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Antihyperglycemic Effect of a Herbal Mixture in Rats

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Abstract : Postprandial glycemia is a risk factor of diabetes mellitus. In the present study we aim to evaluate the effect of herbal mixture on fasting glycemia and on oral-induced hyperglycemia in normal rats.
The herbal mixture (*Thymelaea hirsuta* extract, *Urtica dioica* extract and *Argania spinosa* oil; 10 ml/kgb.w.) was administered to normal fasting rats to evaluate its hypoglycemic power. The antihyperglycemic potential of the mixture was assessed on normoglycemic rats using the oral glucose tolerance test.
The results show that the herbal mixture administration significantly decreased (-20.91%) basal glycemia of treated rats at the 6th hour following the intake. Also, the mixture inhibited the hyperglycemic peak following the glucose overload. Area under curve analysis shows a significantly decreased (-25.94%) plasmatic glucose availability in mixture-treated rats.
Our findings support the efficiency of this herbal mixture in enhancing glucose tolerance in normal rats which could be helpful in managing postprandial glycemic state.
Keywords : Antihyperglycemic, hypoglycemic, postprandial state, herbal mixture, *Argania spinosa*, *Urtica dioica*,*Thymelaea hirsute.*

Introduction

Postprandial state is a crucial period for both normal and diabetic people due to its association with high risk factors of various diseases and mainly with diabetes mellitus complications (cardiovascular diseases, retinopathy and nephropathy)[1-2-3].

Monitoring postprandial state is actually one of the relevant therapeutic strategies used to attenuate postprandial metabolic events linked to hyperglycemia and hyperlipemia (glucolipotoxic state)[4]. In Morocco, such as in many developing countries, medicinal plants extracts are used to treat diabetes symptoms and complications as it was previously described[5].

In diverse studies, it has been reported that *Thymelaea hirsuata* aqueous extract (ThAE), *Urtica dioica* aqueous extract (UdAE) and *Argania spinosa* kernel oil (AsKO) had, separately, antihyperglycemic effects on normal and diabetic glucose overloaded rats[6-7-8].

In the present study, we exclusively examine the acute effect of a single dose treatment of an herbal mixture containing ThAE, UdAE and AsKO on basal fasting glycemia and against oral induced hyperglycemia by glucose overload in normal rats.

Material and Methods

Herbal mixture preparation

The herbal mixture was prepared by emulsifying 20% of Moroccan virgin argan oil (*Argania spinosa* L.) in 78% of commercial drinking water, and then, 1% of *Thymelaea hirsuta* (L.) and 1% of *Urtica dioica* (L.) aqueous extracts of their respective shade-dried powdered aerial parts were added to the oil-water emulsion.

Hypoglycemic effect assessment

Overnight fasted Wistar rats were subdivided into three groups. The first one served as control group, received a commercial drinking water (10 ml/kg b.w.). Group II, the test group, received the plant mixture (10 ml/kg). Group II served as standard reference group and received glibenclamide (2 mg/kg). Fasting plasma glucose was monitored by collecting blood from incised rat tail at 1, 2, 4 and 6 h after oral administration of the mixture. Glycaemia was assessed by glucose oxidase-peroxidase enzymatic commercial test kit (Glucose, Biosystems, Barcelona, Spain)

Oral glucose tolerance test

The oral glucose tolerance test was performed on overnight faster normoglycemic rats. The animals were subdivided into three groups. Group I, the control group, was orally treated by commercial drinking water (10 ml/kg b.w.). Group II and II were treated, respectively, by the mixture (10 ml/kg) and glibenclamide (2 mg/kg). Oral glucose overload (1 g/kg) was given to all groups 30 min after treatment administration. Fasting glycaemia was assessed before treatment administration and plasma glucose level was monitored after glucose overload by use of enzymatic oxidase-peroxidase commercial Kit (Glucose, Biosystems, Barcelona, Spain).

Results and Discussion

Oral administration of the herbal formulation (10 ml/kg b.w.) induced a hypoglycemic effect in normal rats (**Error! Reference source not found.**). Fasting glycemia has been significantly decreased in treated rats (4.31 ± 0.27 mM; $p<0.05$) at the 6th hour after the mixture administration compared to normal untreated control rats. The standard medication (glibenclamide, 2 mg/kg) induced a significant decrease in glycemia ($p<0.05$) at the 2nd hour after its administration.

Table 1. Effect of single dose herbal mixture (Mixt 10 ml/kg) and glibenclamide (Glib 2 mg/kg) on basal glycaemia in normoglycemic rats.

	Time (h)				
Treatment	**0**	**1**	**2**	**4**	**6**
Control	5.78± 0.50	6.16± 0.40	6.11± 0.66	5.88 ± 0.50	5.45 ± 0.40
Mixt (10 ml/kg)	5.77 ± 0.63	5.37 ± 0.45	5.15 ± 0.41	4.62 ± 0.32	4.31 ± 0.27*
Glib (2 mg/kg)	4.76± 0.46	4.53± 0.57*	3.72± 0.42*	3.66± 0.65*	3.33± 0.80*

Values are mean ± SEM (n=6).
*$P\leq0.05$ compared to control group.

The herbal mixture administration showed an antihyperglycemic effect in normal glucose overloaded rats (**Error! Reference source not found.**). The oral administration of the mixture attenuated the hyperglycemic peak at 60 min following the glucose gavage in treated rats (**Error! Reference source not found.**.A). Similarly, glibenclamide (2 mg/kg b.w.) significantly inhibited glycemic peak following the glucose administration ($p<0.05$). The area under curve ($AUC_{glucose}$) analysis showed a significantly decreased plasmatic glucose availability when rats are treated by the mixture ($p<0.01$) or glibenclamide ($p<0.001$) compared to normal control ones (**Error! Reference source not found.**.B).

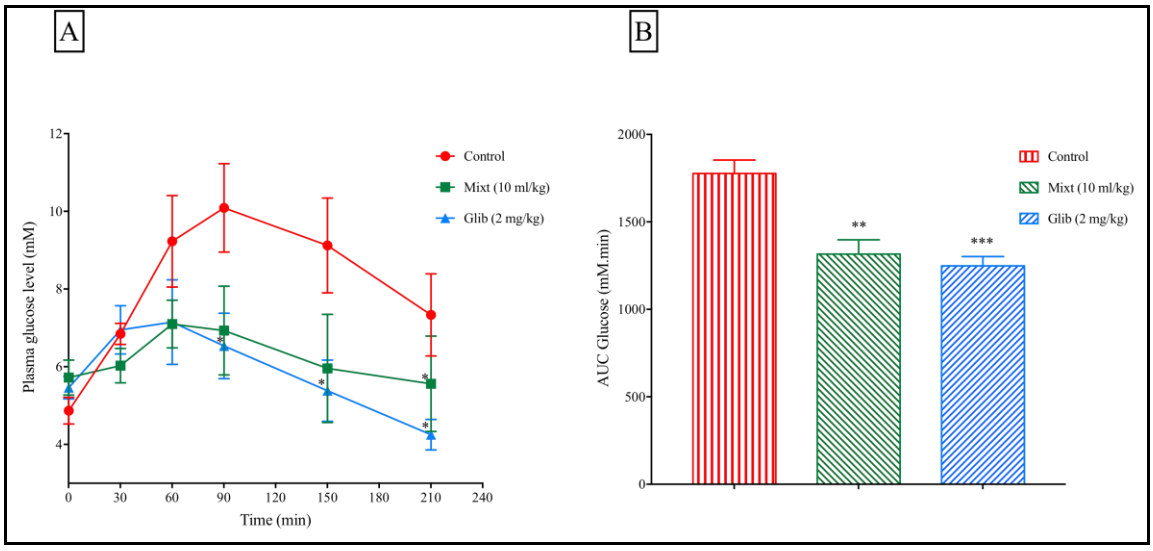

Figure 1. Effect of single dose herbal mixture (Mixt 10 ml/kg) and glibenclamide (Glib 2mg/kg) on plasma glucose level (A) and Area under curve ($AUC_{glucose}$) (B) in normal rats. Values are mean ± SEM (n=6). *$P \leq 0.05$, **$P \leq 0.01$and ***$P \leq 0.001$ compared to control group.

It has been shown that Argan oil has an antihyperglycemic effect on both normal and STZ-diabetic rats[3]. This effect were, partially, due to the inhibition of glucose gut absorption but the major effect of Argan oil could be in the insulinosecretagogue power of its fatty acids and phenolic compounds. Similar effects were observed when ThAE and UdAE were administered to normal rats[5-6].

In an *in vitro* study, it has been demonstrated that *Urtica dioica* (powdered leaves) aqueous extract has a glucose-dependent insulinotropic effect on isolated Langerhans'islets[9]. Another study showed that *Thymelaea hirsuta* ethanolic extract attenuates oral induced hyperglycemia by a partial inhibition of the glucose gut absorption[10].

The antihyperglycemic effect of this herbal mixture might be explained by a partial inhibition of instestinal glucose absorption in one hand. In the others hand, this effect might be due to a glucose-dependent insulinotropic action or an insulinomimetic active compounds which could be beneficial in enhancing glucose uptake by the insulin-sensitive organs. However, the hypoglycemic effect might be principally due to a glucose independent insulin secretion and/or an insulinomimetic effect inducing a higher glucose uptake by insulin sensitive organs.

Conclusion

The results of the present study demonstrate the effectiveness of our herbal mixture in decreasing basal glycaemia in normal rats. Also, the mixture helped normal rats to be more tolerant to glucose overload which could be useful in managing glycaemia during the postprandial period; and consequently, preventing the glucotoxic effect.

More studies should be done to confirm this effect *in vitro* and *in vivo* by use of more advanced experimental cellular and animal diabetes models.

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Conflict of interest

The authors declare no conflict of interest.

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