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Effect of a controlled food-chain mediated exposure to cadmium and arsenic on oxidative enzymes in the tissues of rats

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ABSTRACT

Objective: The present study aims to investigate the effect of cadmium and arsenic through a controlled food chain on the activities of some oxidative enzymes (Sulphite oxidase SO, Aldehyde oxidase AO, Monoamine oxidase MO and Xanthine oxidase, XO) in the liver, kidney, testes, heart and brain of rats.
Materials and methods: Fish (the first trophic level) were exposed to both metals (singly and in mixture) using cadmium chloride ($CdCl_2$) as the source of cadmium and arsenic trioxide (AS_2O_3) as the source of arsenic at a concentration of 0.4 mg of metals/100 ml of water for 1 month and then sacrificed. The contaminated fish were then used as a source of protein in compounding the experimental diet to which the rats (the second trophic level) were exposed to for a period of 1 and 3 months. The Cd- and As-load in the feed and tissues of rats as well as the activities of the oxidative enzymes were subsequently analyzed in the various tissues after both period of exposure.
Results: Metal analysis on the tissues of rats showed that the metals accumulated more in the liver than in other organs after the 1 month exposure but accumulated more in the kidney after the 3 months exposure. The activities of the oxidative enzymes in the liver were significantly ($P < 0.05$) decreased in all test groups after the 1 and 3 months exposure. However, after the 1 month exposure, the kidney, testes and heart showed an initial increase in the activities of these enzymes which were decreased after the 3 months exposure. In the brain, the activities of these enzymes were increased in both duration of study.
Conclusion: From the results obtained in the current study, it could be concluded that exposure to cadmium and arsenic through the food chain leads to accumulation of these metals in the tissues of experimental rats leading to the inhibition of oxidative enzymes, thus affecting several normal metabolic processes.

1. Introduction

Heavy metals occur as natural constituents of the earth crust. They are persistent environmental contaminants [28]. Once liberated into the environment, heavy metals can be taken into the body via inhalation, ingestion and skin absorption [7,49]. If heavy metals enter and accumulate in body tissues faster than the body's detoxification pathways can dispose of them, then a gradual build-up of these toxins occurs. As heavy metal accumulation occurs in body tissues gradually, it can reach toxic concentration levels over time, much beyond the permissible limits [77]. The agency for Toxic Substances and Disease Registry (ATSDR) lists arsenic and cadmium among the top seven of the 275 most hazardous substances in the environment [56].

Cadmium is considered one of the most toxic substances in the environment due to its wide range of organ toxicity and long elimination half-life of 10–30 years [47]. Cadmium was identified as a contaminant at 776 of the 1467 EPA National Priorities List sites [2]. Cadmium has been shown to be highly toxic to living cells and tissues even at low levels [6,7,55]. It is an underground metal and did not enter the air, water, or even food in significant amounts until it was unearthed as part of zinc deposits. It has become a widespread environmental contaminant [56,7,85]. It is said to be a global threat because it is ubiquitous in virtually all ecosystems [44]. Cadmium has no essential biological function and is extremely toxic to humans.

Arsenic (As) is a member of group V of the periodic table of elements along with nitrogen, phosphorus, antimony, and bismuth. It is found in the natural environment, being present in soil, ground-

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water and plants [12]. Arsenic appears in both inorganic and organic compounds, differing in their physical and chemical properties [17,34,35]. The inorganic and organic arsenic compounds differ significantly in their toxicity, since the organic arsenic compounds exhibit very low toxicity [34]. Consequently, the potential adverse effects of arsenic to animal and human health are determined by the amount of inorganic arsenic present in food [12]. The chemistry of arsenic is rather complex, and the compounds it forms are numerous. This is largely because arsenic possesses several different valence or oxidation states, which result in the markedly different biological behavior of its compound. Arsenic compounds are used in pigments and dyes, as a preservative of animal hides, in glass manufacture, agricultural pesticides, and various pharmaceutical substances [3].

Heavy metal bioaccumulation in the food chain can be especially highly dangerous to human health. These metals enter the human body mainly through two routes: inhalation and ingestion, with ingestion being the main route of exposure to these elements in human population [1]. Heavy metals intake by human populations through the food chain has been reported in many countries with this problem receiving increasing attention from the public as well as governmental agencies, particularly in developing countries [23,38]. The introduction of these metals into the food chain may affect human health, and thus, studies concerning heavy metal accumulation through the food chain have received increasing importance [24]. Since the dietary intake of food may constitute a major source of long-term low-level body accumulation of heavy metals, the detrimental impact might become apparent only after long period of exposure. Regular monitoring of these metals from effluents, sewage, in vegetables and in other food materials is essential for preventing excessive buildup of the metals in the food chain [11].

Fish are exposed to varying concentrations of Cd and As in their natural habitats and have an ability to accumulate metal burdens exceeding aquatic levels [66,18,67,71,27]. Fish may therefore be an important vector of Cd and As transfer to higher levels of the food chain, including humans. Moreso, fish has been described as a good bio-indicator because it can be obtain easily in large quantity, easy to sample and can accumulate metals for analysis [13] of which humans are exposed to via food web. Since toxicity studies of this nature cannot be carried out directly on humans, and rats feed very well on fishes, rats were used for this purpose as the sensitivity of the test animals represents, at best, the average sensitivity of the highly heterogeneous human population of which it could be much higher for some members of the human population [54]. Various studies [73,5,42,39,15] have been carried out using fish as a feed source in terms of contamination for rats. Since fish is capable of accumulating Cd and As and thus may contribute to the intake of these metals, it is therefore important to determine their absorption and toxicity when consumed through fish. However, studies on the possible toxicity of these metals when provided in fish are scarce in literature. This forms the basis of the current study.

Xenobiotic metabolizing enzymes play central role in the biotransformation, metabolism and detoxification of xenobiotics or foreign compounds that are introduced to the human body. These enzymes protect or defend the body against the potential harmful insults from the environment [72]. Xenobiotic metabolizing enzymes enzymatically transformed foreign compounds to less harmful excretable compounds. This biotransformation process occurs mostly in the hepatic tissues and to a lesser extent, some extra hepatic tissues [82]. In the phase I reactions in xenobiotic biotransformation, oxidation reactions are probably the most common. These reactions require a group of non-specific, cytochrome P-450 dependent mixed functionoxidases (MFO). Aldehyde, xanthine, and sulphite oxidases are molybdenum and haem containing soluble enzymes that are present in the liver and other tissues and are also involved in the oxidation of xenobiotics [70,41]. Monoamine oxidase carries out the biotransformation of aromatic monoamines, including classical neurotransmitters such as serotonin, adrenalin, histamine and dopamine [7]. Despite the role played by these important oxidative enzymes in the biotransformation of xenobiotics, animal studies on the effect of cadmium and arsenic on these enzymes through the food chain are missing. Thus, the present study examines the effect of the exposure to cadmium and arsenic (singly and in mixture) on the activities of these oxidative enzymes (viz Sulphite oxidase (SO), Aldehyde oxidase (AO), Monoamine oxidase (MO) and Xanthine oxidase, (XO)) in the liver, kidney, testes, heart and brain through the food chain using rat as the animal model.

2. Materials and methods

2.1. Treatment of fish and preparation of diets

Catfish were gotten from a local fish pond in Imoje-Orogun, Delta State, Nigeria. These fish were exposed to both cadmium and arsenic in the form of cadmium chloride ($CdCl_2$) and arsenic trioxide (AS_2O_3), respectively, in plastic trough for 4 weeks and subsequently used as sources of protein in wholly compounded diets (Table 1). The fishes were divided into four (4) groups and left to acclimatize for 1 week before the commencement of the experiment. In Group A (Control), fishes were kept in fresh water. In Groups B, C and D, fishes were kept in water (100 l) contaminated with 0.4 mg cadmium/100 ml of water, 0.4 mg arsenic/100 ml of water and 0.4 mg arsenic + cadmium/100 ml of water, respectively. This concentration is equivalent to a dose of 4 ppm. For each group, the water was changed and re-contaminated every 24 h for 4 weeks. All the fishes received normal commercial feed for the duration of the 4 weeks after which they were sacrificed and dried in an oven and used as protein source in the compounded experimental diet.

Table 1
Composition of experimental diets.

Ingredients	Percentage (%) composition			
	Control	Cadmium (Cd)	Arsenic (As)	Combined (Cd + As)
Control fish	20	–	–	–
Cadmium-contaminated fish	–	20	–	–
Arsenic-contaminated fish	–	–	20	–
Cadmium + Arsenic-contaminated fish	–	–	–	20
Corn starch	45	45	45	45
Sugar	10	10	10	10
Palm oil	10	10	10	10
Fibre (dried groundnut husk)	10	10	10	10
Multi vitamin/mineral mix	5	5	5	5

The Cd and As contents of these diets were determined by atomic absorption spectrophotometry.