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Original Research Article

Comparative Analysis of Phytochemicals and Nutritionally Essential Metals in Coconut Oil and Coconut Water Fractions

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ABSTRACT

The nutritional benefits of coconut oil have not been well reported. This study compared the status of nutritionally essential elements, phytochemicals, and antioxidant activities in coconut oil (CNO) and coconut water (CNW) fractions. Elemental constituents of the CNO and CNW were determined using atomic absorption spectrophotometry, while the levels of DPPH and the total antioxidant capacity were determined spectrophotometrically. There was no significant ($p>0.05$) difference in the DPPH scavenging ability of CNO (50.44 ± 0.44 %) and CNW (49.41 ± 0.07 %). The total antioxidant capacity of CNO (35.57 ± 1.54 mg/dl) was significantly ($p<0.05$) higher than in CNW (24.78 ± 0.40 mg/dl). Levels of Ca, Na, Fe, Mg, Zn, Cr and Mn (83.86 ± 1.93 mg/L, 10.89± 0.25 mg/L, 8.71± 0.17 mg/L, 7.56 ± 0.19 mg/L, 0.73 ± 0.03 mg/L, 0.08 ± 0.01 mg/L and 0.77 ± 0.03 mg/L respectively) in CNW were significantly ($p<0.05$) higher than in CNO (23.61± 0.78 mg/L, 6.22± 0.14 mg/L, 3.95± 0.11mg/L, 2.83 ± 0.06 mg/L, 0.17 ± 0.04 mg/L, 0.04 ± 0.02 mg/L and 0.5 ± 0.01 mg/L respectively). It could be concluded that CNW contains essential elements and could be used to optimize metabolism in deficient individuals.

***Keywords*:** Coconut; phytochemicals, antioxidants, minerals, beverage

Introduction

Coconut is the fruit of *C. nucifera* (coconut palm), it belongs to the monocotyledon family *Arecaceae* (*Palmaceae*) and sub-family *Cocoideae*.[1] It is believed to originate from Indo-Malaya and is now widely distributed in the tropical coastal regions.[2] The major varieties of coconut are the tall, dwarf, and hybrid species. It grows to about 30m long with pinnate leaves and pinnae of about 400-600 cm and 60-90 cm, respectively.[3] It is consumed worldwide for its water, milk, or meat.[4] Its by-products such as husk, shell, wood, leaves, spikelet, and many others have all contributed meaningfully to human life.[5] Coconut forms parts of our daily diet as the oil is commonly used for cooking, skin, and hair treatment. Coconut water is consumed as a beverage due to its refreshing taste and acclaimed medicinal benefits. Coconut's kernel (white meat) is often consumed raw or processed as snacks. Coconut's palm contributes significantly to the earnings and livelihood of many of farmers and industries.[6]
Coconut oil has been reported to be rich in medium-chain fatty acids that can help with weight reduction, lower cholesterol, and lower cardiovascular disease.[7] This type of fatty acid is known to create satiety and prevent excessive eating.[8] More so, they are easily digested and are not deposited into the adipose tissue, since they are transported directly through the bloodstream to the liver where they are stored.[9]

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Coconut water has been reported for its numerous pharmacological benefits, such as treating diarrhoea due to its saline nature and the presence of electrolytes in it.[10] It has also been reported for the treatment of high blood pressure.[11]
Although coconut water is highly nutritious and available in the sterile form from the endocarp; it is often discarded when the meat is processed into snacks in the industry.[12] Current research on coconut water is rare and there are no published studies that compared the essential mineral elements present in coconut water and oil. Hence, this study was aimed to determine essential and potentially toxic metals in the products to assess their nutritional integrity. Provision of this vital information will create more awareness of the health benefits of consuming coconut by-products and consequently to increase its value chain.

Materials and Methods

Biological Materials
Coconut water was obtained after breaking the endocarp, while the oil was extracted from the dehydrated coconut meat. The oil was obtained from Sabo Market, Ikorodu, Lagos, Nigeria. The samples were collected in July 2022.

Phytochemical screening
Levels of tannin, saponin, steroids, terpenoids, flavonoids, alkaloids and glycosides were determined by the methods of Ogunjobi *et al*.[13] and Sofowara.[14]

Antioxidant screening
DPPH radical scavenging assay
1mL of extract was added to 1mL of 0.135mM DPPH, and the resultant solution was vortexed properly and incubated at room temperature for 30 minutes. The absorbance was measured at 517nm using ascorbic acid as a reference.[15]

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DPPH radical scavenging activity (%) = [(Abs control – Abs sample)/ (Abs control)] x 100

Determination of Total Antioxidant Activity (TAC)

The principle was based on the production of a green phosphomolybdate (V) complex in an acidic medium. 3 mL of the reagent (0.6 M sulphuric acid, 28 mM sodium phosphate, and 4 mM ammonium molybdate) was added to 0.1 mL of the fraction solution. The tubes were sealed and heated to 95 degrees Celsius for 90 minutes. The tubes were tightly closed and heated to 95°C for 90 minutes. The absorbance of the sample was measured at 695 nm against a blank. At 695 nm, the sample's absorbance was measured in comparison to a blank. The antioxidant capacity was expressed using the ascorbic acid equivalent.[16]

Determination of the concentration of metals

The sample was digested with sulphuric and nitric acid as described by Nanda *et al.*[17] with slight modification. Briefly, 5 mL of the sample was heated in sulphuric and nitric acid in a Kjedahl flask to oxidize the carbonaceous materials. A small amount of nitric acid was added intermittently until all the carbonaceous matter had been completely oxidized. This was determined when the dark solution turns colourless during heating. After that, the solution was cooled and was made up to 100 mL with distilled water. Re-distilled water was used as blank, and AAS (ShimadzuAA 7000, Shimadzu Corporation, Tokyo, Japan) was used to determine the concentration of metal ions.[18] The solution of the sample was aspirated into a burning acetylene flame and consequently, vaporized. The concentration of the metal present was estimated based on the amount of light absorbed at the same wavelength compared to the amount of light emitted by the element in its excited states. Specific standard solutions were assayed, and the values were used to plot graphs.

Statistical analysis

Version 21 of SPSS was used for the statistical analysis. The statistical comparison of the data from CNO and CNW was carried out using Student's t-test. All data were expressed as mean ± standard error of the mean. Values of $p<0.05$ were considered significantly different.

Results and Discussion

The status of the phytochemical constituents of CNO and CNW are shown in Table 1 below. It was observed that CNO contained flavonoids, steroids, alkaloids, and terpenoids; while CNW contained saponins, alkaloids, and terpenoids. This agree with several studies that reported tannins, saponins, alkaloids, and terpenoids in coconut.[19-21] This study revealed the pharmacological benefits and phytochemical constituents of coconut that have always been the concern of many scientists. Phytochemicals such as polyphenols in the CNO and CNW can reduce the risk of cancer and inflammation in humans and animals.[22]

The percentage DPPH (free radical scavenging ability) of CNO (50.44 ± 0.44 %) was significantly different ($p>0.05$) compared with CNW (49.41 ± 0.07 %). Meanwhile, the radical scavenging activities of CNO and CNW were significantly ($p < 0.05$) lower compared with L-ascorbic acid (Figure 1). Figure 2 shows that the total antioxidant capacity of CNO (35.57 ± 1.54 mg/dl) was significantly higher ($p<0.05$) compared with CNW (24.78 ± 0.40 mg/dl).

Table 1: Phytochemical constituents of coconut oil and coconut water

Phytochemicals	CNO	CNW
Tannins	-	-
Glycosides	-	-
Saponins	-	+
Flavonoids	+	-
Steroids	+	-
Alkaloids	+	+
Terpenoids	+	+

Coconut oil = CNO ; coconut water = CNW

DPPH radical scavenging activity of CNO and CNW were similar. However, significantly a total antioxidant capacity was observed in CNO compared to CNW. This corroborates the report of Karunasiri et al.[23] that CNO contains a high amount of phenolic antioxidants. Higher levels of terpenoids and alkaloids observed in the CNO used for this study might also contribute to a significantly higher total antioxidant capacity. Therefore, this study could hypothesize that CNO, being used as body cream in some parts of Africa may serve as a source of antioxidants to prevent oxidative damage to the skin.

Figures 3-6 show the levels of Ca, Na, Fe, Mg, Zn, Cr, and Mn (83.86 ± 1.93 mg/L, 10.89± 0.25 mg/L, 8.71± 0.17 mg/L, 7.56 ± 0.19 mg/L, 0.73 ± 0.03 mg/L, 0.08 ± 0.01 mg/L and 0.77 ± 0.03 mg/L respectively) in CNW were significantly ($p<0.05$) higher compared with CNO (23.61± 0.78 mg/L, 6.22± 0.14 mg/L, 3.95± 0.11 mg/L, 2.83 ± 0.06 mg/L, 0.17 ± 0.04 mg/L, 0.04 ± 0.02 mg/L and 0.5 ± 0.01 mg/L respectively). Levels of K and Cu were not significantly ($p>0.05$) different in CNW (6.88 ± 0.17 mg/L and 0.01 ± 0.00 mg/L) compared with CNO (7.10 ± 0.15 mg/L and 0.01 ± 0.00 mg/L). Metals are major constituents of important biomolecules. The essential metals have proven to be important in immune stimulation, growth, catalysis, blood clotting, osmoregulation, and regulation of other vital physiological processes.[24] Virtually all essential trace metals were found in significantly higher quantities in CNW. This could be because metal ions have greater affinities for water and can enhance the reactivity of chemical groups near or at the active sites of enzymes. Their charges can interact with water to make it acidic by acting like a proton. In hydrolases, proton can polarise water to generate hydroxyl ions which can serve as a nucleophile to attack the substrate.[25] This corroborates the findings from previous studies which show that several oxidative stress-related enzymes require metals as cofactors.[26] Nnorom *et al.*[27] reported that 13.56 mg/L, 5.97 mg/L, 0.99 mg/L, and 0.19 mg/L as the daily recommended intakes for iron, zinc, chromium, and copper, respectively.

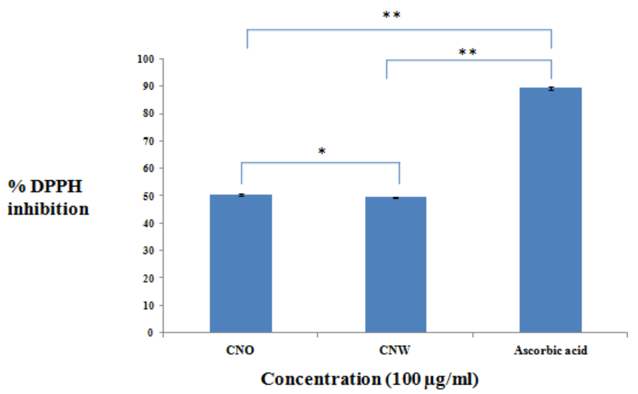

Figure 1: Percentage of DPPH radical scavenging activity of coconut oil and coconut water.
* Significantly different; Coconut oil = CNO ; coconut water = CNW

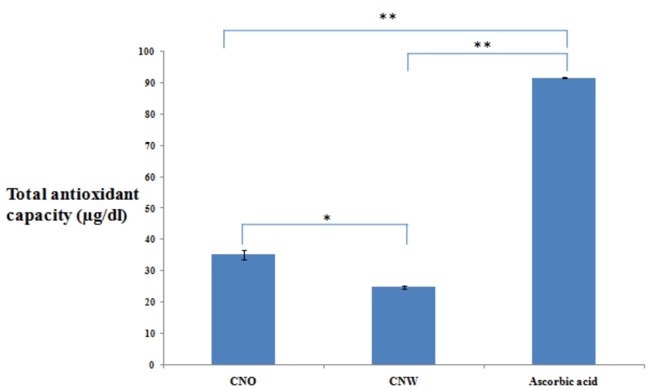

Figure 2: Total antioxidant capacity of coconut oil and coconut water.
* Significantly different

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The concentration of iron (8.7 $\pm$ 0.17 mg/L) found in CNW could be considered a good source of iron to meet the 8.0 mg recommended as a dietary daily allowance for men. Higher values of most of the metals were observed in CNW compared with CNO. Since virtually all physiological processes require either metalloenzymes or metal-activated enzymes, consuming CNW would be nutritionally beneficial to man and animals. The iron content of the CNW could also be useful in the peroxidase catalytic cycle and catalase antioxidant activity.[28] Ewansiha *et al.*[29] have also reported the presence of calcium, magnesium, sodium, potassium, iron, manganese, and zinc in a coconut shell. Calcium and magnesium found in higher concentrations in our CNW has been reported as mineral needed for the structure| of organisms and for bone formation, muscle contraction, blood clotting and regulation of hormone actions. Iron is an integral component of haemoglobin, myoglobin, transferrin, and hemoproteins. In carbohydrate metabolism, energy production depends on magnesium to catalyze the conversion of ATP to ADP.[30] 80% of diabetes patients are magnesium deficient. Taking magnesium supplements can improve insulin and glucose levels in diabetic patients.[31] Thus, magnesium consumption helps lessen the severity of the disease that may occur because of its deficiency, such as fatigue, nervousness, heart problems, weakness, and cramps.[32] Significantly higher levels of sodium could indicate that CNW may be useful in treating sodium deficiency conditions.

Zinc plays important roles in cell proliferation, gene expression, and metabolism of macromolecules, growth, and development.[26] The immune system, wound healing, and vision are just a few of the essential biological functions that zinc is required for, along with the metabolism of proteins and carbohydrates. Zinc is a cofactor of over 100 enzymes and is required for synthesising of haem molecules.[33] Zinc is mostly used in energy metabolism to activate the enzymes in the chemical reactions involved in the metabolic process. For instance, it improves insulin release, allowing the cells to metabolize glucose and produce ATP. Additionally, zinc is crucial to the treatment of diarrhoea. A severe zinc deficiency may be a factor in stunted growth.[34] This study could recommend CNW as a good source of zinc. Significantly higher levels of zinc were observed in CNW could be evidence of its benefits in disease prevention and management.

Manganese promotes both the thyroid hormone and blood sugar metabolism. Manganese is used by the body to activate most enzymes necessary for energy metabolism. For instance, the body uses the manganese-containing enzyme pyruvate carboxylase to convert proteins and lipids into glucose. Manganese is known for the role it plays in the activation of phosphoenolpyruvate in glucose metabolism.[35] Significantly higher levels of manganese in CNW could contribute to its importance in herbal medicine.

Chromium plays a critical role in the metabolism of biomolecules. Chromium potentiates the activity of kinase in insulin receptor and consequently enhances insulin signalling. pI3-kinase enhances the translocation of Glut4 to the cell surface. Studies show that people with type-2 diabetes have lower levels of chromium when compared to non-diabetics.[36] 0.5 mg of chromium found in CNW is sufficient for the daily recommended intake. Therefore, coconut water could be recommended as a source of chromium in the management of diabetes mellitus.

Copper is an essential component of various enzymes that play key roles in the development of bone, skeletal mineralization, and maintenance of integrity of the connective tissues. It is a component of several metalloenzymes i.e. superoxide dismutase[37]. Its variable oxidative state makes it useful in redox reactions.[38] Similar levels of copper were observed in CNW and CNO used for this study. 0.1 mg of copper in CNW is within the recommended daily allowance for children, men, and pregnant women.[39] The CNW and CNO showed adequate levels of copper. Therefore, CNW and CNO are good sources of copper that can enhance normal physiological processes.

Conclusion

This study concluded that coconut water contains higher levels of nutritionally essential elements (calcium, sodium, zinc, iron, manganese, and magnesium) needed to promote health and prevent diseases. Because of high levels of antioxidants in coconut oil, it could be used in formulations of body creams to prevent oxidative damage to the skin. The abundance of essential electrolytes in CNW might be beneficial to athletes when used as a natural sports drink.

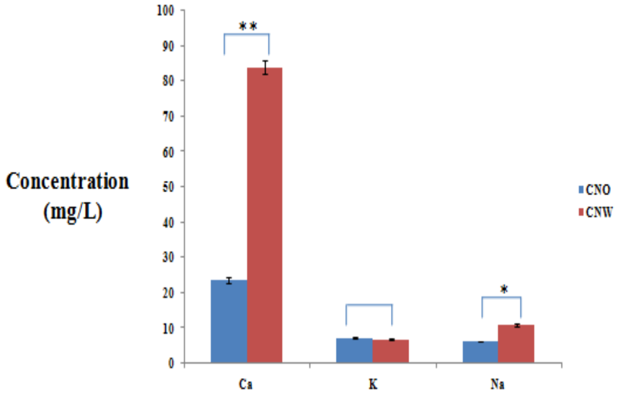

Figure 3: Concentrations of Ca, K, and Na ions in coconut oil and coconut water
* Significantly different

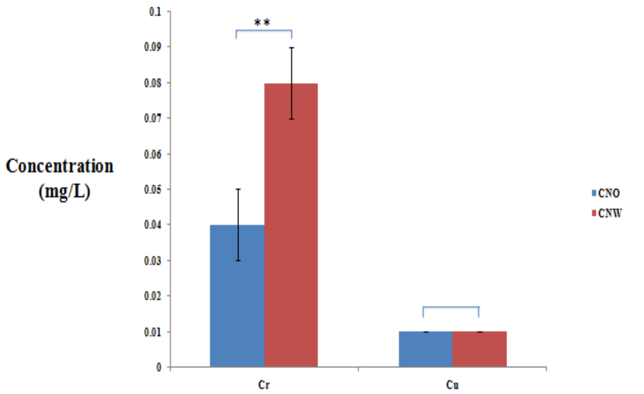

Figure 4: Concentrations of chromium and copper in coconut oil and coconut water
* Significantly different

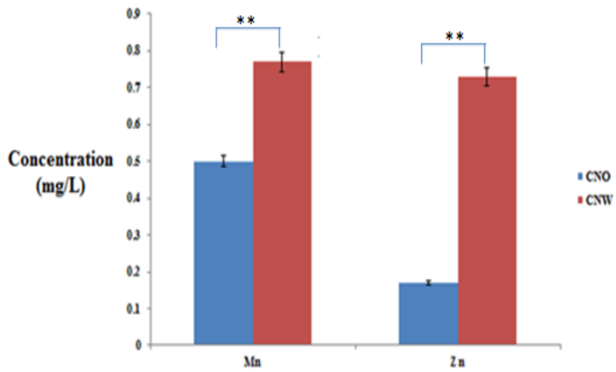

Figure 5: Concentrations of manganese and zinc ions in coconut oil and coconut water
* Significantly different

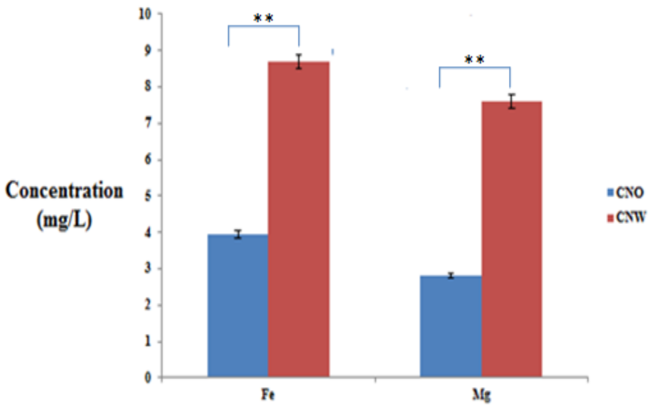

Figure 6: Concentrations of iron and magnesium ions in coconut oil and coconut water.
* Significantly different

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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References

1. Ezedom T. Coconut (*C. nucifera*) and Moringa (*M. oleifera*) Oils Protect Against Cadmium-induced Toxicity in Albino Rats. Trop J Nat Prod Res. 2018; 2(4):158-161.
2. Siramon P, Wongsheree T. Chemical Composition, Tyrosinase Inhibitory Activity and Antibacterial Activity of Coconut Coir Dust Extract. Trop J Nat Prod Res. 2022;6(7):1135 –1139.
3. Prades A, Dornier M, Diop N, Pain JP. Coconut water uses, composition and properties: A review. Fruits. 2012;67(2):87–107.
4. Patil U, Benjakul S. Coconut Milk and Coconut Oil: Their Manufacture Associated with Protein Functionality. J Food Sci. 2018;83(8):2019–27.
5. Udayana SK, Naorem A, Singh NA. The Multipurpose Utilization of Coconut By-Products in Agriculture: Prospects and Concerns. Int J Curr Microbiol App Sci. 2017;6(6):1408–15.
6. Moreno ML, Kuwornu JKM, Szabo S. Overview and Constraints of the Coconut Supply Chain in the Philippines. Int J Fruit Sci. 2020;20(S2):S524–41.
7. Uba BO, Chukwura EI, Iheukwumere IH, Okeke JJ, Akaun IP. Evaluation of Marine Wastewater and Aromatic Hydrocarbons Toxicity using a Battery of Assays. Research & Reviews: J. Toxicol. 2020;10(2):1-3.
8. Jadhav HB, Annapure US. Triglycerides of medium-chain fatty acids: a concise review. J Food Sci Technol. 2023;60(8):2143–52.
9. da Silva Lima R, Block JM. Coconut oil: What do we really know about it so far? Food Quality and Safety. 2019;3(2):61–72.
10. Elekwa I, Ude VC, Emmanuel O, Amachaghi VO, Ugbogu EA. *In vivo* studies on the ameliorative effect of coconut water against carbon tetrachloride induced toxicity in rats. Biomarkers. 2021;26(6):570–7.
11. Airaodion AI, Ogbuagu EO. Ameliorative Effect of *P. biglobosa* (African Locust Bean) against Egg-Yolk Induced Hypertension. Int J of Bio-Sci & Bio-Tech. 2020;12(5):17–25.
12. Halim HH, Dee EW, Dek MSP, Hamid AA, Ngalim A, Saari N, Jaafar, AH. Ergogenic attributes of young and mature coconut (*C. nucifera* l.) water based on physical properties, sugars and electrolytes contents. Int J Food Prop. 2018;21(1):2378–89.
13. Ogunjobi KM, Abdulwahab SO, Gakenou OF, Thompson OE, Olorunfemi O. Qualitative and quantitative evaluation of the phytochemical constituents of three wood species in Ogun state, Nigeria. J Soc Trop Plant Res. 2020;7(3):627-33.
14. Sofowora A. Research on medicinal plants and traditional medicine in Africa. J Alt Comp Med. 1996;2(3):365–72.
15. Song L, Li T, Yu R, Yan C, Ren S, Zhao Y. Antioxidant activities of hydrolysates of *Arca subcrenata* prepared with three proteases. Mar Drugs. 2008;6(4):607–19.
16. Aloanis AA, Karundeng M. Antioxidant Properties of Beringin (*F. Benjamina* Linn.) Fruit. Fullerene J Chem. 2021;6(2):165-170.
17. Nanda V, Sarkar BC, Sharma HK, Bawa AS. Physico-chemical properties and estimation of mineral content in honey produced from different plants in Northern India. J Food Comp Anal. 2003;16(5):613–9.
18. Arinola OG, Olaniyi JA, Akiibinu MO. Evaluation of antioxidant levels and trace element status in Nigerian sickle cell disease patients with Plasmodium parasitaemia. Pakistan J. Nutr. 2008;7(6):766–9.
19. Obidoa O, Joshua PE, Eze NJ. Phytochemical analysis of *C. nucifera* L. J Pharm Res. 2010;3(2):280–6.
20. Singla RK, Dubey AK. Phytochemical profiling, GC-MS analysis and α-amylase inhibitory potential of ethanolic extract of *C. nucifera* linn. Endocarp. Endocr Metab Immune Disord Drug Targets. 2019;19(4):419–42.
21. Misrahanum M, Alfiyani N, Helwati H, Sadli S. Phytochemical, GC-MS Analysis, and Antibacterial Activity of Ethanol Extract Coir and Shell U Groh (*C. nucifera L.*). Majalah Obat Tradisional. 2022;27(3):172–80.
22. Briguglio G, Costa C, Pollicino M, Giambò F, Catania S, Fenga C. Polyphenols in cancer prevention: New insights. Int J Funct Nutr. 2020;1(2):1–11.
23. Karunasiri AN, Senanayake CM, Hapugaswatta H, Jayathilaka N, Seneviratne KN. Protective Effect of Coconut Oil Meal Phenolic Antioxidants against Macromolecular Damage: *In Vitro* and *in Vivo* Study. J Chem. 2020;2020:1-8.
24. Elmadfa I, Meyer AL. The role of the status of selected micronutrients in shaping the immune function. Endocr Metab Immune Disord Drug Targets. 2019;19(8):1100–15.
25. Raj SB, Ramaswamy S, Plapp BV. Yeast Alcohol Dehydrogenase Structure and Catalysis. Biochemistry. 2014;53(36):5791–803.
26. Sisodia NS. . Effect of Heavy Metal Toxicity on Environment & Health. International. J Res Appl Sci Biotech. 220;7(6):248-254.
27. Nnorom IC, Nnadozie C, Ugwa R, Obike AI. Proximate and trace metal analysis of coconut (*C. nucifera*) collected from Southeastern, Nigeria. ABSU J Env Sci Tech. 2023;3:357-361.
28. Adeoye RI, Okaiyeto K, Oguntibeju OO. Global mapping of research outputs on nanoparticles with peroxidase mimetic activity from 2010–2019. Inorg Nano-Metal Chem. 2023;53(2):199–211.
29. Ewansiha CJ, Ebhoaye JE, Asia IO, Ekebafe LO, Ehigie C. Proximate and mineral composition of coconut (*C. nucifera*) shell. Int J Pure Appl Sci Technol. 2012;13(1):57–60.
30. Spriet LL, Heigenhauser GJ. Regulation of pyruvate dehydrogenase (PDH) activity in human skeletal muscle during exercise. Exer Sport Sci Rev. 2002;30(2):91–5.

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ISSN 2616-0692 (Electronic)

31. Morais JB, Severo JS, de Alencar GR, de Oliveira AR, Cruz KJ, do Nascimento Marreiro D, de Carvalho CM, Frota KD. Effect of magnesium supplementation on insulin resistance in humans: A systematic review. Nutrition. 2017;38:54–60.
32. Barbagallo M, Veronese N, Dominguez LJ. Magnesium in aging, health and diseases. Nutrients. 2021;13(2):1–20.
33. Liu G, Sil D, Maio N, Tong WH, Bollinger JM, Krebs C, Rouault TA. Heme biosynthesis depends on previously unrecognized acquisition of iron-sulfur cofactors in human amino-levulinic acid dehydratase. Nat Commun. 2020;11(1):6310.
34. Chasapis CT, Ntoupa PSA, Spiliopoulou CA, Stefanidou ME. Recent aspects of the effects of zinc on human health. Arch Toxicol. 2020;94(5):1443–60.
35. Farag MA, Hamouda S, Gomaa S, Agboluaje AA, Hariri MLM, Yousof SM. Dietary micronutrients from zygote to senility: Updated review of minerals' role and orchestration in human nutrition throughout life cycle with sex differences. Nutrients. 2021;13(11).
36. Hua Y, Clark S, Ren J, Sreejayan N. Molecular mechanisms of chromium in alleviating insulin resistance. J Nutr Biochem. 2012;23(4):313–9.
37. Wang Y, Zhang W, Yao Q. Copper-based biomaterials for bone and cartilage tissue engineering. J Orthop Translat. 2021;29:60–71.
38. Ishida T. Antiviral activities of Cu^{2+} ions in viral prevention, replication, RNA degradation, and for antiviral efficacies of lytic virus, ROS-mediated virus, copper chelation. World Scientific News. 2018;99:146–148.
39. Bhattacharya PT, Misra SR, Hussain M. Nutritional aspects of essential trace elements in oral health and disease: an extensive review. Scientifica. 2016;2016:1–12.