NJBMB (2022) 37(3) 175-180

Nigerian Journal of Biochemistry and Molecular Biology

The Official Publication of the Nigerian Society of Biochemistry & Molecular Biology (NSBMB). Journal homepage: https://www.nsbmb.org.ng/journals

e-ISSN: 2659-0042

Research Article

Curative Influence of Natural Honey Bee on Liver Function Parameters in Aluminium Nitrate-induced Wistar Rats

Lisa I. Ekakitie[1], Osuvwe C. Orororo[2*], Joel Okpoghono[3]

[1]*Department of Biochemistry, College of Sciences, Afe Babalola University, Ado-Ekiti, Nigeria*
[2]*Department of Chemical Sciences, Faculty of Science, Edwin Clark University, Kiagbodo, Nigeria*
[3]*Department of Chemical Sciences, Faculty of Natural and Applied Sciences, Novena University, Ogume, Nigeria*

OPEN ACCESS

CORRESPONDENCE
Orororo, O.C.
osuvwec@yahoo.com
+234-806-230-6783

ARTICLE HISTORY
Received: 25/03/2022
Reviewed: 23/05/2022
Revised: 20/06/2022
Accepted: 24/08/2022
Published: 30/09/2022

CITATION
Ekakitie, L.I., Orororo, O.C. and Okpoghono, J. (2022). Curative Influence of Natural Honey Bee on Liver Function Parameters in Aluminium Nitrate-induced Wistar Rats. *Nigerian Journal of Biochemistry and Molecular Biology*. 37(3),175-180

ABSTRACT

The search for antidotes for Al toxicity is on-going. Thus, this study investigated the curative influence of natural honey bee on liver function parameters in aluminium nitrate-induced Wistar rats. Thirty (30) Wistar rats (150±6g) were divided into six groups: Group one served as control and received only feed and water. Groups 2-6 served as the test groups and received single dose of Al(NO3)3 (6.5 mg/kg body weight). Groups 3-6 received varying doses of NBH (10 %, 25 %, 50 % diluted with distilled water and 100 % natural BH orally at a dose of 2.5 g/kg respectively) 24 h after Al(NO3)3 intoxication for 14 consecutive days. The activities of alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase in the plasma and liver and the levels of total protein, albumin and globulin were evaluated. Exposure to aluminium significantly ($p< 0.05$) increased the activities of ALT, AST and ALP relative to rats in the control group. However, the treatment of Al-exposed rats with varying doses of NBH significantly reduced the activities of the enzymes, compared to rats maintained on Al alone, with the exception of Al-exposed rats given 100 % NBH. Albumin concentrations were significantly higher in control rats than in rats exposed to Al. However, the administration of 50% NBH to Al-exposed rats significantly ($p< 0.05$) increased albumin concentration relative to rats exposed to Al alone. This study showed that NBH has significant positive effects on aluminum toxicity in rats with the 50 % NBH treatment having the greatest effect.

Keywords: *Aluminium, Honey, Liver, Albumin*

INTRODUCTION

The environment in which animals and humans live is contaminated with many chemicals and heavy metals of which Aluminum (Al) is of great concern (Al Dera, 2016). Al makes up about 8% of the earth's mineral component being the third most abundant element on the planet (WHO, 2010; Al-Olayan *et al.*, 2015). In addition, due to its wide application in several industrial processes and products ranging from antiperspirants, food additives, antacids, shampoos, packaging materials, toothpaste, vitamins, treatment of water, cosmetics, wood preservation and plastic fillers, humans and animals are inevitably exposed to Al (AbdelMoneim *et al.*, 2013; Lentini *et al.*, 2017; Bulan *et al.*, 2019).

Till date, aluminum has not been shown to play known physiological role in the body, but has been shown to trigger several adverse effects effects (Turgut *et al.*, 2004; Yousef *et al.*, 2019). Al bio-accumulates in several organs such as liver, kidney and brain, where it results in toxic effects, which have been shown to occur via increase in oxidative stress (Yousef *et al.*, 2019; Al-Kahtani *et al.*, 2020; Ekakitie *et al.*, 2021). Though Al is not a redox metal, it interacts

with membranes. It aids the formation of reactive oxygen species and disturbs the normal body function of essential trace metals (such as iron and zinc) and antioxidant enzymes (Zhu *et al.,* 2012). In addition, Al has the ability to attach itself to nucleic acid molecules and can inhibit the activity of alkaline phosphatases, phosphodiestrases and hexokinase (Akpanyung *et al.,* 2018; Wang *et al.,* 2018).

The liver is a major organ where Al toxicity is manifested because it plays central role in the metabolism of xenobiotics (Sivakumar *et al.,* 2012; Bhasin *et al.,* 2014) and as such, several studies have screened some natural products, with proven antioxidant prowess, and demonstrated their protective effects against Al-induced hepatic injury. Such natural products include saffron, melatonin, propolis, gingerol, quercetin, royal jelly and Nigella sativa (Shati and Alamri 2010; Shrivastava, 2013; Al-Qayim *et al.,* 2014; Alqayim,2015; Oda 2016; Sharma *et al.* 2016; Yakubu *et al.,* 2016; Dass and Ramoji, 2017).

The antioxidant capacity of natural bee honey (NBH) against Al-induced oxidative stress in the tissues of rats has also been demonstrated (Erejuwa, 2012; Ekakitie *et al.,* 2021), but studies reporting the effects of varied concentrations of NBH on liver function parameters of Al-exposed rats are rare. Honey is made by honeybees using nectar gotten from different flowers, digested and enriched with salivary and enzymatic secretions. Thus honey contains several compounds such as proteins, phenolic acids, volatile chemicals, lipids, carbohydrates, flavonoids (quercetin, kaempferol, luteolin), enzymes (phosphatases, catalase, glucose oxidase, invertase), amino acids, organic acids (acetic acid, gluconic acid) and vitamins (pyridoxine, niacin, ascorbic acid etc.) with powerful free radical scavenging and antioxidant effects (Blasa *et al.,* 2006; Fiorani *et al.,* 2006). This study therefore investigated the influence of natural honey bee on liver function parameters in aluminum nitrate-induced Wistar rats.

MATERIALS AND METHODS

Chemicals and Reagents

Analytical grade chemicals and assay kits used for this study were products of BDH chemical laboratory England and Randox laboratories limited, Antrim, England.

Experimental Animals and Bee Honey

Thirty (30) Wistar rats (150±6g) procured from the Animal House, Faculty of Basic Medical Sciences, Delta State University, Abraka were used for this study. Standard animal house with plastic cage and exposed to 12 hours light was used. The animals were divided into 6 groups with five rats in each group and acclimatized for one week before the commencement of the experiment. The animals were handled in accordance to standard protocols for animal care and were given free access to feed (grower's mash) and drinking water. Natural bee honey was obtained from trusted dealers in Abraka, Ethiope East Local Government Area of Delta State, Nigeria.

Experimental Design

Group one served as control and received only feed and water. Groups 2-6 served as the test groups and received single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight), intraperitoneally. In addition, rats in groups 3-6 received varying doses of NBH (10 %, 25 %, 50 % diluted with distilled water and 100 % natural BH orally at a dose of 2.5 g/kg respectively) 24 h after $Al(NO_3)_3$ intoxication for 14 consecutive days. Table 1 below shows the experimental design:

Table 1. Experimental Design

Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Control (Feed and Water only)	$Al(NO_3)_3$ control: Single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight) only	$Al(NO_3)_3$ + 10 % natural bee honey: Single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight) and 10% of NBH for 14 consecutive days	$Al(NO_3)_3$ + 25 % natural bee honey: Single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight) and 25 % of NBH for 14 consecutive days	$Al(NO_3)_3$ + 50 % natural bee honey: Single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight) and 50% of NBH for 14 consecutive days	$Al(NO_3)_3$ + 100 % natural bee honey: Single dose of $Al(NO_3)_3$ (6.5 mg/kg body weight) and 100% of NBH for 14 consecutive days

At the end of the last treatment, blood and liver samples were obtained from the rats after sacrificing them by cervical dislocation and processed for biochemical examinations.

Biochemical Assays

The biochemical assays conducted include: the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in the plasma and liver as well as the levels of total protein, albumin and globulin. The activities of ALT and AST in the plasma and tissues were assayed by the method of Reitman and Frankel (1957), with the activity of the aminotransferases expressed in units/ml.

The method of Annino and Giese (1976) was employed in the determination of the activity of alkaline phosphate (ALP) with the activity of the enzyme expressed in units/g tissue

based on the principle that a unit of the enzyme represents the quantity of the enzyme that produced a micromole of p-nitrophenol per minute. The concentration of albumin in the serum and liver was determined according to the method of Doumas *et al*. (1971), while total protein levels were determined through the method of Tietz (1999). Thereafter, the concentration of globulin in serum was calculated as the difference between total protein and albumin concentrations.

Statistical analysis

Descriptive statistics and the one-way analysis of variance (ANOVA) were performed followed by the Least Significant Difference (LSD) test to locate significant difference between the groups. Statistical analysis was done using the Statistical Package for Social Sciences SPSS-(version 22.0). Results are presented as Mean ± SD and statistical significance was set at $p< 0.05$.

RESULTS AND DISCUSSION

The curative influence of natural honey bee on the activities of ALT, AST and ALP in the liver of aluminium nitrate-induced Wistar rats is presented in Table 2. Exposure to aluminium (groups 2-6) significantly ($p< 0.05$) increased the activities of the enzymes relative to rats in the control group. However, the treatment of Al-exposed rats with varying doses of NBH significantly reduced the activities of the enzymes, compared to rats maintained on Al alone, with the exception of Al-exposed rats given 100% NBH (Group 6). The activity of AST in Al-exposed rats was restored to normal (as in the control; group 1) by the administration of 50% NBH (group 5).

Table 2: The Curative Influence of Natural Honey Bee on the Activities of ALT, AST and ALP in the Liver of Aluminum Nitrate-Induced Wistar Rats.

Expt Group	Liver ALT (U/L)	Liver AST (U/L)	Liver ALP (U/L)
Group 1	83.10 ± 2.65 [a]	55.10 ± 4.21[a]	260.14 ± 19.21[a]
Group 2	150.20 ± 3.58[b]	110.20 ± 17.49 [b]	570.14 ± 20.09[b]
Group 3	138.10 ± 5.98[c]	90.00 ± 12.71[c]	415.25 ± 48.81[c]
Group 4	112.26 ± 4.60[d]	72.10 ± 9.28[d]	345.27 ± 17.00[d]
Group 5	100.15 ± 3.33[e]	59.35 ± 8.30[a]	325.32 ± 4.81[e]
Group 6	152.20 ± 26.79[b]	112.15 ± 3.70[b]	573.54 ± 6.22[b]

Values are represented in mean ± SD. n=5. Mean values with different superscript alphabet in the same column differ significantly at p<0.05. Key: Group 1; Control; Group 2: Aluminum nitrate control; Group 3: Aluminum nitrate + 10% honey; Group 4: Aluminum nitrate + 25% honey; Group 5: Aluminum nitrate + 50 % honey; Group 6: Aluminum nitrate + 100% honey.

The curative influence of natural honey bee on the activities of ALT, AST and ALP in the serum of aluminum nitrate-induced Wistar rats is shown in Table 3. As observed in the liver, the activities of ALT, AST and ALP in the serum was significantly elevated ($p< 0.05$) in rats exposed to Al (groups 2-6) compared with the control (group 1). Significant reduction ($p< 0.05$) in the activities of the enzymes was observed when rats maintained on Al alone (group 2) were given varying concentrations of NBH. Again, the 50 % treatment showed the greatest positive effect; it restored the activity of ALP to levels comparable with that of control rats.

Table 3. The Curative Influence of Natural Honey Bee on the Activities of ALT, AST and ALP in the Serum of Aluminum Nitrate-Induced Wistar Rats.

Expt Group	Serum ALT (U/L)	Serum AST (U/L)	Serum ALP (U/L)
Group 1	50.20 ± 11.50[a]	33.00 ±14.33 [a]	297.22 ± 18.18 [a]
Group 2	111.30 ± 26.51[b]	100.20 ±7.82[b]	348.22 ± 81.30[b]
Group 3	90.10 ± 11.32[c]	78.30 ± 22.82[c]	324.52 ± 10.34[c]
Group 4	65.40 ± 10.50[d]	68.10 ± 6.62[c]	316.39 ± 70.00[d]
Group 5	80.32 ± 22.01[e]	42.40 ± 7.04[d]	291.20 ± 10.83[a]
Group 6	108.20 ± 10.11[b]	96.40 ± 3.32[b]	347.15 ± 15.50[b]

Values are represented in mean ± SD. n=5. Mean values with different superscript alphabet in the same column differ significantly at p<0.05. Key: Group 1; Control; Group 2: Aluminum nitrate control; Group 3: Aluminum nitrate + 10 % honey; Group 4: Aluminum nitrate + 25 % honey; Group 5: Aluminum nitrate + 50 % honey; Group 6: Aluminum nitrate + 100 % honey.

Table 4 shows the influence of natural honey bee on the concentrations of total protein and albumin in the liver of aluminum nitrate-induced Wistar rats. Total protein concentrations were significantly higher in control rats than in rats exposed to Al. This was also observed for albumin concentration. The albumin concentration in Al-exposed rats was not significantly increased with administration of 10 %, 25 % and 100% NBH, however, the administration of 50% NBH to Al-exposed rats significantly ($p< 0.05$) increased albumin concentration relative to rats exposed to Al alone (group 2) and to a level comparable to that in the control group. This also shows that the 50 % NBH treated had the greatest curative effect against Al-induced toxicity. Levels of total protein were significantly increased in Al-exposed rats by the administration of 25 % and 50 % NBH, but no changes were observed in Al-exposed rats given 10 % and 100 % NBH compared to rats exposed to Al alone (group 2)

Table 4. The Curative Influence of Natural Honey Bee on the Concentrations of Total Protein and Albumin in the Liver of Aluminum Nitrate-Induced Wistar Rats.

Experimental Group	Liver Albumin (g/dl)	Liver total protein (g/dl)
Group 1	50.40 ± 04.83 [a]	58.36 ± 02.09 [a]
Group 2	36.20 ± 12.15[b]	30.26 ± 02.52[b]
Group 3	32.60 ± 09.40[b]	35.40 ± 05.23[b]
Group 4	38.45 ± 09.20[b]	37.36 ± 3.39[c]
Group 5	42.25 ± 10.87[a]	43.30 ± 12.47[d]
Group 6	34.15 ± 06.70[b]	31.28 ± 09.82[b]

Values are represented in mean ± SD. n=5. Mean values with different superscript alphabet in the same column differ significantly at p<0.05. Key: Group 1; Control; Group 2: Aluminum nitrate control; Group 3: Aluminum nitrate + 10 % honey; Group 4: Aluminum nitrate + 25 % honey; Group 5: Aluminum nitrate + 50 % honey; Group 6: Aluminum nitrate + 100 % honey

The influence of natural honey bee on the concentration of total protein, albumin and globulin in the serum of aluminum nitrate-induced Wistar rats is presented in Table 5. Exposure to Al significantly ($p< 0.05$) decreased the concentration of total protein, albumin and globulin compared to the control. Treatment of Al-exposed rats with 25% and 50% NBH significantly increased total protein, albumin and globulin concentrations relative to untreated rats (group 2), but no significant changes in the levels of total protein, albumin and globulin when Al-exposed rats were treated with 10% and 100% NBH. Again, the 50% NBH treatment was observed to be more effective incurring Al-induced toxic effects.

Table 5. The Curative Influence of Natural Honey Bee on the Concentration of Total Protein, Albumin and Globulin in the Serum of Aluminum Nitrate-Induced Wistar Rats.

Expt. groups	Serum Albumin (g/dl)	Serum total protein (g/dl)	Serum globulin (g/dl)
Group 1	38.26 ±13.54 [a]	52.38 ± 05.06 [a]	14.12 ± 03.09 [a]
Group 2	20.28 ± 8.40 [b]	27.36 ± 03.00 [b]	07.22 ± 09.52 [b]
Group 3	22.36 ± 3.00 [b]	30.46 ± 01.00 [b]	08.10 ± 05.23 [b]
Group 4	28.96 ± 9.00 [c]	39.32 ± 03.02 [c]	10.36 ± 05.39[a]
Group 5	37.28 ± 4.35 [a]	49.22 ± 02.78[a]	11.94 ± 12.47[a]
Group 6	24.00 ± 7.01[b]	29.42 ± 01.22 [b]	05.45 ± 09.82 [b]

Values are represented in mean ± SD. n=5. Mean values with different superscript alphabet in the same column differ significantly at p<0.05. Key: Group 1; Control; Group 2: Aluminum nitrate control; Group 3: Aluminum nitrate + 10 % honey; Group 4: Aluminum nitrate + 25 % honey; Group 5: Aluminum nitrate + 50 % honey; Group 6: Aluminum nitrate + 100 % honey

Discussion

In this study, the curative influence of natural honey bee on liver function parameters in aluminum nitrate-induced Wistar rats was assessed. Exposure to aluminum lead to a significant ($p< 0.05$) increase in the activities of the ALT, AST and ALT. This result is in consonance with the reported toxic effect of Al on these enzymes (Othman *et al.*, 2020; Bakour *et al.*, 2017; Shati and Alamri 2010; Al-Kahtani and Morsy, 2019). It is well known that these liver enzymes are biomarkers of liver injury (Yousef *et al.*, 2019; Abdel Moneim *et al.*, 2013). Thus exposure to Al may have caused injury to the liver with the resultant leakage of these enzymes into the blood (Cheraghi and Roshanaei, 2019; Abdel-Wahab, 2012). The increase in their activity in the liver may be as a result of increased synthesis to compensate for the lost activity (Okail *et al.*, 2020).

The results of this study also showed that the treatment of Al-exposed rats with varying doses of NBH significantly reduced the activities of the enzymes, compared to rats maintained on Al alone, with the 50 % NBH treatment producing the greatest curative effect. This can be attributed to the reported antioxidant properties of NBH (Ekakitie *et al.*, 2021; Bakour *et al.*, 2017; Erejuwa, 2012; Fiorani *et al.*, 2006). In a similar study by Al-Waili *et al.*, (2006) honey had a preventive effect on the elevation in AST and ALT activities due to the toxic effects of CCl_4. The several antioxidant compounds present in NBH may have helped in mopping up free radicals released due to Al administration thereby aiding in the stabilization of cellular redox state. In addition, the works of Achuba and Nwokogba (2015) and El Rabey *et al.* (2013) showed the protective ability of natural honey against toxicity induced by hydrocarbon and melamine respectively.

As shown in Tables 4 and 5, exposure to Al significantly reduced the concentration of total protein and albumin in the liver and serum. Similar result was seen in globulin levels in the serum indicating that Al had negative effects on protein metabolism. Similar results were reported by Yousef (2004) and Okail *et al.*, (2020). In their study, Al induced significant increase in levels of albumin relative to control. This was attributed to Al-induced alterations in the liver (confirmed by increase in the activities of ALT, AST and ALT) which may have affected the synthesis/metabolism of proteins. However, the administration of 50% NBH to Al-exposed rats significantly ($p< 0.05$) increased albumin concentration relative to rats exposed to Al alone (group 2) and to a level comparable to that in the control group. This appreciable raise in levels total protein and albumin in both the liver and serum following treatment with NBH is probably due to the health-promoting components of NBH and it agrees with other studies (El-Khayat and Ahmed, 2000; El Rabey *et al.*, 2013).

CONCLUSION

This study showed that NBH has positive influence on toxicity due to aluminum in rats. The administration of NBH to Al-exposed rats ameliorated the increase in liver marker enzymes and normalized protein levels. These effects are largely connected to the many health-promoting components of NBH. The 50 % NBH treatment had the greatest curative effect against Al-induced toxicity.

AUTHORS' CONTRIBUTIONS

Authors LIE and JO designed the experiment. LIE carried out the laboratory work. Author OCO wrote and edited the manuscript. All the authors read and approved the final version for publication.

FUNDING STATEMENT

None

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

ACKNOWLEDGEMENT

The authors are grateful to the staff at Primary Health Centers in Calabar, Cross River State, Nigeria for their technical assistance throughout the study duration.

REFERENCES

Abdel-Moneim, A. E., Othman, M. S. Mohmoud, S. M. and El-Deib, K. M. (2013). Pomegranate peel attenuates aluminum-induced hepatorenal toxicity. *Toxicology Mechanisms and Methods*, 23(8): 624–633.

Abdel-Wahab, W. M. (2012). $AlCl_3$-induced toxicity and oxidative stress in liver of male rats: protection by melatonin. *Life Sciences*, 9(4): 1173–1182.

Achuba, F. I. and Nwokogba, C.C. (2015). Effects of honey supplementation on hydrocarbon-induced kidney and liver damage in Wistar albino rats. *Biokemistri*, 27(1): 50–55.

Akpanyung, E. O., Nwaokonko, D. U., Ekong, M. B. and Ekpo, M. M. (2018). Evaluation of the protective effect of *Moringa oleifera* leaf extract against aluminium induced liver damage in male albino Wistar rats. *International Journal of Sciences*, 7(2): 21-31.

Al Dera, H. S. (2016). Protective effect of resveratrol against aluminum chloride induced nephrotoxicity in rats. *Saudi Medical Journal*, 37(4): 369–378.

Al-Kahtani M. and Morsy, K. (2019). Ameliorative effect of selenium nanoparticles against aluminum chloride-induced hepatorenaltoxicity in rats. *Environmental Science and Pollution Research*, 26(31): 32189–32197.

Al-Kahtani, M., Abdel-Daim, M. M., Sayed, A. A. El-Kott,A. and Morsy, K. (2020). Curcuminphytosome modulates aluminum-induced hepatotoxicity via regulation of antioxidant, Bcl-2, and caspase-3 in rats. *Environmental Science and Pollution Research International*, 27(17):21977–21985.

Al-Olayan, E. M., El-Khadragy, M. F., and Abdel Moneim, A. E. (2015). The protective properties of melatonin against aluminium-induced neuronal injury. *International Journal of Experimental Pathology;* 96(3):196–202.

Al-Qayim M., Ghali, L. and Al-Azwai, T. (2014). Comparative effects of propolis and malic acid on hematological parameters of aluminum exposed male rats. *Global Journal of Bioscience and Biotechnology*, 3(1):6–11

Alqayim, M.A.J. (2015). Propolis cardioprotective role from the impact of aluminium chloride in female rabbits. *Basic Journal of Veterinary Research*,14(2):136-149.

Al-Waili, N. S., Saloom, K. Y., Akmal, M., Al-Waili, F., Al-Waili, T. N., Al-Waili, A. N. and Ali, A. (2006). Honey ameliorates infliuence of hemorrhage and food restriction on renal and hepatic functions, and hematological and biochemical variables. *International Journal of Food Science and Nutrition*, 57(5–6):353–362.

Annino, J. S. and Giese, R. W. (1976) Clinical chemistry, principles and procedures, 4th edition, Little Brown and Company, Boston. pp. 76-82.

Bakour, M., Al-Waili, N. S., El Menyiy, N., Imtara, H., Figuira, A. C., Al-Waili, T. andLyoussi, B. (2017). Antioxidant activity and protective effect of bee bread (honeyand pollen) in aluminum-induced anemia, elevationof inflammatory makers and hepato-renal toxicity. *Journal of Food Science and Technology*, 54(13): 4205–4212.

Bhasin, P., Singla, N. and Dhawan, D. K. (2014). Protective role of zinc during aluminum-induced hepatotoxicity. *Environmental Toxicology*, 29(3): 320-327.

Blasa, M. Candiracci, M. Accorsi, A. Piacentini, M. P. Albertini, M. C.and Piatti, E. (2006). Raw Millefiori honey is packed full ofantioxidants.*Food Chemistry*, 97(2): 217–222.

Bulan, Ö. K. Bayrak, B. B. Sarikaya-Ünal, G. and R. Yanardağ (2019). The influence of melatonin supplementation againstaluminum-induced toxicity in brains of male rats. *Journal of Research in Pharmacy*, 23(2): 275–283.

Cheraghi, E. and Roshanaei, K. (2019). The protective effect of curcumin against aluminum chloride-induced oxidative stress and hepatotoxicity in rats. *Pharmaceutical and Biomedical Research*, 5(1): 6–13.

Dass, A. P. and Ramoji, P.C. (2017). The effect of aqueous ginger extract on aluminium chloride ($AlCl_3$) induced alteration in lipid profile of male Wister rats. *International Journal of Basic and Clinical Pharmacology*, 6: 1-4.

Doumas, B. T., Watson, W. A. and Biggs, H. G. (1971). Albumin standards and the measurement of serum albumin with bromcresol green. *Clinica Chimica Acta*, 31(1): 87-96.

Ekakitie, L. I., Okpoghono, J., Orororo, O. C. and Ekakitie, O. A. (2021). Ameliorative prowess of bee honey in the

tissues of rats administered aluminium nitrate. *Scientific African*, 12, e00782.

El Rabey, H. A.,Al-Seeni, M. N. and Al-Solamy, S.M. (2013). Bees' Honey Protects the Liver of Male Rats againstMelamine Toxicity. *BioMed Research International Volume* 2013, Article ID 786051, 8 pages.

El-Khayat Z. and Ahmed, H. H. (2000). Antitumer efficacy of edible *Portulacaoleracea* and bees honey in mice inoculated with Ehrlich ascttestumer cells. *Journal of Union of Arab Biologists*, 13: 583–605.

Erejuwa, O. O., Sulaiman, S. A. and AbWahab, M. S. (2012). Honey: a novel antioxidant. *Molecules*, 17(4):4400–4423.

Fiorani, M. Accorsi, A. Blasa, M. Diamantini, G. and Piatti, E. (2006). Flavonoids fromItalianmultifloral honeys reduce the extracellular ferricyanide in human red blood cells. *Journal of Agricultural and Food Chemistry*, 54(21): 8328–8334.

Lentini, P. Zanoli, L. Granata, A. Signorelli, S. S. Castellino, P. and Dellaquila, R. (2017). Kidney and heavy metals - the role of environmental exposure (review). *Molecular Medicine Reports*, 15(5): 3413–3419.

Oda, S. S. (2016). The influence of Omega3 fatty acids supplementation against aluminum-induced toxicity in male albino rats. *Environmental Science and Pollution Research Internationa*l, 223(14): 14354–14361

Okail, H. A., Ibrahim, A. S. and Badr, A. H. (2020). The protective effect of propolis against aluminum chloride-induced hepatorenal toxicity in albino rats. *The Journal of Basic and Applied Zoology*, 81(1): 1-11.

Othman, M. S., Fareid, M. A., Abdel Hameed, R. S. and Abdel Moneim, A. E. (2020). The protective effects of melatonin on aluminum-induced hepatotoxicity and nephrotoxicity in rats. *Oxidative Medicine and Cellular Longevity*, 2020, Article ID 7375136, 12 pages.

Reitman, S. and Frankel, S. A. (1957). Colomentric method for determination of serum glutamic oxalacetic acid and glutamic pyruvic transaminases. *American Journal of Clinical Pathology*, 28: 56–63.

Sharma, D. R., Wani, W. Y., Sunkaria, A., Kandimalla, R. J., Sharma, R. K., Verma, D., Bal, A. and Gill, K. D. (2016) Quercetin attenuates neuronal death against aluminum-induced neuro degeneration in the rat hippocampus. *Neuroscience*, 324: 163–176.

Shati, A. A. and Alamri, S. A. (2010). Role of saffron (Crocus sativus L.) and honey syrup on aluminum-induced hepatotoxicity. *Saudi Medical Journal*, 31(10): 1106–1113.

Shrivastava, S. (2013). Amelioration of aluminium induced toxicity by *Allium sativum*. *Scientific Research and Assays*, 8(4): 168-177.

Sivakumar, S., Khatiwada, C. P. andSivasubramanian, J. (2012). Bioaccumulations of aluminum and the effects ofchelating agents on different organs of *Cirrhinusmrigala*. *Environmental Toxicology and Pharmacology*, 34(3): 791-800.

Tietz, N. W. (1999). Fundamental of clinical chemistry. 3rd ed. Carl AB, Edward RA (ed.). W. B. Saunders, Co,

Turgut, G., Kaptanoglu, B., Enli, Y. and Genc, O. (2004). Effect of chronic aluminum administration on blood and liver iron related parameters in mice. *Yonsei Medical Journal*, 45(1): 135-9

Wang, X. Gong, J. Gui, Z. Hu, T. and Xu, X. (2018). Halloysitenanotubes-induced Al accumulation and oxidative damagein liver of mice after 30-day repeated oral administration. *Environmental Toxicology*, 33(6): 623–630.

WHO (2010). Aluminium in drinking water. Geneva Switzerland, p. 1.

Yakubu, O.E., Nwodo, O.F. C., Imo, C., Abdulrahaman, M. and Uyeh, L. B. (2016). Effects of *Vitexdoniana* leaf extract on aluminium induced toxicity in male albino Wistar rats. *Journal of Applied Biology and Biotechnology*, 4(5): 37-40

Yousef, M. I. (2004). Aluminium-induced changes in hemato-biochemicalparameters, lipid peroxidation and enzyme activities of male rabbits: Protective role of ascorbic acid. *Toxicology*, 199(1): 47–57.

Yousef, M. I. Mutar, T. F. and. Kamel, M. A. E. L. N (2019). Hepatorenal toxicity of oral sub-chronic exposure to aluminum oxide and/or zinc oxide nanoparticles in rats. *Toxicology Reports*, 6: 336–346.

Zhu, W., Jia, Q., Wang, Y., Zhang, Y., and Xia, M. (2012). The anthocyanincyanidin-3-O-b-glucoside, a flavonoid, increases hepatic glutathione synthesis and protects hepatocytes against reactive oxygen species during hyperglycemia: Involvement of a cAMP-PKA-dependent signaling pathway. *Free Radical Biology and Medicine*, 52: 314–327.