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GOLD NANOPARTICLE APPLIED TO BRACHYTHERAPY

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ABSTRACT

Cancer is a global public health problem, that consists in a disease is characterized by the uncontrolled growth of anomalous cells that impair the functioning of the body. One of the treatments for cancer is the brachytherapy. This technique a non-invasive treatment in which the radiation is placed close or in contact with the region to be treated, brachytherapy may save the healthy tissues and consequently reduces the amount of side effects. An unexplored strand is nanobrachytherapy, that unites the advantages of brachytherapy with the small size in the nanoparticle (NP), resulting in an even less invasive treatment. Nanotechnology is the science that studies the properties of nanometric materials with the aim of creating new materials with different properties of interest. In view of the synthesis of the NP and their applicabilities, there is a fundamental role that is made to coatings, which have the function of avoiding the aggregation of particles, stabilize and also control their functional properties. Besides being able to add molecules of interest, such as antibiotics and anti-inflammatories. Among the range of coatings, the most outstanding are polyethylene glycol (PEG). PEG improves the surface properties of NP and presents high stability under biomedical conditions. The NP have their size controlled, which facilitates their penetration into the vasculature, in addition to being a non-toxic coating. After the synthesis of gold nanoparticles (Au-NP) was developed, PEG were successfully incorporated into the surface. Incorporation was confirmed by DLS, FT-IR and HRTEM.

1. INTRODUCTION

Cancer is characterized by anomalous growth of cells in organism impairing the functioning of the body.[1] When discovered in early stages, the disease can be treated using less invasive methods with better or equal results when compared with traditional procedures, such as chemotherapy, radiotherapy, and surgery. The simpler approach is highly desirable especially because the main side effects are pain, abbreviation of life and death. [2]

A type non-invasive treatment is brachytherapy. This treatment uses radiation in close contact or inside the tumor.[3] It can be classified as a permanent or temporary implant. In permanent implants, the dose is released during the whole radioactive decay. Temporary implants the dose is calculated in function of treatment time and number of sessions.[3] The main advantage of brachytherapy is the direct delivery of radiation into the target, sparing the healthy surround tissues and, consequently, reduces the amount of side effects.[3, 4]

For example, the size of the seed used in prostate brachytherapy is in millimetric scale. They are inserted in the prostate 3-5 at a time through a needle. Since around 100 seed are inserted, the needle punctures the peritoneum approximatively 25 causing pain and discomfort to patient.

With the size issue in mind, the IPEN's brachytherapy sources production group is using its experience combined with nanotechnology. The nanometric scale have unique properties and promotes alteration in physical, chemical and biological aspects of the atoms/ molecules used.[5] The properties of materials, such as melting point, electrical conductivity, magnetic permeability, and chemical reactivity, are size-dependent (quantum effects rule).[6] By synthetizing a radioactive nanoparticle, a nanosource is created and can be used to treat cancer in a direct and easy way.

2. OBJECTIVES

The project is based on the development and validation of a new radioactive nanoparticle, wich will be used for the treatment of cancer. The great advantage of nanotechnology, when compared to classic brachytherapy method is the small size of the emitting source and the possibility of adding other molecules of interest to the coating. The objective of the work is to study more deeply coatings widely used for use in nanobrachytherapy and others Nano systems: Polyethynele glycol and study your stability on a radioactive system.

3. METHODOLOGY

3.1 Synthesis

The synthesis of gold nanoparticles is a new method developed in IPEN based on Turkevich's method; $HAuCl_4$, sodium citrate, 2,3-meso-dimercaptosuccinic acid (DMSA), sodium hydroxide (granules) and NH_2-PEG-SH are used. All reagents are used without further purification. All glass products and magnetic stir bars must first be cleaned with royal water (HCl and HNO_3 in a 3: 1 volumetric ratio) and thoroughly rinsed with reverse osmosis water prior to use. The same reverse osmosis water was used to prepare aqueous solutions. $HAuCl_4$ was only treated with plastic spatulas to prevent corrosion. 50 ml of $HAuCl_4$ (0.1 mM) containing 100 µL of NaOH (1 M) is prepared in a 100 ml three-necked flask equipped with a reflux condenser. The solution should be boiled (80-90 ° C) while stirring with a magnetic stir bar coated with PTFE. Then, 5 mL of Na 3 Ctr (34 mM) is added rapidly. The reaction turns from light yellow to light black, black and dark until the solution reaches the red color of the wine. The reaction allows to continue for another 7 minutes (completing 10 in total). After 10 minutes the vial should be removed from the heating plate and allowed to cool for 10 minutes still under reflux. After this period, the reflux system is turned off and the analysis in the DLS is performed. For the coating reaction, 1 ml of the nanoparticle solution is mixed with 1 ml of the coating (PEG 0.05% w / v)

3.2 Characterization

The nanoparticle were characterized by Dinamic Light Scattering (DLS), evaluating potential Z, particle diameter and polydispersity index and transmission electronic microscopy (TEM). To evaluate the coating reaction was performed Infrared spectroscopy.

4. RESULTS AND DISCUSSION

4.1 Synthesis

The synthesis was succesfull, in the reaction the rapid color change was observed, the final wine-red color indicates that all solution gold ions were consumed by reaction.

4.2 Characterization

The DLS characterization of the nanoparticles presented these results:
The uncoated nanoparticles had a size of 16±4, polydispersity index of 23% and Z potential of -42±4. The nanoparticles coated with PEG showed size of 25±2 nm, polydispersity index of 25% and Z potential of -44±2.

The FTIR was performed, the coat PEG and nanoparticles coated with PEG were compared with the spectrometer. Peaks clearly coincide with clear indication of a successful coating reaction. As shown in figure 1.

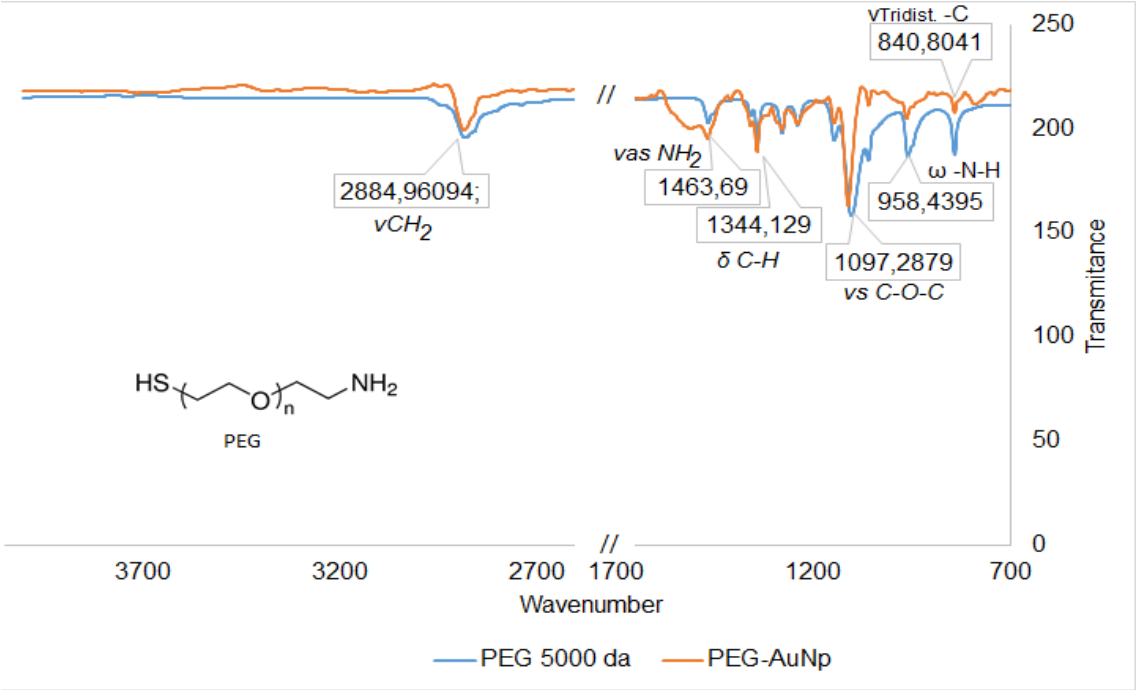

Figure 1: FTIR of PEG and PEG-AuNPs

Transmission electron microscopy presented regular, unattached and uniform nanoparticles, as shown in figure 2 and 3.

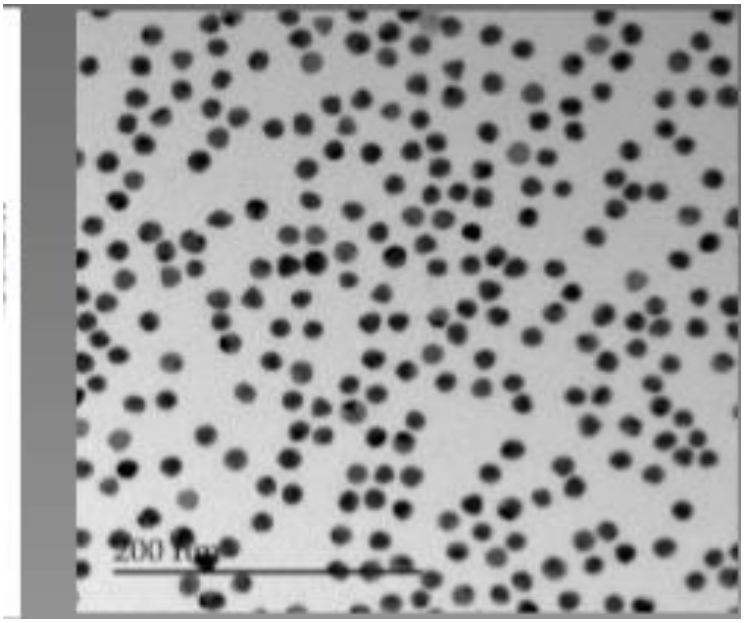

Figure 2: TEM of Uncoated AuNPs

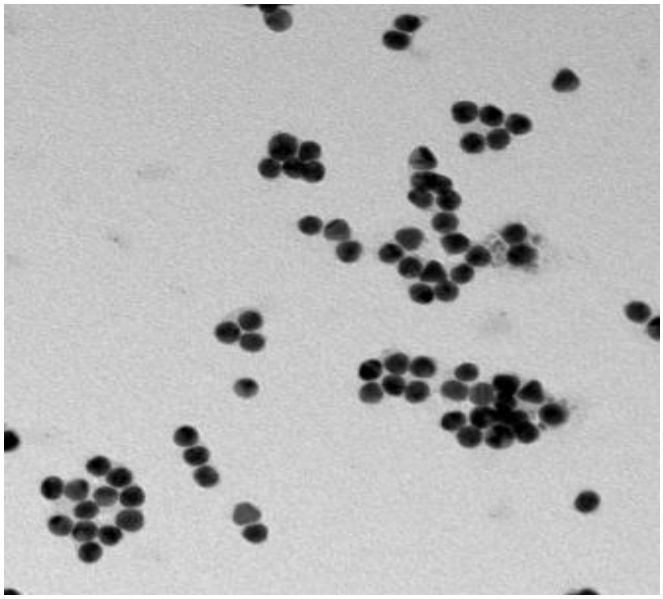

Figure 3: TEM of PEG-AuNP

5. CONCLUSIONS

The two nanoparticles presented excellent results, both in their size, polydispersity of up to 25%, indicating that the family of nanoparticles present there, are mostly of the same size, and Z negative potential, below -30 indicating that the repulsion force between the particles is strong enough that they do not aggregate.

The PEG coating produced particles within the desirable size, had good polydispersity and Z potential. In the infrared spectroscopy analysis the binding peaks coincided, with clear indication of a successful coating reaction. The TEM presented excellent results, confirming that the reaction and the production of the nanoparticles were successful.

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