CLAIMS

What is claimed is:

1. A composition comprising a mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprising:
β-cyclodextrin substituted with eight hydroxypropyl groups (“DS-8”);
β-cyclodextrin substituted with nine hydroxypropyl groups (“DS-9”);
β-cyclodextrin substituted with ten hydroxypropyl groups (“DS-10”);
β-cyclodextrin substituted with eleven hydroxypropyl groups (“DS-11”);
β-cyclodextrin substituted with twelve hydroxypropyl groups (“DS-12”);
β-cyclodextrin substituted with thirteen hydroxypropyl groups (“DS-13”); and
β-cyclodextrin substituted with fourteen hydroxypropyl groups (“DS-14”),
wherein the composition comprises less than 1% β-cyclodextrin substituted with seven hydroxypropyl groups (“DS-7”).

2. The composition of claim 1, wherein the composition comprises less than 1% β-cyclodextrin substituted with six hydroxypropyl groups (“DS-6”), 1% β-cyclodextrin substituted with five hydroxypropyl groups (“DS-5”), β-cyclodextrin substituted with four hydroxypropyl groups (“DS-4”), β-cyclodextrin substituted with three hydroxypropyl groups (“DS-3”), β-cyclodextrin substituted with two hydroxypropyl groups (“DS-2”), and β-cyclodextrin substituted with one hydroxypropyl group (“DS-1”).

3. The composition of claim 1 or 2, wherein the DS-10 has the highest concentration in the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules as compared to DS-8, DS-9, DS-11, DS-12, DS-13, and DS-14.

4. The composition of any preceding claim, wherein:
(a) the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 6% to about 12% DS-8;
for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 7% to about 11% DS-8; and/or
(b) the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 18% to about 24% DS-9; for example, wherein the mixture of

isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 19% to about 23% DS-9; and/or

(c) wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 24% to about 30% DS-10; for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 25% to about 29% DS-10; and/or

(d) wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 18% to about 24% DS-11; for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 19% to about 23% DS-11; and/or

(e) wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 10% to about 16% DS-12; for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 11% to about 15% DS-12; and/or

(f) wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 4% to about 10% DS-13; for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 5% to about 9% DS-13; and/or

(g) wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 0% to about 6% DS-14; for example, wherein the mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprises about 1% to about 5% DS-14.

5. The composition of any preceding claim, wherein the average degree of substitution of the mixture of isomerically-purified hydroxypropyl β-cyclodextrin is about 9 to about 10;

for example, wherein the average degree of substitution of the mixture of isomerically-purified hydroxypropyl β-cyclodextrin is about 9.65.

6. The composition of any preceding claim, wherein about 15% to about 21% of the hydroxypropyl substitutions in the hydroxypropyl β-cyclodextrin molecules are located at the 3-O- position;

for example, wherein about 16% to about 20% of the hydroxypropyl substitutions in the hydroxypropyl β-cyclodextrin molecules are located at the 3-O- position.

7. The composition of any preceding claim, wherein about 79% to about 85% of the hydroxypropyl substitutions in the hydroxypropyl β-cyclodextrin molecules are located at the 2-O- position;

for example, wherein about 80% to about 84% of the hydroxypropyl substitutions in the hydroxypropyl β-cyclodextrin molecules are located at the 2-O- position.

8. The composition of any preceding claim, wherein:

(a) the composition has an HPLC-CAD chromatogram of FIG. 28, optionally wherein the composition has a mean retention time of about 15.4 minutes; and/or

(b) the composition has a -ESI-MS spectrum with peaks at about 770 m/z, about 798 m/z, about 828 m/z, about 857 m/z, about 885 m/z; and/or

(c) the composition has a +ESI-MS spectrum with peaks at about 803 m/z, about 831 m/z, about 861 m/z, about 889 m/z, and about 919 m/z; and/or

(d) the composition has a ESI-MS spectra of FIG. 29; and/or

(e) the composition has a MALDI-TOF spectrum with peaks at about 1614 m/z, about 1673 m/z, about 1733 m/z, about 1792 m/z, about 1852 m/z, about 1912 m/z, and about 1971 m/z; and/or

(f) the composition has a MALDI-TOF spectrum of FIG. 30, optionally wherein:

(i) the area of DS-8 is 8.53%; and/or

(ii) the area of DS-9 is 21.33%; and/or

wherein the area of DS-10 is 26.58%; and/or

wherein the area of DS-11 is 20.90%; and/or

wherein the area of DS-12 is 13.31%; and/or

wherein the area of DS-13 is 6.74%; and/or

wherein the area of DS-14 is 2.60%; and/or

(h) the composition has a 1H-NMR spectrum of FIG. 26; and/or

(i) the composition has a DEPT-edited HSQC spectrum of FIG. 27.

9. The composition of any preceding claim, wherein the osmolality of the composition is about 635–695 mOs/kg; and/or wherein the true density of the composition is about 1.096 – 1.098 g/cm^3

10. The composition of any preceding claim, wherein:

(a) the composition comprises no more than 10 ppb of propylene glycol as measured by HPLC; and/or

(b) the composition comprises no more than 10 ppb propylene glycol as measured by gas chromatography; and/or

(c) the composition comprises no more than 10 ppb propylene glycol as measured by PG/EG-ratio of propylene glycol to ethylene glycol; and/or

(d) the composition comprises no more than 1 ppm propylene oxide; and/or

(e) the total amount of other unspecified impurities is less than or equal to 0.05% as measured by HPLC; and/or

(f) the composition comprises between 0 and 10 ppm chloride; for example, wherein the composition comprises between 0 and 1 ppm chloride.

11. The composition of any preceding claim, wherein the composition has a conductivity between 0 and 8 μS/cm;

for example, wherein the composition has a conductivity between 0 and 4.5 μS/cm;

for example, wherein the composition has a conductivity between 0 and 3 μS/cm;

for example, wherein the composition has a conductivity between 0 and 1.5 μS/cm.

12. The composition of any preceding claim, wherein the composition is nanofiltered, optionally wherein:

(a) the nanofiltrated composition has no substantial difference observed in HPLC-ELSD after nanofiltration as compared to before nanofiltration; or

(b) the nanofiltrated composition has no substantial difference observed in NMR after nanofiltration as compared to before nanofiltration.

13. A composition comprising a mixture of isomerically-purified hydroxypropyl β-cyclodextrin molecules comprising:

about 6% to about 12% β-cyclodextrin substituted with eight hydroxypropyl groups (“DS-8”);

about 18% to about 24% β-cyclodextrin substituted with nine hydroxypropyl groups (“DS-9”);

about 24% to about 30% β-cyclodextrin substituted with ten hydroxypropyl groups (“DS-10”);

about 18% to about 24% β-cyclodextrin substituted with eleven hydroxypropyl groups (“DS-11”);
about 10% to about 16% β-cyclodextrin substituted with twelve hydroxypropyl groups (“DS-12”);
about 4% to about 10% β-cyclodextrin substituted with thirteen hydroxypropyl groups (“DS-13”); and
about 0% to about 6% β-cyclodextrin substituted with fourteen hydroxypropyl groups (“DS-14”).

14. A composition according to any preceding claim for use in therapy.

15. Use of a composition according to any one of claims 1 to 13 in the manufacture of a medicament for treating or preventing a disease or condition selected from Niemann-Pick disease Type C, liver disease, cardiovascular disease, familial hypercholesterolemia, and/or cholesterol deposits.