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A Review on Gold Nanoparticles (GNPS) and their Application in Cancer Therapy

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Abstract

Global Cancer Treatment (GLOBOCAN) claims that almost 18 million new cases of cancer are recorded each year. Chemotherapy, radiation, and surgery have historically been the most popular types of cancer treatment. The maximum tolerable dose is now the guideline for treating patients. It will be critical to address normal tissue toxicity, which is one of the major problems with both chemotherapy and radiation therapy. The development of contemporary nanoparticle-based approaches could help with this. Due to the fact that they release chemotherapeutics under controlled conditions, devices based on gold nanoparticles (GNP) are particularly beneficial in further strengthening chemotherapy. Nonetheless, by aiming the GNPs at the tumor, the local radiation dosage may be increased. More than 20 therapeutic drugs based on nanotechnology have entered the clinical stage in the past 20 years. Using a GNP-based therapeutic system more swiftly in clinical settings while lowering normal tissue toxicity and increasing treatment effectiveness is the main objective of this review paper. Nanomedicines will enhance and lessen the side effects of future cancer therapies.

Key word :- Gold Nanoparticle , Synthesis , Cancer therapy

Introduction

The development of the fictionalization of chemistry with state-of-the-art NPs and their wide applications in the treatment of various human ailments have attracted interest on a global scale [1]. Nanotechnology offers several untapped uses in medical research and prescription, and it is crucial for the delivery of medicinal substances. There are numerous uses for NPs in the field of nanomedicine, such as drug formulation, cancer treatment, and research methods [2]. NPs are a highly suggested option for cancer therapy due to their distinct physicochemical properties, which show promise for the future advancement of infection cure in cancer therapy with minimal side

effects. Since a higher size-to-volume ratio, NPs units utilized in the nano-technology with ranges of size between 1nm and 100nm exhibit entirely novel or innovative properties.

For treating cancer at a specific target site, experimental decisions are being made regarding metal NPs. Nanocarriers, cutting-edge cancer therapy techniques, are applied in specific target areas. The development of several distribution tools, including nanoparticles, nanodendrimers, nanorods, and nanotubes, over the years has involved a range of NPs. The development of nanotechnology holds the possibility of modernizing clinical trials, medicine delivery, and pharmaceutical manufacturing [3] .

Researchers are learning how the materials act oddly at a particular component or cell, which reveals the massive therapeutic potentials of the nano-scale approaches [4]. Despite the fact that almost all research is currently standstill, experts in the fields of drug carriers, drug synthesis, toxicity reduction, target indications, and tool optimization are creating innovative tools and methods [5, 6]. NP therapy for cancer has a special function, especially these made of gold. It was demonstrated why GNPs offer unique synthetic and somatic capacities for pharmaceuticals delivery and release [7, 8]. The fact that the gold core of GNPs is largely latent and harmless is the fundamental advantage of employing them as medication carriers. Moreover, mixing ease and the functionalization position of GNPs, which frequently complete thiol connections, favor their selection. When observed in their photographs, somatic features can most clearly cause a distant location's medication release [9].

Gold Nanoparticles (GNPs)

One of the first metals to be shown is gold. However, a few thousand years have gone since the exploration and discovery of Gold Ages. The oldest reports of colloidal gold come from Chinese, Arabic, and Indian scientists who attempted to produce the substance as early as fifth and fourth century. For therapeutic and other uses, scientists have utilized colloidal gold. Colloidal gold has been studied then applied at all of the European chemical research facilities. Functionalized GNPs are being researched for applications in the medical field, including various immune systems, biosensors, genomics, experimental clinical sciences, drug delivery, laser therapy of cancer cells and tumors, scanning, imaging, antigens, and DNA, control of the cancer tissues and cells using cutting-edge indication methods [10].

GNPs are now understood to be a desired option for drug particles' delivery to selected target cells. As a result of their excellent capabilities, especially in the transportation and release of drugs to their targeted cells, GNPs have been selected as an ideal option for therapeutic agent delivery. The therapeutic particles should be much smaller and embedded in the drug particles or large bio-molecules like nucleic acids, RNA, DNA or amino acids for a therapy to be effective [11].

Usually, the GNPs have an incredibly high surface-to-volume ratio because of their inertness and biocompatibility, and they could unquestionably be functionalized with a broad variety of different functional groups. Because of this, they have the potential to be important adjuvants in the medical profession, boosting the immunogenic effects, lowering the toxic effects, and ensuring storage stability of medications and other drugs that are used in the vaccinations [12].

Because of their success in cancer treatment and drugs' administration, the GNPs have grown to be the most well-known. Thanks to bases of functional moieties and their competence in distributions of the amino acids, nucleic acids, proteins, and gene therapy in vivo cures and symptoms, GNPs were able to forge their own path from discovery to therapy in today's medications [12]. The outer functionalization of the GNPs is crucial for biological applications since it enables the GNPs to precisely interact with other cells or biomolecules and transform them into the outlined disease zones. A high surface zone to sum proportion, measure and figure-subordinate physical properties, measure and figure-subordinate optical and electrical aspects, and the next GNPs all display these intriguing traits [13]. Surfaces that may be quickly adjusted and ligands holding important assemblies, like phosphines, amines, and thiols

that have preference for the gold faces. In order for those practical groups to attach ligands, extra moieties such as amino acids, antibodies, dinucleotides and proteins, are needed [4, 14]. The wide range of uses for GNPs is supported by their exceptional somatic and synthetic characteristics. The surface plasmon vibrations of GNPs [2], which are related to linked excited conductive electrons, have an impact on their optical properties in a wide range, from the visible to the infrared (IR), depending on their shape, size, and molecular structure. Figure 1 describes the shapes and applications of the various GNPs.

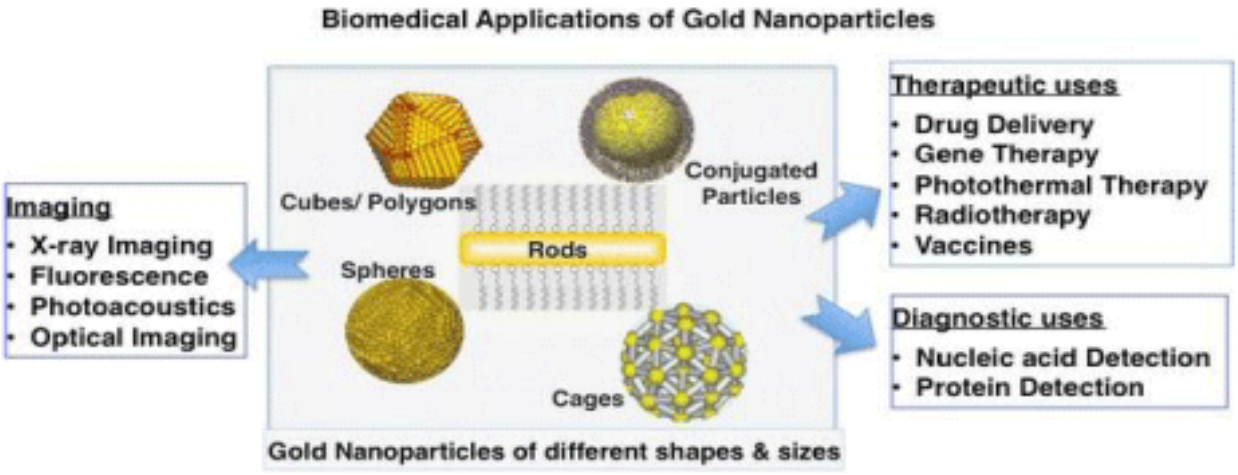

Figure1: PBiomedical applications and various GNP shapes [14].

Methods for GNP synthesis

The next procedures are typically used in order to create GNPs:

Chemical techniques: The sort of chemical technique most frequently used to synthesize GNPs is the Turkevich method, which is also extremely promising when compared to other techniques. In this procedure, mild reducing agents including ascorbic acid [15], citrate [16], and tannic acid [17] are utilized to lower Au+3 ions. As shown in Figure 2, compact and biocompatible GNPs are produced using the Turkevich method. It is crucial to control the process's variables, including temperature, pH, and concentration, in order to produce GNPs [18]. Schiffrin and Brust created the Brust-Schiffrin method for the first time in 1944. Through this method, low dispersion, controlled, thermally stable, and air-stable GNPs may be easily synthesized. In this procedure, AuCl4 was reduced with NaBH4 with the existence of dodecanethiol after being transferred from aqueous phase to toluene with the use of the tetra-octylammonium bromide (TOAB) as phase-transfer agent. In the presence of reducing agents, organic phase transforms from the orange to the deep brown [19].

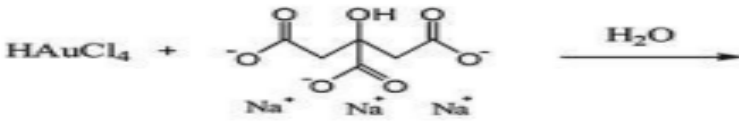

Figure2: Diagram of GNP synthesis by Turkevich approach.

Another technique for creating GNPs with a limited size distribution and a diameter of 5–40 nm is seeding growth. It is feasible to control the particle size and generate particles with a size range of 5–40 nm by the variation of the ratio of the seed to metal salts [20]. This approach offers benefits since it is quick, easy, and affordable [21].

The most popular methods for producing metallic nanoparticles in biology are chemical ones. The expense of reducing and stabilizing drugs restricts their use. Moreover, the biological uses of chemically generated nanoparticles may be hazardous [22]. As a result, it's important to develop straightforward, economical procedures for making safe nanoparticles. In recent years, the production of nanoparticles by biological processes has gained popularity as a green and ecologically friendly technology. Nanoparticle synthesis is often carried out by bacteria, plant extracts, plants, and enzymes in biological processes [23].

Since they are less harmful, more affordable, and environmentally acceptable, plants are increasingly being used to create nano-particles in the past few years. Plants like Azadirachta indica, Medicago sativa, Aloe Vera, Cinnamomum camphora, Pelargonium graveolens, Coriandrum sativum, lemongrass and Terminalia catappa [22 - 23] were utilized recently for producing NPs by biosynthesis. GNPs synthesis using plant extracts, like Memecylon umbellatum, Citrus reticulata and Citrus sinensis, Citrus limon, Terminalia chebula, Memecylon edule, Nyctanthes arbor-tristis, Cinnamomum zeylanicum, Mangifera indica, Piper pedicellatum, Brevibacterium casei, Cochlospermum gossypium, and Macrotyloma uniflorum [24].

Cancer therapy

Cancer is a common illness and a substantial cause of death. Every year, it claims the lives of around 8–10 million people worldwide. Each year, there are around 19.3 million new cases of these deaths that are recorded. Thus, there is an urgent need for effective cancer treatment. The current treatments are still largely conventional and include surgery, which frequently entails a number of radical procedures and can cause a patient to lose function in particular areas; chemotherapy, radiotherapy, and other harsh treatments, which frequently result in the destruction of sizable amounts of healthy tissue. [25]

Although conventional chemotherapy is quite successful, it often comes with serious side effects. Toxicity is caused by the nonselective absorption of hazardous chemotherapy medicines into both normal and dysplastic cells found in organs and tissues. With the introduction of nanomedicine, significant progress has been made in recent years. By functioning as a medication delivery agent and not causing extensive damage but instead aiding to preserve normal tissue due to its great specificity, it offered a significant improvement over chemotherapy [26].

Doxorubicin (DOX) is a popular and frequently utilized antineoplastic medicine, even though it is prone to cause treatment resistance in tumor cells. Stabilizer-modified AuNPs are conjugated to DOX by covalent or noncovalent interactions in several investigations. It may also help prevent drug resistance in case of conjugation. Research suggests as well a link between cancer cells that are resistant to treatment and intracellular accumulation of DOX. To address multidrug resistance, for instance, AuNPs and NH2 have been first PEGlycated with the DOX and then grafted onto this combination [27]. Magneto-gold-fluorescent NPs (MGFs-LyP-1) were produced recently with the use of solvent-mediated technique. Those particles caused the formation of autophagosomes, which caused real autophagy to occur. They worked well along with DOX. By increasing autophagy flux, they increased chemotherapy at nontoxic dosages with minimal harm of the mice's essential organs [28]. As a result, medication delivery keeps improving, with new developments focusing on removing resistance.

The main factor behind GNPs' appeal in drug delivery is that they are simple to make thanks to surface alterations using a variety of ligands that aid in focused and precise distribution. The paper goes on to address the physical-chemical characteristics of photodynamic treatment, contrast imaging, and thermal ablation. Hence, early illness detection is possible using tailored nanoparticles. Due to the inherent multifunctionality of GNPs, all these

characteristics demand that we approach them from several angles [29].

Nanotechnology advancements in cancer management will aid in early diagnostics, targeted treatments with fewer restrictions, and effectiveness, as well as lowering exorbitant treatment costs, making them widely accessible to the general public. [30]

PTT is utilized as a stand-alone treatment because it induces targeted hyperthermia, and we can induce tumor ablation thanks to the variety of GNPs that can be manufactured. An additional advantage is that the nanoparticles build up inside the cells, resulting in continued activity in tumor environment [31]. Due to their stronger adhesion to sick cells, the smaller injected particles have consistent biological effects, whereas the larger AuNPs have better optical properties [32]. PTT's applications are nevertheless restricted because it has no effect on metastatic lesions or a large surface area. As a result, additional procedures, including ionizing radiation and other supplemental therapeutic approaches, are included [33]. Ion radiotherapy uses ion beams as its radiation source. Both "light ions" like hydrogen and helium as well as "heavy ions" like carbon and/or oxygen make up these beams. Although they commonly harm healthy tissue as well, these ions help destroy cancerous cells. The quantity of radiation deposited in cancerous tissues can be increased when GNPs are utilized as radiosensitizers, which merely enhance the radiation's effects on those tissues. [34] Significant X-ray interaction up to 1 MeV and ion interactivity are both present in AuNPs. According to Monte Carlo simulations, AuNPs might boost radiation sensitivity. The radiation beam was shown to deliver a lower dose after passing through the zone containing AuNPs, suggesting that AuNPs might increase radiation sensitivity. It was found that after passing through the zone containing AuNP, the radiation beam will deliver a lower dose. The therapeutic ratio increases as a result [35].

The body absorbs NPs, which serve two purposes: they aid in imaging by helping to target specific tissues, and they also have a number of therapeutic applications. Extracellular matrix (ECM) with abnormal vasculature and an aggregation of many cell types makes up the tumor microenvironment (TME). The TME is hypoxic due to the deformed function and appearance of the ECM. There are also fibroblasts, which contribute significantly to the TME and have a major impact on the development and management of tumors. The microenvironment is constantly hypoxic because of aberrant vasculature, which causes an immune-suppressive condition to start by an accumulation of immune-suppressive cells secreting immune-suppressive chemicals, which ultimately inhibit dendritic cells, which are crucial for antigen presentation in the body. This results in a pathological fibrosis due to an aberrant macrophage phenotype [36]. Different cell types interact with GNPs, which have an immunostimulatory function that causes a range of responses. They are commonly used as vaccine adjuvants due to their ability to generate specific antibody responses to certain antigens when conjugated with an appropriate molecule type. This quality could be advantageous for cancer immunotherapy [37].

Photodynamic treatment, which was initially suggested more than 100 years ago, is another option. The creation of ROS is currently a universally accepted as effective and safe therapeutic approach, notably for skin problems [38]. Overproduction of ROS leads to oxidative stress. It causes necrosis or apoptosis in the cells, which kills them. In the case when GNPs are closely examined, they have as well an apoptotic effect on the tumor itself, which causes the cell shrinkage, DNA breakage, and other signs that finally result in the production of apoptotic cells, which are after that phagocytosed through the macrophagic cells (39).

The attachment of GNPs to photosensitizers, which results in oxidative stress, eliminates the numerous drawbacks of the use of a single photosensitizer. The disadvantage of the photodynamic treatment without the GNPs include a development of photosensitizers in bodily media which impairs the yield of singlet oxygen and non-targeted dispersion throughout the body. Attachment to an AuNP ensures the stability of such photosensitizers, improves their cell selectivity, and significantly improves the efficacy of photodynamic treatment [40].

Conclusion

A better potential for cancer treatment in numerous human body sections is provided by using GNPs. As an adjuvant, GNPs are essential in the medical field because they increase immunogenicity, lessen toxicity, and provide storage stability for medications and other compounds used in vaccinations. They also have an excessive amount of potential.

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