



## Haematological Indices, Blood glucose levels and lipid profile of rats administered Tartrazine E102

KE Imafidon<sup>1</sup>, S Wuruyai<sup>1</sup>, S Odudu<sup>1</sup>, S Ighodalo<sup>1</sup>, SO Atewe<sup>1</sup>, IJ Akuneatiwu<sup>1</sup>, BI Egede<sup>1</sup>

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### Correspondence to

KE Imafidon;  
katevbu@gmail.com

### ABSTRACT

This work was done as a part of safety assessment to determine the effects of Tartrazine E102 on some haematological indices, glucose levels and blood lipid profile in rats. An animal model was used as a basis for interpreting the situation in humans. Consequently, 40 albino rats were divided into 5 groups of 8 rats each. All the animals were fed rats' mash and water and administered 0, 10, 20, 40 and 80mg/kg body weight of Tartrazine E102 respectively. Weekly measurements of body weight were recorded. Results obtained showed a significant reduction in body weight gain and blood glucose levels compared with the control. A non-dose dependent effect was observed on total cholesterol, LDL cholesterol, total white blood cells and monocytes. A slight but significant increase was observed in haematocrit at the highest dose levels. Conclusively, Tartrazine E102 exhibited a hypoglycemic effect in rats, no negative effect was observed on lipid profile.

**KEY WORDS:** *Tartrazine E102; glucose; haematological; cholesterol; triacylglycerol*

### INTRODUCTION

Tartrazine E102 is a synthetic orange-yellow coloured azo-dye, readily soluble in water. It is a trisodium salt of 3-carboxy-5-hydroxy-1-(p-sulphophenyl)-4-(p-sulphophenylazo) pyrazole. It is one of the most commonly used food colourant. A food additive is only approved for human consumption after studying its acute, subacute and chronic toxicity. Post-marketing surveillance of its effects must be kept for a long time. Individual response varies not only according to dose, age, gender, nutritional status and genetic factors, but also according to long term exposure to low doses<sup>1,2</sup>. Acute oral toxicity has been assessed in rats; the LD50 was defined as > 2000 mg/kg body weight<sup>2</sup>.

Some studies have linked asthma with tartrazine sensitivity; in one of such studies, four children with aspirin – induced asthma were tested for sensitivity to other substances including tartrazine, two of the children tested positive for reactions to tartrazine<sup>3</sup>. In another study, ten asthmatic children with a history of cough and wheeze after orange drinks were tested for

tartrazine sensitivity. On separate days, either oral tartrazine (1mg) or a placebo capsule was used in the tests. Bronchial reactivity was measured before the test and at thirty and sixty minutes after ingestion. They found that there was no change in baseline lung function after tartrazine administration but histamine sensitivity increased significantly in four of the children<sup>4</sup>.

Tartrazine undergoes metabolic reduction by intestinal microflora<sup>5</sup>, the reductive cleavage of the azo linkage produces sulfanilic acid and aminopyrazolone. The pyrazolone fragment is further degraded by intestinal bacteria to yield a second molecule of sulphanic acid<sup>6</sup>. Some work has been done on the biochemical effects of Tartrazine; Tartrazine was found to adversely affect and alter biochemical markers in vital organs of rats, not only at higher doses but also at low doses<sup>7</sup>.

An inflammatory effect on the gastric mucosa was reported on administration of Tartrazine which increased lymphocytes in the chorion. The maximum permitted intake of Tartrazine E102 in various foodstuffs is between 50-500 mg/kg; 200 mg/kg is the value permitted in alcoholic beverages, up to 100 mg/kg in non-alcoholic beverages and 500 mg/kg body weight in solid food<sup>8</sup>. This study was undertaken using sub lethal doses to determine the effect of Tartrazine on blood lipids, glucose levels and some haematological indices.

## MATERIALS AND METHODS

### Source of Materials/Animals

Tartrazine E102 was obtained from Rovet Scientific Limited, Benin City, Edo State. Forty albino rats used for this study were obtained from the Animal House of Pharmaceutical Chemistry Department, University of Benin, Edo State. The chows used were the product of Edo Feed and Flour Mill, Ewu, Edo State. The chow contains crude protein 14.50%, crude fat

4.80%, crude fibre 7.2%, crude ash 8.00%, Calcium 0.80%, phosphorus 0.52%, sodium 0.15%, lysine 0.60%, methionine 0.29%, vitamin E 15mg, vitamin B12 4mg, vitamin C 50mg, manganese 30mg and zinc 30mg.

### Treatment of Animals

The animals (40) were divided into five groups of eight rats each. They were acclimatized for two weeks on rats' chows and water ad libitum. Groups I – V were administered 0, 10, 20, 40, and 80 mg/kg body weight of Tartrazine respectively. Weekly measurements of weights were recorded. The animals were properly housed in well-ventilated cages and allowed unlimited access to feed and water. The principles of laboratory animal care<sup>9</sup> were adhered to.

### Collection of samples

The rats were subjected to an overnight fast, weighed and then anaesthetized. Blood was collected by cardiac puncture into containers with or without anticoagulant.

### Chemicals

All chemicals used were of the analytical grade (Aldrich Chemicals, Germany), diagnostic kits used were products of Randox Laboratories Limited, London, UK.

### Biochemical analysis

A glucometer (Accu-chek Active blood glucose meter, Roche Diagnostics, Germany) was used to measure the concentration of glucose. Total cholesterol, triacylglycerol and HDL cholesterol levels were determined using the enzymatic end point method<sup>10,11</sup>. LDL cholesterol was estimated using Friedewald equation<sup>12</sup>. Haematological indices were estimated using the automated method (Sysmex-kx-21N automated haematological analyser).

**Statistical analysis**

All data were expressed as means  $\pm$  SEM. One-way analysis of variance was used to test for differences among all the groups. Duncan multiple range tests were used to test for significant differences among the means. A p-value  $< 0.05$  was considered statistically significant.

**RESULTS**

**Table 1** shows the effect of Tartrazine on body weight changes and glucose levels of rats. There were significant reductions in weight gain of test rats compared with control. At dose level 10 mg/kg, blood glucose level was not significantly altered compared with the control. However at 20, 40 and 80 mg/kg dose levels, blood glucose levels of rats were significantly reduced compared with control.

**Table 1: Effect of Tartrazine E102 on body weight changes and blood glucose levels**

Treatment	Weight gain	Blood glucose level (mmol/L)
Control	16.63 $\pm$ 2.20 <sup>a</sup>	6.06 $\pm$ 0.68 <sup>a</sup>
10 mg/kg	2.97 $\pm$ 0.82 <sup>b</sup>	4.50 $\pm$ 0.19 <sup>a,b</sup>
20 mg/kg	1.77 $\pm$ 0.51 <sup>b</sup>	3.96 $\pm$ 0.27 <sup>b</sup>
40 mg/kg	9.83 $\pm$ 3.70 <sup>c</sup>	4.23 $\pm$ 0.23 <sup>b</sup>
80 mg/kg	6.03 $\pm$ 1.20 <sup>d</sup>	4.13 $\pm$ 0.29 <sup>b</sup>

Results are expressed in mean  $\pm$  SEM. Different superscripts denotes significance at  $p < 0.05$

Effect of Tartrazine on blood lipid profile is presented in **table 2**. A non-dose dependent increase was observed in total cholesterol and LDL cholesterol at the 40mg/kg dose levels. Others were not significantly altered. Haematocrit were significantly increased at the highest dose of 80mg/kg compared with the control. Other parameters were not significantly altered compared with control (**table 3**).

**Table 2: Effect of graded doses of Tartrazine E102 on blood lipid profile (mmol/l) of rats**

	Control	10mg/dl	20mg/dl	40mg/dl	80mg/dl
Total chol.	1.27 $\pm$ 0.06 <sup>a</sup>	1.25 $\pm$ 0.42 <sup>a</sup>	1.24 $\pm$ 0.18 <sup>a</sup>	1.72 $\pm$ 0.28 <sup>b</sup>	1.22 $\pm$ 0.32 <sup>a</sup>
Triacylglycerol	2.23 $\pm$ 0.09 <sup>a</sup>	1.81 $\pm$ 0.20 <sup>a</sup>	2.10 $\pm$ 0.04 <sup>a</sup>	2.43 $\pm$ 0.02 <sup>a</sup>	2.79 $\pm$ 0.08 <sup>a</sup>
HDL Chol.	0.13 $\pm$ 0.04 <sup>a</sup>	0.10 $\pm$ 0.02 <sup>a</sup>	0.14 $\pm$ 0.01 <sup>a</sup>	0.21 $\pm$ 0.01 <sup>a</sup>	0.15 $\pm$ 0.03 <sup>a</sup>
LDL Chol.	1.14 $\pm$ 0.03 <sup>a</sup>	1.15 $\pm$ 0.02 <sup>a</sup>	1.10 $\pm$ 0.01 <sup>a</sup>	1.51 $\pm$ 0.01 <sup>b</sup>	1.07 $\pm$ 0.02 <sup>a</sup>

Results are expressed in mean  $\pm$  SEM. Different superscripts denotes significance at  $p < 0.05$

**Table 3: Effects of graded doses of Tartrazine E102 on some haematological indices**

	Control	10mg/dl	20mg/dl	40mg/dl	80mg/dl
RBC ( $10^6$ /ul)	6.50 $\pm$ 0.18 <sup>a</sup>	6.59 $\pm$ 0.19 <sup>a</sup>	7.18 $\pm$ 0.21 <sup>a</sup>	6.96 $\pm$ 0.17 <sup>a</sup>	7.38 $\pm$ 0.27 <sup>a</sup>
Haematocrit (%)	41.48 $\pm$ 1.12 <sup>a</sup>	41.22 $\pm$ 1.15 <sup>a</sup>	44.32 $\pm$ 1.39 <sup>a</sup>	42.92 $\pm$ 1.56 <sup>a</sup>	46.92 $\pm$ 2.26 <sup>b</sup>
WBC ( $10^3$ /ul)	4.72 $\pm$ 0.28 <sup>a</sup>	4.64 $\pm$ 0.30 <sup>a</sup>	6.22 $\pm$ 1.04 <sup>b</sup>	5.00 $\pm$ 0.92 <sup>a</sup>	5.40 $\pm$ 0.97 <sup>a</sup>
Lymphocytes ( $10^6$ /ul)	4.18 $\pm$ 0.21 <sup>a</sup>	3.92 $\pm$ 0.27 <sup>a</sup>	4.46 $\pm$ 0.39 <sup>a</sup>	3.56 $\pm$ 0.22 <sup>a</sup>	4.90 $\pm$ 0.89 <sup>a</sup>
Neutrophil (%)	0.40 $\pm$ 0.10 <sup>a</sup>	0.56 $\pm$ 0.14 <sup>a</sup>	0.50 $\pm$ 0.16 <sup>a</sup>	0.32 $\pm$ 0.04 <sup>a</sup>	0.36 $\pm$ 0.07 <sup>a</sup>
Hgb (g/dl)	13.54 $\pm$ 0.44 <sup>a</sup>	13.64 $\pm$ 0.28 <sup>a</sup>	14.82 $\pm$ 0.53 <sup>a</sup>	14.56 $\pm$ 0.49 <sup>a</sup>	14.82 $\pm$ 0.66 <sup>a</sup>
RDW (%)	15.96 $\pm$ 0.30 <sup>a</sup>	16.04 $\pm$ 0.20 <sup>a</sup>	16.16 $\pm$ 0.18 <sup>a</sup>	15.62 $\pm$ 0.42 <sup>a</sup>	15.86 $\pm$ 0.41 <sup>a</sup>

Results are expressed in mean  $\pm$  SEM. Different letters denotes significance at  $p < 0.05$

## DISCUSSION

Weight loss observed in experimental rats may be due to non-palatability of experimental diet or a negative effect on appetite. At dose levels 10, 20, 40 and 80 mg/kg body weight, Tartrazine significantly reduced blood glucose levels demonstrating a hypoglycemic effect. This result is contrary to the report of some workers; some workers<sup>7,13</sup> reported that high dose of Tartrazine of up to 500 mg/kg caused no significant increase in serum glucose concentration.

The results of this study show non-dose dependent effect of Tartrazine on total cholesterol and LDL cholesterol, triacylglycerol and HDL cholesterol levels were not significantly altered. Some workers<sup>13</sup> observed significant increases in serum total lipids, cholesterol and triacylglycerol levels in rats whose diets were supplemented with mixtures of four synthetic dyes, Imafidon *et al*<sup>14</sup> reported an increase in LDL cholesterol and a reduction in HDL cholesterol on administration of sudan iv dye. The mechanism by which Tartrazine reduced blood glucose level is not known. Tartrazine may have exerted some effects on insulin release and sensitivity either directly or indirectly.

Slight but significant increase was observed in haematocrit at the highest dose level of 80 mg/kg, but there was no concomitant increase in red blood cells and haemoglobin levels. Swelling of the red blood cells secondary to hyperglycemia or hypernatremia may produce elevated haematocrit. Excessively elevated WBC counts may also alter the haematocrit. From the results of this study, it is clear that Tartrazine demonstrated a hypoglycemic effect, also WBC count were not significantly affected. Therefore, hypernatremia is suspected. Adverse effect of Tartrazine on the kidney has been reported<sup>13</sup>.

## CONCLUSION AND RECCOMENDATIONS

These results show a possible hypoglycemic effect of Tartrazine. Also a positive effect on blood lipid profile was observed. So intake of Tartrazine at the doses administered may not produce adverse effects on glucose, blood lipids and haematological indices. This work was done using an animal model; lower animals are used in some biomedical research work as a basis for interpreting the situation in humans. Any implication of potential lack of effects in humans will require human studies in which biomarkers like glucose, cholesterol, etc. are monitored on administration of Tartrazine.

### Author affiliations

<sup>1</sup>Biochemistry Department, Faculty of Life Sciences, University of Benin, Edo State, Nigeria

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