What is claimed is:

1. An analytical method for analyzing the presence and quantity of impurities present in a preparation of dianhydrogalactitol comprises the step of analyzing a preparation of dianhydrogalactitol by subjecting the preparation to high performance liquid chromatography (HPLC) on an HPLC column using elution with a mobile phase gradient to separate dianhydrogalactitol from dulcitol and other contaminants of the preparation;
wherein the high performance liquid chromatography employs evaporative light scattering detection (ELSD); and
wherein the HPLC column is a silica gel column bonded to C18 compounds and finished with an endcapping procedure employing Lewis acid-Lewis base chemistry.

2. The analytical method of claim 1 wherein elution is performed with a gradient of 95% water/5% acetonitrile to 70% water/30% acetonitrile, returning to 95% water/5% acetonitrile.

3. The analytical method of claim 2 wherein the time schedule for varying the eluent is as follows: 0 minutes, 95% water/5% acetonitrile; 15 minutes, 95% water/5% acetonitrile; 15.1 minutes, 70% water/30% acetonitrile; 20 minutes, 70% water/30% acetonitrile; 20.1 to 35 minutes, 95% water/5% acetonitrile.

4. The analytical method of claim 1 wherein the method detects a monoepoxide degradation product of dianhydrogalactitol, a monoepoxide dimer, and dulcitol.

5. The analytical method of claim 4 wherein the method also detects a dimer of dianhydrogalactitol and condensed products.

6. The method of claim 1 wherein the peaks resulting from HPLC are analysed by LC-MS.

7. The method of claim 1 wherein the method further comprises a step of determining the relative concentration of one or more peaks resolved by high performance liquid chromatography that represent compounds other than dianhydrogalactitol itself.

8. The method of claim 1 wherein the column temperature is about 30° C.

9. The method of claim 1 wherein the flow rate is about 0.5 mL/min.

10. The method of claim 1 wherein the ELSD detector is operated in cooling mode with the drift tube temperature of 35° C and gain 400, 2 pps, 45 PSI.

11. The method of claim 1 wherein Mobile Phase A and Mobile Phase B are employed, with Mobile Phase A being 0.05% formic acid in water and Mobile Phase B being 100% methanol.

12. The method of claim 11 wherein elution is performed from 0 minutes to 25 minutes with 100% of 0.05% formic acid in water, from 25 minutes to 25.1 minutes with 90% of 0.05% formic acid in water and 10% of 100% methanol, from 25.1 minutes to 35 minutes with 10% of 0.05% formic acid in water and 90% of 100% methanol, and from 35.1 minutes to 50 minutes with 100% of 0.05% formic acid in water.

13. The method of claim 1 wherein the method further comprises the preparation of an external calibration standard curve for an impurity.

14. The method of claim 11 wherein the method further comprises the preparation of an external calibration standard curve for an impurity.

15. The method of claim 13 wherein the impurity is selected from the group consisting of dulcitol, a monoepoxide degradation product of dianhydrogalactitol, and a dimer of dianhydrogalactitol.

16. The method of claim 14 wherein the impurity is selected from the group consisting of dulcitol, a monoepoxide degradation product of dianhydrogalactitol, and a dimer of dianhydrogalactitol.

17. The method of claim 1 wherein, for an unknown impurity, the content of the unknown impurity is estimated using a calibration standard curve established by chromatography of dianhydrogalactitol reference material.

18. The method of claim 11 wherein, for an unknown impurity, the content of the unknown impurity is estimated using a calibration standard curve established by chromatography of dianhydrogalactitol reference material.

19. The method of claim 12 wherein, following the elution sequence, an additional elution sequence is performed as follows: from 0 minutes to 7.5 minutes with 100% of 0.05% formic acid; from 7.5 minutes to 7.6 minutes with 97% of 0.05% formic acid and 3% of methanol; and from 7.6 minutes to 20 minutes with 100% of 0.05% formic acid.

20. The method of claim 19 wherein the column temperature for HPLC is about 30° C, the sample temperature for HPLC is about 5° C, the flow rate for HPLC is about 0.5 mL/min, and the injection volume is about 10-100 μL.

21. The method of claim 19 wherein, for ELSD, the gain is about 400, the drift tube temperature is about 45°C, the gas pressure is about 35 PSI of nitrogen, the nebulizer is set to cooling, the data rate is 2 points per second, and the Rayleigh factor is about 6.0.

22. The method of claim 19 wherein standards of 2.0% dulcitol, 1.6% dulcitol, 1.0% dulcitol, 0.60% dulcitol, 0.20% dulcitol, and 0.10% dulcitol are employed to determine the sensitivity and linearity of the system.

23. The method of claim 19 wherein the retention time for dulcitol is about 6.4 minutes and the retention time for dianhydrogalactitol is about 12.1 minutes.

24. The method of claim 19 wherein the amount and percentage of a dulcitol impurity are determined from the results of HPLC and ELSD.

25. The method of claim 19 wherein the amount and percentage of an unknown impurity other than dulcitol are determined from the results of HPLC and ELSD.

CLAIMS

1. An analytical method for analyzing the presence and quantity of impurities present in a preparation of dianhydrogalactitol comprises the step of analyzing a preparation of dianhydrogalactitol by subjecting the preparation to high performance liquid chromatography (HPLC) on an HPLC column that is a silica gel column bonded to C18 compounds and finished with an endcapping procedure employing Lewis acid-Lewis base chemistry, using elution with a mobile phase gradient to separate dianhydrogalactitol from dulcitol and other contaminants of the preparation;
wherein the high performance liquid chromatography employs evaporative light scattering detection (ELSD).

2. The analytical method of claim 1 wherein elution is performed with a gradient of 95% water/5% acetonitrile to 70% water/30% acetonitrile, returning to 95% water/5% acetonitrile.

3. The analytical method of claim 2 wherein the time schedule for varying the eluent is as follows: 0 minutes, 95% water/5% acetonitrile; 15 minutes, 95% water/5% acetonitrile; 15.1 minutes, 70% water/30% acetonitrile; 20 minutes, 70% water/30% acetonitrile; 20.1 to 35 minutes, 95% water/5% acetonitrile.

4. The analytical method of claim 1 wherein the method detects a monoepoxide degradation product of dianhydrogalactitol, a monoepoxide dimer, and dulcitol.

5. The analytical method of claim 4 wherein the method also detects a dimer of dianhydrogalactitol and condensed products.

6. The method of claim 1 wherein the peaks resulting from HPLC are analysed by LC-MS.

7. The method of claim 1 wherein the method further comprises a step of determining the relative concentration of one or more peaks resolved by high performance liquid chromatography that represent compounds other than dianhydrogalactitol itself.

8. The method of claim 1 wherein the column temperature is about 30°C.

9. The method of claim 1 wherein the flow rate is about 0.5 mL/min.

10. The method of claim 1 wherein the ELSD detector is operated in cooling mode with the drift tube temperature of 35° C and gain 400, 2 pps, 45 PSI.

11. The method of claim 1 wherein Mobile Phase A and Mobile Phase B are employed, with Mobile Phase A being 0.05% formic acid in water and Mobile Phase B being 100% methanol.

12. The method of claim 11 wherein elution is performed from 0 minutes to 25 minutes with 100% of 0.05% formic acid in water, from 25 minutes to 25.1 minutes with 90% of 0.05% formic acid in water and 10% of 100% methanol, from 25.1 minutes to 35 minutes with 10% of 0.05% formic acid in water and 90% of 100% methanol, and from 35.1 minutes to 50 minutes with 100% of 0.05% formic acid in water.

13. The method of claim 1 wherein the method further comprises the preparation of an external calibration standard curve for an impurity.

14. The method of claim 11 wherein the method further comprises the preparation of an external calibration standard curve for an impurity.

15. The method of claim 13 wherein the impurity is selected from the group consisting of dulcitol, a monoepoxide degradation product of dianhydrogalactitol, and a dimer of dianhydrogalactitol.

16. The method of claim 14 wherein the impurity is selected from the group consisting of dulcitol, a monoepoxide degradation product of dianhydrogalactitol, and a dimer of dianhydrogalactitol.

17. The method of claim 1 wherein, for an unknown impurity, the content of the unknown impurity is estimated using a calibration standard curve established by chromatography of dianhydrogalactitol reference material.

18. The method of claim 11 wherein, for an unknown impurity, the content of the unknown impurity is estimated using a calibration standard curve established by chromatography of dianhydrogalactitol reference material.

19. The method of claim 12 wherein, following the elution sequence, an additional elution sequence is performed as follows: from 0 minutes to 7.5 minutes with 100% of 0.05% formic acid; from 7.5 minutes to 7.6 minutes with 97% of 0.05% formic acid and 3% of methanol; and from 7.6 minutes to 20 minutes with 100% of 0.05% formic acid.

20. The method of claim 19 wherein the column temperature for HPLC is about 30° C, the sample temperature for HPLC is about 5° C, the flow rate for HPLC is about 0.5 mL/min, and the injection volume is about 10-100 μL.

21. The method of claim 19 wherein, for ELSD, the gain is about 400, the drift tube temperature is about 45°C, the gas pressure is about 35 PSI of nitrogen, the nebulizer is set to cooling, the data rate is 2 points per second, and the Rayleigh factor is about 6.0.

22. The method of claim 19 wherein standards of 2.0% dulcitol, 1.6% dulcitol, 1.0% dulcitol, 0.60% dulcitol, 0.20% dulcitol, and 0.10% dulcitol are employed to determine the sensitivity and linearity of the system.

23. The method of claim 19 wherein the retention time for dulcitol is about 6.4 minutes and the retention time for dianhydrogalactitol is about 12.1 minutes.

24. The method of claim 19 wherein the amount and percentage of a dulcitol impurity are determined from the results of HPLC and ELSD.

25. The method of claim 19 wherein the amount and percentage of an unknown impurity other than dulcitol are determined from the results of HPLC and ELSD.