Research Journal of Pharmacology 4 (1): 21-25, 2010
ISSN: 1815-9362

Antidiabetic and Hypolipidaemic Effects of *Cinnanomum verum* Bark on Hyperglycaemic and Diabetic Rats

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Abstract: The aqueous and methanolic extracts of the bark of *C. verum* were studied for their hypoglycaemic and hypolipidaemic effects in hyperglycaemic (type II) and in streptozotocin diabetic rats (type I). The hypoglycaemic effect was determined following the Glucose Tolerance Test (GTT) model and the results were compared to the control. The results of this research in type II showed an early and persistent hypoglycaemic effect, since the first hour and throughout the experiment. Both doses of the aqueous extract and dose 200 mg kg^{-1} of the methanolic extract, revealed the highest significant glucose lowering effect ($p<0.001$) as compared to the control, followed by dose 400 mg kg^{-1} of the methanolic extract, which reduced blood glucose significantly ($p<0.05$) throughout the experiment. The onset of hypoglycaemic effect in diabetic rats was slow but highly significant as started at the 12th h. The reference drugs revealed no significant hypoglycaemic effect throughout the experiment. Regarding blood cholesterol, the onset of the hypocholesterolaemic effect in type II started with a significant reduction ($p<0.05$) at the 2nd h post dosing and continued till the 4th h post dosing. Glibenclamide reduced blood cholesterol significantly ($p<0.05$) at the 2nd h only. Both extracts of *C. verum* showed no significant cholesterol reduction in type I diabetic rats. Insulin reduced blood cholesterol significantly ($p<0.05$) at the 2nd h only. Concerning the effect of *C. verum* on the level of blood triglycerides, the aqueous and methanolic extracts, reduced blood triglycerides of hyperglycaemic rats, significantly ($p<0.05$) and ($p<0.001$), respectively at the 2nd h post dosing as compared to the control. In diabetic rats, the aqueous extract reduced blood triglycerides significantly ($p<0.001$) at the 2nd and 4th h post dosing. The effect of the methanolic extract was highly significant ($p<0.001$) but slower in its action, as it started at the 4th h. In conclusion, the bark of *C. verum* confirmed its traditional use in herbal medicine as an antidiabetic agent which can be more effective than the commonly used hypoglycaemic drugs.

Key words: Hyperglycaemic, rats, cholesterol, herbal medicine, *C. verum*

INTRODUCTION

Diabetes is world-wide in distribution and its incidence is rising. In the year 2000, 150 million people world-wide had diabetes and this is expected to double by 2010 (Christopher *et al*., 2002). In spite of the introduction of synthetic hypoglycaemic agents, diabetes and the related complications continue to be a major medical problem (Satyanarayana *et al*., 2004). Therefore, the search for more effective and safer hypoglycaemic agents has continued to be an important area of active research. Many medicinal plants have been found to be successful in management of diabetes (Subramanian *et al*., 1996). However, search for new antidiabetic drugs continue.

Cinnanomum verum: Family (Lauraceae) is a moderate sized tree. The bark is smooth, light pinkish brown and thin, with a strong, pleasant small and spicy, burning taste. Its habitat is India. Its active ingredient is a water soluble poly phenol compound called MHCP. This compound mimics insulin, activates its receptor and works synergistically with insulin in cells. Cinnamon can improve glucose and cholesterol (Alam, 2003). In folkloric medicine, *C. verum* is used for treatment of renal diseases,

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diabetes mellitus, productive cough and is also used as a CNS stimulant, memory activator and menstrual cycle stimulant (Elghazali *et al*., 1998). The essential oil in Cinnamon has demonstrated strong antibacterial and antifungal properties (Bruneton, 1995). Cinnamon bark has also shown strong lipolytic activity, hydrolysing fats (Leung and Foster, 1996).

MATERIALS AND METHODS

Plants: The bark of *C. verum* (Lauraceae*)* was obtained from Omdurman General Market and was authenticated by the botanists at the Medicinal and Aromatic Plants' Research Institute in Khartoum.

Preparation of the aqueous extract: About 100 g of the bark of *C. verum* were weighed, immersed in cooled boiling distilled water and then incubated in a water bath at 60°C for 4 h after which they were filtered. The filtrate was freeze dried (Bruneton, 1995).

Preparation of the methanolic extract: Sixty grams of the bark of *C. verum* were weighed and packed in Soxhlet apparatus using 500 mL of petroleum ether followed by chloroform, as solvents to separate lipids and terpenoids. The sample was then extracted using methanol as a solvent to get the polar constituents of the plants. The extract was evaporated till dryness using a rotatory evaporator (Harborne, 1973).

Animals: Adult male wistar albino rats weighing 70-300 g were used in this study. Rats were obtained from the Faculty of Pharmacy, University of Khartoum. They were divided into groups of tens among the controls, standards and subgroups of samples. They were supplied with a standard pellet diet and tap water *ad libitum.*

Experimental type II diabetes mellitus (Glucose tolerance test): Rats were divided into groups of tens among the controls, standards and samples. After 18 h fast, blood samples were obtained from the retro orbital plexus of rats (Khanna *et al*., 1992.) using heparinized capillary tubes. The zero time sample was collected and then all groups of animals were over loaded with (2 g kg^{-1}) of 50% glucose intraperitoneally; the control was given distilled water, the standard was given (10 mg kg^{-1}) of Glibenclamide, while the tested groups were given (400 and 200 mg kg^{-1}) of the aqueous and methanolic extracts orally. The 1, 2 and 4 h samples, were collected and the plasma obtained after centrifugation was estimated for glucose, cholesterol and triglycerides.

Experimental type I diabetes mellitus (Streptozotocin induced diabetes): In this experiment, induction of diabetes in rats was achieved by destruction of the pancreatic cells using an intraperitoneal injection of Streptozotocin (STZ), at a dose of 60 mg kg^{-1} (by wt), dissolved in the citrate buffer at a concentration of 20 mg mL^{-1} to provide a pH of 4.5 (Rakieten *et al*., 1963; Heor and Jahuke, 1967).

Soluble insulin at a dose of 3 U kg^{-1} diluted 100 times was used as standard (reference drug) and samples were collected at 0, 4, 8 and 12 h (Suba *et al*., 2004). Samples were then analysed biochemically for glucose (Trinder, 1969), Cholesterol (Richmond, 1973) and triglycerides (Vad, 1960).

Statistical analysis: Data were expressed as mean±SE of means using paired student's t-test (Mendenhall, 1971).

RESULTS AND DISCUSSION

Phytochemical screening revealed presence of triterpenes alkaloids, tannins and saponin. In type II, both doses of the aqueous extract and dose 200 mg kg^{-1} of the methanolic extract, showed a highly significant hypoglycaemic effect ($p<0.001$) throughout the experiment as compared to the control. Dose 400 mg kg^{-1} of the methanolic extract showed a significant reduction ($p<0.05$), throughout the experiment, while Glibenclamide showed a slower significant reduction ($p<0.05$) at the 4th h post dosing (Table 1 and 2).

In diabetic rats both doses of the aqueous extract and dose 400 mg kg^{-1} of the methanolic extract reduced blood glucose significantly ($p<0.001$) at the 12th h post dosing. Insulin showed no significant reduction at all (Table 3 and 4).

Concerning blood cholesterol, the two extracts of *C. verum* showed a significant reduction ($p<0.05$) at the 2nd h post dosing in type II and the effect continued till the 4th h post dosing. Glibenclamide reduced blood cholesterol significantly ($p<0.05$) at the 2nd h only (Table 1 and 2).

Both extracts of *C. verum* showed no significant reduction in type I diabetic rats. Insulin reduced blood cholesterol significantly ($p<0.05$) at the 2nd h only (Table 3 and 4). Regarding blood triglycerides. The aqueous and methanolic extracts of *C. verum*, reduced blood triglycerides of hyperglycaemic rats, significantly ($p<0.05$) and ($p<0.001$), respectively at the 2nd h post dosing as compared to the control (Table 1 and 2). In diabetic rats, the aqueous extract reduced blood triglycerides significantly ($p<0.001$) at the 2nd and 4th h

Table 1: Effects of the aqueous extract of *C. verum* on the blood glucose, cholesterol and triglycerides of hyperglycaemic rats

	Blood glucose (mg dL^{-1})			
	0	1	2	4
Name of groups	(h)			
Control (water)	110±8.9	166.8±7.51	129.4±17	110.4±8.5
Glibenclamide (10 mg kg^{-1})	105±5.8	141.7±32.8	87.38±2.89	86.7±10.45*
C. verum (400 mg kg^{-1})	73.9±9.9	93.5±1.9**	92.7±2**	87.5±9.7**
C. verum (200 mg kg^{-1})	93.6±7.5	88.8±7.9**	85±2.3**	72.5±4.1**
Cholesterol (mg dL^{-1})				
Control (water)	75.8±6.7	104.2±16.8	107.2±6.4	83.5±6.4
Glibenclamide (10 mg kg^{-1})	88±8.87	87±8.2	83.6±2.8*	86.4±21.2
C. verum (400 mg kg^{-1})	69.4±5.1	111.8±20.5	92.6±17.9*	86.7±1.4*
C. verum (200 mg kg^{-1})	70.2±3.7	72.8±4.6*	90.4±1.8*	80.6±6.9*
Triglycerides (mg dL^{-1})				
Control (water)	108±13.6	118.5±11.2	135.2±19.4	122.2±16.5
Glibenclamide (10 mg kg^{-1})	132.2±10.5	140.6±10.2	134.8±16.3	144.4±9.4
C. verum (400 mg kg^{-1})	138.4±11	144±4.5	121±14.2*	115±10.0
C. verum (200 mg kg^{-1})	131.2±10.9	129.2±6	136.8±8.5	120.2±7.5

Table 2: Effects of the methanolic extract of *C. verum* on the blood glucose, cholesterol and triglycerides of hyperglycaemic rats

	Blood glucose (mg dL^{-1})			
	0	1	2	4
Name of groups	(h)			
Control (water)	110±8.9	166.8±7.51	129.4±17	110.4±8.5
Glibenclamide (10 mg kg^{-1})	105±5.8	141.7±32.8	87.38±2.89	86.7±10.45*
C. verum 400 mg kg^{-1})	108.6±8.3	122.5±1.2*	90.6±16.2**	90.7±11.2*
C. verum (200 mg kg^{-1})	97.6±7.6	104.2±15**	91.2±7.4**	78±5.5**
Cholesterol (mg dL^{-1})				
Control (water)	75.8±6.7	104.2±16.8	107.2±6.4	83.5±6.4
Glibenclamide (10 mg kg^{-1})	88±8.87	87±8.2	83.6±2.8*	86.4±21.2
C. verum (400 mg kg^{-1})	69.4±5.1	92.6±17.9	101.8±20.5	86.7±1.4*
C. verum (200 mg kg^{-1})	70.2±3.7	72.8±4.6	90.4±1.8*	80.6±6.9*
Triglycerides (mg dL^{-1})				
Control (water)	108±13.6	118.5±11.2	135.2±19.4	122.2±16.5
Glibenclamide (10 mg kg^{-1})	132.2±10.5	140.6±10.2	134.8±16.3	144.4±9.4
C. verum (400 mg kg^{-1})	138.4±11	124±4.5	111±14.2**	105±10.0
C. verum (200 mg kg^{-1})	131.2±10.9	129.2±6	116.8±8.5**	108.2±7.5

Table 3: Effects of the aqueous extract of *C. verum* on the blood glucose, cholesterol and triglycerides of diabetic rats

	Blood glucose (mg dL^{-1})			
	0	4	8	12
Name of groups	(h)			
Control (water)	286.2±18.2	226.6±12.5	202.8±56.5	277±56.5
Glibenclamide (10 mg kg^{-1})	311.8±46.3	221.2±55	259.8±64.9	266.6±49.4
Soluble insulin (3U kg^{-1})	273.6±18.3	286.8±6.6	226±2	222±6.6
C. verum (400 mg kg^{-1})	303±7.2	254.4±23.4	182.4±62.8	156.2±42.2**
C. verum (200 mg kg^{-1})	293.8±7.7	269.2±45.1	202.8±31.5	186±18.7**
Cholesterol (mg dL^{-1})				
Control (water.)	66±10.2	61±3.7	53±5.4	56.8±5.9
Glibenclamide (10 mg kg^{-1})	98.6±18.6	112±17.4	97.4±15	56.8±4.9
Soluble insulin (3U kg^{-1})	40.4±2.5	31.4±3*	34.2±.8	42 ±2.1
C. verum (400 mg kg^{-1})	95.8±6.5	79±20.6	50.6±6.7	50±1.6
C. verum (200 mg kg^{-1})	100.4±53	73.2±13.8	58.6±19.3	54.4±19.2
Triglycerides (mg dL^{-1})				
Control (water)	247.2±35.7	227.8±20.3	187±15.3	284±54.3
Glibenclamide (10 mg kg^{-1})	123.2±22.5	222.4±52.3	247±55.9	230.4±61.5
Soluble insulin (3 U kg^{-1})	57.8±12.8	33.2±4.8*	33.6±2.5*	42±6.5*
C. verum (400 mg kg^{-1})	285.8±34.8	305±47.1	88.6±19.2**	165±64.7**
C. verum (200 mg kg^{-1})	186.8±65.7	227.8±20.3	88.2±29.5**	88.6±28**

(Data are expressed in mean±standard error of mean). * = ($p<0.05$), ** = ($p<0.001$)

post dosing. The effect of the methanolic extract was highly significant ($p<0.001$) but slower in its action, as it started at the 4th h (Table 3 and 4). In accordance to the recommendations of the Expert Committee (2002) on diabetes mellitus, it is important to investigate the hypoglycaemic action for plants which were traditionally used in traditional medicine (Alarcon-Aguilara *et al*., 1998). The limited efficacy and the draw back of the currently used hypoglycemic agents prompted the scientists world-wide to search for more effective phytomedicenes (Rahman and Zaman, 1989). More than 1200 species of plants have been used ethno-

Table 4: Effects of the methanolic extract of *C. verum* on the blood glucose, cholesterol and triglycerides of diabetic rats

	Blood glucose (mg dL^{-1})			
	0	4	8	12
Name of groups	(h)			
Control (water)	286.2±18.2	226.6±12.5	202.8±56.5	277±56.5
Glibenclamide (10 mg kg^{-1})	311.8±46.3	221.2±55	259.8±64.9	266.6±49.4
Soluble insulin (3 U kg^{-1})	273.6±18.3	286.8±6.6	226±2	222±6.6
C. verum (400 mg kg^{-1})	235.4±12.4	315.6±31.9	206.2±54.1	203.6±57.1**
C. verum (200 mg kg^{-1})	239.4±15.4	220.4±25.9	205.6±32.3	187.4±41.7
Cholesterol (mg dL^{-1})				
Control (water. 10 mL kg^{-1})	66±10.2	61±3.7	53±5.4	56.8±5.9
Glibenclamide (10 mg kg^{-1})	98.6±18.6	112±17.4	97.4±15	56.8±4.9
Soluble insulin (3U kg^{-1})	40.4±2.5	31.4±3	34.2±.8	42±2.1
C. verum (400 mg kg^{-1})	58.4±8.2	51.8±7.1	45.2±5.9	42.6±1.7
C. verum (200 mg kg^{-1})	79±3.4	48.6±5.1	52.8±2.5	47.8±2.9
Triglycerides (mg dL^{-1})				
Control (water)	247.2±35.7	227.8±20.3	187±15.3	284±54.3
Glibenclamide (10 mg kg^{-1})	123.2±22.5	222.4±52.3	247±55.9	230.4±61.5
Soluble insulin (3 U kg^{-1})	57.8±12.8	33.2±4.8*	33.6±2.5*	42±6.5*
C. verum (400 mg kg^{-1})	210.8±51.2	283.4±16.2	165.2±22.6	165.8±43.7**
C. verum (200 mg kg^{-1})	179.8±65	195±57.9	223.2±61.4	165.2±43.1**

(Data are expressed in mean±standard error of mean) * = ($p<0.05$), ** = ($p<0.001$)

pharmacologically or experimentally to treat symptoms of diabetes mellitus. They represent >725 genera in 183 families. The most frequently sited families are Asteraceae, Fabaceae, Poaceae, Laminaceae and Liliaceae (Thorne, 1981). According to the taxonomy of Elghazali *et al.* (1998), *C. verum* belongs to the family Lauraceae.

The biologically active components of plants with hypoglycaemic action include; flavonoides, alkaloids, glycosides, polysaccharides, peptidoglycans, steroids and terpenoides (Grover *et al.*, 2002). In this study, phytochemical screening of *Cinnanomum verum* revealed presence of triterpenes alkaloids, tannins and saponin. In addition Oliver-Bever and Zahnd (1979) reported presence of volatile oil, cinnamic aldehyde and terpenoides.

Thus components, such as alkaloid, salicylic may be responsible for the hypoglycemic activity of hypoglycaemic plants (Shani *et al.*, 1974). Coumarin an active constituent of *Trigonella* was found to have a profound hypoglycemic activity in normal and alloxan diabetic rats (Shirwaikar *et al.*, 2004). Thus presence of alkaloids and coumarin in *Cicer arientinum* are probably responsible for its hypoglycaemic activity.

Many plants are recently studied for their hypoglycaemic effects. The leaf alcohol extract of the plant *Annona squamosa* was investigated for its anti-diabetic activity in diabetic rats. The findings showed the significant anti diabetic potential of the extract in monitoring the diabetes rats (Lemela *et al.*, 1985).

In studying the antihyperglycemic, effect of the ethanol extract of *G. montanum* leaves to diabetic rats, the results indicatated a positive role of *G. montanum* as atherapeutic agent for diabetes (Ramkumar *et al.*, 2007). The results of this current study showed that the extracts of the bark of *C. verum* possess blood glucose lowering effect in both hyperglycaemic (Table 1 and 2) rats and in diabetic rats (Table 3 and 4).

CONCLUSION

The folk use of *C. verum* may be validated by this study. The bark of this plant seems to have a promising value for the development of potent phytomedicine for diabetes.

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