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NANOMEDICINE ALCHEMY: EXPLORING THE THERAPEUTIC POTENTIAL OF GOLD AND SILVER NANOTECHNOLOGY

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Abstract
Surface modifications and coatings using metal nanoparticles have gained significant attention in recent years for enhancing the biocompatibility of polymers. This innovative approach facilitates the creation of nanofilms, which greatly improve the interaction between living cells and biomaterials. Specifically, these modifications positively influence cell adhesion and proliferation. In conjunction with the regulation of material porosity, the incorporation of metal nanoparticles promotes vascularization and facilitates the growth of cells within the biocompatible materials. This paper explores the integration of key biological processes, such as protein adsorption and cell proliferation, through chemical methods applied to modify the surface properties of biocompatible materials. The adoption of nanotechnology in medical science has led to remarkable advancements in drug delivery and diagnostics, revolutionizing the field.

Keywords: surface modifications, metal nanoparticles, biocompatibility, nanofilms, cell adhesion, cell proliferation, porosity

Introduction

The surface modifications for polymers or applying coatings using metal nanoparticles increase the biocompatibility properties, nanofilms since favor interaction of living cells with the biomaterial, especially for its beneficial effect on cell adhesion and proliferation. Along with the control of porosity in these materials, the application of metal helps allow vascularization and the growth of cells inside. The key biological processes integration, protein adsorption and cell proliferation, is the use of chemical methods to modify the properties of the surface of biocompatible materials, (Variola, Vetrone, Ricert, Jedrzejowski, Yi, Zalzal, Clair, Sarkissian, Perepichka, Wuest, Rosie, & Nanci, 2009), Nanotechnology had tremendous impact on medical science and has resulted in phenomenal progress in the field of drug delivery and diagnostics, (Doshi, & Mitragotri, 2009).

Within the biocompatible metals are used to increase the biocompatibility properties of the various polymers found as Ag, Au, Cu, Ti, Ni, etc. A metal is considered biocompatible when it is:

- Accepted by the body without rejection reaction.
- Not toxic
- Inert or stable.

Gold and silver are precious metals that have been used by people for thousands of years in medical applications, for example the ancient Greeks used silver coated to store and preserve water and wine

containers, Hippocrates the father of medicine manuscripts wrote about the beneficial health properties and cure of diseases featuring silver, ancient Roman placed Silver coins in containers with water for his crusades to preserve, in the first world war Silver compounds were used for infections caused by injury, and Silver sulfadiazine is currently used for burns, (Pulit, Banach, & Kowalski, 2011). New technologies, especially nanotechnology has increased use with silver compounds primarily in medical applications due to its antibacterial properties. Silver nanoparticles with sizes below 100 nm are used widely in consumer products, biomedical devices, and other textile products, and that having a larger surface area provides increased contact and hence increased antimicrobial properties.
The Gold is another metal that is used at nanoparticles level due to its physical properties and corrosion resistance, which is one of its greatest attributes. The materials manufactured at the nanoscale have unique and beneficial properties for the medical sector in the area of implants, tissue engineering, organs, etc, due to its properties gold nanoparticles are subject to great interest in applied fields of Physics, Chemistry, Biology, and especially in the Medical Sector, (Scobczak, Dagmara, Malgorzata, & Zbigniew, 2011). Advances in the field of nanotechnology have provided new forms of Gold and Silver available for use in biosensors or implantable devices (Kleps, Danila, Angelescu, Miu, Simion, Ignat, Bragaru, Dumitru, & Teodosiu, 2007).

Silver

Nomotechnology is a most promising field for generating new applications in medicine. However, only nanoproducts are currently in use for medical purposes.
A most prominent nanoproduct is nanosilver. Nanosilver particles are generally smaller than 100 nm and contain 20-15000 silver atoms. At nanoscale, silver exhibits remarkably unusual physical, chemical and biological properties. Due to its strong antibacterial activity, nanosilver coatings are used on various textiles but as well as coating on certain implants. Further, nanosilver is used for treatment of wounds and burns or as a contraceptive and marketed as water disinfectant and room spray, (Shluesener, 2008). Silver has always been an excellent antimicrobial and has been used for the purpose for ages. The unique physical and chemical properties of silver nanoparticles only increase the efficacy of silver. Through there are many mechanisms attributed to the antimicrobial activity shown by silver nanoparticles, the actual and most reliable mechanism is not fully understood or cannot be generalized as the nanoparticles are found to act on different organisms in different ways, (Prabhu, & Poulose, 2012). The ability of the silver particles to kill microbes because airway block or break the outer walls of the bacteria has become one of the most important property or factor for the development of technologies level nanoparticles. Application of nanoparticles based on coatings of medical devices where silver has bactericidal effects and disinfectants, hence its current importance, silver nanoparticle coatings are currently used as antibacterial additives in poly-methylmethacrylate, the polymer used to manufacture bone implants (prosthetic knees, hips, etc), (Rai, Yadav, & Gade, 2009).
The antibacterial mechanisms of silver nanomaterials are not fully elucidate, but the prevailing paradigm suggest various conbinations:

1- Silver ion release followed by cellular uptake and cascade of intracellular reactions.
2- Extracellular and intracellular generations of ROS (reactive oxygen species).

3- Direct interactions between nanoscaled silver and cell membranes.

At sub micromolar concentrations, silver ions are internalized and react with thiol groups of cellular proteins, wich lead to uncoupling of ATP synthesis from respiration, loss of proton motive force, and interference with the phosphate efflux system. At milli molar levels, silver nanoparticles induce detachment of the cell wall menbrane from the cytoplasm, possible release of intracellular content, DNA condensation and loss of replication ablity. ROS (reactive oxygen species) produce oxidative stress resulting in membrane lipid and DNA damage.

Finally, silver nanoparticles increase cell membrane permeability and, subsequently, penetrate inside cells to induce any one or the entire cascade of effects just described, (Marambio-Jones, & Hoek, 2010). Silver ions can lead to denaturing of protein and cell death because of their reaction with nucleophilic amino acid residues in proteins, and attach to sulfhydryl, amino, imidazole, phosphate and carboxyl groups of membrane or enzyme proteins, silver also blocking the cells respiration, inhibit a number of oxidative enzymes and produce the cell membrane rupturing for the attachment of silver ions or nanoparticles to the bacteria base on electrostaic interations, (Dastjerdi, & Montazer, 2010; Dubas, Wacharanad, & Potiyaraj, 2011; Rujitanaroj, Pimpha, & Supaphol, 2009).

The constantly expanding field of silver nanocomposites has been proven to become of significant importance mainly due to their well proved antimicrobial properties and great potential for aplications as antimicrobial coatings and agents. Among the many experimental routes that have been proposed, all goal is to have some advantages as well as drawbacks. In general, the goal is to identify the method that allows the preparation of composites with biocompatible, biodegradable, and non toxic matrix, synthesized through non toxic manomers and precursors with well attached silver nanoparticles, (Dallas, Sharma, & Zboril, 2011; Lok, Ho, Chen, He, Yu, Sun, Tam, Chiu, & Che, 2007).

The application of nanoscale materials and structures, usually ranging from 1 to 100 nanometers (nm), is an emerging area of nanoscience and nanotechnology. Nanomaterials may provide considerably changed physical, chemical and biological properties; Gold, Silver and Copper have been used mostly for the synthesis of stable dispersions of nanoparticles, which are useful in areas such as photography, catalysis, biological labeling, medical application like cancer diagnosis and therapy, (Sharma, Yngard, & Lin, 2009).

Nanosilver has biological properties which are significant for consumer products, food technology (e.g., food processing equipment, packaging materials, food storage), textiles/fabrics (antimicrobial clothing), and medical applications (wound care products, implantable medical devices).

In addition, nano-silver has unique optical and physical properties that are not present in bulk silver, and which are claimed to have great potential for medical applications (diagnostics, drug delivery, and imaging). Due to the properties of silver at the scale, nanosilver is nowdays used in an increasing number of consumer and medical products. Because silver is a soft white lustrous element, an important used of silver nanoparticles is to give products a silver finish. Still, the remarkably strong antimicrobial activity is the major diretion for development of nanosilver products, Of more than 800 consumer products that contain nanomaterials, roughly 30% are claimed to contain silver particles. Examples are food packaging materials and food suplements, odor resistant textiles, eletronics and housed appliances, water desinfectants, room sprays, cosmetics and medical devices, (Wijnhoven, Peijnenburg, Herberts, Hagens, Oomen, Heugens, Roszek, Bisschops, Gosens, Van de Meent, Dekkers, De Jong, Zijverden, Sips, & Geertsma, 2009).

The silver nanoparticles applications for a medical propose requires stabilization in various substrates depend of the used, polymer matrices are well suited for this propose. In general, many polymeric matrices have been used for the synthesis of silver/polymer antibacterial nanocomposites, including dendrimers, an plastics (poliacrilamide, poliurethane, hydroximetilacrilamide, etc), the polymer matrix plays a multiple role because it acts as a stabilizer, template and protective agent against agglomeration. Advanced and dendrimers with functional groups which allow the reduction of silver cations that are attached and dispersed on the surface of the matrix polymers giving antibacterial properties, (Dallas, Tucek, Jancik, Kolar, Panacek & Zboril, 2010).

The implantation of indwelling devices is often complicated by infections with biofilm forming microbes that are resistant to a number of antimicrobial agents, biofilms are glue like sustances composed of a matrix of excreted polymeric compounds called exopolysaccharides formed by bacteria, the biofilm allows bacteria to adhere to medical implants composed of metallic, polimeric, ceramic, composite substances and potentially protects bacterial colonies from antimicrobial therapies. A variety of active and passive strategies including the use of antibitics, inorganic salts, and different compounds have been employed to implant antimicrobial properties for devices.

Silver, in a variety of forms, is among the device base antimicrobial solutions that are currently commercially available, and it has a successful history of safe and effecacious use against a broad spectrum of gram positive and gram negative microbial agents, exposure to relatively low concentrations, silver can result in a substantial reduction of viable microbial organisms, (Qureshi, Monroe, Lopez, James, Dasa, Park, Amirsadeghi, & Hayes, 2011).

Nanosilver (NS), comprising silver nanoparticles, is attracting interest for a range of biomedical applications owing to its potent antibacterial activity. It has recently been demonstrated that NS has useful anti-inflammatory effects and improves wound healing, which could be exploited in developing better dressings for wounds and burns. The key to its broad-acting and potent antibacterial activity is the multifaceted mechanism by which NS acts on microbes. This is utilized in antibacterial coatings on medical devices to reduce nosocomial infection rates. Many new synthesis methods have emerged and are being evaluated for NS production on medical applications, (Chaloupka, Malam, & Seifalian, 2014).

Nowadays, antimicrobial effects are intensively studied due to an enormously increasing bacterial resistance against excessively and repeatedly used classical antibiotics. Silver nanoparticles may be of promising help in this struggle as they effectively eliminate bacteria at relatively low concentration that are non toxic for human cells, (Prucek, Tucek, Kilianova, Panacek, Kvitek, Filip, Kolar, Tomankova, & Zboril, 2011).

Gold

The medical benefits of gold date back many thousands of years ago, ancient cultures, such as India and Egypt used medicinal preparations containing gold, in China Gold is used in the treatment of diseases such as smallpox, ulcers skin and measles. In Japan, tradition suggests that thin sheets of gold placed in tea, sake and food are beneficial to health, (Ravishankar, & Jamuna, 2011).

Apart from the obvious use of gold alloys in dental restorations, gold nanoparticles are currently being utilized in several technologies applications and are gaining popularity, there are a large number of direct gold applications in medical devices, due to the excellent biocompatibility of this metal, applications include wires for pacemakers, gold-plated stents used in the treatment of heart disease, etc, (Parida, & Nayak, 2012). Gold has a high degree of resistance to bacterial colonization and this is because the material of choice for implants that are at risk of infection, such as the inner ear. Gold has a long tradition of use in this application and is considered a precious metal in microsurgery of the ear, its compounds have historically been also used in medicines to treat a range of ailments, (Giasuddin, Jhuma, & Mujibul, 2012). Gold nanostructures have proven to be a versatile platform for a broad range of biomedical applications, with potential use in numerous areas including: diagnostics and sensing, in vitro and in vivo imaging, and therapeutic techniques. These applications are possible because of the highly favorable properties of gold nanostructures, many of which can be tailored for specific applications, (Cobley, Chen, Cho, Wang & Xia, 2011).

Recent developments concerning the attractive properties of nanoparticles have increased interes about their applicability in biosensin areas resulting in a great progress of nanomaterial-based biosensors. The used of metal nanoparticle superstructures for the organization of electrochemical sensing devices is an extremely promising prospect. Metal nanoparticles provide some important functions including the roughening of the conductive sensing interface and some catalytic properties that result in the aplication of electrochemical signal. Gold nanaoparticle is a kind of metal nanoparticle that can help proteins retain their biological activity upon absortion. Because of its large surfase area and good electronic properties, Gold nanoparticles can be defined as a good biocompatible material since modification of electrode surfaces with this metal nanoparticle provides a suitable microenvironment similar to that redox protein. Moreover gold nanoparticle is claimed to reduce the insulating effect of protein shell by providing direct electron transfer through the conducting tunnels of gold nanocrystals. On the other hand, the activities of the immobilized antibodies can be largely influenced by the surface properties of the transducer in clinical inmunoassays, It was demostrated that use of gold favored a particle enhanced immobilization of antibodies, (Tiwari, Ramalingam, Kobayashi, & Turner, 2012).

Nanomaterials are increasingly used in biomedical fiels because of their remarkable physicochemica properties on the nanometer scale, nanorods, nanocages , or nanocomposites composed of dielectric core and outer thin metal shell can be sharply increased by near-IR (infrared) laser illumination because of the surface plasmon resonance effect, also potential benefits of multimodal functionality in biomedical applications, researchers would like to design and fabricate multifunctional magnetic nanoparticles, (Wang, Chen, Talavage, & Irudayaraj, 2009). Currently, there are two strategies to fabricate magnetic nanoparticle-based multifunctional nanostructures. The first, molecular functionalization, involves attaching antibodies, proteins, and dyes to the magnetic nanoparticles. The other method integrates the magnetic nanoparticles with other functional nanocomponents like gold nanoshell, and it meet the dual tasks of cancer detection by Magnetic Resonance Imagingand and cancer treatment by hyperthermia, (Lee, Yang, Ko, Oh, Kang, Son, Lee, Lee, Yoon, Suh, huh, & Haam, 2008; Gao, Gu, & Xu, 2009).

Radiation dose assessment is essential for several medical treatments and diagnostic procedures. In this context, nanotechnology has been used in the development of improved radiation sensors, with higher sensitivity as well as smaller sizes and energy dependence. The application of the nanocomposites as radiation detectors was evaluated by the electron spin resonance technique. The sensitivity is improved almost 3 times in the case of the nanocomposite containing 3% (w/w) gold, so it can be easily tuned by changing the amount of gold nanoparticles in the nanocomposites, In conclusion, the featured properties, such as homogeneity, nanoparticle size stability, and enhanced sensitivity, make these nanocomposites potential candidates for the construction of small-sized radiation sensors with tunable sensitivity for application in several medical procedures (Guidelli, Ramos, Zaniquelli, Nicolucci, & Baffa, 2012).

Gold nanoparticles show entirely different properties in comparison with their bulk counterparts. Gold nanoparticles have a capability of binding strongly to bio molecules like proteins, peptides, antibodies, olinucleotides, and pathogens susch bacteria, virues, etc. these particles could be used as biomarkers to detect diseases and to deliver a suitable drug to cure the disease. The use of functionalized gold nanoparticles as biomarkers and their binding capacity to biomolecules is opening new fesibilities, (Panyala, Pena-Mendez, & Havel, 2009).

It has been almost 4 decades since the “war on cancer” was declared. It is now generally believed that personalized medicine is future for cancer patient management. Possessing unprecedented potential for early detection, accurate diagnosis, and personalized treatment of cancer, nanoparticles have been extensively studied over the last decade. Gold nanoespheres, nanoroads, nanoshells, nanocages, nanoestructures and nanocomposes are the key feature for medical aplications like vitro assays, ex vivo and in vivo imaging, cancer diagnosis, cancer therapy, target drug delivery. Multifunctionality is the key feature of nanotechnology, targeting ligands, imaging labels, therapeutic drugs and other properties can all be integrated to allow for targeted molecular imaging and molecular therapy of cancer. A multifunctional platform based on gold nanotechnology, with multiple receptor targeting, multimodality imaging, and multimodality therapeutic entities, holds the promise for a magic gold bullet against cancer, (Cai, Gao, Hong, & Sun, 2008). Gold nanoparticles (Au NPs) have been studied for both photothermal therapy and imaging. Efficient photothermogenic response to near-infrared light is necessary for in vivo applications, due to the multiple interactions of mirror images of localized surface plasmons, closely spaced multiple Au NPs exhibited enhanced photothermogenic properties in the longer wavelength region even when the Au NPs were small, (Kojima, Watanabe, Hattori, & Iida, 2011).

Gold nanoparticles (GNPs) with controlled geometrical, optical, and surface chemical properties are the subject of intensive studies and applications in biology and medicine. Todate, the ever increasing diversity of published examples has included genomics and biosensors, immunoassays and clinical chemistry, photothermolysis of cancer cells and tumors, targeted delivery of drugs and antigens, and optical bioimaging of cells and tissues with state-of-the-art nanophotonic detection systems (Dykman, & Khlebtsov, 2012).

Biomedical applications of plasmonic metal nanostructures represent new and exciting directions of research and development. For instance, Photothermal Ablation Therapy (PTA) based on metal nanomaterials has been actively explored for treating cancer with encouraging success. PTA relies on heat generated from light for destroying cancer cells and thus requires strong optical absorption and high efficiency of photothermal conversion. Desired metal nanostructures for PTA should have strong and tunable SPR, low toxicity, ease of delivery, and convenience for bioconjugation for actively targeting cancer cells.

Nanostructures of noble metals, for example, gold and silver, show great promise for PTA applications, including nanoparticles, nanorods, nanoshells, nanocages, and hollow nanospheres, (Zhang, 2010; Tian, Tang, Sun, Zou, Chen, Zhu, Yang, Wang, Wang, & Hu, 2011; Yuan, Khoury, Wilson, Grant, Bennett, & Vo-Dinh, 2012).

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Conclusion

In recent years, the use of nanoparticles, particularly metal nanoparticles have expanded in biomedical research. They are used in diagnosis and therapeutics due to their unique properties of small size, large surface area to volume ratio, high reactivity to the living cells, stability over high temperatures and translocation into the cells, etc, (Pooja, Komal, Vida, & Shree, 2011).

Inorganic and organic nanostructures, nanoparticles and nanocomposites with different shapes, sizes, and consisting of various metal, metal compound, semiconductor materials, organic materials are finding increasing application in a diverse range of medical industry fields. The use of gold and silver nanoparticles, nanoshells, and nanowires as substrates for surface-enhanced Raman spectroscopy in sensing and diagnostics is presently the subject of intense research interest, (Berkel, Piekarski, Kierstead, Pressly, Ray, & Hawker 2009). Thix new research field is not only nanoparticles, it is more (nanostructures, nanocompounds, nanofilms, etc), it is a new technology (nanotechnology) that has gained widespread acceptance.

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