Toxicology Reports 5 (2018) 401–410

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Bioactive profiling and therapeutic potential of mushroom (*Pleurotus tuberregium)* extract on Wistar albino rats (*Ratus norvegicus*) exposed to arsenic and chromium toxicity

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ARTICLE INFO

Keywords:
Arsenic
Chromium
Pleurotus tuberregium
Haematological and redox markers

ABSTRACT

Mushroom species are valued in gourmet traditions around the world for their unique taste, aroma, nutritional value and medicinal potentials. The bioactive profiling of *P. tuberregium* mushroom was evaluated to determine it therapeutic effect on Wistar albino rats exposed to arsenic (As) and chromium (Cr) toxicity. Proximate analysis of *P. tuberregium* showed high composition of carbohydrate (80.24) followed by moisture (21.16), protein (11.46), ash (3.03) and fibre (0.25) content. Phytochemical analysis revealed the presence of polyphenols (2.58), alkaloid (2.46), oxalate (4.25), flavonoid (1.68), tannin (0.38) and Saponin (trace) in trace amount. Mineral analysis yielded variable amounts of Na, Mg, K and Ca. Therapeutics assessment of *P. tuberregium* to Wistar albino rats exposed to As-Cr toxicity showed improved feed and water intake during the exposure duration. Haematological indices revealed significant increase in platelet (PLT), granulocytes and monocytes while lymphocyte (LY) and red cell distribution width (RDW) were low. Biochemical and redox marker of liver and kidney profiles showed decrease in alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) in the liver. Creatinine and urea in the kidney also decrease while total protein increased significantly. Malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), glutathione S-transferase (GST) decrease in the liver and kidney of the therapeutic group when compared with As-Cr treated rats. The presence of alkaloids and flavonoids in significant amount may have contributed in the therapeutic changes observed in all the parameters. Therefore, our findings conclude that *P. tuberregium* possessed remarkable effect against As-Cr induced toxicity in albino rats and may be useful in metal toxicity treatment in man and may be concluded that they are therapeutically effective.

1. Introduction

Africa population is highly vulnerable to frequent exposure to heavy metal pollution because of rapid industrialization and urbanization. Heavy metals are significant environmental pollutants and have become a major public health threat because they are persistent in the environment and can lead to serious wildlife and human health effects and even death. Two recent incidents that highlighted the vulnerability of African population to large scale metal exposure is the lead (Pb) poisoning that occurred in Zamfara State, Nigeria in 2010 from informal artisanal gold mining activities [69] and Dakar, Senegal between November 2007 and March 2008 from informal lead-acid battery dismantling and recycling [44]. Heavy metals enter the environment through natural and anthropogenic means. Anthropogenic activity has contributed significantly to the elevated environmental concentrations of heavy metals in Africa. As and Cr are predominantly products of anthropogenic insults that have become ubiquitous in natural ecosystems. They affect global health due to their toxicity and carcinogenicity [9,19,20,48,49,65,68,106]. As and Cr exist in the environment at low concentrations in soil, water, air, and food such that humans are constantly exposed to this contaminant through the food chain.

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https://doi.org/10.1016/j.toxrep.2018.03.004
Received 17 July 2017; Received in revised form 11 February 2018; Accepted 5 March 2018
Available online 15 March 2018

Arsenic is a toxic metalloid which represents a global environmental health threat. It is the twentieth most abundant element on earth and can exists in organic and inorganic forms with different oxidation or valence states [111]. The valence states of arsenic compounds relevant to human health are the trivalent (As III) and pentavalent (As V) states [111]. The inorganic forms such as arsenite and arsenate compounds are prominently lethal to living organisms. As is released into the terrestrial and aquatic ecosystems through a combination of natural and anthropogenic processes such as mining and processing of ores and humans may be exposed by natural, industrial, or from unintended sources [53]. Accidental consumption of Arsenic through food chain may result in acute and chronic arsenicosis typically defined by classical dermal stigmata and internal disorders.

Chromium also is one of the most toxic heavy metals and 7th most abundantly element in the environment [76,82,93]. It also occurs in several oxidation states in the form of divalent Cr (II), trivalent (Cr III) and hexavalent (Cr VI) [94,108]. The most commonly occurring forms are Cr (III) and Cr (VI), with both states highly toxic to animals, humans and plants [76] due to their ability to accumulate in tissues of organisms. Cr occurs naturally by the burning of oil and coal, petroleum from ferro chromate refractory material, pigment oxidants, catalyst, chromium steel, fertilizers, oil well drilling and metal plating tanneries. Anthropogenically, Cr is released into the environment through sewage and fertilizers [38,108]. Cr (III) is immobile in its reduced form and is insoluble in water whereas Cr (VI) in its oxidized state is highly soluble in water and thus mobile [116]. The health hazards associated with Cr exposure are dependent on its oxidation state, ranging from the low to high toxicity of the hexavalent form which has been classified as a carcinogen possessing mutagenic and teratogenic properties [108,112]. Cr has nutritive importance [57] in very small amount and plays an important role in glucose metabolism by serving as a cofactor for insulin action.

Most heavy metal poisoning treatment has primarily been by chelation therapy. The chelating agents bind to toxic metal ions to form complex structures which are easily excreted in urine and faeces from the body [32]. However, the use of natural products as alternative chelating agents in heavy metal toxicity treatment has not been fully explored. Mushrooms a source of biologically active compounds of medicinal and therapeutic values occur naturally in Nigeria during the early and late rainy seasons [35] and are usually found in forests, grasslands, damp rotten logs etc. *P. tuberregium* are common species widely consumed for their nutritional value, taste, aroma and nutraceuticals/medicinal properties [66,113]. Nearly 80% of the world's population relies on traditional medicines for primary health care, most of which involve the use of plant extracts [98]. A variety of compounds with important pharmacological properties have been isolated from mushroom, which include polysaccharides, polysaccharopeptides, polysaccharide-protein with immuno-enhancing and anticancer properties [114]. Also, other isolates have shown potential antiviral, antibacterial, antiparasitic, anti-inflammatory, and antidiabetic properties in preliminary studies [70]. Various researches have shown that mushroom lectin is a powerful scavenger of the superoxide anion, the hydroxyl radical and nitrogen dioxide [56]. *Pleurotus* spp. has been proven to have anticholesterolemic and antioxidant properties [4], blood lipid lowering effects [46,90], antihepatoma and antisarcoma activities [113].

Effects of heavy metals on several biochemical and haematological parameters have been studied by many researchers [47,51,81,95,102,110] however therapeutic role of mushrooms in heavy metal toxicity remain very scanty in literatures. Therefore, this study aims to evaluate the therapeutic application of *P. tuberregium* against arsenic and chromium induced toxicity using a battery of biochemical and haematological tests as valuable biological indicator.

2. Materials and methods

2.1. Experimental animals

Eighteen (18) healthy male albino rats of Wistar strain (*Ratus norvegicus*) of 8–10 weeks old weighing approximately 170–200 g were obtained from the Experimental Animal Unit of the Faculty of Veterinary Medicine, University of Ibadan, Nigeria. The study protocol followed the principles and Guide for the Care and Use of Laboratory animals of the National Institute of Health (NIH) [83]. The rats were acclimatized for 21 days in plastic cages at temperature (22 ± 2 °C), humidity (40 ± 10%) and 12 h light–dark cycle and given laboratory chow and tap water *ad libitum* before the experiment.

2.2. Chemicals

All chemicals used were of the analytical grade. Potassium dichromate ($K_2Cr_2O_7$) (Mol. wt., 294.18, CAs No. 7778-50-9) and Sodium arsenite (Na_2AsO_2, Mol. Wt., 129.9 As 57.6% CAS No 7784-46-5) were purchased from Rovet Scientific Limited Benin City, Nigeria.

2.3. Collection of fungi

Fresh fruiting bodies of *P. tuberreguim* were collected from Enwan community in Akoko-Edo Local Government area of Edo State. They were identified in the Department of Plant Biology and Biotechnology, University of Benin. Samples were taken to the laboratory of Ecotoxicology and Environmental Forensics for preparation of extract, determination of phytochemical properties and therapeutic bioassay test.

2.4. Preparation of extract

The methanol extract of *P. tuberregium* was prepared according to the method described by Ref. [107] with slight modifications. Briefly, freshly harvested whole matured mushrooms were thoroughly washed with cold sterile water and disinfected by treating with Mercury (II) chloride ($HgCl_2$) and washed again. The edible portions were carefully removed, cut into small piece using a stainless-steel blade and then air dried in shade under room temperature for seven days. Samples free of moisture and had crunchy appearance were separately crushed into fine powders using a blender. 100 g of crushed samples were mixed with 200 ml of pure methanol and were kept in a shaker (IKA400i, Germany) at 120 rpm and 30 °C for 48 h. The liquid extracts were filtered using Whatman No. 4 filter paper. The residue was then extracted with two additional 200 ml portions of methanol, as described earlier. The combined methanolic extracts were evaporated using a rotary evaporator (R-215, BUCHI, Switzerland) under a reduced pressure (100 psi) at a controlled temperature (40 °C) to remove the solvent and obtain the soluble components of the samples in a paste form. Each extract (the concentrated) (47.51%) extract (mass of extract × 100/mass of powder) was stored in a sterile container and preserved in a refrigerator at 4 °C for further use.

2.5. Chemical and bioactive profiling of mushroom

2.5.1. Proximate and mineral analysis

P. tuberregium edible mushroom species was analysed for food composition according to the method of Association of Official Analytical Chemists [5]. These include the determination of crude protein, fat, moisture content, ash, fibre, carbohydrate and minerals. Values for heavy metals were determined using Atomic Absorption Spectrophotometer (AAS). The percentage of all the fractions (crude protein, crude fat, minerals and ash) were added together and subtracted from 100 to obtain the total carbohydrate percentage.