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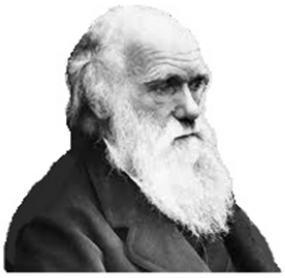

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Study on the preparation of a compound based on five traditional Chinese medicines and its *in vivo* hypoglycenic activity

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ABSTRACT

In this work, we obtained the water extracts of *Dendrobium officinale* Kimura et Migo, *Astragalus membranaceus* (Fisch.) Bunge, the leaves of *Morus alba* L., *Pueraria lobata* (Willd.) Ohwi, *Panax notoginseng* (Burk) F. H. Chen. Respectively. Then, we made a compound with these water extracts of *Dendrobium officinale* Kimura et Migo (13.33 %), *Astragalus membranaceus* (Fisch.) Bunge (29.17 %), the leaves of *Morus alba* L. (12.5 %), *Pueraria lobata* (Willd.) Ohwi (20.83 %), *Panax notoginseng* (Burk) F. H. Chen (6.95 %), accessory materials (17.22 %). Subsequently, we tested its *in vivo* hypoglycenic activity, and the results showed that this compound can reduce the blood sugar of the model mouse without toxicity.

***Keywords*:** *Dendrobium officinale* Kimura et Migo, *Astragalus membranaceus* (Fisch.) Bunge, the leaves of *Morus alba* L., *Pueraria lobata* (Willd.) Ohwi, *Panax notoginseng* (Burk) F. H. Chen, water extract, compound, hypoglycenic activity

1. INTRODUCTION

Diabetes mellitus(MD) is a non-communicable metabolic disorder that is chronic where there is derangement of insulin action, secretion, or both. A lack of Insulin results in disturbed carbohydrate, protein, and fat metabolism. There are genetic and environmental factors at play

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for the development of diabetes mellitus. The decrease in insulin secretion, reduction in glucose utilization, or increased gluconeogenesis ultimately result in hyperglycemia and harmful changes in different organs [1, 2].

The diabetes mellitus (MD) are generally classified as two types (type 1 and type 2 diabetes). At present, The diabetes mellitus (MD) is globally becoming increasingly prevalent in the general population. Especially, it is becoming increasingly in the young persons. It is estimated that approximately 537 million pepole globally have DM. Every year there are 1.6 million fatalities linked directly to diabetes. As per data obtained in studies done throughout the world, an estimation has been made by the International Diabetes Federation that by the year 2045, there will be about 693 million cases of diabetes in the age range of 18-99 years [3].

Long term high blood sugar can lead to chronic damage and dysfunction of various tissues: such as the eyes, kidneys, heart, blood vessels, and nerves. So it is very essential to develop hypoglycemic drugs.

Traditional Chinese medicines are usually used in clinics for a long history, and it is a trend to development of hypoglycemic drugs from Traditional Chinese medicines, especially from the medicinal and edible homologous plants.

Dendrobium officinale Kimura et Migo, *Astragalus membranaceus* (Fisch.) Bunge, the leaves of *Morus alba* L., *Pueraria lobata* (Willd.) Ohwi, *Panax notoginseng* (Burk) F. H. Chen. are the five traditional Chinese plant medicines and they have a wide spectrum of biological activities [4-20]. The Notice of the Ministry of Health on Further Standardizing the Management of Health Food Raw Materials lists them as the materials that can be used for health food.

Thus, in this work, we mainly obtained the water extracts of these five plant medicines, and then made a compound with different ratio of the extracts for the developent of hypoglycemic drugs.

2. EXPERIMENTAL SECTION

2. 1. Materials and instruments

Dendrobium officinale Kimura et Migo was obtained from Xiamen Tasman Bio-Tech Co. Ltd.), *Astragalus membranaceus* (Fisch.) Bunge, the leaves of *Morus alba* L., *Pueraria lobata* (Willd.) Ohwi, *Panax notoginseng* (Burk) F. H. Chen were marketable availability, other reagents are analytical pure and marketable availability.

2. 2. Experimental processes for extracts

2. 2. 1. The water extract for *Dendrobium officinale* Kimura et Migo

12 g powdered *Dendrobium officinale* Kimura et Migo was added into a 150 mL round-bottom flask. Subsequently, 100 mL pure water was added and the mixture was reflux at 90 °C for 3h.

Then, the water layer was removed. The residue was extracted as the above process for twice. The water layers were combined and concentrated under the reduced pressure to 50 mL. Then, it was dried by freezing spray method to obtain 1.92 g light yellow solid (marked **A**). The yield is 16%.

2. 2. 2. The water extract for *Astragalus membranaceus* (Fisch.) Bunge

14 g powdered *Astragalus membranaceus* (Fisch.) Bunge was added into a 150 mL round-bottom flask. Subsequently, 100 mL pure water was added and the mixture was reflux at 90 °C for 3h. Then, the water layer was removed. The residue was extracted as the above process for twice.

The water layers were combined and concentrated under the reduced pressure to 50 mL. Then, it was dried by freezing spray method to obtain 4.2 g light yellow solid (marked **B**). The yield is 30%.

2. 2. 3. The water extract for the leaves of *Morus alba* L.

10 g powdered leaves of *Morus alba* L. was added into a 150 mL round-bottom flask. Subsequently, 100 mL pure water was added and the mixture was reflux at 90 °C for 3h. Then, the water layer was removed. The residue was extracted as the above process for twice. The water layers were combined and concentrated under the reduced pressure to 50 mL. Then, it was dried by freezing spray method to obtain 1.8 g dark green solid (marked **C**). The yield is 18%.

2. 2. 4. The water extract for *Pueraria lobata* (Willd.) Ohwi

12 g powdered *Pueraria lobata* (Willd.) Ohwi was added into a 150 mL round-bottom flask. Subsequently, 100 mL pure water was added and the mixture was reflux at 90 °C for 3h. Then, the water layer was removed.

The residue was extracted as the above process for twice. The water layers were combined and concentrated under the reduced pressure to 50 mL. Then, it was dried by freezing spray method to obtain 3.0 g white solid (marked **D**). The yield is 25%.

2. 2. 5. The water extract for *Panax notoginseng* (Burk) F. H. Chen

4 g powdered *Panax notoginseng* (Burk) F. H. Chen was added into a 150 mL round-bottom flask. Subsequently, 100 mL pure water was added and the mixture was reflux at 90 °C for 3h. Then, the water layer was removed. The residue was extracted as the above process for twice. The water layers were combined and concentrated under the reduced pressure to 50mL. Then, it was dried by freezing spray method to obtain 1.0 g brown solid (marked **E**). The yield is 25%.

2. 3. The process for preparation of the compound

A (53.33 g), B (116.67 g), C (50.0 g), D (83.33 g), E (27.78 g), microcrystalline cellulose (64.49 g) and magnesium stearate (4.0 g) was added into a mixer, and the mixture was grinded and mixed evenly to obtain the compound. Then, the compound was made into 1000 particles, and each particle is 0.4g(containing 0.0533g **A**, 0.11667g **B**, 0.05g **C**, 0.08333g **D**, and 0.02778g **E**).

2. 4. Hypoglycemic activity test

The hypoglycemic activity was finished by the Health Food Function Testing Center of the College of Applied Arts and Science of Beijing Union University. The detailed processes were listed below:

2. 4. 1. Acute oral toxicity test

The 20 Kunming mice (18-22g) with half male and half female were selected for experiment, and the mice were feeded to confirm that all mice are normal. Before experiment, the mice were fasted for 4 hours and only drank freely. During the experiment, the mice were free to consume food and water, and the compound was administered by gavage with the maximum concentration of 0.3 g/mL twice per day with an interval of 4 hours between each gavage, and the maximum gavage volume of 40 mL/kgBW, which is the 400 times the recommended dose for the humans.

After the last gavage, the mice were fasted for 2 hours, and they were observed for 14 days for recording their general state, weight changes, toxic signs, and death.

2. 4. 2. Hypoglycemic activity test

The 210 Kunming mice (25-28g) with half male and half female were selected for experiment, and the basic blood glucose value for the experimental mice is 6.9 ± 0.5 mmol/L. After being raised for a period and the mice have adapted to conditions, they were divided for three groups (The first group was conducted to investigate the effect of fasting blood glucose on normal mice; the second group was conducted to investigate the effect of fasting blood glucose on high glucose model mice; while the third group was conducted to investigate the effect of the glucose tolerance in high glucose model mice).

3. RESULTS AND DISCUSSION

3. 1. The acute oral toxic result

The acute oral toxic result was listed in **Table 1**. From **Table 1**, we can know that the experimental mice are normal and no poisoning and death occurred.

Table 1. The acute oral toxic result

Sex	Dose (g/kgBW)	Mice numbers	Changes of the body weight (X±SD)		Death numbers	MTD (g/kgBW)
			Initial weight (g)	Final weight (g)		
male	24.00	10	19.5±1.0	38.7±1.9	0	＞24.00
female	24.00	10	20.6±1.0	34.0±1.2	0	＞24.00

3. 3. The hypoglycemic results

3. 3. 1. The effect of the compound on the fasting blood glucose of normal mice

The effect of the compound on the fasting blood glucose of normal mice was listed in **Table 2**. From **Table 2**, we can know that there is no significant difference in blood glucose values between before and after the experiment for 32 days.

Table 2. The effect of the compound on the fasting blood glucose of normal mice.

Groups for different doses	Mice numbers	Blood glucose values (X±SD)				The percentage of blood glucose loss(%)	P value
		Before experiment	P value	After experiment	P value		
0 g/kgBW	12	7.1±0.5	–	7.6±0.9	–	-7.1±11.2	–
1.8 g/kgBW	12	7.1±0.7	0.808	7.8±0.6	0.513	-11.3±8.8	0.318

3. 3. 2. The effect of the compound on the fasting blood glucose of high glucose model mice

The effect of the compound on the fasting blood glucose of high glucose model mice was listed in **Table 3**. From **Table 3**, we can know that there is no significant difference in blood glucose values between before and after the experiment for 32 days.

Table 3. The effect of the compound on the fasting blood glucose of high glucose model mice.

Groups for different doses	Mice numbers	Blood glucose values (X±SD)				The percentage of blood glucose loss(%)	P value
		Before experiment	P value	After experiment	P value		
0 g/kgBW	12	13.4±3.1	–	15.1±3.0	–	-13.3±6.1	–
0.3 g/kgBW	12	13.4±3.3	1.000	15.0±3.4	1.000	-12.3±3.6	0.915
0.6 g/kgBW	12	13.5±3.4	1.000	14.8±3.3	0.990	-9.8±5.3	0.183
1.8 g/kgBW	12	13.5±3.3	1.000	14.7±3.1	0.984	-9.6±3.6	0.150

3. 3. 3. The effect of the compound on the fasting blood glucose of the model mice with glucose

The effect of the compound on the fasting blood glucose of the model mice with glucose was listed in **Table 4**. From **Table 4**, we can know that the blood glucose values reduced after oral administration of different doses of the compound to high glucose model mice for 32 days. This result proved that the compound in the high dose(1.8 g/kgBW) has hypoglycemic activity.

Table 4. The effect of the compound on the fasting blood glucose of the model mice with glucose

Groups for different doses	Mice numbers	Blood glucose values after administering glucose (mmol/L) (X±SD)					
		0h	P value	0.5h	P value	2h	P value
0 g/kgBW	12	15.0±3.2	–	27.0±3.4	–	17.5±3.2	–
0.3 g/kgBW	12	14.6±3.3	0.988	26.0±3.0	0.820	17.2±2.8	0.994
0.6 g/kgBW	12	14.8±3.3	0.998	25.4±3.0	0.548	16.7±2.9	0.865
1.8 g/kgBW	12	14.7±3.2	0.993	22.5±4.6	*0.009	16.5±3.3	0.778

4. CONCLUSION

From the above results, we can know that after oral administration of different doses of the compound to the hyperglycemic model mice for 32 days, this compound can reduce the blood glucose levels in hyperglycemic model mice that were administrated glucose at 1.8g/kgBW. However, this compound did not show toxicity to the experimental mice, and no effect on the weight and fasting blood glucose. This compound can be deeply developed for the development of sugar reducing snacks and beverages.

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