[0006] In an additional embodiment, the invention is directed to a method of preparing powdered exosomes. The method comprises centrifuging bovine milk to form a lipid fraction top layer, a whey fraction middle layer, and a first pellet of cells and debris, separating the whey fraction and centrifuging the separated whey fraction to remove additional fat, casein aggregates and debris and form a substantially clear whey fraction, microfiltering the substantially clear whey fraction to remove residual debris, centrifuging the microfiltered whey fraction to obtain a pellet containing exosomes, incubating the exosome-containing pellet in aqueous medium to dissolve the pellet without disrupting exosome bilayer membranes to provide an exosome suspension, and drying the suspension to obtain the powdered exosomes.

[0007] In another embodiment, the invention is directed to a method of preparing a powdered nutritional composition. The method comprises dry blending a powder composition comprising protein, fat, and carbohydrate with powdered exosomes isolated from bovine milk.

[0008] In further embodiments, the invention is directed to a method of lowering a risk of developing insulin resistance, prediabetes, or diabetes in a subject, or treating insulin resistance, prediabetes, or diabetes in a subject. The method comprises administering to a subject at risk of developing, or having, insulin resistance, prediabetes, or diabetes the exosomes according to the invention or the nutritional composition of the invention, wherein the administered amount of exosomes is effective to lower the risk of development of, or treat, respectively, insulin resistance, prediabetes, or diabetes.

[0008a] In one aspect, provided herein is a composition comprising bovine milk-isolated powdered exosomes comprising intact exosomes, wherein at least 50 wt % of the bovine milk-isolated powdered exosomes in the composition are intact.

[0008b] In another aspect, provided herein is a nutritional composition comprising protein, carbohydrate, and/or fat, and bovine milk-isolated exosomes, wherein the exosomes are provided by addition of the composition as described herein.

[0008c] In another aspect, provided herein is bovine milk-isolated powdered exosomes comprising intact exosomes, wherein at least 50 wt % of the bovine milk-isolated powdered exosomes in the composition are intact, obtainable by the method comprising: centrifuging bovine milk to form a lipid fraction top layer, a whey fraction middle layer, and a first pellet of cells and debris; separating the whey fraction and centrifuging the separated whey fraction to remove additional fat, casein aggregates and debris and form a substantially clear whey fraction; microfiltering the substantially clear whey fraction to remove residual debris; centrifuging the microfiltered whey fraction to obtain a pellet containing exosomes; incubating the exosome-containing pellet in aqueous medium to dissolve the pellet without disrupting exosome membranes to provide an exosome suspension; and drying the suspension to obtain the powdered exosomes.

[0008d] In another aspect, provided herein is a use of the nutritional composition as described herein, or the composition as described herein, in the manufacture of a medicament for lowering

a risk of developing insulin resistance, prediabetes, or diabetes in a subject, or treating insulin resistance, prediabetes, or diabetes in a subject.

[0008e] In another aspect, provided herein is the nutritional composition as described herein, or the composition as described herein for use in therapy.

[0009] The bovine milk-isolated exosomes of the invention are advantageous in providing bioactive agents in a convenient and stable form, and, in certain embodiments, in a nutritional

WHAT IS CLAIMED IS:

1. A composition comprising bovine milk-isolated powdered exosomes comprising intact exosomes, wherein at least 50 wt % of the bovine milk-isolated powdered exosomes in the composition are intact.

2. The composition of claim 1, wherein the intact exosomes comprise miRNA.

3. The composition of claim 2, wherein, after storage at 37°C for 3 weeks, the bovine milk-isolated powdered exosomes comprise a greater amount of miRNA than fresh milk exosomes stored at 37°C for 3 weeks.

4. The composition of any one of claims 1-3, wherein the bovine milk-isolated powdered exosomes comprise freeze dried intact exosomes.

5. The composition of any one of claims 1-4, wherein greater than 90% of the exosomes in the composition are from about 10 nanometers to about 250 nanometers in diameter.

6. A nutritional composition comprising protein, carbohydrate, and/or fat, and bovine milk-isolated exosomes, wherein the exosomes are provided by addition of the composition of any one of claims 1-5.

7. The nutritional composition of claim 6, comprising from about 0.001 to about 10 wt % of the bovine milk-isolated exosomes, based on the weight of the nutritional composition.

8. The nutritional composition of claim 6 or 7, wherein the protein comprises milk protein and/or soy protein.

9. The nutritional composition of any one claims 6-8, wherein the carbohydrate comprises fiber.

10. The nutritional composition of any one of claims 6-9, wherein the fat comprises at least one omega-3 fatty acid.

11. The nutritional composition of claim 10, wherein the at least one omega-3 fatty acid of the composition is selected from the group consisting of eicosapentaenoic acid, docosahexaenoic acid, arachidonic acid, and alpha-linolenic acid.

12. The nutritional composition of any one of claims 6-11, wherein the nutritional composition is in the form of a powder.

13. The nutritional composition of any one of claims 6-11, wherein the nutritional composition is in the form of a liquid.

14. Bovine milk-isolated powdered exosomes comprising intact exosomes, wherein at least 50 wt % of the bovine milk-isolated powdered exosomes in the composition are intact, obtainable by the method comprising:

centrifuging bovine milk to form a lipid fraction top layer, a whey fraction middle layer, and a first pellet of cells and debris;

separating the whey fraction and centrifuging the separated whey fraction to remove additional fat, casein aggregates and debris and form a substantially clear whey fraction;

microfiltering the substantially clear whey fraction to remove residual debris;

centrifuging the microfiltered whey fraction to obtain a pellet containing exosomes;

incubating the exosome-containing pellet in aqueous medium to dissolve the pellet without disrupting exosome membranes to provide an exosome suspension; and drying the suspension to obtain the powdered exosomes.

15. Use of the nutritional composition according to any one of claims 6-13, or the composition of any one of claims 1-5, in the manufacture of a medicament for lowering a risk of developing insulin resistance, prediabetes, or diabetes in a subject, or treating insulin resistance, prediabetes, or diabetes in a subject.

16. The use of claim 15, wherein the subject is obese or has sarcopenia.

17. The nutritional composition according to any one of claims 6-13, or the composition of any one of claims 1-5 for use in therapy.