Claims

1. A composition comprising:
   a. triiodothyronine, or a pharmaceutically acceptable salt thereof,
   b. hydroxypropyl methyl cellulose acetate succinate (HPMC-AS) and/or hydroxypropyl methyl cellulose (HPMC)in a total amount of 0.1% to 20% by weight, and
   c. polyethylene oxide (PEO) in an amount from 80 to 99.9% by weight.

2. The composition according to any one of the claims 1, wherein triiodothyronine or a pharmaceutically acceptable salt thereof is present in an amount between 1 and 100 µg, such as between 2 and 70 µg, for example between about 5 and 50 µg, such as 5 to 7 µg, such as 7 to 9 µg, such as 9 to 11 µg, such as 11 to 13 µg, such as 13 to 15 µg, such as 15 to 17 µg, such as 19 to 21 µg, such as 21 to 23 µg, such as 23 to 25 µg, such as 25 to 27 µg, such as 27 to 29 µg, such as 29 to 31 µg, such as 31 to 33 µg, such as 33 to 35 µg, such as 35 to 37 µg, such as 37 to 39 µg, such as 39 to 41 µg, such as 41 to 43 µg, such as 43 to 45 µg, such as 45 to 47 µg, such as 47 to 50 µg.

3. The composition according to any one of the preceding claims, wherein the HPMC-AS is present in an amount of about 1% to 20%, such as about 2% to 20%, such as about 5% to 15%, such as about 6% to 14%, such as about 7% to 13%, such as about 8% to 12%, such as about 9% to 11%, for example about 10%.

4. The composition according to claim 3, wherein the composition does not comprise HPMC.

5. The composition according to any one of claims 1 to 2, wherein the hydroxypropyl methyl cellulose is present in an amount of about 1% to 20%, such as about 2% to 20%, such as about 5% to 15%, such as about 6% to 14%, such as about 7% to 13%, such as about 8% to 12%, such as about 9% to 11%, for example about 10%.

6. The composition according to claim 5, wherein the composition does not comprise HPMC-AS.

7. The composition according to any one of the preceding claims, wherein the HPMC_AS and/or hydroxypropyl methyl cellulose is present in a total amount of about 1% to 20%, such as about 2% to 20%, such as about 5% to 15%, such as about 6% to 14%, such as about 7% to 13%, such as about 8% to 12%, such as about 9% to 11%, for example about 10%.

8. The composition according to any one of the preceding claims, wherein the PEO has an average molecular weight between 10 kDa to 2000 kDa, such as 50 kDa to 1000 kDa, such as 100 kDa to 500 kDa, such as 150 kDa to 300 kDa.

9. The composition according to any one of the preceding claims, wherein PEO is present in an amount of about 80 to 99%, such as 85% to 86%, such as 86% to 87%, such as 87% to 88%, such as 88% to 89%, such as 89% to 90%, such as 90% to 91%, such as 91% to 92%, such as 92% to 93%, such as 93% to 94%, such as 94% to 95%, such as 95% to 96%, such as 96% to 97%, such as 97% to 98%, such as 98% to 99%.

10. The composition according to any one of the preceding claims, wherein the weight ratio between PEO and the total amount of HPMC and/or HPMC-AS is between about 8:2 and about 9:0.1.

11. The composition according to any one of the preceding claims, wherein the composition is a uniform dispersion of the triiodothyronine, or a pharmaceutically acceptable salt thereof; the HPMC and/or HPMC-AS; and the PEO.

12. The composition according to any one of the preceding claims, further comprising
    a. one or more further polymers each independently selected from the group consisting of polyethylene oxide glucomannan, galactan, glucan, polygalacturonic acid, polyhdyroxyalkanoates, polyxylane, polygalactomannans, rhanogalacturonan, polyxyloglycan, arabinogalactan, starch, alginates, xhanthan gum, carrageenan, agar, dextran, pectins, cellulose, polyvinyl alcohol, polyvinyl butyral, polyvinyl pyrrolidone, methylcellulose, ehtylcellulose, hydroxypropyl cellulose, hydroxypropyl

methylcellulose stearate, carboxymethyl cellulose, carbomers, polyacrylic acid, poly(methylacrylic) acid, poly(methylmethacrylate), polyhydroxybutyrate, polyhydroxyvalerate, polyhydroxyphenylvalerate, polylactic acid, polyglycolic acid, a polyacrylic amide, and derivatives or copolymers thereof; and/or

b. further comprising one or more additional excipients, such as one or more excipients selected from the group consisting of: binders, fillers, lubricants, release-controlling excipients, stabilizers, antioxidants and preservatives.

13. The composition according to any one of the preceding claims, wherein the composition is selected from the group consisting of a tablet, a mini-tablet and a micro-tablet, such as a monolithical tablet or a monlithical cylindrical tablet, optionally wherein the tablet has a total weight of 50 to 800 mg, such as 50 to 250 mg, such as 100 to 200 mg, such as 150 mg; and/or the tablet has a volume/weight ratio between 10 and 200, such as 130 to 170, for example 140 to 160, such as 150.

14. The composition according to any one of the preceding claims, further comprising a coating, optionally wherein the coating comprises one or more selected from the group consisting of: polyacrylates, polyacrylate derivatives and copolymers thereof, cellulose, cellulose derivatives; and shellac.

15. The composition according to any one of the preceding claims, wherein the composition is a single-unit oral dosage form, or a multiple-unit oral dosage form.

16. A method of manufacturing a composition comprising the steps of:

a. preparing a melt uniform dispersion comprising i) PEO, ii) hydroxypropyl methyl cellulose and/or HPMC-AS and iii) triiodothyronine or a pharmaceutically acceptable salt thereof, wherein the weight ratio between PEO and the total amount of HPMC and/or HPMC-AS is between about 8:2 and about 9:0.1; and

b. cooling the melt to obtain a solid composition.

17. A method of manufacturing a composition comprising the steps of:

a. mixing powders of triiodothyronine or a pharmaceutically acceptable salt thereof, HPMC and/or HPMC-AS; and PEO, wherein the weight ratio between PEO and the total amount of HPMC and/or HPMC-AS is between about 8:2 and about 9:0.1; and

b. compacting the mixture to obtain uniform dispersion of components in a matrix.

18. Use of the composition according to any one of claims 1 to 15 in the manufacture of a medicament.

19. Use of the composition according to any one of claims 1 to 15 in the manufacture of a medicament for the treatment of hypothyroidism.

20. The use according to claim 19, wherein wherein the hypothyroidism is drug-induced hypothyroidism or the hypothyroidism is caused by one or more selected from the group consisting of autoimmune disease, radiation treatment, treatment with other medications, surgical removal of part or all of the thyroid gland, congenital disease and pregnancy.

21. The use according to any one of claims 19-20, wherein the composition
a) is administered between 18h and 00h, such as between 20h and 22h, for example at 21h;
b) is administered during dinner or after dunner, such as within 3 hours after dinner, such as 2 hours after dinner, such as within 1 hour after dinner such as within 30 minutes after dinner;
c) is administered prior to a major sleep episode such as within 3 hours before a major sleep episode, such as within 2 hours before a major sleep episode, for example within 1 hour before a major sleep episode, such as within 30 minutes before a major sleep episode;
d) is administered once daily; and/or
e) is administered on an empty stomach.

22. The use according to any one of claims 19-21, wherein the composition
a) provides an increase in T_{max} of triiodothyronine, as compared to an equivalent amount of triiodothyronine administered as an immediate release formulation, such as the T_{max} of triiodothyronine is increased by at least about 1 hour, such as at least about 2 hours, for example at least about 3 hours, such as at least about

4 hours as compared to an equivalent amount of triiodothyronine administered as an immediate release formulation; and/or

b) provides a C_{max} of triiodothyronine between 150 and 400 ng/dL, such as between 200 and 350 ng/dL.

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