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Nanomaterial Chemistry and Technology

Short Commentry

Metallic Nanoparticles for Targeted Drug Delivery

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Introduction

Targeted drug delivery aims at increasing therapeutic efficacy, achieving controlled distribution, improving drug localization and reducing drug toxicity (Figure 1) [1]. In this regard, metallic nanoparticles offer a new dimension towards the fulfillment of these aims in treating various diseases and their simplicity and ease of preparation has precipitated their interest in the scientific community [2]. Diseases such as cancer as well as several ocular diseases display many similarities in potential nano-based therapeutic intervention owing to their unusual chemistry and a variety of design considerations. Their physiochemical similarities, such as the over-expression of angiogenic factors, have inspired the design and development of pharmaceutical agents for targeted delivery where the drugs can safely reach their targets and deliver the cargo at the site of need with little to no interaction to surrounding structures and cells [3]. In addition to this, metallic nanoparticles with magnetic properties can also be used as drug delivery agents while under the influence of a magnetic field [4]. When looking specifically at ovarian cancer, the delivery of siRNA in a nanoscale metallic framework along with cisplatin manifests tremendous potential in re-sensitizing ovarian tumor cells to chemotherapy [5]. The application of these frameworks in conjunction with photodynamic therapy promises a great deal from the standpoint of cancer targeting as well ocular disease therapeutics [6,7].

Gold Nanoparticles (AuNPs)

The rationale behind targeted drug delivery is to produce a system that can deliver drugs at rates finely tuned to the biological requirements of the body [6] with high specificity and efficacy [1]. The primary objective is to develop a system that protects the payload and improves the therapeutic index [8,9]. In this regard, gold nanoparticles (AuNPs) have come into the spotlight of targeted pharmaceuticals. Amongst the wide range of nanomaterials used for anticancer therapy, AuNPs hold tremendous importance [7] due to their unique ability to respond to a variety of different stimuli, such as molecular binding or changes in ionic concentration, and release cargo instantaneously [10]. AuNPs can also be combined with targeting ligands in roder to reach sub-cellular compartments in specific tissue(s) [8].

A class of peptides, called integrins, are known to mediate intracellular signaling and gene expression. In recent studies, their role as highly amenable target molecules for cancer therapy has become evident [9]. Conjugation of these integrin peptides to the surfaces of AuNPs, as well as other metallic nanoparticles, holds significant promise in anticancer medicine [11]. Moreover, integrin targeted radiotracers can be used in tumor imaging by single photon emission computed tomography (SPECT) [12]. As integrins are prime targets for synaptic drug delivery, they can be functionalized on the surface of AuNPs to also provide theranostic application [1].

On the other hand, research in ocular disease treatment has also witnessed a significant perusal of AuNPs. Their self-therapeutic properties were utilized by Song *et al* to inhibit vascular angiogenesis in mice with oxygen-induced retinopathy. The surface properties of these nanoparticles were fine-tuned for Optical Coherence Tomography (OCT) imaging, and showed significant suppression of Vascular Endothelial Growth Factor (VEGF) *in vivo* [13]. Also, AuNPs designed by Karthikeyan *et al* demonstrated promising blockage of VEGF-induced cell proliferation in bovine retinal pigment epithelial (RPE) cells [14]. Additionally, VEGFR2 suppression in animal models of

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Nanoparticle	Size (nm)	Description	Application	Ref
GND	162 ± 3.3	Gold nanodisks	Ocular neovascularization	Song et al, 2017 (13)
Au-NP	50	Purified gold nanoparticles	Ocular neovascularization	Karthikeyan et al, 2010 (14)
cRGD + CLIO	28 ± 3	Cyclic RGD and cross-linked iron oxide nanoparticles	Cancer	Montet et al, 2006 (11)
PLA-PEG-Mal anti-HER-2 Affibody	85 ± 5	Poly (D,L lactic acid), poly(ethylene glycol), a maleimide terminal group and anti-HER-2 Affibody	Cancer	Alexis et al, 2008 (3)
Au-tiopronin	2.6	Ultra-small gold nanoparticles with tiopronin	Cancer	Huang et al, 2012 (18)
Au-Dox	2.7	Ultra-small gold nanoparticles with Doxorubicin	Cancer	Zhang et al, 2011 (19)

Table 1: Examples and characteristics of nano-based drug delivery systems to treat various diseases (i.e. cancer and ocular neovascularization).

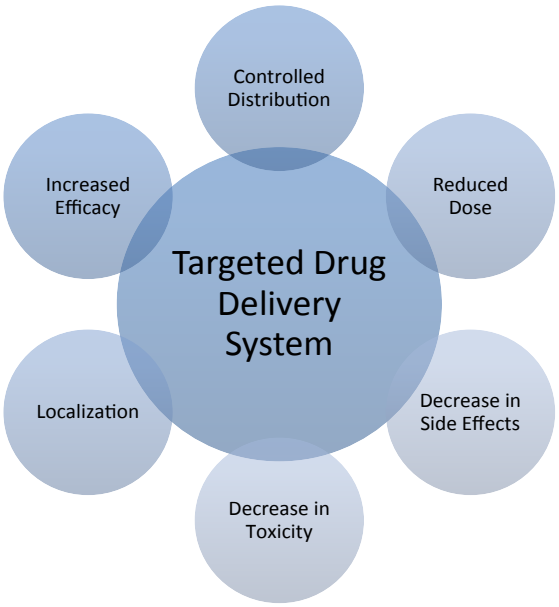

Figure 1: Ideal characteristics of a nano-based targeted drug delivery system.

retinopathy of prematurity (ROP) via AuNPs, designed by Kim *et al,* provides promising evidence of the effectiveness of gold-based nanoparticles in the area of ocular disease treatment [15].

Magnetic Nanoparticles (MNPs)

From the standpoint of biomedical imaging, the behavior of magnetic nanoparticles (MNPs) is affected by size, shape, surface defects and coating [2]. They provide a non-invasive means of achieving biological control at the nanoscale. The category of MNPs includes metallic, bimetallic and superparamagnetic iron oxide nanoparticles (SPIOs). Alongside their tunable magnetic properties, MNPs can be made to target tissues via biocompatible coatings [16]. One can also purposely increase their concentration in the tumor cells. In addition, they can be made to target the posterior segment of the eye as well, by means of functionalizing the surface of these MNPs with VEGF to enable transcytosis into posterior layers of the retina [17]. Once inside, they can specifically localize in the site of interest.

Nanoscale Metal-Organic Frameworks (NMOFs)

The union of organic compounds with a nanoscale metal framework has recently been reported for the treatment of ovarian cancer [5]. Acquired resistance to chemotherapy is the major reason behind the dismal prognosis in ovarian cancer cases [20]. After the discovery of small interfering RNAs (siRNAs) in 1998, it is now possible to silence certain genes. Thus, RNA interference has been shown to undo cisplatin resistance in ovarian cancer cells [21]. A Metal Organic Framework (MOF) is a class of self-assembling porous materials. Their properties can be tuned to construct molecular building blocks [22]. At the nanoscale, these NMOFs serve as nano-carriers of chemotherapeutics and imaging contrast agents [23]. A study by Liu *et al.* investigates NMOFs in cancer treatment in combination with photodynamic therapy (PDT) [24]. As PDT was approved for use in Age-Related Macular Degeneration (AMD) about 10 years ago [25], the use of NMOFs in treating posterior segment diseases of the eye is not far away. It is evident that their structural and chemical properties open up far-reaching avenues in the field of cancer targeting and ophthalmic disease treatment by making possible the co-delivery of chemotherapeutics, such as Cisplatin, and nucleic acids, such as siRNA, microRNA and plasmid DNA.

Conclusion and Future Perspectives

To summarize, targeted drug delivery has the potential to increase therapeutic efficacy while achieving controlled distribution as well as improving drug localization, thus reducing drug toxicity. Gold and magnetic nanoparticles demonstrate tremendous potential in not only treating diseases, but also performing diagnostic testing, as well as, real-time imaging. A variety of nanoparticle formulations show the promise of nanotechnology in achieving targeted drug delivery (Table 1). Although significant challenges still remain, especially in terms of reproducing similar results in clinical trials, the studies reported thus far manifest far-reaching capabilities of nanomedicine in cancer, ophthalmology and targeted drug delivery.

References

1. Kumar Anil, Zhang Xu, L Xing-Jie. Gold nanoparticles: Emerging paradigm for targeted drug delivery system (2013) Biotechnology Advances 593-606.
2. Mody Vicky V, Singh Ajay, Wesley Bevins. Basics of magnetic nanoparticles for their application in the field of magnetic fluid hyperthermia (2013) European Journal of Nanomedicine 11-21.
3. Alexis F, Basto P, Levy-Nissenbaum E, Radovic-Moreno AF, Zhang L, et al. HER-2-targeted nanoparticle-affibody bioconjugates for cancer therapy (2008) Chem Med Chem 1839-1843.
4. Mody VV, Arthur Cox, Samit Shah, Ajay Singh, Wesley Bevins, et al. Magnetic nanoparticle drug delivery systems for targeting tumor (2014) Applied Nanoscience 385-392.

5. Chunbai He, Kuangda Lu, Demin Liu, Wenbin Lin. Nanoscale Metal−Organic Frameworks for the Co-Delivery of Cisplatin and Pooled siRNAs to Enhance Therapeutic Efficacy in Drug-Resistant Ovarian Cancer Cells (2014) Journal of the American Chemical Society 136: 5181-5184.

6. Cunliffe D, Kirby A, Alexander C. Molecularly imprinted drug delivery systems (2005) Advanced Drug Delivery Reviews 57: 1836-53.

7. Cobley CM, Chen J, Cho EC, Wang LV, Xia Y. Gold nanostructures: a class of multifunctional materials for biomedical applications (2011) Chemical Society Reviews 40: 44-56.

8. Schroeder A, Heller DA, Winslow MM, Dahlman JE, Pratt GW. Treating metastatic cancer with nanotechnology. (2012) Nature Reviews Cancer 12: 39-50.

9. Garanger E, Boturyn D, Dum P. Tumor targeting with RGD peptide ligands-design of new molecular conjugates for imaging and therapy of cancers (2007) Anti-Cancer Agents in Medicinal Chemistry 7: 552-558.

10. Dreaden EC, Megan AM, Xiaohua Huang, Bin Kanga , El-Sayed MA. Beating cancer in multiple ways using nanogold (2011) Chemical Society Reviews 40: 3391-3404.

11. Montet X, Montet-Abou K, Reynolds F, Weissleder R, Josephson L. Nanoparticle imaging of integrins on tumor cells (2006) Neoplasia 8: 214-222.

12. Zhou Y, Chakraborty S, Liu S. Radiolabeled cyclic rgd peptides as radiotracers for imaging tumors and thrombosis by SPECT (2011) Theranostics 1: 58-82.

13. Song HB, Wi JS, Jo DH, Kim JH, Lee SW. Intraocular application of gold nanodisks optically tuned for optical coherence tomography: inhibitory effect on retinal neovascularization without unbearable toxicity (2017) Nanomedicine: Nanotechnology, Biology, and Medicine, 13: 1901-1911.

14. Karthikeyan B, Kalishwaralal K, Sardarpasha S, Venkataraman D, Ravinarayanan H. Gold nanoparticles downregulate VEGF- and IL-1β-induced cell proliferation through Src kinase in retinal pigment epithelial cells (2010) Experimental Eye Research 91: 769-778.

15. Kim JH, Kim MH, Jo DH, Yu YS, Lee TG. The inhibition of retinal neovascularization by gold nanoparticles via suppression of VEGFR-2 activation (2011) Biomaterials 32: 1865-1871.

16. Mamiya H, Jeyadevan B. Hyperthermic effects of dissipative structures of magnetic nanoparticles in large alternating magnetic fields (2011) Scientific Reports 1: 157.

17. Giannaccini M, Pedicini L, De Matienzo G, Chiellini F, Dente L. Magnetic nanoparticles: a strategy to target the choroidal layer in the posterior segment of the eye (2017) Scientific Reports 7: 43092.

18. Keyang Huang, Huili Ma, Juan Liu, Shuaidong Huo, Anil Kumar. Size-dependent localization and penetration of ultrasmall gold nanoparticles in cancer cells, multicellular spheroids, and tumors in vivo (2012) ACS Nano 6: 4483-4493.

19. Xuan Zhang, Hicham Chibli, Randall Mielke, Jay Nadeau. Ultrasmall gold-doxorubicin conjugates rapidly kill apoptosis-resistant cancer cells (2011) Bioconjugate Chemistry 22: 235-243.

20. D Roberts, J Schick, S Conway, S Biade, P B Laub. Identification of genes associated with platinum drug sensitivity and resistance in human ovarian cancer cells (2005) British Journal of Cancer 92: 1149–1158.

21. Yellepeddi VK, Vangara KK, Kumar A, Palakurthi S. Comparative Evaluation of Small-molecule Chemosensitizers in Reversal of Cisplatin Resistance in Ovarian Cancer Cells (2012) International J Cancer Res Treatment 32: 3651-3658.

22. Hailian Li, Mohamed Eddaoudi, M O'Keeffe, OM Yaghi. Design and synthesis of an exceptionally stable and highly porous metal-organic framework (1999) Nature 402: 276–279.

23. Rieter WJ, Taylor KM, An H, Lin W, Lin W. Nanoscale Metal−Organic Frameworks as Potential Multimodal Contrast Enhancing Agents (2006) Journal of the American Chemical Society 128: 9024–9025.

24. Jingjing Liu, Yu Yang, Wenwen Zhu, Xuan Yi, Ziliang Dong. Nanoscale metal−organic frameworks for combined photodynamic & radiation therapy in cancer treatment. (2016) Biomaterials 97: 1-9.

25. Lang GE, Mennel S, Spital G, Wachtlin J, Jurklies B. Different indications of photodynamic therapy in ophthalmology (2009) Klin Monbl Augenheilkd 226: 725-739.