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Assessment of the Anti-hypertensive and Hyperhomocysteinemic Activity of Aqueous Extracts of Tomato (*Lycopersicon esculentum MILL*) Grown in Ivory Coast

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Abstract: The tomato (*Lycopersiconesculentum* Mill) is a herbaceous plant of the Solanaceae family widely cultivated for its fruit. It is one of the most consumed fruits in the world because of its nutritional potential. Indeed, tomato is rich in secondary metabolites and compounds with antioxidant power known for their beneficial effects on health. This study aims to evaluate the antihypertensive and antihyperhocysteinemic activity of two varieties of tomatoes grown in Côte d'Ivoire, namely *Locale côtelette* and *Cobra F1*. To do this, rats made hypertensive and hyperhomocysteinemic were treated at a dose of 50 and 100 mg/kg bw for 8 days with the extracts of these tomatoes. At the end of this treatment, the results indicate a decrease in the serum level of LDL-cholesterol and creatinemia respectively of 79.92% and 18.82% in comparison with those of hypertensive rats which did not undergo any treatment. In addition, serum homocysteine level decreased by 35% compared with untreated hyperhomocysteinemic rats. Moreover, a 13.33% increase in serum HDL-cholesterol was observed. In view of the results obtained, regular consumption of tomatoes could help fight against high blood pressure, atherosclerosis, renal failure and prevent cardiovascular complications such as thromboembolic diseases.

Keywords: *Lycopersiconesculentum*, Homocysteine, Thromboembolic Diseases, LDL-cholesterol, HDL-cholesterol

1. Introduction

Native to the fertile valleys of Mexico, the tomato (*Lycopersiconesculentum* Mill.) has long been considered an ornamental plant because of its resemblance to the mandrake. It is from the XIXth century that the consumption of the tomato knew a considerable rise thanks to the transborder trade. Today, with an increasing production [1], it occupies the 2nd place as a vegetable crop in the world after the potato.

The nutritional interest of tomato lies in the fact that this fruit contains many secondary metabolites and other compounds with antioxidant power including, flavonoids such as rutin and hydroxycinnamic acid derivatives [2]. In addition, tomato contains carotenoids such as lycopene and β-carotene which are responsible for the red and yellow color of tomatoes, respectively [3].

Lycopene represents the majority carotenoid in human plasma [4]. Its protective effects against cancer and cardiovascular diseases have been demonstrated by several studies [5-7]. For this purpose, clinical studies have revealed that the amount of lycopene in blood plasma is inversely proportional to the risk of developing prostate cancer [6]. It has also been shown that when cancer is already declared, lycopene significantly reduces its aggressiveness [7]. Also, a correlation has been established between the consumption of tomatoes or tomato-based foods and the reduction of diseases such as cardiovascular diseases, gastrointestinal infections and epithelial cell infections [8]. The major risk factors for cardiovascular disease are hyperhomocysteinemia and hypertension [9, 10].

Homocysteine is a sulfur-containing amino acid produced during the catabolism of methionine [11]. After its formation, it can either undergo remethylation to give back methionine itself or undergo trans-sulfuration to give cysteine. These transformations are catalyzed by certain enzymes (methionine synthase, β-cystathionine synthase) as well as their enzymatic cofactor (Vitamin B12 and Vitamin B6). The deficiency of one or more of these enzymes and/or cofactor can lead to an increase in plasma homocysteine concentration (hyperhomocysteinemia) that can exceed 50 µmol/L in cases of severe hyperhomocysteinemia [12]. This high level can result in developmental delay, osteoporosis, early arteriosclerosis [13] and a change in the anticoagulant phenotype of the endothelial cell to a pro-coagulant phenotype [14, 15]. In addition, dietary factors may impact plasma homocysteine levels due to their content of vitamins B12, B6, and folate. Some of these factors may regulate renal function [16], blood glucose [17], and blood plasma lipid profile [18].

Hypertension is defined as an abnormal and permanent elevation of blood pressure, i.e. when systolic (SBP) and diastolic (DBP) blood pressures are higher than 140 mmHg and 90 mmHg respectively [19]. This elevation leads to arterial stiffness which causes hyperactivity of the heart. According to Diop [20], the number of hypertensive people will increase to 150 million by 2025 in sub-Saharan Africa. In Côte d'Ivoire, the prevalence of this pathology is growing exponentially. In fact, in 2015, data indicated a rate of 20.4% of hypertensives within the Ivorian population [21-23]. These pathologies being among the major causes of mortality and morbidity in the world, therefore deserve special attention. This necessarily requires the implementation of preventive measures in order to curb these pathologies in their devastating momentum within the population. Several studies around the world have demonstrated the existence of a correlation between the consumption of tomato and its derivatives, and the risk of appearance of various diseases including prostate cancer [24, 25]. In addition, tomato extracts induce a decrease in blood pressure [26]. However, in Côte d'Ivoire, very few data remain available on the anti-hyperhocysteinemic and anti-hypertensive activity of tomatoes. Therefore, this study was conducted to evaluate the effects of tomato extracts grown in Ivory Coast on blood pressure and plasma homocysteine concentration of Wistar rats with respect to the determination of blood glucose, triglycerides, cholesterol, urea, creatine, electrolytes (Na+, K+, Cl-) as well as serum homocysteine level.

2. Materials and Methods

2.1. Material

2.1.1. Plant Material

The two varieties of tomatoes that were the subject of this study are from the Yamoussoukro plantations (Lakes Region, Côte d'Ivoire). They are the species *Lycopersiconesculentum* Mill. var. Cobra 26 F1 and *Lycopersiconesculentum* Mill. var. Locale côtelette commonly called African tomato. These tomatoes were cut and dried in an oven at 60°C for 48 hours before being ground in a porcelain mortar to a powder.

2.1.2. Animal Material

The experiments were conducted on Wistar rats of the species *Rattusnorvegicus*, aged 2 to 3 months. A total of 92 rats with average weights ranging from 120 to 200 g were used in this study. These animals were raised in plastic cages and acclimated to the experimental laboratory conditions. They were fed with pellets provided by the Ivorian Society for the Manufacture of Animal Feed (FACI) and watered with tap water without discontinuity.

2.2. Methods

2.2.1. Preparation of Aqueous Tomato Extracts

Two extracts were prepared from the powders of dried tomato samples. The aqueous extract by maceration and the aqueous extract by decoction according to the method described by Bidié *et al.* [27].

2.2.2. Induction of Animals to Adrenaline and Methotrexate®

The animals were divided into three groups. The first group of 66 rats received intraperitoneal 0.5 mL of adrenaline at a daily dose of 8.33 10^{-3} mg/kg body weight for 6 days. In addition, the second group of 16 rats received orally (gavage) 1 mL of methotrexate® at a daily dose of 1 mg/kg body weight for 3 days. A third group of 10 uninduced rats constituted the control group.

2.3. Treatment of Hypertensive and Hyperhomocysteinemic Animals with Aqueous Tomato Extracts

2.3.1. Evaluation of the Anti-Hypertensiveactivity of Tomato Extracts

The adrenaline-treated animals were divided into 11 batches of 6 rats each. The first batch did not receive treatment (untreated hypertensive batch (UHT)).

Instead, they received tap water. The second and third batches received 1 mL of Nifedipine® (reference antihypertensive) at a dose of 10 and 20 mg/kg body weight by gavage for 8 days, respectively. The other 8 batches received 1 mL of aqueous tomato extract by gavage at a dose of 50 and 100 mg/kg body weight for 8 days.

2.3.2. Evaluation of the Anti-Hyperhomocysteinemic Activity of Tomato Extracts

The 16 rats that received methotrexate® by gavage for 3

days were divided into four batches of 4 rats according to their body weight. Each batch received daily by gavage 1 mL of aqueous extract at a dose of 100 mg/kg body weight for 7 days. The HHNT (untreated hyperhomocysteinemic) and control batches received only tap water during treatment.

2.4. Determination of Biochemical Parameters of Animal Blood

After the treatments, the animals were fasted for 12 hours before being decapitated. Blood samples were collected in appropriate tubes and immediately transported to the laboratory for determination of biochemical parameters.

2.4.1. Determination of Biochemical Parameters

Biochemical parameters such as blood glucose, urea, creatinine and lipid compounds were determined using the HITACHI 704 (France) multiparameter automaton according to the protocol described by Nhanes, [28].

2.4.2. Determination of Electrolytes

The determination of electrolytes such as sodium, potassium and chlorine was performed with a flame spectrophotometer of the HospitexScreen brand (France).

2.4.3. Determination of Homocysteine

Serum homocysteine was assayed according to the Diazyme method of enzymatic cycling described by Dou *et al.* [29], using the Cobas c-311 biochemistry machine (Roche Diagnostics, France).

2.5. Statistical Analysis

Statistical analysis was performed by performing a one-factor analysis of variances (1-factor ANOVA) for all data (mean of each assayed parameter). This analysis was performed using GraphPad Prism 7 software. Comparisons of means were performed by the Newman-Keuls test at the 5% significance level.

3. Results and Discussion

The effect of aqueous tomato extracts on the blood glucose levels of rats made hypertensive by adrenaline injection is shown in Figure 1. In most cases, there was no significant ($p > 0.05$) variation in blood glucose levels between the rats in the different batches treated with tomato extracts and those in the control batch. The blood glucose values recorded were between 0.74 and 0.91 g/L. On the other hand, there was a significant decrease ($p < 0.05$) in the blood glucose level of the batches of rats treated with the decoctate of the local chop variety (DYLCO 50) in comparison with that of the hypertensive rats that received no treatment, which was 0.91 g/L compared with 0.74 g/L. The results also indicate that hypertensive rats have higher blood glucose levels than normotensive rats (control rats). This elevation of blood glucose is due to an abnormality in the flow of glucose to the target cells for storage. This abnormality would be the result of a vasoconstriction of the arteries which would prevent the normal circulation of glucose [30]. Indeed, several studies have shown that hypertensive animals have elevated blood glucose [31]. These results once again confirm the elevation of blood glucose in hypertensive animals. It is important to note that the aqueous tomato extracts used for the treatment of hypertensive rats resulted in a decrease in blood glucose levels to normal levels (control blood glucose). These extracts would thus have a hypoglycemic activity.

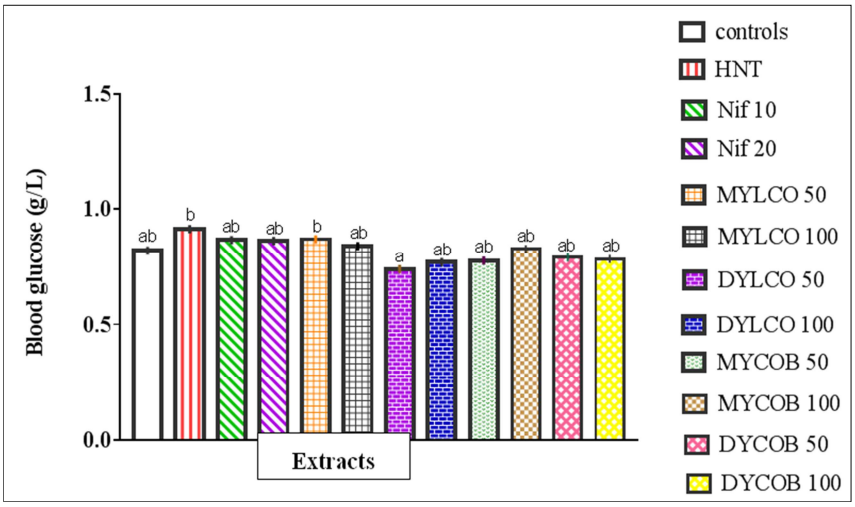

Figure 1. *Effect of tomato extracts and Nifedipine on blood glucose in hypertensive rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

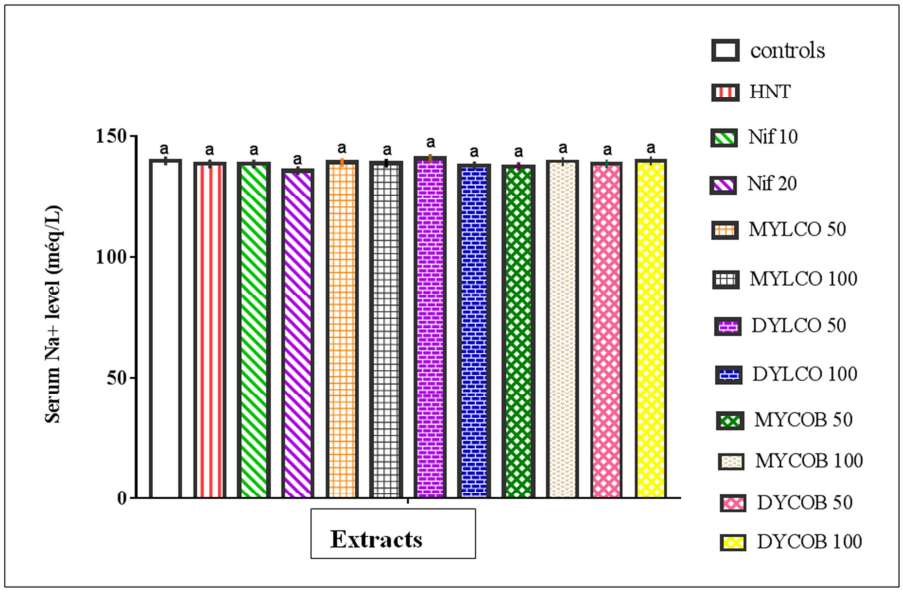

Figure 2. *Effect of tomato extracts and Nifedipine on serum Na^+ level of hypertensive rats.*

Each histogram represents the mean ± SME, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

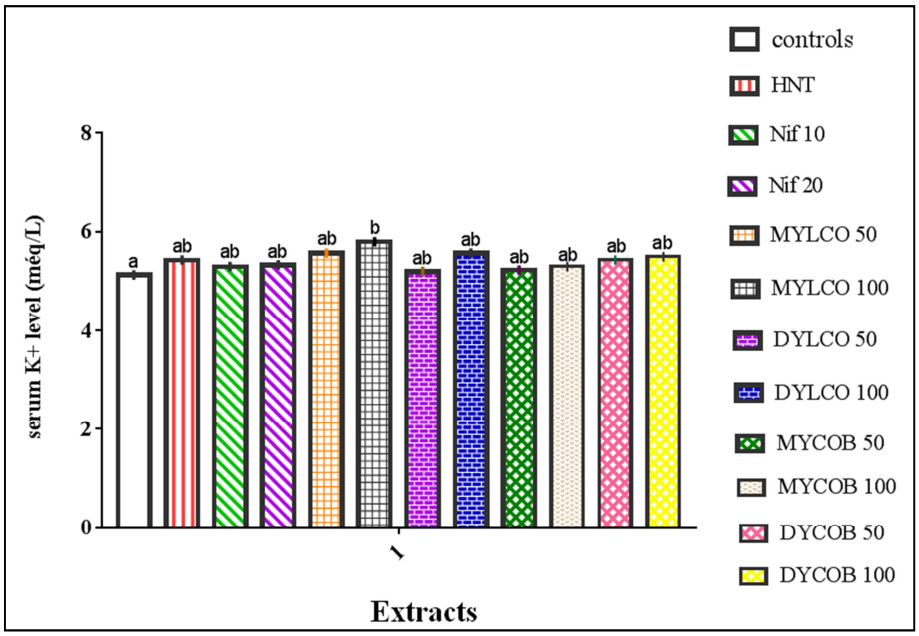

Figure 3. *Effect of tomato extracts and Nifedipine on serum K^+ levels of hypertensive rats.*

Each histogram represents the mean ± SME, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

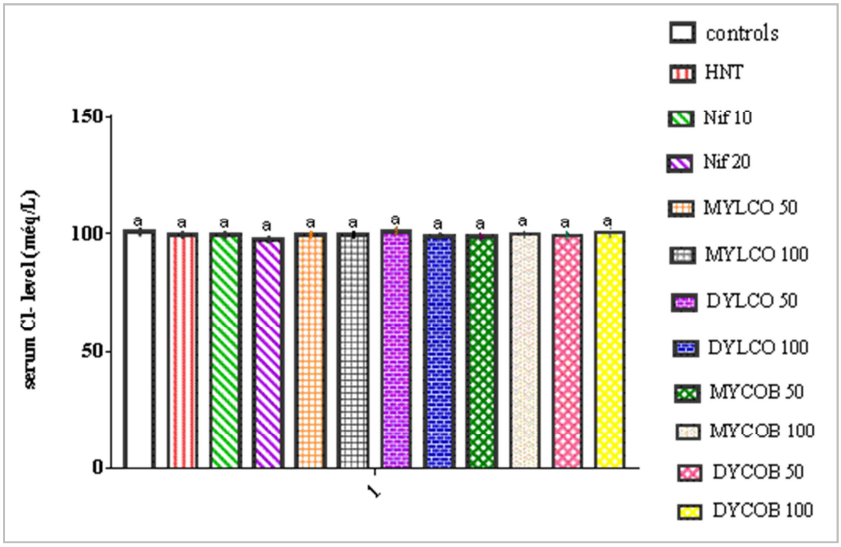

Figure 4. *Effect of tomato extracts and Nifedipine on serum Cl⁻ level of hypertensive rats.*

Each histogram represents the mean ± SME, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

Figures 2, 3, and 4 show the effect of aqueous tomato extracts on serum electrolyte (Na^+, K^+, Cl^-) levels of rats rendered hypertensive following injection of adrenaline. The serum sodium, potassium and chlorine levels of hypertensive rats were not significantly different from those of control rats ($p> 0.05$). Also, the serum sodium and chlorine levels of the batches treated with the aqueous tomato extracts did not differ significantly at the 5% significance level compared with those of the HNT batch and those treated with the reference antihypertensive (Nifedipine). However, the rat lot treated with the macerate of the Local chop variety at the dose of 100 mg/kg bw had a significantly different potassium level than the control lot at the 5% significance level. The hemodynamic balance of the body is due in part to the electrolytes sodium, potassium and chlorine. Potassium is the main intracellular cation, hence its low plasma level. This cation plays an important role in the regulation of blood pressure in hypertensive subjects by increasing natriuresis [32, 33]. The increase in blood potassium levels in hypertensive rats shows that the injection of adrenaline disturbed the ionic balance between the extracellular and intracellular milieu. This disturbance would result from a renal attack following the increase in arterial pressure. Indeed, potassium, like other electrolytes, is essentially eliminated by the kidneys. An incapacity of the kidneys to eliminate potassium normally would be at the origin of this hyperkalemia. In addition, potassium reduces blood pressure by suppressing renin and inhibiting certain angiotensin II converting enzymes [34, 35]. Treatment of hypertensive animals with aqueous extracts promoted constant maintenance of serum potassium levels. This result would imply that these extracts would regulate the blood level of potassium and thus restore normal kidney function.

The results of the effect of aqueous tomato extracts on the serum lipid profile of rats rendered hypertensive are shown in Figures 5 and 6. Adrenaline-induced hypertension significantly increased serum triglyceride, total cholesterol, and LDL-cholesterol levels at the significance level ($p<0.05$). However, this induction decreased serum HDL-cholesterol levels. With increasing doses of extract during treatment, there was a decrease in serum triglyceride, total cholesterol, LDL-cholesterol while HDL-cholesterol increased. The lowest levels of total cholesterol and LDL-cholesterol were found in animals treated with the macerate of the traditional Local Chop variety. Also, the animals treated with the decoctate of the Cobra F1 variety at the dose of 100 mg/kg bw had the highest HDL-cholesterol level with 0.61±0.03 g/L. This value corresponds to an increase in serum HDL-cholesterol of 22.95% and 29.51%, respectively, compared with HDL-cholesterol in normotensive and hypertensive rats.

Adrenaline-induced hypertension resulted in increased serum triglyceride, LDL-cholesterol, total cholesterol, and decreased HDL-cholesterol compared to the corresponding control batches. These results are in agreement with those of several authors including Ugawa *et al.* [36] and Oyedepo [37], who conducted work on hypertensive rats.

Atherosclerosis is the major consequence of increased serum LDL cholesterol and triglyceride levels. It is one of the major risk factors for high blood pressure. Indeed, macrophages consider oxidized LDL-cholesterol as a "non-self". These LDL are therefore captured by a metabolic pathway called 'SCAVENGER pathway' where they

aggregate to give rise to foam cells [38]. These cells will then accumulate in the walls of the arteries forming atheromatous plaques that obstruct the arteries and promote an increase in blood pressure [39]. In addition, fat mobilization in adipose tissue may be due to glucose underutilization as a result of hyperlipidemia associated with hyperglycemia [40]. The effect of aqueous tomato extracts in increasing blood levels of HDL-cholesterol and decreasing LDL-cholesterol, triglycerides and total cholesterol is thought to be due to the inhibition of LDL-cholesterol oxidation. This inhibition may be responsible for the reduction of oxidative stress [41]. The increase in HDL-cholesterol following treatment with aqueous tomato extract could be beneficial in the prevention of various pathologies, particularly atherosclerosis. In view of these results, these extracts could help fight against oxidative stress and atherosclerosis.

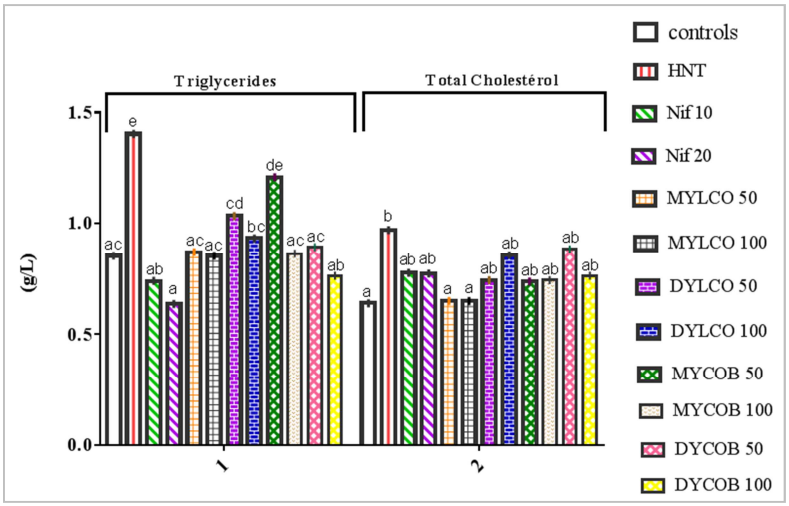

Figure 5. *Effect of tomato extracts and Nifedipine on serum triglyceride and total cholesterol levels in hypertensive rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

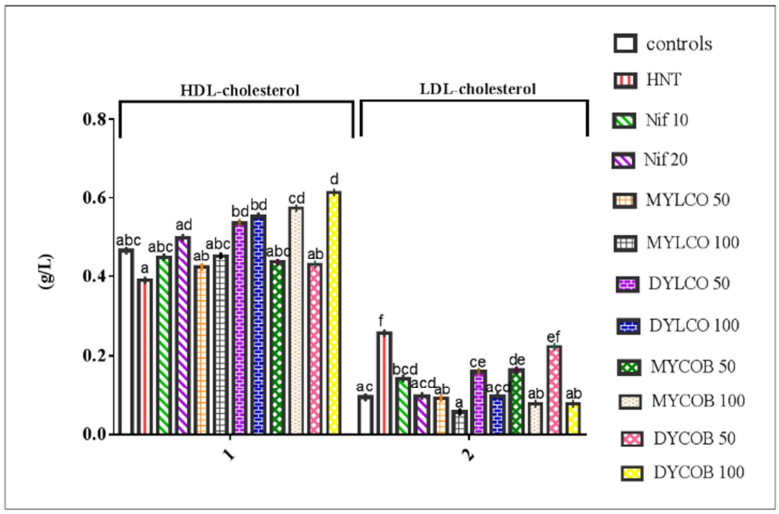

Figure 6. *Effect of tomato extracts and Nifedipine on serum HDL-cholesterol and total LDL-cholesterol levels in hypertensive rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

The results of the effect of aqueous tomato extracts on the indicators of renal function of the hypertensive rats are shown in Figures 7 and 8.

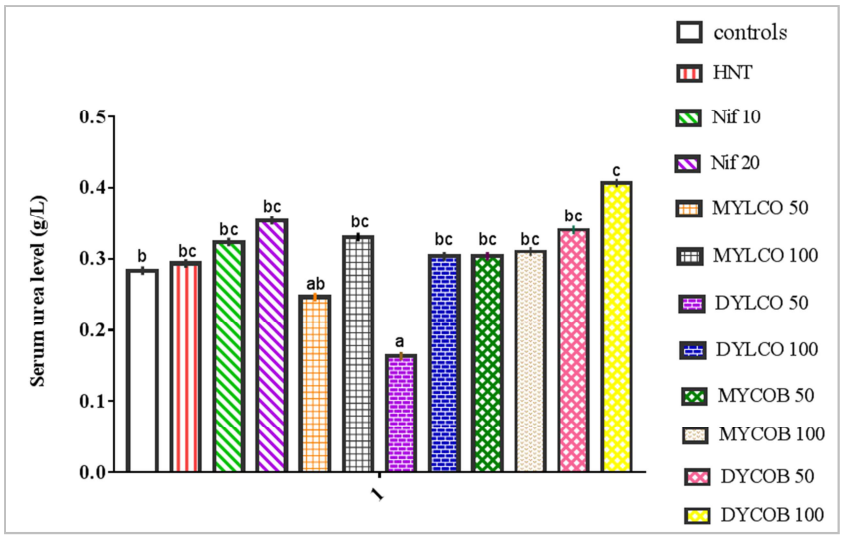

Figure 7. *Effect of tomato extracts and Nifedipine on serum urea levels in hypertensive rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

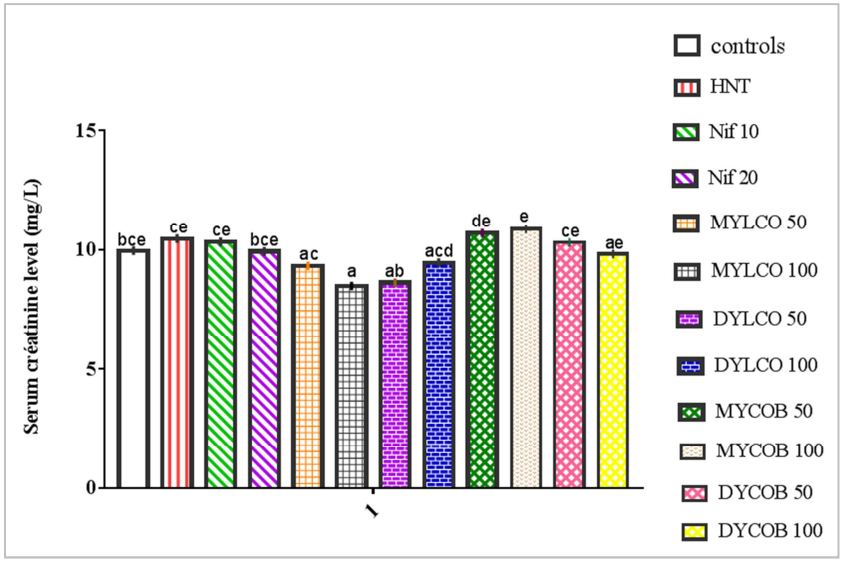

Figure 8. *Effect of tomato extracts and Nifedipine on serum creatinine levels in hypertensive rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; Nif 10: Hypertensive batch treated with Nifedipine 10 mg/kg bw; Nif 20: Hypertensive batch treated with Nifedipine 20 mg/kg bw; MYLCO 50: Hypertensive batch treated with macerate of the local chop variety at a dose of 50 mg/kg bw; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 50: Hypertensive batch treated with decoctate of the local chop variety at a dose of 50 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 50: Hypertensive batch treated with Cobra F1 macerate at a dose of 50 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bw; DYCOB 50: Hypertensive batch treated with Cobra F1 decoctate at 50 mg/kg bw; DYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

In hypertensive rats, there was a slight increase in urea and creatinine levels compared with those of control rats. However, this increase was not significant at the 5% significance level. The serum urea value increased from

0.28±0.02 g/L in normotensive rats to 0.29±0.02 g/L in hypertensive rats, a percentage increase of 3.45%. The same observation was made with creatinine, where rats made hypertensive had their serum creatinine levels elevated to 10.47±0.40 mg/L versus 9.97±0.06 mg/L in normotensive rats, an increase of 4.77%.

Treatment of hypertensive rats with aqueous tomato extract and nifedipine did not result in a significant change in either indicator in most cases. Nevertheless, with increasing doses of aqueous tomato extract and nifedipine, there was a decrease in serum urea and creatinine levels. The aqueous extract by decoction of the local chop variety at a dose of 50 mg/kg bw caused a significant decrease in urea from 0.29±0.02 g/L in hypertensive rats to 0.16±0.05 g/L, i.e. a percentage decrease of 44.82%. Also, the aqueous extract by maceration of the Local chop variety at the dose of 100 mg/kg bw resulted in a decrease in serum creatinine level of 18.82% compared to that of hypertensive rats.

Adrenaline injected into the animals also caused an increase in serum urea and creatinine levels. These elevated values would be the result of renal dysfunction. Indeed, urea and creatinine are compounds eliminated mainly by the kidneys through urine following glomerular filtration [42, 43]. They are good markers of renal function.

Therefore, an elevated concentration in the blood indicates renal damage [43]. The decrease in urea and creatinine levels in batches treated with tomato extracts therefore shows that these extracts could protect the kidneys against the complications of high blood pressure.

Figure 9 shows the effect of aqueous tomato extracts on serum homocysteine levels in hyperhomocysteinemic rats. Rats rendered hyperhomocysteinemic following induction with methotrexate® at a dose of 1 mg/kg bw for 3 days had a serum homocysteine level of 21.56±0.05 µmol/L. This value is high compared to the control lot (10.19±2.74 µmol/L) with a percentage increase of 52.73%. Hyperhomocysteinemic rats treated with aqueous extracts at a dose of 100 mg/kg bw for 7 days showed a decrease in serum homocysteine levels. However, this decrease is more pronounced with the aqueous extracts of the Cobra F1 variety than with those of the Locale côtelette variety. Indeed, the value of serum homocysteine level of rats treated with aqueous extracts of the Local chop variety is higher than that of the control rats. On the other hand, the serum homocysteine level of rats treated with aqueous extracts of the Cobra F1 variety is lower than that of control rats. The serum homocysteine level decreased by 38.27% for rats treated with the aqueous extract by decoction of the Locale chop variety and by 64.8% for rats treated with the aqueous extract by maceration of the Cobra F1 variety compared to hyperhomocysteinemic rats. The hyperhomocysteinemia following methotrexate® induction in rats indicates that homocysteine metabolic pathways are disrupted. This disruption is thought to be due to the inhibition by methotrexate® of the activity of methylene tetra-hydrofolate reductase, which is the catalytic enzyme for homocysteine remethylation [15]. This high plasma homocysteine level will result in an increased thromboembolic risk that can lead to cardiovascular complications. The decrease in serum homocysteine levels in rats treated with aqueous extract could result from the activation of the enzymatic reaction that was previously inhibited by the action of methotrexate. These results show that aqueous extracts, especially those from Cobra F1 variety, could help to fight against hyperhomocysteinemia, thus preventing cardiovascular complications.

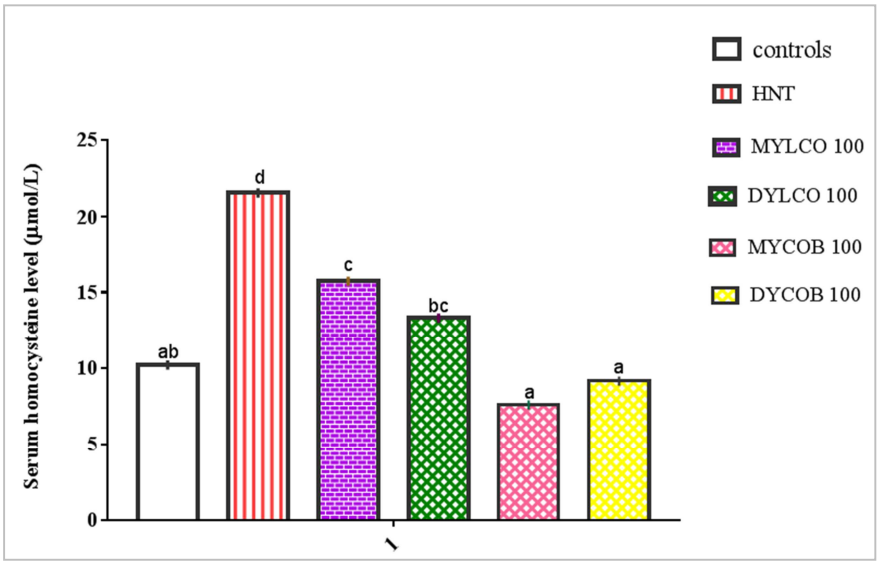

Figure 9. *Effect of tomato extracts on serum homocysteine level of hyperhomocysteinemic rats.*

Each histogram represents the mean ± MSE, n=6. Those assigned the same letters are not significantly different at the P>0.05 threshold.
HNT: untreated hypertensive batch; MYLCO 100: Hypertensive batch treated with macerate of the local chop variety at a dose of 100 mg/kg bw; DYLCO 100: Hypertensive batch treated with decoctate of the local chop variety at a dose of 100 mg/kg bw; MYCOB 100: Hypertensive batch treated with Cobra F1 macerate at a dose of 100 mg/kg bwDYCOB 100: Hypertensive batch treated with Cobra F1 decoctate at 100 mg/kg bw.

4. Conclusion

This study revealed that tomato consumption can promote the regulation of certain biological parameters. Several compounds with antihypertensive and antihyperhomocysteinemic activity would be involved in this regulation of pressure indicators and serum homocysteine level. It appears from this study that the tomatoes studied, whether they are of the improved or traditional variety, can help the organism to protect itself from the deleterious effects of hypertension and hyperhomocysteinemia. They could be used in the diet of hypertensive and hyperhomocysteinemic patients as part of the prevention of these pathologies.

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