

Claims

1. An implantable medical device with a surface having a coating comprising:
a first coating layer comprising an immobilized heparin moiety and
a second particulate coating layer comprising elutable paclitaxel and at least one organic additive,
wherein at least a portion of the second particulate coating layer is in contact with at least a portion of the first coating layer.
2. The implantable medical device according to claim 1, wherein the medical device is a tubular medical device.
3. The implantable medical device according to claim 1 or claim 2, wherein the first coating layer comprises a polymer.
4. The implantable medical device according to claim 3, wherein the heparin moiety is covalently attached to the polymer.
5. The implantable medical device according to claim 3 or claim 4, wherein the polymer is a cationic polymer.
6. The implantable medical device according to any one of claims 3 to 5, wherein the heparin moiety is covalently end-point attached to the polymer, wherein suitably the end-point attached heparin moiety is connected through its reducing end.
7. The implantable medical device according to any one of claims 1 to 6, wherein the or each organic additive is non-polymeric and hydrolytically stable.
8. The implantable medical device according to any one of claims 1 to 7, wherein at least a proportion of the second particulate coating layer comprising paclitaxel and at least one organic additive melts as a single phase at a lower temperature than the melting point of paclitaxel and the at least one organic additive when in pure form;
and/or the second particulate coating layer is surfactant-free;
and/or the second particulate coating layer is polymer-free;
and/or the or each organic additive are in crystalline form.
9. The implantable medical device according to any one of claims 1 to 8, wherein the or each organic additive is independently selected from the list consisting of p-aminobenzoic acid, saccharin, ascorbic acid, methyl paraben, caffeine, calcium salicylate, pentetic acid, creatinine, ethylurea, acetaminophen, aspirin, theobromine, tryptophan, succinic acid, adipic acid, glutaric acid, theophylline, and saccharin sodium, and is suitably independently selected from the list consisting of p-aminobenzoic acid, methyl paraben, caffeine, calcium salicylate and succinic acid, for example is caffeine or succinic acid.

10. The implantable medical device according to any one of claims 1 to 9, wherein the implantable medical device is a stent and is suitably composed of a metal alloy such as nitinol or stainless steel;
or the implantable medical device is a stent-graft, wherein the stent-graft comprises a stent member and a graft member.
11. The implantable medical device according to any one of claims 1 to 10, wherein the coating is applied to a surface of the device which is composed of ePTFE.
12. The implantable medical device according to any one of claims 1 to 11, wherein at least a portion of the second particulate coating layer is applied on top of at least a portion of the first coating layer.
13. The implantable medical device according to any one of claims 1 to 12, wherein the first coating layer is applied to the medical device before the second particulate coating layer.
14. The implantable medical device according to any one of claims 1 to 13, wherein the second particulate coating layer is applied to the medical device by dissolving the paclitaxel and the at least one organic additive in a solvent to form a solution, applying the solution to the medical device and then evaporating the solvent, wherein the solvent is suitably selected from water, acetone and mixtures thereof.
15. An implantable medical device according to any one of claims 1 to 14 for use in the prevention or treatment of stenosis or restenosis in a blood vessel of the human body.
16. A process for preparing a coated implantable medical device comprising the steps of:
 - i) treating the medical device to provide a first coating layer comprising an immobilized heparin moiety; and further
 - ii) treating the medical device to provide a second particulate coating layer comprising elutable paclitaxel and at least one organic additive,wherein at least a portion of the second particulate coating layer is in contact with at least a portion of the first coating layer.
17. The process according to claim 16, wherein step i) comprises the steps of:
 - a) treating the medical device to provide a polymer coating layer; and then
 - b) reacting said polymer layer with a heparin moiety to immobilize the heparin moiety to the polymer coating layer.
18. The process according to claim 16 or claim 17, wherein in step ii) the second particulate coating layer is applied to the medical device by dissolving the paclitaxel and the at least one organic additive in a solvent to form a solution, applying the solution to the medical device and then evaporating the solvent, wherein the solvent is suitably selected from water, acetone and mixtures thereof.

19. The process according to claim 17, wherein the heparin moiety is covalently attached to the polymer coating layer.
20. The process according to claim 19, wherein the heparin moiety is covalently end-point attached to the polymer coating layer wherein the end point attached heparin moiety is suitably connected through its reducing end.