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SELECTED RENAL OXIDATIVE STRESS MARKERS AND LIPID PROFILE CHANGES DUE TO LONG TERM CONSUMPTION OF INSTANT NOODLES IN ADULT WISTAR RATS

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ABSTRACT

Reports have linked the levels of renal antioxidant markers to the development of kidney disease. Though the effects of instant noodles consumption on the levels of these markers and serum lipid profile remain vague and poorly established, this study sought to investigate the long term consumption of instant noodles on selected oxidative stress markers and lipid profile levels of Wistar rats. Fifty (50) adult wistar rats of an average weight of 200g were purchased for the study. After fourteen (14) days of acclimatization, the rats were then grouped into five (5) groups of ten (10) rats each. While Group A was fed with cooked instant noodle (Type A), group B received cooked instant noodles mixed with its spice, whereas, group C and D were respectively fed with cooked instant noodles (type B) and type B with spice. Lastly, group E (Control) rats received standard rat chow and the other animals were given water *ad libitum*. At the end of administration of test substances, rats were sacrificed (by cervical dislocation) and kidney tissue harvested and homogenized for assay of selected oxidative stress markers [Catalase, Malonyldialdehyde (MDA), Glutathione Peroxidase (GPx) and superoxide Dismutase (SOD)]. Blood sample was also collected and subjected to biochemical analysis of various levels of lipid profile [Triglycerides (TG) Total Cholesterol (TC), High Density Lipoprotein (HDL), and Low Density Lipoprotein (LDL)]. After data collation, result showed a statistically insignificant increase ($p < 0.05$) in serum lipid levels of all treated animals as against those of the control group. Renal antioxidant enzyme levels, we observed a statistically significant ($p < 0.05$) decrease in Catalase, SOD and GPx concentrations in the treatment group. However there was a significant ($p < 0.05$) increase in MDA levels in the treatment groups as compared with control, which was a strong indication that renal cortical structures were compromised. Study also observed a statistically significant ($p < 0.05$) increase in all assayed lipid profiles levels. We strongly recommend further studies aimed at corroborating these findings.

KEYWORDS: Kidney, Instant Noodles, Lipid profile, Oxidative stress markers.

INTRODUCTION

Indomie instant noodle (produced by Indofood) is one of the world's largest instant noodle from Indonesia.[1] The fast food is sold all through Australia, Malaysia, the United States, Indonesia, Nigeria, and several other countries. Indomie noodle is reportedly nutritious; containing colours, flavourings, high measures of monosodium glutamate (MSG) and certain preservatives.[2] It is relatively easy to cook and can be eaten either as a normal meal, or as snack. It is attractive to most people; both at home, at work, or in school.[3]

Nutritionally, noodles are high in carbohydrate (< 70%) and low in protein, fibre, vitamins and minerals.[4&5] However, long term consumption of instant noodles fast food has been reported to affect the vital function of glomerular filtration, thereby resulting to morphological changes in the kidney followed by severe histopathogenesis.[6] For instance, report has it that one of the active ingredients in indomie; monosodium glutamate (MSG) can trigger an unfavourably susceptible response in 1 to 29% of global populace with hypersensitive individuals consuming sensations, tranic and facial flushing or torment and cerebral pains from it.[7]

The Kidneys are paired organ whose functions include removing waste products from the blood and regulating the amount of fluid in the body.[8] The basic units of the kidneys are microscopically thin structures called nephrons, which filter the blood and cause wastes to be removed in the form of urine. Together with the urinary

bladder, two ureters, and the single urethra, the kidneys make up the body's urinary system. Human beings, as well as members of all other vertebrate species, typically have two kidneys; which are dark red in colour and have a shape in which one side is convex, or rounded, and the other is concave, or indented.[8] The kidneys of adult humans are about 10 - 13 cm (4 - 5 inches) long and about 5 - 7.5 cm (2 - 3 inches) wide of about the size of a computer mouse.[9]

The kidneys lie against the rear wall of the abdomen, on either side of the spine. They are situated below the middle of the back, beneath the liver on the right and the spleen on the left. Each kidney is encased in a transparent, fibrous membrane called a renal capsule, which helps protect it against trauma and infection.[8 & 9] The concave part of the kidney attaches to two of the body's crucial blood vessels the renal artery and the renal vein and the ureter, a tube-like structure that carries urine to the urinary bladder.[8]

The primary function of kidneys is the removal of poisonous wastes from the blood. Chief among these wastes are the nitrogen-containing compounds urea and uric acid, which result from the breakdown of proteins and nucleic acids. Life-threatening illnesses occur when too many of these waste products accumulate in the bloodstream. Fortunately, a healthy kidney can easily rid the body of these substances. Eating well is an important part of kidney health condition and it helps to avoid complication of renal disease such as fluid overload, high blood potassium, bone disease, and weight loss.[10] Healthy and functioning kidney requires all the forms of food types in an appropriate proportions for the enhancement of its prolong health and functions.

Aim of Study

Current study aimed at investigating the alterations in liver function markers and selected lipid profiles due to long term consumption of instant noodles in adult wistar rats. Specifically, this study;

i. Determined the changes in selected renal oxidative stress marker activities in long term consumption of instant noodles in adult Wistar rats.
ii. Examined the lipid profile levels [Total Cholesterol, Triglyceride, High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL)] in long term consumption of instant noodles.

MATERIALS AND METHODS

Animals

Fifty (50) adult wistar rats of an average weight of 180g were procured from the animal holdings of the Department of Anatomy and Cell Biology, Delta State University Abraka. The rats were then maintained in the Animal holding of the Department of Public and Community Health, Novena University, Ogume, Delta State, Nigeria.

Study Design

After two weeks period of acclimatization, animals were randomly assigned into five (5) groups: group A, B, C, D and E of ten rats per group. The treatment group (Group A) received cooked instant noodle (Type A) only; whereas, those in group B received cooked instant noodles with its spice. Group C received cooked instant noodles type B only. Group D received cooked instant noodles type B with its spice while rats in the control group E were fed with grower marsh obtained from Animal care services, Konsult (Nig Ltd), Asaba, Delta State for 30 days. The animals were given water liberally.

Ethical Clearance

Ethical approval was obtained from the Research and Ethics committee of the college of Health Sciences, Novena University, Ogume, Delta State. Guidelines on use and handling of laboratory animals were also strictly followed, ensuring that no animal live was unduly wasted without actual need for it.

Sample preparation

After bulk purchase from local markets, Noodle samples were taken randomly from the composite pack and sun-dried for 24 hours, following which it was grinded to powder form using mortar. The ground solid samples (5 g each) were placed in crucibles and then made into various samples; for addition to rat feeds based on study design

Preparation of tissue homogenate

The different kidney sample from each group of the experimental animals were dissected out, homogenized in a mortar and pestle with a pinch of acid washed sand and a total of 5mls of normal saline (0.9%) added sequentially during the homogenization process. The homogenates were centrifuge at 3500rpm for five minutes with the aid of a centrifuge. The clear supernatants were collected using a micropipette and transferred into an empty specimen container and refrigerated till needed for the assay.

Collection of Blood Sample

Blood samples were collected from the orbital sinus of the animals through ocular puncture, following which serum was separated by centrifuging at 6000 rpm for 15 min. various biochemical analyses [Catalase, Malonyldialdehyde (MDA), Glutathione Peroxidase (GPx) and superoxide Dismutase (SOD)] were thereafter conducted on obtained serum.

Biochemical Assay

Lipid Profile Determination

Excerpt from refrigerated serum was obtained, analysed for total cholesterol, triglyceride, and High Density Lipoprotein (HDL-cholesterol) levels by precipitation and possibly modified enzymatic processes. Cholesterol and triglyceride concentrations were determined using enzymatic calorimetric assay kits. High density

lipoprotein cholesterol was measured using precipitation method while low density lipoprotein was obtained by calculation using Friedwald's formula (LDL mg/dl = Total cholesterol – HDL - TG/5).

Superoxide Dismutase (SOD)

Activities of the SOD in kidney tissues were determined by the method of Misra and Fridovich, (1972).[11] An aliquot (0.04mls) of the supernatant was added to 5mls of 0.05m carbonate buffer (pH 10.2) equilibrated in the spectrophotometer for 2-3 minutes. The reaction was then initiated by the addition of 0.6mls of freshly prepared adrenaline as substrate to the buffer-supernatant mixture which was quickly mixed by inversion and the absorbance taken. The reference cuvette contained 5ml of the carbonate buffer, 0.6m of the substrate and 0.4ml of distilled water. The increase in absorbance of 420nm due to the adenochrome formed was monitored every 30 seconds for 120 seconds. 1 unit of SOD activity was given as the amount of SOD necessary to cause 50% inhibition of the auto-oxidation of adrenaline to adenochrome during 120 seconds.

Catalase Assay

The method of Cohen *et al.*, (1970) was adopted.[12] Aliquots of the homogenate supernatant (0.05ml) were added into ice cold test tubes while the blank contained 0.05 ml distilled water. The reactions were initiated by adding sequentially at fixed intervals, 5 ml of cold 30 nM hydrogen peroxide that was mixed thoroughly by inversion. The test samples and the blank were taken one at a time, and 7ml of 0.01M potassium permanganate was added which was mixed twice by inversion and absorbance at 480nm. It was read within 30-60 seconds. The spectrophotometer standard was prepared by adding 7ml of 0.01M phosphate buffer with pH 7.0 and 1ml of 6M - Tetraoxosulphate (VI) acid solution. The spectrophotometer was zeroed with distilled water and the activity of enzymes was estimated.

Peroxidase Assay

The assay was based on the method of Junqueira, and Carneiro (2004) in which 0.4ml of the sample homogenate was added into clean test tubes, follow the addition of 5ml phosphate buffer and then 5ml hydrogen peroxide which was subsequently followed by 3ml of distilled water.[13] Lastly, the addition of 5ml of pyrogallol and the absorbance was taken at 330nm. The blank was prepared by the addition 0.5ml of phosphate buffer, follow by 5ml of hydrogen peroxide. 3ml of distilled water was then added and finally, pyrogallol which was used to zero the spectrophotometer before taking the absorbance of the test

Malonyldialdehyde (MDA) Assay

MDA level was estimated in terms of thiobarbituric acid reactive species using malonlydialdehyde (MDA) as standard by the method of Beuge and Aust, (1978).[14] 1.0ml of a sample extract was added with 2ml of the TCB- TBA reagent (15%w/v TCA, 0.375% (W/V) TBA and 0.25N HCl). The contents were boiled for 15minutes, cooled and centrifuge at 10,000rpm to removed precipitate. The absorbance was read at 535nm and the Malonlydialdehyde coefficient of 1.56×10^5 M^{-1} Cm^{-1}.

Statistical Analysis

Results obtained from the study were recorded and compared statistically using the unpaired sample t-Test and symmetric measured t -Test of the Statistical Package for Social Sciences (SPSS). The results from the various assay were also analysed and taken the significant level of ($p < 0.05$) as taken below variables.

RESULTS

Table I: Effect of Indomie Instant Noodles on Oxidative Stress Makers of the Kidney.

	A	B	C	D	E (Control)	F	p
SOD	15.26 ± 1.35^{ab}	9.37 ± 1.23^{a}	17.43 ± 1.68^{bc}	12.56 ± 0.70^{ab}	23.85 ± 2.12^{c}	13.412	0.000
Catalase	12.69 ± 0.69^{a}	11.88 ± 0.71^{a}	6.90 ± 1.10^{b}	13.27 ± 0.27^{a}	17.42 ± 1.11^{c}	20.151	0.000
MDA	13.05 ± 1.31^{ab}	14.36 ± 1.03^{a}	10.08 ± 0.17^{ac}	14.07 ± 0.75^{a}	9.15 ± 0.23^{c}	8.317	0.000
GSH	2.92 ± 0.16^{a}	2.22 ± 0.24^{a}	2.40 ± 0.19^{a}	2.21 ± 0.21^{a}	4.29 ± 0.20^{b}	18.692	0.000

Values are expressed as Mean ± SEM; Mean with different superscript are statistically significant @p<0.05.

Table II: Average levels of selected lipid profile in the Kidney of instant Noodles Fed Rats.

	A	B	C	D	E (Control)	F	p
Total Cholesterol	126.00 ± 3.29^{ab}	139.80 ± 5.05^{b}	117.00 ± 9.84^{a}	126.10 ± 1.39^{ab}	83.40 ± 3.32^{c}	15.417	0.000
Triglyceride	109.32 ± 2.39^{a}	132.97 ± 5.58^{b}	94.80 ± 2.36^{ac}	86.48 ± 9.57^{c}	62.68 ± 1.44^{d}	25.156	0.000
High Density Lipoproteins	51.45 ± 3.01^{a}	38.22 ± 2.63^{b}	32.03 ± 3.88^{bc}	71.77 ± 7.46^{cd}	20.86 ± 3.06^{d}	19.954	0.000
Low Density Lipoproteins	52.08 ± 6.28^{ab}	77.68 ± 1.48^{c}	66.01 ± 7.12^{bc}	37.03 ± 6.88^{a}	50.22 ± 2.87^{ab}	8.266	0.000

Values are expressed as Mean ± SEM; Mean with different superscript are statistically significant @p<0.05

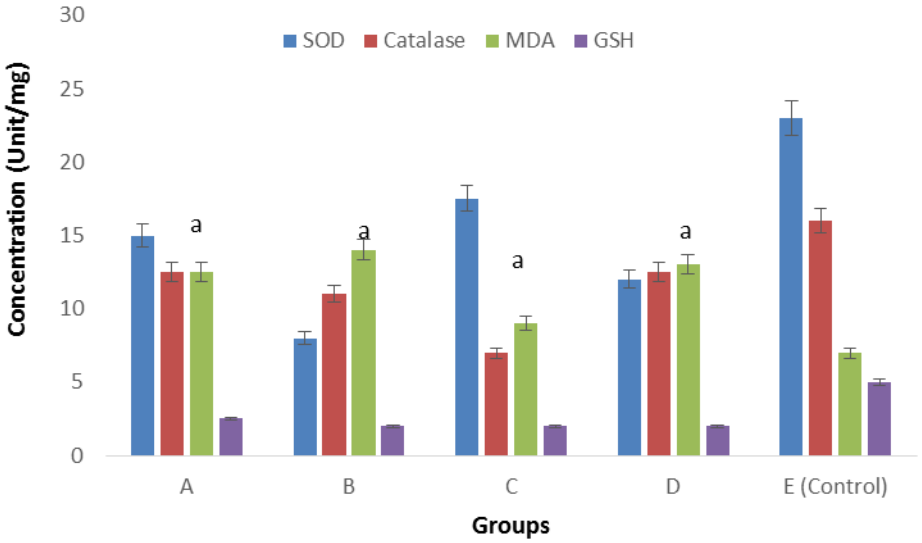

Figure I: Comparative Changes in selected Antioxidant Enzyme Activities of Instant Noodles fed Rats.
a = Statistically significant increase in compared with control group

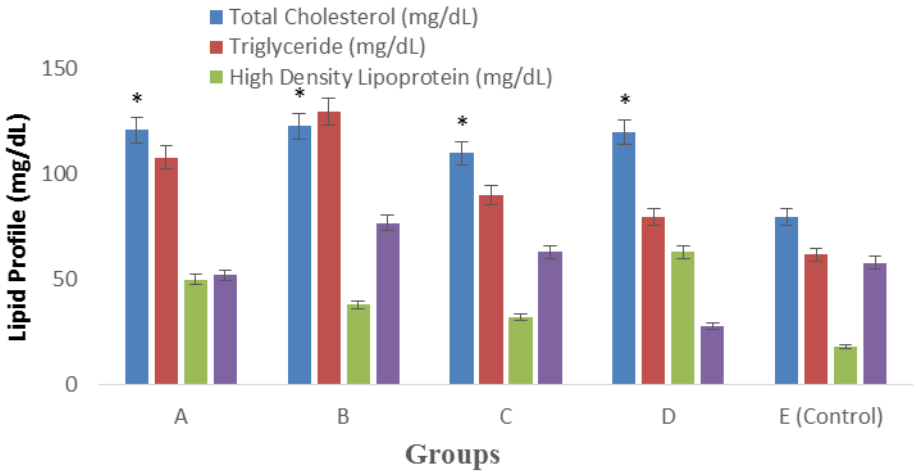

Figure II: Comparative Changes in selected Lipid profile levels of Instant Noodles fed Rats.
** = Statistically significant increase in compared with control group*

DISCUSSION

The proper functioning of the kidney is essential for healthy living, and composition of food, nutrients and drugs may alter these functions. The modern diet composition is resulting in renal damage and metabolic diseases.[10] Consumption of Monosodium glutamate (MSG) in instant noodles may have some deleterious effects on the kidney of adult Wistar rats at higher doses and by extension may affect the functions of the kidney.[8]

In humans, several toxic substances ingested or are eliminated by the combination of hepatic metabolism and renal excretion, and kidney happens to be among the major organs of metabolism in the body.[13] Kidney plays a significant role in food breakdown. It is also important in drug and electrolyte excretion in the body. From the result of our study (Figure II above), we observed a statistically significant increase ($p < 0.05$) in all assayed lipid profile levels, except for High Density Lipoprotein (good cholesterol). Huge deposits of lipid were also observed in the kidney, suggesting that increased level of LDL deposition and the resultant renal damage may be due to long term consumption of instant noodles. By implication; in fat metabolism, lipoproteins, phospholipids and cholesterol formation are known to take place along with oxidation of free fatty acids. For the process of synthesis of cholesterol and other substances, fatty acids produced by digestion of lipids are used.

The combination of the noodle and the seasoning caused a greater damage to the wall of the blood vessels, thereby leading to the narrowing of the lumen of the blood vessels, almost blocking it, hence causing renal arteriosclerosis, which causes Ischaemia damage to the kidney.[9] This Ischaemia damage to the kidney can lead to renal failure and increase in blood pressure.[14] Additionally, the group that was given instant noodles and its seasoning plus feed showed a more severe effect

on the kidney when compared with the other group. This outcome reasonably informed us that if large amount of seasoning is being added to noodle meal may be detrimental to the kidney.

Also from figure II, the effects of long term consumption of instant noodle on total Cholesterol, LDL and HDL levels are shown. The result shows a statistically significant difference in Total Cholesterol level in all experimental groups when compared with control (group E). In addition, when treated and control groups were compared for HDL levels; there was a statistically significant decrease. The same result was seen in Triglyceride, implying that instant noodles consumption may significantly affect the deposition of Total Cholesterol and Triglyceride in the kidney and adipose tissues. Result also show a significant difference in HDL level in all experimental groups when compared with control. Also when experimental groups were compared for HDL level, there was a statistically significant decrease, implicating minimal changes in brands as well as the application of noodle spices to have also contributed to the changes in HDL, LDL and triglyceride level of the animals.

A recent report by Adjene *et al*. (2017 & 2010).,[15 & 16] has it that the continuous consumption of instant noodles and soda pop drink may be detrimental to the health of an individual and that long-term consumption of indomie noodles have significantly ($p < 0.05$) increases the body weight and decrease in brain weight of adult wistar rats. Eze *et al*., (2017) also reported that the morphological changes induced by instant noodles food on kidney showed that the consumption of instant noodles may lead to pathological changes in the kidney.[17] These reviewed studies are certain in consonance with the present study.

It has been reported that Instant noodle and its flavouring sauce base contain high amount of Monosodium Glutamate (MSG), which causes neuroplacental neurotoxic effect, causes cataract, causes induced retinal lesions and causes genotoxicity.[9] This present study focused on evaluating the possible morphological and biochemical effects of long term consumption of indomie noodles on the kidney of adult wistar rats.

Several toxic substances ingested or eaten by humans are limited by the combination of hepatic metabolism and renal excretion, and the kidney happens to be among the major organ of metabolism in the body.[17 & 18] Kidney plays a significant role in food breakdown. It's also important in drug excretion in the body. The combination of the noodle and the seasoning caused a greater damage to the wall of the blood vessels, thereby leading to the narrowing of the lumen of the blood vessels, almost blocking it, hence causing renal arteriosclerosis, which causes ischemia damage to the kidney. This ischaemia damage to the kidney can lead to renal failure and increase in blood pressure.[19] Additionally, the group that was given instant noodles and its spices showed a more severe effect on the kidney when compared with the other group. This outcome reasonably informed us that if large amount of seasoning is being added to noodles meal may be detrimental to the kidney.

The study further revealed that there were significant differences in the effects of long term consumption of different forms of noodles on the biochemistry (SOD, catalase, MDA and GSH activities) of the animals ($p < 0.05$). Sanni *et al*., (2013) had observed that the effects of chronic administration of Indomie instant noodles on the activities of kidney oxidative stress markers, showing that, there was a decrease in kidney activity of the enzyme.[19] This agrees with the findings in the present study.

The results showed that oxidative stress measured as MDA was found to have significantly increased ($P<0.05$) in all the treated tissues as compared with their controls. This finding corroborates the previous works of adjene *et al.,* (2017) who demonstrated that efavirenz exerts its toxic effect by promoting oxidative stress in the colliculi and geniculate bodies of adult Wistar rats.[20] The antioxidants level is lower while pro-oxidant polyunsaturated fatty acids are higher in the CNS relative to other tissues. Therefore, the CNS is exceptionally at risk of oxidative damage. The antioxidant enzymes such as catalase, glutathione peroxidase, G6-PDH, LDH and SOD are responsible for the brain's basic functions, both physical and cognitive.[21 & 22] It is known that the activities of antioxidant enzymes are significantly modified in the CNS during intoxication, whereby a decrease in activity may indicate oxidative modification of the enzymatic proteins. It is worthy to note that the increase in the activity of the antioxidant enzymes may often be due to adaptive response to excess free radicals. Further catalase may be unreliable in this respect because the decrease in its activity may be due to enhancement of protein synthesis as a confounding factor.[22]

CONCLUSION

This research work has shown that chronic consumption of instant noodles could pose deleterious effects to health. Much intake of it could lead to copious serum surge of malonaldehyde levels which could oxidatively damage the kidney. This may however vary by mode of preparation and feed, depending on addition of spice. The effects may thus alter the physiological state of the animal. Results from this study revealed oxidative stress on the kidney via significant increase in MDA levels, whilst posing a significant decrease in SOD levels. Subsequently, long term administration of instant noodles also revealed a significant ($p < 0.05$) decrease in the concentrations of catalase and GSH. Furthermore, there was a significant increase ($p < 0.05$) in lipid profile levels of treated animals as compared with control

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