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Synergistic Ameliorative Capabilities of Quercetin and Ascorbic Acid on Hepatic and Pro-Inflammatory Markers of Arsenic-Induced Toxicity in Obese Wistar Rats

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Abstract

Obesity and arsenic exposure have been linked to many health issues. However, arsenic poisoning severity and susceptibility may depend on Body Mass Index (BMI), oxidative state, food supplements, and other factors. This study examines how quercetin and ascorbic acid can improve arsenic-induced health dysfunctions in normal and high BMI male Wistar rats. A total of 70 male Wistar rats weighing between 135 - 220 g were divided into 10 groups. A: Control group; B: sodium arsenite group; C: quercetin + sodium arsenite group; D: ascorbic acid + sodium arsenite group; E: sodium arsenite + quercetin + ascorbic acid; F: obese group; G: obese + sodium arsenite group; H: obese + sodium arsenite + quercetin group; I: obese + sodium arsenite + ascorbic acid group; J: obese + sodium arsenite + quercetin + ascorbic acid group, all treatments were administered orally daily for twenty-eight (28) days. The doses administered were 595 mg/kg body weight of ascorbic acid (10 % LD50), 50 mg/kg body weight of quercetin (5 % LD50), and 0.75 mg/kg body weight of sodium arsenite (5 % LD50). Concentrations of interleukin-1β (IL-1β), interleukin 6 (IL 6), TNF-alpha (TNF-α), COX-2, nitric oxide (NO), total bilirubin (TBL) and activities of alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), and gamma-glutamyl transferase (GGT) were determined in plasma. Upon the completion of the experiment, serum IL-1β, IL 6, TNF-α, COX-2, NO, TBL concentrations and ALP, AST, ALT, and GGT activities increased significantly ($p<0.05$) across the groups and treatment with quercetin and ascorbic acid ameliorated the pathological alteration elicited or caused by sodium arsenite. The findings showed that arsenic exposure altered pro-inflammatory and hepatic function indices in high BMI rats, while treatment with quercetin and ascorbic acid exhibited an ameliorative effect against this obesity and arsenic-induced health dysfunctions.

Keywords: Body Mass Index, Dysfunctions, Sodium arsenite, Inflammation

Introduction

Arsenic, the 33rd element on the periodic table, is recognized as a heavy metal in toxicology, belonging to the group of metals classified as human carcinogens (Xian *et al.,* 2017). Its global prevalence in nature raises significant health concerns due to its association with various detrimental effects on organisms (Mandal & Suzuki, 2017). Being a natural component of the environment, animals are frequently exposed to

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relatively low levels of arsenic through sources such as food, air, and water, which is not immediately detectable because arsenic compounds lack colour or smell, posing a significant human health risk due to their toxic nature (Hughes *et al.,* 2011; Jomova *et al.,* 2011). Even low to moderate levels of arsenic in water can contribute to a wide range of health dysfunctions, illnesses, and degenerative diseases (Hughes *et al.,* 2011; Naujokas *et al.,* 2013). Although the primary toxic mechanism of arsenic remains unspecified, inflammatory dysfunctions have been suggested as potential factors. Inflammation plays a role in the pathogenesis of numerous degenerative diseases, including cardiovascular diseases, metabolic syndrome, chronic kidney and liver diseases, and cancer (Coussens, 2002; Black, 2003; Leemans *et al.,* 2014; Steinmaus *et al.,* 2015). Arsenic has been implicated to induce inflammatory responses and compromise the immune cells (Oyewo *et al.,* 2017), which might be the mechanism of arsenic-induced health dysfunction and diseases. Various factors such as dose, diet, co-exposure, and age of the individual could determine the extent of arsenic poisoning, which also varies widely from person to person (Jomova *et al.,* 2011; Research Council, 2014).

However, most of the variability in susceptibility and the influence of lifestyles on arsenic metabolism in humans are poorly understood. Although the influence of arsenic toxicity in individuals with elevated BMI is not well understood, studies have revealed that BMI, an indicator of overall nutritional status, is positively associated with arsenic methylation capacity (Gomez-Rubio *et al.,* 2011). The pathological processes linked to arsenic and obesity, such as inflammation and oxidative stress, are thought to play a role in diseases caused by each. Elevated BMI has been shown to exacerbate oxidative stress and inflammatory responses that have been associated with some types of cancer (De Pergola & Silvertris, 2013; Marseglia *et al.,* 2015). Quercetin, a major flavonoid found in edible plants (fruits and vegetables) is one of the most potent antioxidants present in plants and has unique biological properties that may improve mental/physical performances and decline infection risk (Erdman *et al.,* 2007; Davis *et al.,* 2008). It is found abundantly in foods like onions, hot peppers, apples, tea, and broccoli (Sampson *et al.,* 2002) and has also been documented to exhibit various physiological effects, including antioxidative properties (Ciz *et al.,* 2008), anti-inflammatory effects (Nair *et al.,* 2006), anti-pathogenic activity (Chiang *et al.,* 2003), anti-microbial effects (Cushine & Lamb, 2005), anti-carcinogenic potential (Neuhouser, 2004). This highlights the significant potential of quercetin in enhancing mammalian health. Ascorbic acid is an antioxidant that has been reported to possess free radical scavenging potential (Diego *et al.,* 2014). Studies have shown that obese individuals have ascorbic acid deficiency which strongly correlated positively with abdominal obesity, body fat, waist circumference and waist-hip ratio (Canoy *et al.,* 2005; Aashiem *et al.,* 2008). Thus, quercetin coupled with ascorbic acid may be beneficial in the treatment of arsenic toxicity and obesity. Given the interplay between the pathological mechanisms of arsenic and elevated BMI coupled with the anti-inflammatory and anti-oxidative potentials of quercetin and ascorbic acid, this study, therefore, assessed the synergistic ameliorative capability of quercetin and ascorbic acid on arsenic-induced toxicity with respect to BMI in apparently healthy male Wistar rats.

Materials and Methods

Material Reagents Kits and Chemicals

All chemicals used were of analytical grades and purchased from Central Research Laboratory, Ilorin, Kwara State, Nigeria. Arsenic, ascorbic acid, and Quercetin were purchased from Biobridge Laboratory, Ilorin. Reagents for analysis such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (TBL) and gamma-glutamyl transferase (GGT) were procured from Randox Laboratories Ltd Crumlin, United Kingdom.

Experimental Animals

Seventy (70) male Wistar rats weighing 135-220 g were procured from the animal house College

of Health Sciences, Osun State University, Osogbo. These rats were accommodated in the animal house within the Department of Biochemistry at Osun State University, Osogbo. The animals were acclimatized for two weeks, during which they were fed with commercial pellets (obtained from Vita Feeds Nig. Ltd) and clean tap water *ad libitum*. The animals were maintained at a constant room temperature with a twelve-hour light/dark cycle, relative humidity of 60 ± 5 % and made obese by feeding with a high-fat diet (60 % normal rats feed + 40 % cholesterol-dense oil) for two weeks. The experimental protocol used was approved by the Osun State Health Research Ethical Committee (OSHREC/PRS/569T/518).

Experimental Design

The rats were randomly divided into ten groups of seven per group based on their BMI as illustrated in Table 1, distinguishing between normal BMI (N-BMI/NON-OBESE) and high BMI (H-BMI/OBESE). The classification was determined by BMI values of 0.45-0.60 g/cm^2 for non-obese and greater than 0.68 g/cm^2 for obese rats; these were achieved by dividing the body weight in grams (using a digital weighing scale) by the length (using a tape measure) in cm^2. All treatments were administered orally daily for twenty-eight (28) days. The experimental groups and their treatments were presented in Table 1 {the doses administered were 595 mg/kg body weight of ascorbic acid (10 % LD50), 50 mg/kg body weight of quercetin (5 % LD50), and 0.75 mg/kg body weight of sodium arsenite (5 % LD50)}.

Collection of Serum

Following the administration, rats underwent an overnight fast and were anesthetized with diethyl ether. The chest cavity was promptly opened, and blood was drawn by puncturing the heart with a new syringe for each animal. The collected blood samples were placed into plain bottles and centrifuged at 4000 revolutions per minute (rpm) for 10 minutes to separate the serum from the whole blood. The resulting serum, constituting the supernatant, was carefully decanted into labeled sample bottles using a micropipette. These bottles were then promptly placed in a refrigerator below 4 °C for subsequent analysis.

Determination of Liver Markers Activities

Activities of ALT, AST, ALP, GGT, and T.BIL concentration in the rats' serum were determined in tandem with the principle described by Reitman and Frankel, (1957) using Randox kits.

Assessment of Pro-inflammatory Markers in Rats

IL-1β, IL-6, TNF- α, COX-2 and NO analyses were done using the ELISA method as specified in the kit manual based on the sandwich immunoassay principle.

Statistical Analysis

Data obtained from this study are expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was used to assess the difference between means, followed by Tukey's multiple comparison test. GraphPad Prism 6.0 was the statistical package used for the analysis; p-values < 0.05 were considered statistically significant for differences in means.

Results

Activities of ALT, AST and ALP in Non-obese and Obese Wistar Rats Administered Sodium Arsenite and Treated with Quercetin and Ascorbic Acid

The serum activities of ALT, AST and ALP in non-obese and obese Wistar rats treated with quercetin and ascorbic acid to determine the arsenic-induced toxicity is shown in Figure 1. In non-obese rats there is a significant difference in the ALT activity in rats administered sodium arsenite as compared to rats treated with sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid ($p < 0.05$). Similarly, in obese rats, there is a significant reduction in the ALT activity in rats administered with sodium arsenite, sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite +

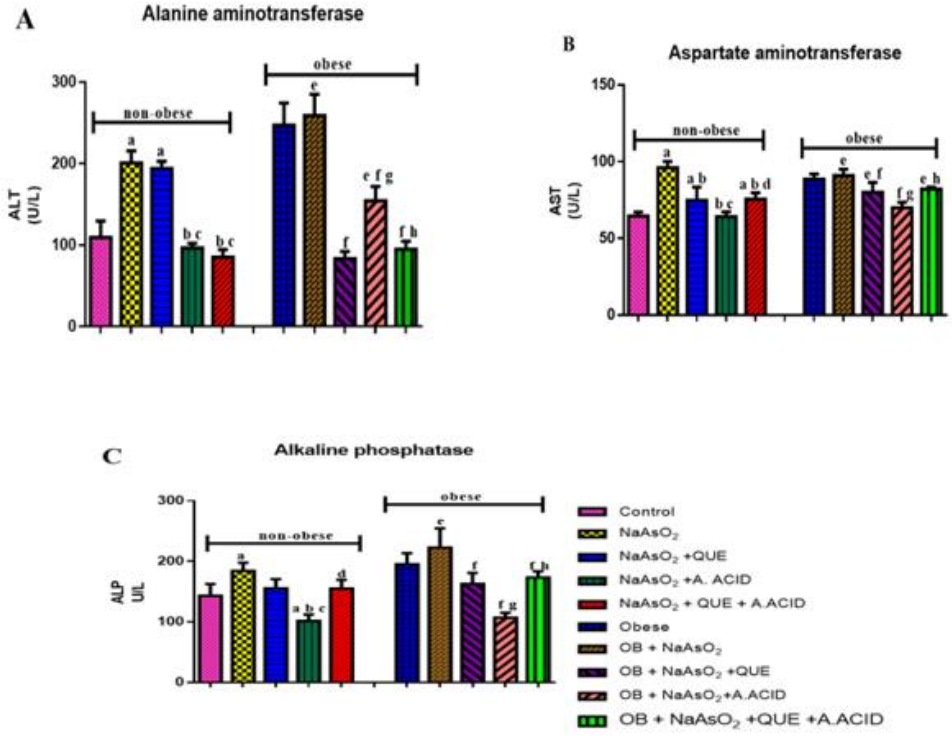

Figure 1: Changes in the levels of serum ALT (A), AST (B) and ALP (C) of arsenic-induced toxicity in non-obese and obese Wistar rats treated with quercetin and ascorbic acid. Results are represented as Mean ± SD (n = 7).

quercetin + ascorbic acid ($p < 0.05$). Notably, AST and ALP activities were significantly reduced in the ALT activity in rats administered with sodium arsenite, sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid ($p < 0.05$). Notably, AST and ALP activities significantly reduced in both non-obese and obese rats administered with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid as compared to rats administered sodium arsenite ($p < 0.05$). a: significantly different from control, b: significantly different from non-obese + sodium arsenite + quercetin, c: significantly different from non-obese + sodium arsenite + quercetin, ascorbic acid, d: significantly different from non-obese + sodium arsenite + ascorbic acid, e: significantly different from obese, f: significantly different from obese + sodium arsenite, g: significantly different from obese + sodium arsenite + quercetin, h: significantly different from obese + sodium arsenite + ascorbic acid ($p< 0.05$).

Activities of GGT and Total Bilirubin in Non-Obese and Obese Wistar Rats Administered Sodium Arsenite and Treated with Quercetin and Ascorbic Acid

The levels of GGT and total bilirubin in non-obese and obese Wistar rats treated with quercetin and ascorbic acid to determine the arsenic-induced toxicity is shown in Figure 2. In non-obese rats, there is a significant difference in the GGT activity in rats administered sodium arsenite as compared to rats treated with sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid ($p < 0.05$). Similarly, in obese rats, there is a significant reduction in the GGT activity in rats administered with sodium arsenite, sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid ($p < 0.05$). Furthermore,

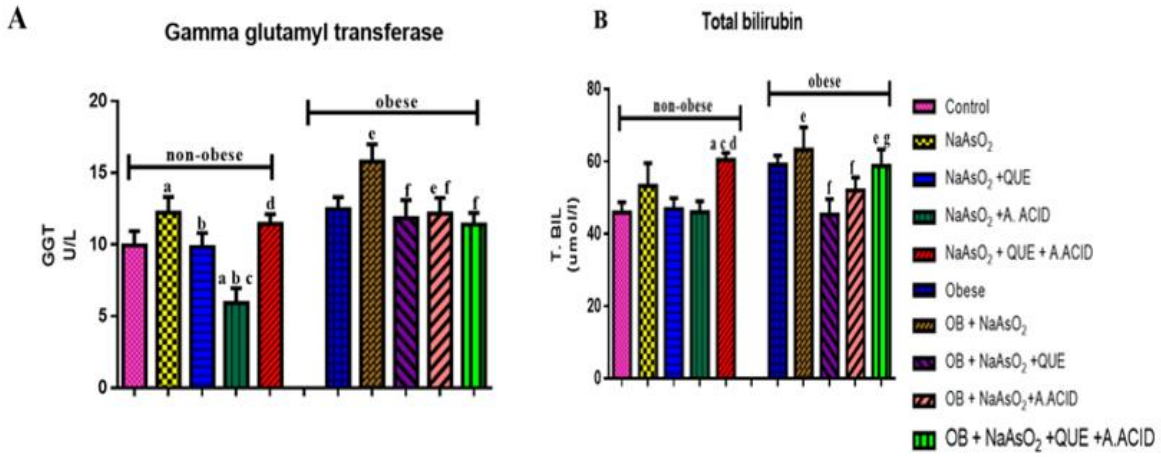

Figure 2: Changes in the levels of serum GGT (A) and T.BIL (B) of arsenic-induced toxicity in non-obese and obese Wistar rats treated with quercetin and ascorbic acid. Results are represented as Mean ± SD (n = 7). Bars with different superscripts (a-h) are significantly different ($p < 0.05$)

the total bilirubin level was significantly reduced in non-obese and obese rats administered sodium arsenite + quercetin and sodium arsenite + ascorbic acid compared to rats that received sodium arsenite. Notably, in non-obese rats, total bilirubin increased significantly in rats treated with sodium arsenite + quercetin + ascorbic acid compared to the rats that received sodium arsenite ($p < 0.05$).

The Levels of Serum Il-1beta, Il 6 and Tnf-Alpha in Non-Obese and Obese Wistar Rats Administered Sodium Arsenite and Treated with Quercetin and Ascorbic Acid

The level of IL-1, IL-6 and TNF-alpha in non-obese and obese Wistar rats treated with quercetin and ascorbic acid to determine the arsenic-induced toxicity is shown in Figure 3. In non-obese rats, there is a significant reduction in the level of IL-1 in rats administered sodium arsenite + ascorbic acid and sodium arsenite + quercetin + ascorbic acid as compared to rats treated with sodium arsenite ($p < 0.05$). Similarly, in obese rats, there is a significant reduction in the level of IL-1 in rats administered with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid as compared to rats treated with sodium arsenite ($p < 0.05$). Notably, the level of IL-6 significantly reduced in both non-obese and obese rats administered with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid as compared to rats administered sodium arsenite ($p < 0.05$). Furthermore, in obese rats, TNF-alpha reduced significantly in rats administered with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, and sodium arsenite + quercetin + ascorbic acid as compared to rats administered sodium arsenite ($p < 0.05$).

The Levels of Serum Cox-2 and no in Non-Obese and Obese Wistar Rats Administered Sodium Arsenite and Treated with Quercetin and Ascorbic Acid

The levels of serum COX-2 and NO in non-obese and obese Wistar rats treated with quercetin and ascorbic acid to determine the arsenic-induced toxicity are shown in Figure 4. In non-obese rats, the level of serum COX-2 did not change considerably in the rats administered sodium arsenite, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid ($p > 0.05$). Similarly, in obese rats, there is a significant

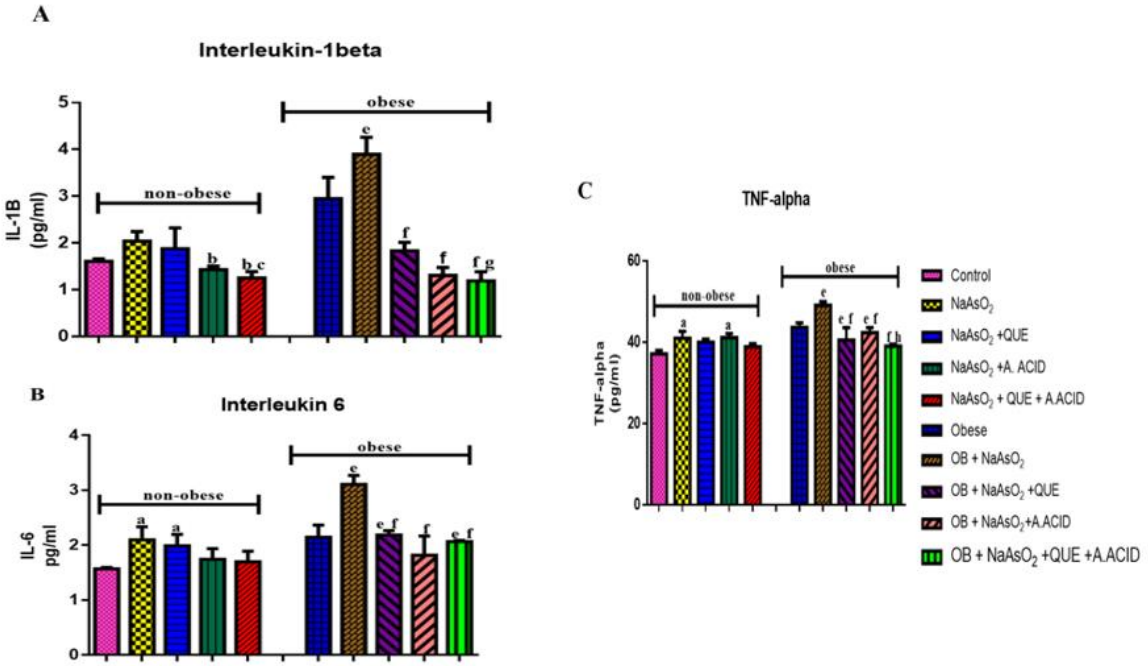

Figure 3: Changes in the levels of serum IL-1beta (A), IL 6 (B) and TNF-alpha (C) of arsenic-induced toxicity in non-obese and obese Wistar rats treated with quercetin and ascorbic acid. Results are represented as Mean ± SD (n = 7). Bars with different superscripts (a-h) are significantly different ($p < 0.05$).

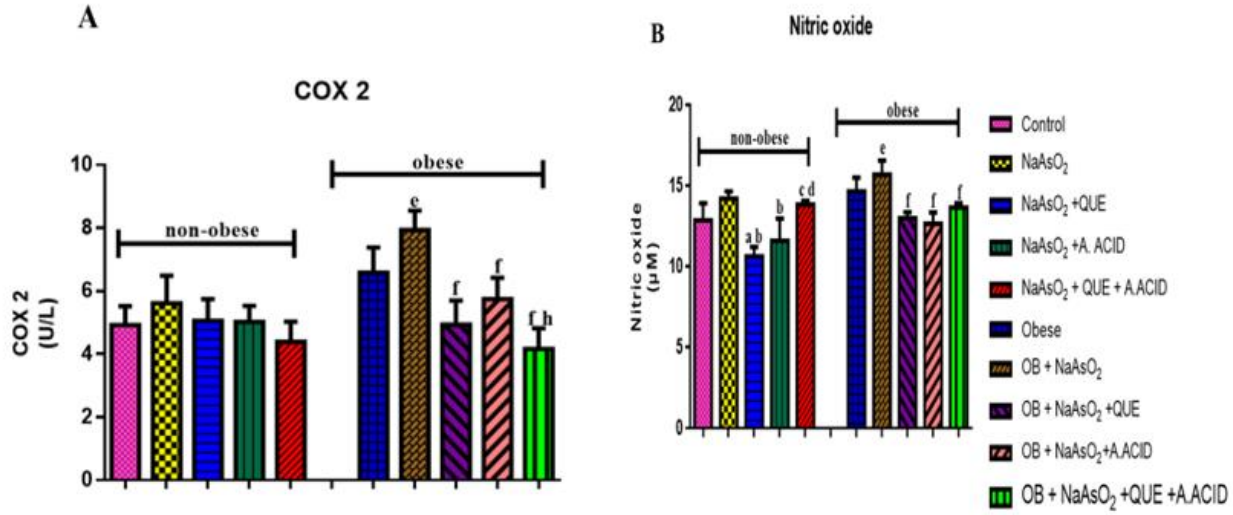

Figure 4: Changes in the levels of serum COX-2 (A) and NO (B) of arsenic-induced toxicity in non-obese and obese Wistar rats treated with quercetin and ascorbic acid. Results are represented as Mean ± SD (n = 7). Bars with different superscripts (a-h) are significantly different ($p < 0.05$).

eduction in the level of serum COX-2 in rats administered with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, sodium arsenite + quercetin + ascorbic acid as compared to rats administered sodium arsenite ($p < 0.05$). Furthermore, the level of NO significantly reduced in non-obese rats administered with sodium arsenite + quercetin and sodium arsenite + ascorbic acid as comapred to rats that received sodium arsenite. Also, in obese rats, the level of NO decreased significantly in rats treated with sodium arsenite + quercetin, sodium arsenite + ascorbic acid, and sodium arsenite + quercetin + ascorbic acid compared to the rats the received sodium arsenite ($p < 0.05$).

Discussion

One of the heavy metals known to be human carcinogens is arsenic. Arsenic is widely distributed in the environment due to natural processes like volcanic eruption and human and industrial activities like mining and smelting. Arsenic's oxidative state and chemical forms are integral to its toxicity mechanism. Reactive oxygen species (ROS) such as intracellular peroxide, hydrogen peroxide, superoxide anion radicals, and hydroxyl free radicals, as well as reactive nitrogen species (RNS), are produced by cellular exposure to arsenic (Adewale *et al.,* 2018), which cause changes to the native conformation and physiology of cellular macromolecules likes proteins, lipids, and nucleic acids. These changes can affect the hepatic markers, trigger pro-inflammatory and pro-fibrogenic cytokines, and attack the mitochondrial respiratory chain, which obstructs the antioxidant defence system and taints cellular DNA and proteins (Mandal & Suzuki, 2017). In this study, a significant increase in the activities of alanine aminotransferase and aspartate aminotransferase was observed after exposure of the normal rats to arsenic; these effects were more pronounced with higher concentrations in the obese rats treated with arsenic. These findings coincide with the report of Adewale *et al.* (2018), and these may later cause changes in lipid morphology and physiology that result in resistance to insulin and the phenomenon of lipotoxicity, which causes the cellular metabolism to be decoupled from the generation of signalling cascades linked to the start of programmed cell death processes as well as elevated AST activity (Maulucci *et al.,* 2016). This is demonstrated by a significant ($p<0.05$) decrease in the levels of ALT and AST when treated with quercetin and ascorbic acid separately and in combination, thus making both effective in preventing arsenic toxicity as well as reducing the possible harmful impact of arsenic poisoning in Wistar rats, both non-obese and obese. The group exposed to both arsenic and obesity exhibited higher serum GGT activity than any other groups, indicating a potential biliary blockage due to the enzyme's primary presence in the bile canaliculi. This suggests that biliary obstruction likely occurred in the obese and arsenic-exposed group. Furthermore, the concentration of GGT was observed to decrease when treated with quercetin and ascorbic acid separately and in combination. As per reports, fatty acids might exhibit cytotoxicity independently, particularly without adequate metabolic control, leading to pathophysiological consequences such as liver damage (Houben *et al.,* 2017). This is likely the underlying reason for the elevated ALP activity observed in obese rats exposed to arsenic compared to their normal-weight counterparts. The reduced serum GGT and ALP activity observed in post-treatment can be attributed to the anti-inflammatory attributes of quercetin and the enhanced bioavailability of ascorbic acid. The primary byproduct of haemoglobin breakdown, bilirubin, is elevated in the serum in cases of liver injury from hepatic biliary hemolysis, alcoholic hepatopathy, viral hepatitis, and neonatal jaundice. A significant increase in total bilirubin level was detected in the serum of both obese rats as compared to non-obese rats given arsenic; this reflects hepatic toxicity and may result in a reduction in the concentration of total protein due to liver disorders (Oyewole *et al.,* 2015). Both the non-obese and obese rats that were arsenic-intoxicated showed a significant($p<0.05$) reduction in total bilirubin levels upon individual and co-administration of quercetin and ascorbic acid. Arsenic exposure is believed to induce inflammation, leading to increased secretions of

pro-inflammatory cytokines (Singh *et al.,* 2010; Oyewo *et al.,* 2017). In both humans and rodents, arsenic exposure is associated with the activation of inflammatory cytokines linked to immune-related disorders. The toxic effects of arsenic include the secretion of cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β), and interleukin-6 (IL-6), contributing to inflammatory responses. (Singh *et al.,* 2010; Das *et al.,* 2012; Afolabi *et al.,* 2013; Oyewo *et al.,* 2017). Proapoptotic protein activation, growth factor, transcription factor, tumor progression, and other biological and cellular comebacks are all mediated by these pro-inflammatory mediators. Furthermore, growing epidemiologic data showed that exposure to arsenic, even at low concentrations, raised the chance of getting cardiovascular conditions including atherosclerosis (Medrano *et al.,* 2010; Moon *et al.,* 2013). Atherosclerosis begins when endothelial cells are activated by several stimuli, such as cytokines and elevated reactive oxygen species (ROS). Because of the functions that various cytokines, chemokines, and immune cells play in the evolution of the disease, arthritis is thought to include persistent inflammation-related diseases. An essential pro-inflammatory chemokine and cytokine involved in both innate and adaptive immunity is tumor necrosis factor-alpha (TNF- α), owing to its pro-inflammatory nature, it plays a role in drawing and triggering inflammatory cells at the sites of injury. It is generally known that cytokines produce reactive oxygen substances (ROS) and that the exposure and metabolism of arsenic can produce high ROS levels, which in turn causes tissue fibrosis and may also trigger the creation of TNF- α. The results of this study are similar to the report of (Yueshui *et al.,* 2017; Castriota *et al.,* 2018), as a significant ($p<0.05$) increase in the level of TNF-α was recorded in the liver tissues of non-obese rats given arsenic. Nevertheless, the liver of obese rats exposed to arsenic showed a greater level of TNF-α as compared to other groups. Quercetin and ascorbic acid, given alone or in combination to non-obese and obese rats exposed to arsenic, significantly lower TNF- α levels, indicating the ability to control the inflammatory reactions brought on by both the arsenic and the obesity, which may be due to ability of quercetin to inhibits the production of TNF-α, which in turn stimulates anti-inflammatory cytokines by blocking NF-κB activation (Maria *et al.,* 2022). However, this is in contrast to Oyewo *et al.*'s (2021) findings, which showed quercetin does not affect pro-inflammatory biomarkers. Although multiple researches had established that IL-6 is a separate risk factor for coronary artery disease (Afolabi *et al.,* 2013; Maria *et al.,* 2022). It is said to be correlated with factors that are important for the advancement of atherosclerosis, including both metabolic and inflammatory factors. Depending on its expression level, IL-6 can have either an anti-inflammatory or pro-inflammatory effect; however, at high concentrations, it has been shown to have a pro-inflammatory function. It has been linked to a number of pathological disorders, including an elevated risk of heart attack, stroke, and atherosclerosis. In this study, kidney and liver IL-6 levels were significantly increased in both non-obese and obese rats exposed to arsenic. This increase was most pronounced in the obese rats, indicating a pro-inflammatory response to the toxin amplified by obesity. This result is consistent with the report by Afolabi *et al.* (2013), who found that rats exposed to arsenic had an elevated level of IL-6. Treatment with ascorbic acid and quercetin alone or in combination was able to reduce the level of IL-6 in both normal and obese rats. The heightened levels of IL-1β observed in both normal and obese rats exposed to arsenic in this study indicate a potential link between obesity and an increased susceptibility to arsenic-induced inflammatory responses, as chemokines and cytokines play a crucial role in the early stages of atherosclerotic plaque formation (Singh *et al.,* 2013). Individual and co-administration of quercetin and ascorbic acid were able to reduce the concentration of IL-1β in both obese and non-obese rats. This result is consistent with the previous findings of Zhang *et al.,* 2023, that quercetin demonstrated high efficacy or is effective in lowering circulating inflammation markers, including IL-1β, following an 8-week administration). Also, Quercetin has been demonstrated to inhibit NF-κB-mediated pathways associated with cell survival, thereby reducing the

expression of pro-inflammatory cytokines, which ultimately contributes to the prevention of cancer formation. (Costa, 2019; Maria *et al.,* 2022). In addition to its effects on adipose tissue, quercetin has been demonstrated to possess and exert its anti-inflammatory properties over an extended period, making it a recognized long-lasting anti-inflammatory agent (Abdelkareem and Fadda, 2013; Wu *et al.,* 2021). Nitric oxide (NO) reacts with water and molecular oxygen to produce nitrite and nitrate, two stable oxidized products. The enzyme NO synthases (NOS) is in charge of producing NO from the terminal guanidino nitrogen atom of L-arginine. Because NO retains an unpaired electron and functions as a free radical, it is essential as a transcellular messenger in a number of physiological processes. When NO is exposed to arsenic, it quickly combines with O_2 to form a toxic substance called peroxynitrite anion, which oxidizes sulfhydryl groups and thioethers, further damaging DNA. Three pathways, including the creation of N-nitroso compounds, which lead to DNA alkylation, interference with the main amino group of DNA, which results in deamination, and lastly, the generation of ROS, such as hydroxyl and peroxynitrite radicals, are involved in DNA damage caused by NO. Depending on the type of cell under investigation, either NO, ROS, or possibly both are the perpetrators causing arsenic-induced DNA strand cleavage (Obinaju, 2021). Results from these findings demonstrate that when obese rats are exposed to arsenic, their production of NO rises noticeably, which may lead to oxidative stress and inflammation caused by obesity, which may also be contributing factors. However, quercetin and ascorbic acid alone or in combination reflect the down-regulation of NO levels in the liver of non-obese and obese rats. As a result, enhanced oxidative stress may change the integrity of biological membranes.

Conclusion

This research demonstrated that arsenic intoxication coupled with obesity resulted in hepatic damage, as indicated by alterations in its markers and pro-inflammatory markers. However, quercetin and ascorbic acid were found to exhibit a synergistic ameliorative potential in combating the toxicity and lowering body mass index.

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Conflict of interest

The author(s) did not reveal any potential conflict of interest.

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