tissues of the organism.

SUMMARY

In one aspect, the present disclosure provides a use of a compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally occurring amino acids in the single, oligomeric or polymeric form, in the manufacture of a medicament for treating skeletal conditions, in particular in the regeneration of hard tissues.

In another aspect, the present disclosure provides an implantable scaffold comprising a compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally occurring amino acids in the single, oligomeric or polymeric form.

In yet another aspect, the present disclosure provides a pharmaceutical formulation comprising a compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally occurring amino acids in the single, oligomeric or polymeric form, for its use in the treatment of skeletal conditions, in particular in the regeneration of hard tissues.

DESCRIPTION OF THE INVENTION

A class of hyaluronic acid derivatives, in which this molecule is associated with at least one heterocyclic compound derived from a purine or pyrimidine base and with at least another organic compound consisting of a naturally occurring amino acid, in single, oligomeric or polymeric form, is described in EP1525244 with the procedures for its preparation.

The above mentioned derivatives of hyaluronic acid, a glycosaminoglycan (GAG) naturally present in the extracellular matrix (ECM), constitute a more stable form than the native one because the compounds associated with it are found in the target sites of the lytic hyaluronidase enzyme, normally responsible for its degradation, making its action more difficult. Furthermore, depending on the type of heterocyclic compounds and amino acids selected, these derivatives show a particular three-

dimensional structure, which makes them able to modify the micro-environment of the EMC.

Object of the present invention is therefore the use of said derivatives of the hyaluronic acid in the regeneration of the bone and cartilage tissues, thanks to the high regenerative potential on said tissues highlighted in the experimental section accompanying the present description.

The compounds of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, associated with at least one different organic compound selected from the naturally occurring amino acids in the single, oligomeric or polymeric form, thus are used, according to the present invention, in the treatment of the skeletal conditions, in particular in the regeneration of hard tissues.

According to the present invention, the hyaluronic acid derivatives the use of which is object of the present invention, are high molecular weight hyaluronic acid, in the range between 400,000 and 4 million Da, preferably between 800,000 and 3.5 million Da, more preferably between 1.5 and 3 million Da.

Optionally, the hyaluronic acid derivatives the use of which is object of the present invention, consist of low molecular weight hyaluronic acid, for example, in the range between 80,000 and 400,000 Da.

CLAIMS

1. Use of a~~A~~ compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally occurring amino acids in the single, oligomeric or polymeric form, in the manufacture of a medicament for ~~its use in the treatment~~ treating ~~of~~ skeletal conditions, in particular in the regeneration of hard tissues.

2. The ~~compound for the~~ use according to claim 1, wherein said at least one heterocycle is thymine.

3. The ~~compound for the~~ use according to claim 1 or 2, wherein said at least one different organic compound is lysine.

4. The ~~compound for the~~ use according to anyone of the preceding claims, wherein the bond between said hyaluronic acid, said heterocycle and said naturally occurring amino acid is a chemical bond of ionic type.

5. The ~~compound for the~~ use according to anyone of the preceding claims, wherein said compound of the hyaluronic acid is T-LysYal®, which comprises hyaluronic acid in combination with lysine and thymine.

6. The ~~compound~~ use according to anyone of the preceding claims, for ~~its use in~~ the induction and stimulation of cell differentiation in the osteogenic and chondrogenic lineage of mesenchymal stem cells.

7. The ~~compound for its~~ use according to claim 6, wherein said mesenchymal stem cells are stem cells of the dental germ.

8. An implantable scaffold comprising a compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally occurring amino acids in the single, oligomeric or polymeric form.

9. The implantable scaffold according to claim 8, for its use in the treatment of skeletal conditions, in particular in the regeneration of hard tissues.

10. A pharmaceutical formulation comprising a compound of hyaluronic acid and at least one heterocycle derived from purine and/or pyrimidine, said compound being further associated with at least one different organic compound selected from naturally

occurring amino acids in the single, oligomeric or polymeric form, for its use in the treatment of skeletal conditions, in particular in the regeneration of hard tissues.