

Nanotheranostics: A Light at the End of a Tunnel: A Review

Yesoda Aniyam K*, Krithika C. L, Anuradha Ganesan

SRM Dental College, SRM University of Science and Technology, Bharathi Salai, Chennai-600089,
Tamil Nadu, India

Abstract

Nanotheranostics encompasses the combined efforts of diagnostic imaging and therapy in one system. It is also a science of which adequate awareness and research are still lagging. It is a type of personalized medicine, wherein molecular understanding of the disease and conforming the treatment, is based on the patients' genes, proteins and metabolites. It uses nano-sized particles in various polymer conjugations, dendrimers, micelles, liposomes, metal and inorganic nanoparticles, carbon nanotubes, and nanoparticles of biodegradable polymers for uninterrupted, restrained and targeted co-delivery of agents. A current literature search of the entire database was performed using MEDLINE/PubMed/ Cochrane with "nano theranostics", "nano theranostics in dentistry", "nano theranostics in imaging" and "nano theranostics in diagnosis and therapy" as keywords, in March 2019. Current literature has forayed into cancer detection and management, diagnostic imaging as well and autoimmune disease remedies. This review of literature aspires to address the importance of such an approach, a boon to Oral Medicine and Radiology.

Keywords: *Nanotheranostics, Nanotheranostics in Dentistry, Nanotheranostics in Imaging, Nanotheranostics in Diagnosis and Therapy.*

Introduction

Nanotheranostics encompasses the combined efforts of diagnostic imaging and therapy in one system. It is a type of personalized medicine, wherein molecular understanding of the disease and conforming the treatment, is based on the patients' genes, proteins and metabolites [1]. This diagnostic and therapeutic modality utilizes nanotherapeutics, that capitalize polymer conjugations, dendrimers, micelles, liposomes, metal and inorganic nanoparticles, carbon nanotubes, nanoparticles of biodegradable polymers for uninterrupted, restrained and targeted co-delivery of agents. This concept will have fewer side effects which is ideal for any therapeutic measure [2].

This review of literature aspires to address the importance of such an approach, a boon to Oral Medicine and Radiology.

Methodology

A current literature search was performed using MEDLINE/PubMed/ Cochrane databases with "nano theranostics", "nano theranostics in dentistry", "nano theranostics in imaging" and "nano theranostics in diagnosis and therapy" as keywords, in March 2019. Both original research and review articles were selected for reporting recent techniques for the development of nanotheranostics. Only the most representative publications indexed in PubMed/MEDLINE or Scopus, written in English were considered. Other relevant research articles were manually obtained from previous publications.

Discussion

Nanotheranostics has the potential to add another dimension to the field of Oral Medicine and Radiology. As for current literature, it has forayed into cancer detection and management, diagnostic imaging as well as autoimmune disease remedies.

Cancer

Cancer, a convoluted, diverse, and destructive disease, is globally recognized as overwhelmingly demanding in terms of early diagnosis and management. A preeminent system, nano theranostics can first diagnose the type of cancer class, image the heterogeneity of the tumour, and apply a tailored treatment based on the diagnostic and imaging results. It is also adept at monitoring the treatment efficacy [3].

The mechanism of action of nanoparticles: oral or intravenous ingestion followed by circulation in blood. They further accumulate in the tumour by vascular extravasation due to irregular blood vessels and increased vascularity. These particles further penetrate tissue in the tumour microenvironment and internalize within the cells, further releasing the drug intracellularly [4, 5].

Xue et al reported the development and successful trial of a dual size/charge-transformable, nanoparticle for delivery of ultra-small, fully active pharmaceutical constituents (drug) with interspersed bimodal imaging and trimodal therapeutic functions. The dual size allowed ease in blood circulation and size transformation enables tumour accumulation via extravasations from blood vessels. The trimodal therapeutic functions included targeted drug delivery to the tumour site, photodynamic effect and synergistic action with chemotherapy [6].

The genomic markers released by malignant cells are identified by the programmed nanoparticles, enabling targeted delivery to the tumor site. This in turn alleviates the drug-induced toxicity to other organ systems simultaneously amplifying drug efficacy [4].

Additionally, Eyvazzadeh et al in a study reported the ability of nanoparticles to act as radiosensitizers in radiotherapy [5]. With these sterling qualities to recommend, early cancer diagnosis, imaging and treatment are just beyond the horizon.

Imaging

Nanotheranostics has forayed into imaging as well. A metabolic by-product of the presenting pathology such as matrix metalloprotease, produced in cancer metabolism is identified. Organic nanoparticle fluorophores are sensitive to such by-products, which then accumulate within the lesion based on AIE (Aggregation emission). Additional advantages of these nanoparticles include emitting non-ionizing radiation during fluorescence, photostability and biocompatibility. In photodynamic therapy, this principle is applied. Hence, simultaneous to the optical imaging during fluorescence, the heat generated by laser activation, causes therapeutic cell death [7]. Xia Q et al have investigated this modicum and reported great application prospects in cell tracking, tumour imaging and image-guided treatment [8].

In CT imaging, gold nanoparticles (AuNP) have been proven for used as a contrast agent. It is facilitated owing to biocompatibility, higher atomic number and X-ray absorption coefficient. Kim et al presented a novel multifunctional AuNP for targeted molecular CT imaging and therapy of prostate cancer [9, 10].

MRI is one of the primary oncology imaging modalities. Magnetic iron oxide (IO) nanoparticles have been proven effective as target-specific MRI T2 contrast agents [10]. They are more efficient than Gadolinium-DTPA as relaxation promoters and their magnetic properties can be manipulated by controlling the sizes of the core and coating surface. More importantly, IO nanoparticles have a long blood retention time, biodegradability and low toxicity [11].

Autoimmune Disease

Autoimmune diseases are protracted, detrimental diseases that can cause functional disability and eventual multiple organ failure. Despite compelling advances in the multitude of therapeutic agents, constraints in the routes of administration, the need for incessant long-term dosing and meagre targeting options resulted in suboptimal effects, systemic adverse reactions and patient non-compliance [12, 13, 14]. In the context of autoimmunity, nanoparticles primarily target the immune cells [15, 16]. They have demonstrated uses as antigen-linked nanoparticles in artificial apoptotic antigen-presenting cells, peptide MHC-based nano-vaccines and targeting dendritic cells [17, 18, 19]. Also, cellular toxicity associated with certain nanomaterials has been used to kill or inhibit pathogenic cell types by preferential accumulation into specific sub-cellular compartments of immune cell types. This principle avails the potential to enhance the desired biological activity while limiting the off-target toxicity of drugs. Some of the key autoimmune disorders clinically

References

[1]. Kim, T., Lee, S., Chen, X., 2013. Nanotheranostics for personalized medicine. *Expert Rev. Mol. Diagn.* 13 (3):257–269.

[2]. Mahesh, K. P., 2018. Nanotheranostics--Novel Modality for Integrating Diagnosis and Therapy for Oral Cancer. *Acta Scientific Dental Sciences.* 2 (9): 57-58.

[3]. Silva, C., Pinho, J., Lopes, J., Almeida, A., Gaspar, M., Reis, C., 2019. Current Trends in Cancer Nano-theranostics: Metallic, Polymeric, and Lipid-Based Systems. *Pharmaceutics.* 11: 22.

[4]. Xue, X., Huang, Y., Bo, R., Jia, B., Wu, H., Yuan, Y., Wang, Z., Ma, Z., Jing, D., Xu, X., Yu, W., Lin, T. Y., Li, Y., 2018. Trojan Horse nanotheranostics with dual transformability and multifunctionality for highly effective cancer treatment. *Nat Commun.* 7;9(1):3653.

tested include type 1 diabetes, multiple sclerosis, systemic lupus erythematosus and rheumatoid arthritis [17, 19, 20].

Autoimmune diseases are extremely challenging to control and cure is next to impossible by contemporary standards [21, 22]. However, with nano theranostics, the disadvantage of the current treatment protocol is becoming a thing of the past.

Conclusion

Nanotheranostics and their advantages are multiplying by the second. Its potential to benefit multiple challenging diseases and disorders in Oral medicine and to revolutionize diagnosis through Radiology is staggering. However, its relative neoteric aspect and the compounding cost of this therapy is a limiting factors.

Conflict of Interest

None.

Acknowledgement

None.

[5]. Eyvazzadeh, N, Shakeri-Zadeh, A, Fekrazad, R, Amini, E., Ghaznavi, H., Kamran Kamrava S., 2017. Gold-coated magnetic nanoparticle as a nanotheranostic agent for magnetic resonance imaging and photothermal therapy of cancer. *Lasers Med Sci.* 32(7):1469-1477.

[6]. Abiodun-Solanke, I., Ajayi, D., Arigbede, A., 2014. Nanotechnology and its application in dentistry. *Ann Med Health Sci Res.* 4 (Suppl 3):S171-7.

[7]. Wang, L. S., Chuang, M. C., Ho, J. A., 2012. Nanotheranostics--A review of recent publications. *Int J Nanomedicine.* 7:4679-95.

[8]. Xia, Q., Chen, Z., Zhou, Y., Liu, R., 2019. Near-Infrared Organic Fluorescent Nanoparticles for Long-term Monitoring and Photodynamic Therapy of Cancer. *Nanotheranostics* 2;3(2):156-165.

- [9]. Vadivel, J. K, Govindarajan, M, Somasundaram, E, Muthukrishnan, A., 2019, Mast cell expression in oral lichen planus: A systematic review. *J Investig Clin Dent.* 10: e12457. doi:10.1111/jicd.12457113.
- [10]. Peng, X et al.2008. Targeted magnetic iron oxide nanoparticles for tumor imaging and therapy. *Int J Nanomedicine.*3(3): 311–321.
- [11].Rogers, W. J., Basu P.2005. Factors regulating macrophage endocytosis of nanoparticles: implications for targeted magnetic resonance plaque imaging. *Atherosclerosis.*178(1):67-73.
- [12]. Gharagozloo, M., Majewski, S., Foldvari, M., 2015. Therapeutic applications of nanomedicine in autoimmune diseases: from immunosuppression to tolerance induction. *Nanomedicine.* May;11(4):1003-18.
- [13].Serra, P., Santamaria, P., 2015. Nanoparticle-based autoimmune disease therapy. *Clin Immunol.*160(1):3-13.
- [14].Badea, I., Virtanen, C., Verrall, R. E., Rosenberg, A., Foldvari, M., 2012. Effect of topical interferon- γ gene therapy using gemini nanoparticles on pathophysiological markers of cutaneous scleroderma in Tsk/+ mice. *Gene Ther.*19(10):978-87.
- [15].Rao, V, Bowman, S., 2013. Latest advances in connective tissue disorders. *Ther Adv Musculoskelet Dis.* 5(4):234-49.
- [16]. Klippstein, R., Pozo, D., 2010. Nanotechnology-based manipulation of dendritic cells for enhanced immunotherapy strategies. *Nanomedicine: Nanotechnology, Biology, and Medicine.* 6: 523-529.
- [17].Lutterotti, A., Yousef, S., Sputtek, A., Stürner, K. H., Stellmann, J. P., Breiden, P., Reinhardt, S., Schulze, C., Bester, M., Heesen, C., Schippling, S., Miller, S. D, Sospedra, M, Martin, R., 2013. Antigen-specific tolerance by autologous myelin peptide-coupled cells: a phase 1 trial in multiple sclerosis. *Sci Transl Med.* 5;5(188):188ra75.
- [18].Tsai, S. S., Yamanouchi, A., Clemente-Casares, X., Wang Serra, P., Yang, Y., Medarova, Z. M., Santamaria, A. P., 2010. Reversal of autoimmunity by boosting memory-like autoregulatory T cells. *Immunity* 32:568-580.
- [19].Look, M., Saltzman, W. M., Craft, J., Fahmy, T. M., 2014, The nanomaterial-dependent modulation of dendritic cells and its potential influence on therapeutic immunosuppression in lupus. *Biomaterials.*35(3):1089-95.
- [20].Clemente-Casares, X., Tsai, S., Huang, C., Santamaria, P., 2012. Antigen-specific therapeutic approaches in Type 1 diabetes. *Cold Spring Harb Perspect Med.* 2(2): a007773.
- [21].Yesoda Aniyani K , Krithika C.L,Anuradha G,Kannan A,Swathi K.V. (2022). A systematic review of randomized controlled trials on the Efficacy of purslane for the treatment of systemic disorders. *International Journal of Chemical and Biochemical Sciences.* 21: 219-223
- [22]. Anuradha Ganesan, et al., 2024. Exploring the Relationship between Psychoneuroimmunology and Oral Diseases: A Comprehensive Review and Analysis. *Journal of Lifestyle Medicine.*14(1):13-19.