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AMELIORATIVE EFFECTS OF GREEN TEA ON POTASSIUM BROMATE INDUCED PANCREATIC DAMAGE OF ADULT WISTAR RATS

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ABSTRACT
Bromate is a byproduct of ozonation process that is sometimes used for the disinfection of municipal drinking water. Potassium bromated is metabolized into harmful substances within different organs, and generally target those specific places once produced. This led to the study of its effects on the pancreas following oral administration of honey. Twenty wistar rat weighing averagely 150g were divided into four groups (n=5). Group A served as the control group while groups (B, C, D) were the experimental groups which received potassium bromate only, group C received green tea extract only while group D received green tea extract and potassium bromate all using orogastric tube, usually between the hour of 9am to 10am at concentration of 1.0ml for green tea extract and 0.7ml for potassium bromate. The result of the study showed acute inflammation of the islet of Langerhans with few regeneration pancreatic tissue in the honey treated group.
Keywords: *potassium bromate, pancreas, honey.*

INTRODUCTION
Potassium bromate ($KBrO_3$) is a bromate of potassium and takes the form of white crystals of powder. It is produced by passing bromine into a solution of potassium hydroxide. Alternatively, it can be created as a byproduct of potassium bromide production by absorption of bromine of ocean water into potassium carbonate. Potassium bromate has the ability of causing cancer within the body and can also cause cough and sore throat (Atkins, 1993). Abdominal pain, diarrhea, vomiting, kidney failure, hearing loss, bronchial and ocular problems, are some of the non cancer health problems associated with ingestion of potassium bromate (Atkins, 1993). Studies have reported that it can cause cancer in experimental animals and in humans (Watson 2000) potassium bromate was reported to give positives for mutagenicity in the Ames test, chromosome aberration test and micronucleus test but gave negative results in the Rec-assay and in a silk worm assay (Kawachi*et al.,* 1980; Ischidate*et al.,* 1981).Potassium bromate has been investigated as a tumorigen and mutagen (Environmental Health and safety, 2010). On inhalation, it causes irritation to the respiratory tract and symptoms may include coughing and

shortness of breath. Ingestion causes irritation to the gastrointestinal tract.
Herbal medicines derived from plant extracts are being increasingly utilized to treat a wide variety of clinical disease (Gupta et al., 2004). More attention has been paid to the protective effects of natural antioxidants against drug-induced toxicities especially whenever free radical generation is involved (Frei and Higdon, 2003). Flavonoids have been found to play important roles in the non-enzymatic protection against oxidative stress (Okada et al., 2001; Babich et al., 2005), especially in case of cancer. Flavonoids are group of polyphenolic compounds that occur widely in fruit, vegetables, tea, cocoas and red wine (Arts et al., 1999; Bearden et al., 2000; Matito et al., 2003). Tea is second only to water in popularity as a beverage. Green tea (Camellia sinensis) extract is fast becoming ubiquitous in consumer products supplemented with green tea such as shampoos, creams, soaps, cosmetics, vitamins, drinks, lollipops and ice creams (Mukhtar and Ahmad, 2000). Fresh tea leaves are rich in flavanol monomers known as catechins such as epicatechins (Graham, 1992), which are 13.6 g/100 g in green tea and 4.2 g/100 gm dry weight in black tea (Peterson, et al., 2005). Catechins have beneficial effects in prevention of cardiovascular diseases including LDL oxidative susceptibility, serum lipids and lipoprotein concentrations (Wan et al., 2001).

Green tea consumption has also been linked to the prevention of many types of cancer, including lung, colon, esophagus, mouth, stomach, small intestine, kidney, pancreas, and mammary glands (Koo et al., 2004).Studies using animal models show that green tea catechins provide some protection against degenerative diseases (Vanessa et al., 2004). Some studies indicated that green tea has an antiproliferative activity on hepatoma cells and a hypolipidemicactivity in hepatoma-treated rats, as well as the prevention of hepatoxicity and as a preventive agent against mammary cancer post-initiation (Vanessa et al., 2004).

MATERIALS AND METHOD

Twenty apparently healthy wistar rats weighing about 100g to 150g which was considered fit to withstand the experiment were used. Normal rat chow and water was provided ad libitium throughout the experimental period. 25g of potassium bromate manufactured by windia speciality chemical (Chennae) PVT LTD, T amilwadu India was purchased from a reputable shop in Onitsha. This was then dissolved into 1000ml (1L) of distilled water. The green tea leaf which was gotten from Everyday supermarket in Owerri, Imo state was processed by drying in the sun, then

blending and washing out with water. The lethal dose of potassium bromate in male wistar rats is 160 – 190mg/kg/bw (Kurokawa*et al* 1990) while the adverse effect level is 63mg/kg-day.

The rats were randomly divided into four groups (A, B, C, D) each group containing five rats. The control group did not receive any treatment, while the test groups were given oral doses of 0.7 ml of $KBrO_3$ only, 1ml of green tea only, and 0.7 ml of $KBrO_3$ solution and 1ml of green tea extract, respectively for 28 days via orogastric tube.

Termination of the experiment

24 hours after the last administration for each group, the rats were anesthetized using ignasia method. The pancreas was dissected, processed for paraffin wax embedding and routinely stained for histological study using haematoxylin and eosin technique

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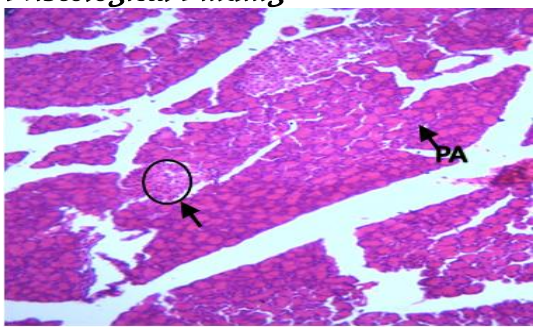
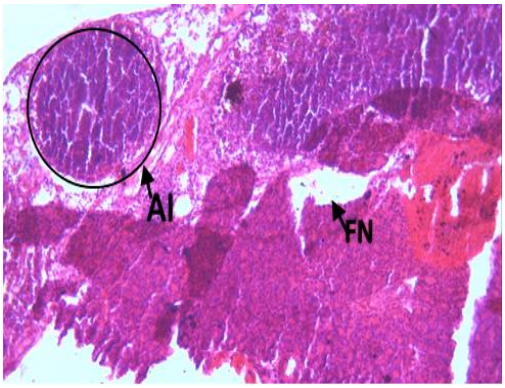
RESULTS

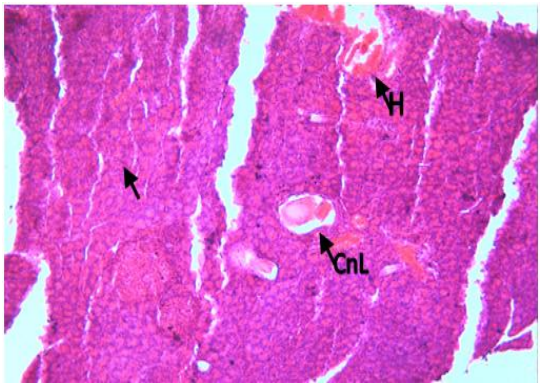
Histological Finding



A



B1



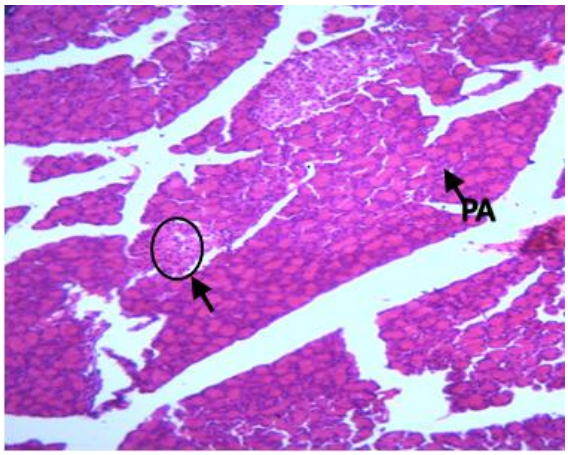
B2

Plate 2. Photomicrograph of Pancreas administered with 0.7mls of potassium bromate and their control (H&E) mag x150 for all plates

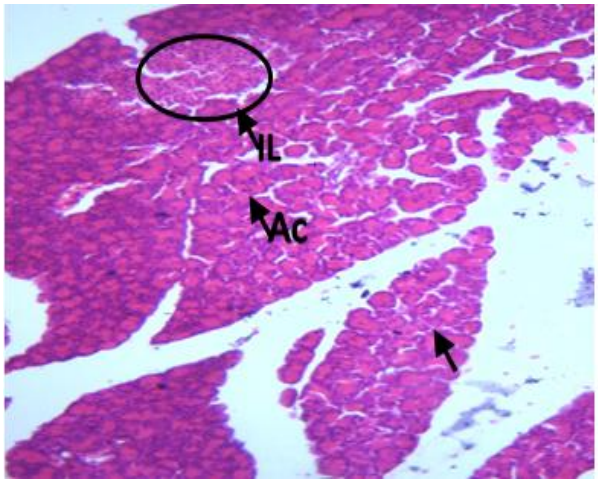
A Shows normal morphology of the pancreas

B1 Shows severely damaged pancreatic tissue with several consolidated focal aggregate of inflammatory exudent (arrow), focal area of hemorrhage (H)

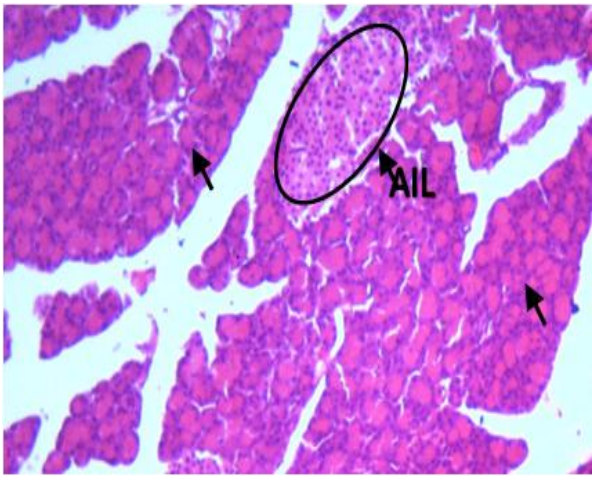
B2 Shows coagulative necrosis of islet s of Langerhans (CnL).



A



C1



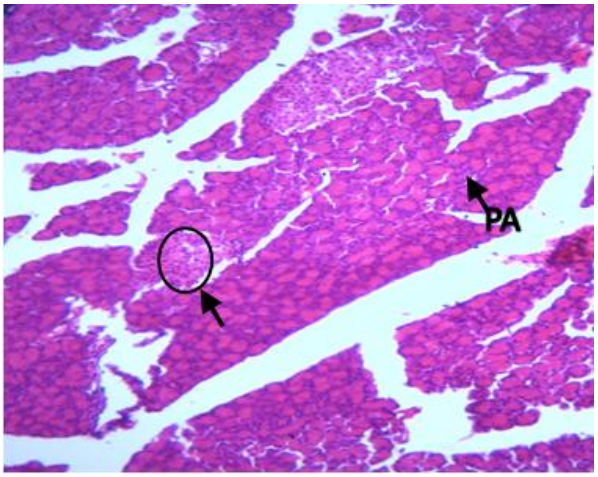
C2

Plate 3 Photomicrograph of pancreas administered with green tea extract of 1.0 ml (x150)(H/E)

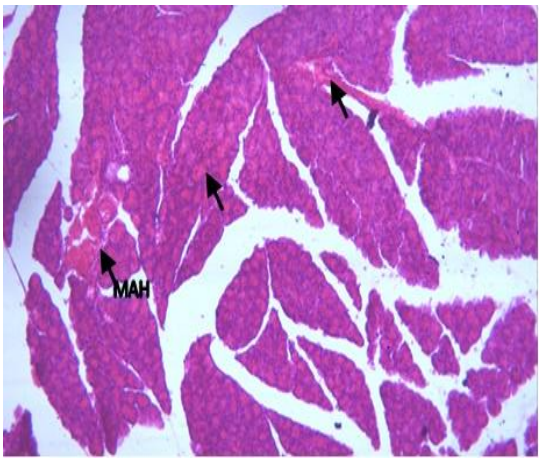
A Shows normal morphology of the pancreas

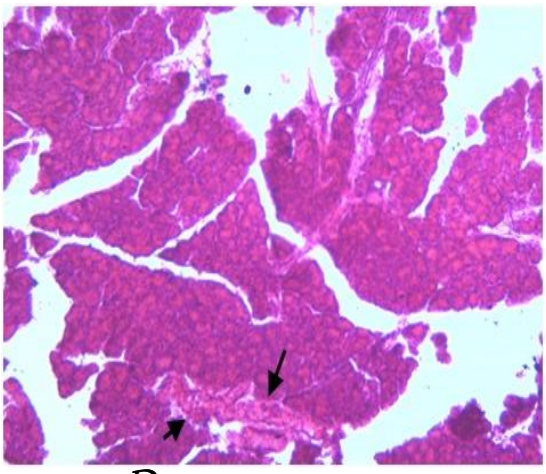
C1 Shows normal appearance of acinar cell (AC), with mild inflammation of islet of Langerhans

C2 Shows restoration of pancreatic tissue following acute inflammation of the islet of Langerhans (AIL)



A





D1 D2

Plate 4 Photomicrograph of pancreas administered with green tea extract of 1.0ml and 0.7ml of potassium bromate for 3 weeks (x150)(H/E)

A Shows normal morphology of the pancreas

D1 Shows moderately regenerated pancreatic tissue. However there are mild areas of hemorrhage (MAH).

D2 Shows regeneration of islets of Langerhans (arrow)

DISCUSSION

An oxidizing cellular microenvironment can cause apoptotic or necrotic cell death. Apoptosis may occur with relatively moderate oxidative stimuli, while necrosis can result from more severe oxidative challenges leading to the loss of the cell's ability to effectively defend itself against oxidative stresses. Reactive oxygen/nitrogen species generated within an inflamed organ have an unfavorable impact on cells, and may potentially induce apoptosis or necrosis. An oxidizing cellular microenvironment can cause apoptotic or necrotic cell death. Apoptosis may occur with relatively moderate oxidative stimuli, while necrosis can result from more severe oxidative challenges leading to the loss of the cell's ability to effectively defend itself against oxidative stresses. Reactive oxygen/nitrogen species generated within an inflamed organ have an unfavorable impact on cells, and may potentially induce apoptosis or necrosis (Sledzinski et al., 2000). In the present study, histological staining of pancreatic tissue showed coagulative necrosis of islet s of Langerhans which may result from oxidative challenges as stated by Sledizinski et al., (2000).

Acute pancreatitis remains a serious pathological condition with significant mortality rate, depending on the severity of the disease. The main cause of morbidity and mortality are sepsis and multi-organ failure. It has been shown that the systemic manifestation of the disease is mediated by inflammatory cytokines (Gross et al., 1993). From the present study, group treated with 0.7mls of potassium bromate showed focal aggregate of inflammatory exudent which may lead to acute pancreatitis. Cellular degenerative changes resulting from either necrosis or apoptosis may cause pyknosis of the islet of Langerhans (Kumar et al. 2005; Kroemer et al. 2009), which may have been induced by $KBrO_3$ administration. However, regeneration of pancreatic tissue observed in group D treated with green tea extract of 1.0ml and 0.7ml of potassium bromate for 3 weeks may result from the anti-inflammatory properties of the green tea extract. Inflammation is often a precursor to cancer. EpigallocatechinGallate (EGCG) and Epigallocatechin (ECG) which highly found in green tea have anti-inflammatory effects as they induce apoptosis in monocytes at concentrations of 10 to 50 μM (Kawai et al., 2005) EGCG is the primary focus for the activity behind green tea consumption. EGCG can inhibit cancer in animal models (Nakazato et al., 2005; Sukhthankar et al., 2008). It also can reduce inflammation, causing a decrease in oxidative and inflammatory markers in rat model (Ran et al., 2008).

CONCLUSION

Despite the relatively well defined histological progression of pancreatic damage in the rat model, the

intracellular events leading to cellular apoptosis and necrosis of the islet of Langerhans remain inadequately defined. However, ingestion of aqueous extract of green tea has showed to salvage the toxic effect of potassium bromate on the pancreas.

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