Antidiabetic effects of *Thymus praecox* subsp. *skorpilii* var. *skorpilii* on streptozotocin/nicotinamide-induced rat model of type II diabetes

Muhammet Emin Cam^{1,*}, Sila Yildiz¹, Busra Ertas¹, Turgut Taskin², Levent Kabasakal¹

¹Department of Pharmacology, Faculty of Pharmacy, Marmara University, Istanbul, Turkey

²Department of Pharmacognosy, Faculty of Pharmacy, Marmara University, Istanbul, Turkey

*e-mail: muhammet.cam@marmara.edu.tr

BACKGROUND

- Owing to perceived effectiveness, minimal side effects in clinical experiences and also relatively low cost, plants are attractive sources for the development of novel safe and effective medicines for DM.
- Studies demonstrated that the *Thymus* species could have anti-inflammatory, antifungal, antiviral, antioxidant, anticancer and antidiabetic effects (1).
- Thymus praecox* subsp. *skorpilii* var. *skorpilii* is a medical plant having strong antioxidant activity and the leaves of the plant have been utilized for the treatment of diabetes as in the form of decoction in Turkey.
- In this study, we aimed to investigate the potential antidiabetic actions of *Thymus praecox* subsp. *skorpilii* var. *skorpilii* extract (TPSE) on STZ/NA-induced type-2 diabetic rats and to clarify the mechanisms accompanied with the related effects.

METHOD

- The aerial parts of TPS were extracted using the maceration method with methanol solvent for 7 days.
- A single intraperitoneal injection of nicotinamide (100 mg/kg), followed after 15 min by STZ (55 mg/kg) were given to induce type-2 diabetes in rats (2).
- Sprague Dawley rats were randomly divided into 4 groups as to be 6 animals for each group; Control group (C), Diabetes group (DM), TPSE group (100 mg/kg) and Positive control group (400 mg/kg metformin).
- In ITT, after 12 h of fasting, animals received 1 UI/kg of insulin (i.p.) and blood glucose level was measured just before insulin injection and at 15, 30, 60, 90 min after injection from tail vein (2).
- In OGTT, after 12 h of fasting, treatments were carried out and a single dose of glucose (2g/kg) was given by gavage 30 minutes later. The levels of blood glucose measured 30, 60, 120 and 180 min after glucose intake (3).
- To determine the most effective dose for TPSE, OGTT was applied (4).
- Following 3 weeks, rats were decapitated, tissue and blood samples were collected for ELISA (Figure 1).

Figure 1: Schematic representation of the experimental design. "12-h" indicates 12-h fasting.

RESULTS

Figure 2: The levels of insulin (a), AMPK (b) and PEPCK (c). Values are expressed in Mean $\pm$ SEM (n=6 animals for each for groups). One-way ANOVA was carried out followed by post hoc Tukey multiple comparison test. Values are represented statistically, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, compared to diabetes group; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to control group.

Figure 3: The levels of GLUT-2 (a), SGLT-1 (b) and SGLT-2 (c). Values are expressed in Mean $\pm$ SEM (n=6). One-way ANOVA was carried out followed by post hoc Tukey multiple comparison test. Values are represented statistically, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to diabetes group; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to control group.

Table 1: The Effects of TPSE on Oral Glucose Tolerance Test in Diabetic Rats

Blood glucose levels (mg/dl)					
Groups	0 min	30 min	60 min	120 min	180 min
Control	86 $\pm$ 2.9	146 $\pm$ 8.9	123 $\pm$ 5.1	90 $\pm$ 2.8	85 $\pm$ 3.7
DM	135 $\pm$ 23.1	347 $\pm$ 61.0 ^a	317 $\pm$ 52.9 ^a	225 $\pm$ 50.1 ^{a2}	183 $\pm$ 47.4 ^{a1c2}
DM+TPSE	98 $\pm$ 3.3	288 $\pm$ 19.9 ^{a3}	235 $\pm$ 19.2 ^{a1}	94 $\pm$ 8.6 ^{a24d2}	95 $\pm$ 2.8 ^{a4g2}
DM+M	101 $\pm$ 5.0	145 $\pm$ 13.9 ^{a4c3}	128 $\pm$ 10.6 ^{a4c1}	80 $\pm$ 4.8 ^{a3}	86 $\pm$ 4.2 ^{a1b4}

Values are mean $\pm$ SEM, n=6, ^acompared to control; ^bcompared to diabetes; ^ccompared to TPSE; ^dcompared to Metformin; ^ecompared to 30 min; ^fcompared to 60 min; ^gcompared to 120 min; ^hcompared to 180 min. ¹p<0.05; ²p<0.01; ³p<0.001; ⁴p<0.0001.

Figure 4: Effects of TPSE treatment on blood glucose (a), insulin tolerance test (b) and body weight (c). Each group (n=6) represents Mean $\pm$ SEM. Data was analyzed by using two-way ANOVA followed by Bonferroni posttests; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 and compared to diabetes group; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to control group.

CONCLUSION

- Based on the findings presented here, it is concluded that TPSE has potent antidiabetic effects on STZ/NA-induced diabetic rats via influencing different pathways and processes existed in the development of T2DM.

REFERENCES

- Soleimani Farsani M, Behbahani M, Isfahani HZ. The Effect of Root, Shoot and Seed Extracts of The Iranian *Thymus* L. (Family: Lamiaceae) Species on HIV-1 Replication and CD4 Expression. Cell journal. 2016; 18(2): 255-61.
- Adam SH, Giribabu N, Rao PV, Sayem AS, Arya A, Panichayupakaranan P, et al. Rhinacanthin C ameliorates hyperglycemia, hyperlipidemia and pancreatic destruction in streptozotocin-nicotinamide induced adult male diabetic rats. European journal of pharmacology. 2016;771:173-90.
- Shewamene Z, Abdelwahab M, Birhanu Z. Methanolic leaf extract of *Osteoglossum integrifolium* Benth reduces blood glucose levels in diabetic, glucose loaded and normal rodents. BMC complementary and alternative medicine. 2015; 15: 19.
- Korec R. Diabetes diagnosis following intravenous and oral glucose load: animal experiment principles. Zeitschrift für die gesamte innere Medizin und ihre Grenzgebiete. 1988; 43(15): 427-9.