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Chronic Maltex Drink and Tomato Paste Therapy Effects on Blood Glucose, Haematological and Biochemical Indices in Normal and Alloxan- Induced Diabetic Wistar Rats.

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ABSTRACT

There has not been a study that has directly assessed the potentially health promoting of tomato paste and maltex drink mixtures therapy and disease- preserving properties. In order to directly extrapolate the findings to everyday human health practices the effect of chronic ingestion of tomato paste and maltex drink mixtures on blood glucose, haematological and biochemical profiles in normoglycaemic and alloxan induced diabetic rat's model system are compared. Results revealed that after 35 days, tomato paste and maltex drink mixture therapy and/or maltex therapy significantly ($p<0.05$) lowered blood glycaemic load in normoglycaemic rats when compared with that of tomato paste therapy or control; while maltex drink therapy have significant anti-diabetic potential in both normoglycaemic and diabetic rats. Overall, the treatments ameliorate cholesterol and body weight lowering with corresponding improvement in some haematological parameters in both normoglycaemic and diabetic rats, with tomato paste and maltex drink mixture therapy having significant anti-obese effect. The anti-hyperglycaemic, anti-cholesterolaemic, anti-obese and erythropoietin-potentiating activities of maltex drink and tomato paste mixture therapy after 35 days, as demonstrated in the present study, may have important clinical implications for improving chronic diseases particularly type 2 diabetes and its complications.

Keywords: Maltex drink, tomato paste, type 2 diabetes, cholesterol, blood indices, obesity, alloxan

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INTRODUCTION

Most of the populations worldwide use several plants as dietary medicinal plants in primary health care in treating a number of diseases without knowledge on its proper bio-active constituents. Even though this practice may be due to their fewer side effects, accessibility, availability, affordability or effectiveness compared to the synthetic orthodox agents, the popularity of the herbal medicine in the modern medical practices appear to be less popular and probably may be unrelated to lack of scientific and clinical data, which provide its efficacy and safety. Nevertheless, among rapidly urbanizing communities in sub-Saharan Africa, Nigeria in particular, maltex drink and tomato paste (*Solanum lycopersicum or lycopersicon esculentum*) therapy traditionally, has been acclaimed to show potentially a myriad of health promoting and disease- preventing properties including the various pathological conditions such as hypertension, diabetes, atherosclerosis, obesity, inflammation, anaemia and even in some cancers prevention. However, the molecular mechanism(s) responsible for this health promoting activity has not been yet elucidated.

While vitamins C and E, and in addition, phenolic and flavonoid compounds found in tomatoes has been suggested to consist antioxidant properties that have beneficial therapeutic effects in many diseases [1,2,3] Aside, the carotenoid, beta-carotene and lycopene responsible for the colour of tomato are considered as scavenging free radicals which have antioxidant effects that reduce oxidative stress and play an important role in prevention of diabetes and cardiovascular diseases[4,5]. Maltex drink, a non alcoholic drink is a carbonated malt beverage, brewed from barley, hops, yeast and water. Accordingly, barley one of the active ingredients has been suggested by Food and Drug Administration to provide health benefits of serum cholesterol lowering effects Furthermore, it has been suggested that barley contains insoluble fibres which reduce the risk of type 2 diabetes; while on the other hand, the soluble fibres may reduce the risk of coronary health disease and can lower cholesterol[6]. Thus, based on the local application, the aim of this work therefore, was to elucidate the health benefit linked with tomato paste and maltex drink therapy on blood glucose, haematological and biochemical profile in normoglycaemic and alloxan diabetic rats.

MATERIALS AND METHODS

Albino wistar strain rats of either sex weighing between 140-200g aged 10 weeks were enrolled for the study. The animals were housed in large spacious, hygienic polypropylene cages linked with husk, renewed every 24 h under 12/12 h light/dark cycles at 25–30°C and at 45%–55%

relative humidity in the animal house, Department of Human Physiology, during the course of the experimental period. The experimental animals maintained their regular diet during the study and drank tap water at *ad libitum*

The National Institutes of Health guidelines for care and use of animals and Guidelines on Ethical Standards for Investigation of Experimental in Animals (NIH, 1985) were followed.

Alloxan induction of diabetes:

Diabetes was induced in Wistar albino rats of both sexes with a freshly prepared solution (110 mg/kg body weight) of alloxan monohydrate (Sigma Chemical Co, St Louis, MO, USA) in 0.1ml sterile normal saline solution and administered intraperitoneally to overnight fasted adult rats and after being confirmed diabetic, animals were orally treated with maltex drink daily for 35 days. Blood glucose was measured after 72 hours by one-touch glucometer (Accu-chek sensor of Roche Diagnostics, Germany). Rats showing fasting blood glucose (FBG) levels > 200 mg/dL after alloxanisation were selected for the study. Glucose level was assessed in diabetic rats compared with non-diabetic induced rats before the treatments of the animals (initials) and subsequently weekly for five (5) weeks.

Experimental design:

Albino Wistar rats of both sexes were randomly divided into two major groups of males and females and five sub- groups of 5 rats, sub group 1 serving as control and received physiological saline (0.9% NaCl; 5ml/kg.b.w.p.o) while sub-group 2 received tomatoes paste, group 3 mixtures of tomatoes and malt drink, group 4 malt drink only and group 5 diabetic rat treated with maltex drink; once a day for a period of 5 weeks (35 days) consecutively. The albino Wistar rats of both sexes were treated orally with maltex drink (16.5cl) or tomato paste (10g, De-Rica brand) or both, taking cognizance that the amount of lycopene contained in a serving of tomato paste exceeds the average dietary intake and which represents a physiologically relevant dose that compares favorably to doses used in human studies (Xaplanteris et al., 2012).

Measurement of weight variations and sugar level:

Blood glucose and body weights were measured on the 1st, 7^{th}, 14^{th}, 21^{st}, 28th and 35th day respectively or for 5 weeks. Thereafter, blood samples were collected from the tail tip vein of the rats by strip method weekly till the end of the study for the determination of the blood glucose level. The variations in weight were measured for both diabetic and normal rats using the kitchen scale weighing balance.

Blood glucose, Blood chemistry and Heamatological studies:

After the experimental regimen the animals were fasted overnight and sacrificed by cervical

dislocation under mild anaesthesia using chloroform. Blood was collected on decapitation in two different tubes, one with anticoagulant for plasma and another without anticoagulant for serum separation. Serum and plasma samples was separated by centrifugation at 5000 rpm for 10 mins, and utilized for biochemical studies. All other chemicals and reagents were of analytical grade. Blood glucose level, total serum cholesterol, total protein, packed cell volume (PCV), haemoglobin concentration (Hb), Red Blood Cell (RBC), White Blood Cell (WBC), neutrophil, lymphocytes and eosinophil counts were assessed with routine methods and assayed as an index for the study. For instance, blood glucose level analysis was employed as diabetic indices.

Serum biochemistry was performed on each sample by standard enzymatic assay methods using Agappe Diagnostic kits and Selector Junior Automated Chemistry Analyzer (Vital Scientific Ltd, Dieren, and The Netherlands). The total cholesterol level was analysed by precipitation and modified enzymatic procedures from Agappe Diagnostic kits chemistry autoanalyser. Total-protein (T-PROTEIN) was determined using enzymatic spectroscopic method.

The haemotological parameters; packed cell volume (PCV), haemoglobin concentration (Hb), red blood cell (RBC) count and white blood cell (WBC) count (total and differential) were analyzed using the Automated Haematological Analyzer, Sysmex KX-21 (Japan). PCV tubes were filled by capillary action to the mark with whole blood and the bottom of the tubes sealed with plasticine and centrifuged for 4 - 5 min using haematocrit centrifuge. The percentage cell volume was read by sliding the tube along a “critocap” chart until the meniscus of the plasma intersects the 100% line. Haemoglobin contents were determined using Cyanmethaemoglobin (Drabkin) method. The relationship: - [Hb] = 1/3{PCV} was applied as a check on haemoglobin concentration [Hb] .

Statistical Analysis:

All the values in the test are presented as mean ± SEM (Standard Error of the Mean). The data between the control and treated animals were statistically analyzed using analysis of variance (ANOVA) and post-hoc LSD tests with the SPSS program (SPSS 17.0, USA) for multiple comparisons. The level for statistical significance/ differences between the means of the various groups were set at value of $p < 0.05$.

RESULTS AND DISCUSSION

The aim of the present study was to explore the scientific basis for the therapeutical potential of daily ingestion of maltex drink and tomato paste mixtures in health promotion and disease-preventing properties in normal and alloxan induced diabetes mellitus in experimental animal

model. In the study, either tomato paste, maltex drink or tomato paste and maltex drink mixtures were administered to normoglycaemic rats on one hand, and maltex drink to alloxan- induced diabetic rats, on the other hand, during which the animals were exposed to their regular diet and water *ad libitum* for five weeks. The percentage relative change in blood glucose following the administration of tomato paste therapy and maltex drink therapy in normoglycaemic and diabetic rats respectively during the 35 days of the study in relation to the base value in week one are compared in figure 1.

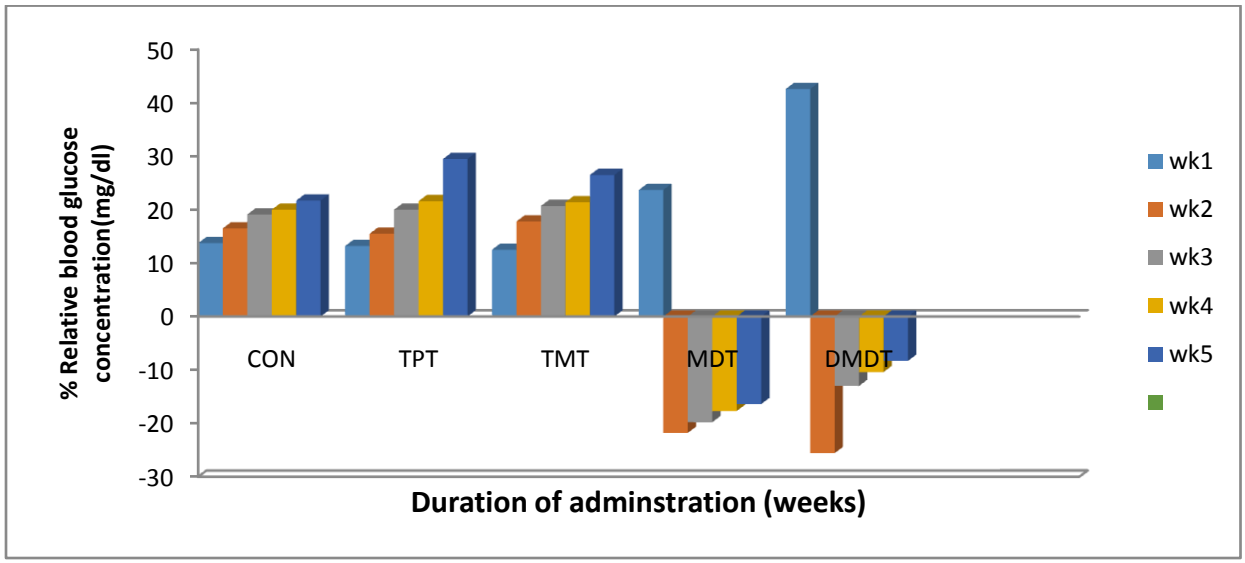

Figure.1. Effect of administration of maltex drink and tomato paste on *blood glucose level* in normal and alloxan-diabetic rats for 35 days.

Control = CON; tomato paste therapy =TPT; tomato paste with maltex drink therapy = TMT; maltex drink therapy = MDT and diabetes treated with maltex drink therapy = DMDT.

Administration of tomato paste or tomato paste and maltex drink mixtures statistically significantly ($p < 0.05$) duration-dependently increased blood glucose level from the base value at one week of 4.0% and 9.1% to 36% and 22.1% respectively after 35 days in normoglycaemic rats, while daily tomato paste and maltex drink mixtures tended in long term, to reduce blood glucose load compared with that of tomato paste therapy. The observation in the present study, that tomato paste therapy increased blood glycaemic load in normoglycaemic rats is of interest as it helps to explain patho-physiologically that in long- term, but not in short- term, it has the potential to increase the predisposition of an individual to developing high blood glucose level. In fact, it contributed to establish the importance of the influence of over nutrition or obesity and overweight [7,8]- associated - sedentary lifestyle (lack of exercise training) and cardiometabolic-stress impact on the increased risk of the prevalence of various modern lifestyle disorders

affecting both industrialized and developing countries. The result therefore supports the notion that chronic ingestion of maladaptive diet consisting of foods that are calorie-dense, phytochemical-depleted, highly processed and rapidly absorbable, often results in metabolic syndrome, a physiological state encompassing a cluster of metabolic abnormalities including central obesity and glucose intolerance.

Conversely, to our anticipation, although, at week one, blood glucose concentration for the diabetic and normoglycaemic rats was initially higher, the commencement of maltex drink therapy resulted in a steady decline of this factor to approach the control value (Figure.1). The reduction in blood glucose in normoglycaemic and alloxan-induced diabetic rats was from the base value of 72.4% and 209.8% in week one to 24.4% and 61.8% respectively after 35 days compared with control. The beneficial long-term rather than short term effect of maltex drink therapy on blood glucose is consistent with the previous report[6] and is suggestive that it possesses anti-hyperglycaemic property and plausibly can prevent oxidative stress with concomitant increase in antioxidant [5,9] and this may consequently avert macrovascular and microvascular complications as in diabetes. Additionally, as far that there was lowering of fasting blood glucose largely governed by insulin sensitivity, it is possible that maltex drink therapy acted by some yet undetermined mechanisms apart from stimulating insulin production from the pancreatic islets since these would have been severely damaged by alloxan. Alloxan induces diabetes mellitus by damaging the insulin secreting β-cells of the pancreas, and provoke a state of primary deficiency of insulin without affecting other islet types with the resultant decrease in endogenous insulin release [10] Although, the results from the present study revealed that maltex drink therapy delivers insulin into the bloodstream and lowers blood glucose concentrations thus providing a therapeutic approach for diabetes treatment, it's promising anti-hyerglycaemic properties remains speculative; therefore warrants further investigation to unravel the pathway of its hypoglycaemic action and the bio-active constituents responsible for its action.

Table 1 depict the effects of administration of maltex drink and tomato paste on some haematological and biochemical indices. The administration of tomato paste (group 2), tomato paste and maltex drink mixture (group 3), maltex drink (group 4) or ingestion of maltex drink by alloxan diabetic rats (group 5) statistically significantly ($p<0.05$) reduced cholesterol level (by 30.9%) and on the other hand, ingestion of maltex drink by alloxan-diabetic rats (group5) significantly ($p<0.05$) reduced the level of total protein (by 12.6%) after 35 days relative to control (group 1).

Table 1. Effect of administration of maltex drink and tomato paste on *some* biochemical and haematological indices in normoglycaemic and alloxan-induced diabetic rats.

Parameters	Group 1 (Control)	Group 2 (Tomatoes)	Group 3 (Malt +Tomatoes)	Group 4 (Maltex)	Group 5 (Alloxan + Maltex)
Cholesterol (mg/dl)	39.09 ± 5.06	26.56 ± 7.29	27.76 ±5.22	25.3 ± 7.32	27.5 ± 5.01
Total Protein (g/dl)	7.2 ± 0.27	7.91 ± 0.13	7.6 ± 0.34	7.3 ± 0.36	6.29 ± 0.26
PCV (%)	41.38 ± 3.38	45.38 ± 2.72	45.88 ± 2.52	44.50 ± 3.61	43.25 ± 1.38
Haemoglobin (g/dl)	13.26 ± 1.19	13.78 ± 0.96	15.55 ± 1.19	13.65 ± 1.42	13.05 ± 0.06
RBC x 10^9/L	4.09 ± 0.65	4.84 ± 0.73	4.39 ± 0.73	4.12 ± 0.98	4.17 ± 0.23
WBC (g/dl)	4.98 ± 0.13	4.67 ± 0.31	4.75 ± 0.40	4.86 ± 0.50	5.28 ± 0.43
Neutrophil (%)	36.75 ± 1.11	43.25 ± 6.50	40.00 ± 1.08	45.25 ± 3.43	55.25 ± 2.06
Lymphocytes (%)	60.75 ± 0.85	57.50 ± 6.04	58.75 ± 2.50	58.50 ± 5.42	40.25 ± 0.85
Eosinophil (%)	2.25 ± 0.35	2.25 ± 0.48	2.65 ± 0.57	2.50 ± 0.48	1.75 ± 0.25

The observed beneficial long- term effects of the theses treatments on cholesterol a key element for the development of atherosclerosis, is in consonance with previous reports in humans and experimental animals [11,12,13,5,4] suggesting plausible atheroprotective/ cardioprotective and prevention of the development of many other complications including diabetes mellitus potential of these medicinal plants.

As observed in the present study, the administrations of tomato paste and maltex drink significantly improved the level of the following haematological parameters: RBC, Hb, PCV, (also MCH, MCV and MCHC results not shown) and WBC, while the functional indices neutrophil were elevated (by about 8.8% to 50.4%) compared with that of the control. The treatment groups decreased the amount of lymphocytes (by about 4.1% in normoglycaemic rats and by 33.8 % in diabetic rats) and eosinophil (by 22.2% in diabetic rats) compared with control. These perhaps might be due to decreased blood glucose level or to increased immune-potentiating effect of maltex drink, tomato paste or both. In the present study, maltex drink therapy slightly reduced haemoglobin concentration (by 2.8%) in diabetic rats which can be compared with the report of Bose and Agrawal (2006)[13] who reported that in type 2 diabetic, patients who had prolonged administration of tomato, lycopene had reduced glycoslated haemoglobin (HbA1c), cholesterol among others and in contrast, increases antioxidant enzymes like superoxide dismulase (SOD) and glutathione peroxidase (GSH-Px).

Interestingly, in the present study, tomato paste (TPT), maltex drink (MDT) or tomato paste and maltex drink mixtures (TMM) duration- dependently reduced the relative body weight of the normoglycaemic and alloxan-diabetic rats ($p<0.05$) compared with that of the control (figure. 2). The percentage body weight gained after 35 days was ranked control (CON) > maltex drink - alloxan diabetic therapy (DMDT) > maltex drink therapy (MDT) > tomato paste therapy (TPT) >

maltex drink and tomato paste mixtures (TMM) therapy.

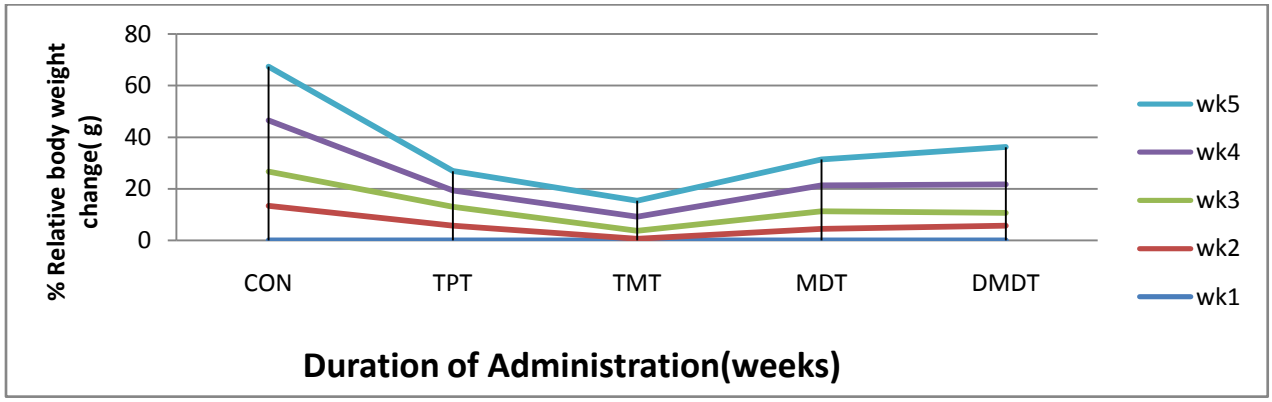

Figure.2. Effect of prolonged administration of maltex drink and tomato paste on body weight of normal and alloxan-diabetic rats.

Control = CON; tomato paste therapy =TPT; tomato paste with maltex drink therapy = TMT; maltex drink therapy = MDT and diabetes treated with maltex drink therapy = DMDT.

Although, the treatments concomitantly promoted weight loss, chronic ingestion of maltex drink and tomato paste mixture therapy after 5 weeks drastically reduced the body weight of the experimental animals in comparison with either that of tomato paste or maltex drink therapy alone, and which may in turn enhance insulin sensitivity. Invariably, the result demonstrated that tomato paste and maltex drink mixture therapy have tremendous benefits for people that are overweight and obese, an independent risk factor for cardiovascular disease (CVDs) and/or diabetes and possibly those with metabolic syndrome. The strong cooperative additive/synergetic anti-obesity effects of tomato paste and maltex drink mixture therapy may plausibly be attributed to modulation of cardiovascular risk factors- principally, endothelial dysfunction, an important underlying precursor of atherosclerosis, by inhibiting lipid uptake into adipocytes, decreasing fatty acid synthesis, and increasing lipid oxidation [4,14,15]. An alternative mechanism explaining our results of the weight loss may be that the treatment allowed the tissues access to glucose utilization and/or an indication of the inhibition of polyphagic condition and loss of weight due to excessive protein metabolism [16]

Insofar tomato and maltex drink mixtures are of plant origin, their beneficial effects may be attributed to strong cooperative additive/synergetic activities of antioxidant/ phytochemical dynamics associated - specific bio-active constituents in the body, preventing the incidence of diseases associated with oxidative stress [11,2,13,17,18,10,5,9,4]

CONCLUSION

the present findings show that daily maltex drink and tomato paste consumption in long term

lowers blood glucose and cholesterol level and can improve body weight and some haematological indices whilst maltex drink possesses anti- hyperglycaemic properties. This is of some interest as it helps to explain the rational of the local daily tomato paste and maltex drink consumption in health promotion and disease preventing which may be of clinical interest in the management of blood glucose, blood chemistry and anaemia for diabetic population in cardiac rehabilitation.

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