

## Effect of Sub-acute Exposure to Volatile Organic Compounds on Biochemical Indices in Wistar Rats

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### ABSTRACT

Petroleum hydrocarbons' exposure has been associated with the development of non-communicable diseases including cardiovascular diseases, allergies, cancers, immune toxicities and reproductive problems. However, little is known about their effects on metabolic dysregulation especially glucose homeostasis. This study therefore investigated the effect of volatile organic compounds (VOCs) on glycemic dysregulation in Wistar rats. A total of 30 adult albino rats were used and grouped into 5 groups of 6 rats each. The rats were individually exposed to 5% v/v of VOCs for a period of four weeks. The effects on body weight lipid profile, antioxidant enzymes, fasting plasma insulin,  $\beta$ -cell function, insulin resistance, inflammatory markers were evaluated and histological studies was carried out. The result indicated significant ( $p < 0.05$ ) increase in total cholesterol, triglyceride, and low density lipoprotein cholesterol in all VOCs exposed rats compared to control rats. Moreover, there was no significant ( $p > 0.05$ ) difference in SOD activity of VOCs exposed rats compared with control rats. Malondialdehyde (MDA) level was significantly ( $p < 0.05$ ) high with significantly ( $p < 0.05$ ) low catalase activity in control rats compared to all VOCs exposed rats. Level of Inflammatory markers IL-6, VEGF and TNF $\alpha$  were significantly high in all VOCs exposed rats with significant ( $p < 0.05$ ) increase in insulin resistance and  $\beta$  cell dysfunction compared to control rats. Histological examination of pancreas revealed changes in the cyto-architecture of pancreas of all VOCs exposed rats except toluene exposed rats. Therefore, exposure to benzene, hexane and xylene components of crude oil could cause glycemic dysregulation.

**Keywords:** Body weight, fasting blood glucose, inflammatory cytokines, oxidative stress, VOCs.

### 1.0 INTRODUCTION

Crude oil contains significant amount of volatile organic compounds with varied physical and chemical properties, producing different biochemical and physiological effects (Osibemhe *et al.*, 2024). At ambient temperature and pressure, they vaporize and are known to play role in photochemical reaction. They are abundantly found in crude oil products such as petrol, kerosene, diesel, solvents, paints, glues, tobacco products, and vehicle exhaust. Nowadays, they are increasingly utilized for economic and industrial purposes as solvents, cleansing agents, herbicides, insecticide, and intermediate for the production of rubber and plastics and a variety of purposes (Wesley *et al.*, 2019; Masoud *et al.*, 2015

The increasing human population growth, modernization, agricultural mechanization, industrialization, and increasing usage of vehicles, brought about increased exploration and refining of crude oil which has led to increase release of VOCs into the environment at a dangerous proportion (Ismail *et al.*, 2021). The risk of chronic, sub-chronic, acute and sub-acute toxicity in human generally exist during exploration, production, distribution, storage and

utilization of crude oil products (Okoye and Awunor, 2022; Mashoud *et al.*, 2015; Ita *et al.*, 2014; Orisakwe *et al.*, 2004).

In Nigeria, petroleum is a primary source of revenue that derives major transformational objectives of modern Nigeria and acts as fastest means of economic booms, rapid industrial revolution and affordable works (Osibemhe *et al.*, 2024; Salahuddeen *et al.*, 2024; Maduka and Paul, 2021). However, toxicity arise as a result of exposures and application of petroleum hydrocarbon at varied levels (Okoye and Awunor, 2022; Kim *et al.*, 2021; Jardel *et al.*, 2022). Reproductive and developmental problems, infertility, systemic toxicity, genotoxicity, hepatotoxicity, nephrotoxicity, immune toxicity, respiratory problems, have been reported following exposure to petroleum hydrocarbons (Osibemhe *et al.*, 2024; Salahuddeen *et al.*, 2024; Nwanjo and Ojiako, 2007; Abdel Aziz *et al.*, 2006; Akinosun *et al.*, 2006; Brauthar *et al.*, 2006; Neghab and Stacey, 1997). Take for instance, elevated activity of liver enzymes, creatinine, and urea have been reported in laboratory animals exposed to crude oil (Osibemhe *et al.*, 2024; Okoye and Awunor, 2022).

Further, epidemiological studies have reported increasing prevalence of diabetes mellitus in communities and individuals with residential or occupational exposures to petroleum hydrocarbons (Jardel *et al.*, 2022; Kim *et al.*, 2021; Maduka and Paul, 2021).

With the growing exposures to VOCs and increasing prevalence of diabetes in recent years, toxicity risk assessment of exposures especially on metabolic disturbance (glucose homeostasis) as well as assessment of their effects on gross structure of the pancreas is crucial. Generally, issue of potentials of VOCs on metabolic disturbance and gross pancreas structure has not been thoroughly investigated, and little information exists in this regard. This study, was undertaken to address this issue in response to concerns raised by public regarding the increased prevalence of diabetes, as well as morbidities and mortalities due to diabetes in spite of the treatment undertaken by patients. Thus, the present study investigated the effect of sub-acute exposures to 5%v/v each of VOCs on glucose and other biochemical indices.

## 2.0 MATERIALS AND METHODS

### 2.1 Materials

#### 2.1.1 Chemicals

All the chemicals used in this study were of analytical grade. Benzene, hexane, toluene and xylene were purchased from Sigma Aldrich, Germany and BDH chemicals.

#### 2.1.2 Experimental Animals

A total of thirty (30) adult male albino rats weighing between 130-180g were purchased from animal house, Department of Pharmacology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria. They were fed normal rat chow and allowed access to clean water *ad libitum*. The rats were kept in wire mesh cages for a period of two weeks to acclimatize before the commencement of the experiment.

### 2.2.0 Methods

#### 2.2.1 Preparation of 5% VOCs

Exactly 5% v/v each of benzene, toluene, xylene and hexane was prepared by pouring 5ml in a separate container of each of the earlier mentioned VOCs into 95 ml of distilled water once daily for 28 days.

#### 2.2.2 Animal Grouping and Experimental Protocol

The rats were grouped into 5 groups of 6 rat each according to a study by Jardel *et al.* (2022) with

modification where rats were exposed to 5%v/v as follows:

Group 1: Normal control rats, received food and water only.

Group 2: Rats were given food and water, exposed to 5% v/v benzene for four weeks.

Group 3: Rats were exposed to 5%v/v xylene, given food and water for four weeks

Group 4: Exposed to 5% v/v toluene, given food and water for four weeks

Group 5: Rats were exposed to 5% v/v hexane, given food and water for four weeks.

The exposure was oral ingestion through drinking water for four weeks.

#### 2.2.3 Fasting Blood Glucose Measurement

Fasting blood glucose of the exposed rats was measured weekly using the ACCU CHEK glucometer with compatible strip. Rats with FBG >8.0 mmol/l were considered diabetic (Osibemhe *et al.*, 2024).

#### 2.2.4 Body Weight

The body weight of all the rats before and during exposures was weekly recorded using digital weighing balance M-METLAR (QC PASS KH03).

#### 2.2.5 Blood Sample Collection and Clinical Chemistry

After the last treatment, rats were fasted overnight; body weight and fasting blood glucose were measured and recorded. They were then anaesthetized by placing individual rat in a plastic jar containing a cotton wool saturated with diethyl ether vapor. The rats were then removed from the jar and blood sample collected through cardiac puncture by opening the stomach along greater curvature; a 3 ml syringe was used to withdraw blood into labelled plastic specimen bottles containing heparin. It was then centrifuged at 4000 g for ten minutes to obtain plasma which were pipetted in to specimen test tubes for other biochemical analyses.

#### 2.2.6 Determination of Biochemical Parameters

Plasma total cholesterol, triglyceride, and high density lipoprotein were estimated with the method of Allain *et al.* (1974) method reported by Osibemhe *et al.* (2018). Low density lipoprotein cholesterol was estimated with Fredewald *et al.* (1972) formula reported by Muhammad *et al.* (2018). Catalase activity (CAT) and superoxide dismutase levels were estimated according to the methods of Aebi (1984) and Fridovich (1989) as reported by Muhammad *et al.* (2018). GSH was determined using the method of Ellman (1959) as reported by Omoboyowa *et al.* (2017). Assessment of  $\beta$ -cells function and insulin resistance were with the

method of Wesley *et al.* (2019). Insulin, Vascular endothelial growth factor (VEGF), interleukin-6 (IL-6) and Tumor necrosis factor (TNF- $\alpha$ ) were determined using ELISA kits according to manufacturers' instructions.

### 2.2.7 Statistical Analysis

The data obtained were expressed as mean  $\pm$  standard error of mean, and analyzed using SPSS version 22 software. The significance among groups was determined by One Way Analysis of Variance (ANOVA). LSD post hoc test for multiple comparison was used to ascertain the significance of the difference in the means.

### 2.2.8 Histopathology

The histological examination revealed changes in the cyto-architecture of pancreas of all VOCs exposed rats except toluene exposed rats where the pancreas was found unaffected. There was tissue necrosis, congestion and inflammation in benzene, hexane and xylene exposed rats.

## 3.0 RESULTS

Tissue sample of the pancreas was fixed in 10 per cent formalin. The formalin fixed specimen was embedded in paraffin, sectioned and stained with haematoxylin and eosin. The histological sections were examined under microscope and then photographed at magnification 400 (Osibemhe *et al.*, 2024).

### 3.1 Observation for Symptoms of Toxicity

Exposure of rats to volatile organic compounds, did not produced any grossly negative behavior such as restlessness, convulsion, respiratory distress, coma or mortality. However, the exposed rats were observed sleeping upon placement in individual VOCs cages.

### 3.2 Body Weight Changes with VOCs Exposure

The body weight changes of rats exposed to the individual VOCs (Table 1). This research revealed no significant ( $p>0.05$ ) change in body weight of all exposed rats, but there was fluctuation in body weight of all VOCs exposed rats compared with control group who had a progressive increase in body weight (Table 1).

### 3.3 Effect of the VOCs on Fasting Blood Glucose Level

Fasting blood glucose level of rats exposed to the individual VOCs is presented in Table 2. From the result, it was found that there was slight increase in the level of fasting blood glucose of the exposed rats compared with the control rats although the increased

was not significant ( $p>0.05$ ) (Table 2). The initial and final values for xylene was  $4.76\pm 0.58$  and  $5.46\pm 1.03$ ;  $4.82\pm 0.38$  and  $6.2\pm 0.78$  for hexane;  $4.74\pm 0.29$  and  $5.8\pm 0.24$  for toluene;  $5.08\pm 0.24$  and  $6.45\pm$  for benzene. Histological examination showed necrosis of pancreas in benzene exposed rats (plate 1b). There was moderate necrosis of pancreas in hexane exposed rats (plate 1c), and slight necrosis of pancreas cells in xylene exposed rats (plate 1e). Toluene exposed rats had normal feature of pancreas (plate 1d).

### 3.4: Plasma Lipid Profile of Experimental Rats Exposed to VOCs

The result of the effect of VOCs exposure on lipid profile is presented in Table 3. The result shows no statistically ( $p>0.05$ ) significant difference in cholesterol content of the VOCs exposed rats compared to control rats. However, there was higher triglyceride content in benzene exposed rats ( $92.83\pm 3.12$ ) than all other groups ( $41.32\pm 1.96$  for control;  $64.92\pm 2.41$  for xylene exposed rats;  $32.83\pm 1.94$  for hexane exposed rats;  $30.90\pm 2.39$  for toluene exposed rats), with a statistically significant ( $p<0.05$ ) difference in HDL content in hexane and benzene exposed groups compared with normal control rats. Of all the VOCs exposed rats, HDL content was lowest in benzene exposed rats.

### 3.5 Effect of VOCs Exposure on Antioxidant Profile of Experimental Rats

Antioxidant profile of control and experimental rats exposed to VOCs was presented in table 4. From the result, GSH content was significantly ( $p<0.05$ ) high in control rats compared to VOCs exposed rats. There was no statistically significant ( $p>0.05$ ) increase in SOD activity across all group. While catalase activity was significantly ( $p<0.05$ ) low in control group compared to all VOC exposed rat.

### 3.6 Effect of exposure of VOCs on Insulin level, $\beta$ cell function and insulin resistance in experimental rats

The effect of VOCs exposure on Insulin level,  $\beta$  cell function and insulin resistance in experimental rats was presented in Table 5. The data obtained showed that benzene and hexane exposed rats had a higher fasting blood glucose (FBG) content than other VOCs. Insulin content was high for hexane and xylene.  $\beta$  cell function was comparatively low for benzene exposed rats (Table 5).

### 3.7 Effect of VOCs Exposure on Cytokine levels of experimental rats

The effect of VOCs exposure on cytokine levels in experimental rats was presented in table 6.

VEGF was high for all VOCs exposed rats, though no significant ( $p>0.05$ ) difference compared with the normal control rat compared with the normal control rat.

However, IL-6 and TNF $\alpha$  for all exposed rats was significantly ( $P<0.05$ ) high compared with normal control rat.

**Table 1: Body Weight Changes Associated with Exposure to 5% VOCs.**

Group	Weekly Weight (g)				
	Initial	1	2	3	4
Control	132.4 $\pm$ 1.97 <sup>a</sup>	148.2 $\pm$ 5.18 <sup>a</sup>	169.6 $\pm$ 2.72 <sup>a</sup>	196.0 $\pm$ 5.90 <sup>a</sup>	205.6 $\pm$ 6.39 <sup>a</sup>
Xylene	117.28 $\pm$ 2.32 <sup>a</sup>	125.7 $\pm$ 3.48 <sup>a</sup>	123.83 $\pm$ 8.40 <sup>b</sup>	157.0 $\pm$ 6.84 <sup>b</sup>	125.8 $\pm$ 4.51 <sup>b</sup>
Hexane	118.5 $\pm$ 3.43 <sup>a</sup>	135.1 $\pm$ 4.47 <sup>a</sup>	131.34 $\pm$ 3.66 <sup>b</sup>	135.9 $\pm$ 3.31 <sup>b</sup>	132.4 $\pm$ 3.93 <sup>b</sup>
Toluene	104.7 $\pm$ 2.86 <sup>a</sup>	113.5 $\pm$ 2.91 <sup>a</sup>	115.7 $\pm$ 4.02 <sup>b</sup>	133.5 $\pm$ 4.06 <sup>b</sup>	136.3 $\pm$ 3.71 <sup>b</sup>
Benzene	107.5 $\pm$ 3.41 <sup>a</sup>	118.2 $\pm$ 4.76 <sup>a</sup>	117.6 $\pm$ 3.31 <sup>b</sup>	128.8 $\pm$ 2.95 <sup>b</sup>	126.0 $\pm$ 4.39 <sup>b</sup>

Values are mean  $\pm$  SEM for 5 rats per group. Different superscript in the same column are statistically significant from control at  $p<0.05$ .

**Table 2: Fasting Blood Glucose Profile of Experimental Animals Exposed to VOCs.**

Group	Weekly Fasting Blood Glucose (mmol/L)				
	Initial	1	2	3	4
Control	4.4 $\pm$ 0.19 <sup>a</sup>	4.86 $\pm$ 0.12 <sup>a</sup>	4.82 $\pm$ 0.13 <sup>a</sup>	4.90 $\pm$ 0.08 <sup>a</sup>	4.84 $\pm$ 0.29 <sup>a</sup>
Xylene	4.76 $\pm$ 0.26 <sup>a</sup>	5.58 $\pm$ 0.18 <sup>a</sup>	4.90 $\pm$ 0.16 <sup>a</sup>	5.12 $\pm$ 0.11 <sup>a</sup>	5.46 $\pm$ 0.46 <sup>a</sup>
Hexane	4.82 $\pm$ 0.16 <sup>a</sup>	6.15 $\pm$ 0.25 <sup>a</sup>	4.90 $\pm$ 0.18 <sup>a</sup>	5.51 $\pm$ 0.31 <sup>a</sup>	6.21 $\pm$ 0.34 <sup>a</sup>
Toluene	4.74 $\pm$ 0.12 <sup>a</sup>	4.64 $\pm$ 0.16 <sup>a</sup>	4.94 $\pm$ 0.26 <sup>a</sup>	6.02 $\pm$ 0.21 <sup>a</sup>	5.80 $\pm$ 0.11 <sup>a</sup>
Benzene	5.08 $\pm$ 0.11 <sup>a</sup>	5.84 $\pm$ 0.26 <sup>a</sup>	6.30 $\pm$ 0.14 <sup>a</sup>	5.84 $\pm$ 0.16 <sup>a</sup>	6.45 $\pm$ 0.11 <sup>a</sup>

Values are mean  $\pm$  SEM for 5 rats per group. Different superscript in the same column are statistically significant from control at  $p<0.05$ .

**Table 3: Plasma lipid profile of experimental rats exposed to VOCs**

Group	Parameters			
	Cholesterol(mg/dl)	Triglyceride(mg/dl)	HDL(mg/dl)	LDL(mg/dl)
Control	37.54 $\pm$ 2.24 <sup>a</sup>	41.32 $\pm$ 2.72 <sup>a</sup>	8.00 $\pm$ 0.62 <sup>a</sup>	20.08 $\pm$ 2.42 <sup>a</sup>
Xylene	29.08 $\pm$ 2.84 <sup>a</sup>	64.92 $\pm$ 2.41 <sup>ab</sup>	9.38 $\pm$ 0.76 <sup>a</sup>	22.70 $\pm$ 2.42 <sup>a</sup>
Hexane	27.07 $\pm$ 2.63 <sup>a</sup>	32.83 $\pm$ 1.94 <sup>a</sup>	5.30 $\pm$ 0.47 <sup>a</sup>	17.07 $\pm$ 1.78 <sup>a</sup>
Toluene	51.65 $\pm$ 2.20 <sup>a</sup>	30.90 $\pm$ 2.39 <sup>a</sup>	9.38 $\pm$ 0.96 <sup>a</sup>	34.83 $\pm$ 3.82 <sup>a</sup>
Benzene	40.75 $\pm$ 2.32 <sup>a</sup>	92.83 $\pm$ 3.12 <sup>b</sup>	3.50 $\pm$ 0.67 <sup>a</sup>	18.65 $\pm$ 1.42 <sup>a</sup>

Values are mean  $\pm$  SEM for 5 rats per group. Different superscript in the same column are statistically significant from control at  $p<0.05$ .

**Table 4: Antioxidants profile of control and experimental rats exposed to 5% VOCs**

Sample	SOD (u/ml)	GSH ( $\mu$ /ml)	MDA (nmol/ml)	CAT (u/ml)
Control	10.04 $\pm$ 0.54 <sup>a</sup>	16.80 $\pm$ 0.91 <sup>a</sup>	58.8 $\pm$ 1.58 <sup>a</sup>	3.04 $\pm$ 0.36 <sup>c</sup>
Xylene	15.90 $\pm$ 0.21 <sup>a</sup>	10.28 $\pm$ 0.19 <sup>b</sup>	51.94 $\pm$ 1.52 <sup>a</sup>	8.02 $\pm$ 0.16 <sup>b</sup>
Hexane	11.53 $\pm$ 1.01 <sup>a</sup>	7.37 $\pm$ 0.74 <sup>b</sup>	70.20 $\pm$ 2.71 <sup>b</sup>	7.30 $\pm$ 0.36 <sup>b</sup>
Toluene	16.70 $\pm$ 1.01 <sup>a</sup>	6.25 $\pm$ 0.77 <sup>b</sup>	30.65 $\pm$ 2.21 <sup>a</sup>	20.35 $\pm$ 0.63 <sup>a</sup>
Benzene	15.30 $\pm$ 0.19 <sup>a</sup>	9.63 $\pm$ 0.25 <sup>b</sup>	84.73 $\pm$ 2.24 <sup>b</sup>	7.90 $\pm$ 0.48 <sup>b</sup>

**Table 5: Fasting plasma glucose, insulin and  $\beta$  – cell function of rats exposed to VOCs.**

Treatment	FBG (mMol/L)	Insulin(mIu/mL)	HOMA-IR	HOMA- $\beta$
Normal control	4.84 $\pm$ 0.29	118.6 $\pm$ 1.02 <sup>a</sup>	25.52 $\pm$ 0.25 <sup>a</sup>	1757.2 $\pm$ 2.41 <sup>a</sup>
Xylene	4.46 $\pm$ 0.46	164.2 $\pm$ 1.07 <sup>b</sup>	32.69 $\pm$ 0.11 <sup>b</sup>	1678.3 $\pm$ 1.62 <sup>a</sup>
Hexane	6.20 $\pm$ 0.35	242.7 $\pm$ 2.51 <sup>c</sup>	67.75 $\pm$ 0.16 <sup>c</sup>	1802.9 $\pm$ 2.28 <sup>a</sup>
Toluene	5.80 $\pm$ 0.11	116.9 $\pm$ 0.72 <sup>a</sup>	31.03 $\pm$ 0.08 <sup>b</sup>	971.1 $\pm$ 2.45 <sup>b</sup>
Benzene	6.45 $\pm$ 0.11	123.0 $\pm$ 1.64 <sup>a</sup>	35.31 $\pm$ 0.11 <sup>b</sup>	849.9 $\pm$ 2.05 <sup>b</sup>

Values are mean  $\pm$  SEM for 5 rats per group. Values are mean  $\pm$  SEM for 5 rats per group. FBG: Fasting Blood Glucose; HOMA\_IR: Homeostasis Model Assessment of Insulin Resistance; HOMA- $\beta$ : Homeostasis Model Assessment of  $\beta$  cell.

**Table 6: Effect of VOCs exposure on cytokines levels of experimental rats**

Parameters

Treatment	VEGF (pg/mL)	IL6 (pg/mL)	TNF (pg/mL)
Control	542±10.98 <sup>a</sup>	79.93±1.44 <sup>b</sup>	301.99±8.31 <sup>b</sup>
Xylene	927.9±12.36 <sup>a</sup>	87.22±2.21 <sup>ab</sup>	744.0±11.74 <sup>a</sup>
Hexane	1347.3±19.46 <sup>a</sup>	98.13±1.25 <sup>a</sup>	545.6±8.33 <sup>ab</sup>
Toluene	576.84±5.51 <sup>a</sup>	87.01±1.94 <sup>ab</sup>	308.4±2.95 <sup>ab</sup>
Benzene	760.9±8.38 <sup>a</sup>	97.11±2.37 <sup>a</sup>	334.9±8.58 <sup>ab</sup>

Values are mean ± SEM for 5 rats per group. Different superscript in the same column are statistically significant from control at  $p < 0.05$ .

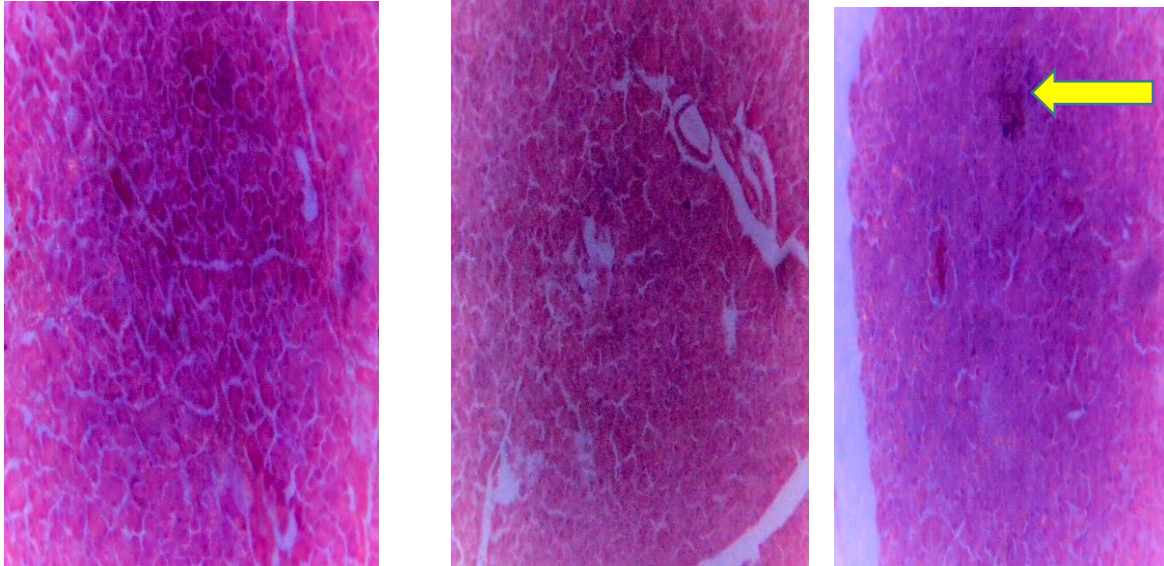


Plate 1a: Normal features of islet cells Plate 1b: Moderate changes of islet cells Plate 1c: Inflammation and necrosis

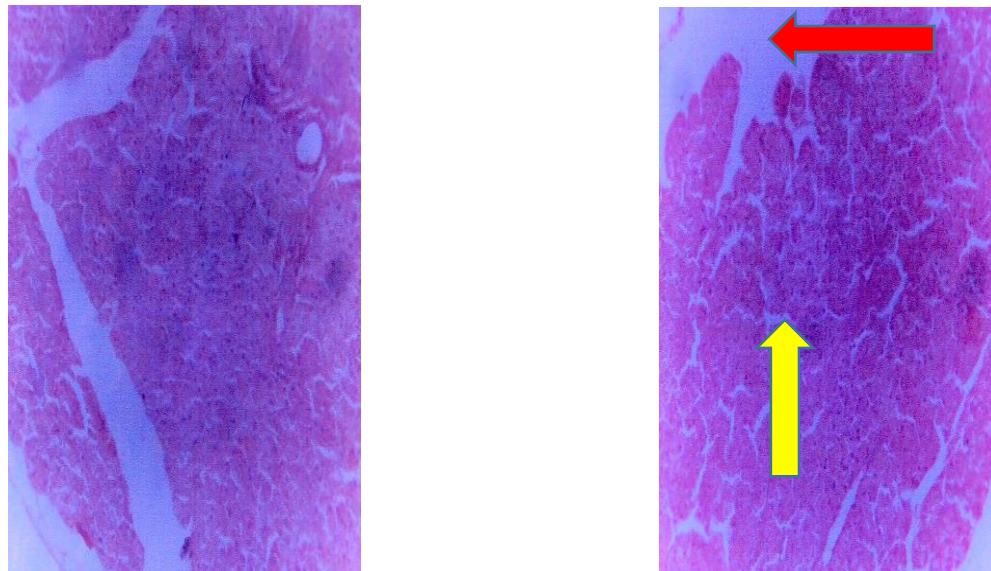


Plate 1d: Normal features of islet cell

Plate 1e: Necrosis of islet cells

Plate 4.2: Histological examination of pancreas of control and experimental animals exposed 5% VOCs for four weeks. Normal control group (1a); benzene exposed animals (1b); hexane exposed rats (1c); toluene exposed rats (1d); xylene exposed rats (1e).

#### 4.0 DISCUSSION

Considering the increasing morbidity and mortality burden from diabetes mellitus, the present study

evaluated the potentials of VOCs exposure in the pathogenesis of diabetes mellitus. Generally, the concentrations of VOCs in crude oil were estimated at

18% w/w and about 30% v/v (Jardel *et al.*, 2022; Kim *et al.*, 2022). In the present study, rats were exposed to 5% v/v to represent the percentage of each of the VOCs in crude oil according to previous study by Jardel *et al.*, (2022). It is reported that people in oil exploring areas and other parts of Nigeria are exposed to VOCs during their life either acutely, sub-acutely or chronically at sub-threshold limit value levels through petrol, diesel, kerosene, glues, paints, and solvents.

The findings in the present study show fluctuation in body weight of all VOCs exposed rats compared to control rats that had a progressive gain in body weight (Table 1). The fluctuation in body weight of VOCs exposed rats indicates that exposure to VOCs impaired feed utilization ratio. This agrees to a study conducted by Wesley *et al.* (2019). It agrees also with a study by Ubah *et al.* (2009). Osibemhe *et al.* (2018). Saidu *et al.* (2010) reported progressive gain in body weight of control rats.

Moreover, fasting blood glucose was not significantly increased in all the exposed groups compared with the control group (Table 2). However, there was slight fluctuations of the glucose level during the weeks of exposure. This may suggest effects of the VOCs in impairing glucose homeostasis. Increased fasting blood sugar above normal generally reflects hyperglycemia and abnormal glucose homeostasis (Osibemhe *et al.*, 2018; Muhammad *et al.*, 2018). The result is in line with the findings of Wesley *et al.* (2019) who found increased fasting plasma glucose and insulin resistance in rats exposed to benzene inhalation for two weeks. The disparity of our results could be attributed to differences in the route of exposure. It could also be due to the short exposure duration. Presence of food in the stomach of the rats could interfere with the toxicity of the VOCs as it might have impede gastric absorption of the VOCs; and may increase activity of the toxicant metabolizing enzymes thereby prolonging manifestation of the effect of exposure in the rats.

Alteration of lipid metabolism has been postulated to occur in animals exposed to petroleum hydrocarbons/crude oil (Osibemhe *et al.*, 2024; Ita *et al.*, 2014). Furthermore, there was significant increased level of triglyceride content of benzene and xylene exposed rats. This suggests that they have effect on lipid metabolism. Of all the VOCs exposed groups, benzene exposed group had the lowest content of functional HDL-C, suggesting its higher tendency to cause cardiovascular disease and related complications. Kim *et al.* (2022) found increase of stroke prevalence due to residential exposure to petroleum refining in the

southern United States. It is also in line with the study by Wesley *et al.* (2019) who found that inhalation of volatile benzene for a period of 2 to 6 weeks caused insulin resistance.

Exposure to petroleum hydrocarbons contributes to increase oxidative stress which decreases the antioxidant profile of exposed organisms (Ismail *et al.*, 2021; Maduku and Paul, 2021). In the current study, there was significant increase in the activities of superoxide dismutase and while catalase activity increased significantly in all exposed rats compared with control rats. The increased activities of enzymes might be attributed to increase generation of free radical that activates production of more of the enzymes to scavenge free radicals generated as a result of exposure (Osibemhe *et al.*, 2024). GSH and related enzymes have the potential to prevent cellular damage due to its detoxification and antioxidant properties (Muhammad *et al.*, 2018; Omoboyowa *et al.*, 2017). In this study, exposure to all VOCs had depleted the GSH content. The decreased GSH content might be attributed to the increase generation of superoxide, hydroxyl radicals and H<sub>2</sub>O<sub>2</sub> generated as a result of VOCs ingestion/exposure which in turn subject the pancreas to oxidative stress burden thereby affecting the structure of the pancreas as seen from the histological examination.

Insulin secretion and utilization has been postulated to be affected by VOCs due to anticipated damage on pancreas (Jardel *et al.*, 2022). In the present study, insulin level was high in hexane and xylene exposed rats. The low insulin level of benzene exposed rats, though not significantly different from control may suggest decline of  $\beta$ -cell function. This is in line with a study reported by Wesley *et al.* (2019). In the same vein, benzene and hexane exposed rats had higher fasting plasma glucose level. The result suggests insulin resistance for all VOCs exposed rats compared with control rats. The high insulin resistance observed could be linked to the effect of VOCs in raising oxidative stress markers known to affect insulin receptors and the downstream signaling pathways (Wesley *et al.*, 2019; Jardel *et al.*, 2022; Okoye and Awunor, 2022; Kumar *et al.*, 2022; Ozougwu *et al.*, 2013).

Cytokines are generally glycoproteins and polypeptides secreted by leucocytes into the extracellular compartment, with increased expression due to vascular changes and proteolytic cascades mediated by ROS, which are interlinked to act as intra and inter cellular signals (Fatemah *et al.*, 2023). Acute, chronic and sub-acute exposure to VOCs have been postulated to cause activation of inflammation pathways which affects various organs leading to different disease conditions.

Cytokines are generally markers of identifying possibility of the development of disease complications (Fatemah *et al.*, 2023; Kumar *et al.*, 2021; Veruscka *et al.*, 2016; Lei *et al.*, 2015). In the present study, vascular endothelial growth factor (VEGF) level was high for hexane, xylene and benzene exposed rats compared with control rats. In contrast, it was low for toluene exposed rats. The increased VEGF level could be attributed to the individual effect of the VOCs of activating nuclear translocation of HIF-1 $\alpha$ , and HIF-1 $\alpha$  dimerization which up regulates VEGF level (Fatemah *et al.*, 2023). The increased level of IL-6 may be connected to the recruitment of macrophages as a result exposure of the individual VOC. Tumor necrosis factor (TNF- $\alpha$ ) was high for xylene and hexane exposed rats but no significant difference in TNF $\alpha$  level of toluene and benzene exposed rats compared with normal control rats. The increased level of TNF $\alpha$  generally promotes NF-k $\beta$  activation of gene expression for inflammation of pancreas, which may affect  $\beta$ -cells function due to inflammation. Such exposure can be said to have aggravate the inflammation process which in turn altered the structure of pancreas as revealed in the histology plates.

The changes in the cyto-architecture of pancreas observed may also be attributed to the effect of VOCs in increasing permeability and fluidity of the pancreas cells associated with increase in oxidative indices. This in turn cause deoxyribose oxidation, protein cross links, inhibition of protein synthesis, loss of enzyme function, DNA strand breakage, inhibition of protein synthesis with consequent loss of cell functionality. This is in line with a study by Wesley *et al.* (2019) who reported insulin resistance in ice exposed to benzene. It is also in line with study by Jardel *et al.* (2022) who reported increased prevalence of insulin resistance in southern United States where over 288 million gallons of crude oil spilled in to Mexico.

## 5.0 CONCLUSION

In conclusion, the present data show that VOCs exposure can affect pancreas structure and function by up-regulating pathways of inflammation, oxidative stress and hyperlipidemia. This study raises the possibility that residential and occupational exposure to VOCs may be associated with heightened risk of diabetes morbidity and mortality due to its effect on pancreas. However, further scientific studies are required to define the low-dose, and long-term effects of these chemicals on pancreas and specifically, their diabetogenic effects. Also, studies that use biological monitoring information, and environmental information may be employed to understand the pathways involved

for the development and progression of diabetes linked to VOCs exposures.

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## COMPETING INTEREST

The authors declare that they have no competing interests

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## References

- Abdel Aziz I.L., Al Agha S.Z., Shehwan O.A. (2006). Hematological and biochemical studies for gasoline toxicity among gasoline workers in Gaza Strip. *J Al-Aqsa Univ*; 10(S.E), 41-9.
- Akinosun O.M., Arinola O.G., Salimonu L.S. (2006). Immunoglobulin classes and liver function tests in Nigerian petrol workers. *Indian J Occup Envir Med*; 10:58-61.
- Aebi, H.E. (1984). Catalase In: *Methods of enzymatic analysis*, Bergmer H.U (Ed.) vol.3 Weinheim, Germany, Verlag Chemie pp. 273-286.
- Allain, C.C., Poon, L.S., Chan, C.S., Richmond, W., Fu, P.C. (1974). Enzymatic determination of total serum cholesterol. *Clin Chem*. 20(4), 4-5.
- Brautbar N., Wu M.P., Gabel E., Regev I. (2006). Occupational Kidney cancer exposure to industrial solvents. *Ann N Y Acad Sci*, 1076, 753-64.
- Ellman G.D. (1959). Tissue sulfhydryl groups. *Archives of Biochemistry and Biophysics*, 82, 70-77.
- Fatemeh S.J., Zahra Z. and Mehrdad A. (2023). A review on the effect of garlic on diabetes, BDNF, and VEGF as a potential treatment for diabetic retinopathy. *Chinese Medicine*, 18, 18.
- Fridewald, W.T., Levy, R.I., Fredrickson, D.S. (1972). Estimation of concentration of low density lipoprotein cholesterol in plasma, without use of preparative ultracentrifuge. *Clinical chemistry*, 18, 499-502.
- Fridovich I. (1989). Method for the Determination of Superoxide Dismutase Activity in Tissues. *Journal of Biological chemistry*, 32, 102-106.
- Ismail H.Y., Farouq, A.A., Rabah A.B., Muhammad, A.B. and Aliyu, R.U. (2021). Effect of soil contamination with crude petroleum on cowpea: An insight into the Prospects of Crop Production in

- Nigerian Frontier Basins. *Journal of Environmental and Agricultural Studies*, 2(2), 50-62.
- Ita S.O., Aluko E.O., Olubobokun T.H., Okon U.A., Antai A.B., Osim E.E.(2014). The relationship between Nigerian Bonnylight Crude Oil-Induced Hypoglycemia and Endogenous Serum Insulin Concentration in Male Wistar Rats: The Role of Antioxidant Vitamins C and E. *American Journal of Molecular Biology*, 4, 81-88.
- Jardel, H.V., Engel, L.S., Lawrence, K.G., Stewart, P.A., Stenzel, M.R., Curry, M.D., Kwok, R.K., Sandler, D.P. (2022). The association between oil spill cleanup-related total hydrocarbon exposure and diabetes. *Environ Res.* 2022. Doi: 10.1016/j.envres.2022.113591
- Kim H., Natalia F., Kate B., Dae C.K., Thomas M.G. and Michelle L.B. (2022). Residential exposure to petroleum refining and stroke in the southern United States. *Environ. Res. Lett.* 17, 094018.
- Kumar P., Amel G., Mohammad T.A., Virendra K.Y., Snigdha S., Krishna K.Y., Mottahir A., Vinars D., Satish P., Parul M., Yongtae A., Byong-Hun J and Marina M.S. (2022). Environmental and human health implications of metals: Source identification, contamination, toxicity, and sustainable clean-up technologies. *Frontiers in Environmental Science.* DOI10.3389/fenvs.2022.949581
- Lei M., Lun Z., Jianjun L., Liang Z., Jiahui L., Zheng W., and Zheng W. (2015). Overview of Emerging Contaminants and Associated Human Health Effects. *BioMed Research International*, Article ID 404796 13 pages. <http://dx.doi.org/10.115/2015/404796>
- Maduka O. and Paul, J.N. (2021). Is There a Relationship between residence in Oil Bearing Communities and the Prevalence of Diabetes Mellitus? *Journal of Epidemiological Society of Nigeria Special conference edition.* 2022, 1:43-47.
- Mashoud N., Kiamars H., and Jafar H. (2015). Early Liver and Kidney Dysfunction Associated with Occupational Exposure to Sub-Threshold Limit Value Levels of Benzene, Toluene, and Xylenes in Unleaded Petrol. *Safety and Health at Work*, 1-5.
- Muhammad I., Ibrahim, K. M., Ibrahim, A. Y., Salahuddeen Y., Abdullahi N., Suleiman L. Bilbis and Yahya A, Abbas (2018). Development of Okra-based antidiabetic nutraceutical formulations from *Abelmoschus esculentus* (L.) Moench (Ex-maradi variety). *Tropical Journal of Natural Product Research*, 2(2):80-86.
- Neghab M., Stacey N.H. (1997). In vitro interference with hepatocellular uptake of bile acids by xylene. *Toxicology in vitro*, 21, 782-8.
- Nwanjo H.U., Ojiako OA. (2007). Investigation of the potential health hazards of petrol station attendants in Owerri Nigeria. *J Appl Sci Environ Manage*, 11, 197-200
- Okoye O.C. and Nyemike, A. (2022). Is exposure to hydrocarbons associated with chronic kidney disease in young Nigerians? A case control study. *Frontiers in Nephrology*, 1-8.
- Orisakwe, O.E., Njan, A.A., Afonne, O.J., Akumka, D.D., Orish, V.N., Udemezue, O.O. (2004). Investigation into the Nephrotoxicity of Nigerian Bonny Light Crude Oil in Albino Rats. *Int. J. Environ. Res. Public Health*, 1(2), 106-110.
- Osibemhe M., Balkisu, O.A., Salahuddeen Y. (2024). Crude oil exposure affects hepatic function of diabetic rats treated with metformin and *Allium sativum*. *Bulletins of Natural and Applied Science*, 1(2), 32-40.
- Osibemhe M., Bello, O.M., Lawal, N. (2018). Prognosis of diabetes complications and efficacy of *Guiera senegalensis* aqueous leaf extract in streptozocin induced-diabetic rats. *Journal of Applied Sciences and Environmental Management*, 22 (8), 1325-1329.
- Omoboyowa, D.A., Aja, O.A., Vining-Ogu, I.C., and Alum, A.A. (2017). Anti-hyperglycemic Activity of Methanol Seed Extract of *Dioclear reflexa* in Alloxan-induced Diabetic Rats. *Nigerian Journal of Biochemistry and Molecular Biology*, 32(1):32-43.
- Ozougwu, J. C., Obimba, K. C.2, Belonwu, C. D.3, and Unakalamba, C. B. (2013). The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *Journal of physiology and pathophysiology*, 4(4), 46-57. DOI 10.5897/JPAP2013.0001
- Saidu Y., Nwachukwu, F.C., L.S. Bilbis, Faruk, U.Z. and Abbas, A.Y (2010). Toxicity Studies of the Crude Aqueous Root Extract of *Albizzia chevalieri* Harms in Albino Rats. *Nigerian Journal of Basic and Applied Science*, 18(2), 308-314.
- Salahuddeen, Y., Osibemhe, M., Balkisu, O.A. (2024). Nephrotoxic effect of crude oil exposure in Diabetic rats treated with metformin and *Allium sativum* extract. *Bulletins of Natural and Applied Science*, 1(2), 41-48.
- Veruscka L., Ilaria C., Erika A.L., Walter R., and Ivo L. (2016). Occupational chemical exposure and diabetes mellitus risk. *Toxicology and Industrial Health*, 1-28.
- Wesley, T.A., Nalinie S.W., Srinivas D.S., Daniel, J.C., Zhengzhi, X., Aruni B., Sanjay, S., and Timothy E.O.T. (2019). Benzene Exposure Induces Insulin Resistance in Mice. *Toxicological Sciences*, 167(2), 426-437.

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