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Rejuvenation of Cadmium Induced Electrolyte Imbalance by Mentha Piperita

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Abstract- Health hazards caused by heavy metals have become a great concern to the population. Excessive industrial effluents, pesticide application and biomedical activities load a large amount of metals and metalloids to the environment. Cadmium is one of these, with high rate of bioaccumulation and extreme toxicity at low concentration. Cadmium is exposed to air and water through a number of industrial sources including mining, pesticides, alloys, electroplating, food and cigarette-smoking etc. WHO permitted limit for cadmium in drinking water is 0.005 mg/L whereas in Indian standard it is 0.01 mg/L. In India there are some places where groundwater cadmium concentration is far beyond this limit. Pali, in Rajasthan is a place where this concentration is reported to be 0.224 mg/L.

Present study has been designed with the aim of social welfare as well as an eco-healthy approach to find out impact of orally administered cadmium on the hepatic enzymatic system in model organism albino rat and its amelioration by *Mentha piperata*.

Acute and sub-acute cadmium administration induces a significant hyponatremia, hypochloremia and hyperkalemia in albino rat, which were brought to normalcy after pretreatment with *Mentha piperata*, containing terpenoids as an antioxidant after acute and sub acute treatment.

Experimental results therefore reveal protective effect of pretreatment with *Mentha piperata* under stress of cadmium in albino rat.

Index Terms- Cadmium, *Mentha piperita*, serum electrolytes, albino rat.

I. INTRODUCTION

Natural and anthropogenic activities have being contributing to the spread of toxic chemicals into the environment, including several toxic metals and metalloids (Fig. 1) (Roy and Saha, 2002). Pollution due to heavy metal is the major challenge of present scenario. Cadmium is the industrially applicable heavy metal; most of electronic and electric goods consist of a noticeable amount of cadmium. Rechargeable Batteries contains about 6% of cadmium. Indiscriminate and illegal disposal of these goods have introduced a heavy flow of these metals in ground water table and thus in food chain. Major sources of cadmium exposure are mining, batteries, electronic and electrical goods, electroplating, vapor lamps, engraving, fertilizers, smoking, soldering, and old galvanized PVC water supply pipes etc.

Among possible target organs of heavy metals, the kidney and CNS appear to be the most sensitive ones. Any alteration in kidney or the part of kidney due to induction of cadmium may be responsible for improper renal functioning. Evaluation of serum electrolytes provides vital information about renal functions, hence have been considered as possible biomarkers of renal dysfunctioning

The various indigenous system of medicines such as Siddha, Ayurveda, Uanai and sometimes allopathy use several plant species for the treatment of degenerative diseases (Bhakta *et al*., 2001), *Mentha piperita* (pippermint) is one of them. These medicines are commonly used to obviate profound side effects of modern drugs (Abebe, 2002). It is a perennial herb that grows up to 1 meter (3 feet) high and has slightly hairy serrated leaves with pinkish-mauve flowers arranged in a long conical shape. It has underground runners by which it easily propagates. Peppermint oil is extracted from the whole plant above ground just before flowering by steam distillation

II. MATERIALS AND METHODS

Eighty adult male Wister albino rats (*Rattus norvegicus*) of almost same age and weight (100 ± 10 gm), were procured from inbred colony. They were acclimatized at room temperature with 12 hr dark/light cycle and fed on standard diet and water *ad-libitum.* All experiments were performed as per animal institutional ethical committee (**360/01/CPSEA/2001**).

The experimental compound cadmium was obtained from Merck, India and its LD_{50} was calculated to be 88 mg/Kg body weight by log dose /probit regression line method (Finney, 1971).

Mentha aerial parts were collected from local fields and subjected to hydro distillation for obtaining essential oil. Further, the oil was analyzed by GC/MS to find the major constituents. A safety trial was performed to set the safe dose of oil and it was found to be 500 mg/100 gm body weight.

Animals of acute and sub-acute sets were divided into four groups viz. control, cadmium treated, Mentha + cadmium treated and Mentha treated. Doses of respective sets and groups are listed in Table – 1.

Table – 1: Acute and sub-acute doses of cadmium chloride and *Mentha piperata* for *Rattus norvegicus*

Groups / Sets	Group-A (Control)	Group- B (Cadmium treated)	Group- C (Mentha treated)	Group- D (Mentha + cadmium treated)
Set: I Acute (1 d)	Water	8.8 mg/kg body weight	500 mg/kg body weight	500 mg/kg body weight + 8.8 mg/kg body weight
Set: II Sub-acute (7 ds)	Water	1.26 mg/kg body weight	500 mg/kg body weight	500 mg/kg body weight + 1.26 mg/kg body weight
Set: III Sub-acute (14 ds)	Water	0.63 mg/kg body weight	500 mg/kg body weight	500 mg/kg body weight + 0.63 mg/kg body weight
Set: IV Sub-acute (21 ds)	Water	0.42 mg/kg body weight	500 mg/kg body weight	500 mg/kg body weight + 0.42 mg/kg body weight

At the end of designated days the animals of respective sets were sacrificed to determine the renal functions. The blood samples were collected from the ventricle of heart and serum was separated for the determination of **serum Na^+** and **K^+** by colorimetric method (Bassir, 1971) and **Serum Cl^-** by thiocyanate method (Skeggs and Hochstrassman, 1964).

The data were analysed using one-way analysis of variance (ANOVA) followed by student Newman–Keul's (SNK) test. Differences with $P<0.05$ were considered as significant (Glantz, 1992).

III. RESULTS

Results in Table-2 show that cadmium intoxication induces significant hyponatremia, hypochloremia and hyperkalemia, after acute (1 day) and sub-acute (7, 14 and 21 days) treatments. However these altered levels of serum electrolytes were brought to normalcy preceding treatment with Mentha.

Table – 2: Effect of Mentha piperita against cadmium intoxication on serum electrolytes of albino rats.

Serum Electrolytes	Treatment days	Control	Cadmium treated	Mentha treated	Mentha + Cadmium treated
Na^+ (mEq/l)	1 day	141 ± 1.15	137 ± 0.58*	140.33 ± 0.33	138 ± 0.57*
	7 days	142 ± 1.00	135.33± 0.88*	140.66 ± 0.88	138.66 ± 0.33
	14 days	142 ± 1.52	134 ± 1.15*	141 ± 1.15	139 ± 0.23
	21 days	141 ± 0.58	132 ± 0.58*	142 ± 1.15	140 ± 1.15
K^+ (mEq/l)	1 day	4.17 ± 0.03	4.54 ± 0.04*	4.20 ± 0.01	4.44 ± 0.01*
	7 days	4.19 ± 0.02	4.82 ± 0.01*	4.21 ± 0.01	4.38 ± 0.02*
	14 days	4.18 ± 0.02	5.18 ± 0.10*	4.16 ± 0.02	4.35 ± 0.02
	21 days	4.17 ± 0.01	5.84 ± 0.07*	4.21 ± 0.01	4.30 ± 0.03
Cl^- (mEq/l)	1 day	103 ± 1.15	98 ± 0.57*	102.5 ± 1.04	99.66 ± 0.33*
	7 days	102 ± 1.15	97 ± 1.00*	101.16 ± 0.68	100 ± 0.91
	14 days	102 ± 1.15	94 ± 0.57*	101.5 ± 0.76	98 ± 1.00
	21 days	103 ± 1.00	93 ± 0.57*	101 ± 1.15	99 ± 1.00

values are expressed as mean ± SEm.
* P < 0.05

IV. DISCUSSION

Rate and health effects of cadmium depend on its route of exposure. Cadmium is a cumulative toxin with a slow rate of elimination, accumulating mainly in the liver and kidneys. Cadmium poisoning is not reversible. It stays in the system for a very long time and excreted very slowly via metallothionein, the major excretory protein of kidney. Its biological half-life is 10 years, staying for a larger part of life. (Longe, 2005; Darwish et al., 2002) Besides cadmium's long half-life, the body lacks ability to metabolize it properly. Replacement of zinc and calcium inside the body is also an important mechanism of cadmium toxicity (Sutoo et al., 2002).

Cadmium is known to increase oxidative stress by being a catalyst in the formation of reactive oxygen species, changing body metabolism of different biochemicals. Toxicity is caused by lipid peroxidation, free radical production and depleting glutathione and protein-bound sulfhydryl groups. Cadmium inhibits glutathione peroxidases resulting in reduced defense against the lipid peroxidation. (Novelli et al., 2000, Congui et al. 2000) Cadmium also stimulates the production of inflammatory cytokines and downregulates the protective function of nitric oxide formation (Navas-Acien *et al.* 2004).

Cadmium intoxication caused significant hyponatremia, hypochloremia and hyperkalemia that might be due to attachment of cadmium with proteins of renal tubular epithelium and thus producing ROS. Cadmium causes peroxidation of polyunsaturated fatty acids (PUFA) in biological membranes, leading to decrease in membrane fluidity and membrane integrity which delocalizes the enzyme Na-K ATPase from basolateral to apical membrane, resulting in electrolyte imbalance (Schnellman and Kelly, 2008).

Besides cadmium damages juxtaglomerular apparatus, due to which renin secretion gets decreased, and probable disturbance in renin – angiotensinogen pathway generally causing aldosteron reduction resulting in electrolyte imbalance (Rhods and Tadnner, 1995; Wang and Giebisch, 1996 and Ellison, 2008).

Cadmium promotes lipid peroxidation, producing free radicals which damage the glomerular filtration membrane and ultimately reduces GFR (Hussain, 2002). Damage in tubular epithelium causes diffusion and backleak of the filtrate across the tubular basement membrane back into interstitium and circulation. Thus both decreased GFR and backleak of filtrate leads to imbalanced serum electrolytes.

GC/Ms analysis of *Mentha piperita* reveals that terpenoids including hydrocarbon and oxygen derivatives of mono and sesquiterpenoids like terpinol, limonene and p-cymene etc. are its major constituents. These terpenoids are found to possess antioxidant property (Youdin *etal.*,2002; Grassman *etal.*,2005 and Vickers *etal.*,2009).They may arrest oxidative stress at several levels of endogenous antioxidant mechanism. Being lipophilic in nature, they stabilizes hydrophobic interactions in the membrane thus minimizes lipid peroxidation. (Vickers *etal.*,2009) Reduction in oxidative stress could be well understood as below-

$$SOOH + metal \longrightarrow SOO^{\bullet} + metal^{(n-1)} + H^+$$
$$SOO^{\bullet} + AH \longrightarrow SOOH + A^{\bullet}$$
$$A^{\bullet} + x^{\bullet} \longrightarrow \text{Non radical complex}$$

Where, S = Substance oxidized
AH = Antioxidant molecule
$A^{\bullet}$ = Antioxidant radical
$x^{\bullet}$ = another radical

Inhibition of ROS stabilizes the membrane integrity, reverting Na^+- K^+ ATPase back at its location and recovery of Jxtraglomarular apparatus thus in turn regaining the electrolyte imbalance.

The present findings conclude that *Mentha piperita* prevents the oxidative damage by cadmium induced ROS, due to its antioxidant property. Further, ameliorating the impaired renal functions associated with cadmium toxicity in albino rats and offers itself as a novel drug for future.

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