Life Science Informatics Publications

Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences

Journal Home page http://www.rjlbpcs.com/

RJLBPCS

ISSN 2454-6348

Original Review Article **DOI: 10.26479/2018.0404.41**

GOLD NANOPARTICLES AND THEIR NOVEL BIOMEDICAL POTENTIAL: A SHORT REVIEW

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ABSTRACT: Nanotechnology and nanomaterial have created revolution in almost all areas of research. Gold nanoparticles are used as therapeutic materials from ancient times. Currently nanotechnology brought a boom in synthesis and studying of gold nanoparticles and thus created a leap in the application of these materials. This review addresses the use of gold nanoparticles in three major health issues of the world which are Cancer, AIDS and Diabetes.

KEYWORDS: Nanotechnology, Gold nanoparticles, Cancer, Diabetes, HIV.

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1.INTRODUCTION

Nanotechnology has created a paradigm shift in all aspects of research like energy, medicine and electronics research. The unique property of these materials like tunable morphology, composition and optical properties made them promising candidates for clinical and biomedical applications. Specifically the size, shape, biocompatibility and light-scattering and absorptive properties of nanoparticles, which in turn make these materials ideal for use in therapeutic and imaging techniques. Nanomaterials are generally classified into quantum dots, nanowires, self assembled layers, polymer nanocomposites and metallic nanoparticles. Among these, metallic nanoparticles attained wide research interest due to their eco friendly synthetic methods, tunable properties and extraordinary physical and chemical behavior. All these features make metallic nanoparticles as promising candidates for future biomedical research.

Gold nanoparticles (Au NP's):What makes them special?

Gold is always special for mankind due to its fascinating property associated with metallic character. There is no other metal than Gold which is closely associated with human civilization because the preparation and use of gold can be consistently correlated with the evolution of mankind, especially the advancement of science and technology. The role of gold in medicine can be traced back to ancient vedic civilization and chinese civilization and they are used in ayurvedic system of medicine where the medical formulations contains gold particles which are purified by long procedures of medicine preparation. Charaka Samhita is one of the ancient standard text which mentions the use of processed gold for treatment purposes. Galib et al. describe the use of gold in ancient times with as mentioned in Charaka Samhitha[1]. It is observed that the toxicity associated with these heavy metals like gold are removed and purified during the complex and sophisticated manufacturing process of medicines described in Ayurvedic system of medicine. The form of Gold used in ayurveda is mentioned as 'Bhasma' which is the processed form of raw metallic gold. It is constituted of metallic Gold (96.76%), silica (1.14%), ferric oxide (0.14%), phosphates (0.78%), potash (0.16%), salt (0.078%), and traces of copper and magnesium [2].Elemental form of Gold has been used as an anti-pruritic agent as a remedy for itching palms in old time. The property of gold for the in vitro inhibition of *Mycobacterium tuberculosis* was first studied by Robert Koch during 1980. This vital observation paved the path to in vivo trials on arthritis and lupus erythematosus. Other properties of gold has been also a matter of interest in the ancient medical world. It is observed that use of Gold compounds will decrease the concentrations of rheumatic factors and has a profound effect on the immunological responses.[3] It has also been established that gold suppresses the anaphylactic release of histamine more effectively than gluco-corticoids[4]. Sodium aurothio malate (water soluble preparation) was introduced around 25 years ago to treat arthritis, and is administered through IM injections. Its pharmacokinetics were not clear but, but are probably due to its antimicrobial effects and stimulatIon of the Reticulo Endothelial system[5].All these qualities of elemental gold can be successfully and effectively implemented by using gold nanoparticles by the advancement in nanotechnology. From the wide variety of synthetic methods available for the synthesis (as shown in figure 1), Phytochemical methods are gaining more attention due to its cost effective and ecofriendly features. Modern scientific literature shows plenty of successful methods for the ecofriendly or green synthesis of Au NP's. Most of these methods are based on phytochemical approaches which use plant extracts in synthesis [6-15].

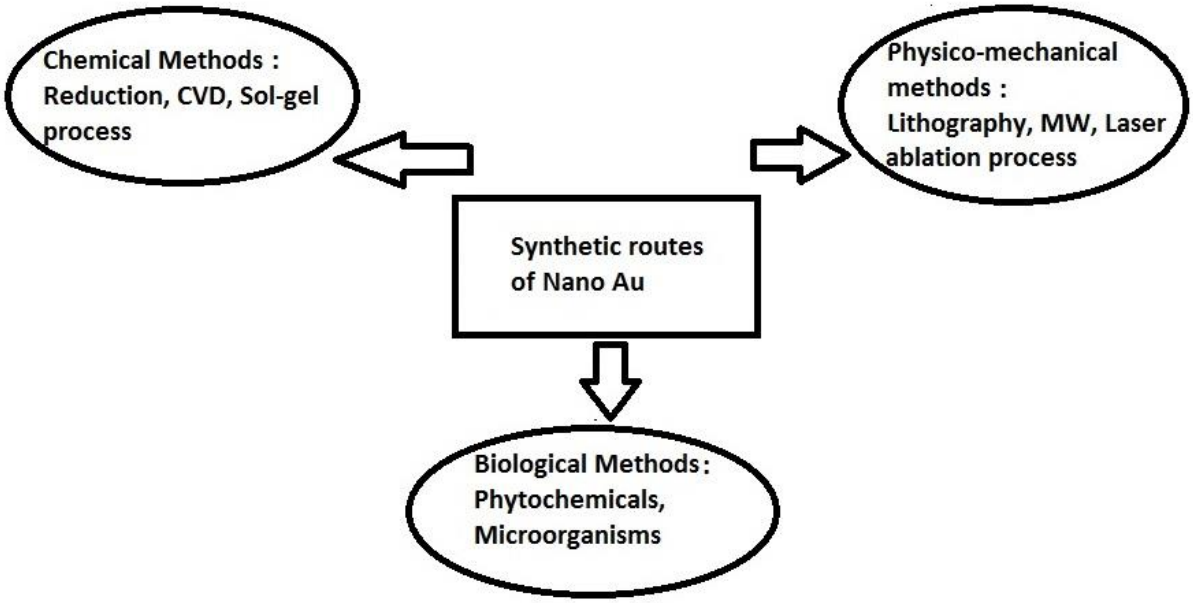

Figure 1: Preparative methods for Gold nanoparticles

1.1 Cancer

Despite of all the efforts with the advancement of science and technology research, cancer is still remaining as the major health issue responsible for the deaths of millions of people in both developed and third world countries.According to cancer statistics 2010 done by American Cancer Society, estimated new cancer cases were 1,529,560 and 569,490 death in both males and females in the US [16]. The characteristic feature of cancer cells is the abnormal cellular division or mitosis. Under the absence of specific growth inhibitory or mitogenic signals, the cell division of normal cells stops. On the contrary, cancer cells are relatively inured to such signals compared to normal healthy cells. Literature shows the use of Au NP's for both imaging and therapeutic activity in oncology especially in drug delivery applications. The most unique features of Au NP's that are employed in diagnostic and imaging techniques are [17]

1. Surface Plasmon resonance- used in Ligand receptor interaction, DNA hybridization, Single molecule detection etc
2. Magnetic properties- Used in MRI contrasting agents, CT-MRI, diagnosis and imaging of malignant and solid tumors etc
3. Fluorescence properties- Used in drug screening, immunological assay, imaging etc

When we go through the use of Au NP's in therapeutic activities of cancer, we can see that the major uses are credited to employing Au NP's for drug delivery applications. Brown et.al has been studied the use of gold nanoparticles for the Improved Anticancer Drug Delivery of the Active Component of Oxaliplatin [18]. Oxaliplatin is a platinum based drug which is a widely used chemotherapy drug. This drug has the disadvantage of physiological side effects and also develops faster drug resistance with the tumors. They used functionalized nanoparticles of gold with a thiol containing

poly(ethylene glycol) (PEG) monolayer which is further capped with a carboxylate moiety. This study showed thatthe platinum-tethered nanoparticles possess cytotoxicity which is very much improved than pure oxaliplatin drug in all of the studied cell lines such as A549 (lung epithelial cancer) and HCT116, HCT15, HT29, and RKO (colon cancer). Another interesting and significant feature observed is that it has an unusual ability to penetrate the cell nucleus in the lung cancer cells. These drugs can be further tuned for its activity by incorporatingdrug-delivery vehicles which can target cancer cells actively or passively depending on the application. Another interesting study showed thatWater-soluble, doxorubicin (DOX) conjugated gold nanoparticles (DOX conjugated Au NPs) exhibits a significant pH-responsive drug release activity. Agasti et al studied the photoregulated release of caged anticancer drugs from gold nanoparticles [19].They have used an anticancer drug 5-fluorouracil which is conjugated to the surface of gold nanoparticles through a photocleavable *o*-nitrobenzyl linkage. In this system, the particle serves as both cage and carrier for the therapeutic, providing a nontoxic conjugate that effectively releases the moiety upon long wavelength UV irradiation. Dendrimers are also used as effective encapsulated partners for glutathione triggered release of anticancer drugs [20]. The dendrimer-encapsulated gold nanoparticles (DEGNPs) are effectively used for the release of Thiol-containing drugs such as captopril and 6-mercaptopurine which showed an “Off–On” release behavior in the presence of thiol-reducing agents such as Glutathione andDithiothreitol. Also, the selected DEGNPs showed excellent biocompatibility on several cell lines.

1.2. HIV

HIV/AIDS continues to be a curse upon mankind with no cure or preventive vaccine against it. World Health Organization (WHO) says that HIV infection in humans is considered to be at pandemic levels. More than 33 million people are believed to be living with HIV, and 2 million population suffered AIDS-related death in the year 2008. Gold nanoparticles are not studied extensively in anti HIV research and there is not enough literature available for its potential activity against HIV. Gianvincenzo et.al used Gold nanoparticles capped with sulfate-ended ligands as anti-HIV agents [21]. They employed Au NP’s coated with multiple copies of an amphiphilic sulfate-ended ligand which binds the HIV envelope glycoprotein gp120. This is measured by surface plasmon resonance (SPR) and showed in vitro inhibition of the HIV infection of T-cells at nanomolar concentrations.Bowman et.al reported the inhibition of HIV fusion with multivalent gold nanoparticles [22]. This study suggests that multivalent presentation of small molecules on gold nanoparticles surface can convert inactive drugs into potent therapeutics. Another study reports Gold glyconanoparticles as carrier for anti-HIV prodrugs [23]. Here, the drugs-containing glyconanoparticles were characterized and the pH-mediated release of the drug from the nanoparticles has been determined. Literature also shows the feasibility of using gold nanoparticle (NP)-based assays for improving detection sensitivity of human immunodeficiency virus type 1

(HIV-1) p24 antigen [24]. All these studies suggest the scope of a further exploration of gold glyconanoparticles as a new multifunctional tool in the world of drug-delivery system against HIV.

1.3. Diabetes

Diabetes consumes an ever increasing proportion of national and international health care budgets in most of the countries. It is believed to become one of the world's main disablers and killers within the next 25 years. It is most common serious metabolic disease in the world. The number of people suffering from the disease worldwide is increasing at an alarming degree with a probable 552 million people likely to be diabetic by the year 2030 as against 366 million estimated in 2011 [25]. Ninety percent of these patients suffer from type 2 diabetes, which is characterized by a resistance to insulin.The use of Au NP's against diabetes is an area which still remains much unexplored. Eventhough there are some literature showing the use of gold nanoparticles for the treatment of diabetes, the potency of Au NP's against diabetes is still not studied in depth by scientific community. Venkatachalam et.al studied the use of Functionalized gold nanoparticles as an antidiabetic nanomaterial [26]. In their investigation, functionalization of gold nanoparticles synthesized using propanoic acid 2-(3-acetoxy-4,4,14-trimethylandrost-8-en-17-yl) (PAT) an active biocomponent isolated from *Cassia auriculata* is studied in detail. It has been reported thatPlasma glucose level, cholesterol and triglyceride were significantly ($p < 0.001$) reduced in experimental animals treated with gold nanoparticles at dosage of 0.5 mg/kg body weight and plasma insulin increased significantly. Also, the newly synthesized gold nanoparticles by green methods exhibit remarkable protein tyrosine phosphatase 1B inhibitory activity. Some In Vivo studies are also available which reports the effect of biologically synthesized gold nanoparticles on alloxan-induced diabetic rats [27]. They reported that AuNPs has shown significant reduction in blood glucose level on diabetic rats. Daisy et.al studied phytochemically synthesized gold nanoparticles using *Cassia fistula* aqueous extract as hypoglycemic treatment for diabetes mellitus [28].They reported the Use of gold nanoparticles synthesized from *C. fistula* stem bark for the treatment of rats with streptozotocin-induced diabetes reduced serum blood glucose concentrations, induced favorable changes in body weight, improved transaminase activity, achieved a better lipid profile, and reversed renal dysfunction to a greater extent that did aqueous extracts from the same plant. This study indicates that phytochemically synthesized gold nanoparticles are better hypoglycemic agents in the treatment of diabetes mellitus and its associated complications.

2. CONCLUSION

This review focused the three major health issues across the world which is not having a successful cure despite of all the advancement of science and technology. The emergence of nanotechnology and its advancement has been created a revolution in medical and biological research but the use of these techniques for the making an efficient and successful cure for these diseases still needs thorough and extensive research. Thus nanotechnological principles provide golden opportunities

for researchers and academic world to employ and create fruitful results for biological threats.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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