Effect of Feeding Granulated Sugar and Gari on Some Hepatic Enzymes in Albino Rats (*Rattus norvegicus*)

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Abstract: Seventy albino rats divided into seven groups of five albino rats per group were fed normal rat diet mixed with sugar (Granulated) and gari (a dried cassava product) at concentrations of 10%, 20%, 40%, 60%, 80% and 100%, while the last groups were fed normal rat diet and distilled water to serve as control to determine the sugar and gari concentrations that will repress induction of hepatic enzymes through glucose effect. The hepatic enzymes aspartate amino transferase (AST), alanine amino transferase (ALT), gamma glutamyl transpeptidase (GGT) and alkaline phosphatase (ALK PHOS) activities with albumin and total protein were monitored in the animals. There was significant dose increase (P<0.05) with variations in alkaline phosphate, (ALK), aspartate amino transferase, (AST), alanine amino transferase, (ALT) and dose dependent decrease (P>0.05) with variations in albumin and total protein in sugar and gari treated albino rats compared with their respective controls. The induced gamma glutamyl transpeptidase (GGT) levels showed variations compared with its control. The study showed that sugar and gari caused glucose effect at 20% concentrations by lowering of enzymes at this concentration through reducing cAMP concentrations. Therefore feeding sugar and gari can repress enzymes induction through the process of glucose effect at this concentration.

Key words: Glucose effect • Enzymes • Hepatic • Gari • Sugar

INTRODUCTION

Feeding varieties of carbohydrates (Glucose, sucrose and fructose) to mammals and bacteria result in blocking the induction of many enzyme systems. It has been shown that glucose feeding causes in both man and microorganism profound changes in metabolism include inhibition of induction of several enzymes, stimulation of others and blockage of most effects of glucocorticods [1]. The reduction of gene expression by glucose (catabolite repression) has been studied in various microorganisms [2]. Glucose, usually an excellent carbon source for growth, interferes with the synthesis of many secondary metabolites. Because of parallels with the well known suppression by glucose of catabolic enzymes that use less preferred substrates [3] this has been referred to as catabolite repression.

Glucose is known to repress a large number of inducible enzymes in many different bacteria. Meyer et al. [4] showed that not only the dietary regulated concentrations of serum glucagons and insulin but also the carbohydrate compound in principle might be able to exert control over the gene expression of this important glycogenic enzyme, the physiological significance is probably only apparent after refeeding glucose when the concentration may be as high as 20mM in the portal vein. Glucose supplementation has been found to restore cytochrome P₄₅₀ 2E1 expression but further suppressed GSTA2 expression during water deprivation, while glucose feeding instead of food during dehydration prevented P₄₅₀ 2E1 induction in the absence of recovery plasma insulin level [5] The short term deprivation of carbohydrate has the effect of decreasing rates of oxidative metabolism due to depletion of cofactors [6].

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However chronic high carbohydrate diets decrease P₄₅₀ activities in a pattern contrasting with that seen for protein [7, 8, 9] Sucrose, glucose or fructose when given in drinking water to mice maintained on a rodent chow was reported to decrease drug metabolism rates *in vivo* and *in vitro* [10].

Gari is a starchy food prepared from cassava (Manihot utilisima) tubers and is widely consumed in West Africa. Cassava is a staple food in human diets in over 80 countries [11] Sugar cane juice has been used successfully in the fattening of pigs as the principal source of carbohydrates, replacing completely the cereal grains normally used for this purpose [12, 13]. Sugar cane juice has also been used on the same basis as with pig feeding, giving the juice free choice together with restricted amounts of a protein supplements [14].

This study is aimed at determining the sugar and gari concentrations likely to repress enzymes induction through glucose effect in albino rats using Aspartate amino transaminase (AST), Alanine amino transaminase (ALT), Alkaline Phosphatase (AlkPhos), Gamma glutamyl Transpeptidase (GGT), Albumin (Alb) and Total Protein (T.Prot) as indicator.

MATERIALS AND METHODS

Test Animals: Seventy Wistar albino rats of 0.195kg average body weight on normal rat diet were obtained from the animal house of the department of Pharmacology and Toxicology, University of Port Harcourt. These rats were fed adlibitum with normal rat pellet and water and acclimatized to laboratory conditions for a period of 14days prior to commencement of study. The granulated sugar (produced by Dangote Sugar Nigeria PLC) and the Gari used in this study were purchased from Mile 3 Market, Port Harcourt.

Determination of Glucose Effect Concentration: Seventy (70) albino rats averaging 0.195kg in body weight were used for the determination of glucose effect in sugar and gari concentrations. The test animals were divided into thirty five (35) rats each for sugar and for gari. The rats were further divided into seven groups of five test animals per group each and fed with rat diet mixed with sugar and gari respectively at concentrations of 10%, 20%, 40%, 60%, 80% and 100% w/w. The last group was fed normal rat diet with distilled water to serve as control (0.00g/kg) for 3 weeks. The animals were sacrificed, blood collected and taken to the laboratory for analysis.

Biochemical Studies: Determination of ALT and AST was done by monitoring the concentrations of pyruvate hydrazone formed with 2,4, dinitrophenylhydrazine [16] Alkaline Phosphatase by Phenolphthalein Monophosphate method [17], Gamma Glutamyl Transpeptidase by Modified Szasz method [18], Total Protein by Biuret method [19] and Bromocresol green (BCG) method by Doumas *et al.* [20] for albumin in all the samples.

Statistical Analysis: The biochemical data were subjected to some statistical analysis. Values were reported as Mean±SEM while student's t-test was used to test for differences between treatment groups using Statistical Package for Social Sciences (SPSS) version 16.A value of P<0.05 was accepted as significant.

RESULTS

The effect of various concentrations of sugar and gari on hepatic protein levels in albino rats are as shown in Tables 1 and 2. The results showed that generally increasing concentrations of sugar and gari increased mean enzymes concentrations and decrease mean proteins concentration especially at 80% and 100% with little exception.

The Alkaline phosphatase activity (U/L) showed dose dependent increase. The alkaline phosphatase activity of 48.00±7.60 of the control albino rats was increased when the albino rats were fed sugar diet at 10% concentration to 58.00±4.77 but was reduced to 44.00±3.56 at 20%. This activity further increased to 58.00±5.99, 84.00±14.58, 86.00±11.80 and 90.80±4.49 at concentrations of 40%, 60%, 80% and 100% respectively. Also the alkaline phosphatase (U/L) activity increased in albino rats fed gari diet from 48.00±7.60 of the control rats to 66.40 ±8.80 at 10% concentration but reduced to 59.60±5.60 at 20% before it increases in activities to 69.40±6.00,81.60±3.82, 109.20±4.54 and 112.40±2.29 at concentrations of 40%, 60%, 80% and 100% respectively (Table 1).

The aspartate aminotransferase (U/L) activity of 18.00±2.59 of the control rats were reduced to 16.60±2.56 when fed sugar diet at 10% concentration which was further reduced to 16.00±2.68 at 20%. The activities were then increased to 19.00±3.26, 28.00±5.86, 82.00±4.77 and 74.00±4.93 at concentrations of 40%, 60%, 80% and 100% respectively. The aspartate aminotransferase (U/L) activity were increased in albino rats fed gari diet from 18.00±2.59 of the control rats to 25.80 ±4.15 at 10%

Table 1: Eeffect of sugar and gari on alkaline phosphatase, aspartate amino transferase and alanine amino transferase activities in albino rats

	Alkaline phosphatase(u/l)			Aspartate amino transferase (u/l)			Alanine amino transferase (u/l)		
Concentration (%)	Sugar Fed	Gari Fed	P Value	Sugar Fed	Gari Fed	P Value	Sugar Fed	Gari Fed	P Value
0.00	48.00±7.60	48.00±7.60	1.000	18.00±2.59	18.00±2.59	1.000	10.00±1.95	10.00±1.95	1.000
10	58.00 ±4.77	66.40±8.80	0.532	16.60 ± 2.56	25.80±4.15	0.227	13.40 ± 2.31	17.60±2.94	0.271
20	44.00±3.56	59.60±5.60	0.140	16.00 ± 2.68	19.60±2.01	0.489	8.60±0.93	14.00±3.36	0.130
40	58.00±5.99	69.40±6.00	0.154	19.00 ± 3.26	23.40+0.66	0.365	10.80 ± 0.97	13.60±2.64	0.452
60	84.00±14.58	81.60±3.82	0.875	28.00± 5.86	24.80±2.59	0.656	13.80 ± 1.85	17.40±1.44	0.250
80	86.00±11.80	109.20±4.54	0.123	82.00± 4.77	26.80±2.17	0.000	15.60±1.03	16.40±2.80	0.825
100	90.80±4.49	112.40±2.29	0.003	74.00 ± 4.93	25.00±1.79	0.000	24.80±2.65	17.40±3.14	0.221

Table 2: Effect of sugar and gari on gammaglutamy ltranspeptidase activity, total protein and albumin concentrations in albino rats

	Gammaglutamyl transpeptidase(u/l)			Total protein (g/l)			Albumin (g/l)		
Concentration (%)	Sugar fed	Gari fed	P value	Sugar fed	Gari fed	P value	Sugar fed	Gari fed	P value
0.00	493.00±59.45	493.00±59.45	1.000	68.00±1.87	68.00±1.87	1.000	36.00±1.76	36.00±1.76	1.000
10	232.40±70.45	309.60 ±93.09	0.372	65.60±2.48	66.00±4.20	0.926	34.60±1.53	35.20±1.02	0.818
20	373.00±90.30	470.80±96.96	0.189	71.00±1.58	68.00±3.45	0.208	38.00±0.84	37.60±1.72	0.836
40	382.00±63.52	504.00±106.09	0.470	74.00±1.70	67.20±2.58	0.056	37.00±1.10	36.80±1.25	0.002
60	228.00±28.91	355.00 ± 50.79	0.157	71.00±2.67	64.80±2.06	0.061	37.00 ± 1.05	36.20±1.69	0.456
80	235.00±28.91	322.00±46.95	0.151	63.00±1.73	63.00±0.89	1.000	36.00±1.30	34.80±1.36	0.547
100	191.00±18.28	250.00±34.06	0.208	61.00±3.49	62.80 ± 1.02	0.647	32.00±1.30	35.20±1.02	0.030

concentration but reduced to 19.60±2.10 at 20% before it increased inactivities to 23.40±2.66,24.80±2.59,26.80±2.17 and 25.00±1.79 at concentrations of 40%, 60%, 80% and 100% respectively (Table 1).

The alanine aminotransferase (U/L) activity of 10.00 ± 1.95 of the control rats were increased to 13.40 ± 2.31 when fed sugar diet at 10% concentration which was further reduced to 8.60 ± 0.93 at 20%. The activities were then increased to 10.80 ± 0.97 , 13.80 ± 1.85 , 15.60 ± 1.03 and 24.80 ± 2.65 at concentrations of 40%, 60%, 80% and 100% respectively. The alanine aminotransferase (U/L) activity were increased in albino rats fed gari diet from 10.00 ± 1.95 in the control rats to 17.60 ± 2.94 at 10% concentration but reduced to 14.00 ± 3.36 at 20%. The other activities are 13.60 ± 2.64 , 17.40 ± 1.44 , 16.40 ± 2.80 and 17.40 ± 3.14 at concentrations of 40%, 60%, 80% and 100% respectively (Table 1).

The gammaglutamyl transpeptidase (U/L) activity of 493.00±59.45 of the control rats was reduce to 232.40±70.45 when fed sugar diet at 10% concentration. The activity of 373.00 + 90.30 at 20% were then increased to 382.00±63.52 at 40%.At 60%,80% and 100%,the 228.00±28.91, 235.00±28.91 activities were 191.00±18.28 The respectively gammaglutamyl transpeptidase (U/L) activity were decreased in albino rats fed gari diet from 493.00±59.45 in the control rats to 309.60±93.09 at 10% concentration but increased to 470.80 ± 96.96 at 20% and 504.00 ± 106.09 at 40%. The other activities include 355.00±50.79, 322.00±46.95 and 250.00±34.06 at concentrations of 60%, 80% and 100% respectively (Table 2). Total protein (g/L) concentration of 68.00±1.87 of the control rats were decreased to 65.60±2.48 when fed sugar diet at 10% concentration. The concentration of 71.00 + 1.58 at 20% were then increased to 74.00±1.70 at 40%, while it reduced to 71.00±2.60, 63.00±1.73 and 61.00±3.49 at concentrations of 60%,80% and 100% respectively. Total protein (g/L) concentration in the control was 68.00±1.87 which decreased in albino rats fed gari diet to 66.00±4.20 at 10% concentration but increased to 68.00±3.45 at 20%. The concentrations now reduced to 67.20±2.58, 64.80±2.06,63.00±0.89 and 62.80±1.02 at 40%,60%,80% and 100% respectively (Table 2). There was dose dependent decrease in albumin concentration (g/l) of both sugar and gari fed rats. Albumin (g/L) concentration of 36.00±1.76 of the control rats were decreased to 34.60±1.53 when fed sugar diet at 10% concentration which was increased to 38.00±0.84 at 20% then decreased to $37.00\pm1.10,37.00\pm1.05,36.00\pm1.30$ and 32.00±1.30 at concentrations of 40%, 60%,80% and 100% respectively. The albumin (g/L) concentration of the control in gari fed albino rats was 36.00±1.76 which decreased in albino rats fed gari diet to 35.20±1.02 at 10% concentration but increased to 37.60±1.72 at 20%. The concentrations now reduced to 36.80 ± 1.25 36.20±1.69,34.80±1.36 and 35.20±1.02 at 40%,60%,80% and 100%, respectively (Table 2).

DISCUSSION

There was dose dependent increases in the enzymes ALKPHOS, AST and ALT in sugar and gari fed albino rats with slight variations while the GGT, an inducible microsomal enzyme behaved differently. While other liver damage marker enzymes were increasing in concentration, the GGT level was reducing only showing peak induction at 40%. There was dose dependent decrease in albumin and total protein. The concentration of sugar that caused glucose effect was 20% as shown by the lowering of enzymes and increase protein at this concentration. This is similar to the study by Benkel and Hickey [21] which showed that amylase activity in Drosophila melanogaster larvae was dramatically repressed simply by adding 10% glucose to their diet and that the magnitude of the response is both large and strain-specific. The effect of varying the composition of carbohydrate in the diet upon various enzymes including transaminases in the blood of healthy humans has been studied previously by Irwin and Staton [22] and Porikos and Van Itallie [23] Studies have shown that diet can have an effect upon hepatic enzymes both in animals [24, 25, 26] and in healthy humans [27, 22, 23].

Michaelis and Szepesi [28] reported dose dependent increase in hepatic glucose 6 phosphate dehydrogenase (G6PD), Malic enzyme and relative liver weight when rats were fed various concentrations of glucose, sucrose, galactose, fructose and lactose. Their study showed that 10% of glucose, fructose and sucrose gave the least enzyme concentration while 50% of carbohydrate gave the highest enzyme induction. Yamada et al. [29] showed that Gamma glutamyl transpeptidase activity varied inversely with the dietary carbohydrate level with 63% carbohydrate and 11% carbohydrate inducing the lowest and highest GGT levels respectively in rats to suggest that dietary carbohydrate levels influence hepatic gamma glutamyl transpeptidase (GGT) levels. Tschurdy et al. [30] have shown that carbohydrate administration decreased the level of the mitochondrial enzyme ä- aminolaevulinic acid synthetase in liver. Dietary carbohydrate also affected hepatic dimethylaminoazobenzene reductase in a similar manner [31] while an elevated level of hepatic phosphoenolpyruvate carboxykinase was suppressed by administration of glucose or glycerol [32, 33].

Gari is a high carbohydrate; high fibre and low protein food that contains trace amounts of cyanogens. Its effects on some liver microsomal enzymes in the rat over a period of prolonged ingestion have been reported [34]. Chilaka et al. [34] also reported that changes were observed in the activity rates of glucose-6-phosphatase, NADPH-cytochrome C (P-450) reductase, NADPHdichlorophenolindophenol reductase, cytochrome P₄₅₀ peroxidase, aniline hydroxylase and glucose-6phosphatase in rats fed Gari (56%w/w) for 9 weeks. Ezeji et al. [35] reported an overall reduction in the activity of the mitochondrial electron transport system namely, succinate dehydrogenase and cytochrome C oxidase in albino mice fed on maize (control) and gari (a dried cassava product) based diets for 5 weeks. The reduction in activity was more pronounced in Cytochrome C oxidase while gari fed mice had reduction in the mitochondrial respiratory control ratio (RCR). The choice of Gari as a source of carbohydrate in this study is because it is the staple food of people in West African region. The concentration of gari that caused glucose effect was 20% as shown by the lowering of enzymes and increase protein. Purkins et al. [36] also reported that amount of sucrose in the high-carbohydrate diet rather than starch was the cause of rise in transaminases and triglycerides. The high carbohydrate high calorie diet was also reported to produced small but significant rises in ALP and GGT activities as suggested previously by Irwin and Staton [21]. Gordon [37] and Nillson et al. [38].

Glucose represses the induction of inducible operons by inhibiting the synthesis of cyclic Adenosine monophosphate (cAMP) a nucleotide that is required for the initiation of transcription of a large number of inducible enzyme systems including the Lac operon. Cyclic AMP (cAMP) is required to activate an allosteric protein called catabolite activator protein (CAP) which binds to the promoter CAP site and stimulates the binding of Ribonucleic acid (RNA) polymerase to the promoter for the initiation of transcription, but cAMP must be available to bind to CAP which binds to Deoxyribonucleic acid (DNA) to facilitate transcription. In the presence of glucose, adenylase cyclase (AC) activity is blocked. AC is required to synthesize cAMP from Adenosine Triphosphate (ATP) [41, 42]. Therefore if cAMP levels are low, CAP is inactive and transcription does not occur. In the absence of glucose, cAMP levels are high, CAP is activated by cAMP and transcription occurs (in the presence of lactose). Thus the effect of glucose in suppressing these inducible enzymes is by lowering cyclic AMP level.

Rats fed sugar had insignificant lower enzymes concentration than the gari fed albino rats. This is similar

to study by Ezeji et al. [35]. Ezeji et al. [35] had suggested that cyanide affects some important enzymes of the mitochondrial electron transport system which are used as markers of the organelle. Their study also showed that the rate of oxygen consumption is lowered upon prolonged gari feeding. Grace [43] had reported that continual dependence on gari (and other cassava related foods) as staple food may lead to protein and vitamin deficiencies. Therefore, the presence of cyanogens in the gari caused the slight elevations seen in enzymes in gari fed albino rats.

The objective of this study includes determination of sugar and gari concentration likely to cause glucose effect by repressing the induction of enzymes. The 20% sugar and gari repressed the induction of inducible hepatic enzymes as shown in this study. This study thus showed that 20% sugar or 20% gari lowered the cyclic AMP level causing the glucose effect.

CONCLUSION

This study has shown that 20% concentrations of glucose and gari will repress the induction of inducible enzymes due to glucose effect. These repressions depend on the type of carbohydrate.

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Conflict of Interest: No conflict of interest associated with this work.

Contribution of Authors: We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

We hereby declare that

- Solomon A. Braide (Ph.D) carried out the entire literature and analysis of this study
- Adebayo O.Adegoke (Ph.D) did the entire animal study and report of this study
- Olugbenga E. Bamigbowu (M.Sc) carried out the biochemical analysis of this study.

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