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MODULATING BLOOD PROFILES: THE PROTECTIVE ROLE OF *CUCUMEROPSIS MANNII* SEED OIL IN ALBINO RATS EXPOSED TO CISPLATIN TOXICITY

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ABSTRACT
This research work was designed to determine the modulatory effect of *Cucumeropsis mannii* seed oil (CMSO) on hematological parameters of cisplatin induced toxicity in albino rats. A total of 36 albino rats were randomly assigned into six experimental groups. Group1 (normal control) was fed on pellet and allowed free access to water; Group2 (cisplatin only) received 20mg/Kg body weight of cisplatin only; Group3 (treated group) received 20mg/Kg body weight of cisplatin and 5ml/Kg b.w. of CMSO; Group4 (treated group) received 20mg/Kg body weight of cisplatin and 2.5 ml/Kg b.w. of CMSO; Group5 (treated group) received 20mg/Kg body weight of cisplatin and 7.5ml/Kg b.w. of CMSO; Group6 (CMSO only) received 5ml/Kg body weight of CMSO only. All the animals were allowed free access to water and feed without restriction. The administrations were done by oral intubation once daily for three weeks. The results showed that administration of cisplatin to albino rats caused a significant ($p<0.05$) decrease in the levels of red blood cell count and significantly ($p<0.05$) increase in the level of white blood cell count when compared to controls. The results also showed that administration of cisplatin to albino rats showed a significant ($p<0.05$) decrease in the levels of hemoglobin and PCV in relation to controls. However, concurrent administration of cisplatin and CMSO showed a significant ($p<0.05$) reversal in the trends of these parameters to a level comparable to the level observed in the control group when compared to group that received cisplatin alone. The result also revealed that there was no significant ($p>0.05$) difference in the group administered CMSO only when compared with the normal controls. It's recommended that *Cucumeropsis mannii* seed oil could be used to manage hematological imbalance in cisplatin administrations.

Keywords: Hematology, Imbalance, Cisplatin and *C.mannii*

Introduction
Chemotherapy uses cyclophosphamide, an alkylating agent, to treat various cancer types. It is known to have adverse effects on the liver and kidneys, leading to hepatorenal damage (Giri *et al.,* 2016). This damage is due to oxidative stress, which leads to inflammation of the liver and kidneys. The metabolization of cyclophosphamide produces reactive oxygen species (ROS), which in turn cause oxidative stress (Mustafa and Gopalakrishnan, 2013). These ROS cause damage to cells, proteins, and DNA, leading to inflammation and tissue damage. This can result in hepatorenal damage, including liver fibrosis, kidney tubular damage, and kidney failure (Li *et al.,* 2016).

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Cisplatin is a chemotherapeutic drug that is used in the treatment of various types of human cancers such as Ovarian, lung, head and neck, testicular and bladder (Aldossory, 2019).The mechanism of action of cisplatin has been associated with the ability to crosslink with the purine bases on the DNA to form DNA adducts, preventing repair of the DNA leading to cell death. Cisplatin is a multi-organ toxicant at high doses. Cisplatin overdose leads to various toxic side effects includinghepato-toxicity, nephrotoxicity, cardiotoxicity, nausea and neurotoxicity (Aldossory, 2019).

High dosage of Cisplatin may lead to hepatoxicity (Dos-Santos *et al.,* 2007). Oxidative stress is the main reason for Cisplatin-induced toxicity possibly due to depletion of reduced glutathione (GSH). Many studies reported that there was significant elevation in the hepatic malondialdehyde (MDA) and reduction in the level of antioxidant enzymes in rats treated with cisplatin (Mansour *et al.,* 2006). The most sensitive biomarkers directly concerned in causing cellular damage and toxicity are transaminases, because they are cytoplasmic in location after cellular damage. Elevation of hepatic enzymes level in serum and bilirubin are the indicators of impaired liver functions (Iseri *et al.*, 2007).

Several antioxidant agents have been used to inhibit the formation of free radicals, and they can also be used to prevent or reduce the adverse effects caused by cisplatin (Arivarasu *et al.,* 2013). There are many studies which demonstrated the use of antioxidants in mitigating the adverse effects related to Cisplatin (Dos-Santus *et al.,* 2012; Leonetti *et al* 2003).

Medicinal plants have formed the basis of health care throughout the World since the earliest days of humanity and are still widely used and have a considerable importance in international trade. Medicinal plants are health aids that have been in use for a long time in developing countries (Hoareau and DaSilva, 1999). The use of these herbs for treatment of diseases is popular in developing countries for historical and cultural reasons and is more economical because of the rising cost of orthodox drugs in the maintenance of personal health and wellbeing (Hoareau and DaSilva, 1999). Herbal medicine has allowed for research into pharmacological activities of plants and their metabolites that influence biological processes and reverse disease states. A variety of bioactive compounds and their derivatives such as phenolic compounds, terpenes, steroids, alkaloids, glycosides, fats and oils have been shown to inhibit oxidative stress in the number of experiments or studies (Hoareau and DaSilva, 1999).

CMSO is a vegetable oil obtained from the seeds of C. mannii, a tropical African plant also known as African white melon (*Ogunsanwo et al.,2012)*. It is used as a source of essential fatty acids for both culinary and cosmetic purposes. CMSO is rich in oleic acid, linoleic acid, and linolenic acid, as well as other fatty acids (Ajiboye *et al.,* 2020). This study was designed to investigate the Modulatory Effects of CMSO on Hematological Profiles in Albino Rats Subjected to Cisplatin-Induced Toxicity.

Materials and Methods

Equipment and Instruments

The equipment and instruments used in this study were of good analytical quality/grade.

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Chemicals and Reagents

The chemicals and reagents used were of analytical quality. The chemicals were sourced from May and Baker, England; BDH, England and Merck, Darmstadt, Germany. The reagents used were commercial kits and products of Randox, QCA, USA and Biosystem Reagents and Instruments, Spain.

Biological Materials

Albino rats and *C. mannii* seed oil are the biological materials used in this study.

Collection and Authentication of Biological Materials

Fresh seeds of *C. mannii* were collected from Oko in Anambra State, South Eastern Nigeria and was identified by a Taxonomist in the Department of Applied Biology, Ebonyi State University, Abakaliki, Ebonyi State, Nigeria. The albino rats used were purchased from the Animal Unit, NnamdiAzikiwe University, Awka, Anambra State, Nigeria. The rats were acclimatizatized for one week before the commencement of experiment.

Methods

Extraction of *C. mannii* Seed Oil

The seed oil of the *C. mannii* were extracted from the dried seed using mechanical pressing method according to Mathangi **(**2018). In the first step, seeds were cleaned, to remove the dirt and stones. In the second step, seeds were dried under the shade in an open space. In the third step, seeds were powdered and finally, the theory of diffusion was applied to extract the oil through continuous pressing of the powdered sample.

Experimental Design for the Study

After adaptation, a total of 36 albino rats were randomly divided into six experimental groups of 1-6 ($N = 6$). Group 1 (normal control): rats were fed on pellet and allowed free access to water; Group 2 (cisplatin only): the animals received 20 mg/Kg body weight of cisplatin only (Hong *et al.,* 2020). Group 3 (cisplatin + 5 ml/Kg b.w. of CMSO): the rats received 20 mg/Kg body weight of cisplatin (Hong *et al.,* 2020) and 5 ml/Kg b.w. of CMSO; Group 4 (cisplatin + 2.5 ml/Kg b.w. of CMSO): the rats received 20 mg/Kg body weight of cisplatin (Hong *et al.,* 2020) and 2.5 ml/Kg b.w. of CMSO; Group 5 (cisplatin + 7.5 ml/Kg b.w. of CMSO): the rats received 20 mg/Kg body weight of cisplatin (Hong *et al.,* 2020) and 7.5 ml/Kg b.w. of CMSO; Group 6 (CMSO): the animals received 5ml/Kg body weight of CMSO only. All the administration was done by oral intubation once daily for six weeks.

Determination of Hematological Parameters (PCV and HB)

Determinations of hematological parameters were carried out according to the method of Dacie and Lewis (2000).

Statistical Analysis

Data were expressed as mean ± standard deviation. The means of the parameters were compared using one-way ANOVA and $p<0.05$ was considered statistically significant levels in the Turkey analysis.

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RESULTS

Effects of CMSO on some Hematological Parameters of Cisplatin Induced Toxicity in Albino Rats

The results showed that administration of cisplatin to albino rats caused a significant ($p<0.05$) decrease in the levels of red blood cell count and significantly ($p<0.05$) increase in the level of white blood cell count when compared to controls. The results also showed that administration of cisplatin to albino rats showed a significant ($p<0.05$) decrease in the levels of hemoglobin and PCV in relation to controls. However, concurrent administration of cisplatin and CMSO showed a significant ($p<0.05$) reversal in the trends of these parameters to a level comparable to the level observed in the control group when compared to group that received cisplatin alone as shown in Table 1 and 2. The result also revealed that there was no significant ($p>0.05$) difference in the group administered CMSO only when compared with the normal controls as shown in Table 1 and 2.

Table 1: RBC and WBC Levels of Cisplatin Induced Toxicity in albino rats Treated with CMSO. Data are shown as mean ± S.D (n=6). Values with Different Superscript are significantly different at p<0.05.

GROUPS	RBC ($\times10^6$)	WBC ($\times10^9$mm^3)
Group 1: FEED AND NORMAL WATER	5 ± 0.10^a	8 ± 0.01^c
GROUP 2: 20 mg/Kg B.W. CISPLATIN ONLY	2 ± 0.62^b	14 ± 0.52^d
Group 3: CISPLATIN + 7.5ml/Kg B.W. CMSO	5 ± 0.45^a	8 ± 0.46^c
GROUP 4: CISPLATIN +5ml/Kg B.W. CMSO	4 ± 0.53^a	9 ± 0.72^c
Group 5: CISPLATIN + 2.5ml/Kg B.W. CMSO	5 ± 0.43^a	7 ± 0.65^c
Group 6: 5 ml/Kg B.W. of CMSO ONLY	4 ± 0.11^a	8 ± 0.51^c

KEY:
B.W. = Body weight
CMSO = *Cucumeropsis mannii* Seed Oil

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Table 2: Hemoglobin and PCV Levels of Cisplatin Induced Toxicity in albino rats Treated with CMSO. Data are shown as mean ± S.D (n=6). Values with Different Superscript are significantly different at p<0.05.

GROUPS	Hemoglobin (g/dl)	PCV (%)
Group 1: FEED AND NORMAL WATER	15 ± 0.01^{a}	35 ± 0.42^{c}
GROUP 2: 20 mg/Kg B.W. CISPLATIN ONLY	5 ± 0.62^{b}	15 ± 0.34^{d}
Group 3: CISPLATIN + 7.5 ml/Kg B.W. CMSO	14 ± 0.65^{a}	35 ± 0.43^{c}
GROUP 4: CISPLATIN + 5 ml/Kg B.W. CMSO	15 ± 0.54^{a}	36 ± 0.71^{c}
Group 5: CISPLATIN + 2.5 ml/Kg B.W. CMSO	15 ± 0.43^{a}	34 ± 0.62^{c}
Group 6: 5 ml/Kg B.W. CMSO ONLY	14 ± 0.22^{a}	34 ± 0.21^{c}

KEY:
B.W. = Body weight
CSMO = *Cucumeropsis mannii* Seed Oil

Discussion

The results showed that administration of cisplatin to albino rats caused a significant (p<0.05) decrease in the levels of red blood cell count and significantly (p<0.05) increase in the level of white blood cell count when compared to controls. The results also showed that administration of cisplatin to albino rats showed a significant (p<0.05) decrease in the levels of haemoglobin and PCV in relation to controls. However, concurrent administration of cisplatin and CMSO showed a significant (p<0.05) reversal in the trends of these parameters to a level comparable to the level observed in the control group when compared to group that received cisplatin alone. The result also revealed that there was no significant (p>0.05) difference in the group administered CMSO only when compared with the normal controls.

These suggest that CMSO may have the potential to stimulate erythropoietin release in the kidney known to enhance RBC production (erythropoiesis) (Sanchez-Eisner *et al.,* 2004).

Our findings is in agreement with the report of Mbaka *et al.* (2010) who reported significant (P<0.05) increase in red blood cells (RBC), packed cell volume (PCV) and haemoglobin (Hb) in the treated animals with extract of *Sphenocentrum jollyanum* leaves compared to the control animals. It also agrees with the findings of Mbaka and Owolabi (2011), who reported that administration of extract of *Sphenocentrum jollyanum* seed resulted to significant increase (P<0.05) in RBC, packed cell volume (PCV) and haemoglobin count (Hb) with increase in dose while WBC did not record appreciable difference compared to the control. This result equally agrees with the report of Mojisola *et al.* (2013), who reported that extract of *Anogeissus leiocarpus* at

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100 and 200 mg/Kg body weight increased the haemoglobin, RBC and PCV levels of treated *P. berghei* infected mice compared to untreated group.

These findings disagrees with that of Mbaka *et al.* (2014), who reported an insignificant (P>0.05) decrease in Red Blood Cell (RBC) count and haemoglobin (Hb) level while White Blood Cell (WBC) showed significant (P<0.05) increase on swiss albino rats treated with aqueous ethanol root extract of *Raphia hookeri*(Palmaceae). It also disagrees with the report of Amidu *et al.* (2008), who reported that there were no significant (P>0.05) differences found in most of the haematological, serum **biochemical parameters** and organ/body weight ratio in rats administered with the extract of ***Sphenocentrum jollyanum*** **root**. It equally disagrees with the report of Sreemoy *et al.* (2015), who reported no significant (P>0.05) differences in haematological and biochemical parameters in animals administered with extract of *Epipremnum aureum*.

This variation in the results could be because of different locations in which the plants were collected or may be attributed to the part or species of the plant used (Ibiam *et al.,* 2017). It may also be directly depended to the plant physiological setup and climatic changes (Goss, 1980). This variation may equally be attributed to the methodology, experimental model or doses of the extracts used (Ibiam *et al.,* 2017).

Conclusion

The result revealed that *Cucumeropsis mannii* seed oil (CMSO) could be used in the management of hematological disorders caused by cisplatin toxicity in albino rats.

Recommendations

1. Further research should be carried out to know the cause of increase or decrease in the studied parameter.
2. *Consumption of Cucumeropsis mannii seed oil (CMSO)* should be encouraged.

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