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Development and Performance Evaluation of Gold Nanoparticles in Radiotherapy

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ABSTRACT:
The synthesis, physicochemical characterization, and performance assessment of gold nanoparticles (GNPs) in radiotherapy were the main objectives of the current work. Another goal was to examine the antibacterial effectiveness of gold nanoparticles against clinical strains of E. coli. Tri sodium citrate is used to manage the reduction of an aqueous HAuCl4 solution to create gold nanoparticles. For physicochemical characterisation, particle size analysis and transmission electron microscopy were utilised. Polymer gel dosimetry was utilised to assess how well the dosage was being absorbed. Investigation of the antibacterial action was conducted using the diffusion technique in agar media. By using several formulations, gold nanoparticles in sizes ranging from 57 nm to 346 nm were produced. A 57 nm-sized gold nanoparticle boosted radiation dosage efficacy by roughly 21%. Nano gold had a remarkable anti-bacterial activity against clinical strains of E. coli at a dose of 400 ppm. Gold nanoparticles can be used as a dosage enhancer in radiotherapy, it is determined. According to research on anti-bacterial effectiveness, clinical strains of E. coli were significantly affected by gold nanoparticles.

Keywords: gold nanoparticle, antibacterial, gel dosimetry, radiation therapy.

I. INTRODUCTION:

The effects of nanotechnology are starting to be felt in the delivery of healthcare. These include brand-new approaches to illness diagnosis, treatment, and prevention known as nanomedicine. [1] Quantum dots, carbon nanotubes, paramagnetic nanoparticles, liposomes, gold nanoparticles (GNPs), and several other nanoparticles have received the greatest research attention. [2] Gold nanoparticles have received a lot of interest recently. They are agents having several uses in biomedicine, including gene and medication delivery, thermal ablation, diagnostic assays, cancer research, and diagnostic assays [3-5]. Nanogold has various distinctive qualities, such as being inert and nontoxic [9], having potent antibacterial, anti-angiogenesis [11], etc. Both "physical" and "chemical" processes have been used to create GNPs. In the "physical" preparation process, GNPs are produced when Au mass is attacked by a powerful force, such as ion irradiation in air or arc discharge in water. chemical process including organometallic complex breakdown, electrochemical routes, and chemical reduction of Au salts. Among these, the chemical reduction approach is straightforward and controlled for producing GNPs in a range of sizes and forms. [12,13]

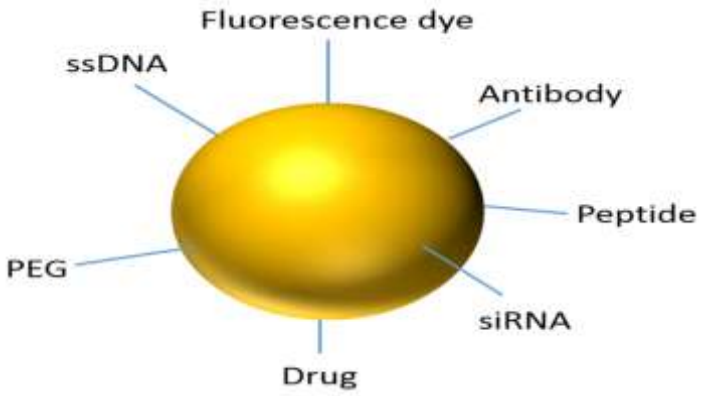

Fig.1: Gold Nanoparticle

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The second greatest cause of mortality in the United States and the third major cause of death overall in industrialised nations is cancer. [2] Chemotherapy, surgery, and radiation are all used in the treatment of cancer. Radiation therapy has been used to treat cancer for almost 100 years and is one of the most popular treatments, although it comes with a number of drawbacks. Therefore, researchers are exploring for novel approaches to improve radiotherapy's effects while minimising harm to healthy cells. [14] Long-term research has been done on the idea of enhancing dosage in cancer radiation utilising high-Z materials. On the possible use of GNPs in combination with radiation treatment, several research have been conducted. [15] This project's goal was to create and characterise GNPs in order to increase their absorption by tumour cells. Investigated was the produced GNPs' antibacterial impact on E. coli clinical strains.

II. MATERIALS AND METHODS:

Materials:

From Indian Platinum Pvt.Ltd. in Mumbai, HAuCl4 was acquired. Tri sodium citrate was procured from the Hygia Institute of Pharmacy pharmaceutics facility in Lucknow. Tetrakis (Hydroxymethyl) Phosphonium Chloride, Gelatin, N, N'-methylenebis-acrylamide (bis) acrylamide (AA), all of which were purchased from Sigma Chemical Company. We bought Mueller Hinton agar from Liofilchem. Water that has been deionized was utilised to make aqueous solutions.

Method:

Development of Gold nanoparticles:

The traditional citrate reduction process was used to create gold nanoparticles (frens method). 20 ml of a 1 mM HAuCl4 water solution were briefly kept boiling. The mixture was then supplemented with various amounts of 1% sodium citrate water solution while being agitated for around 10 minutes to create a suspension of coloured gold nanoparticles. Table 1 displays the various citrate volumes used in the manufacture of GNPs.

Table 1: Particle size and polydispersity index of gold nanoparticles produced using various formulations

Formulation Code	Volume of HAuCl4 1mM(ml)	Volume of Citrate 1% (ml)	Particle Size (nm)	Polydispersity Index
F1	20	1.8	46	1.17
F2	20	1.7	51	1.22
F3	20	1.6	58	1.21
F4	20	1.5	75	1.81
F5	20	1.4	139	1.19
F6	20	1.3	261	1.12
F7	20	1.2	344	1.07

III. CHARACTERIZATION OF GNPS

The mean particle-size values of GNPs were calculated using a laser diffraction particle-size analyser equipped with Wing software. The morphology of the nanoparticles was studied using transmission electron microscopy (TEM). [16] Drops of the gold suspension (formulation F6) were put on a copper grid covered with Formvar and allowed to dry. One of the created colloidal solutions' UV-visible absorption spectra were captured from 400 to 900 nm using a spectrophotometer.

Gel dosimetry

Gel fabrication

Water makes up 89% of the bulk of the gel solution, along with acrylamide, N,N-methylene-bisacrylamide, and gelatin. In a 500 ml beaker, the gel's component parts were combined between 35 and 40 °C. Tetrakis (hydroxyl methyl) phosphonium chloride (THPC), an oxygen scavenger, was added as an antioxidant to the gel mixture at a concentration of 10 mM. In order to create gel with GNPs batch, nano gold (formulation F3) was employed as a component of water in gel preparation.[17] We saw that the GNPs blended evenly throughout the gel. As a control, a different batch of gel was produced without GNPs. After that, the gel was swiftly poured into several tubes.

Irradiation

After being placed in a head and neck phantom, the tubes from both batches were subjected to a CT scan for irradiation. 40, 80, and 120 Gy of radiation were given to the gel samples.[18] The Day CT scanning centre used the

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following parameters to irradiate the gel samples: slice thickness=1 cm, t=0.8 s/turn, mA=200, and kVp=140.

Magnetic Resonance Imaging (MRI)

Irradiated and non-irradiated gel samples were scanned in a 1.5 T MRI scanner to assess the spin-spin relaxation time of the free protons using a head coil. Field of view = 105 120 mm^2, slice thickness = 5 mm (kV X-ray beams), effective echo time TE = 22 ms, turbo factor = 14, field of view = 128 128 matrix, and total imaging time = 20 min were the fast-spin echo parameters that were employed. At least 24 hours had passed since the irradiation before imaging to allow for polymerization. The samples were all scanned at ambient temperature.

Data analysis

The picture was examined using the MATLAB programme (version 3.5.7). Before doing an analysis to identify the region of interest, the software looked over the data. Pixel by pixel calculations of T2 data resulted in T2 maps. By determining the R2 (1/T2), the amounts of polymerization of the irradiation gels with and without GNPs were compared.

Anti-bacterial test

Using the agar-well diffusion technique, antibacterial activity was examined after adding 100 l of bacterial suspension to 20 mL of sterile nutritional Mueller Hinton agar at 45°C and allowing the combination to solidify on a Petri plate. Three wells each measuring 7 mm in diameter and spaced equally apart from one another and from the dish border were drilled into the agar after the medium had set. 150 L of various concentrations of GNPs from formulation F2 were poured into the wells (400 ppm, 200 ppm, 100 ppm). The petri dishes were incubated for 24 hours at 37 °C in a thermostat. After incubation, the diameter of the zone that inhibited bacterial growth was determined. Five clinical strains of E. coli were used in all studies, which were carried out three times.

IV. RESULTS AND DISCUSSION

Physicochemical properties of GNPs

Table 1 illustrates how citrate volume affects particle size. These results showed that when citrate volume increased, the size of the gold nanoparticles decreased. TEM images demonstrate the spherical form of the produced GNPs (Figure1). Utilizing the reduction process, a narrow range of sizes was attained (Figure 2). An absorption maxima at 532 nm proved that GNPs had formed. Their well-dispersed condition in solution was confirmed by the lack of absorbance at wavelengths longer than 600 nm16 (Figure 3).

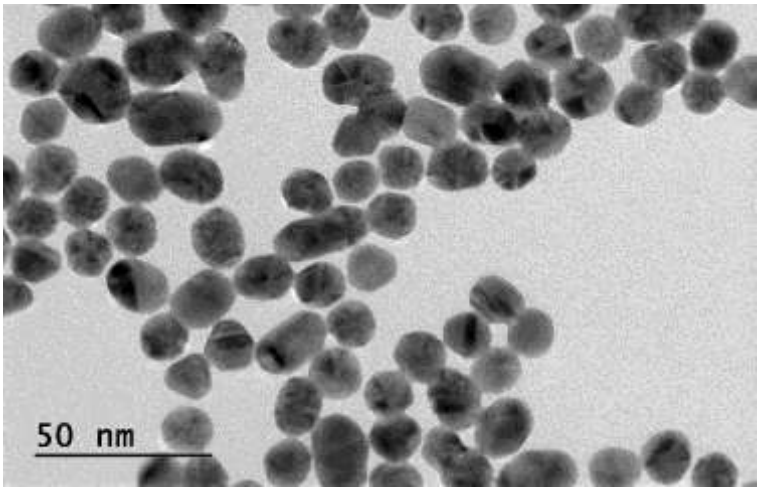

Fig. 2: TEM image of gold nanoparticles (f4)

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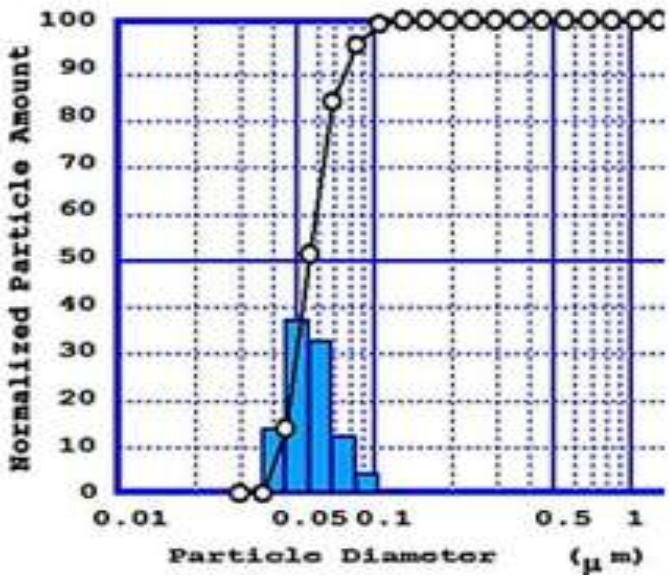

Fig. 3: Particle size distribution of gold nanoparticles (formulation F1)

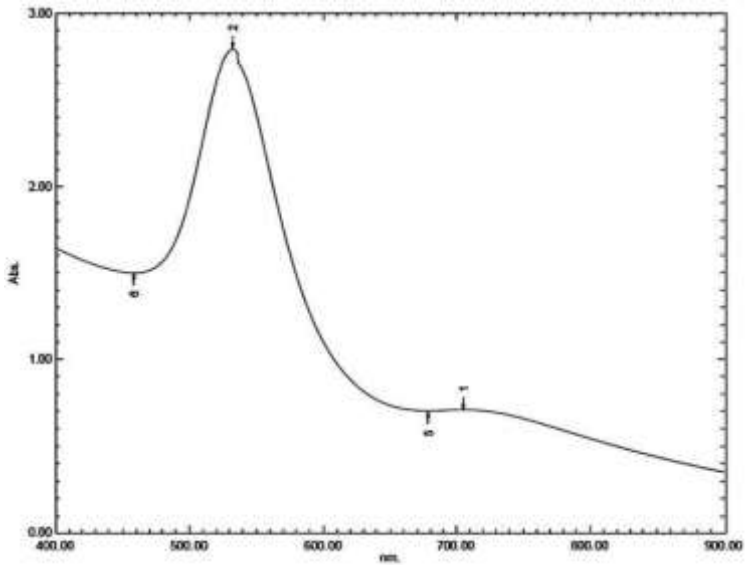

Fig.4: UV– Visible spectra of 250 nm gold nanoparticles (formulation F3)

Gel dosimetry

To describe the impact of GNPs on polymer gel, the connection between the given X-ray dosage and the R2 (spin-spin relaxation rate) was examined. R2 is a function of dosage and equals 1/T2 (spin-spin relaxation time) (dose delivered to water). Delivered dosage and R2 are shown to be correlated linearly (Figure 4). For gel-GNP and pure gel, the dose-response slopes for R2 vs delivered X-ray dosage were computed. The dosage enhancement factor was determined as the ratio of these slopes (DEF). For the dose-response relationship, the DEF was 1.21. High Z material is thought to increase the possibility of the photoelectric contact, which is thought to be the main factor contributing to dose enhancement. The photoelectric interaction cross section will rise when GNPs are introduced to the gel before being exposed to kilovoltage X-rays. This is plainly deduced from the likelihood that these X-ray photons will interact with gold atoms as opposed to a tissue comparable media like water.

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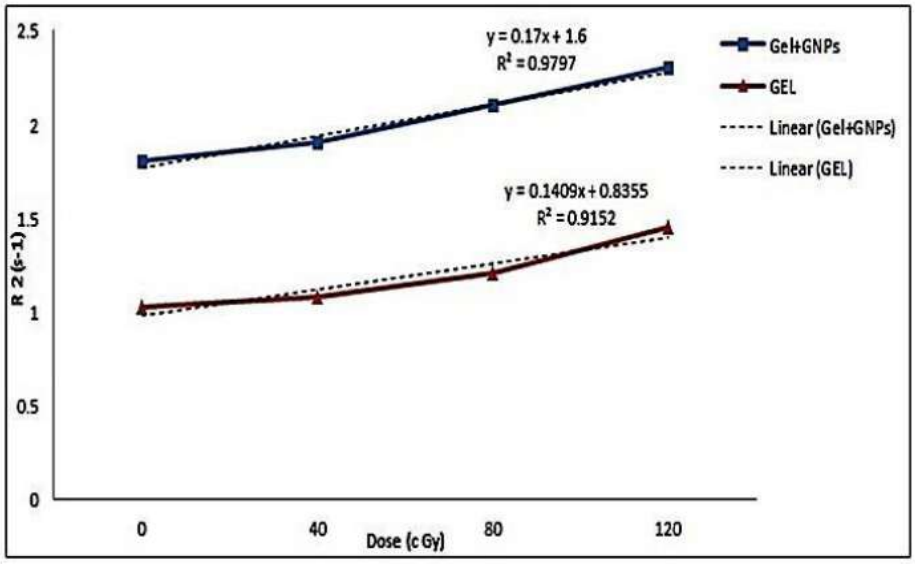

Fig.5: Dose–response curve for pure gel and gel–GNPs

Antimicrobial activity of GNPs against E. coli clinical strains

Table 2 lists the mean inhibitory diameters in relation to various GNP concentrations (formulation F2). GNPs showed good efficacy against E. coli clinical strains at 400 ppm concentration. 100 ppm had essentially no effect, whereas 200 ppm had a negligible impact. GNPs primarily work by two mechanisms to limit ATP synthase activity, shift membrane potential, and decrease ATP levels, all of which point to an overall drop in metabolism. The alternative approach involves blocking the ribosome's subunit's ability to bind tRNA, which shows that a biological process has failed.17 Citric acid was used as a reducing agent and cetyl trimethyl ammonium bromide (CTAB) as a binding agent in Nishat et all reports of a straightforward one-step microwave irradiation technique for the manufacture of GNPs. They tested the nano gold's antibacterial effectiveness against the standard strain of E. coli and found that it had a high level of antibacterial activity with a zone of inhibition of roughly 22 mm. 18 This outcome demonstrated the nano gold's increased antibacterial potency against E. coli.

This discrepancy can be due to the usage of CTAB, a strong anti-microbial agent.

Table 2:Inhibition zone diameter (mm) of various nanogold concentrations placed in plates containing inoculums of E. coli clinical strains

Strain	100 ppm	200 ppm	400 ppm
1	0	7.88	9.91
2	5.4	8	11.13
3	0	7.91	11.43
4	0	5.21	11.43
5	0	3.31	9.15

V. CONCLUSION

Here, we describe how we measured the radiation dose augmentation caused by GNPs using phantom polymer gel dosimeters. This study discovered a considerable dosage augmentation when the GNPs were added to polymer gels exposed to treatment machine kilovoltage X-ray beams. Additionally, GNPs showed strong antimicrobial activity against clinical strains of E. coli at a concentration of 400 ppm.

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