



**AMELIORATIVE EFFECTS OF CURCUMIN TREATMENT ON SELECTED GROWTH INDICES OF MALE WISTAR RATS EXPOSED TO BENZO[A]PYRENE**

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<https://dx.doi.org/10.4314/coast.v7i2.2s>

**Abstract**

The study evaluated the ameliorative effects of curcumin on selected growth performance indices of benzo[a]pyrene treated male Wistar rats. The wistar rats (n=6/group) were divided into five groups. Group 1(Control) rats were given rat feed and normal drinking water whereas groups II, III, IV and V were given benzo[a]pyrene (1mg) only, benzo[a]pyrene (1mg) with 50mg/kg body weight (bw) curcumin, benzo[a]pyrene (1mg) with 100mg/kg bw curcumin, benzo[a]pyrene (1mg) with 200mg/kg curcumin respectively. Rats were acclimatized for 7days before they were orally administered the varying doses of benzo[a]pyrene and curcumin every other day for 6weeks. Growth performance of the animals in the study was evaluated in terms of feed intake, percentage weight gain (%), feed conversion ratio (FCR) and percentage mortality rate. Results of the study showed that benzo[a]pyrene treatment triggered reduced ( $p<0.05$ ) percentage weight gain (PWG), increased ( $p<0.05$ ) feed conversion ratio (FCR) and percentage mortality (PM) in rats but curcumin treatments (50, 100 and 200 mg/kg bw) reversed the effects. Curcumin treatment seemed to be effective in ameliorating the toxic effects of benzo[a]pyrene on growth performance in the rats.

**Keywords:** benzo[a]pyrene, curcumin, growth parameters, wistar rats.

**Introduction**

Food smoking is an ancient traditional food processing method which offers fish consumers fish products with improved taste and aroma (Baten *et al.*, 2020). Regardless of these benefits, an unpleasant consequence of smoking is the generation of some harmful contaminants such as polycyclic aromatic hydrocarbons (PAHs), nitrosamines and heterocyclic amines due to the thermal breakdown of wood and naturally occurring compounds during the thermal processes (Rasheed, 2022). These

harmful substances, majorly PAHs, generated during the smoking process, pose a source of harm to human health when such smoked processed food products are consumed (Adeyeye *et al.*, 2016).

Polycyclic aromatic hydrocarbons are a wide range of organic compounds that possess at least two or more aromatic rings fused together (Hokkanen *et al.*, 2018). They have become an issue of great worry, based on their genotoxic, carcinogenic, mutagenic and immunotoxic effects in humans (Babić *et al.*, 2017).

Benzo[a]pyrene (BaP) is considered a representative PAH, due to its well-studied toxicity, link with other PAHs and a high occurrence in the environment, as a result of both pollution (such as industrial incineration, smoke and automobile exhaust) and natural burning processes (Dzobo *et al.*, 2018; Gao *et al.*, 2015; Yang *et al.*, 2021). It is generated during the burning of fossil fuels, wood, and other organic materials. Emissions of B[a]P primarily originate from human activities, with a smaller contribution from natural sources such as wildfires and volcanic eruptions (Saravanakumar *et al.*, 2022).

BaP is a well-identified human carcinogen (Maier *et al.*, 2022) whose metabolism generates the formation of reactive metabolites that create DNA adducts and disrupt cell cycles, ultimately resulting in uncontrolled cell proliferation and cancer development (Yang *et al.*, 2021). In mammals, B[a]P is readily absorbed in mammal via inhalation, oral administration, and skin contact (Knafla *et al.*, 2006). The main sources of B[a]P exposure for humans are contaminated food air (Bukowska and Sicińska, 2021).

Curcumin (diferuloylmethane), a polyphenolic compound, is a crucial ingredient of turmeric (*Curcuma longa*). Curcumin has been shown to possess chemo-preventive properties, largely due to their antioxidant activities (Hussain, 2017). Various studies have explored the impact of polycyclic aromatic hydrocarbons on the diverse health parameters in rats. However, direct assessments of growth indices such as bodyweight gain, feed intake, feed efficiency ratio following PAH exposure are limited, since most research have focused on biochemical, neurological and genetic effects. Given the scarcity of information on the impact of polycyclic aromatic hydrocarbons on growth performance

indices in rats, this study sought to examine the effects of benzo[a]pyrene on growth performance parameters such as bodyweight gain, feed intake, feed efficiency ratio and mortality rate in wistar rats.

## Materials and Methods

### Materials

Male Wistar rats, aged between 6 and 8 weeks and weighing between 130 g and 140 g, were used for this experiment. These animals were obtained from the Animal House of the Department of Biochemistry, Faculty of Life Sciences, University of Ilorin, Ilorin, Nigeria. Prior to the commencement of the experiment, the rats were acclimatized for one week to laboratory conditions, including feeding regimes and handling procedures. The study utilized industrially purified benzo[a]pyrene (BaP) and curcumin as the primary reagents.

### Methods

Benzo[a]pyrene, a polycyclic aromatic hydrocarbon (PAH), was freshly dissolved in olive oil and administered orally to the experimental rats at a dosage of 1 mg/kg body weight, three times per week over a six-week period. Similarly, curcumin was solubilized in olive oil and administered orally at varying doses of 50 mg/kg, 100 mg/kg, and 200 mg/kg body weight, also given thrice weekly for six weeks.

The experimental study utilized thirty male Wistar rats (*Rattus norvegicus*) with an average body weight ranging between 130 and 140 grams. These animals were obtained from the Small Animal Holding Unit of the Department of Biochemistry at the University of Ilorin, Nigeria. Upon arrival, the rats were acclimatized and then randomly divided into five treatment groups, each consisting of six animals.

The first group served as the control and was maintained on standard feed and tap water without any treatment. The second group received 1 mg/kg body weight of

benzo[a]pyrene orally, three times weekly. The remaining three groups were co-administered benzo[a]pyrene at the same dosage (1 mg/kg body weight) along with curcumin at doses of 50 mg/kg, 100 mg/kg, and 200 mg/kg body weight, respectively, following the same administration schedule. Throughout the experimental period, the growth performance of the animals was assessed by measuring feed intake, percentage weight gain, feed conversion ratio (FCR), and mortality rate. Feed intake was determined by subtracting the quantity of leftover feed from the amount initially provided over a 24-hour period.

#### Percentage Weight Gain

Body weights of rats in all groups were measured at the beginning and the end of the experiment. Percentage body weight gains were calculated using this equation:

$$\% \text{ Weight gain (g)} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

#### Feed Conversion Ratio (FCR)

This was calculated by dividing the mean of the feed consumed by the difference in weight.

$$\text{FCR} = \frac{\text{Final Body Weight} - \text{Initial Body Weight}}{\text{Feed Intake}}$$

#### Percentage Mortality

Mortality refers to total deaths that occurred in a population. Percentage mortality was calculated by dividing the number of deaths that occurred in a given period of time by the size of population amongst which death occurred multiplied by 100.

$$\% \text{ Mortality rate} = \frac{\text{Number of deaths that occurred in a given time period} \times 100}{\text{Size of Population among which death occurred}}$$

#### Results

The mean percentage weight gain of rats treated with benzo[a]pyrene (BaP) was significantly lower ( $p < 0.05$ ) compared with that of control group (Table 1). However, the mean percentage weight gains of rats administered BaP and curcumin (50, 100, and 200 mg/kg bw) were not significantly different ( $p < 0.05$ ) from the control (Table 1). Also, the mean feed conversion ratio (FCR) of rats treated with BaP was significantly higher ( $p < 0.05$ ) than that of control. Meanwhile, the mean FCRs for groups treated with BaP and curcumin (50, 100, and 200 mg/kg bw) were significantly lower ( $p < 0.05$ ) when compared with control group and BaP treated group (Table 1). In addition, rats treated with BaP only and BaP +50mg/kg bw curcumin had mean percentage mortality rates of 33.3 and 16.7% respectively (Table 1).

#### Discussion

Modifications in body weights are common

**Table 1: Selected Growth Performance Parameters of Male Wistar Rats Treated Orally with Benzo[a]pyrene (BaP) and Curcumin**

Groups	Initial Body Weight (g)	Final Body Weight (g)	Weight gain (%)	Feed Conversion Ratio	Mortality Rate (%)
Control	133.95 ± 5.79 <sup>a</sup>	217.00 ± 6.06 <sup>a</sup>	62.0 ± 0.23 <sup>a</sup>	9.58 ± 0.05 <sup>a</sup>	0
BaP Only	128.05 ± 1.72 <sup>a</sup>	198.58 ± 3.9 <sup>b</sup>	55.1 ± 2.13 <sup>b</sup>	10.34 ± 1.62 <sup>b</sup>	33.3
BaP + 50mg/kg bw Curcumin	130.25 ± 6.86 <sup>a</sup>	209.81 ± 3.37 <sup>a</sup>	61.1 ± 0.41 <sup>a</sup>	8.57 ± 0.62 <sup>c</sup>	16.7
BaP + 100 mg/kg bw Curcumin	129.58 ± 6.40 <sup>a</sup>	213.81 ± 5.17 <sup>a</sup>	65.0 ± 1.03 <sup>a</sup>	8.23 ± 0.31 <sup>c</sup>	0
BaP + 200 mg/kg bw Curcumin	130.17 ± 1.40 <sup>a</sup>	217.52 ± 4.13 <sup>a</sup>	67.1 ± 0.18 <sup>a</sup>	7.59 ± 0.05 <sup>c</sup>	0

Values are expressed as mean ± S.D. Values across columns carrying different superscripts are significantly different ( $P < 0.05$ ). ("a", "b", "c") are different superscripts which indicate significant differences across columns ( $P < 0.05$ ). (Significance Threshold "a ≠ b at  $p < 0.05$ "; "b ≠ c at  $p < 0.05$ "; "a ≠ c at  $p < 0.05$ ").

sensitive pointers to the general wellbeing of animals (Onyeabo *et al.*, 2021), since weight gain in animals serves as an index of growth rate (Hassan, *et al.*, 2019). In the present study, reduced body weight gain in rats treated orally with benzo[a]pyrene might be due to diminished desire for food and or decreased absorption of nutrients from the gut (Liu *et al.*, 2015). This outcome is supported by the findings of Li *et al.*, 2019 and Liu *et al.*, 2015 who reported the reduction in body weight gains in experimental animals treated orally with benzo[a]pyrene. Decreased body weight gain in benzo[a]pyrene-treated rats might have been due to the occurrence of oxidative stress, in which the metabolism of benzo[a]pyrene results in the formation of reactive metabolites. These metabolites might have induced diverse intracellular signaling pathways including mitogen-activated protein kinases (MAPKs) and Akt kinase which control cell proliferation, cell survival and cell communication, that are essential for normal growth and development (Vondracek and Machala, 2020). Thus, disruptions in these signaling cascades by benzo[a]pyrene might have affected growth processes in the rats.

The reduced body weight gain of rats treated with benzo[a]pyrene might also have been due to direct unpleasant effects of the metabolites generated from the metabolism of the diverse PAHs on gastrointestinal tracts of the animals (Aztatzi-Aguilar *et al.*, 2018). It might also have been due to alterations in rate of food assimilation as a result of tissue damage due to generated reactive oxygen species (ROS), which may have resulted in a decline in the absorption of nutrients from the gut (Kazemi *et al.*, 2016). However, increased body weight gains in animals co-treated with benzo[a]pyrene and curcumin in varying doses (50 mg/kg bw, 100 mg/kg bw and 200

mg/kg bw), might have been due to stimulated desire for food in the animals by curcumin, besides protecting them against the unpleasant effects of the metabolites of benzo[a]pyrene. This corroborates the findings of Oyewole and Oladele (2017), who reported that curcumin induced desire for food intake in rats treated with curcumin while boosting rate of feeding, leading to improved nutrient biotransformation and utilization thus enhancing growth rate in rats. Feed Conversion Ratio (FCR) also known as feed conversion efficiency, is a parameter that measures an animal's efficiency in converting feed into body mass (Fry *et al.*, 2018). This FCR value, which was observed to be high in rats treated with benzo[a]pyrene, might imply that the rats might have been unable to convert the feed consumed efficiently into useful nutrients needed by the body; thus, this may have been responsible for their reduced final body gain. It might also have been due to the ability of benzo[a]pyrene to induce cytochrome P<sub>450</sub> enzymes which perform a vital role in the metabolism of foreign substances in the body. Thus, there might have been significant induction of the cytochrome P<sub>450</sub> enzymes indicating an increased metabolic burden on the liver (Stoddard *et al.*, 2021). Thus, this heightened metabolic activity might have diverted energy and resources away from growth processes thus potentially impairing the efficient conversion of feed in the rats.

Meanwhile, reduced FCR values in rats co-treated with benzo[a]pyrene and curcumin (at varying doses such as 50mg/kg bw, 100 mg/kg bw and 200mg/kg bw) might suggest that the animals might have effectively converted the feed consumed into useful nutrients needed by the body, even as the FCR values of curcumin treated rats appeared to be dose dependent. This might be an indication of curcumin helping to stimulate and increase appetite in the rats. Curcumin

might have achieved this by triggering the pancreas to produce pancreatic juice which is rich in enzymes such as lipase, amylase and protease to help enhance the breakdown of food molecules such as proteins, fats and carbohydrates. This could have in turn boosted efficient absorption of food nutrients by the walls of the intestine, thus fast tracking the emptying of the stomach, and eventually bringing about hunger and stimulated appetite in the rats (Prabowo *et al.*, 2017).

Mortality can be regarded a crucial endpoint in toxicity studies providing essential data on the harmful effects of substances on an organism (Stoddard *et al.*, 2021). The occurrence of deaths amongst rats orally treated with benzo[a]pyrene, could indicate that the toxicity of benzo[a]pyrene on the experimental animals. Reports have shown that close contact with hazardous compounds such as heavy metals and PAHs, which trigger toxicity in tissues via oxidative stress, which could be a major factor responsible for increased rates of morbidity and mortality (Kanee *et al.*, 2021). And this could be due to a combination of factors that include oxidative stress and DNA damage in which benzo[a]pyrene underwent metabolic activation by cytochrome P450 enzymes to generate ROS (Ramos De Rainho *et al.*, 2013; Olasehinde, and Olaniran, 2022). It could also be due to immunotoxicity in which benzo[a]pyrene tended to suppress the immune system by reducing T-cell function and reducing antibody production as a result of the toxic effects of its metabolites on the immune system (Aztatzi-Aguilar *et al.*, 2018). However, rats co-treated with benzo[a]pyrene and curcumin (at doses of 50 mg/kg bw, 100 mg/kg bw and 200 mg/kg bw) had a lower mortality rate, thus suggesting the protective action of curcumin

against benzo[a]pyrene induced toxicity in the animals. The underlying mechanism of curcumin's chemo preventive action might be due to its good scavenging attributes for free radical generated during the metabolism of these PAHs.

### Conclusion

The outcome of the study indicates that benzo[a]pyrene treatment on rats triggered reduced body weight gains, high feed conversion rates and high incidence of mortality in rats while curcumin ameliorated these unpleasant effects. The study thus concludes that curcumin ameliorated such effects in rats exposed to benzo[a]pyrene. Future studies should explore curcumin's protective effects on other physiological parameters such as organ weights e.g. liver, kidney, heart, brain and spleen; body mass index, hormone levels such as growth hormone, insulin, leptin and thyroid hormones alongside hematological indices.

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