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Research Article

Ngu-Vi-Tieu-Khat decoction, a Vietnamese traditional medicine, possesses hypoglycemic and hypolipidemic effects on streptozotocin-induced type-2 diabetic rat model

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Abstract

This study aims to assess the hypoglycemic effects of Ngu-Vi-Tieu-Khat (NVTK) decoction, a traditional Vietnamese medicine, in a rat model of type-2 diabetes. The NVTK decoction was prepared using the maceration method and tested for its hypoglycemic effects by measuring blood glucose levels, insulin resistance indicators, and pancreatic mass. The results showed that NVTK decoction improved diabetes symptoms, increased insulin levels, reduced insulin resistance, restored pancreatic mass, and decreased total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) while increasing high-density lipoprotein cholesterol (HDL-C). The hypoglycemic effects of NVTK were comparable to those of gliclazide at a dose of 10 mg/kg. In conclusion, NVTK decoction possesses hypoglycemic properties and could be explored as a potential traditional medicine for treating type-2 diabetes in humans.

Keywords

Ngu-Vi-Tieu-Khat, decoction, bioactivity, type-2 diabetes mellitus, traditional medicine

Introduction

Diabetes mellitus, especially type-2 diabetes, is one of the most considerable healthcare problems and provocation because of its high prevalence and its association with numerous health complications (Ogurtsova et al. 2017). Worldwide, 537 million people had been expected to live with diabetes in 2021, and 783 million people will be expected to suffer from diabetes by 2045 (Wild et al. 2004; Sun et al. 2022). Moreover, developing countries experiencing industrial and economic developments are experiencing a significant increase in type-2 diabetes recently (Animaw and Seyoum 2017; Dunachie and Chamnan 2019), which could be due to urbanization, aging, increased adiposity, hypertension, eating habits, and sedentary work (Pham and Eggleston 2016; Ogurtsova et al. 2017). In Vietnam, a rapidly rising prevalence of type-2 diabetes has been noted, with 1 out of 17 adults diagnosed with diabetes and 1 out of 7 adults suffering from prediabetes (Pham and Eggleston 2016). Diabetes in Vietnam is

associated with an elevated waist-to-hip ratio even with a normal body mass index due to undernutrition and overnutrition coexisting (Khue 2015; Nguyen et al. 2015). Therefore, prevention and control measures are urgently needed for type-2 diabetes.

The prevalence of complementary medicine and traditional medicine usage among diabetes patients has been reported to be about 51% (Alzahrani et al. 2021). Herbal treatment of type-2 diabetes possesses several mechanisms, including the increase in insulin secretion, improvement in insulin sensitivity, improved glucose uptake by the adipose and muscle tissues, inhibition of glucose absorption from the intestine, inhibition of glucose production from the hepatocytes, and anti-inflammatory effects (Li et al. 2013; Wang et al. 2013; Tian et al. 2019). In the context of Vietnam, for thousands of years, Vietnamese people have used plants collected from their surroundings to treat a variety of diseases, and herbal traditional medicine is an integral part of the Vietnamese healthcare (kDô~TâtLi and Duñg 1991; Craig 2002; Nguyen et al. 2016, 2021). According to the World Health Organization (WHO), at least 1,863 plant species in 238 families and at least 8,000 specimens of 1,296 plant species, as well as approximately 1,000 different folk remedies have been identified in Vietnam (World Health Organization 1990). To treat and prevent type-2 diabetes, Vietnamese native physicians use herbs and remedies, as well as combinations of them (Van 1997; Tat 2004). Among numerous recipes, Ngu-Vi-Tieu-Khat (NVTK) decoction is the traditional remedy that has been passed for generations of the traditional practitioner Tran Van Thoai at the Mekong delta, Vietnam. NVTK decoction is the combination of *Caulis et folium Gymnemae sylvestris*, *Radix Scrophulariae*, *Herba Physalis Angulatae*, *Herba Gymnanthemum amygdalinum*, and *Cortex Oroxyli*, at a 2:3:4:2:1 weight ratio. All five of these herbs have been used extensively in Vietnamese traditional medicine practices, which possess hypoglycemic effects (Van 1997; Bich et al. 2004; Tat 2004). In Hindi, *Gymnema sylvestre* (Retz.) R.Br. ex Sm. (family Apocynaceae) is commonly referred to as gurmar, which translates to "sugar destroyer". The leaves of this plant have been utilized in Ayurvedic medicine to manage diabetes, cholesterol, and obesity (Radwan et al. 2020). Additionally, worldwide, the Indians have used *Caulis et folium Gymnemae sylvestris* for a long time in type-2 diabetes management (Pothuraju et al. 2014). The primary chemical constituents of these herbal materials include gymnemic acid, tartaric acid, gurmarin, calcium oxalate, glucose, sitosterol, betaine, and choline (Kanetkar et al. 2007). The gymnemoside ND7-9 isolated from this plant showed significant stimulation of 2-NBDG uptake by adipocyte cells 3T3-L1, suggesting further development of these compounds as anti-diabetes agents (Kashima et al. 2017; Pham et al. 2018). Similarly, in the Southeast Asian countries, *Radix Scrophulariae*, the dried root of *Scrophularia ningpoensis* Hemsl., which belongs to the Scrophulariaceae family has been used for many years as a medicinal plant and has been beneficial for reducing insulin resistance and controlling blood sugar (Guo et al. 2022). Scrophulariae Radix mainly contains various components such as iridoid glycosides, phenylpropanoid glycosides, and organic acids (Wang et al. 2018). Bitter leaf (*Gymnanthemum amygdalinum* (Delile) Sch.Bip. ex Walp.) is a plant species (family Compositae) that is widespread throughout tropical regions of Africa. It has been reported to possess antioxidant and anti-inflammatory properties, as well as demonstrated antihyperglycemic effects in both in vivo and in vitro studies. A study conducted by Ong showed that an ethanolic extract of bitter leaf containing 1–5 dicaffeoyl-quinic acid, dicaffeoyl-quinic acid, chlorogenic acid and luteolin 7-O-glucoside exhibited antidiabetic effects in streptozotocin-induced diabetic rats (Ong et al. 2011). *Cortex Oroxyli indici*, the dried stem bark of *Oroxylum indicum* (L.) Kurz. (family Bignoniaceae)(Vietnam Ministry of Health of Vietnam (MoH) 2005), is an herb used in traditional Chinese medicine to treat cardiovascular, urinary, and respiratory diseases. It has analgesic, anti-inflammatory, and blood glucose-lowering effects (Nguyen et al. 2012). The stem bark contains flavones such as oroxylin A, chrysin, and baicalein, along with their respective glucuronide forms. Additionally, it contains scutellarin-7-rutinoside, small amounts of alkaloids, tannic acid, sitosterol, galactose, biochanin-A, and ellagic acid (Harminder et al. 2011). In the study by Iwansyah et al. using *Physalis angulata* L. (family Solanaceae) fruit juice, it was found that the juice had a significant effect in reducing blood glucose levels, while not causing significant changes in body weight (Iwansyah et al. 2022).

Nevertheless, the combination of these 05 plants in the NVTK decoction, although proving clinical hypoglycemic effects, has not been scientifically investigated. Therefore, the purpose of this study was to determine the hypoglycemic and hypolipidemic effects of NVTK decoction on streptozotocin-induced type-2 diabetic rats. Furthermore, the study aimed to enrich the Vietnamese traditional medicine, and provide a theoretical basis for the development of herbal products using the NVTK decoction in the future.

Materials and methods

Materials

The Biochemistry Testing Machine Model 3000 Evolution, capable of measuring total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), was procured from Biochemical Systems International Srl, Italy. Rat-insulin ELISA kits were obtained from Crystal Chem, USA. The blood glucose test strips and One Touch profile meter reader were sourced from Johnson & Johnson, USA. The Human 30TS hematology analyzer was obtained from the Human company, Germany. The Stat Fax 4200 Semi-Automatic ELISA tester was obtained from Awareness company, USA. Gliclazide (Pyme Diapro MR) 30 mg was obtained from Pymepharco company, Viet-

nam. Both normal and high-fat-diet rats were procured from the Military Medical University, Vietnam. The dried herbs were supplied by the Traditional Medicine Hospital of Kien Giang province, Vietnam, and were following the standards outlined in the Vietnamese Pharmacopoeia (Vietnamese Ministry of Health 2018). All other utilized chemicals were of reagent grades or higher.

NVTK decoction preparation

The study utilized dried herbs following the standards from the Vietnamese pharmacopoeia, following a specified remedy ratio of 2:3:4:2:1 w/w/w/w/w. The appropriate amount of herbs was weighed, placed into the extraction system, and hot macerated with distilled water (herb: water ratio of 1:10 w/w) through two boiling periods of 120 min and 60 min, accordingly. The extracts were then filtered, collected, and the extraction process was repeated for two more times. All collected extracts were transferred to the intermediate vessel through a reduced pressure pump and the final product was obtained by distilling the extracts at a temperature of 60 °C, under a vacuum pressure of 50 bar, to achieve a condensed extract with solid:water ratio of 5:1 w/w.

In vivo streptozotocin-induced type-2 diabetic rat model

For the in vivo rat model, 50 Wistar male rats (180–200 g) were individually housed in a specific pathogen-free condition with free access to sterile water and food for 7 days in an air-conditioned room (25 °C and 60% humidity) with a 12-h light-dark cycle prior to performing the experiments.

To induce the type-2 diabetes, rats were fed with a high-calorie, high-fat diet in combination with low-dose streptozotocin for 4 weeks (Nain et al. 2012; Skovsø 2014) (Miaffo et al. 2020). Cholesterol, coconut oil, fructose, lard, cornstarch, yeast, and calcium carbonate were used to formulate the high fat diet, which provides 30% energy from fat and 70% from carbohydrates. In the next step, rats were injected intraperitoneally with streptozotocin at a dose of 35 mg/kg (in 0.1 M citrate buffer, pH 4.5). Then, 72 h after the injection, the rat blood glucose was measured and rats with blood glucose concentrations of ≥ 200 mg/dL were considered to be type 2 diabetic (Ogurtsova et al. 2017).

NVTK decoction test in in vivo rat model

Prior to the test, rats were randomly divided into five groups, with each group consisting of 10 individuals, including (1) the control group, (2) the model group (the disease control group), (3) the gliclazide group (10 mg/kg of gliclazide) (Portha and Serradas 1991), and (4) and (5) the NVTK test groups (low dose [NVTK_L, 7.764 g/kg/day] and high dose [NVTK_H, 15.528 g/kg/day]) (Fig. 1) (Administration of Science, Technology and Training

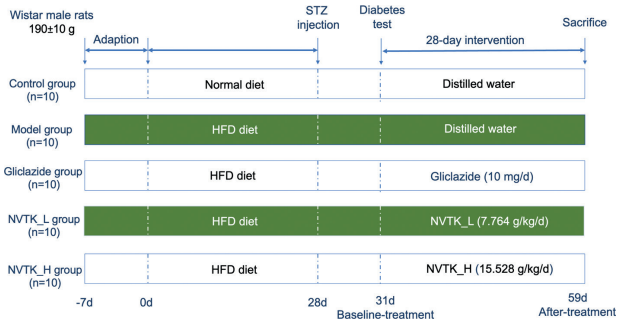

Figure 1. Flow chart of the in vivo study in the streptozotocin-induced high-fat-diet type-2 diabetic rat model. NVTK_L: Ngu-Vi-Tieu-Khat decoction with a low dosage, NVTK_H: Ngu-Vi-Tieu-Khat decoction with a high dosage, HFD: high-fat diet, STZ: streptozotocin.

2015). The control group and the model group received an equal amount of distilled water as a control. The administration of all treatments was performed through gavage, with a volume of 0.2 mL per 25 g body weight.

After 28 days of treatments, the rats were evaluated various parameters, including weight, food intake, water intake, urine volume, blood glucose and insulin levels, lipid profiles (total cholesterol, HDL-C, LDC-C, and triglycerides levels), and pancreas weight and histopathology. The blood glucose and insulin levels were measured in rats that fasted overnight using whole blood taken from their tails. The measurement of insulin levels was performed using an ELISA kit. The evaluation of insulin resistance was performed by calculating indices such as HOMA-IR (homeostatic model assessment of insulin resistance), HOMA-β (homeostatic model assessment of pancreatic β-cell function), QUICKI (quantitative insulin sensitivity check index), and DI (insulin disposition index), according to established guidelines (Muniyappa et al. 2000; Lorenzo et al. 2010; Onishi et al. 2010; Duan et al. 2019). The pancreas was dissected following the blood collection to evaluate its weight.

Ethics approval

The selection of animals, conditions for raising, care, and use, as well as the protocols for animal research were strictly followed the "Guideline for Evaluation of Pre-Clinical Research Results of Modern Drugs, Traditional Drugs, and Vaccines and Medical Biological Products", issued by the Vietnam Ministry of Health. The study protocols were approved by the Medical Science Council of Can Tho University of Medicine and Pharmacy, Can Tho, Vietnam, code 4033/QD-DHYDCT.

Statistical analysis

The data were calculated using the mean values and standard error (mean ± SD). Statistical tests were performed using JASP 16.0 using the Student's t-test, ANOVA test, Kruskal-Wallis's test, and the significance level was set at $p < 0.05$.

Results

Evaluation of streptozotocin-induced type-2 diabetic rat model

At the baseline of the treatment period, the fasting blood glucose levels in the model group were significantly higher ($p < 0.001$) than the control group, with levels exceeding 200 mg/dL. After the intervention, blood glucose levels in the model group remained elevated ($p < 0.05$), whereas no change was observed in the control group ($p > 0.05$) (Table 1). Furthermore, food and water consumption in the model group was higher than that in the control group ($p < 0.01$) (Table 2). The plasma lipid levels (total cholesterol, LDL-C, HDL-C, and triglycerides) in the model group were also significantly different ($p < 0.01$) from the control group (Table 3). The percentage of pancreatic mass in the model group was 43.95% lower compared to the control group ($p < 0.001$) (Table 4). Compared to the control group, the model group demonstrated elevated insulin levels ($p < 0.01$) and altered indicators of insulin resistance, including an increased HOMA-IR index and decreased HOMA-β, QUICKI, and DI ($p < 0.001$) (Table 5). Additionally, the volume of urine in the model group was significantly higher ($p < 0.001$) than in the control group (Fig. 2).

Table 1. Changes in the rat blood glucose levels before and after treatments (mean ± SD, mg/dL).

Group	Baseline	After-treatment	Difference between baseline and after-treatment (p value)
Control	97.59 ± 10.18	98.98 ± 12.17	> 0.05
Model	229.62 ± 13.34***	245.90 ± 13.85***	**< 0.05**
Gliclazide	236.14 ± 17.79***	135.83 ± 13.40***###	**< 0.001**
NVTK-L	234.58 ± 15.13***	142.31 ± 14.91***###	**< 0.001**
NVTK-H	239.63 ± 15.49***	135.80 ± 12.72***###	**< 0.001**

Note: Compared with the control group, *p < 0.05, **p < 0.01, ***p < 0.001; Compared with the model group, #p < 0.05, ##p < 0.01, ###p < 0.001.

Table 2. Changes in the rat body weight (mean ± SD, g), consumption of food (mean ± SD, g/kg/day), and consumption of water (mean ± SD, mL) before and after treatments.

Variable	Group	Baseline	After-treatment
Body weight	Control	220.90 ± 5.51	241.77 ± 7.46
	Model	221.44 ± 6.10	194.08 ± 9.01***
	Gliclazide	219.35 ± 6.91	239.83 ± 9.83###
	NVTK-L	220.13 ± 6.27	235.20 ± 9.74###
	NVTK-H	218.98 ± 5.88	239.10 ± 7.22###
Consumption of food	Control	71.65± 13.34	91.49 ± 12.73
	Model	81.10 ± 13.12	158.01 ± 22.24***
	Gliclazide	75.93 ± 11.31	118.80 ± 15.36***##
	NVTK-L	77.73 ± 10.68	120.64 ± 15.12***##
	NVTK-H	80.10 ± 10.98	119.89 ± 12.52***##
Consumption of water	Control	75.92 ± 11.59	89.29 ± 13.79
	Model	76.15 ± 11.22	217.75 ± 21.36***
	Gliclazide	73.09 ± 10.17	122.44 ± 14.02***###
	NVTK-L	77.31 ± 10.85	132.02 ± 14.97***###
	NVTK-H	79.71 ± 11.89	126.36 ± 19.05***###

Note: Compared with the control group, *p < 0.05, **p < 0.01, ***p < 0.001; Compared with the model group, #p < 0.05, ##p < 0.01, ###p < 0.001.

Table 3. Changes in the rat plasma lipid levels (mean ± SD, mmol/L) after treatments.

Group	Total cholesterol	HDL-Cholesterol	LDL-Cholesterol	Triglyceride
Control	2.21 ± 0.68	0.95 ± 0.29	0.85 ± 0.33	0.91 ± 0.17
Model	3.39 ± 0.72**	0.59 ± 0.13**	2.25 ± 0.57***	1.20 ± 0.19**
Gliclazide	2.64 ± 0.48#	0.74 ± 0.16#	1.46 ± 0.29**###	0.98 ± 0.18#
NVTK-L	2.69 ± 0.51#	0.76 ± 0.14#	1.46 ± 0.35**###	1.03 ± 0.13#
NVTK-H	2.61 ± 0.56#	0.79 ± 0.18#	1.39 ± 0.29*###	0.96 ± 0.21#

Note: Compared with the control group, *p < 0.05, **p < 0.01, ***p < 0.001; Compared with the model group, #p < 0.05, ##p < 0.01, ###p < 0.001

Table 4. Changes in the rat pancreas weights (mean ± SD, g) after treatments.

Group	Weight of pancreas	Decreased compared to the control group	Increased compared to the model group
Control	0.941 ± 0.125	-	-
Model	0.528 ± 0.068***	43.95%	-
Gliclazide	0.893 ± 0.125###	5.11%	69.28%
NVTK-L	0.863 ± 0.116###	8.32%	63.57%
NVTK-H	0.906 ± 0.114###	3.74%	71.74%

Note: Compared with the control group, *p < 0.05, **p < 0.01, ***p < 0.001; Compared with the model group, #p < 0.05, ##p < 0.01, ###p < 0.001.

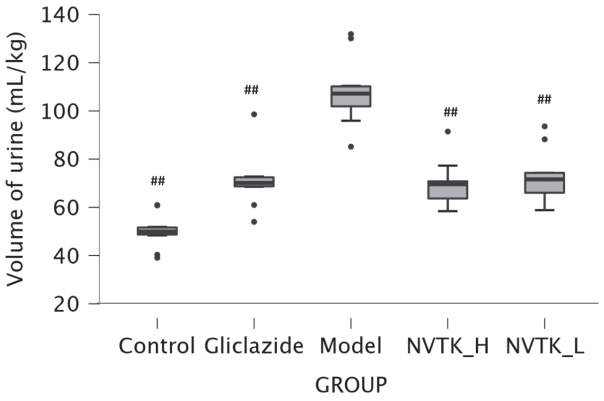

Figure 2. Effects of treatments on the volume of urine in rats. NVTK_L: Ngu-Vi-Tieu-Khat decoction with a low dosage, NVTK_H: Ngu-Vi-Tieu-Khat decoction with a high dosage, ###p < 0.001.

These results suggest that the model group exhibited signs of type-2 diabetes, characterized by hyperglycemia, low insulin levels and insulin resistance, dyslipidemia, polyphagia, polyuria, weight loss, and decreased pancreatic mass. These findings are in line with previous studies (Musabayane et al. 2005; Skovsø 2014; Miaffo et al. 2020) and support the evaluation of the effect of NVTK decoction in a rat model of type-2 diabetes.

Effects of NVTK decoction on rats with type-2 diabetes

Decreasing the blood glucose levels

At the baseline, no significant differences were noted in fasting blood glucose levels between the experimental rat groups. Interestingly, after 28 days of treatment, significant reductions in the blood glucose levels were observed

Table 5. Changes in the rat insulin resistance levels (mean ± SD) after treatments. HOMA-IR: homeostatic model assessment of insulin resistance, HOMA-β: homeostatic model assessment of pancreatic β-cell function, QUICKI: quantitative insulin sensitivity check index, and DI: insulin disposition index.

Group	HOMA-IR	HOMA-b	QUICKI	DI
Control	9.07 ± 2.22	420.68 ± 143.27	0.282 ± 0.009	50.15 ± 25.35
Model	15.41 ± 3.87***	50.96 ± 13.20###	0.264 ± 0.007***	3.32 ± 0.42***
Gliclazide	11.58 ± 2.21*#	177.70 ± 38.49***###	0.273 ± 0.006 *#	15.76 ± 3.73***###
NVTK-L	11.91 ± 2.30*#	159.09 ± 28.42***###	0.272 ± 0.007 *#	14.03 ± 4.37***###
NVTK-H	11.77 ± 2.59*#	178.38 ± 31.15***###	0.273 ± 0.007*#	15.82 ± 4.28***###

Note: Compared with the control group, *p < 0.05, **p < 0.01, ***p < 0.001; Compared with the model group, #p < 0.05, ##p < 0.01, ###p < 0.001.

in the gliclazide, NVTK-L, and NVTK-H groups (p < 0.001), compared with the model group (Table 1). Furthermore, the NVTK possessed comparable effects with the gliclazide. These results suggest that treatments with NVTK decoctions effectively lower the blood glucose levels in rats with type-2 diabetes.

Alleviating diabetes common symptoms

At day 28, compared to the model group, both the gliclazide and NVTK groups showed a significant increase in the rat weight (p < 0.001), a reduction in food and water consumption (Table 2), and a decrement in urine volume (p < 0.001) (Fig. 2). These data suggest that both NVTK and gliclazide are capable of alleviating the common symptoms of diabetes in rats, including polyphagia, polyuria, polydipsia, and unexplained weight loss.

Reducing the plasma lipid levels

After the intervention period, both gliclazide and NVTK showed a reduction in total cholesterol (p < 0.05), LDL-C (p < 0.001), and triglyceride levels (p < 0.05), and an increase in HDL-C levels (p < 0.05), compared to the model group. Neither gliclazide nor NVTK showed significant differences from the control group (Table 3). This indicates that both low and high doses of NVTK can improve dyslipidemia in diabetic rats.

Alternating the pancreatic mass-to-body-weight ratio

A statistically increase in the rat pancreatic mass-to-body-weight was noted in the gliclazide and NVTK groups, compared with the model group (p < 0.001) (Table 4). This suggests that treatment with gliclazide and NVTK had a positive impact on the pancreas weight of the type-2 diabetic rats.

Decreasing the insulin resistance levels

As compared to the model group, rats treated with gliclazide and both doses of NVTK had similar and equivalent levels of insulin (p < 0.01) (Fig. 3). The HOMA-IR index was reduced in the gliclazide and NVTK treated groups (p < 0.05), while the HOMA-β (p < 0.001), DI (p < 0.001), and QUICKI (p < 0.05) indexes increased significantly (Table 5). Despite these improvements, these indicators have not recovered to the same level as the control group. This indicates that treatment with both low and high doses of NVTK and gliclazide has a positive impact on insulin levels and insulin resistance in rats.

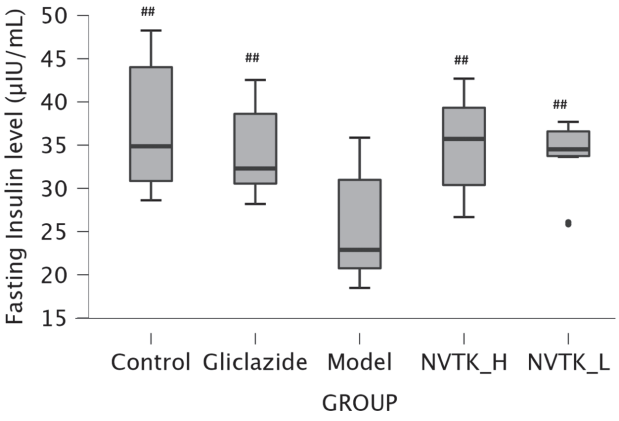

Figure 3. Effects of treatments on fasting insulin level in rats. NVTK_L: Ngu-Vi-Tieu-Khat decoction with a low dosage, NVTK_H: Ngu-Vi-Tieu-Khat decoction with a high dosage, ##p < 0.01.

Discussions

The study employed a rat model of type-2 diabetes mellitus by utilizing a well-known streptozotocin-induced assay, characterized by evident symptoms such as hyperglycemia, polyuria, polydipsia, hypoinsulinemia, insulin resistance, and dyslipidemia. The decreased insulin levels in the body leads to catabolism of fats and proteins, resulting in weight loss. Additionally, low insulin levels reduce the sensitivity of hypothalamic leptin receptors to stimulation, leading to increased food intake and reduced sensitivity to satiety-promoting hormones (cholecystokinin, peptide YY, and glucagon peptide-1). The hyperglycemia leads to excessive excretion of glucose in the urine and water loss, causing an increase in water consumption.

The study results suggest that the reduction of blood glucose levels by NVTK decoction could be achieved through two mechanisms of (1) improvement of both meal-stimulated and post-absorptive insulin secretion, and (2) enhancement of insulin sensitivity (Ma et al. 1989). Furthermore, changes in the body weight and relative weight of the pancreas of diabetic rats after NVTK treatment provide further evidence for the pancreatic mechanisms of action of the decoction.

Type-2 diabetes and insulin resistance are closely related. Type-2 diabetes is predicted most accurately by insulin resistance, which can also be treated once hyperglycemia is present (Taylor 2012). Thus, one of the type-2 diabetes treatment approaches is to improve insulin sensitivity, which could be evaluated by HOMA-IR and HOMA-β

values. In this study, oral administration of NVTK decoction significantly reduced the HOMA-IR values and increased the HOMA-β values, indicating that NVTK could improve pancreatic cell functions and enhance insulin resistance. The QUICKI and DI indices were also increased in rats treated with NVTK decoction orally, which were perfectly in accordance with the evaluation of pancreatic weight and the quantification of plasma insulin.

Regarding the lipid profiles, untreated diabetic rats had significant increases in the plasma TC, LDL-C, and TG levels, whereas the HDL-C was low (Musabayane et al. 2005; Ravi et al. 2005). This is mainly because insulin inhibits HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl coenzyme A reductase), the key enzyme in cholesterol biosynthesis (Goldberg 1981), therefore insulin deficiency or insulin resistance could increase mobilization of fatty acids from adipose tissue, causing hyperlipidemia. Consequently, atherosclerosis might develop due to increased oxidation of low-density lipoprotein, which is a crucial step in developing diabetic macrovascular complications (Jay et al. 2006). To this end, NVTK decoctions had demonstrated their anti-hypolipidemic effects, since they could significantly reduce the TC, TG, and LDL-C levels, while increase the HDL-C level. It may also be suggested that this anti-hyperlipidemic effect of NVTK is through a reduction in intestinal cholesterol absorption or a reduction in cholesterol biosynthesis specifically by reducing the activity of the HMG-CoA reductase inhibitor (Sharma et al. 2003).

The NVTK remedy is a combination of 5 medicinal herbs that have been formulated according to traditional medicinal principles for the treatments of various diseases. Previous studies have demonstrated the individual components of the NVTK remedy's ability to lower blood glucose levels due to their chemical constituents. For instance, *Radix Scrophulariae* has been shown to have blood glucose-lowering effects attributed to its chemical components such as Iridoid and iridoid glycoside (Lee et al. 2021). Furthermore, aqueous extract from *Cortex Oroxyli indici*, rich in flavonoids, has been found to possess therapeutic effects in diabetes treatment (Singh and Kakkar 2013). Additionally, a flavonoid-rich extract from *Herba Gymnanthemum amygdalinum* has been proven to reduce blood glucose levels in Swiss mice (Hanh et al. 2020). Combining these individual herbal components with blood glucose-lowering properties may enhance the efficacy of the NVTK remedy, potentially leading to improved therapeutic outcomes. Moreover, these five herbs, all of which have a long history of use in Vietnamese traditional medicine, are recognized for their hypoglycemic effects. Furthermore, globally, *Caulis et folium Gymnemae sylvestris* has been employed for an extended period in the management of type-2 diabetes by Indian practitioners (Pothuraju et al. 2014). Similarly, in Southeast Asian countries, *Radix Scrophulariae* has enjoyed a long history of medicinal use and has proven effective in reducing insulin resistance and regulating blood sugar levels (Guo et al. 2022).

The study revealed that the NVTK formulation exhibited effects that were comparable to those of gliclazide in reducing blood glucose levels. Moreover, previous studies have demonstrated the efficacy of the individual components of NVTK in reducing hyperglycemia (Iwai et al. 2014; Raju et al. 2015; Devangan et al. 2021; Iwansyah et al. 2022). These findings lend support to the conclusion that NVTK possesses hypoglycemic activity that is comparable to that of gliclazide. Thus, the NVTK formulation has the potential to serve as an effective alternative to gliclazide in the management of hyperglycemia in diabetic patients. Further investigations are necessary to elucidate the underlying mechanism of action of NVTK and its clinical utility. It is important to note that traditional medicine practices should not be used as a substitute for conventional medical treatments, but rather as complementary therapies. Further research is needed to fully understand the efficacy and safety of the NVTK remedy, as well as its individual components. Nonetheless, traditional medicines can provide valuable insight into new treatments and therapies for patients with type-2 diabetes, such as the NVTK remedy.

Conclusions

Our research offers initial support for the efficacy of the traditional formula NVTK in mitigating classical symptoms associated with type-2 diabetes. The study found that oral administration of NVTK decoction led to reductions in hyperglycemia, improvements in plasma lipid levels, enhancements in insulin resistance indicators, and restorations of pancreatic weight in rats. Interestingly, the hypoglycemic effects of NVTK decoction were equivalent to those of gliclazide at a dose of 10 mg/kg. Based on these findings, it may be suggested that NVTK decoction could serve as an adjunct therapy for individuals with type-2 diabetes.

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