Hypoglycemic and Hypolipidemic Effects of *Melastoma dodecandrum ethanol-extract* on Type 2 Diabetic Rats

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Abstract. To observe hypoglycemic and hypolipidemic effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats. Except twelve SPF SD rats were as the control group, the rest eighty type 2 diabetic rats were induced by feeding with high-fat and high-sugar diet and intraperitoneal injection of low-dose streptozotocin (STZ,35mg ·kg^{-1}). According to the values of blood glucose concentration (≧11.1 mmol ·L^{-1}), the rats were randomly divided into diabetic model group, three Melastoma dodecandrum ethanol-extract groups of high dose (40g ·kg^{-1}), medium dose (20g ·kg^{-1}) and low dose (10g ·kg^{-1}), and positive control group (glibenclamide, 0.30mg ·kg^{-1}). During 36 d of continuous intragastric (ig) administration, body weights of the rats were measured weekly, the values of fasting blood glucose (FBG) concentration were measured on 7, 14, 21, 28, 35 d after administration. After the last administration, fasting 10 h, then, the rats were decapitated after anesthesia. Blood of the rats were collected for the analysis of serum insulin(INS), total cholesterol(TC), triglycerides(TG) and low density lipoprotein (LDL-C) levels. Compared with the control group, FBG of model group rats were significantly increased (P<0.01). After administration 21 d, compared with the model group, FBG of Melastoma dodecandrum ethanol-extract groups of high dose and medium dose were significantly lower(P<0.01 or 0.05); after administration 28 d, compared with the model group, FBG of Melastoma dodecandrum ethanol-extract groups of high dose, medium dose, low dose and positive control group were significantly lower (P<0.01 or 0.05). Compared with the control group, INS levels of model group were significantly lower (P<0.01); compared with the model group, INS levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly increased (P<0.05). Compared with the control group, TC, TG and LDL-C levels of model group rats were significantly increased (P<0.01), TG of positive control group was significantly increased(P<0.05). Compared with the model group, TC and LDL-C levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly lower (P<0.05) and TG levels was significantly lower (P<0.01); TG levels of positive control group was significantly lower (P<0.01). Melastoma dodecandrum ethanol-extract can decrease blood glucose, regulate blood lipids in type 2 diabetic rats.

Introduction

Melastoma dodecandrum is the dried whole plants, which mainly grows in Zhejiang, Fujian, Guangdong, Guangxi, Guizhou and so on. Taste sweet, astringent and potency cool. Attributed to heart, liver, spleen and lung. It's function was detoxification, expelling wind and dampness, blood hemostasis. Clinically for treatment some diseases, such as fever, lung abscess, swollen throat, toothache, and so on. The studied results shown that Melastoma dodecandrum contains a variety of chemical constituents, such as polysaccharides, flavonoids, amino acids, pigments, etc, which has some efficacies for anti-tumor, anti-aging, decrease blood glucose and regulate blood lipids and so on[1,2,3]. Researchers found that Melastoma dodecandrum ethanol-extract can decrease blood glucose for alloxan-induced diabetic mice, and also showed that significant hypoglycemic effect for diabetic model mice whom caused by glucose, adrenaline and streptozotocin[4,5], but some reports about effects of melastoma dodecandrum ethanol-extract on type 2 diabetic rats not yet found. In this study,

through observed some changes for weight, FBG, INS, TC, TG and LDL-C content of type 2 diabetic model rats whom be used Melastoma dodecandrum ethanol-extract, discussion the pharmacological effects about Melastoma dodecandrum ethanol-extract on type 2 diabetic rats.

Materials and methods

Animals. A total of 92 SPF SD rats, half of each are male and female, and their body weight were 200 ±20 g, whom were conventional breed in barrier environment, eating and drinking with free state. Water and feed were irradiation and sterilized by ^{60} Co, 12 h / 12 h dark cycle [6].

Reagents and instruments. Melastoma dodecandrum were dry grass which provided by school of medicine. Herbs be put into the 95% ethanol soaked overnight, heating and extracted three times, each time for 1 h, filtered and combined filtrate which recycled and concentrated until no alcohol taste under the reduced pressure, obtained dark green extract which be alternated[5].

Streptozotocin, meter, glucose, glyburide, insulin radioimmunoassay kit, total cholesterol assay kit, glycated serum protein assay kit, triglyceride detection kit, low density lipoprotein test kit and so on.

Modeling and packet administration. Rats be randomized after suitability feeding for a week, control group rats were 12 whom be fed normal diet , and to be made in the model group rats were 80 whom be fed high-fat and high-sugar diet. After the rats were fed four weeks, intraperitoneal injection the STZ for 35mg ŀkg^{-1} which be used to make the model[7]. STZ contains citric acid and sodium citrate buffer solution (PH4.4) and the ratio was 1:1.32[8]. Rats were not prohibit drinking but fasted for 12 h before intraperitoneal injection the STZ, the values of FBG concentration were measured on 96 h after administration. The success criteria of type 2 diabetic model rats is the blood glucose level ≧11.1 mmol Ł$^{-1}$[9, 10]. After testing, a total of 66 rats were produced model with successfully, the blood sugar of control group rats were normal.

After the models were made with successfully, according to the values of FBG concentration, the rats were randomly divided into diabetic model group, three Melastoma dodecandrum ethanol-extract groups of high dose, medium dose and low dose, and positive control group (glibenclamide), the number of each group is 12. Rats in each group be continued to give high-fat and high-sugar diet for two weeks in order to consolidate the model. Initiation of administration after the model was made with successfully, control group and diabetic model group be given saline with 20ml ŀkg^{-1}, positive control group be given glibenclamide with 0.30 mg ŀkg^{-1}, three Melastoma dodecandrum ethanol-extract groups of high dose, medium dose and low dose be given ethanol-extract with 40g ŀkg^{-1}, 20g ŀkg^{-1}, 10g ŀkg^{-1} respectively , intragastric administration once per day and continued for 36 d, during this time, the rats of each group no death. After the last administration, fasting 10 h, the rats were decapitated after anesthesia with 10% chloral hydrate in 3ml ŀkg^{-1} and collected blood, the blood were put into the centrifuge with 3500 revolutions per minute and work for 10 m, erum of the rats were collected for the detection and analysis.

Detection indicators. During 36 d of continuous administration, body weights of the rats were measured weekly.The values of FBG concentration were measured by using the Sino blood glucose meter on 7, 14, 21, 28, 35 d after administration. Follow the instructions to detect the INS content. According to the enzyme assay to detect the TG and TC of serum. By using SUR method to detect the LDL-C.

Statistical Analysis. Using SPSS 13.0 software for statistical analysis of the obtained data, the results of the indicators were expressed by $\bar{x} \pm s$, significance test using the t test and ANOVA. With $P<0.05$ was considered statistically significant and $P<0.01$ as statistically significant difference.

Results

Body weight effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats. Compared with the control group, body weight of model group rats were significantly lower ($P<0.01$). Body weight gradually decreased of rats with Melastoma dodecandrum ethanol-extract of medium

dose group, compared with the control group, body weight of rats significantly lower at 1st and 2nd week (P<0.05),beginning from 3rd week, body weight of rats significantly lower (P<0.01); compared with the model group, body weight of rats significantly increased (P<0.05). Shown in table 1.

Table 1 Body weight effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats（$\bar{x}\pm s$）

Groups	n	Dose /g·kg^{-1}	Weight / g				
			1st wk	2nd wk	3rd wk	4th wk	5th wk
control group	12	—	413±27	428±31	455±30	439±32	427±29
model group	12	—	309±38^{b}	295±35^{b}	277±33^{b}	256±36^{b}	241±30^{b}
Melastoma dodecandrum ethanol-extract group	12	10	305±48	318±42	326±40	311±43	307±41
	12	20	342±25^{a,c}	333±29^{a,c}	328±31^{b,c}	314±30^{b,c}	309±26^{b,c}
	12	40	329±34	318±40	323±36	307±29	289±33
positive control group	12	0.30×10^{-3}	315±29	311±31	301±30	298±27	281±36

Note: compared with the control group, ^{a}P<0 .05 , ^{b}P<0 .01; compared with the model group, ^{c}P<0 .05 , ^{d}P<0 .01 (Table 2 and table3 as the same as table 1)

FBG effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats. Compared with the control group, FBG of model group rats were significantly increased (P<0.01). After administration 21d, compared with the model group, FBG of Melastoma dodecandrum ethanol-extract groups of high dose and medium dose were significantly lower(P<0.01 or 0.05); after administration 28 d, compared with the model group, FBG of Melastoma dodecandrum ethanol-extract groups of high dose, medium dose, low dose and positive control group were significantly lower(P<0.01 or 0.05). Shown in table 2.

INS effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats. Compared with the control group, INS levels of model group were significantly lower(P<0.01). Compared with the model group, INS levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly increased (P <0.05). Shown in table 2.

Table 2 FBG and INS effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats（$\bar{x}\pm s$）

Groups	n	Dose /g·kg^{-1}	FBG/mmol·L^{-1}					INS/ mU·L^{-1}
			7th day	14th day	21st day	28th day	35 th day	
control group	12	—	4.45±1.2	5.23±1.4	6.41±1.3	7.11±1.5	6.89±1.3	358.6±122.4
model group	12	—	11.33±2.51^{b}	20.25±3.10^{b}	18.71±2.63^{b}	19.14±2.34^{b}	18.85±2.25^{b}	115.2±21.5^{b}
Melastoma dodecandrum ethanol-extract group	12	10	11.20±3.01	18.23±2.99	16.52±3.23	15.37±3.44	13.01±3.26^{b,c}	125.4±20.7
	12	20	9.77±3.15	15.32±3.78	14.61±4.01^{c}	12.75±3.87^{c}	12.28±2.99^{b,d}	156.8±39.3^{b,c}
	12	40	10.58±4.11	13.89±4.21	13.12±3.98^{c}	10.62±4.54^{d}	10.09±3.87^{b,d}	153.4±68.5
positive control group	12	0.30 ×10^{-3}	11.12±3.45	17.52±3.31	13.35±3.10	11.66±3.78	10.89±3.56^{b,d}	131.5±30.8

TC,TG and LDL-C effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats. Compared with the control group, TC, TG and LDL-C levels of model group rats were significantly increased (P<0.01), TG of positive control group was significantly increased(P<0.05). Compared with the model group, TC and LDL-C levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly lower (P<0.05) and TG levels was significantly lower (P<0.01); TG levels of positive control group was significantly lower (P<0.01). Shown in table 3.

Table 3 TC,TG and LDL-C effects of Melastoma dodecandrum ethanol-extract on type 2 diabetic rats ($\bar{x}\pm s$)

Groups	n	Dose /g·kg^{-1}	TC/mmol·L^{-1}	TG/mmol·L^{-1}	LDL-C/mmol·L^{-1}
control group	12	—	1.52±0.13	0.66±0.13	0.64±0.12
model group	12	—	2.15±0.10^{b}	1.63±0.44^{b}	1.06±0.17^{b}
Melastoma dodecandrum ethanol-extract group	12	10	2.01±0.47	1.15±0.39	1.02±0.27
	12	20	1.65±0.34^{c}	0.87±0.43^{d}	0.86±0.17^{c}
	12	40	2.05±0.48	1.11±0.45	1.02±0.20
positive control group	12	0.30×10^{-3}	1.01±0.21	1.06±0.34^{a,d,}	1.01±0.21

Discussion

Type 2 diabetic is a metabolic disorders which main feature are elevated blood glucose levels and insulin resistance. Now researchers realized that the pathogenesis are insulin resistance and insulin secretion less which lead to the blood sugar and blood lipid concentration at a high level[11,12]. So, the main efficacy of drugs to treatment of type 2 diabetic were decrease blood glucose and regulate blood lipids[8].

Polysaccharide MD 1 component of Melastoma dodecandrum have strong efficacy to scavenge radical and inhibit erythrocyte membrane lipid peroxidation, which have some effects for anti-aging, anti-ulcer and anti-inflammatory, anti-cancer, decrease blood glucose, regulate blood lipids and other pharmacological effects[13].

The experimental results showed that compared with the model group, body weight of Melastoma dodecandrum ethanol-extract of medium dose group rats significantly increased (P<0.05); after administration 28 d, FBG of Melastoma dodecandrum ethanol-extract groups of high dose , medium dose and low dose were significantly lower(P<0.01 or 0.05); INS levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly increased (P<0.05); TC and LDL-C levels of Melastoma dodecandrum ethanol-extract medium dose group were significantly lower (P<0.05) and TG levels was significantly lower (P<0.01).

Conclusion

These results indicated that Melastoma dodecandrum ethanol-extract can effectively promote insulin secretion, improve insulin resistance and decrease blood glucose, regulate blood lipids in type 2 diabetic, it also open ideas to development new hypoglycemic drugs. About its hypoglycemic mechanism and active ingredients to be further research and exploration.

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