World Journal of
Nanoparticle Research

IDAAM Publications

World J Nanopart Res 2023; 1(1): 10-16

REVIEW ARTICLE

Therapeutic and diagnostic approach of nanoparticles in biomedicine

AKSHAY R YADAV*

Department of Pharmaceutical Chemistry, Rajarambapu College of Pharmacy, Kasegaon, Sangli, Maharashtra, India-415404

***Author for Correspondence:** *Email:* akshayyadav24197@gmail.com

ARTICLE DETAILS

Article history:
Received on 2 March 2021
Modified on 24 March 2021
Accepted on 29 March 2021

Keywords:
Biomedicine,
Nanotechnology,
Medicinal Products,
Nanoparticles,
Nanostructured Designs.

ABSTRACT

Biomedicine has its own set of guidelines for implementing emerging technology for human use, which is understandably conservative. Increased research has helped in the reformulation of existing drugs as well as the creation of new ones. Nanotechnology changes medicine's toxicity, solubility, and bioavailability profile, among other items. However, there is still a long way to go in terms of full regulation, beginning with the development of consistent definitions across the board. The medicinal products come in a wide variety of forms and structures, and they've been used to treat a wide range of acute and chronic diseases. Furthermore, ongoing research is increasingly leading to the emergence of more sophisticated nanostructured designs, which necessitates a detailed understanding of pharmacokinetic and pharmacodynamic properties, which are determined by chemical composition and physicochemical properties, poses additional regulatory challenges.

INTRODUCTION

Nanoparticles are solid colloidal particles with a size of 10 to 1000 nm. Nanoparticles have many advantages over larger particles, including a higher surface-to-volume ratio and improved magnetic properties [1]. The use of nanoparticles in biomedical applications such as targeted drug delivery, hyperthermia, photoablation therapy, bioimaging, and biosensors has seen a steady growth in interest over the last few years. Because of their excellent properties such as chemical stability, non-toxicity, biocompatibility, high saturation magnetisation, and high magnetic resistance, iron oxide nanoparticles have dominated applications such as drug delivery, hyperthermia, bioimaging, cell labelling, and gene delivery. Metallic nanoparticles, bimetallic or alloy nanoparticles, metal oxide nanoparticles, and magnetic nanoparticles will be grouped into four different nanosystems throughout this study. This review examines the use of nanosystems other than iron oxide nanoparticles, such as metallic nanoparticles such as gold (Au) and silver (Ag), bimetallic nanoparticles such as iron cobalt (Fe-Co) and iron platinum (Fe-Pt), and metal oxides such as titanium dioxide (TiO_2), cerium dioxide (CeO_2), silica (SiO_2), and zinc oxide (ZnO) [2].

Biomedical Applications

Targeted drug delivery is a crucial biomedical technology that aims to deliver anticancer drugs to the tumor's exact position while preventing damage to healthy cells in the surrounding area. Iron oxide nanoparticles are actually the most common source of magnetic materials used to deliver anticancer drugs to specific areas. Magnetic hyperthermia treatment is another significant biomedical application of nanoparticles [3]. Magnetic hyperthermia is a procedure that involves heating tumours to temperatures above 42°C in order to kill cancerous cells. The advantage of this method over chemotherapy is that it directly targets the tumour while causing no damage to healthy tissue in the surrounding region. The main material currently used for this treatment is iron oxide (Fe_3O_4) nanoparticles. Other nanosystems, such as Fe–Co and Cu–Ni bimetallic nanoparticles, and magnetic nanoparticles like $Co–Fe_2O_4$, $Mn–Fe_2O_4$, and $Ni–Co_2O_4$, have also been studied. Iron oxide nanoparticles are the key alternative being studied for MRI to replace

gadolinium chelates, which are commonly used. Fe–Co, Fe–Ni, Fe–Pt, $MnFe_2O_4$, and Co Fe_2O_4 are some of the other magnetic nanoparticles being tested as contrast agents. Photoablation therapy kills diseased tissue, such as cancerous tumours, by exposing it to light.

Targeted Drug Delivery

Chemotherapy relies on the circulatory system to transmit cancer-fighting drugs to the tumour. Non-specificity and toxicity of the medication, in which the drugs target healthy cells and organs as well as cancerous cells, are harmful side effects of this therapy. As a result, selective drug delivery is being investigated as a potential alternative to chemotherapy. The purpose of targeted drug delivery is to direct the drug to the exact location of the tumour, raising the amount of drug administered to the tumour site while minimising side effects. Magnetic nanoparticles are used to deliver drugs to particular places in targeted drug delivery. An external magnetic field is used to direct the drug/nanoparticle complex to the particular tumour site after it has been administered. Changes in pH, temperature, or osmolality may cause the drug to be released [4-5].

Magnetic Hyperthermia

Hyperthermia is a treatment procedure in which heat is used to destroy cancerous cells and tissue. To kill cancerous cells without harming healthy cells, the temperature of the infected or diseased area is increased to 41–46°C. Cancerous cells are more temperature sensitive than healthy cells. When cancerous cells are heated to 41–46°C, they undergo apoptosis, which is known as the hyperthermic effect. Thermoablation, or heating the cells to temperatures above 46–48°C, causes necrosis. To treat cancerous cells, hyperthermia is used in conjunction with radiotherapy and chemotherapy. Treatment for hyperthermia can be classified into three groups. Hyperthermia may be localised, regionalized, or all over the body. Heat is applied to a small area of local hyperthermia treatment, which can be achieved using various methods such as radio frequency, microwave, and ultrasound. These methods are used to provide energy to the tumour in order to increase its temperature. Local hyperthermia can also be treated with magnetic nanoparticles. Broad tissue areas are normally treated with regional hyperthermia. External machines are used to heat an organ or limb in this treatment. Whole-body hyperthermia is commonly used to treat cancer that has spread to other areas of the body. The key form of hyperthermia that will be discussed here is local hyperthermia care. Magnetic nanoparticles can be administered to the tumour in four ways for local hyperthermia treatment: arterial injection, direct injection, *in situ* implant development, and active targeting. Arterial injection involves injecting the magnetic nanoparticle-containing fluid through the tumor's arterial supply. The most popular method is direct injection, which involves injecting the fluid containing the magnetic particles directly into the tumour. *In situ* implant formation involves encasing magnetic particles in tumours with injectable formulations that form gels, such as hydrogels (chitosan and sodium alginate) and organogels (Poly (ethylene-co-vinyl alcohol and cellulose acetate). Another way of delivering magnetic nanoparticles to the tumour site is successful targeting. The magnetic nanoparticles are coated with a tumor-specific antibody and then injected into the bloodstream. The antibodies can bind to the target site and are tumour specific. The theory of magnetic fluid hyperthermia is based on the conversion of electromagnetic energy into heat. An alternating magnetic field is used to disperse the magnetic nanoparticles around the target site. This alternating magnetic field provides energy to the magnetic moments in the particles, allowing them to break through the reorientation energy barrier. As the moments in the particles relax to an equilibrium state, energy is dissipated [6].

Bioimaging

For the identification and diagnosis of diseases, bioimaging techniques such as MRI, computed tomography (CT), positron emission tomography (PET), and ultrasound are used. These methods are non-invasive and can provide high-resolution photographs of internal organs in some cases. Contrast agents are widely used in bioimaging techniques to classify the organ or tissue of interest, as well as to differentiate healthy from diseased tissue. The key problem with today's contrasting agents for MRI and CT imaging is their toxicity, as well as their limited retention period and imaging time. Different materials, such as core–shell nanoparticles, have been investigated as potential contrasting agents in order to boost imaging time and increase biocompatibility of contrast agents, as they can provide improved biocompatibility and imaging time. Nuclear magnetic resonance and radio frequency pulses are the foundations of MRI. Certain atomic nuclei have a permanent magnetic dipole moment due to their nuclear

spin. The atoms hydrogen (H), helium (He), carbon (C), oxygen (O), sodium (Na), phosphorus (P), and xenon (X) all have net nuclear spin (Xe). Hydrogen atoms, on the other hand, are the most frequently used since they are plentiful in biological tissue. Water molecules make up the bulk of the human body. Two hydrogen protons are found in these water molecules [7].

Photoablation Therapy: Photodynamic and Photothermal Therapy

Photodynamic therapy (PDT) and photothermal therapy are two forms of photoablation therapy. PDT hires photosensitisers, which are non-toxic light-sensitive compounds that become toxic when exposed to light of a certain wavelength. This drug is specifically used to target cancerous cells. Photo-induced electrons and holes are formed in the PDT process when photosensitisers, such as TiO_2 nanoparticles, are exposed to light at a particular wavelength. Reactive oxygen species (ROS) and singlet oxygen are formed when photo-induced electrons and holes react with hydroxyl ions or water to form oxidative radicals. The production of these species results in cell death, which is unavoidable. Photothermal therapy irradiates tumour cells with a near infrared (NIR) light source. This light energy can be transformed to heat energy, which can result in hyperthermia and cell death. Biocompatibility, chemical stability, and photocatalytic activity are only a few of TiO_2's appealing properties. It is because of these characteristics, especially its photocatalytic activity, that it is a desirable species for use in photothermal therapy.

Biosensors

A biosensor is a type of analytical system used to analyse biological samples. It transforms an electrical signal from a chemical, biological, or biochemical reaction. There are three components that make up a biosensor.

(1) Bioelement or bioreceptor, which are generally made up of enzymes, nucleic acids, antibodies, cells or tissues.
(2) The transducer which can be electrochemical, optical, electronic, piezoelectric, pyroelectric or gravimetric.The electronic unit which contains the amplifier, processor and display.
(3) The bioreceptor detects the target analyte/substrate of interest, and the transducer translates the signal into an electrical signal that can be calculated more easily. When coated with a bioresponsive shell, nanoparticles may be used as bioreceptors. Biosensors are used in a number of industries, including the environmental, bio/pharmaceutical, food, and medical sectors.
(4) Biosensor is composed of three main parts the electronic system, which contains the signal amplifier, processor and display unit, the transducer, which converts the reaction of the sample analyte and bioreceptor into an electrical signal and a bioreceptor, which is composed of a biological substance which targets and or binds to a specific compound.

The biosensor's transducer is calculated by the reaction that occurs between the sample and the bioreceptor. Amperometric biosensors, for example, track changes in current caused by oxidation/reduction reactions. Changes in charge distribution can be detected using potentiometric sensors. Colorimetric biosensors detect changes in light adsorption, while photometric biosensors detect changes in photon production. Piezoelectric sensors are capable of detecting mass changes [8-9].

Biomedical Applications of Metallic, Bimetallic and Metal Oxide Nanoparticles

- **Metallic Nanoparticles**

Throughout history, silver and silver compounds have been commonly used for a number of uses, including utensils, jewellery, and money, as well as medicinal purposes. During the First World War, silver and silver compounds were discovered to have healing and anti-disease properties and were used to combat infection. The use of silver and silver compounds as anti-infection agents faded with the advent of antibiotics. Nanoparticles have been created as a result of developments in science and engineering. As compared to macro-sized silver particles, silver nanoparticles or nanosilver have special physical, chemical, and biological properties. High electrical conductivity, thermal conductivity, chemical stability, catalytic activity, and enhanced Raman scattering were discovered in silver nanoparticles. Antibacterial, antifungal, antiviral, and anti-inflammatory properties have also been discovered in silver nanoparticles. Nanosilver has sparked interest for use in the textile (clothing, underwear, socks) and food industries (food cans, refrigerator surfaces, and chopping boards), as well as medical applications such as wound dressings, surgical instruments,

and bone prostheses, due to its specific properties. However, due to environmental considerations, the use of nanosilver in textiles is strongly discouraged.Use of silver nanoparticles for drug delivery and as cancer therapy. To see whether colloidal silver nanoparticles had a cytotoxic effect, MCF-7 human breast cancer cells were grown and different concentrations of colloidal silver nanoparticles were used. Cell viability was calculated using the trypan blue exclusion process, which is a critical stain used to colour dead cells. Mono-oligonucleosomes, which are protein (histone) related DNA fragments, were used to determine the type of cell death.

The findings revealed that colloidal silver had a dose-dependent cytotoxic effect on a human breast cancer cell line. Apoptosis was found to be the cause of cell death, with no effect on normal cells. MDR cancer is a serious problem in the treatment of the disease since cancer cells can survive chemotherapy. The antitumor effect of silver nanoparticles and modified silver nanoparticles was investigated in both *in vitro* and *in vivo* studies. TAT, a cell penetrating peptide, was used to alter the silver nanoparticles. The silver nanoparticles were combined with thiol-containing TAT and incubated at 37 °C for 2 hours and 30 minutes. The cellular absorption of silver nanoparticles and modified silver nanoparticles was examined in human epithelial colorectal adenocarcinoma (Caco-2), a colon cancer cell line. The inhibitory activity of silver nanoparticles, modified silver nanoparticles, and a positive control (doxorubicin) against skin (B16), cervical (HeLa), and breast (MCF-7 and MCF-7/ADR) cancer cell lines was investigated *in vitro* using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.

The MTT assay is a colorimetric assay for evaluating cell metabolic activity. Female mice were used in the *in vivo* experiments, and B16 melanoma (skin cancer) cells were injected into the mice. Once the tumour had grown to a certain level, it was injected with silver nanoparticles, modified silver nanoparticles, and doxorubicin as a supportive control. The modified silver nanoparticles were found to have improved cellular uptake. Nanosilver's antitumor effect was also shown to be concentration dependent. Both silver nanoparticles and modified silver nanoparticles were found to inhibit cell proliferation in an *in vitro* study. TAT-modified silver nanoparticles blocked tumour growth *in vivo*, according to the results. Gurunathan et al. studied the cytotoxicity of biologically synthesised silver nanoparticles on human breast cancer cells. The silver nanoparticles were made using a Bacillus funiculus culture supernatant and green synthesis. This research used the MDA-MB-231 human breast cancer cell line. Cell viability, metabolic activity, and oxidative stress were used to assess the toxicity of silver nanoparticles to cells. Cell viability was decreased, and membrane integrity was compromised, according to the findings, which were concentration dependent. Cell apoptosis was induced by the activation of lactate dehydrogenase (LDH) and capase-3, as well as the production of reactive oxygen species (ROS). The findings are positive, and the drug may be used as an alternative to chemotherapy in the treatment of breast cancer.

Govindarju et al. looked at how silver nanoparticles created using a green synthesis method influenced cancer cells. By reducing silver nitrate with alginate extract, silver nanoparticles were biosynthesised. The cytotoxicity of silver nanoparticles was studied using cell lines from acute myeloblastic leukaemia (HL60) and cervical cancer (HeLa). The cells and silver nanoparticles were incubated for 5 days before the MTT assay was used to assess cell viability. DNA fragmentation, lipid peroxidation, and apoptosis were among the other experiments used to assess the cytotoxic effect of silver nanoparticles. Apoptosis induced cell death, according to the findings. Microscopy experiments revealed that silver nanoparticles were endocytosed into the nucleus of the cell, causing DNA damage and eventually apoptosis. These results indicate that silver nanoparticles may be used to treat cancer [10-12].

- **Bimetallic or Metal Alloy Nanoparticles**

Researchers are increasingly interested in using Fe–Pt nanoparticles in biomedicine because they have specific magnetic and chemical properties including superparamagnetism, high coercivity, chemical stability, oxidation resistance, and biocompatibility. These properties have prompted increased research into the possible applications of Fe–Pt nanoparticles in biomedical applications such as hyperthermia as MRI contrast agents, drug delivery/cancer therapy, and biosensors [13].

- **Fe–Pt Nanoparticles as Contrast Agents in MRI and Computed Tomography (CT)**

Yang et al. looked into the possibility of using Fe–Pt nanoparticles as MRI contrast agents. High-temperature pyrolysis in tetraethylene glycol (TEG) medium with oleic acid (OA) as a surfactant formed amphiphilic Fe–Pt nanoparticles with both hydrophilic and lipophilic properties. To see if these nanoparticles are toxic, cell viability tests were conducted on cervical cancer (HeLa) cell lines. Magnetic properties including saturation magnetisation (Ms) and transverse relaxation time (T2) were studied as well. The amphiphilic Fe–Pt nanoparticles were found to be biocompatible and cytotoxic in the MTT assay and transmission electron microscopy (TEM) results. Signal enhancement experiments using magnetic resonance (MR) revealed a distinct contrast from the past. The researchers concluded that amphiphilic Fe–Pt nanoparticles could be used as a T2 MRI contrast agent [14].

- **Fe–Pt Nanoparticles in Targeted Drug Delivery and Cancer Therapy**

On gastric and lung cancer cell lines, Fuchigami et al. investigated the effect of magnetic porous Fe–Pt nanoparticles loaded with an anticancer drug for targeted drug delivery. A hydrothermal treatment of Fe–Pt/PDDA Silica composite particles resulted in the creation of a hollow capsule with a Fe–Pt nanoparticle shell, resulting in porous Fe–Pt nanoparticles. The anticancer drug doxorubicin (DOX) was then injected into the hollow cavity, which was then sealed with a lipid membrane to prevent leaks. Gastric (MKN-74) and lung (RERF-A1) cancer cell lines were used to assess the capsules' cytotoxicity. The cell lines were incubated with Fe–Pt–Dox capsules and only doxorubicin in a magnetic field. The results revealed that the Fe–Pt–Dox capsules were driven by a magnetic field and prevented cancer cell growth in both cell lines while also killing over 70% of the cancer cells [15].

- **Fe–Pt Nanoparticles for Magnetic Hyperthermia**

The use of tungsten oxide-coated Fe–Pt nanoparticles in magnetic hyperthermia treatment was investigated by Seeman et al. Fe–Pt nanoparticles with a SiW11O39 coating were prepared and annealed at 700°C. This complex core–shell nanoparticle system was able to move into a highly ordered Fe–Pt core structure coated with an amorphous tungsten oxide layer after high-temperature annealing. The biocompatibility, morphological, and magnetic properties of these nanoparticles were then studied. On rat brain astrocytes, cytotoxicity tests were performed. The morphology of the samples was examined using TEM. The magnetic properties and heating effect of the nanoparticles were calculated using magnetometry and magneto-caloric measurements. When tungsten atoms are neutron activated, they become the radioisotope W-187, which has a promising future as a cancer treatment. The magnetic moment of Fe–Pt nanoparticles increased after high-temperature annealing. This resulted in a magnetic heating effect and a rise in temperature, which is crucial for hyperthermia. The nanoparticles were around 3 nm in size, and the non-neutron activated; amorphous tungsten oxide-coated Fe–Pt nanoparticles were biocompatible, according to the findings. The radiopharmaceutical applications of these nanoparticles looked promising [16, 17].

- **Metal Oxide Nanoparticles**

Titanium dioxide (TiO_2) is a substance that has been thoroughly researched. It has been used in a number of applications, including paint pigments, food colorings, and toothpastes, as well as the cosmetic and pharmaceutical industries. TiO2 has a range of distinguishing characteristics, including good biocompatibility, low toxicity, chemical stability, and photocatalytic properties, making it an appealing commodity for use in the biomedical industry. Because of its special properties, TiO2 nanoparticles have been used in a number of biomedical applications, including drug delivery, PDT, cell imaging, biosensors, and genetic engineering [18].

TiO_2 Nanoparticles as Nanocarriers in Targeted Drug Delivery

Qin et al. investigated whether the drug's performance was influenced by the nanoparticles' drug loading. The first non-covalent complexation (TiO_2/DOX) and the second covalent conjugation (TiO_2–DOX) were used to load doxorubicin (DOX) into TiO_2 nanoparticles. The cytotoxicity, cellular absorption, and intracellular distribution of these two approaches were then contrasted using a rat glioma (C6) cell line. Hydrolysis was used to make TiO_2 nanoparticles coated with oleic acid, resulting in high-quality, mono-crystalline nanoparticles. The oleic acid coating on TiO_2–OA nanoparticles was substituted with carboxylic silane (TETT), TiO_2–TETT, to enhance

the nanoparticles' conjugation to other biomolecules. The formation of an amide bond between the carboxyl group of TiO_2–TETT and the amino group of DOX covalently conjugated DOX to TiO_2–TETT nanoparticles. Electrostatic attraction of the carboxyl group from TiO_2–TETT and the amine group from DOX resulted in the creation of TiO_2–DOX complexes. The non-covalent complexation (TiO_2/DOX) form of loading DOX had higher cytotoxicity than free DOX and covalently conjugated DOX (TiO_2–DOX), according to the findings. DOX from the complexation process (TiO_2/DOX) was contained in the nucleus, according to confocal laser scanning microscopy findings. The conjugation method's DOX (TiO_2-DOX) was often found in the cytoplasm.

This study demonstrates the importance of the process for loading the drug into TiO_2 nanoparticles. Wu et al. explored the use of mesoporous titania nanoparticles for drug delivery. Regulated hydrolysis was used to make the mesoporous titania nanoparticles. Using the human breast cancer (BT-20) cell line and the MTT test, the cytotoxicity of these nanoparticles was examined. The results revealed that the nanoparticles were biocompatible. Titania has a strong preference for phosphate compounds like DNA. For bioimaging, titania nanoparticles were functionalized with flavin mononucleotide (FMN), a phosphate-containing fluorescent molecule. Using the BT-20 cell line, intracellular imaging was performed and analysed using confocal laser scanning microscopy [19].

TiO_2 Nanoparticles as Photosensitiser Agents for PDT

Lagopati et al. studied the use of TiO2 nanoparticles for photocatalytic cancer treatment. A sol–gel system was used to render TiO2 aqueous dispersions. For this study, two breast cancer epithelial cell lines (MCF-7 and MDA-MB-436) were cultured. Different concentrations of TiO2 nanoparticles were seeded onto cultured cell lines and exposed to UV-A light with a wavelength of 350 nm for 20 minutes. These cells were then cultured for another 48 hours before being tested for cell viability, flow cytometry, and western blot analysis [20, 21].

CONCLUSION

There is still no widely accepted definition for biomedicines, and one might never be feasible or useful. The herbal goods come in a wide variety of forms and structures, and they've been used to treat a wide range of acute and chronic diseases. Furthermore, ongoing research is increasingly leading to the emergence of more sophisticated nanostructured designs, which requires a detailed understanding of the pharmacokinetic and pharmacodynamic properties of nanomedicines, which are determined by their chemical composition and physicochemical properties, presenting additional regulatory challenges.

REFERENCES

[1] Pankhurst QA, Connolly J, Jones SK, Dobson J. Applications of magnetic nanoparticles in biomedicine. J Phys D: Appl Phys. 2003; 36:R167–R181.

[2] Yan H, Park SH, Finkelstein G, Reif JH, LaBean TH. DNA-templated self-assembly of protein arrays and highly conductive nanowires. Science. 2003; 301:1882–1884.

[3] Keren K, Berman RS, Buchstab E, Sivan U, Braun E. DNA-templated carbon nanotube field-effect transistor. Science. 2003; 302:1380–1382. Bruchez M, Moronne M, Gin P, Weiss S, Alivisatos AP. Semiconductor nanocrystals as fluorescent biological labels. Science. 1998; 281:2013–2016. Chan WCW, Nie SM. Quantum dot bioconjugates for ultrasensitive nonisotopic detection. Science. 1998; 281:2016–2018.

[4] Wang S, Mamedova N, Kotov NA, Chen W, Studer J. Antigen/antibody immunocomplex from CdTe nanoparticle bioconjugates. Nano Letters. 2002; 2:817–822. Mah C, Zolotukhin I, Fraites TJ, Dobson J, Batich C, Byrne BJ. Microsphere-mediated delivery of recombinant AAV vectors *in vitro* and *in vivo*. Mol Therapy. 2000; 1:S239.

[5] Panatarotto D, Prtidos CD, Hoebeke J, Brown F, Kramer E, Briand JP, Muller S, Prato M, Bianco A. Immunization with peptide-functionalized carbon nanotubes enhances virus-specific neutralizing antibody responses. Chemistry&Biology. 2003; 10:961–966.

[6] Edelstein RL, Tamanaha CR, Sheehan PE, Miller MM, Baselt DR, Whitman LJ, Colton RJ. The BARC biosensor applied to the detection of biological warfare agents. Biosensors Bioelectron. 2000; 14:805–813. doi: 10.1016/S0956-5663(99)00054-8.

[7] Nam JM, Thaxton CC, Mirkin CA. Nanoparticles-based bio-bar codes for the

ultrasensitive detection of proteins. Science. 2003; 301:1884–1886. doi: 10.1126/science.1088755.

[8] Mahtab R, Rogers JP, Murphy CJ. Protein-sized quantum dot luminescence can distinguish between "straight", "bent", and "kinked" oligonucleotides. J Am Chem Soc. 1995; 117:9099–9100.

[9] Ma J, Wong H, Kong LB, Peng KW. Biomimetic processing of nanocrystallite bioactive apatite coating on titanium. Nanotechnology. 2003; 14:619–623.

[10] de la Isla A, Brostow W, Bujard B, Estevez M, Rodriguez JR, Vargas S, Castano VM. Nanohybrid scratch resistant coating for teeth and bone viscoelasticity manifested in tribology. Mat Resr Innovat. 2003; 7:110–114.

[11] Yoshida J, Kobayashi T. Intracellular hyperthermia for cancer using magnetite cationic liposomes. J Magn Magn Mater. 1999; 194:176–184.

[12] Molday RS, MacKenzie D. Immunospecific ferromagnetic iron dextran reagents for the labeling and magnetic separation of cells. J Immunol Methods. 1982; 52:353–367.

[13] Weissleder R, Elizondo G, Wittenburg J, Rabito CA, Bengele HH, Josephson L. Ultrasmall superparamagnetic iron oxide: characterization of a new class of contrast agents for MR imaging. Radiology. 1990; 175:489–493.

[14] Parak WJ, Boudreau R, Gros ML, Gerion D, Zanchet D, Micheel CM, Williams SC, Alivisatos AP, Larabell CA. Cell motility and metastatic potential studies based on quantum dot imaging of phagokinetic tracks. Adv Mater. 2002; 14:882–885.

[15] Sinani VA, Koktysh DS, Yun BG, Matts RL, Pappas TC, Motamedi M, Thomas SN, Kotov NA. Collagen coating promotes biocompatibility of semiconductor nanoparticles in stratified LBL films. Nano Letters. 2003; 3:1177–1182.

[16] Yadav A, Mohite S. Aquasomes as a Self-Assembling Nanobiopharmaceutical Carrier System for Bio-Active Molecules. Research J. Topical and Cosmetic Sci. 2020; 11(2):66-70.

[17] Zhang Y, Kohler N, Zhang M. Surface modification of superparamagnetic magnetite nanoparticles and their intracellular uptake. Biomaterials. 2002; 23:1553–1561.

[18] Gutwein LG, Webster TJ. Affects of alumina and titania nanoparticulates on bone cell function. American Ceramic Society 26 th Annual Meeting Conference Proceedings. 2003.

[19] Roy I, Ohulchanskyy TY, Pudavar HE, Bergey EJ, Oseroff AR, Morgan J, Dougherty TJ, Prasad PN. Ceramic-based nanoparticles entrapping water-insoluble photosensitizing anticancer drugs: a novel drug-carrier system for photodynamic therapy. J Am Chem Soc. 2003; 125:7860–7865.

[20] Han M, Gao X, Su JZ, Nie S. Quantum-dot-tagged microbeads for multiplexed optical coding of biomolecules. Nature Biotechnology. 2001; 19:631–635.

[21] Reich DH, Tanase M, Hultgren A, Bauer LA, Chen CS, Meyer GJ. Biological applications of multifunctional magnetic nanowires. J Appl Phys. 2003; 93:7275–7280.