Summary

The present disclosure provides polymer–flavonoid conjugates, useful in the therapeutic and/or prophylactic treatment of a joint condition in a subject. The present disclosure further provides a process for forming said polymer–flavonoid conjugates.

According to the present disclosure, there is provided the use of a polymer–flavonoid conjugate, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a joint condition in a subject.

According to a first aspect of the present disclosure, there is provided the use of a polymer–flavonoid conjugate, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a joint condition in a subject, wherein the polymer of said polymer–flavonoid conjugate is conjugated to one or more flavonoids at the C2 and/or C6 position of the B ring of said flavonoid(s), and

wherein the joint condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, gouty arthritis, juvenile arthritis, psoriatic arthritis, and ankylosing spondylitis.

In the present disclosure, there is provided a polymer–flavonoid conjugate, or a pharmaceutically acceptable salt thereof, for use in the therapeutic and/or prophylactic treatment of a joint condition in a subject.

Claims

1. Use of a polymer–flavonoid conjugate, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a joint condition in a subject, wherein the polymer of said polymer–flavonoid conjugate is conjugated to one or more flavonoids at the C2 and/or C6 position of the B ring of said flavonoid(s), and wherein the joint condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, gouty arthritis, juvenile arthritis, psoriatic arthritis, and ankylosing spondylitis.

2. The use according to claim 1, wherein said therapeutic and/or prophylactic treatment of the joint condition results in cartilage repair.

3. The use according to claim 1 or 2, wherein said polymer is conjugated to said one or more flavonoids via a linker.

4. The use according to any one of claims 1 to 3, wherein said one or more flavonoids is a monomeric flavonoid or a dimeric flavonoid,

preferably wherein the flavonoid is selected from the group consisting of flavones, isoflavones, flavans, proanthocyanidins, anthocyanidins, (−)-epicatechin, (+)-epicatechin, (−)-catechin, (+)-catechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate, Fisetinidol, Gallocatechin, Gallocatechin gallate, Mesquitol and Robinetinidol, ellagitannin, gallotannin, oolongtheanin, phlorotannin, tannin, theacitrin, theadibenzotropolone, theaflavin, theanaphthoquinone, thearubigins, theasinensin and mixtures thereof.

5. The use according to any one of claims 1 to 4, wherein the polymer is conjugated to the flavonoid via a thiol linker,

preferably wherein said thiol linker further comprises a moiety bound to the polymer, wherein said moiety is selected from the group consisting of an amide, an amine, an alkyl, an alkenyl, an aryl, an ester, a carbonate, an ether, an amido, an amido ester, a carbamate and an acetal group.

6. The use according to any one of claims 1 to 5, wherein the polymer is selected from the group consisting of polysaccharides, polynucleotides, polypeptides, synthetic polymers and mixtures thereof,

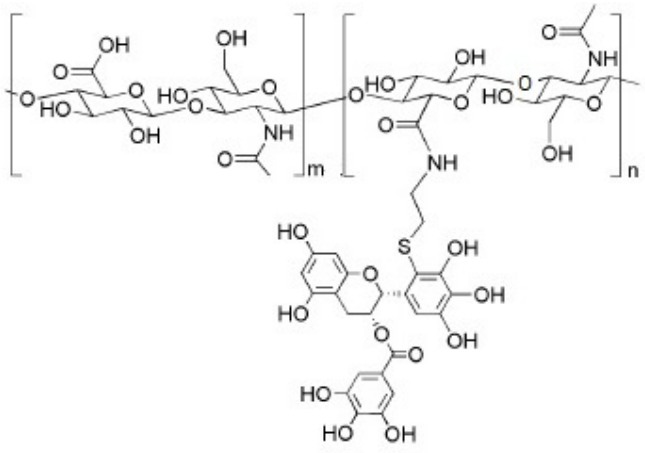
preferably wherein the polysaccharide is selected from the group consisting of hyaluronic acid, dextran, cellulose, amylose, starch, gelatin, alginate, chitosan, carrageenan, cyclodextrin, dextran sulfate, Ficoll, gellan, guar gum, pectin, polysucrose, pullulan, scleroglucan, xanthan and xyloglucan,

preferably wherein the polynucleotide is selected from the group consisting of

aptamers, DNA, small interfering RNA (siRNA), microRNA, peptide nucleic acid (PNA) and small hairpin RNA (shRNA),

preferably wherein the polypeptide is selected from the group consisting of proteins, antibodies, antibody fragments, aptides, peptides and poly(amino acid)s, preferably wherein the synthetic polymer comprises monomers selected from the group consisting of alkenes, ethers, carboxylic acids, imines, amides, amines, anhydrides, carbonates, esters, orthoesters, urethanes,poly(acrylamide),poly(allylamine), polyanhydrides, poly(β-amino ester), poly(butylene succinate), polycaprolactone, polycarbonate, polydioxanone, polyethylenimine, poly(glycerol), polyglycolic acid, poly(3-hydroxypropionic acid), poly(*N*-(2-hydroxypropyl)methacrylamide), polylactic acid, poly(lactic-*co*-glycolic acid), poly(acrylic acid), poly(methacrylic acid), poly(ortho esters), poly(2-oxazoline), poly(sebacic acid), poly(terephthalate-*co*-phosphate), poly(vinyl alcohol), poly(vinylpyrrolidone) and combinations thereof.

7. The use according to any one of claims 1 to 6, wherein the polymer–flavonoid conjugate is of Formula 1:



Formula 1;

wherein:
each n is independently an integer from 0 to 50,000 inclusive; and each m is independently an integer from 0 to 50,000 inclusive, wherein at least n or m is not 0.

8. The use according to claim 7, wherein the polymer-flavonoid conjugate of Formula 1 has a degree of conjugation from 0.1 to 50%.

9. Use of a polymer-flavonoid conjugate, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a joint condition in a subject, wherein the polymer of said polymer-flavonoid conjugate is conjugated to one or more flavonoids at the C2 and/or C6 position of the B ring of said flavonoid(s),
wherein the joint condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, gouty arthritis, juvenile arthritis, psoriatic arthritis, and ankylosing spondylitis, and
wherein said polymer is a polysaccharide and said flavonoid is epigallocatechin gallate.

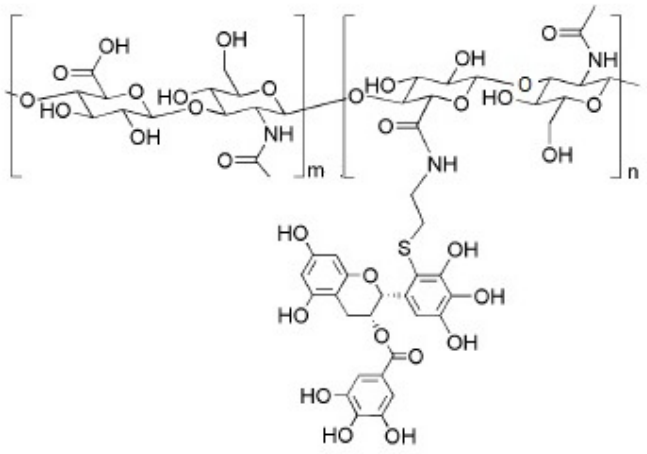
10. The use according to claim 9, wherein the polysaccharide is hyaluronic acid, and the hyaluronic acid is conjugated to at least one epigallocatechin gallate.

11. The use according to any one of claims 9 or 10, wherein the polysaccharide is hyaluronic acid, and the hyaluronic acid is conjugated to two epigallocatechin gallate.

12. The use according to any one of claims 9 or 10, wherein the polysaccharide is hyaluronic acid, and the hyaluronic acid is conjugated to at least one epigallocatechin gallate via a thiol linker.

13. The use according to any one of claims 9, 10 or 12, wherein the polysaccharide is hyaluronic acid, and the hyaluronic acid is conjugated to at least one epigallocatechin gallate at the C2 and/or C6 position of the B ring of said epigallocatechin gallate.

14. The use according to any one of claims 9 to 13, wherein the polymer–flavonoid conjugate is of Formula 1:

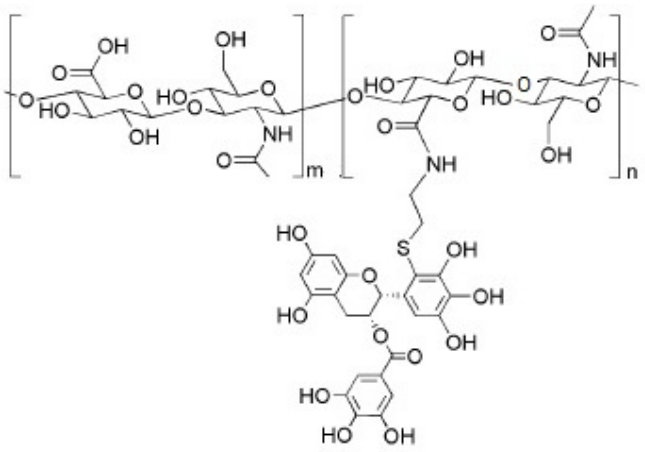


Formula 1;

wherein:

each n is independently an integer from 0 to 50,000 inclusive; and each m is independently an integer from 0 to 50,000 inclusive, wherein at least n or m is not 0.

15. Use of a polymer-flavonoid conjugate of Formula 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a joint condition in a subject:



Formula 1;

wherein:

each n is independently an integer from 0 to 50,000 inclusive; and each m is independently an integer from 0 to 50,000 inclusive, wherein at least n or m is not 0.

16. The use according to claim 14 or 15, wherein the polymer-flavonoid conjugate of Formula 1 has a degree of conjugation from 0.1 to 50%.