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TO STUDY HAEMATOLOGICAL RESTORATION POTENTIAL OF *MENTHA ARVENSIS* AND *MYRISTICA FRAGRANS* AGAINST ARSENIC INDUCED TOXICITY

Sweety Sinha[1], Birendra Kumar[1], Arun Kumar[2], Sunil Kumar[3] and Ranjit Kumar[3*]

[1]Magadh University, Bodh-Gaya.
[2]Mahavir Cancer Sansthan and Research Centre, Patna.
[3]Central University of Himachal Pradesh, Kangra.

***Corresponding Author: Dr. Ranjit Kumar**
Central University of Himachal Pradesh, Kangra.

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ABSTRACT

Arsenic toxicity is a global health problem affecting many millions of people. Since last decade, the wide spread nature of human exposure to arsenic in drinking water has become very apparent in many countries. Very long time exposure to arsenic has been associated with cancer in skin, lungs, urinary bladder, kidney, and liver as well as various non-cancer effects. Various non-cancer effect of arsenic include Keratosis, diabetes, cardiovascular disease, pigmentation. Mentha arvensis are commonly known as mint. It is traditionally used medicinal plants for many diseases since ancient times. Myristica fragrans is commonly known as nutmeg, it possess very high antioxidant property. It is also used in treatment of wide variety of disease. Present study is designed to find comparative hepatoprotective effect of Mentha arvensis and Myristica fragrans against arsenic induced toxicity in rats. Arsenic were administered 8 mg/kg body weight for 8 weeks followed by administration of Mentha arvensis 200 mg/kg body weight for 12 weeks and Myristica fragrans 300 mg/kg body weight for 12 weeks. After scheduled treatment blood were collected for analyzing RBC, haemoglobin, WBC and haematocrit value. Arsenic caused marked increase in RBC, haemoglobin, WBC and haematocrit value, while these medicinal plants were effectively restored the haematological parameters in rats. It is evident from study that Mentha arvensis & Myristica fragrans play a very effective and vital role in controlling deleterious effect caused by sodium arsenite by normalizing the haemotological parameters. Myristica fragrans restores haematological parameters more effectively in comparision to Mentha arvensis.

KEYWORDS: SGPT, hepatotoxicity, arsenic, skin lesions, toxicity.

1. INTRODUCTION

Arsenic toxicity is a global health problem affecting many millions of people. Since last decade, the wide spread nature of human exposure to arsenic in drinking water has become very apparent in many countries. The contamination of groundwater from arsenic and its impact on human health have formerly been recited from 23 regions in different parts of the world. The consequence of this particular problem is found to ascetic in Bangladesh (Mukherjee et al., 2003) ensued by west Bengal, India(Chakraborti et al.,2002) and China (Liu et al, 2010). The transfer of As to the food chain will ultimately remain as long-term risks to human and ecological systems (Tuli et al., 2010). In India, the major or highly affected area from arsenic contamination has been detected in the states of Bihar, Uttar Pradesh, Jharkhand, Assam, Chhattisgarh and Andhra Pradesh(Nikson et al., 2007) and in the river basin of the Ganga, Brahmaputra and Meghana in India and Bangladesh. It was estimated that 25 million people in Bangladesh and 6 million people in West Bengal, India were exposed to arsenic contaminated groundwater (Chakraborti et al, 1987). The previous studies on skin lesion have been cross sectional in complexion and has attention on current vulnerability (Chen et al., 2010). The risk of cancer may be cosequences even without skin lesion, although the state of existence has been seen in present (Environmental Protection Agency(EPA), 1998). Arsenic is equally toxic for all the organs but the most sensitively target organ is kidney. Very long time exposure to arsenic has been associated with cancer in skin, lungs, urinary bladder, kidney, and liver (ASTDR, 2000) as well as various non-cancer effects. Various non-cancer effect of arsenic include Keratosis, diabetes, cardiovascular disease, pigmentation e.t.c. (IARC, 2004)

Myristica fragrans is an aromatic fruit from Myristiceae family that are mainly cultivated in several countries, including Indonesia, Caribbean Island, Malaysia and India. Skin, pulp, mace and seed have been widely used traditionally in Ayurvedic, Chinese and Thai medicine [Somani et al, 2008]. Nutmeg been reported to possess many distinct advantages, some of them are: anti-diarrheal activity, stimulant, antidiabetic, antifungal,

carminative and anti-inflammatory properties (Gowri et al, 2008 and Yanti et al, 2008). Anti-oxidant property of nutmeg is contributed by various phytochemicals, mainly vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignans, simple phenols and phenolic acids (Tan et al, 2013). Myristica fragrans regulates the expression of MMP-1 and type I procollagen in UV-irradiated human skin fibroblasts (Kyung-Eun et al, 2012).

M. arvensis originated in Eurasia. The plant is native to the temperate regions of Europe, western and central Asia. It is commonly known as pudina in Hindi. Traditionally, mint is a very beneficial and important plant, as since ancient times it is extensively used in cuisines, medicaments and cosmetics (Saeed et al, 2006). Leaves of mint is effective in seeking relief from gastric distension, flatulence, dizziness, pregnancy related vomiting and as a cure for various bodily inflammations including bronchitis (Arumugam et al, 2008). The herb was found to be of a great therapeutic benefit when employed as a counteracting agent to flu and inflammation inducing processes of the oropharyngeal region, sinus tracts and cavities and of hepatobiliary and gastrointestinal origin (Rodriguez et al, 2008; Vidal et al, 2007).

Thus the present study is designed to find haematological restoration potential of *Mentha arvensis* and *Myristica fragrans* against arsenic induced toxicity in rat.

2. MATERIAL AND METHODS

2.1 Animals: Rat (Charles foster), weighing 180 g to 250 g of 12 weeks old, were obtained from animal house of Mahavir Cancer Institute and Research Centre, Patna, India (CPCSEA Regd-No. 1129/bc/07/CPCSEA). The research work was approved by the IAEC (Institutional Animal Ethics Committee) with IAEC No. 2015/3E-16/12/15. Food and water to rats were provided ad libitum (prepared mixed formulated food by the laboratory itself). The experimental animals were housed in conventional polypropylene cages in small groups (2 each). The rats were randomly assigned to control and treatment groups. The temperature in the experimental animal room was maintained at 22˚C ± 2˚C with 12 h light/dark cycle.

2.2 Chemicals: Chemicals: Sodium Arsenite (98.5%) manufactured by Sigma-Aldrich, USA (CAS Number: 7784-46-5), was obtained from the Scientific store of Patna of Bihar India.

Medicinal plant used: Leaf extract of *Mentha arvensis* (Mint) and Seed extract of *Myristica fragrans* (Nutmeg) was used as antidote.

2.3 Preparation of *Mentha arvensis* (Mint) and Seed extract of *Myristica fragrans* (Nutmeg) aqueous extract: In the present study, leaf of mint and seed of nutmeg were dried properly and powdered. The doses were dissolved as per requirement on every day for administration.

2.4 Chronic Toxicity Study: Selected pathogen-free rats were sorted and sodium arsenite was administered at the dose of 8 mg/kg body weight dose for 8 weeks by Gavage method. Sacrifices were done at the end of 8th week of Sodium arsenite administration in each group.

2.5 Bioremediation study: Sodium arsenite administration 8 mg/kg body weight for 8 weeks was followed by the administration of leaf extract of *Mentha arvensis* (Mint) for 12 weeks at the dose of 200 mg/kg body weight and Seed extract of *Myristica fragrans* (Nutmeg) for 12 weeks at the dose of 300 mg/kg body weight. Animals were sacrificed on 12th weeks of administration.

2.6 Biochemical Assessment: Blood samples were collected by orbital puncture for carring out haematological alteration. Haematological analysis was performed through standard protocol. RBC, haemoglobin, haematocrit percentage, MCV, MCH, MCHC and WBC were carried out.

2.7 Statistical Analysis: Results are presented as mean ± S.D and total variation present in a set of data was analysed through one-way analysis of variance (ANOVA). Difference among means has been analysed by applying Dunnett's "t" test at 99.9% ($p < 0.05$) confidence level. Calculations were performed with the GraphPad Prism Program (GraphPad Software, Inc., San Diego, USA).

3. RESULTS

R.B.C. count in control rats was 7.17 ± 0.16 X 10^6 cu. mm^3 while in arsenic8 weeks treated group it was 2.77 ± 0.12 X 10^6 cu. mm^3. In *Mentha arvensis* and *Myristica fragrans* administered group of rats R.B.C. count was 4.65 ± 0.23 X 10^6 cu. mm^3 and 5.01 ± 0.19 X 10^6 cu. mm^3after 12 weeks respectively (Table - 1).

Haemoglobin percentage in control rats was 90.8 ± 1.08 g/l while in arsenic8 weeks treated group it was 52.42 ± 0.73 g/l. In *Mentha arvensis* and *Myristica fragrans* administered group of rats haemoglobin percentage was 67.1 ± 2.07 g/l and 74.1 ± 1.83 g/l after 12 weeks respectively (Table - 1).

Haematocrit count in control rats was 272 ± 3.08 % while in arsenic8 weeks treated group it was 148 ± 0.87 %. In *Mentha arvensis* and *Myristica fragrans* administered group of rats haematocrit count was 190 ± 3.14 % and 241 ± 2.91 % after 12 weeks respectively (Table - 1).

MCV count in control rats was 364 ± 18.6 fL while in arsenic8 weeks treated group it was 562 ± 8.96 fL. In *Mentha arvensis* and *Myristica fragrans* administered

group of rats MCV count was 497 ± 6.43 fL and 395 ± 5.78 fL after 12 weeks respectively (Table - 1).

MCH count in control rats was 127 ± 1.40 pg while in arsenic8 weeks treated group it was 202 ± 1.79 pg. In *Mentha arvensis* and *Myristica fragrans* administered group of rats MCH count was 181 ± 2.01 pg and 169 ± 1.97 pg after 12 weeks respectively (Table - 1).

MCHC count in control rats was 33.4 ± 0.036 g/L while in arsenic8 weeks treated group it was 31.6 ± 0.01 g/L. In *Mentha arvensis* and *Myristica fragrans* administered group of rats MCHC count was 32.2 ± 0.034 g/L and 32.9 ± 0.017 g/L after 12 weeks respectively (Table - 1).

W.B.C. count in control rats was 7500 ± 28.9 X 10^3/mm^3 while in arsenic8weeks treated group it was 15169 ± 12.3 X 10^3/mm^3. In *Mentha arvensis* and *Myristica fragrans* administered group of rats W.B.C. count was 10221 ± 7.62 X 10^3/mm^3 and 8705 ± 4.38 X 10^3/mm^3after 12 weeks respectively (Table - 1).

Table-1: Showing haematological analysis in arsenic and *M. arvensis* and *M. fragrans* administered group.

Blood parameters	Control (n= 6)	Arsenic 8 weeks (n= 6)	*Mentha arvensis*12 weeks(n= 6)	*Myristica fragrans* 12 weeks (n= 6)
RBC Counts (10^6 /mm^3)	7.17 ± 0.16	2.77 ± 0.12	4.65 ± 0.23	5.01 ± 0.19
Hb (g/L)	90.8 ± 1.08	52.42±0.73	67.1 ± 2.07	74.1 ± 1.83
Haematocrit percentage (Hct) (%)	272 ± 3.08	148 ± 0.87	190 ± 3.14	241 ± 2.91
MCV (fL)	364 ± 18.6	562 ± 8.96	497 ± 6.43	395 ± 5.78
MCH (pg)	127 ± 1.40	202 ± 1.79	181 ± 2.01	169 ± 1.97
MCHC (g/L)	33.4 ±0.036	31.6 ± 0.01	32.2 ± 0.034	32.9± 0.017
WBC (10^3/mm^3)	7500 ±28.9	15169 ±2.3	10221 ±7.62	8705 ± 4.38

The data are presented as mean ± S.D, n = 6, significance at p< 0.0001.

4. DISCUSSION

Eugenol is a naturally occurring allyl benzene and an active component of leaves of *M. arvensis*. It has been shown to induce detoxification enzymes conjugating many xenobiotics (Yokota et al., 1988).*M. arvensis* has significantly contributes to the free radical scavenging effects of the mint extract (Choudhary et al, 2006). Caffeic acid (3,4-dihydroxycinnamic acid) is among the major hydroxycinnamic acids present in *M.arvensis*. It is recently found to be a potent free-radical scavenger and antioxidant (Ozguner et al., 2006). The ensuing cellular damage or oxidative injury seems to be a major predisposing factor behind a range of ailments like cardiovascular problems, inflammations, viral afflictions, autoimmune disorders, gastrointestinal disorders and diabetes (Bupesh et al, 2007). The anti-inflammatory effect of the compounds can be due to the inhibition of inflammatory mediators which are presumed to have role in the production of reactive oxygen species (ROS), that mint leaves based on ethanol can abate the process of chronic inflammation through their antagonistic effects on oxidation (Arumugam et al, 2008). In present study we find very effective restoration in RBC, WBC, haemoglobin and haematocrit in *M. arvensis* administered group.

Mystica fragrance showed that High dose contains more saponin than the medium and low doses and this may be the reason for non-significant effects observed at the medium and low dosage levels for red blood cell (RBC) count, packed cell volume (PCV), haemoglobin concentration (HbC) (Bamidele et al., 2011). Mystica fragrance also shows the CNS activity, antihelmintic, insecticidal, apoptotic, and protection against DNA damage effects due to presence of myristicin (Morita et al. 2003). Various phytoestrogens, especially isoflavones, have demonstrated beneficial clinical effects against bone loss in both preclinical and clinical studies (Mohammad **e**t al. 2013). Anti-inflammatory and protective effects of macelignan observed in animal models of diabetes and hepatotoxicity (Kareem et al. 2013). It our study least restoration were observed in biochemical profile of liver after *M. fragrance* administration.

8. CONCLUSIONS

It is evident from study that *Mentha arvensis* & *Myristica fragrans* play a very effective and vital role in controlling deleterious effect caused by sodium arsenite by normalizing the haemotological parameters. *Myristica fragrans* restores haematological parameters more effectively in comparision to *Mentha arvensis.*

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