CLAIMS

What is claimed is:

1. A method for preparing a compound bitter melon peptide (BMP) oral medicine for activating insulin and treating diabetes,

wherein the compound BMP oral medicine comprises 20-30 parts by weight of BMP powder comprising 30% or more by weight of BMP;

4-6 parts by weight of *Panax quinquefolius*;

10-12 parts by weight of *Astragalus membranaceus*;

3-5 parts by weight of *Ganoderma lucidum* powder;

8-10 parts by weight of *Dioscorea opposita* powder;

10-15 parts by weight of wheat bran;

10-12 parts by weight of *Psidium guajava* leaf powder;

5-10 parts by weight of an onion extract;

5-10 parts by weight of *Lycium barbarum*;

12-15 parts by weight of a *Gynura procumbens* extract;

1-2 parts by weight of coix seed;

5-8 parts by weight of konjac glucomannan;

8-10 parts by weight of lotus leaf; and

5-8 parts by weight of a xylo-oligosaccharide;

characterized in that the method comprises:

(S100) preparing the BMP powder through steps of:

(S11) soaking a raw material in deionized water at 25°C for 10-12 h, wherein the raw material is selected from the group consisting of fresh bitter melon, dried bitter melon, bitter melon seeds and a combination thereof, and a weight ratio of the raw material to the deionized water is 1:5; and taking out the raw material followed by washing with deionized water 2-3 times;

(S12) drying the raw material followed by crushing and grinding to obtain a pulp;

(S13) mixing the pulp with a buffer solution to obtain a mixed system, and

recording a volume of the mixed system as an initial volume, wherein a weight ratio of the pulp to the buffer solution is 1:(3-5); and adjusting the mixed system to pH 6.8-7 followed by temperature treatment to obtain a bitter melon extract;

wherein the temperature treatment comprises steps of:

(S131) heating the mixed system to 45-55°C and keeping the mixed system at 45-55°C for 45-60 min; cooling the mixed system to 20-25°C, and keeping the mixed system at 20-25°C for 25-30 min; recording a volume of the mixed system at this time as a first volume;

(S132) introducing a first mixed solution to the mixed system, wherein the first mixed solution is composed of deionized water and the buffer solution in a weight ratio of 4:1, and a volume of the first mixed solution is 60% of a difference between the initial volume and the first volume; heating the mixed system to 60-75°C, and keeping the mixed system at 60-75°C for 60-75 min; cooling the mixed system to 45-55°C and keeping the mixed system at 45-55°C for 30-35 min; recording a volume of the mixed system at this time as a second volume; and

(S133) introducing a second mixed solution to the mixed system, wherein the second mixed solution is composed of deionized water and the buffer solution in a weight ratio of 3:1, and a volume of the second mixed solution is 75% of a difference between the initial volume and the second volume; heating the mixed system to 80-90°C, and keeping the mixed system at 80-90°C for 75-85 min; and cooling the mixed system to 60-75°C and keeping the mixed system at 60-75°C for 35-45 min;

(S14) cooling the bitter melon extract to 20-25°C followed by enzymatic hydrolysis to obtain an enzymatic hydrolysis product;

wherein the enzymatic hydrolysis comprises steps of:

adjusting the extract to pH 7.5-8.5; adding trypsin to the extract followed by heating to 35-40°C under stirring at 80-100 rpm and keeping at 35-40°C for 45-60 min to obtain a first enzymatic hydrolysis system, wherein the trypsin is 5% by weight of the extract;

cooling the first enzymatic hydrolysis system to 20-25°C, and adjusting the first enzymatic hydrolysis system to pH 3.0-4.0; adding pectinase to the first enzymatic

hydrolysis system followed by heating to 45-55°C under stirring at 80-100 rpm and keeping at 45-55°C for 40-60 min to obtain a second enzymatic hydrolysis system, wherein the pectinase is 3% by weight of the first enzymatic hydrolysis system; and

cooling the second enzymatic hydrolysis system to 20-25°C followed by adjustment to pH 4.5-5.0; and adding a cellulase to the second enzymatic hydrolysis system followed by heating to 55-60°C under stirring at 80-100 rpm and keeping at 55-60°C for 30-45 min to obtain the enzymatic hydrolysis product, wherein the cellulase is 2% by weight of the second enzymatic hydrolysis system;

(S15) heating the enzymatic hydrolysis product to 90°C followed by keeping at 90°C for 10 min for inactivation, so as to obtain a crude BMP extraction system; adding activated carbon to the crude BMP extraction system followed by uniform stirring, wherein the activated carbon is 4-5% by weight of the crude BMP extraction system; and keeping the crude BMP extraction system at 65°C for 60-90 min followed by centrifugation to collect a first supernatant;

filtering the first supernatant with diatomite at a pressure of 0.2-0.3 MPa to obtain a first filtrate; and adding activated carbon to the first filtrate followed by standing for 45-50 min and centrifugation to collect a second supernatant, wherein the activated carbon is 4-5% by weight of the first filtrate;

(S16) filtering the second supernatant with a ceramic microfiltration membrane having a pore size of 0.5-0.8 μm at 55-65°C to obtain a second filtrate;

filtering the second filtrate with a spiral-wound ultrafiltration membrane at 45-50°C to obtain a third filtrate, wherein the spiral-wound ultrafiltration membrane has a molecular weight cut-off of 100-200 kDa; and

concentrating the third filtrate via a spiral-wound reverse-osmosis membrane with a molecular weight cut-off of 150-1000 Da at a temperature below 40°C to remove water, residual inorganic salts and small molecular impurities, so as to obtain a BMP concentrate; and

(S17) subjecting the BMP concentrate to vacuum freeze drying to obtain the BMP powder.

2. The method according to claim 1, characterized in that the compound BMP oral medicine comprises:

20 parts by weight of the BMP powder;

4 parts by weight of *Panax quinquefolius*;

10 parts by weight of *Astragalus membranaceus*;

3 parts by weight of the *Ganoderma lucidum* powder;

8 parts by weight of the *Dioscorea opposita* powder;

10 parts by weight of wheat bran;

10 parts by weight of the *Psidium guajava* leaf powder;

5 parts by weight of the onion extract;

5 parts by weight of *Lycium barbarum*;

12 parts by weight of the *Gynura procumbens* extract;

1 part by weight of coix seed;

5 parts by weight of konjac glucomannan;

8 parts by weight of lotus leaf; and

5 parts by weight of the xylooligosaccharide.

3. The method according to claim 1, characterized in that the compound BMP oral medicine comprises:

30 parts by weight of the BMP powder;

6 parts by weight of *Panax quinquefolius*;

12 parts by weight of *Astragalus membranaceus*;

5 parts by weight of the *Ganoderma lucidum* powder;

10 parts by weight of the *Dioscorea opposita* powder;

15 parts by weight of wheat bran;

12 parts by weight of the *Psidium guajava* leaf powder;

10 parts by weight of the onion extract;

10 parts by weight of *Lycium barbarum*;

15 parts by weight of the *Gynura procumbens* extract;

2 parts by weight of coix seed;

8 parts by weight of konjac glucomannan;

10 parts by weight of lotus leaf; and

8 parts by weight of the xylo-oligosaccharide.

4. The method according to claim 1, characterized in that the compound BMP oral medicine comprises:

25 parts by weight of the BMP powder;

5 parts by weight of *Panax quinquefolius;*

11 parts by weight of *Astragalus membranaceus*;

4 parts by weight of *the Ganoderma lucidum powder*;

9 parts by weight of *the Dioscorea opposita powder*;

12 parts by weight of wheat bran;

11 parts by weight of the *Psidium guajava* leaf powder;

7 parts by weight of the onion extract;

8 parts by weight of *Lycium barbarum*;

13 parts by weight of the *Gynura procumbens* extract;

1.5 parts by weight of coix seed;

7 parts by weight of konjac glucomannan;

9 parts by weight of lotus leaf; and

7 parts by weight of the xylo-oligosaccharide.

5. The method according to claim 4, characterized in that in step (S11), the raw material is soaked at 25°C for 10.5 h.

6. The method according to claim 4, characterized in that in step (S13), the weight ratio of the pulp to the buffer solution is 1:4.

7. The method according to claim 4 or 6, characterized in that in step (S131), the mixed system is heated to 50°C, kept at 50°C for 55 min, cooled to 22°C and kept at 22°C for 28 min;

in step (S132), after the first mixed solution is added, the mixed system is heated to 65°C, kept at 65°C for 65 min, cooled to 50°C and kept at 50°C for 32 min; and in step (S133), after the second mixed solution is added, the mixed system is heated to 85°C, kept at 85°C for 80 min, cooled to 70°C and kept at 70°C for 40 min.

8. The method according to claim 1, characterized in that the buffer solution is phosphate buffered saline (PBS).

9. The method according to any one of claims 1-4, characterized in that step (S100) further comprises:

preparing the *Gynura procumbens* extract is prepared through steps of:

(S21) selecting a *Gynura procumbens* plant without mildew, spots, diseases and insect pests followed by washing and drying at 100°C in an oven for 60-90 min; and crushing a dried *Gynura procumbens* plant followed by sieving with a 30-50 mesh sieve to obtain *Gynura procumbens* powder;

(S22) mixing the *Gynura procumbens* powder, an enzyme and water in a weight ratio of 1:0.5:30 followed by stirring to obtain a mixed system, recording a weight of the mixed system as initial weight; and subjecting the mixed system to temperature treatment to obtain an enzymatic hydrolysis product;

wherein the temperature treatment comprises steps of:

(S221) heating the mixed system to 35-45°C, and keeping the mixed system at 35-45°C for 45-60 min; cooling the mixed system to 20-25°C, and keeping the mixed system at 20-25°C for 25-30 min; and recording a weight of the mixed system at this time as first weight;

(S222) adding a first mixed solution to the mixed system, wherein the first mixed solution is composed of deionized water and ligninase in a weight ratio of 1:0.03, and a weight of the first mixed solution is 50% of a difference between the initial weight and the first weight; heating the mixed system to 50-55°C, and keeping the mixed system at 50-55°C for 60-75 min; cooling the mixed system to 35-55°C and keeping the mixed system at 35-55°C for 30-35 min; and recording a weight of the

mixed system at this time as second weight;

(S223) adding a second mixed solution to the mixed system, wherein the second mixed solution is composed of deionized water and cellulase in a weight ratio of 1:0.05, and a weight of the second mixed solution is 50% of a difference between the initial weight and the second weight; heating the mixed system to 55-60°C, and keeping the mixed system at 55-60 °C for 45-60 min; cooling the mixed system to 35-40°C, and keeping the mixed system at 35-40°C for 30-40 min, and recording a weight of the mixed system at this time as third weight; and

(S224) adding a third mixed solution to the mixed system, wherein the third mixed solution is composed of deionized water and pectinase in a weight ratio of 1:0.04, and a weight of the third mixed solution is 50% of a difference between the initial weight and the third weight; heating the mixed system to 45-50°C and keeping the mixed system at 45-50°C for 60-70 min; and cooling the mixed system to 20-25°C, and keeping the mixed system at 20-25°C for 30-35 min to obtain the enzymatic hydrolysis product;

(S23) filtering the enzymatic hydrolysis product to obtain a first filtrate and a first filter residue;

(S24) subjecting the first filter residue to ultrasonic extraction in a first solution at 30-35°C and an ultrasonic power of 100 KW for 35-45 min followed by vacuum filtration to obtain a second filtrate and a second filter residue, wherein the first solution is a 60%(v/v) ethanol solution, and a weight ratio of the first filter residue to the first solution is 1:(20-25);

subjecting the second filter residue to ultrasonic extraction in a second solution at 30-35°C and an ultrasonic power of 100 KW for 20-30 min followed by vacuum filtration to obtain a third filtrate and a third filter residue, wherein the second solution is a 60%(v/v) ethanol solution, and a weight ratio of the second filter residue to the second solution is 1:(15-20); and

combining the first filtrate, the second filtrate and the third filtrate to obtain a *Gynura procumbens* crude extract; and

(S25) subjecting the *Gynura procumbens* crude extract to separation and

purification through simulated moving bed chromatography to obtain a purified *Gynura procumbens* extract; concentrating the purified *Gynura procumbens* extract via a vacuum concentrator at 70-75°C to obtain a *Gynura procumbens* concentrate; subjecting the *Gynura procumbens* concentrate to spray drying by using a spray dryer to obtain the *Gynura procumbens* extract, wherein an inlet air temperature of the spray dryer is 120-130°C and an outlet air temperature of the spray dryer is 40-50°C.

10. The method according to claim 9, characterized in that in step (S221),

the mixed system is heated to 40°C, kept at 40°C for 50 min, cooled to 20-25°C, and kept at 20-25°C for 25-30 min;

in step (S222), after the first mixed solution is added, the mixed system is heated to 52°C, kept at 52°C for 65 min, cooled to 45°C and kept at 45°C for 30-35 min;

in step (S223), after the second mixed solution is added, the mixed system is heated to 55-60 °C, kept at 55-60 °C for 50 min, cooled to 37°C, and kept at 37°C for 35 min; and

in step (S224), after the third mixed solution is added, the mixed system is heated to 45-50°C, kept at 45-50°C for 60-70 min, cooled to 20-25°C, and kept at 20-25°C for 30-35 min.

11. A method according to any one of claims 1-3, further comprising:

(S200) weighing individual ingredients of the compound BMP oral medicine;

(S300) immersing *Panax quinquefolius*, *Astragalus membranaceus*, the *Ganoderma lucidum* powder, the *Dioscorea opposita* powder, the wheat bran, the *Psidium guajava* leaf powder, the onion extract, coix seed, lotus leaf and *Lycium barbarum* in water for 5-8 h followed by boiling for 1-2 h and filtration to obtain a first filtrate and a first filter residue, wherein a ratio of a total weight of the *Panax quinquefolius*, *Astragalus membranaceus*, *Ganoderma lucidum* powder, *Dioscorea opposita* powder, wheat bran, *Psidium guajava* leaf powder, onion extract, coix seed, lotus leaf and *Lycium barbarum* to a weight of the water is 1:(5-8);

(S400) drying the first filter residue; and soaking the first filter residue in a

70%(v/v) ethanol solution for 1-2 h followed by heating to 55-65°C, extraction for 1.5-2 h, standing at 6-9°C for 24 h and filtration to obtain a second filtrate and a second filter residue, wherein a weight ratio of the first filter residue to the 70%(v/v) ethanol solution is 1:(2-3), and during the extraction, stirring is performed once every 10 min at 200-250 rpm;

(S500) soaking the second filter residue in a 70%(v/v) ethanol solution for 3-5 h followed by heating to 60-70°C, extraction for 2.5-3 h each for 1-2 h, standing at 6-9°C for 24 h and filtration to obtain a third filtrate and a third filter residue, wherein a weight ratio of the second filter residue to the 70%(v/v) ethanol solution is 1:(0.8-1); and combining the first filtrate, the second filtrate, and the third filtrate;

(S600) filtering a combined filtrate with an ultrafiltration membrane having a molecular weight cut-off of 6000-10000Da, or with diatomite to obtain a fourth filtrate; adding the BMP powder and *Gynura procumbens* extract to the fourth filtrate to obtain a raw material mixture; and subjecting the raw material mixture to vacuum concentration at 50-60°C in a vacuum concentration tank to obtain a concentrate with a relative density of 1.10-1.15 at 80°C; and

(S700) mixing the concentrate, the konjac glucomannan and the xylo-oligosaccharide in a compounding tank under stirring followed by boiling to obtain the compound BMP oral medicine with a relative density of 1.05-1.10 at 60°C.

12. The method according to claim 11, characterized in that the step (S600) further comprises:

subjecting the concentrate to standing at 4°C for 36 h or more and centrifugation at 15000-18000 rpm for 3 -5 min.