The Inhibitory Effects of *Salvia Triloba* and *Thymus Praecox* subsp. *skorpilii* var. *skorpilii* on Acetylcholinesterase Activity in Diabetic Rats

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Introduction

- Type 2 Diabetes Mellitus (T2DM) is the result of insulin resistance in which there is relative or absolute inability of the body cells to use insulin effectively. It has been estimated that 20–70% of patients with DM have cognitive deficits and 60% are at higher risk of dementia.
- Acetylcholine (ACh)** plays an important role in memory function and has been implicated in aging-related dementia.
- Hypoinsulinemia and insulin resistance** is the reason of the decreased level of ACh and contribute the possible biochemical link between DM and cognitive disorders including Alzheimer's disease (1, Fig 1).
- Studies with plants have shed light on the correction of cognitive functions of diabetes mellitus with increased AChE activity.
- Some *Salvia* and *Thymus* species of Lamiaceae family have antidiabetic effects.

Figure 1: The etiology of brain injury with hyperglycemia is multifactorial.

Objectives

- We aimed to investigate the effects of *Salvia triloba* methanolic extract (STE) and *Thymus praecox* subsp. *skorpilii* var. *skorpilii* methanolic extract (TPSE) on brain acetylcholinesterase activities (AChE) on STZ/NA-induced type-2 diabetic rats.

Method

Figure 2: The AChE enzymatic assay was determined according to the method of Ellman et al in prefrontal cortex (2).

Results and Discussion

Evaluation of blood glucose and insulin levels

Figure 3: Effects of *T. praecox* (TPSE) and *S. triloba* (STE) treatment on blood glucose (a) and insulin level (b). Data are shown as the mean $\pm$ SEM (n=6). Data was analyzed by using two-way ANOVA followed by Bonferroni posttests; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to control; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 and compared to diabetes group

- Thymus praecox* (100 mg/kg) in methanolic extract considerably decreased (p<0.0001) blood glucose levels compared to diabetic rats and performed this drop for 3 weeks.
- Salvia triloba* (200 mg/kg) in methanolic extract considerably decreased (p<0.0001) blood glucose levels compared to diabetic rats and performed this drop for 3 weeks.

Acetylcholinesterase enzyme activity

Figure 4: The effect of *T. praecox* (TPSE) and *S. triloba* (STE) treatment on acetylcholinesterase (AChE) activity in T2DM rats. Data are shown as the mean $\pm$ SEM (n=6). Data was analyzed by using one-way ANOVA *p<0.05, ***p<0.001 compared to control group; ***p<0.001 compared to diabetes group.

- The diabetic group exhibited a significant increase (p<0.001) in AChE activity in prefrontal cortex compared to the control and the treatment groups.
- The metformin group decreased (%47, p<0.001) AChE activity compared to diabetic groups.
- Thymus praecox* (100 mg/kg) was able to prevent the increase in AChE activity induced by diabetes compared with diabetes.

- Salvia triloba* (200 mg/kg) reverted this increase (p<0.001) in AChE activity induced by diabetes after 3 weeks of treatment. *Salvia triloba* extract (%37, p<0.001) showed a considerable decrease in AChE activity compared to diabetic group.

Results showed;

The reestablishment of AChE activity by *Salvia triloba* extract and *Thymus praecox* subsp. *skorpilii* var. *skorpilii* extract which demonstrated antidiabetic activities for the first time can contribute to the maintenance of cholinergic signaling in diabetic rats.

Conclusion

- Taking into consideration the above-mentioned findings, it seems that the increase in AChE activity in T2DM rat model can be linked to depletion in cholinergic actions leading to defective neurotransmission and cognitive dysfunction as a result of decreased levels of ACh in the synaptic cleft.
- In our study, acetylcholine deficiency, known as an early sign of Alzheimer's disease, was found to be associated with insulin resistance.

Future Plans

- With the help of our results, we want to elucidate the possible mechanisms underlying the protective effect of TPSE and STE against diabetes-induced brain injury.
- Furthermore, we would like to show the effects of TPSE and STE treatment on cognitive impairment in diabetes model with behavioral studies in the future.

References

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