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Silver and Titanium Nanoparticles Used as Coating on Polyurethane Catheters

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Abstract. Silver nanoparticles have been used in the medical area due to their remarkable antimicrobial properties. In this sense titanium dioxide nanoparticles obtained by the sol-gel method were used as coating of catheters for subsequent impregnation of silver nanoparticles with gamma irradiation and electron beam at 25 and 50 kGy. This work aimed to study the use of the silver nanoparticles and titanium dioxide as coating of polyurethane Central Venous Catheter (CVC) for antimicrobial activity. Furthermore the amounts of titanium and silver present in the coated catheters had been evaluated by Inductively Coupled Plasma – Optical Emission Spectrometry (ICP OES). Therefore the Raman spectrometry was used to identify the polymorph of titanium oxide, rutile.

Introduction

The objective of this work has focused on the ionizing radiation study used in bactericidal central venous catheters coated with silver nanoparticles, providing reduction of severe sepsis, septic shock and other infections associated with contamination of central venous catheters inserted into the blood stream.

Since its description by Niederhuber, 1982 [1], Central Venous Catheters (CVC) have become valuable therapeutic instruments for a variety of clinical conditions, such as cancer, renal disease requiring replacement therapy and malnutrition. These products ensure prolonged central venous access, continuous or intermittent infusion and to exchange liquid, total parenteral nutrition or medication. Peripherally inserted central catheters are particularly useful to administer antibiotics and other chemotherapeutic agents in outpatients. They have advantages by avoiding venous punctures repetition, helping to preserve the integrity of the venous network. The multiple advent paths, ease of maintenance and the discreet appearance of the professionals bandage, the feasibility and management procedures. It also increases acceptance and fulfillment of these therapies by patients [1].

Central Venous Catheters (CVC) are normally employed in critical patients to administer fluids, blood products and parenteral nutrition. The use of these devices is associated with the most infections of the bloodstream. The catheter body is made with high quality materials, integrity and sufficient rigidity, flexibility and consistency accurate for a correct insertion. They have characteristics as resistance to prevent folds and fractures ensuring free way for the introduction therapies under use of the normal conditions, avoiding mechanical irritation in the vascular system. Furthermore they have wide thermal stability, sufficient chemical resistance and level of adhesion / fixation cells and tissues low and thrombogenicity. These characteristics are among those used to judge which is the most appropriate type of catheter for each situation. Both polyurethane and silicone catheters have great biostability and low thrombogenicity. The polyurethane central venous catheters allows thinner walls. Moreover, they allow increased lumen diameter. They are more rigid and resistant, have high resistance to bending, show least variation in the elastic properties, and have increased chemical resistance. However it has a use restriction with antiseptic solutions with alcoholic base, such as chlorhexidine, which increase the risk of fracture / breakage of the catheter [2].

Polyurethanes have been widely used in medicine for the coating and packaging and other implantable medical devices. The poly(ether urethane), particularly, have superior mechanical properties and are biocompatible, but in common with other medical materials they are susceptible to microbial film formation. The poly(ether urethane) can be synthesized with silver lactate and silver sulfadiazine functional groups to produce a bacterially resistant polymer without sacrificing the useful mechanical properties of poly (ether urethane). The silver ions can be covalently incorporated into the polymer during the extension of the prepolymer chain. The mechanical properties, hydrophilicity, *in vitro* stability and antibacterial action in polymers were investigated and the results indicated that both of their silver salts have been incorporated successfully in the polymer structure, without significant effect on the mechanical properties and with giving acceptable bacterial resistance. Additionally, polymers with modified mechanical properties had their materials integrity maintained saved in solution, for *in vitro* exposure. Although the silver content in the membranes is low, significant antibacterial activity was observed [3].

As the catheters are an important source of bloodstream infections in hospitalized patients, microbial adhesion is essential for the formation of biofilm, however, this membership depends on the ionic interaction between the organism and the surface which it has been shown that a negative charge attracts bacteria, suggesting that a positively charged surface will repel bacteria and thereby will inhibit the adhesion [4].

The first silver nanoparticles were prepared for more than a century, and nowadays, electrochemical, photochemical methods, chemical, radiation, laser ablation, among others, are used for their preparation. Nanocrystalline silver is inactivated more slowly by biological fluids than the ionic form and therefore can provide a prolonged antimicrobial action in medical applications [5].

Silver nanoparticles are one of the most prominent products in medicine because unusual physical-chemical properties and displays a large biological activity. Silver deposition technology has an inovactive which was applied to temporary polyurethane catheters for haemodialysis. Therefore, working conditions were reproduced in catheters by means of laboratory equipment that ensured the flow of purified water and simulated body fluid within the lumens in the body temperature. The growth and adherence of *Staphylococcus aureus* on the surface of the device were studied, such as the amount of the silver released from the substrate and the coating stability throughout the life of the device [6].

Silver nanoparticles are used in various polymers such as polyurethane and silicone, resulted in an excellent antimicrobial activity against a broad spectrum of organisms *in vitro*. The type of catheter material is related to the grip and the most easy biofilm formation. It has been shown by *in vitro* studies that the catheters of poly (vinyl chloride), are more susceptible to microbial adhesion than those of silicone or polyurethane [7].

Among the many nanoparticles, titanium dioxide (TiO_2) is often used in medical fields and one of the various methods described in the literature, the sol-gel method is the most widely used [8]. Studies with silicone catheters coated with Ag / titanium dioxide, and photocatalysis on both the inner wall and the outer wall, produced excellent results with UV irradiation [9]. Therefore in this study titanium oxide nanoparticles were used as a coating of catheters for subsequent impregnation of silver nanoparticles.

Raman spectrometry has enabled identifying the polymorph of TiO_2, the rutile [10].

Tests with (ICP OES) were performed on catheters with titanium oxide coating on catheters coated and impregnated titanium oxide nano-silver, and irradiated at 25 and 50 kGy.

Ionizing radiation, used in this work, was from a ^{60}Co γ rays, irradiator for impregnation of silver nanoparticles coated polyurethane catheter with titanium oxide and it also the electron accelerator, for sterilization of catheters with titanium oxide coating, containing silver nanoparticles, for subsequent evaluation of antimicrobial activity.

Economically viable irradiation processes for industrial application, based on gamma radiation obtained by disintegration of ^{60}Co radionuclide (range of ^{60}Co sources) and radiation from high-energy electrons (electrons accelerated), called "electron beam" generated in particle accelerators devices (electron accelerators) [11,12].

Usually, these catheters are sterilized with ethylene oxide, and one of its manufacturers is the Biomedical Equipment and Medical-Surgical Products Ltda[13], however the use of ionizing radiation, obtained these sterilized catheters could be a viable possibility and the greatest advantage of the use of the irradiation process. It does not need additives, which means a clean process.

Experimental

Material and Methods

Polyurethane, PU, used in this current work is present in central venous catheters (CVC), JOHNSON & JOHNSON [13] and the supplier of catheters is the *Biomedical equipment and Medical-Surgical Products Ltd* [13].

Polyurethane CVC coating with pure titanium oxide was performed by the sol gel method as titanium tetraisopropoxide IV [8] and it is confirmed by scanning electron microscopy by way of the SEM JEOL JSM-7401F FESEM.

Samples with titanium oxide coated catheters were impregnated with silver nanoparticles, NpAg_925, provided by TNS, Competence in Nanotechnology, single antimicrobial product; as aqueous emulsion; non-toxic; solid content of approximately 1000 ppm; yellowish brown color; about pH 4.0; density at 25 °C of 1.0 g/cm^3; average size of 10 nm; maximum wavelength of 400 to 410 nm, by irradiation with gamma radiation coming from a radiator "Gammacell 220".

The final sterilization of the catheter was performed with an electron beam using an electron accelerator Dynamitron JOB 188 of 0.5 to 1.5 MeV and 0.3 to 25 mA current with dose 25 kGy.

Optical emission spectrometry analysis by inductively coupled plasma (ICP OES), were performed using ICP OES spectrometer, Radial, Spectro brand, model emission line Arcs: 334.941 nm. The samples passed through the acid digestion process (or opening) to remove organic compounds present and the amount of sample required depends on the concentration of the elements whose concentrations should be determined, it is essential that the samples are homogeneous.

Raman spectrometry analyses were performed out to identify polymorphic titanium dioxide, rutile, in a Micro Raman spectrometer Renishaw InVia Reflex, with type detector CCD (*charge coupled device*).

Results and discussion

An evaluation of the titanium oxide coating on Central Venous Catheter (CVC) is shown in the micrograph of Fig. 1.

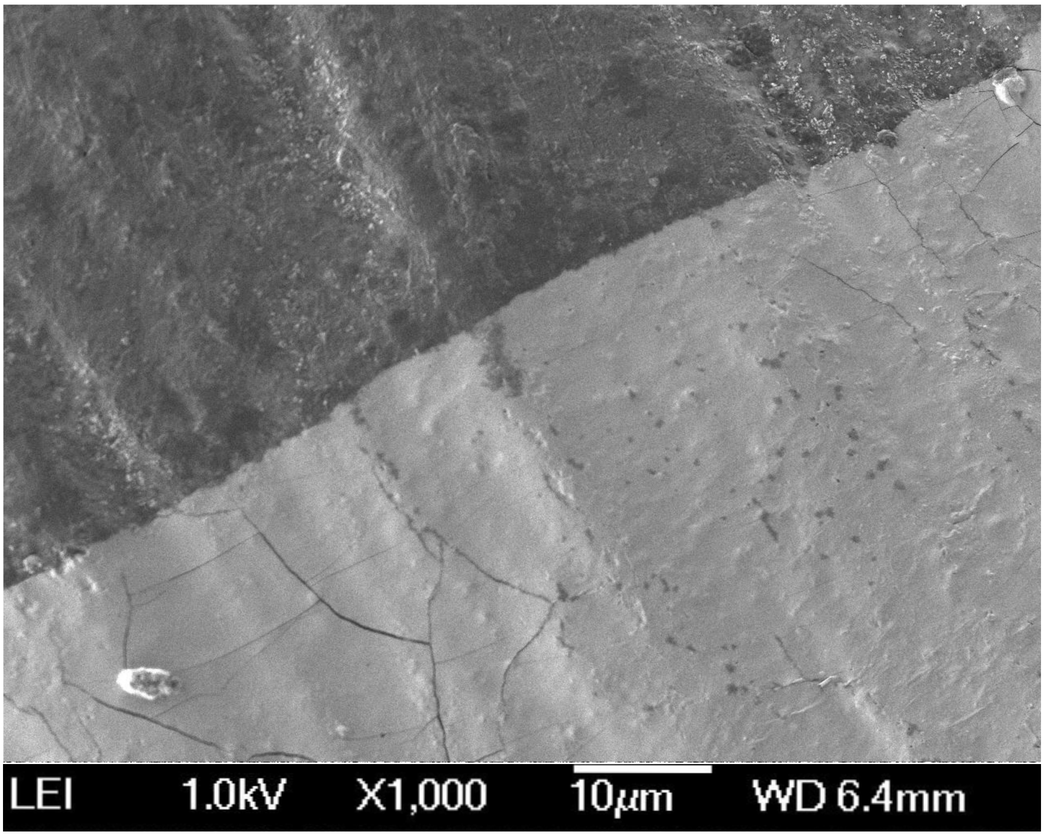

Figure 1. Micrograph Central Venous Catheter (CVC) with TiO_2 coating

Tests (ICP OES) were performed on catheters with titanium oxide coating, and catheters with titanium oxide coating impregnated with nanosilver, and irradiated at 25 and 50 kGy, whose results are presented in Table 1.

Table 1. Ti and Ag determinations of CVC coated with TiO_2 and nanosilver by ICP OES

ELEMENT	RESULT 1	RESULT 2	25 (kGy)	50 (kGy)
TITANIUM (Ti)	1.10 %	1.14 %	0.96 %	0.96 %
SILVER (Ag)	-	-	1.15 %	< 0.01ppm

The Raman lower frequency corresponds to vibrations of TiO_2, and the bands 445 and 614 cm^{-1} correspond to the polymorph rutile which is formed in greater quantity. The presence of the polymorph anatase would be verified by the presence of bands in 395, 514 and 637 cm^{-1}, which are not present in any point of the sample [10]. The intense band in 987 cm^{-1} corresponds to the symmetrical stretching of the sulfate group from barium sulfate, employed in polymers, which is present in all analyzed points with some differences in relative intensity [14] as shown in Fig. 2.

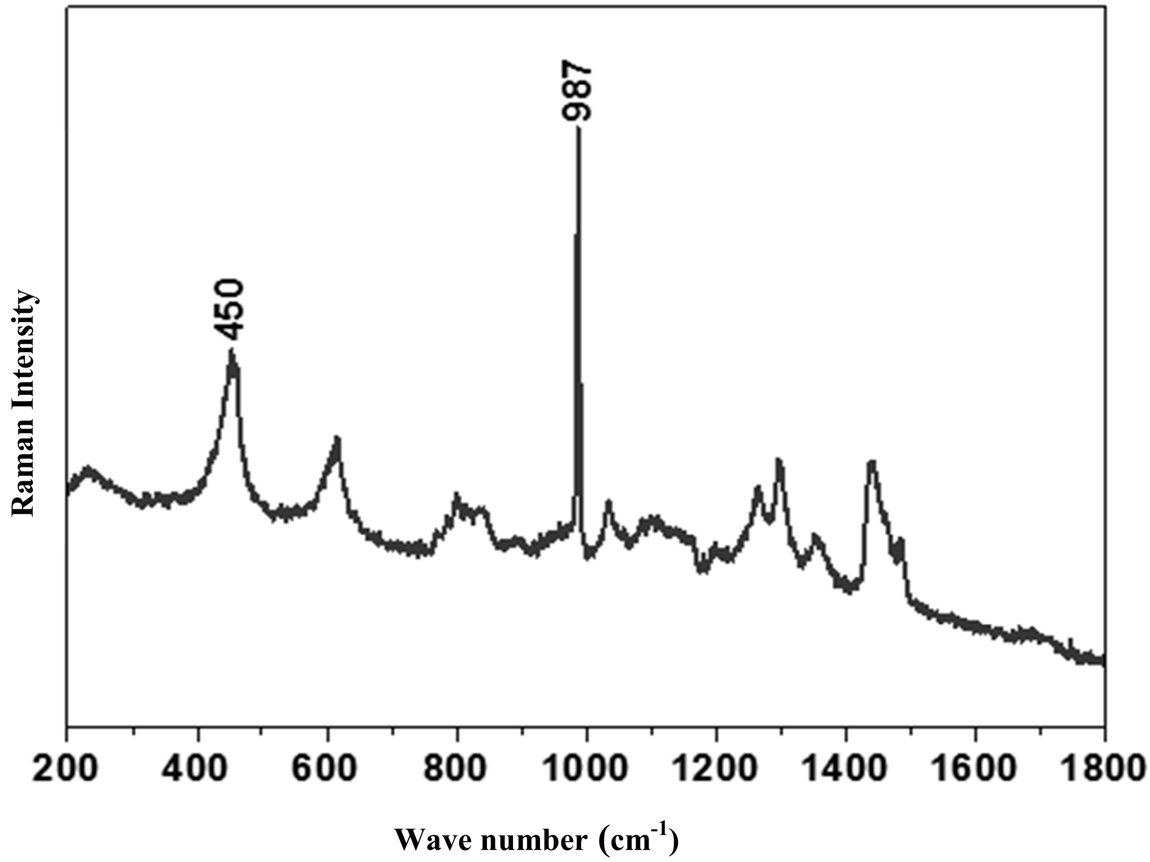

Figure 2. Raman Spectrum Central Venous Catheter (CVC) coating with TiO_2

The Raman spectra of titanium oxide coated catheter in aqueous solution of silver nanoparticles, NpAg_925, irradiated at 25 and 50 kGy, evidenced the same bands referred to previously as shown in Fig. 3.

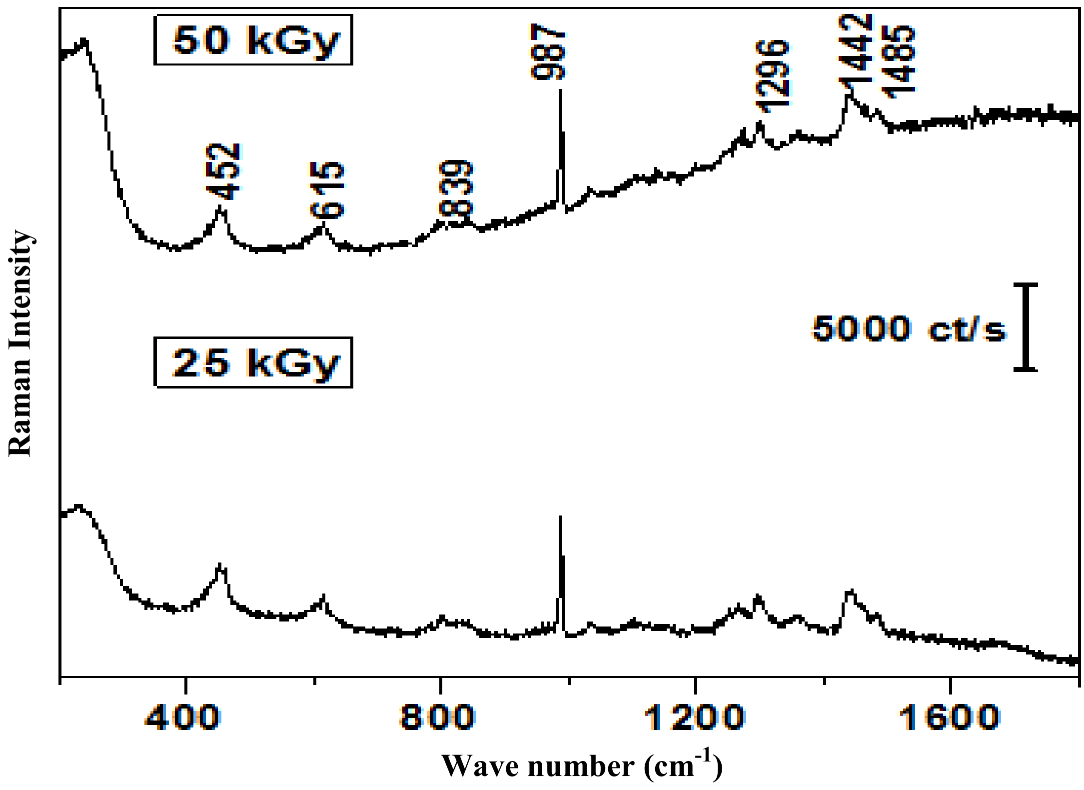

Figure 3. Raman Spectrum Central Venous Catheter (CVC) with TiO_2 coating and silver nanoparticles, irradiated at 25 and 50 kGy

Conclusion

The coating with TiO_2 evidenced the central venous catheter surface modification, provides a better silver nanoparticles adherence, resulting in a viable concentration of titanium, and silver as well, after irradiation. According to the concentration of silver nanoparticles emphasized an ideal concentration for antimicrobial activity. Furthermore, adherence of the titanium oxide by means of ionizing radiation will be studied later in future work. We can say that the radiation doses used in this work were low doses and they do not affect the structure of polyurethane catheters. In addition, the characterizations performed in previous work were observed that polyurethane present in central venous catheters (CVC), did not suffer any changes [15]. Raman spectrometry analysis performed in the higher frequency region and it was not observed the band in 1732 cm^{-1} reported as stretching (N = C = O) bands related to PU, on the other hand, this band can be observed in the spectrum IR according to Kawano [16] at 1700 cm^{-1} corresponding to stretching (C = O) of the urethane group. Raman spectrometry was the technique used to identify the polymorph titanium dioxide, rutile and the aromatic group-related bands were not observed to 1612 and 1530 cm^{-1}.

It should be noted that the use of ionizing radiation from high-energy electrons (electrons accelerated), extends the knowledge to define this form of sterilization showing the advantage of being a clean process.

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