DOI: 10.7860/JCDR/2017/21796.9671

Review Article

Physiology Section

Moringa oleifera Leaf Extract: Beneficial Effects on Cadmium Induced Toxicities - A Review

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ABSTRACT

Environment has been contaminated by heavy metals ever since the original magma of earth has solidified. One such toxin is cadmium. Cadmium that has been around since the industrial age, is considered hazardous both to us and to the environment. From time immemorial man is dependent on plants available in nature for several health benefits. *Moringa oleifera*, has nutritional, pharmacological and antioxidant properties, thus having several medicinal applications. In the present article, we discuss the dose and time dependent damage due to exposure to cadmium on kidneys, liver, testis, lipid profile and haematological parameters in adult Wistar rats and the protective effects of *Moringa oleifera* (pre-treatment) on cadmium induced damage.

Keywords: Haematological parameters, Kidney, Lipid profile, Liver, Testis

INTRODUCTION

Cadmium is a toxic metal occurring in the environment naturally and as a pollutant originating from industrial and agricultural sources. In today's non-smoking population worldwide, food has been found to be the main source of cadmium intake. The bioavailability, retention and toxicity of this environmental dangerous metal are affected by many factors, nutritional status such as low iron levels in the body being one of the most important factors. Cadmium is effectively retained in the kidney and its concentration is directly proportional to that in urine [1]. Furthermore, recent data also suggests that there is an increased mortality rate in environmentally exposed populations mostly due to the fact that there is actually no margin of safety between the point of release and the exposure levels of cadmium in the general population [1]. Pure cadmium is a soft, silver-white metal. The levels of this toxic hazardous metal in the environment have increased dramatically in the last few years as it is naturally emitted into the environment through volcanic activities, forest fires and generation of sea salt aerosols. Cadmium is mostly used in the production of batteries, pigments, coatings and platings, stabilizers for plastics, nonferrous alloys and photovoltaic devices. Studies have also shown that tobacco leaves accumulate high levels of cadmium from the soil. Cadmium is a major concern for people living near cadmium-emitting industries. Highest risk of occupational exposure occurs from processes involving heating cadmium containing materials such as smelting and electroplating. Exposure to this environmental pollutant can be prevented through personal protective equipment, though cigarette smoking is known to double the toxic effects [2]. Humans are generally exposed to cadmium by two main routes, inhalation and ingestion. Absorption of cadmium by skin is relatively insignificant [3]. This metallic toxicant accumulates in the target organs and affects cell physiology and growth [4,5]. The injurious effect of cadmium is related with diverse clinical manifestations like renal and hepatic dysfunctions, bone diseases, anaemia, immune toxic effects along with the alterations of the lipid profile, pulmonary oedema and testicular damage [6-8].

Numerous plants in nature possess medicinal properties. One among many is *Moringa oleifera*. This *Moringa oleifera* plant is one of the naturalized species of Moringaceae family. The tree thrives best under the tropical insular climate. *Moringa oleifera*, originally from India, is now distributed throughout the world. In some parts, it is often referred to as the drumstick or the kelor tree while in other places it is also known as Shagara al Rauwaq [9].

Best known as miracle tree, *Moringa* is an important tropical crop that is used as human food, medicine and in oil production [9]. It has a wide range of health benefits and hence extracts from different parts of *Moringa oleifera* could be used to combat various metal intoxications like cadmium, arsenic, lead etc., [10,11]. The leaves of this miraculous plant are a source of protein, β-carotene, vitamins (A,B,C,E, riboflavin), nicotinic acid, folic acid, pyridoxine, amino acids, minerals, various phenolic compounds. Leaves of *Moringa oleifera* are known to have hypolipidemic, anti atherosclerotic, antioxidant, hypotensive, tumour suppressive and immune boosting effect and also for its role in the prevention of cardiovascular diseases [12].

Pre treatment with *Moringa oleifera* leaf extract in cadmium exposed rats act against kidney injury and has a positive effect on anaemia. *Moringa oleifera*, the most widely distributed species especially in Asian countries, is known to have a wide range of pharmacological properties with significant nutritional values and hence have been scientifically evaluated for various medicinal applications [13,14]. It not only has a positive effect in lowering the lipid levels but also alters the levels of the liver enzymes and hence can also improve the liver functions [15,16]. It causes alterations in the testosterone levels, preventing testicular damage and hence is capable of protecting against the toxic effects of this hazardous material [8].

It is therefore in this light, we seek to establish the detailed correlation between biochemical alterations occurring in these organs on cadmium exposure and their normal functions on one hand and the therapeutic effects of aqueous leaf extract of *Moringa oleifera* on the other hand.

Antihepatotoxic Effects

Cadmium stimulates and binds to numerous organic elements like proteins and non-protein sulfhydryl groups, macromolecules and metallothionein [17]. Large numbers of enzymatic activities are influenced by cadmium and the mechanism of this effect has been hypothesized to be due to the displacement of a beneficial metal from the active site in the enzyme itself [18]. Exposure to cadmium for a short period of time affects the liver and therefore after exposure the liver is the primary organ that takes up the greatest quantity of cadmium during initial hours [19,20]. The liver damage is because of severe toxicity which is controlled by apoptosis and necrosis, the different forms of cell death [19]. Toxic action of cadmium on the liver is evidenced by the elevation in the levels of plasma

Aspartate Aminotransferase (AST) or Serum Glutamic-Oxaloacetic Transaminase (SGOT) and Alanine Aminotransferase (ALT) or Serum Glutamic Pyruvic Transaminase (SGPT) which indicates liver damage and this may be due to hepatocellular necrosis, which causes increase in the permeability of the cell membrane resulting in the release of transaminases in the blood stream. The increase in alkaline phosphatase activity represent general hepatic toxicity [21,22]. The therapeutic effects of *M.oleifera* include anti hepatotoxic effect as well. Inspite of having a toxic effect on the liver by itself, which is seen as an increase in the plasma AST and ALT levels [16,23].

Moringa oleifera shows a decrease in the plasma levels of AST and ALT activities in substantial amounts in cadmium induced liver damage [24]. The efficiency of *Moringa oleifera* leaf extract could be due to the antagonistic effects of antioxidants on cadmium induced necrosis [25]. The reversal of elevated serum intracellular enzyme levels by *Moringa oleifera* extract may be attributed to the stabilizing ability of the cell membrane preventing enzyme leakages as earlier postulated [26]. Previous study reported hepatoprotective effect was due to presence of Quercetin and kaempferol [27].

Erythropoietic Effects

Cadmium exposure causes toxic effects on the haematological parameters. An appreciable decrease in the Red Blood Cell (RBC) count, Packed Cell Volume (PCV) (as it increases lipid peroxidation, thereby causing destruction of cell membrane of the erythrocytes), Haemoglobin (Hb) concentration is evidenced, with an increase in the Mean Corpuscular Volume (MCV) and a reduction in the Mean Corpuscular Haemoglobin (MCH) [14,28]. The fall in haemoglobin (Hb) concentration can be attributed to the production of Reactive Oxygen Species (ROS) [29]. All these can lead to cadmium induced anaemia [28]. *Moringa oleifera* leaf preparations have been cited in the scientific literature as having medicinal values of which communities take advantage of and the antioxidant properties of *Moringa oleifera* leaves have been evaluated and hence the plant extracts have been recommended for use in treatment of various diseases [30-33]. Therefore, the role of *Moringa oleifera* on blood parameters was evaluated as well. Literature has shown that, the leaves of this miraculous plant are an outstanding source of vitamins (A,B,C), iron and proteins [34,35]. So, pretreatment with *Moringa* leaf extract, presented a remarkable increase in the haematological parameters, like RBC count, Haemoglobin (Hb) concentration, PCV, MCH and a decrease in MCV [14].

Accordingly the *Moringa oleifera* aqueous leaf extract, acts against cadmium induced anaemia.

Hypolipidemic Effects

Cadmium induces lipid peroxidation by stimulating the production of superoxide anions and inhibits antioxidants such as glutathione peroxidase and superoxide dismutase and cause accumulation of free radicals that damage the cells and produce chronic disease [36]. The lipid profile too gets altered by cadmium exposure as the lipid and lipoprotein abnormalities play significant role in the pathogenesis and progression of atherosclerosis and cardiovascular diseases [37,38]. Administration of cadmium causes a dose dependent increase in the plasma triglyceride levels with increased concentrations of Low Density Lipoproteins (LDL) and Very Low Density Lipoprotein (VLDL) cholesterol fractions along with increase in plasma total cholesterol levels and a marked reduction in the High Density Lipoprotein (HDL) cholesterol level, suggesting that lipid profile was affected by cadmium exposure [15]. The modulation in lipid levels might be due to cadmium induced oxidative stress leading to a high level of hydroperoxides (LOOH), low paraoxonase activity, etc. Studies have demonstrated that the toxicity of cadmium may partly be due to its disruption of lipid metabolism as there is modulation of cholesterol homeostasis as well as interference with lipid transport. Some of these dysfunctional states elicited by cadmium may be linked to its ability to induce oxidative stress in cellular systems [39].

Since research has shown a strong independent relation between plasma triglyceride concentrations and the likelihood of cardiovascular disease, the therapeutic effects of aqueous leaf extract of *Moringa oleifera* were considered as it has an amelioratic effect on lipid profile [40]. This effect is chiefly due to its potential to control the mechanisms involved in elimination of lipids from the body [41,42].

As a result, pretreatment with *Moringa oleifera* leaf extract presented a decrease in the total cholesterol level, triglyceride, LDL and VLDL cholesterol fractions with an increase in the HDL cholesterol levels thereby having beneficial effect on lipid profile in cadmium exposed rats [15].

Antinephrotoxic Effect

Exposure to cadmium can lead to the absorption of this metal in huge amounts and produce toxic actions on the organism [43]. The most harmful effect is probably renal tubular damage [44,45]. Cadmium produced considerable local haemorrhage of the renal tissues [46]. In cadmium alone treated rats, the increase in the serum urea and creatinine levels are observed, which indicates nephrotoxicity [47]. This in turn is suggestive of a definitive oxidative stress on the kidneys.

Moringa oleifera leaves are found to be a potential source of natural antioxidants and are therefore reported to possess antinephrotoxic effects [48]. Pretreatment with *Moringa oleifera* leaf extract in cadmium exposed rats, presented a noteworthy decrease in the levels of serum urea and serum creatinine levels indicating antinephrotoxic potential [13]. The leaves of this plant are a good source of phenolic compounds, β carotene etc., which may be the reason of this decrease, although the actual mechanism of action may be more complex and multifaceted [49].

Therefore, pretreatment with *Moringa oleifera* leaf extract enhances the kidney functions.

Effect on Male Reproductive System

In addition to various health hazards, cadmium is known to cause toxic effects on testis as well. More than a few reports have revealed that testicular toxicity of cadmium results in male spermatogenic and steroidogenic impairment [50,51]. On an oral administration of cadmium, a severe testicular toxicity was seen. Additionally cadmium is proven to also directly trigger destruction to the hypothalamus-pituitary gonadal axis leading to atrophy of the accessory sex organs such as the prostate as well [52,53]. The outcome of this will be a reproductive dysfunction. This impairment is characterised by destruction of germ cells and seminiferous tubules, vascular congestion, focal necrosis of tissue, reduction of spermatocytes, pyknosis, destruction of nucleus, oedema in the seminiferous tubules and interstitial tissue. A reduction in the testicular weight/body weight, testosterone levels and increase in the testicular content of Malondialdehyde (MDA) is also observed [8]. When exposed to cadmium, testis get toxicity by generating reactive radicals, the consequences being cellular damage like diminution of the enzyme activities, damage to the lipid bilayer and DNA and hence amounting to the amplified damages in the proteins and DNA due to oxidative stress [54]. This may explain the reduced testis weight/body weight and plasma testosterone levels [55,56]. For this reason, increase in testicular level of MDA proved that cadmium caused oxidative stress leading to testicular injury. Evaluation of lipid peroxidative activities in tissues is constantly employed as a biomarker for tissue damage and the disruption of the testes-pituitary axis contributes to the testicular and pituitary destructions [57]. Exposure of animals to cadmium induced oxidative stress, stimulates the synthesis of cadmium binding proteins metallothioneins (MT) and heat proteins [17]. *Moringa oleifera* due to its antioxidative potential prevented the toxicity brought about by cadmium exposure and this is evidenced

by an increase in the plasma testosterone levels coupled with a decrease in the testicular MDA levels [47].

Studies have revealed that pretreatment with *M.oleifera* leaf extract shields testis from a variety of toxic substances and helps in protecting the testis against oxidative changes brought about by toxic materials [57].

CONCLUSION

Cadmium is an environmental toxin that is hazardous to health. Nutritional status of the body is one of the most important factors affecting its bio-availability, retention and toxicity. Cadmium exposure for a short period of time affects mainly the liver though lung cancer has been found in a lot of workers exposed to cadmium in the air. Its exposure can also lead to cadmium induced anaemia along with the modulation in lipid levels mostly due to its ability to induce oxidative stress in cellular systems. Cadmium is known to cause kidney tubular damage along with bone damage, either via a direct effect on bone tissue or indirectly as a result of renal dysfunction. *Moringa oleifera,* is a medicinal plant for the treatment of a wide variety of conditions. In cadmium exposed adult Wistar Albino rats, pretreatment with aqueous leaf extract has been found to play *a* protective role. The leaves of this plant have antioxidant properties which facilitates it to combat cadmium induced toxicity on kidneys, liver, blood, testis and also on lipid profile, like HDL and LDL levels.

However, detailed mechanisms triggering these therapeutic effects need to be explored.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jul 22, 2016**
Date of Peer Review: **Oct 30, 2016**
Date of Acceptance: **Nov 30, 2016**
Date of Publishing: **Apr 01, 2017**