# THE EFFECT OF BIOCOMPATIBLE MATERIALS ON SILVER NANO-RODS USED IN PHOTOTHERMAL THERAPY

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***ABSTRACT—*** *Photothermal therapy (PTT) is a medical method of treating cancer by laser radiation in the NIR region. To enhance the efficiency of the heat generation, nanoparticles are used as photothermal agents. Biocompatible Materials are substances, that are used to cover any foreign bodies that are injected inside the human body, so that they would not be rejected. Noble metal nanoparticles can intensely absorb radiation, when they are inserted into the cancer tumors, they increase the possibility that the cells will be burned by radiation. Silver nano-rods (AgNRs) like all silver nanoparticles in general, are anti-microbial, therefore they are considered to be a perfect choice for multiple medical applications. The AgNRs were modeled under the same conditions and with the same dimensions, but with different biocompatible materials, consequently the heat generated differed for each biocompatible material.*

***Keywords—***biocompatible material, photothermal therapy, surface plasmon resonance, silver nanorods.

## I. INTRODUCTION

Photothermal therapy (PTT) is a medical method of treating cancer by laser radiation in the NIR region. The process of PTT focuses on raising the temperature of the cancer cells to exceed 42◦C, by subjecting them to a laser beam in the NIR region. Because at the NIR region, there is minimum radiation absorption and scattering by the human body. Therefore, the human cells become almost transparent. To enhance the efficiency of the heat generation, nanoparticles are used as photothermal agents. Noble metal nanoparticles can intensely absorb radiation, when they are inserted into the cancer tumors, they increase the possibility that the cells will be burned by radiation. Gold nanoparticles are the most common. But the probability of toxicity issues in the long run, is a drawback for the implementation of most metal nanoparticles in PTT [1]. Therefore, silver nanoparticles are good alternative since they are found to have anti-microbial characteristics [2]. Metalic nanoparticles that have high SPR are found to have encouraging characteristics to be used as photothermal agents. But still the development of photothermal agents that are biocompatible and high photothermal conversion efficiency are a great research issue. In general, the use of any biocompatible material is restrained by a number of features, some of them are due to the characteristics of the human tissue itself and the characteristics of the biocompatible material and the site the period of time the tissue will be exposed to the treatment [3].

In general toxicity issues of the nanoparticles has to be considered, therefore the application of a surrounding biocompatible medium is very important. The rate of toxicity and of nanoparticles is affected by many factors such as the dimensions of the nanoparticle, the number of particles per unit area, and dosage [4]. Also applying biocompatible materials enhances the photothermal stability, and the biocompatibility of the nanoparticles.

Surface plasmon resonance (SPR) is electromagnetic waves produced by the propagating of electrons along the surface of a thin metal layer of the metallic nanoparticle employing the interaction of light photons with free electrons (surface plasmons) to quantify the change in the concentration of biomaterial on the surface. SPR is also responsible for the enhanced scattering and absorption of light in the visible to NIR wavelength regions [5]. The SPR in metal nanoparticles is a function of the metal's optical properties of the metal and the structure and dimensions of the nanoparticles. The dielectric of the surrounding medium also affects the SPR.. SPR can also be implemented plasmonic-driven thermal sensing, and SPR-based detection [6].

Nanoparticles are any particles having a size in the range of 1nm to100 nm, is known as a nanoparticle. The properties of nanoparticles differ from the properties of the same bulk material, due to the large surface area to volume ratio. This leads to increased strength, chemical, and heat resistance. They can be synthesized in may structures, such as nanospheres, nanocubes, nanoshells, nanorods and many other structures. Silver nano-rods (AgNRs) like all other silver nanoparticles, are anti-microbial, therefore they are considered to be a perfect choice for multiple medical applications [5]. The SPR of AgNPs can be measured from the absorption cross section, which is related to the nanoparticles size, and the dielectric of the surrounding medium, which is in this case, the biocompatible material. [7].

At surface plasmon resonance (SPR) frequencies, metal nanoparticles such as AgNRs become thermal nano-sources, therefore they could be used in thermal ablation of the cancer cells [8]. The human cells can absorb radiation in the NIR region, i.e., 700 nm - 900 nm, enabling the radiation to reach the AgNRs inside the cancer cells [1, 9]. After the cancer treatment, the AgNRs do not cause further complications, since they penetrate leaky tumor blood vessels and are easily removed from the human body by the urinary system, since the are smaller than 200 nm [9, 10].

## II. METHODOLOGY

AgNRs were modeled with dimensions of 20 nm in length and 10 nm in width using Matlab. Then the SPR of the modeled AgNRs was measured by its absorbance cross section, $\sigma_{abs}$ (λ) as a function of the wavelength, λ, from the Mie's theory [11]:

$$\sigma_{abs}(\lambda) = 18\pi \frac{V}{\lambda} \varepsilon_m^{1.5} \left[ \frac{\varepsilon_2(\lambda)}{[\varepsilon_1(\lambda) + \varepsilon_m]^2 + \varepsilon_2(\lambda)^2} \right] \qquad (1)$$

Where $V$ is the nanoparticle volume, εm is the permittivity of the surrounding material, ε1(λ) and ε2(λ) are the real and imaginary parts respectively of the complex permittivity of the nanoparticle material.

The real and imaginary parts of the complex dielectric function can be found from Drude's model [12]:

$$\varepsilon_1(\lambda) = \varepsilon_0(\varepsilon_\infty - \varepsilon_h)\left(\frac{1}{1+\tau^2\,(2\pi\frac{c}{\lambda})^2}\right) \quad (2)$$

$$\varepsilon_1(\lambda) = \varepsilon_0(\varepsilon_\infty - \varepsilon_h)\left(\frac{1}{1+\tau^2\,(2\pi\frac{c}{\lambda})^2}\right) + \frac{2\pi c\sigma}{\lambda} \quad (3)$$

Where $\lambda$ is the wavelength, $\tau$ is the relaxation time, $\sigma$ is the electrical conductivity, $\varepsilon_\infty$ is the infinite-frequency relative permittivity, $\varepsilon_h$ is the zero-frequency relative permittivity.

Five biocompatible materials have been chosen in this research in modelling of the AgNRs. These materials are; poly glycol ethylene (PEG 400), propylene glycol (PG), chitosan (CHI), polyvinyl alcohol (PVA) and Teflon (PTFE). There electrical and thermal properties were displayed on table.1.

The radiation power absorbed by the AgNRs can be calculated from the following equation:

$$Q = \sigma_{abs}\, I \quad (4)$$

Where I is the irradiance of the incident light in W/m$^2$

The absorbed radiation power raises the temperature of the AgNRs and this results into heat power generated to the surrounding, which can be found from Stefan's law, which states that the rate at which an object radiates energy is proportional to the fourth power of its absolute temperature. as follows

$$Q_m = 0.9k_B 4\pi R_2{}^2((T_n + \Delta T_n)^4 - (T_m + \Delta T_m)^4) \quad (5)$$

Where $k_B$ is Boltzmann's constant, $T_n$ is the AgNRs temperature, and $T_m$ is the temperature of the surrounding medium and it is equal to the temperature change of the tumor cell. As for the temperature raise inside the AgNRs due to the absorbed radiation, it is controlled by the thermal conductivity of the surrounding medium and the effective radius of the nanoparticle, and is found as follows:

$$\Delta T_n = \frac{Q}{4\pi\, K_0 r_e} \quad (6)$$

Where $K_0$ is the thermal conductivity of the surrounding medium, and $r_e$ is the effective radius of the nanoparticle.

When using photothermal therapy, the temperature of the cancer cell should be in the range from 42˚C to 45˚C in order to start burning and without affecting the surrounding healthy cells [1]. Hence the increase in the cancer cell temperature should be between 4˚C to 8˚C. Penns bioheat transfer equation can be used to find the sufficient heat power for tumor destruction [14].

$$Q_m = \rho c\Delta T - Q_{mt} - Q_p \quad (7)$$

**Table 1 The electrical and thermal properties of the biocompatible surrounding mediums [13]**

| The Material | Dielectric constant in F/m | Electric conductivity in S/m | Thermal conductivity in W/m.K |
|---|---|---|---|
| **PEG 400** | 20.26 | 6.3x10$^{-3}$ | 0.274 |
| **PG** | 32 | 10-6 | 0.206 |
| **CHI** | 17.3 | 9.8x10$^{-6}$ | 0.02 |
| **PVA** | 1.6 | 9.7x10$^{-9}$ | 0.206 |
| **PTFE** | 2.1 | 10$^{-17}$ | 5.86 |

Where ρ is the cell tissue density = 920 kg/m3, c is the cell tissue's specific heat = 3000 J/kg.K

$\Delta T$ is the change in temperature in K

$Q_{mt}$ is the metabolic heat energy generation rate = 33800 J/m3

$Q_p$ is the heat transfer from the blood to the tissue in J

The flow of blood inside the contributes in the adjustment of the body temperature to 37℃.

$$Q_p = \omega_b \rho_b c_b\, \Delta T \quad (8)$$

$\omega_b$ is blood perfusion rate = 0.5, $\rho_b$ is the blood's density = 1000 kg/m$^3$, $c_b$ is the blood's specific heat = 4000 J/kg K

Therefore, from Penns bioheat transfer equation, the calculated value of $Q_m$ that could be used in PTT, should be greater than 3 kJ/m$^3$ in order to burn the cancer cells and less than 6 kJ/m$^3$ so as not to burn the surrounding healthy cells. Therefore, all the parameters of the AgNRs should be adjusted to produce the required value for $Q_m$.

## III. RESULTS AND DISCUSSION

The AgNRs were modeled each time with a different biocompatible material, the results of the absorbance cross section due to the five biocompatible materials were plotted in figure.1 As it can be seen from figure.1, that the materials PG, PEG and CHI had higher absorbance peaks in the visible to NIR region, but the other two materials had no peaks at all.

The AgNRs were illuminated by 85 Watts laser beam for 30 secs in order to raise their temperature, and generate heat. The values of the heat energy generated by the AgNRs due

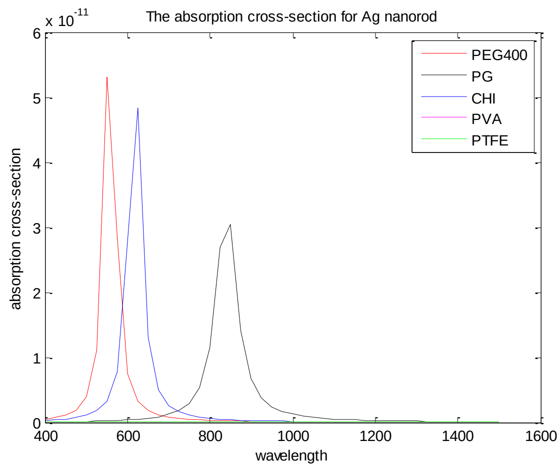


**Figure 1 The absorption cross section for AgNRs**

to the different biocompatible materials is demonstrated on table.2 and figure.3. It was noticed that the energy peak for PEG 400 is very high and can cause dangerous damages to the surrounding healthy cells, and it is also out of the NIR range, therefore it could not be used in PTT applications. The values of the energy peaks for CHI and PG are both equal to 3.134kJ/m3 which is in the range calculated from Penn's bioheat transfer equation (7) and are sufficient enough to be used in PTT. Illuminating the AgNRs for a longer period could produce more efficient results for tumor destruction, but there could be other unwanted results.

The obtained results were compared with the results of [15], where M. A. Behanam and his group, who used carbon nanotubes (CNT) to cover AgNRs. They found that when comparing the absorbance of the AgNRs alone, with CNT on its own and AgNRs and CNT combined together, the absorbance peak for the AgNRs alone was out of the NIR region, but when combined with the CNT, the peak was in the NIR region as can be seen in figure.2, and this result proves that biocompatible materials enhance the absorbance. Also M. A. Behnam and his team found that CNT/Ag NPs were more effective in heat generation than CNTs and Ag NRs [15].

## IV. CONCLUSION

AgNRs were found to be efficient elements for PTT if they were illuminated with the suitable optical power, for the adequate time duration and the accurate biocompatible material was applied, since it affects the SPR of the material and consequently the generated heat. The biocompatible materials CHI and PG are found to be the optimum choice since they enhanced heat generation in the AgNRs to the required value that could be used in PTT. Nanoparticle volume is also an important factor that should be taken under consideration since it also affects the absorbance cross-section and hence the heat generation. But still the development of photothermal agents that are biocompatible and high photothermal conversion efficiency are a great research issue. Hence the biocompatible materials apart from making the AgNRs biodegradable they also enhanced the heat generation.

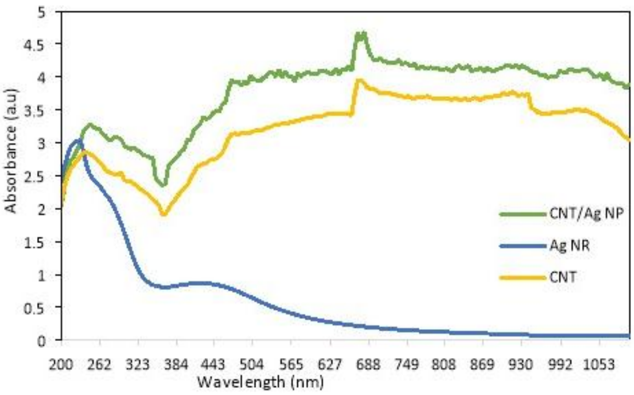


**Figure 2 Comparision between the absorbance of CNT, AgNRs, and AgNRs combined with CNT**

**Table 2 Heat Energy peaks for AgNRs**

| medium | Peak wavelength in nm | Peak value in kJ/m$^3$ |
|---|---|---|
| **PEG 400** | 550 | 21.07 |
| **CHI** | 850 | 3.134 |
| **PG** | 850 | 3.134 |

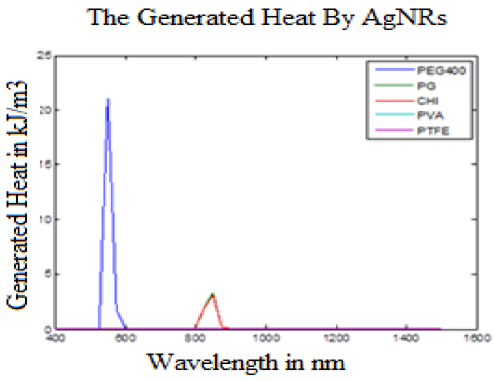


**Figure 3 The energy generated to surrounding by AgNRs**

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