Abstract:
The method for making antibacterial and/or antiviral the surfaces of metal products intended for medical uses comprises: cleaning said surfaces; making said surfaces attached to inorganic agents; applying on said surfaces an inorganic barrier having antibacterial and/or antiviral characteristics, in such a way that said inorganic barrier is placed in between said surfaces and bacteria and viruses; making said application stable.
METHOD FOR MAKING ANTIBACTERIAL AND ANTIVIRAL THE SURFACES OF METAL PRODUCTS INTENDED FOR MEDICAL USES

Technical Field

The invention refers to a method for making antibacterial and antiviral the surfaces of metal products intended for medical uses.

Technological background

It is known that in the medical and veterinary sector, metals of various kinds are used to make products that have to be implanted in the bodies of human beings and animals in order to replace parts of the bone structure or to integrate their functionality.

These products, technically known as prostheses, must have characteristics such as to be able to be placed in direct contact with the tissues and the organs, without, from this contact, phenomena arising that lead to the failure of the prostheses: among these phenomena, the formation of bacterial colonisations are decisive.

The metals used to make the prostheses must also have high mechanical strength but, at the same time, must also be bio-compatible and particularly lightweight so as not to create in the patients conditions of serious inconvenience determined by the fitting of the prostheses which are felt to be foreign bodies.

One of the metals most widely used to make prostheses is titanium, which has a mechanical strength substantially equal to that of the bones and a lightness such as to considerably restrict the problems caused to patients by prostheses implants.

Furthermore, titanium also has high biological compatibility and this characteristic restricts the occurrence of infections that can lead to prostheses failure.

Titanium does not however possess antibacterial characteristics, but the prostheses made with this material are naturally provided with a titanium dioxide coating layer which, when it undergoes a photo-catalytic treatment, does on the other hand have good antibacterial and antiviral characteristics, being in a position to modify the cellular membrane of the bacteria and the viruses which are colonised on the surfaces of the prostheses.

Nevertheless, it has been seen how the antibacterial and antiviral action of the titanium dioxide is slow to develop and limited in time, and for these two reasons, it is possible that bacteria and viruses can attach to and remain on the surfaces of the
prostheses, generating just the same colonies that lead over time to the birth of the previously recalled infective and inflammatory phenomena.

To overcome these drawbacks, crystalline titanium oxides have been used that permit this metal to be more reactive to photo-catalytic treatments. Nevertheless, in this case as well, no particularly advantageous results have been forthcoming because it has not been possible to establish with any precision the behaviour of these crystalline oxides when the irradiation treatment that starts the photo-catalytic processes is interrupted, meaning whether or not their antibacterial and antiviral capacity is able to eliminate already colonised bacteria and viruses.

According to another known technique, the titanium dioxide has been modified using different elements such as calcium, nitrogen, fluoride, silver, copper, tin, vanadium, gold.

In this case as well, the results obtained were unsatisfactory for preventing the formation of infections and inflammation of the tissues in direct contact with the surfaces of the prostheses.

Objects of the Invention

An object of the invention is to improve the state of the art.

Another object is to develop a method for making antibacterial and antiviral, in a constant way, the surfaces of metal products intended for medical or veterinary uses, such as, for example, the prostheses, which is able to prevent the formation of bacteria and viruses colonies on these surfaces, without giving these bacteria and viruses the time to attach to the prostheses.

A further object of the invention is to develop a method for making antibacterial and antiviral, in a constant way, the surfaces of metal products intended for medical or veterinary use, such as, for example, the prostheses, which can be paired with or combined with known methods used to favour a bone growth, such as, for example, the realisation of coatings with solutions that simulate the biological fluids, able to favour the enucleations of phosphated calcium; these known methods can, in some cases, provide for a pre-treatment in alkaline solutions.

According to one aspect of the invention, a method is provided suitable for making antibacterial and/or antiviral the surfaces of metal products intended for medical uses
characterized in that it comprises: applying on said surfaces an inorganic barrier inhospitable to bacteria and viruses, in such a way that said inorganic barrier prevents the attachment of bacteria and viruses to said surfaces; making said application stable. Consequently, the method permits preparing the product surfaces so that the attachment of bacteria and viruses is prevented, meaning that these cannot attach together to form infective colonies.

The method for making antibacterial and antiviral, in a constant way, the surfaces of metal products intended for medical or veterinary uses, such as, for example, prostheses, can also be combined with other known methods to favour bone regrowth, such as, i.e., the making of coatings with solutions that simulate biological fluids, able to favour the enucleation of phosphated calcium.

**Embodiments of the Invention**

Further characteristics and advantages of the invention will appear even more evident from the description of a non limiting example of embodiment of a method for making antibacterial and antiviral the surfaces of metal products intended for medical uses, as indicated below.

**EXAMPLE 1.**

In the execution of the method according to this example, samples have been used of titanium substrates in the form of plates having dimensions of 1 x 1 cm and a thickness of around 0.3 cm.

a) - **Washing.**

During a first stage, the surfaces of the titanium plates undergo:
- cleaning with jets of compressed air;
- washing with ultra-sounds in distilled water for about 15 minutes;
- further double washing with ultra-sounds in acetone for 15 minutes at a time;
- drying in a drying machine at a temperature of around 40°C.

b) - **UV treatment.**

In a second stage, the plates are exposed to Ultraviolet radiations, if necessary integrated with infra-red radiations, with a wavelength between 100 and 290 nm, and are then soaked in distilled water for one hour and 30 minute altogether, and
each face of the plates is exposed to radiations every 30 minutes, so as to obtain complete irradiation on all the plates.

When irradiation has been completed, the plates are rinsed with demonised water.

c) - Change with zinc.

In a third stage, two different solutions are prepared separately: a first solution with 500 ml solution of ammonium chloride 4M and another solution with zinc chloride 0.4M.

The two solutions are then mixed and the pH is brought to value 6.9, adding ammonia until a 1-litre volume is reached.

d) - Plate treatment.

The titanium plates, irradiated with UV rays, are soaked in 100 ml of solution containing zinc for about 30 minutes.

In this specific case, the plates are kept in vertical position in such a way that both faces can be exposed to the solution.

This soaking is done at room temperature and keeping the surfaces exposed to the light.

Once the soaking treatment is completed, the plates undergo a cycle of three washes with demonised water to eliminate any components not adsorbed at the surface.

After completing the three washes, the plates are dried in a heating unit at a temperature of around 40°C.
CLAIMS

1. Method suitable for making antibacterial and/or antiviral the surfaces of metal products intended for medical uses characterized in that it comprises: applying on said surfaces an inorganic barrier inhospitable to bacteria and viruses, in such a way that said inorganic barrier prevents the attachment of bacteria and viruses to said surfaces; making said application stable.

2. Method according to claim 1 wherein said inorganic barrier comprises a sheet coating of an inorganic material.

3. Method according to claim 1 wherein cleaning said surfaces is made before said application; making said surfaces adhesive to said inorganic barrier.

4. Method according to claim 3, wherein said making adhesive comprises pre-treating said attaching surfaces with alkaline solutions.

5. Method according to claim 4, wherein said treating comprises treating in NaOH 4-6M with a temperature comprised between 4°C and 70°C.

6. Method according to any of the claims from 1 to 3, wherein said applying comprises making said sheet coating attached in a stable way to said surfaces.

7. Method according to claim 6, wherein said making attached in a stable way comprises submitting said surfaces to a preventive photo-catalytic treatment, in such a way to generate on said surfaces atoms and/or groups of atoms suitable for binding to corresponding atom and/or molecular bonds of said sheet coating.

8. Method according to claim 7, wherein said preventive photo-catalytic treatment comprises irradiating said surfaces with Ultraviolet rays.

9. Method according to claim 7, wherein said photo-catalytic treatment comprises irradiating said surfaces with Ultraviolet rays together with infra-red rays.

10. Method according to any of the claims 8 or 9, wherein said irradiating comprises irradiating for a time comprised between five minutes and six hours.

11. Method according to any of the claims from 8 to 10, wherein said irradiating comprises irradiating with a wavelength comprised between 400 nm and 100 nm.

12. Method according to claim 1, wherein said cleaning comprises submitting said
surfaces to jets of air; washing said surfaces with ultra-sounds with a first washing liquid for a time comprised between 10 and 20 minutes; drying said surfaces at a temperature comprised between 35 °C and 45 °C.

13. Method according to claim 12, wherein said cleaning comprises, after said washing with a first washing liquid, washing said surfaces with ultra-sounds with a second washing liquid different from said first washing liquid for a time comprised between 1 and 20 minutes.

14. Method according to any of the claims 12 or 13, wherein said first washing liquid comprises distilled water.

15. Method according to any of the claims 12 or 13, wherein said second washing liquid comprises acetone.

16. Method according to claim 13, wherein said washing comprises washing twice consecutively.

17. Method according to claim 1, wherein said metal materials are selected among titanium, titanium alloys, stainless steel, stainless steel alloys.

18. Method according to claim 8, wherein said metal material is titanium.

19. Method according to claim 1, wherein said inorganic agent is selected among oxides of inorganic salts of zinc, manganese, calcium, copper, silver.

20. Method according to claim 10, wherein said oxide is zinc oxide.

21. Method according to any of the claims from 7 to 20, wherein after said preventive treatment said metal products are soaked in a solution for the application of said sheet coating.

22. Method according to claim 21, wherein said solution comprises a mix of a first solution and of a second solution.

23. Method according to claim 22, wherein said first solution comprises: a solution of ammonium chloride in a concentration between 3 and 5 M/litre.

24. Method according to claim 22, wherein said second solution comprises a solution of zinc chloride in a quantity comprised between 0.1 and 0.7 M/litre.

25. Method according to any of the claims from 21 to 24, wherein said application solution has a pH value comprised between 6.5 and 7.3.

26. Method according to claim 24, wherein said pH value is obtained with the
addition of ammonia in said application solution.

27. Method according to any of the claims from 1 to 26, wherein said metal products are kept soaked in said application solution for a time comprised between 1 and 30 minutes.

28. Method according to claim 27, wherein said soaking is done at ambient temperature.

29. Method according to claim 27, wherein said soaking is done with exposure to the light.

30. Method according to any of the claims from 21 to 29, wherein during said soaking in said application solution, said metal materials undergo a final washing cycle with demineralised water.

31. Method according to claim 30, wherein said final washing cycle comprises three consecutive washes.

32. Method according to claim 21, wherein after said soaking said metal products are dried in a heating unit at a temperature comprised between 35°C and 45°C.

33. Method according to claim 1, wherein said inorganic barrier contains calcium and phosphorus.

34. Metal product intended for medical uses characterized in that it has surfaces provided with an inorganic barrier inhospitable to bacteria and viruses, which can be obtained with a method suitable for making antibacterial and/or antiviral the surfaces of metal products intended for medical uses according to any of the claims from 1 to 33.