E-ISSN: 2378-654X

Recent Advances in Biology and Medicine

Original Research Article

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Raw Cucumber (*Cucumis sativus*) Fruit Juice as Possible First-Aid Antidote in Drug-Induced Toxicity

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Received: May 21, 2019; Accepted: Aug 5, 2019

Citation: Olaniyan MF, Ale SA, Uwaifo F. Raw cucumber (*Cucumis sativus*) fruit juice as possible first-aid antidote in drug-induced toxicity. Recent Adv Biol Med. 2019; Vol. 5, Article ID 895463, 6 pages. https://doi.org/10.18639/RABM.2019.895463

Abstract
Raw cucumber (*Cucumis sativus*) fruit juice contains substances that have health-benefit potentials. Fibrinogen is produced in the liver cells. Highest concentrations of lactate dehydrogenase (LDH) are found in the liver, heart, and skeletal muscle, and alanine transaminase (ALT) is a liver enzyme. Overdose of amoxicillin, an antibiotic, can lead to hemolysis, hepatotoxicity, and inflammation. This study was therefore designed to determine the use of raw cucumber (*C. sativus*) fruit juice as a possible first-aid antidote in drug-induced toxicity. Fifteen rabbits of the same gender weighing 0.9-1.4 kg were used for the study. They were divided into three groups of five rabbits each as follows: Group A—five control rabbits; Group B—five rabbits, given 30.0 mg/kgBW subcutaneous injection of amoxicillin every 24 h for seven days and was followed by 30 mL raw cucumber fruit juice supplementation for 14 days; Group C—five rabbits, given 30.0 mg/kgBW subcutaneous injection of amoxicillin every 24 h and raw cucumber fruit juice supplementation for 14 days simultaneously. Plasma LDH, ALT, and fibrinogen were determined in the rabbits by spectrophotometry. There was a significant increase in plasma ALT and LDH and a significant decrease in fibrinogen following amoxicillin overdose compared with the results obtained from the basal samples and the control rabbits. These abnormalities were reversed when raw cucumber fruit juice was administered to the experimental rabbits initially overdosed with amoxicillin ($p < 0.05$). There was a significant increase in the plasma value of LDH in the rabbits when they were supplemented with raw cucumber fruit juice following amoxicillin overdose and when the rabbits were coadministered with raw cucumber fruit juice and amoxicillin overdose compared with their basal samples ($p < 0.05$). There was no significant difference in the plasma value of ALT and fibrinogen when the rabbits were coadministered with raw cucumber fruit juice ($p > 0.05$). This study showed an increase in plasma ALT and LDH, and a decrease in fibrinogen following the administration of subcutaneous injection of amoxicillin; however, these abnormalities were reversed when the rabbits were administered 30 mL of raw cucumber fruit juice. Raw cucumber fruit juice could be applied as first-aid antidote in drug induced toxicity.

Keywords: ALT; LDH; Fibrinogen; Rabbits; Amoxicillin overdose; Raw cucumber (*Cucumis sativus*) fruit juice.

1. INTRODUCTION

Cucumber (*C. sativus*) fruit juice is a rich source of iron, Cu, Ca, potassium, phosphorus, magnesium, vitamin K, vitamin C, phytochemicals, and phytonutrients of useful bioactivities such as antioxidation, antiageing, and antitoxin [1, 2]. Cucumbers are also rich in silica, which is an essential biochemical substance in muscles, ligaments, cartilage, bone, and skin. Some of these bioactive substances are useful as a natural remedy to prevent hypertension and has a powerful alkalizing effect in the body system [3-5].

The large volume of fluid in cucumbers is useful as a detoxifying fluid to remove toxins in the body through urination, to eliminate the bacteria attached to the bowel and bladder, and to hydrate the skin, joints, and tissues when it is taken as juice. Lignans such as lariciresinol, pinoresinol, and secoisolariciresinol found in cucumber fruit can reduce cardiovascular disease, as well as several cancer types including breast, uterine, and ovarian, and dehydration in pregnancy [3-5].

C. sativus, which is rich in fiber and low in calories, can help to maintain a healthy weight and prevent constipation in pregnancy. Additionally, potassium content of cucumbers is useful for removing excess uric acid and metabolic waste through the kidneys. The biochemical constituents of cucumbers can bring about the breakdown of kidney stones and act against the accumulation of toxins. Saponin, which is a phytochemical in the fruit, can lower cholesterol, boost the immune system, and prevent cancer [1, 2].

Amoxicillin is a penicillin-type antibiotic that inhibits the growth of bacteria. Abuse of amoxicillin can decrease antibiotic effectiveness. The antibiotic can be used in combination with other drugs to treat stomach/intestinal ulcers caused by

H. pylori and to prevent relapse. Overdose of amoxicillin can cause jaundice, difficulty in breathing, hairy, severe vomiting, persistent diarrhea, bleeding/hemolysis, and severe oliguria [6-8].

Lactate dehydrogenase (LDH) is an enzyme that catalyzes the interconversion of lactic and pyruvic acids. It has four peptide chains and five isoforms. The enzyme is distributed in the body with the highest concentrations found in the liver, heart, and skeletal muscle. LDH activity is associated with stroke, kidney disease, liver disease, progressive muscular dystrophy, cancer, and intestinal myocardial and pulmonary infarction [9-15].

Alanine aminotransferase (ALT) or serum glutamate pyruvate transaminase (SGPT) has the highest concentration in the liver, with decreasing concentrations found in the kidneys, heart, skeletal muscle, pancreas, spleen, and lung tissue [16-19]. Raised plasma levels of ALT can indicate inflammation of liver cells. Increased plasma transaminases can be caused by myocardial infarction, hepatic disease, muscular dystrophy, and organ damage [16-19].

Fibrinogen is a plasma glycoprotein and an acute phase protein produced by liver cells and the most abundant clotting factor. Plasma fibrinogen is used to determine inherited deficiency, unexplained or prolonged bleeding, and risk of cardiovascular and heart disease [20-27]. Increased fibrinogen concentration can be due to chronic inflammation [20-27].

This study seeks to determine raw cucumber (*C. sativus*) fruit juice as a possible first-aid antidote in drug induced toxicity.

2. METHOD(S)

2.1. Study Area

This study was carried out in the animal house of Achievers University, Owo-Nigeria located in Idasen community in Owo, Ondo State, Nigeria.

2.2. Study Population

The study population includes 15 rabbits of the same gender divided into three groups of five rabbits each. The rabbits were bought from the major animal farm in Owo-Nigeria and were confirmed by the Federal College of Agriculture, Akure, Ondo State capital in Nigeria.

The three groups included the following:

Group A—Five control rabbits that were fed with normal meal and water throughout the study period.
Group B—Five rabbits were administered subcutaneous injection of 30.0 mg/kgBW of amoxicillin every 24 h for seven days and was followed by 30 mL of raw cucumber fruit juice supplementation for 14 days.
Group C—Five rabbits were given subcutaneous injection of 30.0 mg/kgBW of amoxicillin every 24 h and raw cucumber fruit juice for 14 days simultaneously.

2.3. Administration of Amoxicillin

Amoxicillin was bought from a registered pharmaceutical store in Owo-Nigeria. Overdose of 30.0 mg/kgBW of amoxicillin every 24 h for seven days was by subcutaneous injection.

2.4. Preparation of Cucumber (*C. sativus*) Fruit Juice

Cucumber (*C. sativus*) was bought from Hausa fruit vendors in Owo-Nigeria. The fruit was confirmed at the Federal College of Agriculture, Akure, Nigeria. The fruit was washed using sterile water and thereafter sliced into pieces. The sliced cucumber fruit was blended together using an electronic blender. The raw fluid was extracted using a sterile sieve. Thirty (30 mL) milliliters of freshly prepared raw liquid extract was administered orally to the rabbits as juice on a daily basis.

2.5. Specimen (Blood) Collection

Five milliliters of venous blood was collected from each of the rabbits in lithium heparinized bottles for biochemical analysis before and after treatments.

2.6. Biochemical Analysis

2.6.1. Fibrinogen measurement using RANDOX kit by Clauss method

Principle: In the presence of a high concentration of thrombin, the time required for blood clot formation in diluted plasma is inversely proportional to fibrinogen concentration.

2.6.2. Alanine transaminase (ALT/SGPT) measurement using RANDOX kit

Principle: Alanine aminotransferase (ALT) catalyzes the transamination of L-alanine to α-ketoglutarate (α-KG), generating L-glutamate and pyruvate. The pyruvate produced is reduced to lactate by lactate dehydrogenase (LDH) including simultaneous

oxidation of reduced nicotinamide adenine dinucleotide (NADH). The change in absorbance is directly proportional to the ALT activity measured using bichromatic (340, 700 nm) rate technique.

2.6.3. Lactate dehydrogenase measurement using RANDOX kit

Principle: This method determines the oxidation of L-lactate to pyruvate including simultaneous reduction of nicotinamide adenine dinucleotide (NAD). The change in absorbance at 340 nm due to the appearance of reduced NAD (NADH) is directly proportional to the LDH activity that is measured using a bichromatic (340, 383 nm) rate technique.

2.7. Data Analysis

The raw data obtained from this work was analyzed to determine mean, standard deviation, Student's *t*-test, and probability at 0.05 level of significance using a statistical package for social scientist of IBM SPSS 18.0 version.

3. RESULTS

There was a significant increase in plasma ALT and LDH and a significant decrease in fibrinogen following amoxicillin overdose compared with the results obtained from the basal samples and the control rabbits. The abnormalities were reversed when raw cucumber fruit juice was administered to the experimental rabbits initially overdosed with amoxicillin ($p < 0.05$; Tables 1 and 2; Figure 1).

There was a significant increase in the plasma value of LDH in the rabbits when they were supplemented with raw cucumber fruit juice following amoxicillin overdose and when the rabbits were coadministered with raw cucumber fruit juice and amoxicillin overdose compared with their basal samples ($p < 0.05$; Tables 1 and 2; Figure 1).

There was no significant difference in the plasma value of ALT and fibrinogen when the rabbits were coadministered with raw cucumber fruit juice ($p > 0.05$; Tables 1 and 2; Figure 1).

No significant difference was obtained in the plasma value of ALT, LDH, and fibrinogen in the results obtained from the basal samples of the experimental and control rabbits ($p > 0.05$; Tables 1 and 2; Figure 1).

Table 1: Mean and standard deviation of plasma values of alanine transaminase, lactate dehydrogenase, and fibrinogen obtained in the rabbits.

	Control rabbits A	Group B			Group C	
		B1	B2	B3	C1	C2
ALT (U/L)	5.0 ± 0.1	5.2 ± 0.5	10 ± 1.0	5.5 ± 0.5	5.1 ± 0.3	5.6 ± 0.2
LDH (µmol/L)	0.6± 0.05	0.5± 0.02	1.5±0.1	0.7± 0.05	0.6± 0.01	0.7± 0.01
Fibrinogen (g/L)	1.9 ± 0.1	1.7 ± 0.2	0.9± 0.1	1.6 ± 0.1	1.9 ± 0.2	1.8 ± 0.1

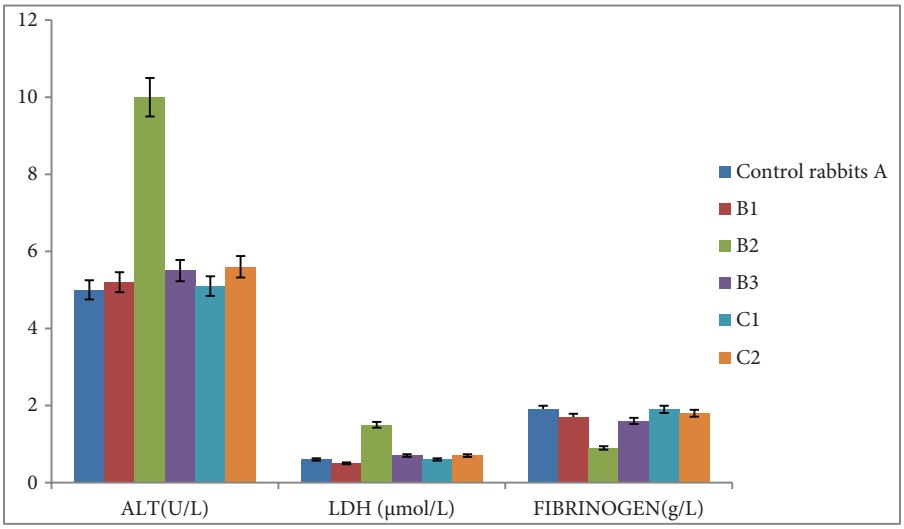
NB: B1 and C1—basal blood samples
B2—blood samples collected after amoxicillin overdose
B3—blood samples collected after raw cucumber juice supplementation following amoxicillin overdose
C2—blood samples collected after simultaneous administration of raw cucumber juice and amoxicillin overdose

Table 2: Comparative analysis of Table 1: Mean and standard deviation of plasma values of alanine transaminase, lactate dehydrogenase, and fibrinogen obtained in the rabbits.

		A vs. B1	A vs. C1	A vs. B2	A vs. B3	A vs. C2	B1 vs. B2	B1 vs. B3	B2 vs. B3	C1 vs. C2
ALT (U/L)	*t*	−0.392	−0.3162	−4.975	−0.98	−2.68	−4.293	−0.42	4.025	−1.3868
	p	0.366	0.391	0.019*	0.215	0.058	0.025*	0.3563	0.028*	0.15
LDH (µmol/L)	*t*	1.857	0	−8.05	−1.414	−1.96	−9.806	−3.71	7.155	−9.39149.
	p	0.102	0.5	0.008*	0.1464	0.10	0.005*	0.033*	0.01*	0. 006*
Fibrinogen (g/L)	*t*	0.894	0	7.0710	2.12	0.707	3.578	0.447	−4.950	0.44721
	p	0.23	0.5	0.010*	0.084	0.276	0.035*	0.349	0.02*	0.3492

 https://doi.org/10.18639/RABM.2019.895463

Figure 1: Comparative description of mean and standard deviation of plasma values of alanine transaminase, lactate dehydrogenase, and fibrinogen obtained in the rabbits.



4. DISCUSSION

This study reveals that there was a significant increase in plasma ALT and LDH and a significant decrease in fibrinogen following amoxicillin overdose compared with the results obtained from the basal samples and the control rabbits, and the abnormalities were reversed when raw cucumber fruit juice was administered to the experimental rabbits initially overdosed with amoxicillin.

Alanine transaminase enzyme is found in plasma and in some body tissues but is found majorly in the liver. The plasma level increases in liver disease, inflammation, and hepatotoxicity. Increase in plasma ALT in this study could be because of hepatotoxicity/inflammation caused by amoxicillin overdose [16-19]. Fibrinogen is synthesized in the liver. Decrease in fibrinogen level in this study after amoxicillin overdose could be associated with the hepatotoxic effect of amoxicillin that can cause a decrease in the physiological function of the liver, which includes the production of fibrinogen [20-27].

Increased plasma LDH following amoxicillin overdose in the rabbits could be also due to possible hepatotoxicity, tissue destruction, and hemolysis because LDH is distributed throughout the body with the highest concentrations in the liver, red blood cells, the heart, and skeletal muscle. Lactate dehydrogenase enzyme has also been associated with kidney disease and liver disease [9-15].

Furthermore, increase in plasma ALT and LDH and a significant decrease in fibrinogen following amoxicillin overdose can be attributed to the potential of amoxicillin overdose to cause hepatotoxicity/liver damage, nephrotoxicity, jaundice, difficulty in breathing, hairy, severe vomiting, persistent diarrhea, bleeding/hemolysis, and a severe decrease in the amount of urine [6-8].

Significant decrease in ALT and increase in fibrinogen following cucumber fruit juice supplementation could be associated with the hepatoprotective activities of cucumber (*C. sativus*) fruit juice, as ALT is majorly found in the liver in which its plasma level increases in hepatotoxicity/hepatocellular damage or inflammation while fibrinogen is produced by the liver, the function that was earlier affected by amoxicillin overdose and possibly resolved when the rabbits were administered raw cucumber (*C. sativus*) fruit juice. This is because raw cucumber (*C. sativus*) fruit juice contains phytochemicals and phytonutrients of health-benefit bioactivities such as antioxidation, antiageing, and antitoxin. Cucumber also contains flavonoids and tannins responsible for free radical scavenging and analgesic effects [1, 2].

There was also a significant increase in the plasma value of LDH in the rabbits when they were supplemented with raw cucumber fruit juice following amoxicillin overdose and when the rabbits were coadministered with raw cucumber fruit juice and amoxicillin overdose compared with their basal samples. This may also be attributed to the degree of cellular, tissue, or organ damages caused by amoxicillin overdose leading to persistent increase in LDH because LDH is distributed throughout the body with the highest concentrations in the liver, red blood cells, the heart, and skeletal muscle, which was not resolved upon the administration of raw cucumber fruit juice. LDH has also been linked with kidney disease and liver disease [9-15].

There was no significant difference in the plasma value of ALT and fibrinogen when the rabbits were coadministered with raw cucumber fruit juice. This could be attributed to possible hepatoprotective activity of raw cucumber fruit juice because the juice has antioxidant and antitoxin properties [1, 2], as phytochemical and phytonutrients aqueous extract of *C. sativus* fruits include lycosides; steroids; alkaloids; steroids; flavonoids; carbohydrates; saponins; fisetin; tannins; and vitamins C, A, K,

and B5 as well as manganese, potassium, and magnesium, which have health benefits that fight inflammation, infection, act as antitoxin, and antioxidants and are antiageing [28].

5. CONCLUSION

This study showed an increase in plasma ALT and LDH and decreased fibrinogen following the administration of 30.0 mg/kgBW subcutaneous injection of amoxicillin; however, these abnormalities were reversed when the rabbits were administered 30 mL of raw cucumber fruit juice. Raw cucumber fruit juice could be taken as a first-aid antidote in drug misuse/overdose.

Acknowledgment
No financial or material support.

Author Contributions
MFO conceived the research design, performed literature search, and collected and analyzed data; SAA and FU performed literature search and data collection.

Conflict of Interest
None.

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