

HYPOGLYCEMIANT AND ANTI-HYPERGLYCEMIANT EFFECTS OF THE AQUEOUS EXTRACT OF ROASTED AND GROUND COFFEE BEANS OF *COFFEA CANEPHORA ROBUSTA* IN THE WISTAR RAT

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ABSTRACT

The beverage from the roasted and ground coffee of *Coffea* (coffee), which for a long has been on the dock, alongside alcohol, tobacco and drugs, has been recognized for over a decade as a drink with positive effects on health. Among these benefits is an inverse association between low coffee consumption and a high prevalence of type 2 diabetes. This study aims to evaluate the hypoglycemic and anti-hyperglycemic activities of the various drinks derived from the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta*. A hypoglycemic effect was observed at doses of 5, 20 and 100 mg/kg bw, respectively for the various extracts of ARE, AE and EE administered orally. EE at the dose of 100 mg/kg bw significantly reduced hyperglycemia induced by administration of 3 g/kg bw of glucose, as did glibenclamide at 10 mg/kg bw. The presence of polyphenols, flavonoids and saponosides in the extract may provide an explanation for the hypoglycemic and anti-hyperglycemic effects observed. Moreover, these same effects would explain the preventive action of this drink (coffee) as to the occurrence of diabetes type 2.

KEYWORDS: *Coffea canephora robusta*, diabetes mellitus, hypoglycemia, antihyperglycemia, glibenclamide.

1. INTRODUCTION

Diabetes Type 2 (TD2) prevalence is rapidly increases and prevention of this disease has become a priority public health goal.^[1] This predominantly involves dietary modifications^[2,3] which are: limited caloric intake to prevent or correct excess weight, adequate intake of dietary fiber, preference for complex carbohydrates, limitation of saturated fats and regular of Physical activity. The cessation of smoking^[4] and moderate consumption of alcohol^[5] have also shown a protective effect. Indeed, the use of medicinal therapies is only a second option when lifestyle modifications prove to be insufficient.^[3] The beverage from roasted and ground coffee beans is one of the most consumed beverages in the world, with 500 billion cups of coffee consumed in 2010 according to the International Coffee Organization (ICO).^[6] Its consumption is accompanied by different physiological responses affecting the cardiac, digestive, cerebral, renal, pulmonary and endocrine systems.^[7] Thus, coffee consumption has been associated with a reduction in the frequency and the age at which the Parkinson's disease appears.^[8] Blood pressure, waist circumference, fasting blood glucose and cholesterol were also inversely proportional to coffee consumption.^[9] An inverse and significant relationship

was found between coffee consumption and total, cardiac and cardiovascular mortality rates in a population of type 2 diabetics monitored for 20 years.^[10] Several studies have also shown an association between coffee consumption and the lesser frequency of type 2 diabetes.^[11] However, caffeine, the major bioactive element of coffee, has a paradoxical effect on glucose metabolism. Indeed, chronic caffeine intake by diet does not affect glucose metabolism and is unlikely to contribute to the decreased risk of type 2 diabetes induced by coffee.^[12] Similarly, the effect of caffeine on insulin is more pronounced if caffeine is administered alone rather than by coffee consumption.^[13]

The aim of this study is to assess the short-term the activity of the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta* on the glycemia of normoglycemic rats and rats subjected to the glucose tolerance test.

2. MATERIALS AND METHODS**2.1. Animal Equipment**

The albino rats of Wistar strain were used for this study. These rats come from the Pasteur Institute Adiopodoumé (Abidjan, Ivory Coast), and their weigh between 120

and 150 g. These animals are bred in airy metallic cages at the temperature of $24 \pm 3^\circ\text{C}$, with a photoperiod of 12 hours and a humidity of 50% for 7 days prior to experimentation. The rats have ad libitum access to water and food.

2.2. Plant material

The plant material used is roasted and ground coffee beans of *Coffea canephora robusta*. These coffee beans come from Ivory Coast. The *robusta* coffee is grown in plains in wetter conditions, as the parts of Central and West Africa, Southeast Asia and parts of Brazil^[14]. The cherries of this coffee tree are round, small and thicker than those of Arabicas.^[15] The grains of this variety are sold cheaper on the market and often enter into the composition of soluble coffees.^[16] Robusta coffee accounts for just under 23.6% of world production.^[17]

2.3. Methods

2.3.1. Phytochemical Screening

Phytochemical tests are qualitative tests to characterize the different chemical groups contained in a plant organ. These are physicochemical reactions which make it possible to identify the presence of chemical substances.

2.3.2. Preparation of extracts

2.3.2.1. Preparation of the aqueous extract

The aqueous extract is obtained by the infusion of roasted and ground coffee beans of *Coffea canephora robusta* (*Ccr*). A filter coffee machine Daily collection inox timer isotherme HD7479/20 of Philips brand was used to prepare coffee. The infusion was made with 30 g of roast and ground coffee beans of *Ccr* in 175 ml of distilled water. The filtrate obtained is evaporated in an oven at a temperature of 60°C . The crystals obtained are pulverized. The captured fine powder is kept refrigerated in sterile glass jars sealed. This technique yielded 3g of dry extract, corresponding to a yield of 10%.

2.3.2.2. Preparation of the ethanolic extract 70% (EE) and Residual (ERA)

The 70% ethanolic and residual extracts are obtained by dissolving 5 g of aqueous extract of roasted and ground coffee beans in a mixer during 5 rotations of 1 minute in 100 ml of an aqueous-alcoholic solution (70% methanol).^[18] The captured homogenate is introduced into a separating funnel which allows it to be separated into two phases, a hydro alcoholic phase and the residue. These two phases are subsequently dried in an oven at 50°C . This technique made it possible to obtain 3.655 g of ethanolic extract and 1.045 g of aqueous residual extract, corresponding respectively to a yield of 73.3% and 20.9%.

2.3.3. Study of the activity of Aqueous Extract (AE), Aqueous Residual Extract (ARE) and Ethanolic Extract 70% (EE) on the glucose of the normoglycemic rats'

The evaluation of the hypoglycemic effect was followed in the short term for 4 hours following oral

administration of various increasing doses of Aqueous Extract (AE), Aqueous Residual Extract (ARE) and Ethanolic Extract 70% (EE) of *Coffea canephora robusta*. This experiment was made with 90 Wistar rats distributed in 15 batches of 6 rats.

The blood glucose of the rats is measured using an Accu-Chek Active glucometer and test strips. In this study, the rats were fasted for 12 hours before the experiments. Blood glucose is first determined just before treatment; this is the initial blood glucose (t_0). After treating the animals, blood glucose is measured every hour for 4 hours and the percentage change in blood glucose relative to the initial blood glucose is calculated.

2.3.3.1. Dose-response effect of the Aqueous Extract (AE)

For this study, 30 rats were used. They were divided into 5 lots of 6 rats.

- Lot 1: Normoglycemic control rats receiving distilled water (10 ml/kg bw).
- Lot 2: rats treated with AE at the dose of 20 mg/kg bw.
- Lot 3: rats treated with AE at the dose of 40 mg/kg bw.
- Lot 4: rats treated with AE at the dose of 50 mg/kg bw.
- Lot 5: rats treated with glibenclamide (reference substance) at the dose of 10 mg/kg bw.

2.3.3.2. Dose-response effect of Ethanolic Extract 70% (EE)

For this study, 30 rats were used. They were divided into 5 lots of 6 rats.

- Lot 1: Normoglycemic control rats receiving distilled water (10 ml/kg bw).
- Lot 2: rats treated with EE at the dose of 50 mg/kg bw.
- Lot 3: rats treated with EE at the dose of 100 mg/kg bw.
- Lot 4: rats treated with EE at the dose of 200 mg/kg bw.
- Lot 5: rats treated with glibenclamide (reference substance) at the dose of 10 mg/kg bw.

2.3.3.3. Dose-response effect of the Aqueous Residual Extract (ARE)

For this study, 30 rats were used. They were divided into 5 lots of 6 rats.

- Lot 1: Normoglycemic control rats receiving distilled water (10 ml/kg bw).
- Lot 2: rats treated with ARE at the dose of 5 mg/kg bw.
- Lot 3: rats treated with ARE at the dose of 10 mg/kg bw.
- Lot 4: rats treated with ARE at the dose of 20 mg/kg bw.
- Lot 5: rats treated with glibenclamide (reference substance) at the dose of 10 mg/kg bw.

2.3.4. Effect of AE, ARE and EE during the glucose tolerance test

The evaluation of the various extracts [ARE (5 mg/kg bw), AE (20 mg/kg bw) and EE (mg/kg bw)] of roasted and ground coffee beans of *Coffea canephora robusta*,

on the regulation and peripheral use of glucose in normal Wistar rats, was demonstrated in a state of oral hyperglycaemia. For this study, 72 male rats were divided into 12 batches of 6 rats. The rats were fasted for 12 hours before the experiments.

2.3.4.1. Blood glucose measurement in pretreated rats

Hyperglycaemia is caused by oral administration of glucose to rats at a dose of 3 g/kg body weight. For this study, 30 rats were divided into 6 batches of 5 rats.

- Lot 1: Negative control rats receiving distilled water (10 ml/kg bw) only.
- Lot 2: positive control rats receiving distilled water (10 ml/kg bw), and 30 minutes after, 3 g/kg bw of glucose.
- Lot 3: rats receiving 5 mg/kg bw of ARE, then 3 g/kg bw of glucose 30 minutes later.
- Lot 4: rats receiving 20 mg/kg bw of AE, then 3 g/kg bw of glucose 30 minutes later.
- Lot 5: rats receiving 100 mg/kg bw of EE, then 3 g/kg bw of glucose 30 minutes later.
- Lot 6: rats receiving glibenclamide (10 mg/kg bw), then 3 g/kg bw of glucose 30 minutes later.

The blood glucose levels of the rats in each batch were measured immediately prior to the administration of the substances or distilled water and then, after treatment, at intervals of 30 minutes, for 4 hours. The percentage of induction of hyperglycemia and the percentage of reduction of the induced hyperglycemia are then calculated.

2.3.4.2. Blood glucose measurement in post-treated rats

Sampling is the same as for pretreated rats. However, in this series of experiments, the different batches of rats receive the doses of coffee [ARE (5 mg/kg bw), AE (20 mg/kg bw) and EE (100 mg/kg bw)] or glibenclamide (10 mg/kg bw) 30 minutes after induction of hyperglycemia by oral administration of 3 g / kg glucose bw. The blood glucose of the rats of each batch is measured just prior to administration of glucose and thereafter at intervals of 30 minutes for 4 hours. The percentage of induction of hyperglycemia and the percentage of reduction of induced hyperglycemia are also calculated.

2.4. Statistical Analysis

The statistical analysis was performed using the Graph Pad Prism 5 software (San Diego, USA). The analysis of variance ANOVA (One-way ANOVA) followed by the Student-Newman-Keuls test was used for comparison of results. The difference is considered statistically significant when $P < 0.05$.

3. RESULTS

3.1. Phytochemical Screening

The main chemical groups identified according to the conventional methods of characterization are recorded in Table I. The aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta* reveals the

presence of sterols and polyterpenes, polyphenols, flavonoids, tannins, compounds quinones, saponosides and alkaloids.

3.1. Hypoglycemic tests

The variations of the glycaemia in rats following the oral administration of different doses of AE, glibenclamide (batches tests) or distilled water (control batch) are shown in the graph of Figure 1. Blood glucose in rats receiving only distilled water (control) did not vary significantly ($p > 0.05$) throughout the study (4 hours). It remains at 0.70 ± 0.05 g/L. AE at doses of 20, 40 and 50 mg/kg bw, induces a dose-dependent increase in blood glucose in the treated rats. This increase in blood glucose was significant ($p < 0.05$) one hour after treatment at doses of 40 mg/kg bw and 50 mg/kg bw and not significant ($p < 0.05$) at the dose of 20 mg/kg bw. On the other hand, AE at the same dose of 20 mg/kg bw induced a non-significant decrease ($p > 0.05$) in blood glucose two (2) hours after administration of the substance. This decrease remains significant ($p < 0.05$) up to the 4th hours.

Glibenclamide (reference substance) at the dose of 10 mg/kg bw, also results in decreased blood glucose levels in treated rats. This decrease was significant ($p < 0.05$) one (1) hour after administration of glibenclamide and increased throughout the experimental period. Blood glucose is 0.40 ± 0.04 g/L, 4 hours after administration.

Figure 3 shows variations of glycaemia in rats following oral administration of different doses of EE, glibenclamide (batches test) or distilled water (control batch). EE at doses of 50 and 100 mg/kg bw, induced a decrease in blood glucose in the treated rats. This decrease in blood glucose was significant ($p < 0.05$) at the dose of 100 mg/kg bw and not significant ($p > 0.05$) at the dose 50 mg/kg bw one hour after treatment. This decrease significantly increased ($p < 0.05$) throughout the experimental period up to 4 hours after administration of the extract with reductions of 24.66% and 27.78% at the respective doses of 50 and 100 mg/kg bw.

3. 2. Glucose tolerance test

3.2.1. Antihyperglycemic effect in pretreated rats.

In this series of experiments (Fig 4), the administration or not glibenclamide at 10 mg/kg bw or the different extracts (ARE = 5 mg/kg bw, AE = 20 mg/kg bw and EE = 100 mg/kg bw), 30 min afterwards, did not significantly ($p > 0.05$) modify the blood glucose of the pretreated animals. At this moment, glucose administration at 3 mg/kg bw leads to significant increases ($p < 0.05$) of the glycaemia in all pretreated or untreated animals. The peak of hyperglycemia, appearing 30 minutes after this administration of glucose, is variable depending on whether the rats were pretreated or not with ARE, AE and EE or glibenclamide.

In rats receiving distilled water (positive control), the glucose administered results in an increase in blood

glucose, with a peak of hyperglycemia which is of the order of 0.39 g/L. Subsequently, hyperglycemia is progressively reduced and the basal glucose level is found 3 hours 30 min after administration of the glucose.

AE and ARE respectively at doses of 20 and 5 mg/kg bw did not have significant effects ($p > 0.05$) on glucose-induced hyperglycemia at 3 g/kg bw. Indeed, in rats receiving AE and ARE respectively at doses of 20 and 5 mg/kg bw, the hyperglycemia which appears 30 minutes after the administration of glucose is 0.40 and 0.38 g/L and the return to the initial blood glucose occurred after 3 hours 10 minutes and 2 hours 50 minutes respectively.

On the other hand, the dose of 100 mg/kg bw of EE reduces hyperglycemia induced by subsequent administration of 3 g/kg bw glucose. In this case, the peak of hyperglycemia which appears 30 minutes after the administration of the glucose is respectively 0.30 g/L. Initial blood glucose is reached after 2 hours 20 minutes, followed by hypoglycemia of 0.15 g/L.

When rats are pretreated with glibenclamide at the dose of 10 mg/kg bw, hyperglycemia induced 30 minutes after administration of glucose to 3 g/kg bw is 0.22 g/L. After this, hyperglycemia is gradually reduced as a function of time until the initial blood glucose level is reached after 1 hour 55 minutes, then a hypoglycemia of 0.23 g/L is measured.

Table II gives, as a function of time, the percentages of reductions in glucose-induced hyperglycemia when the animals are pretreated or not with different extracts or glibenclamide.

3.2.2. Anti-hyperglycemic effect in post-treated rats.

Oral administration of glucose at the dose of 3 g/kg bw (Figure 5) provokes an hyperglycemia in post treated or untreated rats with different extracts (ARE = 5 mg/kg bw, AE = 20 mg/kg bw and EE = 100 mg/kg bw) or the glibenclamide. The peak of hyperglycemia, which is 0.42 ± 0.05 g/L, occurs 30 minutes after the administration. Subsequently, this hyperglycemia gradually decreases until it returns to the initial value. The reduction in

hyperglycemia and the time taken to return to the initial value of blood glucose are variable depending on whether the animals were post-treated with the different extracts or glibenclamide.

In rats receiving only glucose (3 g/kg of bw) 30 minutes later, there was a maximum hyperglycemia of 0.40 g/L. Subsequently, this hyperglycemia gradually decreases and the initial blood glucose level is recovered approximately 3 hours after the administration of the glucose.

ARE at a dose of 5 mg/kg bw administered 30 min after oral administration of glucose to animals showed no significant effect ($p > 0.05$) on hyperglycemia (0.38 g/L) induced by the latter and the return to the initial blood glucose occurs after 2 hours 30 minutes.

When glucose administration (3 g/kg bw) is followed 30 minutes after, of EE at the dose of 100 mg/kg bw, glucose-induced hyperglycemia is reduced with time (Figure 5) and the return to the initial blood glucose occurs after 1 hour 50 minutes. Thereafter, hypoglycemia of (0.19 g/L) appears.

On the other hand, when this administration of glucose is followed, 30 minutes later by AE at a dose of 20 mg/kg bw, glucose-induced hyperglycemia increases significantly ($p < 0.05$) one hour after. Thereafter, the decrease in blood glucose appears and the initial blood glucose is found 2 hours 50 minutes after the administration of glucose.

Glibenclamide (10 mg/kg bw) administered 30 min after glucose administration, results in a greater reduction in induced hyperglycemia over time and returns to the initial glucose level after 1 hour 30 minutes. There is then a hypoglycemia of 0.28 g/L.

Table III gives, as a function of time, the percentages of reductions in glucose-induced hyperglycemia when this administration of glucose is followed 30 minutes after those of the different extracts or glibenclamide.

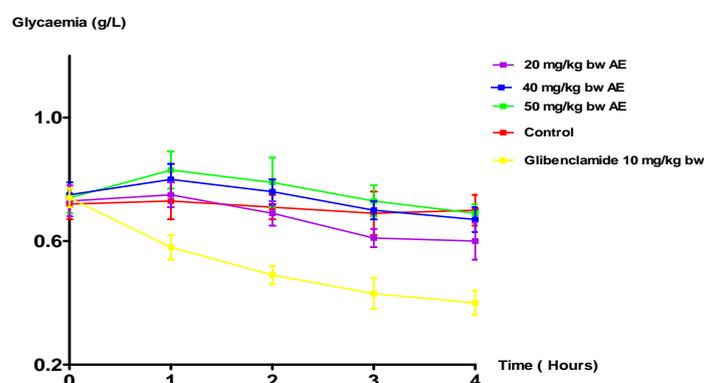


Figure 1: Variations in rats' blood glucose following oral administration of different doses of AE, glibenclamide (tests) or distilled water (control)

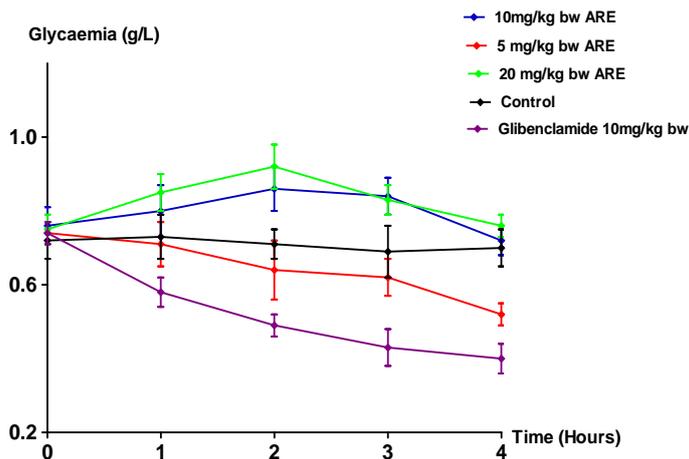


Figure 2: Variations in rats' blood glucose following oral administration of different doses of ARE, glibenclamide (tests) or distilled water (control)

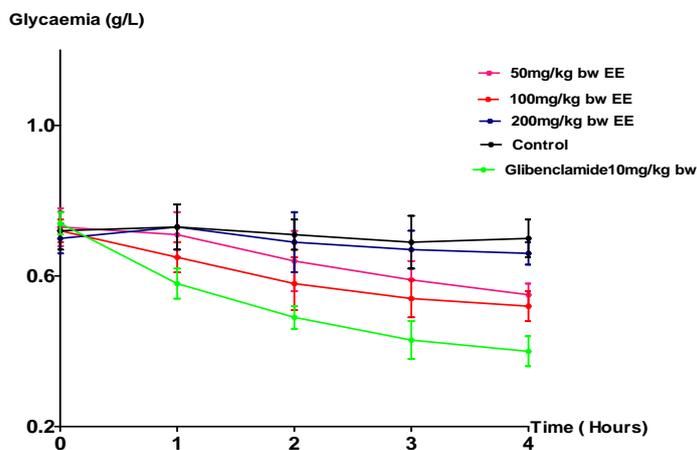


Figure 3: Variations in rats' glucose following oral administration of different doses of EE, glibenclamide (tests) or distilled water (control).

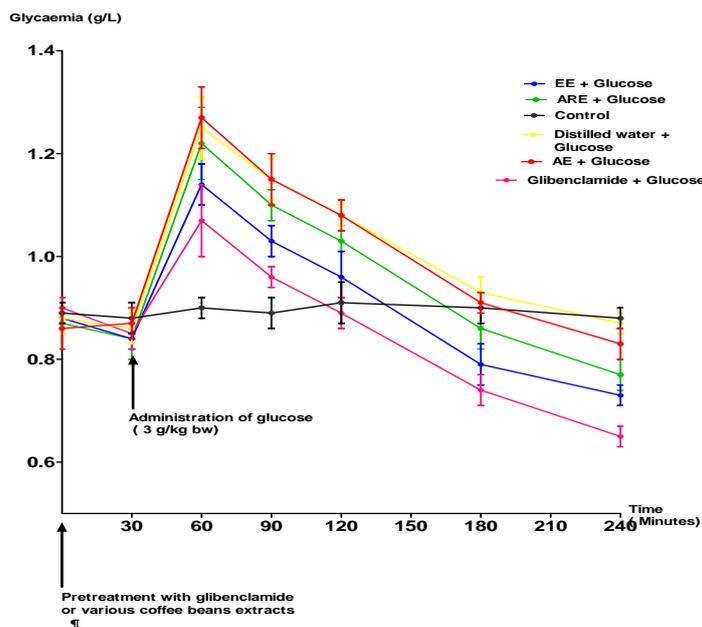


Figure 4: Variation in the glycemia of the rats pretreated by the oral administration of the various extracts AE, ARE, EE and glibenclamide (tests) or distilled water (control) during the glucose tolerance test.

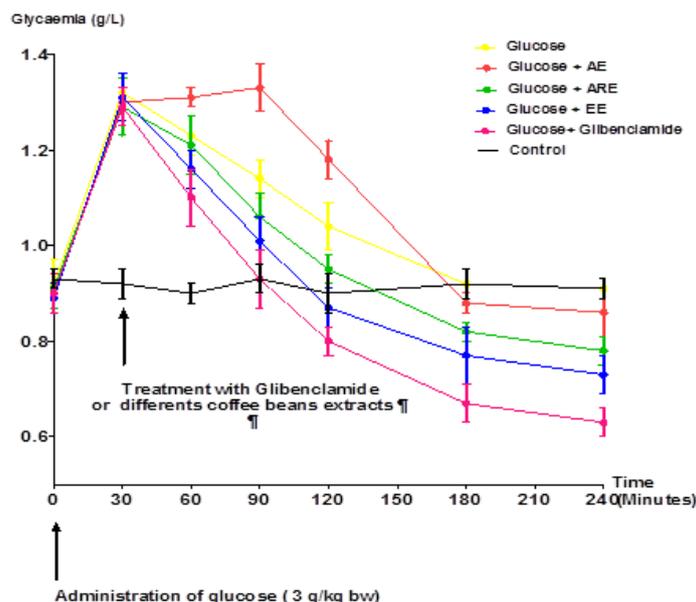


Figure 5: Variation in the glycemia of the rats post-treated by the oral administration of the various extracts AE, ARE, EE and glibenclamide (tests) or distilled water (control) during the glucose tolerance test

TABLE I: Results of the phytochemical screening of the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta*.

Chemical Components		Reagents	Results
Sterols and (polyterpenes)		LIBERMANN	+
Polyphenols		FeCl ₂	+
Tannins	Gal	FeCl ₃	+
	Cat	STIASNY	+
Quinonic Substances		BORNTRAEGEN	+
Alkaloids	D	DRAGENDORFF	+
	B	BOUCHARDAT	+
	VM	VALSEN-MAYER	+
Saponosides		Foam Index	+
Favonoides		Mg ⁺⁺	+

TABLE II: Reduction of glucose-induced hyperglycemia in rats pretreated with extracts AE, ARE, EE or glibenclamide

		Time after glucose administration (minutes)				
		30	60	90	150	210
Percentage of reduction in glucose-induced hyperglycemia (3mg/kg bw)	Hyperglycemic control	0	25.64	43.59	82.05	97.43
	AE (20 mg/kg bw)	0	30	47.5	90	110
	ARE (5 mg/kg bw)	2.4	31.58	50	94.74	118.42
	EE (100 mg/kg bw)	9.56	36.67	60	116.67	136.67
	Glibenclamide (10 mg/kg bw)	14.4	42.31	69.23	126.92	161.54

Table III: Reduction of glucose-induced hyperglycemia in post-treated rats with AE, ARE, EE or glibenclamide extracts

		Time after glucose administration (minutes)					
		30	60	90	120	180	240
Percentage of reduction in glucose-induced hyperglycemia (3mg/kg bw)	Hyperglycemia Control	0	22.5	45	70	98	100
	AE (20 mg/kg bw)	0	0	0	34.88	104.65	109.30
	ARE (5 mg/kg bw)	0	21.05	60.52	89.47	123.68	131.58
	EE (100 mg/kg bw)	0	35.71	71.42	104.76	128.57	138.09
	Glibenclamide (10 mg/kg bw)	0	48.72	92.30	125.64	158.97	169.23

4. DISCUSSION

According to^[19], the chemical compounds contained in the plants are grouped into three classes of secondary metabolites namely phenol compounds, alkaloids and terpenes. These chemical compounds contained in the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta* have been found by other authors who have carried out work on the green and roasted coffee of *arabica* and *robusta* varieties. Thus^[20,21,22,23,24] have demonstrated and even quantified the chemical composition of these three classes of secondary metabolites in green and roasted *Coffea* varieties *arabica* and *robusta*. The leaves of *Coffea canephora robusta* contain various chemical compounds such as sterols, polyterpenes, polyphenols, flavonoids, alkaloids and saponosides.^[25] The physicochemical study of *Mitragyna inermis*, a plant with antidiabetic properties, of the same family as that of the coffee tree revealed the presence of the same chemical constituents contained in the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta*^[26]

The chemical compounds contained in the AE of the roasted and ground coffee beans of *Coffea canephora robusta* would be responsible for the pharmacological activities of this extract.

The increase in blood glucose at doses of 40 and 50 mg/kg bw of AE, could be explained by the action of caffeine. Indeed, HPLC study revealed in the aqueous extract roasted and ground coffee beans of *Coffea canephora robusta*, a high caffeine content of 7.5%^[27], but caffeine inhibits the transport of glucose stimulated by insulin in adipocytes.^[28] This glycemia increase could also be explained by the fact that the ingestion of the coffee drink increases the adrenaline, which can raise blood sugar levels in a short period of time.^[29] Short-term studies have also shown that coffee and caffeine can increase blood sugar and insulin levels.^[30,31,32]

EE at doses of 50 and 100 mg/kg bw induces a significant decrease in blood glucose which could be explained by the presence in this extract of phenol compounds such as polyphenols and flavonoids which are recognized as having hypoglycemic effects.^[33,34,35]

For the glucose tolerance test, the different extracts (AE, ARE and EE) from the roasted and ground coffee beans of *Coffea canephora robusta* induce an increasing decrease in blood glucose levels in normoglycemic rats, as is glibenclamide. Indeed, ingestion of coffee improves glucose tolerance, insulin sensitivity and hyperinsulinemia. This effect could be attributed to a reduction in the expression of inflammatory adipocytokine.^[36] Similarly, some metabolites of chlorogenic acids would have a hypoglycaemic action and stimulate the production of insulin.^[37,38] Our study shows that aqueous residual aqueous and ethanolic extracts of the roasted and ground coffee beans of *Coffea canephora robusta* contain hypoglycemic substances

because they act as the glibenclamide, which is a hypoglycemic sulfonamide. Indeed, it has been reported that sulfonylureas induce hypoglycaemia in normoglycemic rats by stimulating the production of insulin by the beta cells of the pancreas, thus promoting the storage of glycogen in the liver.^[39,40]

The oral administration of glucose per os at a dose of 3 g/kg bw causes a significant increase in blood glucose levels in rats followed by a gradual return to the initial level. Under the same experimental conditions, when animals are pretreated or post-treated with AE (20 mg/kg bw), ARE (5mg/kg bw) and EE (100 mg/kg bw), glucose-induced hyperglycemia is significantly reduced, and the return to the initial blood glucose is much faster. These effects were also observed with glibenclamide at 10 mg/kg bw. Thus, like glibenclamide, the various aqueous (AE), aqueous residual (ARE) and ethanolic (EE) extracts induce a significant reduction in glucose-induced hyperglycemia. These extracts therefore have hypoglycaemic effects and anti-hyperglycemic effects. The similar effects of these extracts with those of glibenclamide on blood glucose suggest that these extracts could act by the same mechanism as the reference anti-hyperglycemic substance used. Thus, hypoglycemia and the reduction of hyperglycemia observed in rats treated with aqueous, residual aqueous and ethanol extracts of the roasted and ground coffee beans of *Coffea canephora robusta* could be explained by a stimulation of insulin secretion by the pancreas^[41] and / or, probably, an increase in the peripheral use of glucose in the presence of these extracts.^[42]

CONCLUSION

This study aims to assess the short-term the activity of the various drinks derived from powder of the aqueous extract of the roasted and ground coffee beans of *Coffea canephora robusta* on the glycemia of normoglycemic rats and rats subjected to the glucose tolerance test. A hypoglycemic effect and an improvement of the tolerance to glucose were observed at doses of 5, 20 and 100 mg/kg bw, respectively for the various extracts of Aqueous Residual (ARE), Aqueous (AE) and Ethanolic 70% (EE) administered orally. A better activity similar of the glibenclamide was observed with the extract ethanolic 70%. The presence of antioxidants (polyphenols, flavonoids and alkaloids) in the extract may provide an explanation for the hypoglycemic and anti-hyperglycemic effects observed. These results demonstrate the importance and the use of this drink (coffee) in the world. Moreover, these same effects would explain the preventive action of this drink (coffee) as to the occurrence of diabetes type 2.

Ethical Approval

The experimental procedures and protocols used in this study were approved by the Ethical Committee of Health Sciences, University Félix Houphouët-Boigny. These guidelines were in accordance with the European Council Legislation 87/607/EEC for the protection of

experimental animals. All efforts were made to minimize animal suffering and reduce the number of animals used.

REFERENCES

- Scheen AJ, Giet D. Prévention du diabète de type 2 : un nouveau défi de santé publique. *Rev Med Liège*, 2005; 60: 383-390.
- Schulze MB, Hu FB. — Primary prevention of diabetes: what can be done and how much can be prevented? *Annu Rev Public Health*, 2005; 26: 445-467.
- Scheen AJ, Letiexhe MR, Ernest Ph. Prévention du diabète de type 2: style de vie ou médicaments? *Rev Med Liège*, 2003; 58: 206-210.
- Magis D, Geronoz I, Scheen AJ. Tabagisme, insulino-résistance et diabète de type 2. *Rev Med Liège*, 2002; 57: 575-581.
- Magis D, Jandrain BJ, Scheen AJ. Alcool, sensibilité à l'insuline et diabète sucré. *Rev Med Liège*, 2003; 58: 501-507.
- Organisation internationale du café (OIC). Statistiques. Répartition des exportations d'Arabica vert et vert Robusta des pays exportateurs des volumes importants de ces deux types de café Juin 2009, Janvier de 2011. www.ico.org.
- Higdon JV, Frei B.— Coffee and health: a review of recent human research. *Crit Rev Food Sci Nutr*, 2005; 46: 101-123.
- Benedetti M D. *Smoking, alcohol, and coffee consumption preceding Parkinson's disease*. *Neurology*, 2000; 55: 1350-1358.
- Hino A. *Habitual coffee but not green tea is inversely associated with metabolic syndrome. An epidemiological study in a general Japanese population*. *Diabetes Res Clin Pract*, 2007; 76: 383-389.
- Bidel S. *Coffee consumption and risk of total and cardiovascular mortality among patients with type 2 diabetes*. *Diabetologia*, 2006; 49: 2618-26.
- Date I H. and al. *The relationship between green tea and total caffeine intake for self reported type 2 diabetes among Japanese adults*. *Ann Intern Med.*, 2006; 144: 554-62.
- Du Y et al. Association of serum caffeine concentrations with serum glucose levels in caffeine drug users and non-users. Results of German National Health Surveys. *Diab Obes Metabol*, 2007; 9: 756-8.
- Batram D S, et al. The glucose intolerance induced by caffeinated coffee ingestion is less pronounced than that due to alkaloid caffeine in men. *J Nutr.*, 2006; 136: 1276-80.
- <http://www.ico.org/prices/ml1.htm> I.C.O., 2011.
- Lambard Ch. « Le café de la terre à la tasse ». Centre de Caféologie. Bordeaux (France), 2003.
- FAO. (Food and Agriculture Organisation) Manual on the application of the HACCP system in mycotoxin prevention and control. Food and Nutrition, 2001; 73. ISSN 0254-4725.
- Costro L, Mourad AL, Oliveira PAPLV, Braddini JPOA, Kletecke RM. Environmental profile of Brazilian green coffee. *International Journal J.L.C.A*, 2006; 11: 16-21.
- G. N. Zirihi, A. M. Kra et F. Guédé-Guina., Évaluation de l'activité antifongique de *Microglossa pyriformis* (LAMARCK) O. KUNZE (ASTERACEAE) « PYMI » sur la croissance in vitro de *Candida albicans* ». *Revue de Med. et Pharm. Afr.*, 2003; 17: 11-18.
- SEIGLER D. S., Secondary metabolites and plant systematics. In: *The biochemistry of plants. A comprehensive treatise*, E. E. COM ed. (Californie), 1981; 7: 139-176.
- Clarke. R.J; "Quality Control in the Food Industry" (Coffee Technology), London. Academic Press, 1987; 4(2): 161-191.
- Viani R; The composition of coffee. In: S. Garattini Ed. *Caffeine, Coffee and Health*. Raven Press, 1993; 1: 17-41.
- Debry. G; Le café. Sa composition, sa consommation, ses incidences sur la santé. Centre de Nutrition Humaine.
- Ky C. L., Louarn J., et al. Caffeine, trigonelline, chlorogenic acids and sucrose diversity in wild *Coffea arabica* L. and *C. canephora* P. accessions. *Food Chemistry*, 2001; 75: 223-230.
- Vasconcelos A. L. S., Franca A. S., et al. A comparative study of chemical attributes and levels of amines in defective green and roasted coffee beans. *Food Chemistry*, 2007; 101: 26-32.
- Koffi N'GUESSAN, Beugré KADJA, et al. Screening phytochimique de quelques plantes médicinales ivoiriennes utilisées en pays Krobou (Agboville, Côte-d'Ivoire). *Sciences & Nature*, 2009; 6(1): 1-15.
- KONKONN G., SIMAGA D., et al. « Etude phytochimique de *Mitragyna inermis* (Willd.) O.Ktze (Rubiaceae), plante à feuille antidiabétique » *Pharm. Méd. Trad. Afr.*, 2006; XIV: 73-80.
- AKA Francis B. A., Amonkan K. A., et al. Acute toxicity of the aqueous extract of roasted and ground beans of *Coffea canephora robusta* in the wistar rat. *The Pharma Innovation Journal*, 2016; 5(12): 01-05.
- Akiba T et al. Inhibitory mechanism of caffeine on insulin-stimulated glucose uptake in adipose cells. *Biochemical pharmacology*, 2004; 68(10): 1929-1937.
- Zaharieva DP, Riddell MC. Caffeine and glucose homeostasis during rest and exercise in diabetes mellitus. *Appl Physiol Nutr Metab*, Aug, 2013; 38(8): 813-22. doi: 10.1139/apnm-2012-0471. Epub 2013 May 14.
- Batram DS, Arthur R, Weekes A, Graham TE. The glucose intolerance induced by caffeinated coffee ingestion is less pronounced than that due to alkaloid caffeine in men. *J Nutr*, May, 2006; 136(5): 1276-80.
- Petrie HJ, Chown SE, Belfie LM, Duncan AM, McLaren DH, Conquer JA, Graham TE. Caffeine

- ingestion increases the insulin response to an oral-glucose-tolerance test in obese men before and after weight loss. *Am J Clin Nutr.*, Jul, 2004; 80(1): 22-8.
32. Robinson LE, Savani S, Battram DS, McLaren DH, Sathasivam P, Graham TE. Caffeine ingestion before an oral glucose tolerance test impairs blood glucose management in men with type 2 diabetes. *J Nutr*, Oct, 2004; 134(10): 2528-33.
 33. Mangambu M. J. D., Mushagalusa K. F., Kadima N. J., Contribution à l'étude phytochimique de quelques plantes médicinales antidiabétiques de la ville de Bukavu et ses environs (Sud-Kivu, R.D.Congo). *Journal of Applied Biosciences*, 2014; 75: 6211-6220.
 34. Kim S. H., Hyun S. H, Choung S.Y, Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. *Journal of Ethnopharmacology.*, 2006; 104(1-2): 119-123.
 35. Huang D. J, Lin C. D, Chen H. J, Lin Y. H, Antioxidant and antiproliferative activities of sweet potato (*Ipomoea batatas* [L.] Lam 'Tainong 57') constituents. *Botanical Bulletin- Academia Sinica*, 2004; 45: 179-186.
 36. Matsuda Y, et al. Coffee and caffeine improve insulin sensitivity and glucose tolerance in C57BL/6J mice fed a highfat diet. *Biosci Biotechnol Biochem*, 2011; 75: 2309-15.
 37. Natella F, Scaccini C. Role of coffee in modulation of diabetes risk. *Nutr Rev.*, 2012; 70: 207-17.
 38. Adisakwattana S, et al. Insulinreleasing properties of a series of cinnamic acid derivatives in vitro and in vivo. *J Agric Food Chem.*, 2008; 56: 7838-44.
 39. Gebreyohannis T., Shibeshi W., Asres K., Effects of Solvent Fractions of *Caylusea abyssinica* (Fresen.) Fisch. & Mey. on Blood Glucose Levels of Normoglycemic, Glucose Loaded and Streptozotocin-induced Diabetic Rodents. *Journal of Natural Remedies*, 2014; 14: 67-75.
 40. Somani R. S., Singhai A. K., Hypoglycaemic and antidiabetic Activities of Seeds of *Myristica fragrans* in Normoglycaemic and Alloxaninduced Diabetic Rats. *Asian Journal Experimental Sciences*, 2008; 22: 95-102.
 41. Jackson J. E., Bressler R., Clinical pharmacology of sulphonylurea hypoglycemic agents. Part I. *DRUG*, 1981; 212: 211-245.
 42. Yasodha K. J., Jayaveera K. N., Ravindra R. K., Rupesh K., Raghavendra D., Anti-diabetic activity of aqueous extract of *Talinum cuneifolium* in rats. *Pharmacologyline*, 2008; 2: 198-206.