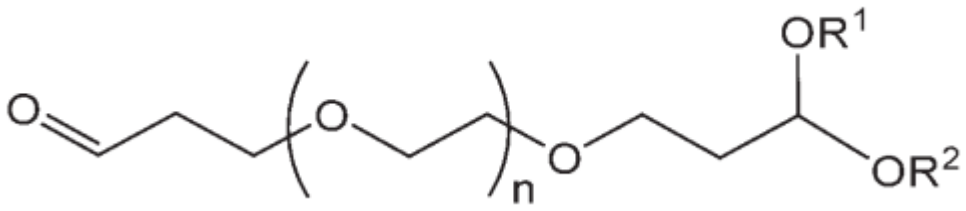
Claims

1. A polyethylene glycol derivative compound of Formula 1:

Formula 1



wherein, in Formula 1, n is a natural number of 30 to 115, and

R^1 and R^2 are C_1-C_5 alkyl that are identical to or different from each other.

2. The polyethylene glycol derivative compound of claim 1, wherein

the C_1 to C_5 alkyl is methyl, ethyl, propyl, or butyl.

3. The polyethylene glycol derivative compound of claim 1, wherein

R^1 and R^2 are each ethyl.

4. The polyethylene glycol derivative compound of any one of claims 1 to 3, wherein

n is a natural number from 50 to 100.

5. The polyethylene glycol derivative compound of claim 4, wherein

n is a natural number from 67 to 83.

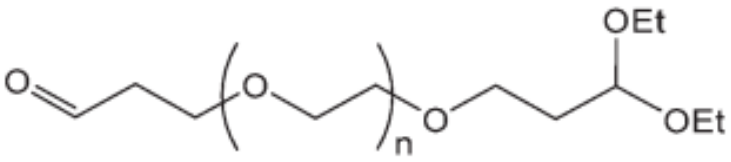
6. A polyethylene glycol derivative composition comprising:

a polyethylene glycol derivative represented by Formula 1A;

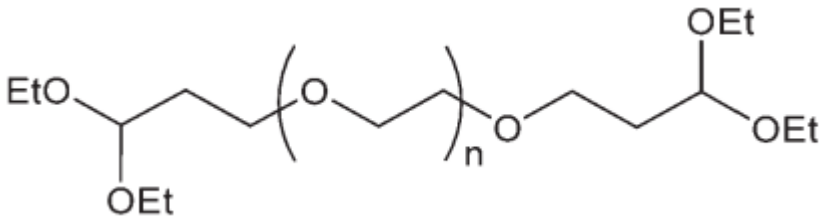
a polyethylene glycol derivative represented by Formula 2; and

a polyethylene glycol derivative represented by Formula 3:

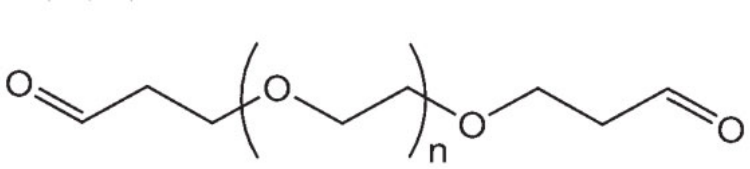
Formula 1A



Formula 2



Formula 3

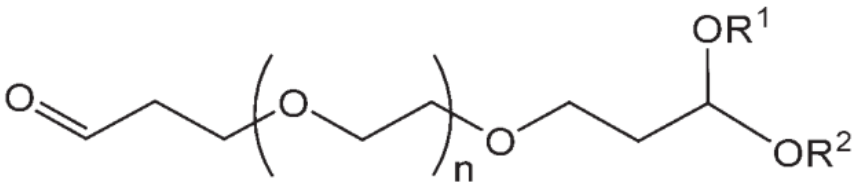


wherein, in the polyethylene glycol derivative composition,
a content ratio of the polyethylene glycol derivative represented by Formula 1A within a range of number average molecular weight of 2950 to 3650 g/mol is at least 70 area% based on high performance liquid chromatography (HPLC),
a content ratio of the polyethylene glycol derivative represented by Formula 2 within a range of number average molecular weight of 2950 to 3650 g/mol is 15 area% or less based on HPLC,
a content ratio of the polyethylene glycol derivative represented by Formula 3 within a range of number average molecular weight of 2950 to 3650 g/mol is 10 area% or less based on HPLC, and
n is a natural number of 30 to 115 in Formula 1A, 2 and 3.

7. The polyethylene glycol derivative composition of claim 6, wherein the number average molecular weight of the polyethylene glycol derivative is in a range of 2950 to 3650 g/mol, the measurements obtained by gel permeation chromatography.

8. The polyethylene glycol derivative composition of claim 7, wherein the number average molecular weight of the polyethylene glycol derivative is in a range of 3000 to 3200 g/mol, the measurements obtained by gel permeation chromatography.

9. A method of preparing a physiologically active polypeptide conjugate, the method comprising:
(a) a pegylation process in which a polyethylene glycol derivative of Formula 1 is reacted with a physiologically active polypeptide to generate a linkage in which the physiologically active polypeptide is covalently conjugated with an aldehyde carbon of the polyethylene glycol derivative of Formula 1;
(b) a hydrolysis process in which the linkage is treated in an acidic aqueous condition to form a linkage hydrolyzate; and
(c) a conjugation process in which the linkage hydrolyzate is reacted with an immunoglobulin Fc fragment or a derivative thereof to generate a conjugate, wherein the conjugate has a structure in which the Fc fragment or the derivative thereof is covalently conjugated with a carbon atom derived from an acetal carbon of the polyethylene glycol derivative of Formula 1 in the linkage hydrolyzate:
Formula 1



wherein, in Formula 1, n is a natural number of 50 to 100, and
R^1 and R^2 are C_1-C_5 alkyl that are identical to or different from each other.

10. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

the physiologically active polypeptide is selected from hormones, cytokines, enzymes, antibodies, growth factors, transcriptional regulators, blood coagulation factors, vaccines, structural proteins, ligand proteins, and receptors.

11. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

the reaction of process (a) is reductive amination, and

the linkage is a material in which an N-terminal nitrogen of the physiologically active polypeptide or a nitrogen atom of an ε-amino group of lysine is covalently conjugated with the aldehyde carbon atom of the compound of Formula 1.

12. The method of preparing a physiologically active polypeptide conjugate of claim 11, wherein

the pegylation of process (a) is carried out at a pH of 3.0 to 9.0.

13. The method of preparing a physiologically active polypeptide conjugate of claim 11, wherein

the hydrolysis in process (b) is performed at a pH of 1.0 to 5.0.

14. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

the conjugation reaction in process (c) is reductive amination.

15. The method of preparing a physiologically active polypeptide conjugate of claim 14, wherein

the reductive amination is carried out at a pH of 5.0 to 8.5.

16. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

the sequence of the Fc fragment or the derivative thereof at the N-terminus is proline.

17. The method of preparing a physiologically active polypeptide conjugate of claim 16, wherein

in the conjugate, a nitrogen atom of the N-terminal proline of the Fc fragment or the derivative thereof is covalently conjugated with a carbon atom derived from the acetal carbon.

18. The method of preparing a physiologically active polypeptide conjugate of claim 17, wherein

the Fc fragment or the derivative thereof has a SEQ ID NO: 2.

19. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

R^1 and R^2 are each ethyl.

20. The method of preparing a physiologically active polypeptide conjugate of claim 9, wherein

n is a natural number from 67 to 83.