like form of inflammation (16). The delivery ofnanogel within cells initiated the acidification process and lowered the pH level ofthe cytosomes or endosomes, releasing the therapeutic agent into Nano gels- claimed by Li *et al*. (17).

b) Thermo Responsive Nano gels: Thermo-responsive prepared Nano gels composed of polymers that exhibit a thermal change response. Dendritic polyglycerol, a reactive polymer nanogel makes changes in the aqueous content where there is a high temperature, resulting in dehydration and reduction of gel (18). Zafar *et al.* explained the use of silver containing nanogels based on N-isopropyl acrylamide as an anti-bacterial agent to prevent the growth of gram-negative bacteria, Escherichia coli and gram positive bacteria, Staphylococcus epidermis (19).

2. Non-Responsive Nanogels

These types of nanogel do not offer much change; they simply swell by absorbing water and releasing the drug. These gels do not show reaction in any conditions as indicated by gels that respond to reactions or change the type of nanogel.

3. Physically Cross-Linked Nanogels

Nanogels can be formed on the basis of hydrogen bonding, Van der Waals' weak energy due to charged particles. These are also known as counterfeit and can be effortlessly remedied through combining structures with opposing sides and copolymers (20). The interaction between the particles creates a nanogel bond, which provides a controlled release. Physically bonded gels are susceptible to the type of polymer and its value, pH and temperature of the material used. These forms of gels are composed of a mixture of polymers.

4. Chemically Cross-Linked Nanogels

These types of nanogels can be prepared by forming durable and strong chemical bonds. Their interactions depend on the active moiety present in the appropriate polymer extracted. Using different types of chemical compounds, many forms of nanogels can be synthesized. Chemically bonded gels are formed as a result of the disulphide-based bonding; amine-based connections or image-linked connections (21). Kumar *et al.* stated that to enhance anticancer activity, nanogels can be combined with disulfide linked for the combined delivery of Etoposide and Vorinostat (22). Zhou *et al*. performed experiment to improve nanogel stability in stomach conditions through chemical interactions using 1- ethyl-3- (3-dimethylaminopropyl) and carbodiimide/N-hydroxy succinimide. Nanogels have shown an improved stability of curcumin with controlled release (23).

5. Polymer Based Nanogels

On the basis of embedded polymers, Nanogels can be dis-assembled, providing a structure-like network to Nanogels. Nanogels formed are based on polyvinyl alcohol (PVA), alginate and chitosan.

a) Alginate Based Nanogels: Nanogels are formed by the fact that poly-lysine is added to the component of “calcium chloride and sodium alginate”. Alginate based Nanogels use a smaller

number of polymers compared to other methods. The availability of nanoparticles is increasing and therefore provides excellent opportunities for the delivery of genetic drugs. Silver-plated alginate silver binding with chitosan nanogels to improve treatment was compared with commercially available formulation by El-feky *et al.* (23). Two reaction nanogels were prepared by using a combination of keratin and alginate in which keratin acts as a cross-linker and alginate properties provided such as drug loading,particle size and stability by Ilanga et al. (24).

b) Chitosan Based Nanogels: "Chitosan" is a polymer obtained by de-acetylation ofa chitin molecule used for delivery of drug by variety of Nano-carriers. Chitosan is cationic in nature and has a hydrophilic property, which gives it a good adhesion through the mucosal membrane. It has the capability to detect strong bonds, which is why it increases bioavailability and reduces toxicity. Curcumin incorporated nanogel properties were enhanced by binding "chitosan and poly-N-isopropyl acrylamide" using a combination of direct response and controlled delivery of biomolecule as performed by Luckanagul et al. (25).

c) Polyvinyl Nanogels: Polyvinyl alcohol (PVA) provides confusing adverse properties either in chemical or physical ways. Cross-linking techniques are tough but still work in the field of delivering drugs. The polyvinyl alcohol molecule can be connected by small poly-lactone chains of decaying polymers. These polymers are then synthesized with tetanus toxoid, serum albumin and cytochrome C to provide continuous release. Senanayake et al. stated that PVA-based nanogelmade by combining with a phosphorylated form of 5-Fluorouracil have enhanced anti-cancer activities (26).

6. Liposome Based Nanogels

The composition of nanogels has been modified by using liposomes, which have beenshown to be an effective treatment for various diseases. A variety of factors can influencethe release of liposomes, for example, temperature, ionic changes or pH changes. At pH 5.5, liposomes formed from succinate polyglycerol release the calcein to cytoplasm.Polyglycidol-based nanogels were prepared showing a maximum yield for the improveddelivery of natural chemical treatments, after the efficient use of liposome designedtemplates (27).

7. Nanogels Based On Micelles

Micelle-based nanogels can be prepared by using a combination of polymeric blocks. This type of nanogel has the characteristics of the middle structure, which is hydrophilic in nature from the inside and lipophilic in nature from the outside. The innermost layer is essential for the formation of hydrogen bond and makes the basic structure around the micelles. The core offers high strength for active drug insertion. Newly developed nanogel micelles with high durability exhibit a strong action against a particular stimulus. The active drug loaded into the lipophilic cavity of nanogels can now easily be protected from attack of water molecules and enzymatic degradation (28).

FABRICATION OF NANOGELS

1. Free Radical Polymerization

In many studies, nanogels have been linked to powerful free polymerization processes. Figure 1 introduces a free radical radical scheme diagram. Depending on the stage in which this process takes place, we refer to free radical polymerization such as dissolving polymerization and precipitation or emulsion polymerization and discuss differently in this review. Both of these processes have been used to prepare well-made nanogels described in the presence of multidisciplinary combinations.

a) Dispersion and Precipitation Polymerization: Polymerization dispersing is a widely used method to create polymers and copolymers by eliminating monomers, stabilizers, and solvents in an inactive organic solvent. Therefore, the reaction mixture starts as a parallel process (29). Precipitation polymerization begins in the same process, where the monomers and the precursors dissolve completely. Different types of nanogels were synthesized using these two methods and were used for the delivery of biomolecules (30, 31).

b) Emulsion Polymerization: It is a type of free flexible polymerization that allows for the preparation of well-defined Nano sized particles by the polymerization of monomers in the form of emulsions. The physical condition of the emulsion system makes it easy to control the process, especially in terms of temperature and viscosity. Moreover, this process has the benefit of being able to gain high molecular weight and high reaction rates, and is divided into a standard emulsion and a flexible emulsion according to the surface area (30). In the case of standard emulsion polymerization, the reaction mixture consists of a liquid phase, a water insoluble monomer, a soluble initiator in a liquid phase, and an emulsifying agent. A medium diameter of 57 nm was prepared using the O/ W emulsion polymerization method and successfully loaded with 5-flurouracil (5-FU), anticancer drug. The 5-FU efficacy of encapsulation detection has been found to reach 61%, indicating pH-emission and heat response of 5-FU (32). Quaternary ammonium groups are introduced into the polyamine gel spine to strengthen the binding of siRNA. Proper dosage of quaternary ammonium groups to high-grade nanogel groups play a key role in gene depletion by providing advanced cellular detection (quaternary ammonium groups) and end-of-life (high amino groups) (33). Stimulus-responsive polymers based on 2-vinylpyridine and divinyl benzene can bind to magnetic nanoparticles of illegal substances. The size of the emerging nanogel was less than 200nm. These pH-response polymers show a difference in their ionization state with a reduced pH, allowing nanogel to be used as a genetic (or drug) delivery system (SR) (34).

2. Controlled/Living Radical Polymerization

Another popular polymerization process is controlled / organic polymerization (CLRP). Since the 1990s, CLRP has been tested to make shortcuts or gels with a well-defined weight of polymer molecules with the inclusion of chemical cross-linking agents and solvents, including protic media such as liquids, can be used to gain maximum control over the process of polymerization, almost identical to the anionic polymerization process, as well as maintaining the tolerance and flexibility of powerful free processes (35). The use of various vinyl monomers allows the production of nanogel with a variety of shapes, sizes, and structures, including core-shell and vanity modification. In addition, active initiators ensure specific localization in the inner part of the NG or above, facilitating bio-conjugation (36).

As discussed in detail by Sanson et al. (37), these factors improve the optimal condition of the number of chains almost identical in all polymerization, which begin almost simultaneously and have the same growth rate: this ensures internal control of molar weight distribution and formation. In addition, the slow CLRP method allows for a gradual redistribution of sleeping chains, allowing them to distribute and distribute evenly. As a result, the dividing points that form NGs are evenly distributed within the Nano network, with a localized polymeric structure, which often exceeds conventional methods (where dense / nodular cross-linking domains occur, producing a different structure) (38). The success of CLRP in the construction of NG is related to the control of network construction: Nano scaffolds can be adjusted to size and molar size. Depending on the concentration of monomers and the cross-linking agent, NG building blocks can have a different range of molar weight and branch structure, which alters the storage and formation of nanogels and thus achieves different structures (39, 40).

3. Physical Self-Assembly Of Interactive Polymer

Self-assembly is a new method developed to prepare nanogels physically connected bythe distribution of various polymers dissolved in water containing hydrophobic elements. Nanogels are formed on the basis of hydrophobic and external hydrophilic shell or vice versa. The facility showcased a variety of facilities suitable for use in the medical and pharmaceutical fields, particularly with the administration of anti-cancer drugs (41). Various natural polymers such as chitosan, pullulan, and mannose have been reported. Chitosan nanogel colloidal was obtained with ammonia gelation made of a phase emulsion reversing the wound of a series of hollow chitosan chains surrounded by partially produced chains that were widely used for natural use (42). Pullulan is a widely used polysaccharide in the field of pharmaceutics due to its low immunogenicity and biodegradability. Nanogels prepared from cholesterol bearing pullulan (CHP) and nanogel-linked substances have been developed as Nano carrier systems for drugs, including peptide-free proteins or molecules (43).

CONCLUSION

Nanogels have proved their important role in various aspects of sustained and controlled drug delivery systems. The study related to the nanogels systems give wide knowledge for theoretical and practical purposes. The study of nanogels based drug delivery systems is necessary to search the better control over properties. In future, improved design of nanogels for specific targeting should be the main objective of the nanogel research.Every new analysis entails discovery of recent polymer and mechanistic approaches with a promising role in therapies and innovation on fabrication of nanogels design. The use of nanogels permits the advance of biopharmaceutical parameters of an entrapped drug. We increase the use of these materials in many fields or other delivery systems. Nanogels are probably one of the better drug delivery systems to provided controlled or sustained release of the drug.

REFERENCES

1. E. Darwin, P. A. Hirt, R. Fertig, B. Doliner, G. Delcanto and J. J. Jimenez. *Int J Trichology.*, 10(2), 51-60 (2018).
2. A. Pourangand N. A. Mesinkovska.*Drugs*, 80(7), 635-646 (2020).
3. A. C. V. Fricke and M. Miteva.Clin.Cosmet.Investig.Dermatol.,8, 397-403 (2015).
4. W. Lu, J. Shiparo, M. Yu, A. Barekatain, B. Lo, A. Finner and K. McElwee.Expert Rev Mol Med.,8(14), 1-19 (2006).
5. S. Y. Chu andY. J. Chen. J. Am. Acad. Dermatol., 65, 949–956 (2011).
6. A. Wipf, N. Boysen and M. K. Hordinsky.J. Cosmet. Laser Ther., 21, 247–254(2019). 14.L. Qiu, M. Qiao, Q. Chen, C. Tian, M. Long, M. Wang, L. Cheng, H. Hum, X. Zhao and D. Chen. Biomaterials,35, 9877–9887 (2014).
7. K. Kono, M. Takashima, E. Yuba, A. Harada, Y. Hiramatsu, H. Kitagawa, T. Otani, K. Maruyama and S. Aoshima. J Controlled Release,216, 69–77 (2015).
8. R. T. Chacko, J. Ventura, J. Zhuang and S. Thayumanavan.Adv. Drug Deliv.Rev., 64,836–851 (2012).
9. F. Sultana, Manirujjaman, Imran-Ul-Haque, M. Arafat and S. Sharmin. J Applied Pharmaceut. Sci.,3, 95 (2013).
10. L. B. Priya, R. Baskaran and V. V. Padma.Nanostruct.Oral Med., 639–668 (2017).
11. A. Sharma, T. Garg, A. Aman, K. Panchal, R. Sharma, S. Kumar and T. Markandeywar. Artific.Cells, Nanomed.andBiotechnol., 2014.
12. B. Adhikari, C. Sowmya, C. Reddy, C. Haranath, H. Bhattaland R. Inturi. World J.Pharm. Pharm. Science., 2016.
13. K. S. Soni, S. S. Desale and T. K. Bronich. J Controlled Release, 240, 109 (2016).
14. P. Sahu,S. K. Kashaw, S. Jain and S. Iyer.J Controlled Release, 253, 122 (2017).

15. A. A. AL-Kinani, G. Zidan, N. Elsaid, A. Seyfoddin, A. W. G. Alani and R. G. Alany. Adv. Drug Delivery Rev., 2017.
16. D. Li, C. F. Nostrum, E. Mastrobattista, T. Vermonden and Hennink. Management ofWEJ.Rel., 259, 16 (2017).
17. P. Sánchez-Moreno, J. Vicente, S. Nardecchia, J. A. Marchal and H. Boulaiz. Nanomaterials, 8(11), 935 (2018).
18. M. Zafar, T. Shah, A. Rawaland E. Siores.Mater.Science. Eng. C., 40, 135-141(2014).
19. H. Zhang,Y. Zhai, J. Wang and G. Zhai.Mater.Sci. Eng. C.,60, 560-568 (2016).
20. A. J. Sivaram, P. Rajitha, S. Maya, R. Jayakumar and M. Sabitha. Wiley interdisciplinary Reviews: Nanomed. Nanobiotechnol., 7, 509 (2015).
21. P. Kumar, L. Wasim, M. Chopra and M. Chhikara.AAPS Pharm. Science.Tech., 19,634 (2018).
22. G. S. El-Feky, S. T. El-Banna, G. S. El-Bahy, E. M. Abdelrazek and M.Kamal.CarbohydrPolym., 177, 194-202 (2017).
23. Z. Sun, Z. Yi, H. Zhang, X. Ma, W. Su, X. Sun and X. Li. Carbohydr. Polym., 175,159-169 (2017).
24. J. A. Luckanagul, C. Pitakchatwong, Q. Wang and P. Rojsitthisak.Carbohydr.Polym.,181, 1119 (2018).
25. T. H. Senanayake, G. Warren, X. Wei and S. V. Vinagradov.J Control.Release, 167,200 (2013).
26. M. A. Phillips, M. L. Gran and N. A. Peppas.Nano Today, 5(2), 143-159 (2010).
27. S. Khoee and H. Asadi.Routledge Handbooks Online, 5266-5293 (2016).
28. J. K. Oh, R. Drumright, D. J. Siegwart and K. Matyjaszewsk. Progress in Polym.Sci.,433, 448 (2008).
29. G. Odian. Wiley Interscience, 1-832 (2004).
30. S. Kawaguchi and K. Ito. Springer,175, 299 (2005).
31. R. K. Madhusudana, B. Mallikarjuna, R. K. S. Krishna, S. Siraj, R. K. Chowdoji and M. C. Subha. Colloids Surf. B. Biointerfaces,102, 891 (2013).
32. G. Tamura, Y. Shinohara and A. Tamura. Polymer Journal,44**,** 240–244 (2012).
33. A. Deka, R. Quarta, L. Falqui, R. Manna and T. Pellegrino.Langmuir, 26(12), 10315-10324 (2010).
34. P. B. Zetterlund, Y. Kagawa and M. Okubo. Chemical Reviews, 108, 3747–3794(2008).
35. K. S. Soni, S. S. Desale and T. K. Bronich. J Control.Release,240, 109-126 (2016).
36. N. Sanson and J. Rieger.Polymeric Chemistry,1, 965-977 (2010).
37. H. Gao and K. Matyjaszewski. Progress in Polym.Sci.,34, 317-350 (2009).
38. Kim and H. D. Sikes. Polymer Chemistry,11, 1424-1444 (2020).
39. C. E. Wang, P. S. Stayton, S. H. Pun and A. J. Convertine.J Control. Release, 219,345–354 (2015).
40. W. Park, S. J. Park and K. Na. Colloids Surf B. B. Biointerfaces,501, 79 (2010).
41. F. Brunel, L. Veron, .Ladaviere, L. David, A. Domard and T. Delair. Langmuir, 25,8935 (2009).
42. N. Kato, U. Hasegawa, N. Morimoto, Y. Saita, K. Nakashima, Y. Ezura,H. Kurosawa, K. Akiyoshi and M. Noda.J Cell Biochem.,101, 1063 (2007).
43. T. Nochi, Y. Yuki, H. Takahashi, S. Sawada, M. Mejima, T. Kohda, N. Harada, I. G. Kong, A. Sato, N. Kataoka, D. Tokuhara, S. Kurokawa, Y. Takahashi, H. Tsukada, S. Kozaki, K. Akiyoshi and H. Kiyono. Nature Mater., 9, 572 (2010).