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Review Article

Bio-materials and Bio-active Nano-particles in Immunotherapy

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ABSTRACT

Immunotherapy is a biological therapy in which the treatment of the disease is achieved by either the activation or suppression of the immune system. In the past decade, this method of therapy has been successfully in use for the treatments of various forms of cancer. Immunity induced against Covid-19 with the vaccination is reported to involve immunomodulatory T cell response. Such vaccine-induced immunity is known to stimulate the natural immune system to fight against the disease. Precision medicine is at the heart of immunotherapy as presently, it is the most researched area for cancer treatment. Despite its effectiveness, for unknown reasons, the therapy has shown responses in the range of 20–50 percentage of patients only. However, the inseparable limitations of conventional immunotherapy are the difficulties of precise dosage control, high cost, insufficient enrichment in tumor tissues, and partial immune response silencing or hyperactivity. Due to these challenges the use of nanomedicines with immunotherapy has acquired interest in research and is reported to enhance the effectiveness of this therapy against the diseases, especially in the treatment of cancers and tumors. Advanced nano biomaterials are found to be important in co-delivery of drugs and immunomodulators. The nanomedicines could precisely target the biological pathways. Thus, apart from enhancing the response range, the application of nano biomaterials will certainly reduce the toxic effects of the drugs. The present review gives an insight of the challenges in the application of immunotherapy and the modification through bioactive nanoparticles.

Key words: Bioactive materials, Cancer, Immunotherapy, Nanocarrier, Nanoparticles.

1. INTRODUCTION

Due to the uncontrolled cell division and weak immune mechanism, cancer is becoming one major peril to human health. The mortality rate has been greatly affected because of recent advancement in the development of various diagnosis and therapy technologies. In cancer immunotherapy, the body's natural immune system is used to recognize and attack cancer cells. The goal of this treatment is to stimulate the natural immune system to fight against cancer. The advancements in cancer immunotherapy have made significant strides in the past decade. Currently, immunotherapy accesses such as cancer vaccines, immune checkpoint blockade (ICB), adoptive cell transfer, monoclonal antibodies therapy, and cytokines therapy showing high potential in preclinical and clinical applications [1]. The combined efforts of pharmacologists, chemists, and material scientists have resulted into the innovation of new approaches to diagnose cancer. Computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, positron emission tomography, single-photon emission CT, and fluorescence imaging are commonly used diagnosis [2]. The concept of co-delivery of immunomodulatory agents with chemotherapeutic agents has shown promising results. However, it remains a challenging area to develop effective and safe cancer immunotherapies. Using nanotechnology, this field can be utilized to develop cancer immunotherapies that are more effective and less toxic. Using nanoparticles (NP) and biomaterials, cancer antigens can be effectively delivered to targeted sites. Due to their unique thermal, magnetic, optical, and chemical characteristics [3], biomaterials play role in improvising the potency of three major strategies of immunotherapy. These are chimeric antigen receptor T-cell therapy, cancer vaccine therapy, and ICB therapy [4]. Among sort of bioactive NP systems for cancer immunotherapy, polymeric NP are the most common. Poly (lactic-co-glycolic acid) (pLGA) due to its nontoxicity and biodegradability, is one of the foremost studied FDA approved polymeric carriers for cancer immunotherapy. In addition to pLGA lipids, Step (polyethylene glycol) is also ordinarily used for the mix of nanocarrier systems as vehicles for immunotherapy. Similar applications of liposomes, virus like particles (VLPs), micelles, dendrimers, inorganic NP have also been studied and well reported. Bioactive NP successfully deliver antigens, adjuvants or other immunotherapeutic agents to the asked target points, such as lymph nodules or other intracellular positions, for the activation of the untouchable response.

1.1. Assorted Biomaterials and Bio-active NPs for Immunotherapy

NP are generally made up of various materials such as polymers, metal, and liposomes. Their primary function is to deliver a targeted product to a specific site by three methods: Passive targeting, active targeting, and physical targeting. Active targeting is conducted by exposing NP to specific receptors. The goal is to stimulate the uptake of the NP by the targeted cell. Physical targeting is achieved by using external sources that guide NP to the specific sites. They can either be bound to the receptor of cancer cells or conjugated to a ligand. Passive targeting follows enhanced permeability and retention effect which is a phenomenon related to the accumulation of NPs within tumor

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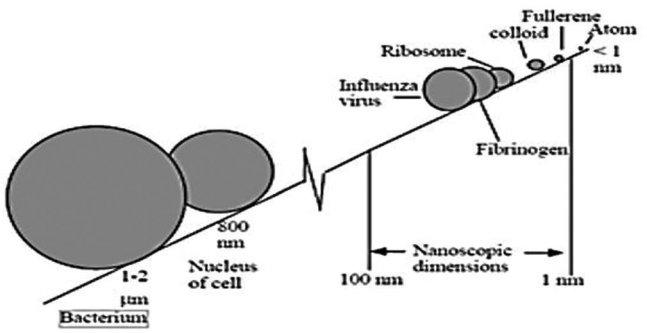
cells. This phenomenon is evidenced by the abnormal vasculatures of cancer cells. Nano formulations can improve a drugs pharmacokinetics by acting at different levels they can prevent drug opsonization by preventing it to occur [5]. Since immunomodulators have a high surface area to volume ratio, so to minimize the drug's effects, a lower concentration is needed. These derivatives can carry high–density peptide major hetero compatibility complex (pMHC) and fastened the re-engagement of dissociated peptide major hetero compatibility complex pMHC [6]. Some factors such as target effective, *in vivo* and *in vitro* toxicity, surface engineering, immune response, the synergistic therapy effect of NP and biomaterials should be considered wisely to begin with therapy design processes. The enhancement of the cross-presentation of neoantigens to antigen-presenting cells triggers a greater immune response it can be utilized for the development of effective vaccines and checkpoint inhibitors. Table 1 [5,7] summarizes various recently developed NP available for immunotherapy of cancer.

2. SYNTHESIS OF NP

NP's are materials having dimensions of the order of 100 nm or less. These NP's exhibits a high surface/volume ratio which has different properties.

Due to technological and fundamental scientific importance, the development of uniform NP has been intensively performed.



Comparison of nano range with other sizes

There are number of chemical methods available and are widely used, but these are often energy-intensive and employ toxic chemicals hence an alternative approach has been introduced via biological route for the synthesis of uniform NP which occurs at ambient pressure, temperature, and at neutral pH. NP's can be produced easily even in reasonable scale because the biomaterial-based routes eliminate the need to use harsh or toxic chemicals. Waste products are relatively non-toxic and easier to dispose of because they are mainly composed of leftover natural plant extracts. Greener synthetic methods involving plant materials that have been used in the synthesis of NP are generally single-pot reactions, without the use of additional surfactants, capping agents, and/or templates. The resulting particles possess increased stability and longevity as they are protected from further reactions and aggregation.

2.1. Gold NP (Au NPs) and Its Alloys

In recent years, gold-based NPs have attracted extensive attentions due to their optical, thermal, and electrical properties [8]. The application of gold-based NPs for biological labeling, therapy, and imaging has been a hot interdisciplinary topic in material science and biomedicine science. With excellent physical properties and low toxicity, gold-based NPs can eventually be metabolized [9]. Like iron-based NPs, plentiful progress has revealed the innate immunogenicity of gold-based NPs which has been related to size and shape of Au NPs. Au NPs have been designed to hold antigen targeting and are reported to be used in cancer nano vaccines to compensate for the monotony of conventional vaccines [10,11]. Jon *et al*. have engineered Au NPs to conjugate with cysteine-modified model antigen, red fluorescent protein, and a sort of immune agonists, toll-like receptor agonists, thiol-modified cytosine-phosphate-guanine oligodeoxynucleotide [10]. A variety of Au NP have been synthesized by banana peel extract which is simple, non-toxic, eco-friendly green material [11]. The chloroauric acid was reduced by boiled, crushed, acetone-precipitated, air-dried banana peel powder. The aggregated NP were observed towards the periphery of the air-dried samples in microcubes and microwire networks. There was involvement of carboxyl, amine, and hydroxyl groups during the synthetic. Nanocomposites of Au NP have also been obtained by using tea extracts. Tea leaf extracts in 1-methyl-2-pyrrolidinone (NMP) solution was used for the fabrication of 20 nm Au NP [12]. These NP were consolidated in NMP solution of polyaniline emeraldine base (PANIEB) to form the nanocomposite films. In polyaniline matrix, the confirmation of the presence of Au NP is done by TEM analysis.

By mixing the Au (III) ion-dissolved rice wine with soda at pH 6.5 at a lightly elevated temperature (25–55°C) Au NP were obtained via completely greener route in the absence of extra protective agents [13], where rice wine was used as a solvent and a reducing agent; soda act as protective agent and as a base catalyst [14].

2.2. Iron (Fe) NP

In clinics, iron-based NPs are commonly used for diagnosis. Based on the finding of ferromagnetic NPs intrinsic peroxidase-like activity, antibody-modified magnetite NPs were first used in a new immunoassay, which provided some important theoretical bases for subsequent research for iron-based NPs applied in immunotherapy [15]. More recently, iron-based NPs are proved to enhance different cell-mediated immune reaction due to intrinsic immunogenicity. Tumor Associated Macrophages are one of the foremost abundant immune cells within the TME, which can be polarized in M1- or M2-like phenotypes with different functions through regulating cytokines. M1-like macrophages have phagocytic function on cancer cells and M2-like macrophages promote tumor cell growth by suppressing immune response [16,17]. Furthermore, iron-based NPs have also

Table 1: Recently developed nanoparticles used for immunotherapy.

Sr. No.	Nanoparticle	Source	Application
1.	Gold NP	$HAuCl_4$	In Cancer Immunotherapy
2.	Iron NP	Magnetite (Fe_3O_4), Haematite (Fe_2O_3)	In Cancer Immunotherapy
3.	Manganese NP	Pyrolusite (MnO_2), Other oxides of Mn like MnO, Mn_3O_4, Mn_2O_3	In Cancer Immunotherapy
4.	Mesoporous silica NP	Tetraethyl orthosilicate (TEOS)	In Cancer Immunotherapy
5.	Titanium oxide NP	Ilmenite ($FeTiO_3$)	Photo-induced Immunotherapy of Tumour cells

been promising candidates for the preparation of nano vaccines. Iron oxide NPs (IONPs) (superparamagnetic Fe_3O_4 NPs) decorated with specific antigen ovalbumin (OVA) was developed as an easy vaccine. OVA formulated with IONPs, promoted the activation of immune cells and cytokines production, which reflected the simple immunogenicity of IONPs based vaccines [17,18]. Ironoxide-zincoxide core-shell NPs incorporated carcinoembryonic antigens were constructed to move into DCs [19] while simultaneously acting as an imaging agent [20]. Variety of NP are being explored for their activity as immunotherapy agents. It has been reported that the extracts of plants and spices can produce Iron nano particles which is an alternative to chemical synthesis protocols and low-cost reductant for synthesizing iron (metallic) nano particles [21]. The effect of iron NP produced from plant extracts of certain leaves, buds, and seeds on the pH have been summarised in Table 2. Studies have shown that mixing of ferric chloride with different plant and spices extract reduces the iron ions which change the pH and color of the solutions and indicate the formation of iron NP. Under the UV-Visible wavelength, NP shows good surface plasmon resonance behavior.

2.2.1. Manganese (Mn)-based NPs

Mn based NPs with the characteristics of acid-induced disintegration, multiple enzyme-mimicking activity, and catalytic-triggering Fenton reaction, make their versatile application in imaging (e.g., MRI), drug delivery, and cancer synergistic therapies. In recent years, Mn-based NPs are reported to be involved in cancer immunotherapy. For instance, an intelligent biodegradable hollow Mn dioxide (MnO_2) nanoplatform with modification of polyethylene glycol (PEG) [22] was prepared to co load a photodynamic agent chlorine (Ce6) and doxorubicin (Dox) [23]. This type of MnO_2 NPs not only enabled MRI-derived accurate diagnosis implementation but also triggered the decomposition of endogenous H_2O_2, leading to an honest effect of chemo-photodynamic therapy synergized with anti-programmed cell death-ligand 1 (PD-L1) antibodies (PD-L1) therapy. $CaCO_3/MnO_2$-based Nano platform not only enhanced oxygen production-derived PDT but also made synergistic benefits from PD-L1 small interfering RNA (siRNA), which improved antitumor immune reaction [2].

2.3. Silver NP (Ag)

Silver NP ranges from 5 to 10 nm in size. It has been synthesized using glutathione under microwave irradiation conditions (Figure 1), which is a cordial antioxidant that serves as the capping agent as well as the reducing agent in aqueous medium [24]. The process takes up to

Table 2: Effect of green synthesis of Iron nano particles on the pH.

S. N.	Plant used	Effect on pH		Result
		Before Reduction	After Reduction	
1	Mango	5.12	2.16	+
2	Clove	4.22	1.88	+
3	Rose	5.75	2.75	+
4	Black Tea	5.00	3.28	+
5	Green Tea	5.37	2.65	+
6	Coffee	4.90	2.20	+
7	Carom Seeds	5.76	3.89	+
8	Champa	4.86	3.22	+
9	Neem	5.69	3.93	+
10	Curry Leaves	4.50	3.23	+

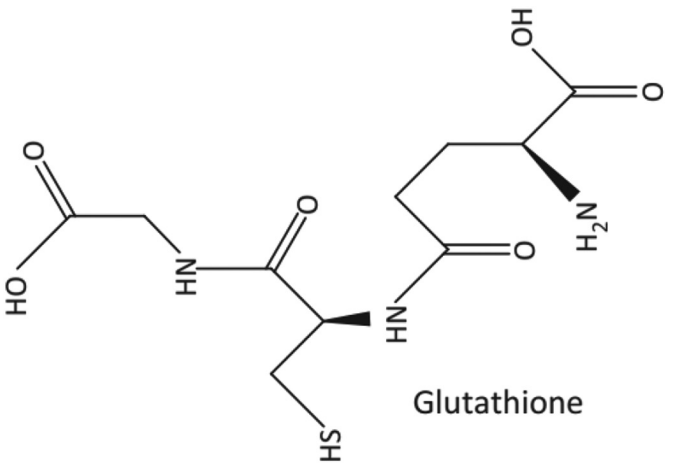


Figure 1: Structure of Glutathione

30–60 min and is also suitable for the synthesis of palladium, platinum, and Au NP. A long with D-sorbitol which increases the stability of the NP, the silver NP are synthesized (at room temperature and 60°C) using

Polyalthia longifolia leaf extract as capping and reducing agent [25]. The synthesized silver NP were more highly toxic to Gram-positive bacteria than Gram-negative bacteria.

2.3.1. Micelles

The use of micelles for cancer therapy has been studied an explored both preclinically and clinically and results of various studies have reported their wide uses as carriers for imaging, chemotherapy, radiotherapy, and immunotherapy. The mix of micelles is comparatively easier than that of other NPs. The biodegradability and non-toxicity of these articulations make them suitable for carrying officinal burdens. Antigen delivery to the cytoplasm ordinarily uses pH-responses liposomes. Studies show that the cytoplasm delivery of antigens is feasible using micelles as carriers. A pH-responsive micelle composed of dilauroyl phosphatidylcholine and deoxycholic acid was synthesized both to deliver antigens to the cytoplasm and to induce an inviolable response. Micelles were taken up by dendritic cells generally via micro pinocytosis and delivered OVA into the cytosol. These micelles are useful for adding the capability of cellular immunity in the treatment of cancer [26].

2.3.2. Dendrimers

Dendrimers are round polymeric macromolecules with defined hyperbranched infrastructure. The fusion of dendrimers is initiated by responding an ammonia core with acrylic acid. The response results in forming a "tri-acid" scruple, that further reacts with ethylenediamine to yield "tri-amine" acid, which further produces "hexa-amine" (generation one) product and so on [27]. Normally, the size of dendrimers ranges from 1 to 10 nm and maximum can reach up to 15 nm. These are used to target nucleic acids. The Studies have reported significant delayed growth of epithelial cancer xenograft by the synthesized dendrimers [28]. Dendrimers in immune-oncology are used in vaccines and immunostimulant. Azabiphosphonate capped dendrimers increase natural killer (NK) cell activity mediated via $CD4^+$ T-cells, thereby killing tumor cells by boosting natural immunity. They also stimulate monocytes and $CD4^+$ T-cells to secrete interleukin (IL)-4 and IL-10 for cell cycle disruption of tumor cells. T-antigen disaccharide conjugated dendrimers (Figure 2) serve as an important biomarker for cancer cells. Besides, peptide conjugated dendrimers have a great impact on dendritic cell stimulation and IL-1β and IL-12 secretion, which are important events in the vaccine delivery system, thus contributing to vaccine delivery in immunotherapy [29].

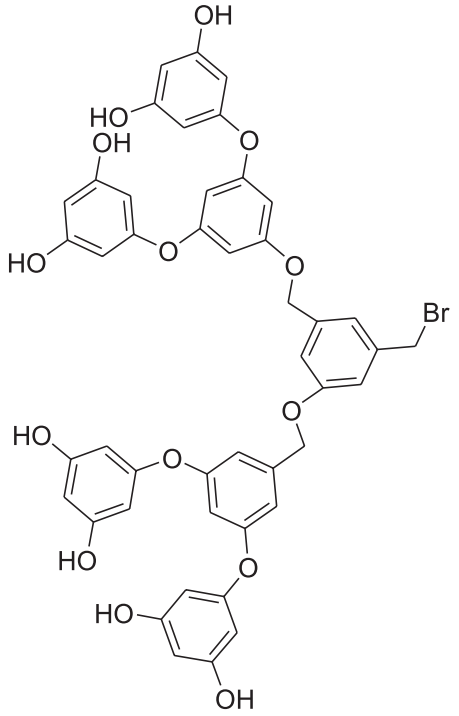


Figure 2: Saccharide conjugated dendrimer for cancer immunotherapy.

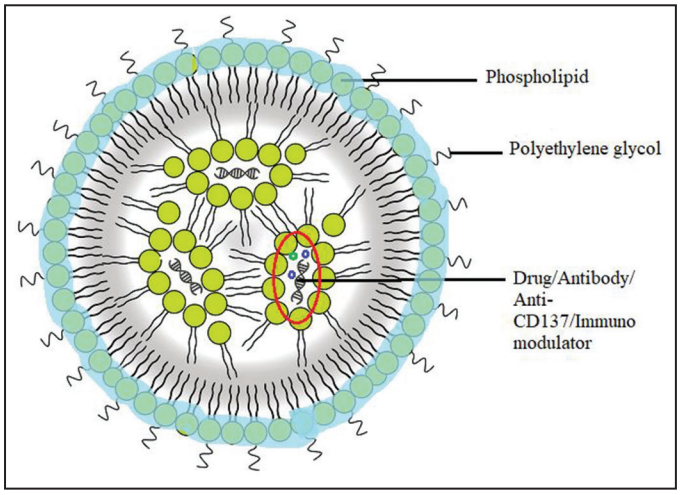


Figure 3: PEGylated liposomes in immunotherapy [29].

2.3.3. Liposomes

Liposomes are global vesicles comprising phospholipids that may be either uni-lamellar or multi-lamellar. The first nano-scale medicine was approved in 1965 [30]. A liposome structure is composed of a "hydrophilic core" and a "hydrophobic phospholipid bilayer". This unique fabric makes it possible for them to entrap both hydrophilic and hydrophobic medicinal [31]. Liposomes are an excellent platform for physic delivery parallel as doxorubicin, paclitaxel, and nucleic acid as well demonstrating late anti-tumor efficiency and enhance bioavailability [32,33]. Liposomes can associate with variety of chemotherapeutics, peptides, and antibodies and can act as platform for controlled release of antigens, immunomodulators, or drugs, which are essential for immunotherapy. Polyethylene glycolated (PEGylated) liposomes (Figure 3) tend to passively accumulate in tumor cells, thus, driving targeted delivery of drugs to these cells, for their disruption. Polyethylene glycolate immunoliposomes conjugated with anti-CD137 (anti-stimulatory receptor factor for tumor) and IL-2Fc enhances anti-tumor immune responses with minimized toxicity [34].

2.3.4. Bacteria and toxicants

Multiplex bacteria have been reported to target, and in some cases, destroys tumors using immunotherapy. Modulating the gut microbiome may impact sequences of cancer immunotherapy, especially for susceptible checkpoint siege-rested therapeutics [35]. Viruses are exquisites nanoscale biomaterials that have been used as considerably promising material as host for cancer antidote, etc. Immunotherapeutic benefits of antidotes have also been studied and reported. As viruses can amplify host exposed responses, release neoplasm-associated antigens, disrupt exposed sufferance so have also been modified as carriers for vaccine delivery [36]. Studies have revealed that Oncolytic virus-based combinations immunotherapies which is under clinical trials, can be used for treatment of multiple types of cancers.

2.3.5. VLPs

VLPs (20–100 nm in size) are artificial nanostructures appearing antivenoms without the competency to replicate. VLPs are immunogenic and can stimulate invincible responses, which provides a new means for cancer immunotherapy. VLP based vaccines can target vulnerable cells and upgrade vaccine productiveness. At present, new cancer vaccines are developed through engineering and combination of VLPs. Lizotte *et al*. first reported that a VLP-rested NPs generated from cowpea mosaic panacea could be directly used as a cancer immunotherapeutic agent rather than delivery vesicle [37].

3. CONCLUSION

In this review, we tried to summarize the application of some bioactive NP and biomaterials in cancer immunotherapy. Recent successes in immunotherapy have attracted the new therapeutics technologies. The complexities of TME, off-target side belongings, and low immunogenicity are still challenges for effective therapy. To resolve these issues designing multiple biomaterials, NPs with enhanced anti-tumor responses is required.

4. ACKNOWLEDGMENT

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5. CONFLICT OF INTEREST

None declared.

6. REFERENCES

1. S. Wang, Z. Sun, Y. Hou, (2021) Engineering nanoparticles toward the modulation of emerging cancer immunotherapy, ***Advanced Healthcare Materials***, **10**(**5**): 2000845.
2. X. Han, K. Xu, O. Taratula, K. Farsad, (2019) Applications of nanoparticles in biomedical imaging, ***Nanoscale***, **11**(**3**): 799-819.
3. W. Fan, B. Yung, P. Huang, X. Chen, (2017) Nanotechnology for multimodal synergistic cancer therapy, ***Chemical Reviews***, **117**(**22**): 13566-13638.
4. S. Yan, Z. Luo, Z. Li, Y. Wang, J. Tao, C. Gong, X. Liu, (2020) Improving cancer immunotherapy outcomes using biomaterials, ***Angewandte Chemie***, **132**(**40**): 17484-17495.
5. H. Maeda, T. Sawa, T. Konno, (2001) Mechanism of tumour-targeted delivery of macromolecular drugs, including the EPR effect in solid tumour and clinical overview of the prototype polymeric drug SMANCS, ***Journal of Controlled Release***, **74**(**1-3**):' 47-61.
6. J. B. Huppa, M. Axmann, M. A. Mörtelmaier, B. F. Lillemeier, E. W. Newell, M. Brameshuber, M. M. Davis, (2010) TCR-peptide-MHC interactions in situ show accelerated kinetics and increased affinity, ***Nature***, **463**(**7283**): 963-967.
7. B. Feng, B. Zhou, Hou, D. Wang, T. Wang, Y. Fu, Y. Li,

(2018), Binary cooperative prodrug nanoparticles improve immunotherapy by synergistically modulating immune tumor microenvironment, ***Advanced Materials***, **30**(**38**): 1803001.
8. X. Bai, Y. Wang, Z. Song, Y. Feng, Y. Chen, D. Zhang, L. Feng, (2020) The basic properties of gold nanoparticles and their applications in tumor diagnosis and treatment, ***International Journal of Molecular Sciences***, **21**(**7**): 2480.
9. S. B. Yaqoob, R. Adnan, R. Rameez Khan, M. Rashid, (2020) Gold, silver, and palladium nanoparticles: A chemical tool for biomedical applications, ***Frontiers in Chemistry***, **8:** 376.
10. P. Velpurisiva, A. Gad, B. Piel, R. Jadia, P. Rai, (2017) Nanoparticle design strategies for effective cancer immunotherapy, ***Journal of Biomedicine***, **2**(**2**): 64.
11. A. Bankar, B. Joshi, A. R. Kumar, S. Zinjarde, (2010) Banana peel extract mediated synthesis of gold nanoparticles, ***Colloids and Surfaces B: Biointerfaces***, **80**(**1**): 45-50.
12. A. B. Afzal, M. J. Akhtar, M. Nadeem, M. ul Hassan, (2009) Investigation of structural and electrical properties of polyaniline/gold nanocomposites, ***The Journal of Physical Chemistry C***, **113:** 17560-17565.
13. C. C. Wu, D. H, Chen, (2007) A facile and completely green route for synthesizing gold nanoparticles by the use of drink additives, ***Gold Bulletin***, **40:** 206-212.
14. O. V. Kharissova, H. V. R. Dias, B. I. Kharisov, B. O. Pérez, V. M. J. Pérez, (2013) The greener synthesis of nanoparticles, ***Trends in Biotechnology***, **31**(**4**): 240-248.
15. J. Liu, L. Yang, X. Cao, M. Chen, J. Li, X. Wang, Z. Zhang, (2021) PEGylated Mn containing MOF nanoparticles for potential immunotherapy of pancreatic cancer via manganese induced activation of anti-tumor immunity, ***Colloid and Interface Science Communications***, **42:** 100409.
16. C. Janko, T. Ratschker, K. Nguyen, L. Zschiesche, R. Tietze, S. Lyer, C. Alexiou, (2019) Functionalized superparamagnetic iron oxide nanoparticles (SPIONs) as platform for the targeted multimodal tumour therapy, ***Frontiers in Oncology***, **9:** 59.
17. Y. Zhao, X. Zhao, Y. Cheng, X. Guo, W. Yuan, (2018) Iron oxide nanoparticles-based vaccine delivery for cancer treatment, ***Molecular pharmaceutics***, **15**(**5**): 1791-1799.
18. T. K. Kishimoto, R. A. Maldonado, (2018) Nanoparticles for the induction of antigen-specific immunological tolerance, ***Frontiers in Immunology***, **9:** 230.
19. R. A. Burga, D. H. Khan, N. Agrawal, C. M. Bollard, R. Fernandes, (2019) Designing magnetically responsive biohybrids composed of cord blood-derived natural killer cells and iron oxide nanoparticles, ***Bioconjugate Chemistry***, **30**(**3**): 552-560.
20. M. Mühlberger, C. Janko, H. Unterweger, R. P. Friedrich, B. Friedrich, J. Band, R. Tietze, (2019) Functionalization of T Lymphocytes with citrate-coated superparamagnetic iron oxide nanoparticles for magnetically controlled immune therapy, ***International Journal of Nanomedicine***, **14:** 8421.
21. M. Pattanayak, P. L. Nayak, () Ecofriendly green synthesis of iron nanoparticles from various plants and spices extract, ***International Journal of Plant, Animal and Environmental Sciences***, **11**: 68-78.
22. B. Ding, J. Yue, P. Zheng, J. Lin, (2021) Manganese oxide nanomaterials boost cancer immunotherapy, ***Journal of Materials Chemistry B***, **9:** 7117-7131.
23. L. Hou, C. Tian, Y. Yan, L. Zhang, H. Zhang, Z. Zhang, (2020) Manganese-based nano activator optimizes cancer immunotherapy via enhancing innate immunity, ***ACS Nano***, **14**(**4**): 3927-3940.
24. Baruwati, B, V. Polshettiwara, R. S. Varma, (2009) Glutathione promoted expeditious green synthesis of silver nanoparticles in water using microwaves, ***Green Chemistry***, **11:** 926-930.
25. Kaviya, S, J. Santhanalakshmi, B. Viswanathan, (2011) Green synthesis of silver nanoparticles using *Polyalthia longifolia* leaf extract along with D-sorbitol: Study of antibacterial activity, ***Journal of Nanotechnology***, **2011:** 152970.
26. E. Yuba, N. Sakaguchi, Y. Kanda, M. Miyazaki, K. Koiwai, (2017) pH-responsive micelle-based cytoplasmic delivery system for induction of cellular immunity, ***Vaccines***, **5**(**4**): 41.
27. K. Y. Kim, (2007) Nanotechnology platforms and physiological challenges for cancer therapeutics, ***Nanomedicine: Nanotechnology, Biology and Medicine***, **3**(**2**): 103-110.
28. S. T. Lo, A. Kumar, J. T. Hsieh, X. Sun, (2013) Dendrimer nano scaffolds for potential theranostics of prostate cancer with a focus on radiochemistry, ***Molecular Pharmaceutics***, **10**(**3**): 793-812.
29. S. R. Bonam, A. Areti, P. Komirishetty, S. Muller, S, (2020) Dendrimers in immunotherapy and hormone therapy, In; ***Pharmaceutical Application of Dendrimers***, San Diego: Elsevier, p233-249.
30. C. Zylberberg, S. Matosevic, (2016) Pharmaceutical liposomal drug delivery: A review of new delivery systems and a look at the regulatory landscape, ***Drug Delivery***, **23**(**9**): 3319-3329.
31. G. Bozzuto, A. Molinari, (2015) Liposomes as nanomedical devices, ***International Journal of Nanomedicine***, **10:** 975.
32. V. Makwana, J. Karanjia, T. Haselhorst, S. Anoopkumar-Dukie, S. Rudrawar, (2020) Liposomal doxorubicin as targeted delivery platform: Current trends in surface functionalization, ***International Journal of Pharmaceutics***, **2020:** 120117.
33. S. Rezasoltani, A. Yadegar, H. A. Aghdaei, M. R. Zali, (2021) Modulatory effects of gut microbiome in cancer immunotherapy: A novel paradigm for blockade of immune checkpoint inhibitors, ***Cancer Medicine***, **10**(**3**): 1141-1154.
34. Z. Gu, C. G. Da Silva, K. Van der Maaden, F. Ossendorp, L. J. Cruz, (2020), Liposome-based drug delivery systems in cancer immunotherapy, ***Pharmaceutics***, **12**(**11**): 1054.
35. C. H. Saroja, P. K. Lakshmi, S. Bhaskaran, (2011) Recent trends in vaccine delivery systems: A review, ***International Journal of Pharmaceutical Investigation***, **1**(**2**): 64.
36. K. Twumasi-Boateng, J. L. Pettigrew, Y. E. Kwok, J. C. Bell, B. H. Nelson, (2018) Oncolytic viruses as engineering platforms for combination immunotherapy, ***Nature Reviews Cancer***, **18**(**7**): 419-432.
37. P. H. Lizotte, A. M. Wen, M. R. Sheen, J. Fields, P. Rojanasopondist, N. F. Steinmetz, S. Firring, (2016) *In situ* vaccination with cowpea mosaic virus nanoparticles suppresses metastatic cancer, ***Review National Library of Medicine***, **11**(**3**): 295-303.

***Bibliographical Sketch**

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