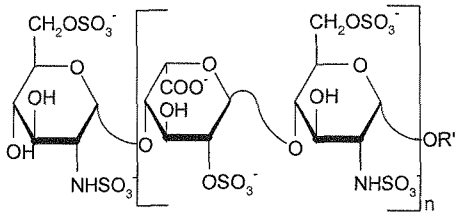
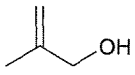
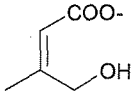
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and

(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or 

n is an integer from 2 to 20

(iii) having a distribution of polysaccharides and their corresponding molecular mass expressed as cumulative % of weight according to the table:

Molecular mass, kDa	Cumulative weight, %
>10	4-15
>8	10-25
>6	22-45
>3	>70

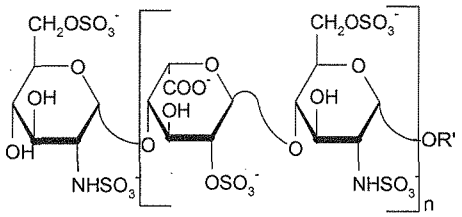
~~wherein the modified heparin or heparan sulfate comprises non-reducing end unsaturated glucosamines that are presented as signals in the interval of 5.0 to 6.5 ppm in a ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4% in relation to the signal at 5.42 ppm from native heparin,~~

for use in combination with ~~an agent capable of promoting myometrial contractions of the uterus~~ oxytocin~~in the treatment of labor arrest~~ wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated with, oxytocin.

In another aspect, there is provided the use of a chemically modified heparin or heparan sulfate with an antifactor IIa activity of less than 10 IU/mg, an antifactor Xa activity of less than 10 IU/mg and an average molecular weight (Mw) from about 4.6 to about 6.9 kDa comprising:

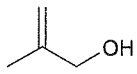
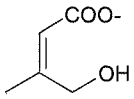
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and

(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or 

n is an integer from 2 to 20

(iii) having a distribution of polysaccharides and their corresponding molecular mass expressed as cumulative % of weight according to the table:

Molecular mass, kDa	Cumulative weight, %
>10	4-15
>8	10-25
>6	22-45
>3	>70

~~wherein the modified heparin or heparan sulfate comprise non-reducing end unsaturated glucosamines that are presented as signals in the interval of 5.0 to 6.5 ppm in a ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4% in relation to the signal at 5.42 ppm from native heparin,~~

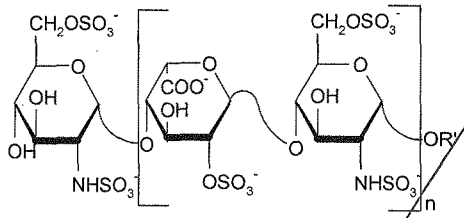
for manufacturing of a medicament for treatment of labor arrest in combination with oxytocin, ~~an agent capable of promoting myometrial contractions of the uterus~~ wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated with, oxytocin.

Brief description of the figures

Figure1 is a graph showing the delivery time in women who received oxytocin and have been treated with a chemically modified heparin or heparan sulfate according to the invention (DF01) or received placebo

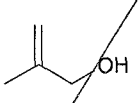
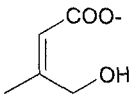
Claims

1. A chemically modified heparin or heparan sulfate with an antifactor IIa activity of less than 10 IU/mg, an antifactor Xa activity of less than 10 IU/mg and an average molecular weight (Mw) from about 4.6 to about 6.9 kDa comprising:
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and
(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or 

n is an integer from 2 to 20

wherein the modified heparin or heparan sulfate comprises non-reducing end unsaturated glucosamines that are presented as signals in the interval of 5.0 to 6.5 ppm in a ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4% in relation to the signal at 5.42 ppm from native heparin,

for use in combination with an agent capable of promoting myometrial contractions of the uterus in the treatment of labor arrest.

2. The chemically modified heparin or heparan sulfate for use according to claim 1, wherein the labor arrest is primary labor arrest.

3. The chemically modified heparin or heparan sulfate for use according to claim 1, wherein the labor arrest is secondary labor arrest.

4. The chemically modified heparin or heparan sulfate for use according to claim 3, wherein the secondary labor arrest is insufficient progress or a complete cessation of progress.

5. The chemically modified heparin or heparan sulfate for use according to claim 3, wherein the secondary labor arrest is due to cephalopelvic disproportion.

6. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-5, wherein the labor arrest appears in a woman who has been induced into labor.

7. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-6, wherein the labor arrest appears in a woman who is nulliparous.

8. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-7, wherein the agent capable of promoting myometrial contractions of the uterus is oxytocin.

9. The chemically modified heparin or heparan sulfate for use according any one of claims 1 to 8, wherein the predominantly occurring polysaccharide chains have between 6 and 12 disaccharide units with molecular weights from 3.6 to 7.2 kDa.

10. The chemically modified heparin or heparan sulfate for use according to any one of claims 1 to 9, wherein at least 70 % of the polysaccharide chains have a molecular weight above 3 kDa.

11. The chemically modified heparin or heparan sulfate for use according to any one of claims 1 to 10, having a distribution of polysaccharides and their corresponding molecular mass expressed as cumulative % of weight according to the table:

Molecular mass, kDa	Cumulative weight, %
>10	4-15
>8	10-25
>6	22-45
>3	>70

12. The chemically modified heparin or heparan sulfate for use according to any one of claims 1 to 11, wherein the modified glucosamine signals are presented at 5.95 ppm and 6.15 ppm in the ^{1}H-NMR spectrum.

13. The chemically modified heparin or heparan sulfate for use according to claim 12, modified glucosamines comprise less than 1% of the total glucosamine content.

14. The chemically modified heparin or heparan sulfate for use according to any one of claims 1 to 13, wherein the chemically modified heparin or heparan sulfate is essentially free of intact non-sulfated iduronic and/or glucuronic acids.

15. The chemically modified heparin or heparan sulfate for use according to anyone of claims 1-14, wherein the at least one chemically modified heparin or heparan sulfate is administered topically in a topical pharmaceutical preparation.

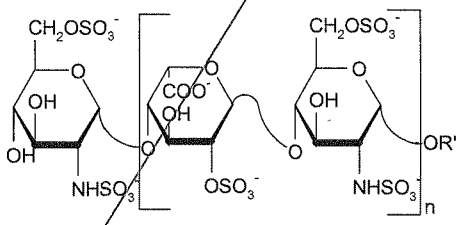
16. The chemically modified heparin or heparan sulfate for use according to anyone of claims 1-14, wherein the at least one chemically modified heparin or heparan sulfate is administered in a parenteral pharmaceutical preparation.

17. The chemically modified heparin or heparan sulfate for use according to any one of claims 1 to 16, wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated

with, another agent useful for promoting or stimulating myometrial contractions of the uterus.

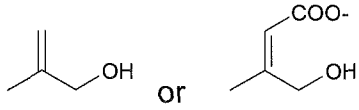
18. The chemically modified heparin or heparan sulfate for use according to claim 17, wherein the chemically modified heparin or heparan sulfate is administered intravenously every 1-4 hours adjunctively with a treatment with oxytocin for up to 36 hours.

19. Use of a chemically modified heparin or heparan sulfate with an antifactor IIa activity of less than 10 IU/mg, an antifactor Xa activity of less than 10 IU/mg and an average molecular weight (Mw) from about 4.6 to about 6.9 kDa comprising:
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and
(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or

n is an integer from 2 to 20

wherein the modified heparin or heparan sulfate comprise non-reducing end unsaturated glucosamines that are presented as signals in the interval of 5.0 to 6.5

ppm in a ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4% in relation to the signal at 5.42 ppm from native heparin,

for manufacturing of a medicament for treatment of labor arrest in combination with an agent capable of promoting myometrial contractions of the uterus.

20. The use according to claim 19, wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated with, another agent useful for promoting or stimulating myometrial contractions of the uterus.

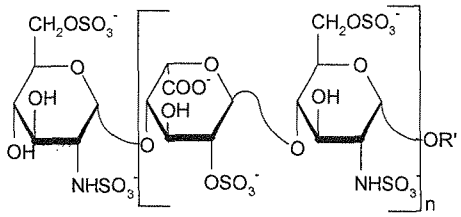
21. The use according to claim 19 or claim 20, wherein the chemically modified heparin or heparan sulfate is administered intravenously every 1-4 hours adjunctively with a treatment with oxytocin for up to 36 hours.

Claims

1. A chemically modified heparin or heparan sulfate with an antifactor IIa activity of less than 10 IU/mg, an antifactor Xa activity of less than 10 IU/mg, and an average molecular weight (Mw) from about 4.6 kDa to about 6.9 kDa, comprising:

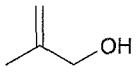
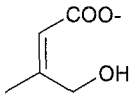
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and

(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or 

n is an integer from 2 to 20, and

(iii) having a distribution of polysaccharides and their corresponding molecular mass expressed as cumulative % of weight according to the table:

Molecular mass, kDa	Cumulative weight, %
>10	4-15
>8	10-25
>6	22-45
>3	>70

for use in combination with oxytocin, wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated

with, oxytocin.

2. The chemically modified heparin or heparan sulfate for use according to claim 1, wherein the labor arrest is primary labor arrest.

3. The chemically modified heparin or heparan sulfate for use according to claim 1, wherein the labor arrest is secondary labor arrest.

4. The chemically modified heparin or heparan sulfate for use according to claim 3, wherein the secondary labor arrest is insufficient progress or a complete cessation of progress.

5. The chemically modified heparin or heparan sulfate for use according to claim 3, wherein the secondary labor arrest is due to cephalopelvic disproportion.

6. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-5, wherein the labor arrest appears in a woman who has been induced into labor.

7. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-6, wherein the labor arrest appears in a woman who is nulliparous.

8. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-7, wherein the predominantly occurring polysaccharide chains have between 6 and 12 disaccharide units with molecular weights from 3.6 to 7.2 kDa.

9. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-8, comprising non reducing end unsaturated glucosamines present as signals in the interval of 5.0 to 6.5 ppm in an ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4 % in relation to the signal at 5.42 ppm from native heparin.

10. The chemically modified heparin or heparan sulfate for use according to claim 9, wherein the glucosamine signals are present at 5.95 ppm and 6.15 ppm.

11. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-10, wherein the chemically modified heparin or heparan sulfate is essentially free of intact non-sulfated iduronic and/or glucuronic acids.

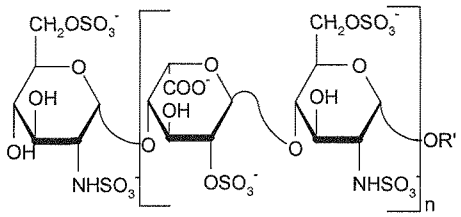
12. The chemically modified heparin or heparan sulfate for use according to any one of

claims 1-11, wherein the at least one chemically modified heparin or heparan sulfate is administered topically in a topical pharmaceutical preparation.

13. The chemically modified heparin or heparan sulfate for use according to any one of claims 1-12, wherein the at least one chemically modified heparin or heparan sulfate is administered in a parenteral pharmaceutical preparation.

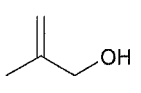
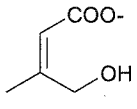
14. The chemically modified heparin or heparan sulfate for use according to claim any one of claims 1-13, wherein the chemically modified heparin or heparan sulfate is administered intravenously every 1-4 hours adjunctively with a treatment with oxytocin for up to 36 hours.

15. The use of chemically modified heparin or heparan sulfate with an antifactor IIa activity of less than 10 IU/mg, an antifactor Xa activity of less than 10 IU/mg, and an average molecular weight (Mw) from about 4.6 kDa to about 6.9 (±10%) kDa , comprising:
(i) polysaccharide chains essentially free of chemically intact saccharide sequences mediating the anticoagulant effect; and
(ii) polysaccharide chains corresponding to molecular weights between 1.2 and 12 kDa with a predominantly occurring disaccharide according to (Formula I),



(Formula I)

wherein,

R'=  or 

n is an integer from 2 to 20, and
(iii) having a distribution of polysaccharides and their corresponding molecular mass expressed as cumulative % of weight according to the table:

Molecular mass,	Cumulative weight,

kDa	%
>10	4-15
>8	10-25
>6	22-45
>3	>70

for manufacturing of a medicament for the treatment of labor arrest in combination with oxytocin, wherein the chemically modified heparin or heparan sulfate is administered as an add-on treatment to, and/or to a woman already being treated with, oxytocin.

16. The use according to claim 15, wherein the labor arrest is primary labor arrest.

17. The use according to claim 15, wherein the labor arrest is secondary labor arrest.

18. The use according to claim 17, wherein the secondary labor arrest is insufficient progress or a complete cessation of progress.

19. The use according to claim 17, wherein the secondary labor arrest is due to cephalopelvic disproportion.

20. The use according to any one of claims 15-19, wherein the labor arrest appears in a woman who has been induced into labor.

21. The use according to any one of claims 15-20, wherein the labor arrest appears in a woman who is nulliparous.

22. The use according to any one of claims 15-21, wherein the predominantly occurring polysaccharide chains have between 6 and 12 disaccharide units with molecular weights from 3.6 to 7.2 kDa.

23. The use according to any one of claims 15-22, comprising non reducing end unsaturated glucosamines present as signals in the interval of 5.0 to 6.5 ppm in an ^{1}H-NMR spectrum with an intensity (% ratio) of less than 4 % in relation to the signal at 5.42 ppm from native heparin.

24. The use according to claim 23, wherein the glucosamine signals are present at 5.95

ppm and 6.15 ppm.

25. The use according to any one of claims 15-24, wherein the chemically modified heparin or heparan sulfate is essentially free of intact non-sulfated iduronic and/or glucuronic acids.

26. The use according to any one of claims 15-25, wherein the medicament is administered topically in a topical pharmaceutical preparation.

27. The use according to any one of claims 15-26, wherein the medicament is administered in a parenteral pharmaceutical preparation.

28. The use according to any one of claims 15-27, wherein the medicament is administered intravenously every 1-4 hours adjunctively with a treatment with oxytocin for up to 36 hours.