World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Research Article
ISSN: 2583-6579
SJIF Impact Factor: 3.454
Year - 2024
Volume: 3; Issue: 3
Page: 120-129

BUCHHOLZIA CORIACEA TERPENOID-RICH SEED EXTRACT POSSESSES ANTIOXIDANT PROPERTIES AND PROTECTS AGAINST ACETAMINOPHEN-INDUCED LIVER DAMAGE INALBINO RATS

Fakoya, Akindele*

Department of Biochemistry, Faculty of Sciences, Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria.

Article Received: 05 May 2024 | | ***Article Revised: 27 May 2024*** | | ***Article Accepted: 19 June 2024***

Corresponding Author: Fakoya, A.
Department of Biochemistry, Faculty of Sciences, Adekunle Ajasin University, Akungba, Akoko, Ondo State, Nigeria.
DOI: https://doi.org/10.5281/zenodo.12627202

ABSTRACT

Acetaminophen is a safe, effective analgesic and antipyretic drug which has been discovered to induce hepatotoxicity in case of overdose. *B. coriacea* is a medicinal plant known to have good antihelmintic, antibacterial, antimicrobial, hypoglycemic and antimalarial effects. In this study, terpenoid-rich extract of air-dried seed of *B. coriacea* was investigated for its potential ameliorative effect on acetaminophen-induced toxicity in the liver of rats using N-acetyl cysteineas a standard drug. In the course of this work, toxicity was induced in the liver of wistar rats at 500mg/kg b.w of acetaminophen to check for the protective effects of terpenoid-rich seed extract of *B. coriacea* at different doses. Group 1 served as basal control which received only normal diet, group 2 received 500 mg/kg b.w of acetaminophen daily. Groups 3, 4 and 5 received 500 mg/kg b.w of acetaminophen each followed by 30, 90 and 210 mg/kg b.w of terpenoid-rich seed extract respectively. Groups 6 and 7 each received 500 mg/kg b.w of acetaminophen followed by 70 and150 mg/kg b.w of N-acetyl cysteine respectively. Groups 8, 9 and 10 received only 30, 90 and 210mg/kg b.w of terpenoid-rich seed extract once daily. These treatments were given orally for three(3) days. The rats were sacrificed, liver was excised, homogenized and the activity of glutathioneperoxidase (GPX), glutathione consumed (GSH), malondialdehyde (MDA) level and total proteinwere determined. The group administered acetaminophen only showed decrease in GPX activity, indicating that there was depletion in glutathione biomolecule which lead to decrease in the activityof the glutathione enzyme. However, the groups administered with terpenoid-rich seed extract of *B. coriacea* elicited increased in the GPX activity. There was increase in total protein level in acetaminophen administered group only due to response caused by acetaminophen. However, the groups administered terpenoid-rich seed extract showed decrease in total protein level compared to the acetaminophen administered group. Acute dose of acetaminophen (500 mg/kg b.w.) significantly elevated the liver MDA level. The results of this study showed that the terpenoid-richseed extract of *B. coriacea* elicited antioxidant effects against liver damage induced by acetaminophen, and could therefore serve as a potent drug in the management and treatment of acetaminophen hepatotoxicity.

KEYWORDS: Malondialdehyde, oxidative, administration, hepatoprotective, cytoplasm.

INTRODUCTION

Buchholzia Coriacea

Medicinal plants are rich in secondary metabolites which are potential sources of drugs and are hence, of therapeutic values. Medicinal plants bear important chemical compounds that are biologically active and effective against diseases. In addition, the alarming development and spread of antibiotics resistance necessitates the search for alternative sources of drugs. Plant-based drugs have enormous therapeutic potentials; they contain chemical compounds that act individually and synergistically, with wider spectrum and fewer side effects when compared with synthetic pharmaceutical agents. *Buchholzia coriacea* was named after Reinhold Wilhelm Buchholz who collected the plants in Cameroon in the late 19th century. It belongs to the family *Capparidacea*. The family *capparidacea* is described from Carpe-Verde Islands. It comprises of 45 genera and approximately 1000 species, distributed in the tropical and sub-tropical regions, especially East Africa and South America. The plant is an evergreen under-storey tree of lowland rainforest, up to 20 m high occurring in Cameroon, Congo, Central African Republic, Gabon, Angola, Nigeria and Ghana among others (Anie *et al*., 2015). It is a shrub or medium-sized tree, evergreen, with a dense crown, large, glossy, leathery leaves arranged spirally and clustered at theends of the branches and conspicuous cream-white flowers in racemes at the end of the branches (Eze *et al.*, 2015).

Wonderful kola

The seed of the plant is used in folk medicine for the treatment of diabetes, ulcer, malaria, helmintic disorders, hypercholesterolemia and other diseases, hence the origin of its common name “wonderful kola”. The plant part commonly eaten is the seed which is either cooked or eaten raw. Studies had shown that the seed extract possess antimicrobial activity (Ezekiel and Onyeoziri, 2009). The antihypercholesterolemic effect of ethanol seed extract of the plant was already established (Olaiya and Omolekan, 2013). The plant leaf extract possesses anti-inflammatory effect. *B. coriacea* seeds are rich in many phytochemicals, some of which possess great antimicrobial effects.

Paracetamol

Paracetamol (an international name used in Europe) and acetaminophen (an international name used in the USA) are two official names of the same chemical compound derived from its chemical name: N-acetyl-para-aminophenol. Acetaminophen was first discovered in Germany in 1887. It was initially rejected in favour of the structurally related phenacetin, as it was considered too toxic.It was only when restudied in the late 1940s that it was recognized as safer than alternative agents.It was first marketed as an antipyretic and analgesic in the USA, as Tylenol, and UK, as Panadol,in the 1950s (Bateman and Dear, 2010). Toxicity from acetaminophen overdose was initially recognized in 1966, about 10 years after marketing, when the first cases were reported in Scotland(Bateman and Dear, 2010). At that time there were no effective therapies, and morbidity and mortality from acetaminophen overdose climbed steadily as overdoses increased. In the1970s therewere a significant number of cases in the Royal Infirmary poisons unit in Edinburgh, and Laurie Prescott and colleagues did important work, allowing rapid progress in knowledge. Initial studies showed the relationship of plasma concentration of acetaminophen to risk of toxicity. Animal studies had suggested both the mechanism of action of acetaminophen and potential antidotes. Studies were then done in the UK and North America evaluating three of these, cysteamine, methionine, and acetylcysteine. By the end of that decade the evidence was clear from UK data that N-acetylcysteine (NAC) was the antidote of choice (Rumack and Bateman, 2012).

N-Acetylcysteine

N-acetylcysteine, NAC, is a precursor to the amino acid L-cysteine and consequently the antioxidant glutathione (GSH) (Pieralisi *et al*., 2016). It is most notably found in plants of the *Allium* species, especially in the Onion (*Allium cepa*, 45 mg NAC/kg) (Campos *et al*., 2003; Diniz*et al*., 2006). The sulfhydryl group (–SH) within the NAC molecule directly scavenges reactive oxygen species (ROS) (Radmska-Lesniewska and Skopinski, 2012), modulates the redox state ofthe N-methyl-D-aspartate (NMDA) and amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors (neurotransmitter effect), and inhibits the nuclear factor kappa-light-chain- enhancer of activated β cells (NF-β) to modulate cytokine synthesis (anti/pro-inflammatory effect)(Guo *et al*., 2013). Unlike -SH itself, NAC has better oral and topical bioavailability (Schmitt *et al*., 2015). Even though it has been used for more than 50 years, there are still many controversiessurrounding it as a medicine as well as a dietary supplement. Several review articles have focusedon various medical uses of NAC, some more general (Mokhtari *et al*., 2017) and others highly specific dealing with NAC use only in a particular condition such as hyperglycaemia-induced oxidative damage (Dludla *et al*., 2017).

The Liver

The liver is the largest solid organ, the largest gland and one of the most vital organs that functions as a center for metabolism of nutrients and excretion of waste metabolites (Ozougwu and Eyo, 2014). Its primary function is to control the flow and safety of substances absorbed from the digestive system before distribution of these substances to the systemic circulatory system (Allen, 2002). A total loss of liver function could leads to death within minutes, demonstrating the liver‘sgreat importance.

TERPENOIDS

This class comprises natural products which have been derived from five-carbon isoprene units. Most of the terpenoids have multi cyclic structures that differ from one another by their functional groups and basic carbon skeletons. These types of natural lipids can be found in every class of living things and therefore considered as the largest group of naturally occurring secondary metabolites (Elbein and Molyneux, 1999). Many of these are commercially interesting because oftheir use as flavours and fragrances in foods and cosmetics (Horborne and Tomasbarberan, 1991).Terpenes are widespread in nature, mainly in plants as constituents of essential oils. Their building block is the hydrocarbon isoprene. Among plant secondary metabolites terpenoids are a structurally most diverse group; they functions as phytoalexins in plant’s direct defense or as signals in indirect defense responses, which involve herbivores and their natural enemies (Mccaskill and Croteau, 1998). Many plants produce volatile terpenes in order to attract specific insects for pollination. Some plants produces less volatile but strongly bitter tasting or toxic terpenes also protect some plants from being eaten by animals (Degenhardt *et al*., 2003). In addition, terpenoids can have medicinal properties such as anticarcinogenic (e.g. perilla alcohol), anti-malarial (e.g. artemisinin), anti-ulcer, hepaticidal, antimicrobial or diuretic (e.g. glycyrrhizin)activity and the sesquiterpenoid anti-malarial drug artimisinin and the diterpenoid anticancer drugtaxol (Dudareva *et al*., 2004).

Laboratory Animals

Forty male white wistar rats were purchased from University of Ibadan, Oyo State, Nigeria. They were housed under standardized environmental conditions. Commercial poultry feed was provided with water three times daily to sustain them for weeks of acclimatization. They were divided intogroups based on their weight which was used to calculate the dosage of *Buchholzea coriacea* extract, acetaminophen and NAC administered. Intubation started after four weeks of

acclimatization for three days. The dose was given to the grouped rats as follows:

Group 1: Rats were given food and water

Group 2: Rats were given 500 mg/kg b.w of acetaminophen daily.

Group 3: Rats were given 500 mg/kg b.w of acetaminophen and 30 mg/kg b.w of terpenoid-richextract daily.

Group 4: Rats were given 500 mg/kg b.w of acetaminophen and 90 mg/kg b.w of terpenoid-richextract daily.

Group 5: Rats were given 500 mg/kg b.w of acetaminophen and 210 mg/kg b.w of terpenoid-richextract daily.

Group 6: Rats were given 500 mg/kg b.w of acetaminophen and 70 mg/kg b.w of n-acetylcysteinedaily.

Group 7: Rats were given 500 mg/kg b.w of acetaminophen and 150 mg/kg b.w of n-acetyl cysteinedaily.

Group 8: Rats were given 30 mg/kg b.w of terpenoid-rich extract daily.

Group 9: Rats were given 90 mg/kg b.w of terpenoid-rich extract daily.

Group 10: Rats were given 210 mg/kg b.w of terpenoid-rich extract daily.

Sacrificing of Laboratory Animals

At the end of three days treatment regimen, the animals were subjected to fasting overnight and were sacrificed after 24 hours. The rats were rendered unconscious by cervical dislocation. The rats were then sacrificed and liver was excised from each experimental animal. The excised tissuewas homogenized and then kept in freezer at 4^{o}C.

Collection and authentication of sample

Fresh seed of *Buchholzia coriacea* was purchased from Idanre Market, Ondo State, Nigeria and were taken to Department of Plant Science and Biotechnology, Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria for authentication. Voucher Number 025 was assigned to *Buchholzia coriacea* (Engler), while a voucher sample was deposited at the University Herbarium.

Preparation of extracts

The seed was washed thoroughly with clean water to remove adhering particles. Thereafter sliced, air-dried and pulverized. The pulverized form was macerated in absolute n-hexane. This was left for 72 hours at room temperature, after which the extract was filtered through a muslin cloth. The filtrate was concentrated at low temperature to obtain the crude extract. The extract was weighed and stored in the fridge before administration. The terpenoid used in the treatment of theexperimental animals were extracted from the method adopted (Akinloye *et al*., 2020). Terpenoidwas extracted from the crude by 85:15 v/v n-hexane / ethylacetate, and silica gel (pore size 230- 400 mesh, Sigma-Aldrich catalog number: 227196). Agilent 6890a GC equipped with an HP5-MScolumn (30m×0.25µm) coupled to an Agilent 5975C Mass Spectral Detector or Flame Ionization Detector (FID) was used for the characterization of the terpenoids.

Malonaldehyde (MDA) determination

The reaction mixture containing 1mL 0.67% thiobarbituric acid (TBA), 500 µL 20% tricarboxylicacids (TCA), and 100 µL sample was incubated at 100° C for 20 min and centrifuged at 12,000 rpm for 5 min. The absorbance of the supernatant was read at 532 nm and MDA concentration wasdetermined by using a molar extinction coefficient of 1.56 × 10^{5}/M/cm and the values were expressed as µM/mg protein (Buege and Aust, 1998).

Total protein determination

40 µl of distilled water was placed into a test tube and 40 µl of standard was placed into anothertest tube and sample was also placed into another test tube. Then 2000 µl of R1 was then added toeach of the three test tubes and the samples

were incubated for 30 minutes and the absorbance of each sample was read at 532 nm against the blank.

Glutathione Activity and Glutathione Consumed Analysis

The 50 ul of 0.026g of sodium azide in 40 ml of water was dispelled to each test tube using micropipette. Phosphate buffer (PH 7.4), 250 ul was added to each test tube, 0.1993 g of GSH wasadded thereafter, 50 ul of hydrogen peroxide (H_2O_2) was added to each test tube, followed by addition of 250 ul of sample to the solution in each test tube after which 300 ul of distilled water was added to each, finally 250 ul of TCA was added to each sample solution, addition of TCA turns the solution brown milky. The samples were centrifuged for 5 mins at 3000 r.p.m. After centrifugation 500 ul of the supernatant was decanted into another set of test tubes, then 1ml of buffer solution was added each. Thereafter, 0.5 ml of 0.016 g of DTNB was added to each test tube. The absorbance of each sample was read at 412 nm against the blank.

Glutathione consumed = 245.84 - GSH remaining Glutathione peroxidase activity = GSH consumed/mg protein.

Statistical analysis

Results were expressed as mean of replicates ± standard deviation. The data were statistically analyzed using One Way Analysis of Variance (ANOVA) and Duncans Multiple Range Tests. Differences were considered statistically significant at $p<0.05$ using the General Linear Model procedure of SPSS (2O17).

RESULTS

Table 1: Changes in glutathione peroxidase activity in the liver of rats treated with terpenoid-rich seed extract of *B. coriacea* and N-acetylcysteine in acute dose ofacetaminophen-induced toxicity.

Groups	GPx (µmol/g)
Control	7.708 ± 0.10^{e}
PCM	0.756 ± 0.17^{a}
PCM+E1	4.053 ± 0.05^{b}
PCM+E2	4.650 ± 0.05^{b}
PCM+E3	6.115 ± 0.01^{d}
PCM+N1	5.228 ± 0.02^{c}
PCM+N2	5.150 ± 0.03^{c}
E1	5.150 ± 0.06^{c}
E2	5.083 ± 0.04^{c}
E3	4.830 ± 0.04^{b}

Values are expressed as means ± SD within each column in each groups carrying different letters aresignificant at $p<0.05$.

Key: PCM= 500 mg/kg body weight of acetaminophen, PCM+E1= 500 mg/kg body weight of acetaminophen and 30 mg/kg body weight of extract, PCM+E2= 500 mg/kg body weight of acetaminophen and 90 mg/kg body weight of extract, PCM+E3= 500 mg/kg body weight of acetaminophen and 210 mg/kg body weightof extract, PCM+N1= 500 mg/kg body weight of acetaminophen and 70 mg/kg body weight of N-acetyl cysteine (N1), PCM+N2= 500 mg/kg body weight of acetaminophen and 150 mg/kg body weight of N- acetyl cysteine (N2), E1= 30 mg/kg body weight of extract, E2= 90 mg/kg body weight of extract, E3= 210mg/kg body weight of extract.

Table 2: Total glutathione consumed in Acetaminophen-Induced Toxicity in Rats' Liver Treated with terpenoid-rich seed extract of *Buchholzia coriacea.*

Groups	GSH Consumed (µmol)
Control	168.91±0.58[d]
PCM	119.34±0.76[a]
PCM+E1	161.70±9.97[b]
PCM+E2	185.50±0.95[e]
PCM+E3	168.08±0.34[d]
PCM+N1	184.36±0.53[e]
PCM+N2	167.29±0.47[d]
E1	164.81±3.26[c]
E2	160.81±1.41[b]
E3	125.92±3.56[a]

Values are expressed as means ± SD within each column in each groups carrying different letters are significant at $p<0.05$.

Key: PCM= 500 mg/kg body weight of acetaminophen, PCM+E1= 500 mg/kg body weight of acetaminophen and 30 mg/kg body weight of extract, PCM+E2= 500 mg/kg body weight of acetaminophen and 90 mg/kg body weight of extract, PCM+E3= 500 mg/kg body weight of acetaminophen and 210 mg/kg body weight of extract, PCM+N1= 500 mg/kg body weight of acetaminophen and 70 mg/kg body weight of N-acetyl cysteine (N1), PCM+N2= 500 mg/kg body weight of acetaminophen and 150 mg/kg body weight of N-acetyl cysteine (N2), E1= 30 mg/kg body weight of extract, E2= 90 mg/kg body weight of extract, E3= 210 mg/kg body weight of extract.

Table 3: Changes in total protein contents in the liver of rats treated with terpenoid-rich seedextract of *B. coriacea* and N-acetylcysteine in acute dose of acetaminophen-induced toxicity

Treatment	Total protein liver (g/dl)
Control[-]	21.78 ± 0.22[a]
PCM	157.93 ± 3.66[e]
PCM+E1	153.24± 2.36[de]
PCM+E2	40.17 ± 0.40[b]
PCM+E3	150.93 ± 1.33[cd]
PCM+N1	150.52 ± 2.86[cd]
PCM+N2	145.64± 3.25[c]
E1	145.60 ± 6.15[c]
E2	149.94 ± 7.11[cd]
E3	154.18 ± 5.95[de]

Values are expressed in mean ± SD (n=4); values with same superscript in the same column are not significantly different at ($p>0.05$) for total protein contents using Duncan test.

Key: PCM= 500 mg/kg body weight of acetaminophen, PCM+E1= 500 mg/kg body weight of acetaminophen and 30 mg/kg body weight of extract, PCM+E2= 500 mg/kg body weight of acetaminophen and 90 mg/kg body weight of extract, PCM+E3= 500 mg/kg body weight of acetaminophen and 210 mg/kg body weight of extract, PCM+N1= 500 mg/kg body weight of acetaminophen and 70 mg/kg body weight of N-acetyl cysteine (N1), PCM+N2= 500 mg/kg body weight of acetaminophen and 150 mg/kg body weight of N-acetyl cysteine (N2), E1= 30 mg/kg body weight of extract, E2= 90 mg/kg body weight of extract, E3= 210 mg/kg body weight of extract.

Table 4: Changes in malondialdehyde levels in the liver of rats treated with terpenoid-rich seed extract of *B. coriacea* and N-acetylcysteine in acute dose of acetaminophen-induced toxicity.

Treatment	Malondialdehyde (µM/mg protein)
Control⁻	0.05 ± 0.00^{c}
PCM	0.20 ± 0.00^{d}
PCM+E1	0.01 ± 0.00^{a}
PCM+E2	0.06 ± 0.01^{c}
PCM+E3	0.01 ± 0.00^{a}
PCM+N1	0.02 ± 0.01^{b}
PCM+N2	0.01 ± 0.00^{a}
E1	0.01 ± 0.00^{a}
E2	0.01 ± 0.00^{a}
E3	0.01 ± 0.01^{a}

Values are expressed in mean ± SD (n=4); values with same superscript in the same column are not significantly different at ($p>0.05$) for the biochemical parameter (MDA) using Duncan test.

Key: PCM= 500 mg/kg body weight of acetaminophen, PCM+E1= 500 mg/kg body weight of acetaminophen and 30 mg/kg body weight of extract, PCM+E2= 500 mg/kg body weight of acetaminophen and 90 mg/kg body weight of extract, PCM+E3= 500 mg/kg body weight of acetaminophen and 210 mg/kg body weight of extract, PCM+N1= 500 mg/kg body weight of acetaminophen and 70 mg/kg body weight of N-acetyl cysteine (N1), PCM+N2= 500 mg/kg body weight of acetaminophen and 150 mg/kg body weight of N-acetyl cysteine (N2), E1= 30 mg/kg body weight of extract, E2= 90 mg/kg body weight of extract, E3= 210 mg/kg body weight of extract.

DISCUSSION AND CONCLUSION

DISCUSSION

Acetaminophen is commonly and widely used analgesic and antipyretic agent. However, acetaminophen toxicity leads to the formation of highly reactive toxic metabolite (N-acetyl p- benzoquinone imine) by cytochrome P450 causing hepatic toxicity (Jaeschke *et al*., 2011).

However, Acetaminophen toxicity leads to the accumulation of N-acetyl-p-benzoquinoneimine, which undergoes conjugation with glutathione. Conjugation depletes glutathione, a natural antioxidant. Thus, Nacetyl- p-benzoquinoneimine in combination with direct cellular proteins leads to cell damage and death. This injury is known as acetaminophen hepatotoxicity in the liver(Lee, 2004). N-acetyl cysteine (NAC) is an effective antidote recommended by United States Foods and Drug Administration as the only standard drug for acetaminophen overdosed patients (Green *et al*., 2013).

The liver is the major source of most of the serum proteins in which the parenchymmal cells are responsible for synthesis of albumin, fibrinogen and other coagulation factors and most the α- andβ-globulins (Ritter, 2000). Albumin, being the most abundant plasma protein account for 60% of the total serum protein and is incorporated in many physiological processes.

Acetaminophen toxicity on total protein level is shown in Table 3 above. There was a significant increase in total protein levels in all the treated groups except basal control and PCM + E2 groups. The PCM treated group had the highest protein content. This may be due to damage of the cell by acetaminophen and or response of the extracts to oxidative damage. From the result, significantly increased total protein levels may result in synthesis of protein for

proper functioning of the liverin the presence of an oxidant (Ekam *et al*., 2011).

The results of liver MDA value on Table 4 revealed that there was an increased level of liver MDAin the group treated only with acute dose of acetaminophen (500 mg/kg b.w.) when compared to the normal control and other groups. However, the groups treated with extract of *B. coriacea* (30 mg/kg, 90 mg/kg and 210 mg/kg b.w.) showed reduced liver MDA levels when compared with thecontrol group. The group given acetaminophen only showed a high MDA value which indicates high oxidative stress when compared to the groups with extracts only. Also, the groups pre-treated with acetaminophen followed by NAC 70 mg/kg and 150 mg/kg also show a significant decreasein liver MDA levels when compared with control group.

The significant decrease in MDA level in the group treated only with *B. coriacea,* was in supportto Liu *et al*., (2012). At 30 mg, 90 mg and 210 mg/kg b.w of *B. coriacea,* there was decreased in MDA levels when compared to acetaminophen treated group only which was in line with the workdone by Fakoya and Olusola (2019), which stated that administration of acetaminophen may trigerexacerbated oxidative damage of the hepatocytes, however, administration of *Buchholzia coriacea*significantly ameliorated the oxidative damage because of the reduced levels of MDA. Glutathione as a biomolecule protect cells by combining with the NAPQI. The reaction is catalyzedby glutathione peroxidase, higher glutathione peroxidase indicate more of the glutathione combining with the NAPQI. Glutathione peroxidase is the main endogenous enzymatic defencesystems for preventing damage by oxidative stress of aerobic cells (Kobayashi *et al*., 2019).

The effect of acute administration of acetaminophen and *Buchoholzia coriacea* seed extract on theliver of wistar rats with respect to the relative Glutathione peroxidase activity and Glutathione consumed is shown in Tables 1 and 2 above. The results showed the antioxidant enzyme had the lowest decreased activity in the group treated with 500 mg/kg b.w acetaminophen due to excessive production of ROS (Warunyo *et al*., 2021). Also, there was decreased in glutathione consumed in group treated with 500 mg/kg b.w acetaminophen compared to the basal control and other treated groups. This work corroborated the hepatoprotective activity of methanol extract of *C. maxima* seeds against paracetamol-induced hepatotoxicity (Jain and Pathak, 2012). The induction of higheractivity of this antioxidant enzyme is suggested for the protection of the liver by reducing oxidative stress on the liver. This protection may be due to the antioxidant properties of the terpenoid-rich seed extract of *B. coriacea*.

CONCLUSION

Acetaminophen abuse and acute administration have been established to cause oxidative stress in this research work. Acetaminophen ingestion and subsequent hepatotoxicity is a critical problem that continues to plague individual across the globe. In this recent study, *Buchholzia coriacea* proved to be a good plant containing important secondary metabolites (terpenoids), a potent medicinal plant in the treatment of acetaminophen-induced hepatotoxicity. These secondary metabolites (terpenoids) could be compounded with acetaminophen to reduce its toxicity during abuse and poisoning.

RECOMMENDATION

Based on this, I recommend that further research should be carried out on *Buchholzia coriacea* inother to know more about its therapeutic effect since it is a medicinal plant and its side effects should also be further investigated.

REFERENCES

1. Akinloye, O. A., Alagbe, O. A., Ugbaija, R. N and Omotainse, S. O. Evaluation of the modulatory effect of *Piper guineense* leaves and seeds on egg albumin-induced inflammation in experimental rat models. *Journal of ethnopharmacology*, 2020; 255: 27-32.
2. Allen, S. E., The liver: Anatomy, Physiology, Disease and Treatment. *North Eastern University Press, USA*, 2002; 161: 361-366.
3. Anie, C. O., Nwabuokei, I. G., Oghenejobo, M and Enwa, F. O., The antibacterial effect of the leaf extract of *Buchholzia coriacae* (Capparidaceae) on gram-negative nasal, 2015.
4. Bateman, D. N and Dear, J., A personal perspective on paracetamol Louis Roche lecture, Stockholm. *Clinical Toxicology*, 2010; 48(2): 97–103.
5. Buege, J.A and Aust, S. D., Microsomal lipid peroxidation. *Methods in Enzymology*, 1998; 51: 303-310.
6. Campos, K. E., Diniz, Y. S., Cataneo, A. C., Faine, L. A., Alves, M. J. Q. F and Novelli, E. L.B., Hypoglycaemic andantioxidant effects of onion, *Allium cepa*: Dietary onion addition, antioxidant activity and hypoglycaemic effects on diabetic rats. *Internaltional Journal of Food Sci*ence *Nutrition*, 2003; 54: 241–246.
7. Degenhardt, J., Gershenzon, J., Baldwin, I. T and Kessler, A., AttractingFriends to feast on foes: Engineering terpene emission to make crop plants more attractive to herbivore enemies. *Current Opinion Biotechnology*, 2003; 14: 169–176.
8. Diniz, Y. S., Rocha, K. K. H. R., Souza, G. A., Galhardi, C. M., Ebaid, G. M. X., Rodrigues, H. G., Novelli Filho, J. L. V. B., Cicogna, A. C and Novelli, E. L. B., Effects of N- acetylcysteine on sucrose-rich diet-induced hyperglycaemia, dyslipidemia and oxidative stress in rats. *Eur. J. Pharmacol*, 2006; 543: 151–157.
9. Dludla, P. V., Nkambule, B. B., Dias, S. C and Johnson, R., Cardioprotective potential of N-acetyl cysteine against hyperglycaemia-induced oxidative damage: a protocol for a systematic review. *Syst. Rev*., 2017; 6: 96.
10. Dudareva, N., Pichersky, E and Gershenzon, J, Biochemistry of plant volatiles. *Plant*, 2004.
11. Elbein, A. D and Molyneux, R. J., Comprehensive Natural Products Chemistry, Vol. 3, Barton D and Nakanishi K, ed. *Amsterdam*, 1999; 129.
12. Eze, J. I, Nwese, N. E and Ekelozie, C. F., Immunomodulatory activity of the methanolic extract of Buchholzia coriacea seeds on Trypanosoma brucei-infected mice. *Global Veterinaria*, 2015; 14(4): 582-588.
13. Ezekiel, O. O and Onyeoziri, N. F., Preliminary studies on the antimicrobial properties of *Buchholzia corriacea* (Wonderful kola). *African journal of Biotechnology*, 2009; 8(3): 472-474.
14. Fakoya, A and Olusola, A. O., Free radicals scavenging potential of *Buchholzia coriacea*extract and ameliorative effect in acetaminophen-induced nephrotoxicity and hepatotoxicity in rats. *International Journal of Research in Pharmacy and Biosciences*, 2019; 6(3): 1-11.
15. Green, J. L., Heard, K. J., Reynolds, K. M and Albert, D., Oral and Intravenous Acetylcyateine for Treatment of Acetaminophen Toxicity, A Systematic Review and Meta-analysis. *The Western Journal of Emergency Medicine*, 2013; 14(3): 218-226.
16. Guo, F., Li, Y., Wang, J., Li, Y., Li, Y and Li, G., Stanniocalcin1 (STC1) Inhibits Cell Proliferation and Invasion of Cervical Cancer Cells. *PLoS One*, 2013; 8: e53989.
17. Harborne, J. B and Tomas-Barberan, F. A, Ecological Chemistry and Biochemistry of PlantTerpenoids, *Clarendon, Oxford*, 1991.
18. Jaeschke, H., McGill, M. R., Williams, C. D and Ramachandran, A., Current issues with acetaminophen

hepatotoxicity a clinically relevant model to test the efficacy of natural products. *Life Sci*., 2011; 88: 737-745.

19. Jain, N and Pathak, A., Hepatoprotective effect of methanolic extract of C. maxima and L. siceraria seeds. *International Journal of Pharmaceutical, Chemical and Biological Science*, 2012; 2(2): 151-154.
20. Kobayashi, E., Ito, J and Schmizu, N., Evaluation of *y*-oryzanol accumulation and lipid metabolism in the body of mice following long-term administration of *y*-oryzanol. *Nutrients*, 2019; 11(1): 104.
21. Langenheim, J. H., Higher plant terpenoids: A phytocentric overview of their ecological roles. *Journal of Chemical Ecolo*gy, 1994; 20: 1223-1280.
22. Lee, N. W., Acetaminophen and the U. S. acute liver failure study group. *Hepathology*, 2004; 40(1): 6-9.
23. Liu, Y., Zhao, H., Zhang, Q., Tang, J., Li, K., Xia, X. J and Lei, X. G., Prolonged dietary Selenium deficiency or excess does not globally affect selenoprotein gene expression and/or protein production in various tissues of pigs. *The Journal of Nutrition*, 2012; 142(8): 1410-1416.
24. Mccaskill, D and Croteau, R., Some caveats for bioengineering terpenoid metabolism in plants. *Trends Biotechnology*, 1998; 16: 349–355.
25. Mokhtari, V., Afsharian, P., Shahhoseini, M., Kalantar, S. M and Moini, A., A Review on Various Uses of N-Acetyl Cysteine. *Cell J*., 2017; 19: 11–17.
26. Olaiya, C. O. and Omolekan, T. O., Antihypercholesterolemic activity of terpenoid rich extract of *Buchholzia coriacea* in rats. *African Health Sciences*, 2013; 13(4): 1084-1090.
27. Ozougwu, J. C and Eyo, J. E., Hepatoprotective effects of Allium cepa extracts on paracetamol-induced liver damage in rat. *African Journal of Biotechnology*, 2014; 13(26): 2679-2688.
28. Pieralisi, A., Martini, C., Soto, D., Vila, M. C., Calvo, J. C and Guerra, L. N., N- acetylcysteine inhibits lipid accumulation in mouse embryonic adipocytes. *Redox Biol*, 2016; 9: 39–44.
29. Radomska-Lesniewska, D. M and Skopinski, P., N-acetylcysteine as an anti-oxidant and anti-inflammatory drug and its some clinical applications.*Cent. J. Immunol.*, 2012; 37: 57–66.
30. Rumack, B. H and Bateman, D. N., Acetaminophen and acetylcysteine dose and duration: past, present and future. *Clin Toxicol*, 2012; 50(2): 91–98.
31. Schmitt, B., Vicenzi, M., Garrel, C and Denis, F. M., Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. *Redox Biol*, 2015; 6: 198–205.