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(54) Title: A CORONARY STENT WITH NANO COATING OF DRUG FREE POLYMER AND A PROCESS FOR PREPARATION THEREOF

(57) Abstract: The present invention relates to a medical device carrying a nano coating by utilizing the same on the coronary stent systems and a process for preparation thereof. The inventive coronary stents can be provided with various advantages/properties and properties thereof. The material coated is a biocompatible bio-formulation which by means of a physical vapor deposition route ensures a very thin coating (5 to 40 nm). *In-vitro* studies on human blood suggest that, the nano coated stent is devoid of platelet adhesion. Such a hydrophobic nano coated stent surface reduces the chances of thrombosis as a result it provides a viable alternative to drug eluting stents.



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TITLE

“A coronary stent with nano coating of drug free polymer and a process for preparation thereof”.

The following specification particularly describes the invention and the manner in which it is to be performed.

FIELD OF INVENTION

This invention relates to a coronary stent with nano coating of drug free polymer and a process for preparation thereof. The present invention relates to medical device comprising atleast one nano polymer/nano polymer composite materials/drug free polymer. By utilizing these nano-materials in the manufacture of the inventive medical devices, certain properties of the nano-particles and/or nano-composites may be exploited in ways particularly advantageous to the medical device.

BACKGROUND OF THE INVENTION

Coronary artery disease (CAD) is the narrowing and hardening of the small coronary arteries that supply blood to the heart muscle. It is the most common type of heart disease, which is the leading cause of death in both men and women, killing more than half a million Americans each year. CAD occurs when the coronary arteries become clogged due to the buildup of fatty deposits, called plaque, on the inner walls. More precisely, this plaque is called atherosclerotic plaque, which literally means growths with a porridge-like consistency. This process of plaque development is referred to as atherosclerosis. As the blood supply is restricted, so is the supply of oxygen to the heart; this leads to angina and heart attacks. Angina is the severe and sharp chest pain people feel as parts of the heart muscle are starved of vital oxygen. A heart attack results from a blockage in a coronary artery, preventing oxygen from reaching a section of the heart muscle and resulting in the death of heart tissue.

Long term damage

The damage accumulates over time, weakening the heart muscle and making it more vulnerable. The damage also contributes to heart failure, where the heart becomes too weak to pump sufficient blood to the rest of

the body. The gradual build-up of damage also increases the likelihood of heart rhythm disturbances, or arrhythmias, as the electrical conduction pathways in the heart become disrupted.

Risk factors

Everyone can reduce the risk of CAD by exercising more, staying slim, eating healthily and not smoking. Other risk factors that can be controlled include high blood cholesterol, high blood pressure and diabetes. Getting old and having a family history of heart disease cannot be controlled, making it all the more important to avoid the other risk factors because the more risk factors you have, the greater your chance of developing CAD.

Signs and symptoms

The most common symptoms of CAD are chest pain or discomfort (angina), pain in one or both arms or the left shoulder, and shortness of breath. The severity of symptoms varies widely.

Treatments

Common treatments for CAD include angioplasty, coronary artery bypass graft surgery (CABG) and medical (drug) therapy. Angioplasty is a procedure used to open blocked or narrowed coronary arteries with a balloon that is threaded into the blocked artery along a catheter. Usually, during angioplasty a stent is placed in the artery to keep it propped open after the procedure. CABG surgery uses arteries or veins from other areas in body to bypass diseased coronary arteries.

In 1975, the invention of a double-lumen catheter fitted with a polyvinylchloride balloon by Andreas Gruentzig revolutionized therapy for CAD. Restenosis is the major limitation of coronary angioplasty, in rates

up to 30% to 60% of patients within the first 6 months. Bare metal stents (BMS) have effectively reduced the restenosis by functioning as a mechanical scaffold that eliminates the elastic recoil and negative remodeling.. BMS demonstrated significant reduction of the major adverse cardiac events (MACE), death, and myocardial infarction (MI).

Currently coronary stents are used in more than 90% of PCI procedures for treatment of CAD. The dramatic increase in the use of BMS identified a new problem, restenosis occurring within the stent. In-stent restenosis (ISR) is defined as lumen diameter loss of greater than 50% within the stent. ISR is also clearly correlated with the degree of stent-induced injury to the vessel wall, strut thickness, patient factors (diabetes, acute coronary syndromes, etc.), and lesion characteristics (small luminal diameter vessel, bifurcation, ostial, restenotic as well as venous graft lesions). In addition, chronic foreign-body inflammatory response as well as gradual long-term corrosion of the metallic stent may have roles in the process of ISR. Drug eluting stents (DES) have reduced ISR and target lesion revascularization (TLR) compared with BMS and launched a revolution in the interventional treatment of symptomatic CAD. However, enthusiasm for this technology has recently been dampened by concerns about late stent thrombosis (LST), incomplete endo-thelialization, coronary artery spasm, and abnormal vasomotor function. Thus, focus has been brought onto the structure and composition of stents and stent coatings with particular interest in how the vessel responds to the foreign device and development of devices with improved biocompatibility and long-term patient outcomes.

The polymer coating is also implicated as a cause for failure in drug eluting stents. The current polymers in use are PLG, Phosphoryl choline of several microns thickness.

A major milestone occurred when the FDA approved the Endeavor drug-eluting stent for Americans with coronary artery disease. The Endeavor stent is the first new drug-eluting stent to be approved by the FDA in more than three years, an endorsement of the safety advantages it delivers for heart disease patients in the United States. As the first in a new generation of drug-eluting stents, the Endeavor stent could again enable millions of patients to benefit from a minimally invasive alternative to bypass surgery. Extensive clinical data shows the new Endeavor stent to be effective at reducing restenosis (the re-narrowing of treated arteries) by more than 50% with excellent long-term safety results. The Endeavor drug-eluting stent was built for safety, effectiveness, and deliverability; the three most important criteria for evaluating these devices. It does so with a safety profile more commonly associated with bare-metal stents which are considered the benchmark for stent safety. In extensive clinical trials, this device has shown to be associated with exceptionally low rates of blood clots and heart attacks, unlike the first generation of drug-eluting stents.

State of the art:

US patent 6364903 relates to a stent/graft composite device including a polymeric coated stent in conjunction with an ePTFE graft. The invention provides a very thin coating on the stent. This is a PTFE graft without macrosized unit.

US5620763 provides a polymer tube having a microstructure of nodes interconnected by fibrils and a wall thickness of less than about 0.20

mm. This invention also concerns a polymer coating but not necessarily the PTFE material of the present invention.

US5888591 discloses a seamless tube of porous PTFE having a wall thickness of less than about 0.20 mm, and a method of making the seamless tube. Fluorocarbon polymer thin film is produced by a pulsed-plasma-enhanced chemical vapor deposition method. Process developed is simple and rapid deposition process. However this process does not result in nano coated films and this invention talks about porous PTFE coating.

Following prior art patents/ publication describe other methods of polymer coating-

In EP0621015 a cylindrical polymer wall is employed around stent surface. In US5466509 an expanded polytetrafluoroethylene sheet is produced by the process of extruding a mixture of polytetrafluoroethylene and a lubricant into a sheet. The invention provides a process for imprinting a predetermined texture on porous and expanded PTFE. In US6364903 a tubular polymer graft is employed. The tubular intraluminal prosthesis comprises an ePTFE tubular structure and a tubular diametrically deformable stent being partially coated with a polymeric powder coating which is in contact with ePTFE tubular structure. This prior art does not conform to the present invention since this is a tubular graft material involving PTFE.

Following prior art patents/publications indicate different methods for coating of nano particles for use in medical devices.

US publication 20090004241 is directed to nanofilm coatings for implantable medical devices comprising a diblock or triblock copolymer (PEO-PMMA or PMOXA-PDMS-PMOXA, respectively). Such nanofilms, may be used, for example, as amphiphilic supports for therapeutic agents. These materials are conducive towards the formation of active substrates for a suite of biological and medical applications. Although nanosized coatings are reported, they do not pertain to PTFE films..

US publication 20090124034 discloses the use of a nanostructured non-silicon thin film (such as an alumina or aluminum thin film) on a supporting substrate which is subsequently coated with an active layer of a material such as silicon or tungsten. The invention provides substrate surfaces that can be produced by relatively straightforward and inexpensive manufacturing processes and which can be used for a variety of applications such as mass spectrometry, hydrophobic or hydrophilic coatings, medical device applications, electronics, catalysis, protection, data storage, optics, and sensors. This coating is a non silicon and alumina based coating and does not concern the use of PTFE coatings.

US publication 20090104434 relates to a device that includes a substrate having an outer surface and a conformal coating of nanoparticle on the outer surface. In particular, the nano-particle coating is substantially a molecular monolayer of a plurality of nano-particles. The filler of a relatively light or inexpensive material may serve as a substrate for a conformal coating of nano-particles of some other bulk material. Although nanocoating is attempted this invention does not involve PTFE films.

US publication 20090104244 discloses therapeutic agent-eluting medical devices having textured polymeric surfaces. US publication 20090118813 provides a bioerodible endoprosthesis which erodes to a desirable geometry that can provide, e.g., improved mechanical properties or degradation characteristics. The medical device includes a surface defining one or more nano-structured patterns defined by local texture discontinuities of spatial frequencies between about 1/500 element/nm and about 1 element/nm forming the pattern of at least one repeating region includes coating the surface with the first material. Coating the surface with the first material can include physical vapor deposition, chemical vapor deposition, printing, spraying, and/or combinations thereof. This invention is basically a polymeric support meant to host drug molecules and these are not PTFE coatings as employed in the present investigation.

US publication 20090005862 relates to a drug release stent and a method for fabricating the same. In the stent of this invention, the diamond-like carbon film preferably has a thickness not less than 10 nm and not more than 300 nm. The diamond-like carbon film can be formed on the stent body 11 by any of known methods such as sputtering, DC magnetron sputtering, RF magnetron sputtering, chemical vapor deposition (CVD), plasma CVD, plasma ion implantation, superposed RF plasma ion implantation, ion plating, arc ion plating, ion beam evaporation or laser abrasion. Thus, the diamond-like carbon film can be prevented from peeling off from the stent body, so that the stent can be used for a long period of time.

US publication 20060129215 relates to medical devices having nanostructured regions, including nanotextured and nanoporous

regions. Nanostructured region is provided by a method that comprises a chemical vapor deposition process wherein chemical vapor deposition process is particle-precipitation-aided chemical vapor deposition process.

Recently Catania stents have been introduced after a first in man 1-year clinical outcome which has a nano thin polyzene-F coating (J.Am.Coll.Cardiol.Intv.2009:2,197-204). The Catania stent is made of Co-Cr alloy and is surface coated with Polyzene-F, a biocompatible, biostable formulation of poly-[bis(trifluoroethoxy) phosphazene]. The surface treatment measures approximately 40 nm thick. Polyzene is a drug free surface treatment and is reported to promote healthy endothelial cellular growth. The present invention discloses a technology for nano polymer coatings on coronary stent systems. This Technology is developed to form an alternative to drug coated stents and to arrest some of the clinical issues encountered in stented patients, ex: thrombosis and restenosis. The present invention is different from the polyzene coating both in term of the composition of the material employed as well as the process technique employed for the deposition of the PTFE layer. Further, control of the minimum thickness of the polymer coating is significantly peculiar to said technique, where thickness down to 20 nm is achieved.

Material selection is thus very important to the therapeutic efficacy of many medical devices since the properties of the materials used often dictates the properties and/or capabilities of the overall device. However, the range of properties available from one, or even a combination of, material(s) is often not as broad as would be desired to provide a corresponding breadth of properties or capabilities in medical device applications. As a result, many medical devices need to be manufactured from a combination of materials, processed in a specific manner, or

subjected to other treatments in order to exhibit the desired and/or required characteristics.

OBJECTS OF THE INVENTION

An object of the invention is to provide coronary stent with nano coating of drug free polymer and a process for preparation thereof with sufficient ease to coat and to control the thickness of the coating.

Another object of the invention is to provide coronary stent with nano coating of drug free polymer and a process for preparation thereof wherein the polymer used is chemically inert.

Yet another object of the invention is to provide coronary stent with nano coating of drug free polymer and a process for preparation thereof that is thermally stable.

Another object of the invention is to have chemical homogeneity of the polymer preserved during the coating on the stent surface.

Another object of the invention is to employ a coating using physical vapor deposition technique.

Another object of the invention is to employ pulsed electron deposition method for large area coating of the stent surface.

Another object of the invention is to control the thickness of the coating from 10 to 40 nanometers.

Another object of the invention is to inhibit the adhesion of platelets on the coated surface.

Another object of the invention is to provide a coating that provides a drug free surface treatment (non drug eluting stent).

Yet another object of the invention is to provide a medical device with nano coating and a process for preparation thereof which can be employed in the treatment of various vascular disorders with proven efficacy and safety in human.

SUMMARY OF THE INVENTION

The present invention provides polymer nano coating on the stent surface. The polymer is chemically inert, thermally stable and can be employed in the treatment of various vascular disorders with proven efficacy and safety in human. The present invention discloses a nano-coating of the preferred polymer using a vapor deposition method which has potential to grow chemically homogeneous and oriented films in nano dimension. The developed coating is cost effective, which can bring down the cost by 95% of the cost required for drug coating polymer on stents and by 80% of the cost compared to the material coated with Catania stents.

The polymer nano-coated stent involves a polymer coating that would prevent cell proliferation and such a biocompatible polymer would enable bio friendly scaffold to the surrounding tissue. The polymer mimics the surface of a red blood cell and coats a unique modular stent engineered from a strong, yet flexible and for ex. cobalt chromium alloy which allows the surface of the stent to be free from roughness. Together these components allow comprehensive healing to take place, enveloping the stent safely in the artery wall away from the blood stream.

BREIF DESCRIPTION OF DRAWINGS

Further objects and advantages of this invention will be more apparent from the ensuing description when read in conjunction with the accompanying drawings and wherein:

FIG. 1a is a longitudinal view of a deployed stent in accordance with the present invention wherein the medical device is a nano-PTFE coated stent employing pulsed electron deposition technique;

FIG. 1b is a close up view of nano-PTFE coated stent (figure 1a), after a 48 hour exposure to human blood. The image demonstrates practically no platelet adhesion to the surface of the stent surface in accordance with the present invention;

FIG. 2a is a longitudinal view of a deployed stent in accordance with the present invention wherein the medical device is a bare metal stent;

FIG. 2b is a close up view of bare metal stent (of figure 2a), after a 48 hour exposure to human blood. The image demonstrates platelet adhesion all over the metal scaffold as reported in the literature;

Figure 3a shows still enlarged view of nano PTFE coated stent practically showing no islands of platelet growth indicating inertness to thrombocytosis;

Figure 3b shows a still enlarged image of bare metal coated stent. Nearly 90% of the surface is showing platelet adhesion suggesting that bare metal surfaces are prone to aid thrombosis;

Figure 4 shows a schematic representation of Pulsed electron beam deposition method.

DETAILED DESCRIPTION OF THE INVENTION WITH REFERENCE TO THE ACCOMPANYING DRAWINGS :

The embodiments of the present invention described below are not intended to be exhaustive or to limit the invention to the embodiments disclosed in the following detailed description. Rather, the same are described so that others skilled in the art understand the principles and practice of the present invention. The nature of the production and therapeutic use of many medical devices can require that the devices exhibit a broad and diverse array of properties and/or be capable of performing many functions. "Coating" for an implantable medical device, such as a stent, can include a drug free-polymer or a drug free layer involving metal-polymer coating. The drug free-polymer layer or the drug free metal-polymer layer can be applied directly onto the stent surface. The drug free-polymer coating involves a long chain fluoro polymer with or without metal particles embedded in it. One example of a polymer having functional groups that can be used for coating is Poly(tetrafluoroethylene) with a general formula $[C_nF_{2n+2}]$ commercially known as TEFLON having excellent chemical and thermal resistance. Their molecules have continuous non-reactive surfaces and are compatible with virtually all chemicals and solvents. They are far more resistant to chemical attack than conventional chlorinated and hydrocarbon polymers, and have far higher service temperatures. Because Teflon is non-reactive, there are no corrosion byproducts or extractables to contaminate processes. It is extremely pure and resists sorption of chemicals. Further, Teflon provides smooth non-wetting hydrophobic surfaces that resist bio-film buildup, and it can also be used with the strongest cleaning solutions and steam-in-place processes. Surfaces of Teflon are easy to clean, and because they resist buildup of process materials, it may be possible to extend intervals between cleanings. While switching from 316L stainless steel (SS) to more costly corrosion-resistant metal alloys, such as Ni based C276 and Fe-based

AL6XN reduces corrosion problems, but it does not eliminate the contamination from metal ions. SS requires expensive passivation and electropolishing to meet validation. Electro polishing smoothes the surface by reducing the height of aspires but not the crannies at the base of these peaks and can even create pits that lead to increase in biofilm adhesion. In contrast, metal contamination from fluoropolymers is nearly undetectable. Fluoropolymers also have greatly reduced biofilm adhesion relative to conventional electropolished 316L SS. Fluoropolymers are based on high purity, high physical integrity and chemical inertness.

Coating of Teflon can be achieved by several methods as a micron thick film. Coating of PTFE in nanometer thickness is a surmountable task and expensive in terms of processing method or with the final composition of the coated film. Often, there is a depletion of fluorine concentration in these films. One of the techniques which has proved to be a useful technique is pulsed electron deposition method. The widespread use of complex oxides in large-scale applications necessitates efficient, reliable and economic processes for the deposition of multi-component materials. Pulsed electron deposition (PED) is an ablation-based film growth technique [1] similar to pulsed-laser deposition but based on much simpler equipment. Use of a pulsed electron beam for the ablation of material from a solid target and the deposition of multi-component thin films were made shortly after the introduction of pulsed laser deposition, and the first applications of PED included the growth of ZrO_2 [2] and $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$ [3, 4], using a pseudo-spark process to generate electrons from a hollow cathode. In this method, magnetically self-pinched electrons are accelerated through a stack of insulating and

metallic rings, while in the subsequently developed channel-spark approach [5, 6] narrow insulating pipes are used for electron acceleration. Electron-beam evaporation techniques require a high vacuum environment and thus, elaborate differential pumping if the deposition is to occur in a background gas. In the present invention, a PED source is integrated with the vacuum chamber for the room-temperature deposition of Teflon films, as shown schematically in figure 4. The pulsed electron source is flange-mounted onto the vacuum chamber, and the electrons are guided to the target via alumina tube. The end of the beam tube is positioned within 2–3mm from the target surface. A typical pulse carries a current of ~1000 A, with a pulse duration of ~100 ns. The stent to be coated is mounted on a substrate platform, perpendicular to the PTFE Plume axis. The following deposition parameters have been employed:

5–20 kV charging potential, 5–30 mTorr (Ar) of background gas pressure required for focused beam propagation, beam energy of 0.2–0.8 J (energy variation $< \pm 20\%$), pulse duration of 100 ns, maximum power density of 1.3×10^8 W/cm², beam cross-section of about 6×10^{-2} cm². The repetition rate of the pulses can be adjusted up to 10 Hz. In PED, the pulse energy increases strongly and arises approximately linearly with the voltage, when operating at 12–15 kV with the beam cross-section of about 9 mm² and the power density (E) at the target is about 6–7 J/cm², during deposition, the chamber pressure is maintained at 5 mTorr by controlled flow of Argon and the substrate temperature is kept at 300 K. The discharge voltage is kept at 12 kV.

Examples:

The invention will now be further illustrated in the following examples, which are not intended to be limiting, but rather, have been chosen and described so that others skilled in the art may appreciate and understand the principles and practices of the present invention.

Example-1- Preparation of PTFE films on stent surface: The deposition, was carried out in a vacuum chamber where the pressure was maintained at 5 mTorr by controlled flow of Argon. The substrate temperature(undeployed stent) was kept at 300 K during deposition. In order to stabilize the working conditions of the source and to clean the target surface, the target was pre ablated by electron beam while masking the substrate for 20 min at 1 Hz. For film deposition, the electron beam operating at 1 Hz was made incident onto a rotating target of PTFE at an incident angle of 45°. The ablated material was allowed to condense on Co-Cr Stent positioned in front of the target, typically 8 cm away. The thickness of the nano coating was evaluated by thickness profilometer and the calibrated thickness was between 5-40 nm. The discharge voltage is kept at 12 kV. SEM microscopic study indicates a smooth coating on the surface of the Co-Cr alloy surface. The coating appears to be two dimensional(as seen from the SEM micrograph) and it does not proceed via island growth. The as prepared nano-coated Stents can be used for in-vitro exposure to human blood.

Example-2- Preparation of Gold-PTFE composite films on stent surface: The deposition was carried out in a vacuum chamber where the pressure was maintained at 5 mTorr by controlled flow of Argon. The substrate temperature (undeployed stent) was kept at 300 K during deposition. A specially designed Gold-PTFE target (having a 2 inch diameter of Teflon target drilled in the middle to hold commercial 99.999% pure Gold pellet

with 8mm diameter, such that gold nano-particles up to 15% may be incorporated into the ablated plume to form the polymeric metal composite) was employed as targets for deposition purpose. In order to stabilize the working conditions of the source and to clean the target surface, the target was pre ablated by electron beam while masking the substrate for 20 min at 1 Hz. For film deposition, the electron beam operating at 1 Hz was made incident onto a rotating target of PTFE at an incident angle of 45°. The ablated material was allowed to condense on Co-Cr Stent positioned in front of the target, typically 8 cm away. The thickness of the nano coating was evaluated by thickness profilometer and the calibrated thickness was between 5-40 nm. The discharge voltage was kept at 12 kV. Gold particles of 5-10 nm size were present as spherical islands on the PTFE matrix. SEM microscopic study indicates a smooth coating on the surface of the Co-Cr alloy surface. The as prepared nanocoated PTFE_Gold nano composite Stents can be used for in-vitro exposure to human blood.

Test Results

The bare metals stents and nanopolymer coated stents were exposed to platelet solution #4024 having a platelet count of 1.2×10^{11} , and the exposure time was extended up to 36 hours at ambient conditions. Upon removal of the stent from platelet solution, the surfaces of the bare metal stent and the nano polymer coated stents were studied under Field emission microscope. The studies indicate that, the surface of the bare metal stents shows islands of platelet adhesion where as the nano polymer coated stents show practically a clear platelet free surface indicating the anti thrombogenic activity of the nano polymer coated surface. FIG. 1a is a longitudinal view of a deployed stent in accordance with the present invention wherein the medical device is a nano-PTFE

coated stent employing pulsed electron deposition technique. FIG. 1b is a close up view of nano-PTFE coated stent (figure 1a), after a 48 hour exposure to human blood. The image demonstrates practically no platelet adhesion to the surface of the stent surface in accordance with the present invention. FIG. 2b shows a close up view of bare metal stent (of figure 2a), after a 48 hour exposure to human blood. The image demonstrates platelet adhesion all over the metal scaffold. FIG. 2a indicates a longitudinal view of a deployed stent in accordance with the present invention wherein the medical device is a bare metal stent.

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It is to be noted that the present invention is susceptible to modifications, adaptations and changes by those skilled in the art. Such variant embodiments employing the concepts and features of this invention are intended to be within the scope of the present invention, which is further set forth under the following claims:-

WE CLAIM:

1. A coronary stent with nano coating of drug free polymer comprising of polymer/polymer-metal layer.
2. A process for preparation of coronary stent with nano coating of drug free polymer by pulsed electron deposition in a vacuum chamber wherein target is pre ablated by electron beam during making of substrate followed by incident of electron beam on said rotating target of coating material for film deposition on the substrate wherein stent is provided with a nano coating comprising of polymer/ metal polymer composite layer.
3. A process as claimed in claim 2, wherein pressure in the vacuum chamber is maintained at 4-15 mtorr by controlled flow of Argon and the substrate temperature was kept at 300 to 350 K.
4. A process as claimed in claim 2 or 3, wherein said deposition of the substrate is carried out for 30-60 min at 3-5 Hz.
5. A process as claimed in any of the preceding claims, wherein said target may be provided with gold/silver pellet for composite film deposition on the stent such as herein described.
6. A process as claimed in any of the preceding claims, wherein the electron beam operating at 5 Hz is made incident onto said rotating target at an incident angle of 45°.
7. A process as claimed in any of the preceding claims, wherein said process involves other deposition parameters such as herein described.

8. A process as claimed in any of the preceding claims, wherein the polymer to metal ratio is for ex: 90:10.
9. A coronary stent with nano coating of drug free polymer and a process for preparation thereof as claimed in any of the preceding claims, wherein said stent is a coronary stent made of cobalt-chromium/stainless steel.
10. A coronary stent with nano coating of drug free polymer and a process for preparation thereof as claimed in any of the preceding claims, wherein said polymer is polytetra fluoroethylene or polytetra fluoroethylene with gold/silver nanoparticles.
11. A coronary stent with nano coating of drug free polymer and a process for preparation thereof substantially as herein described with reference to the accompanying drawings.

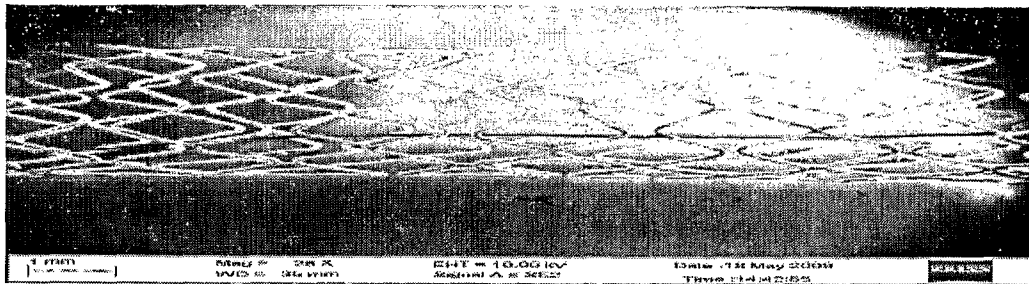


Fig. 1(a)

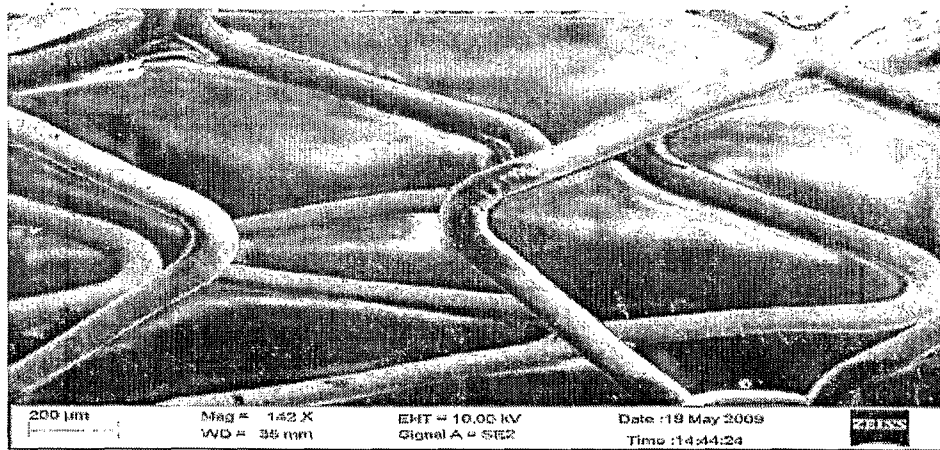


Fig.1(b)

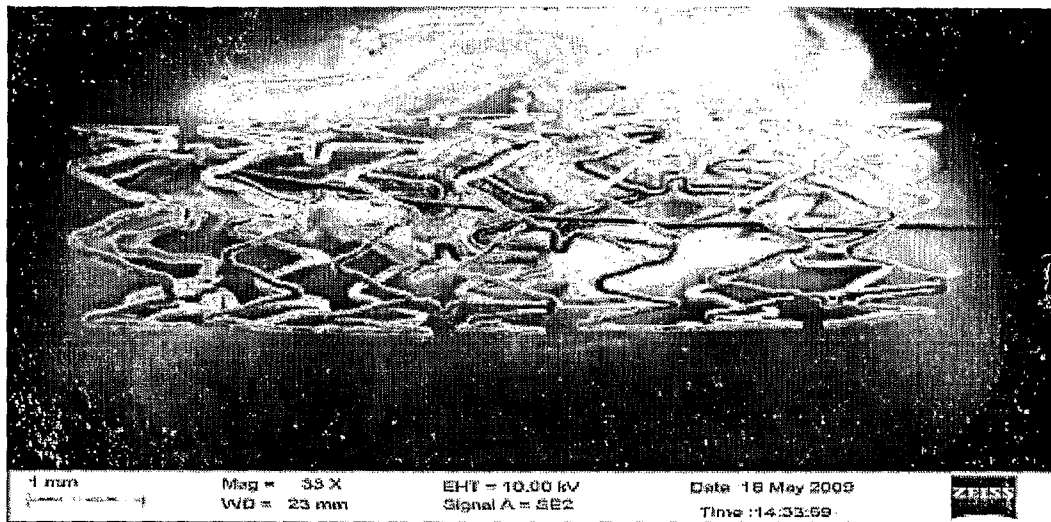


Fig.2(a)

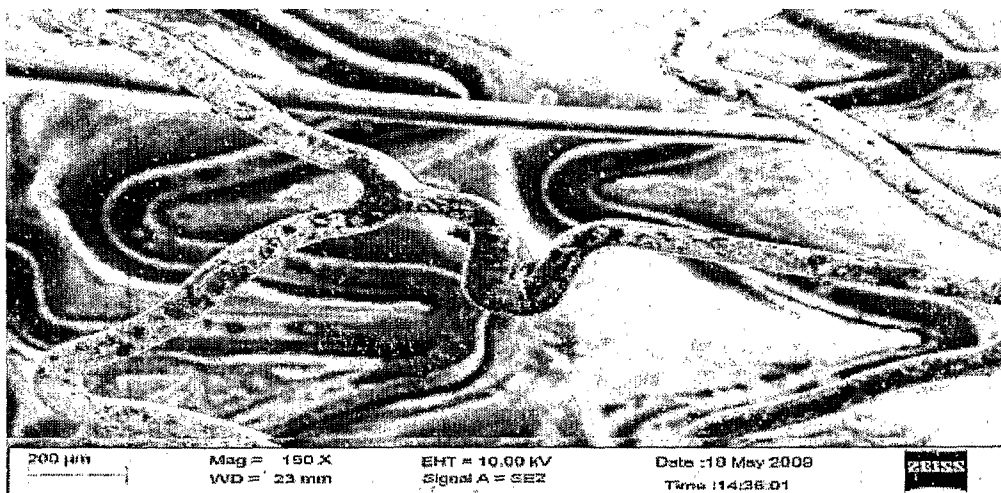


Fig.2(b)

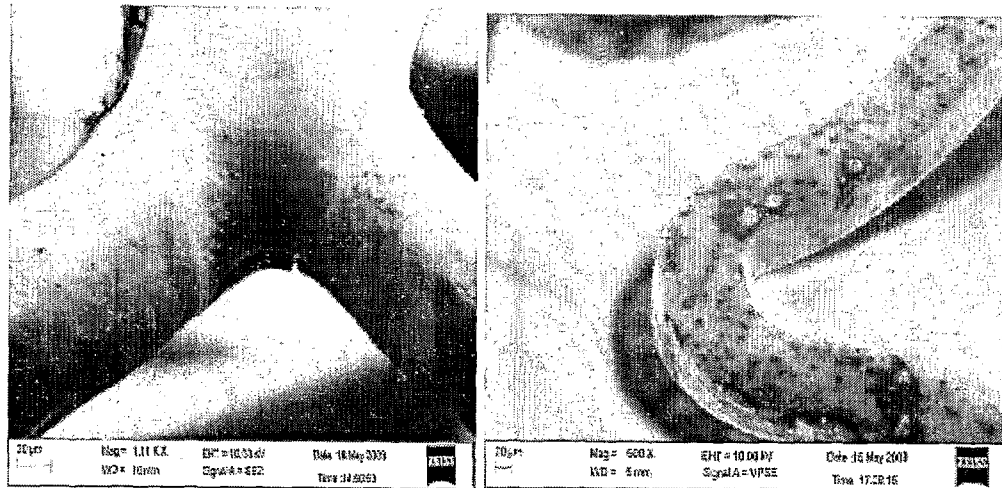


Fig.3(a) & (b)

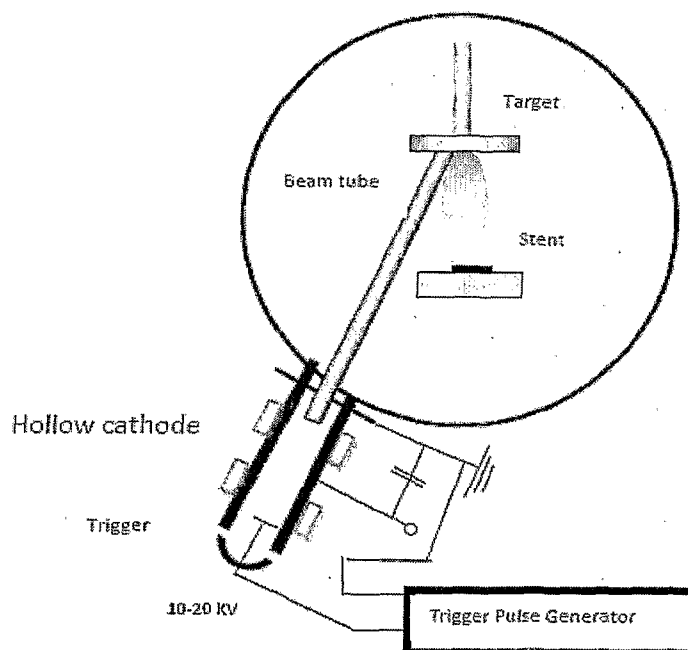


Fig.4