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PROTECTIVE EFFECTOF *CURCUMA AROMATICA* AGAINST NICOTINE-INDUCED OXIDATIVE STRESS IN THE FEMALE RATS

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ABSTRACT

Oxidative stress (OS) has been considered a major contributory factor to the infertility. Oxidative stress is the result of imbalance between the reactive oxygen species (ROS) and antioxidants in the body which can lead to damage to oocytes in developing follicles, or the embryo in the fallopian tube. The protective effect of *Curcuma aromatica* (100 mg/kg bw /day) against ovarian and uterine oxidative stress induced by subcutaneous injection of nicotine (4mg/kg bw/day), was studied. After 30 days of nicotine treatment increased production of malondialdehyde in the nicotine-treated group which was accompanied by marked alterations in the levels of activities of superoxide dismutase, catalase, GPx and GST. Compared to nicotine alone, the combined treatment of nicotine with *Curcuma aromatica* significantly lowered the level of lipid peroxides and enhanced the antioxidant status. The group of rats given *Curcuma aromatica* without exposure to nicotine exhibited no significant changes in the above indices. Thus the results from this study showed that *Curcuma aromatica* exerted a protective action against nicotine-induced oxidative stress and disturbance of ovarian and uterine functions in the rat.

KEYWORDS: Nicotine, ovary toxicity; *Curcuma aromatica*, ovarian and uterine oxidative stress.

INTRODUCTION

Reproduction is an exceptionally complex process being highly vulnerable at many stages. The environmental and life style factor have an adverse effect on fertility.

Smoking has deleterious effects on cardiovascular, pulmonary physiology and reproductive system. In women, smoking is associated with infertility, spontaneous abortion, menstrual abnormalities, ectopic pregnancies and early onset of menopause.[1] Nicotine disrupts antioxidant mechanism.[2] by enhancing Reactive Oxygen Species (ROS) production and thereby decreases the antioxidant level causing peroxidative tissue damages.[3] Oxidative stress (OS) affects multiple physiological processes, from oocyte maturation to fertilization, embryo development and pregnancy. Antioxidants act as scavengers to neutralize free radicals and have generated considerable interest in overcoming the adverse and pathological results of the OS.

Curcuma aromatica is distributed throughout India and is widely used as a flavouring agent, condiment and a source of yellow dye. Medicinally, it possesses strong antimicrobial effect. It is a well listed drug in Ayurveda and other indigenous systems of medicine. The rhizomes of *C. aromatica* possess a reputed property to promote health conditions by arresting ageing and have immunomodulatory effects. From ancient times, it is being used as an antibiotic against various microbial infections.[4] Historically, rhizomes are used as tonic, carminative, and externally in combinations with astringents, bitters and aromatics to brusises, in sprains and in snake-bite. They are also used for skin eruptions and infections.[5] Present study was undertaken to investigate the fertility activity of *Curcuma aromatica* in nicotine induced reproductive toxicity by oxidative stress.

Experimental Design

Normal cycling, healthy albino female rats of 80 days were used for the experiment. The animals were maintained in the standard laboratory conditions and fed with balanced diet as prescribed by Amrut Laboratory Animal Feed, Pranav Agro Industries Ltd., Bangalore, India and water ad libitum at room temperature of 28 ± 2°C. The animals were divided into four groups, each consisting of 4 animals. Based on the earlier studies in our laboratory the effective dose 0.4 mg/100g body weight was selected for nicotine. The treatment was started from estrous phase of the cycle only as the ovarian and uterine activities change markedly from one phase to another phase.

Female rats were divided four groups. Group I control, group II nicotine induced, group III nicotine induced and drug treated and group IV only drug treated. Group II received subcutaneous injection of nicotine tartarate (4mg/kg bw per day for 30 days). Along with nicotine herbal drug was given at the dosage of 100mg per kg.

body weight for Group III rats. The group IV rats received only 100 mg of *Curcuma aromatica*. All the experimental rats were sacrificed by decapitation on 31st day, 24 hours after the final dose. The body weight was recorded. Ovary and uterus were dissected out, freed from adherent tissue and weighed on Anamed electronic balance. The ovaries and uterus were homogenized in chilled 0.1M Tris–Hcl buffer in a Potter- Elvehjem Teflon Homogenizer. The homogenate was used for the assay of the activities of LPO.[6] superoxide dismutase (Misra and Fridovich,1972) (7), catalase (Takahara *et al*.,1960).[8] GPx (Necheles *et al* .,1968).[9] and GST (Habig *et al*., 1974).[10]

RESULTS AND DISCUSSION

The levels of enzymatic antioxidants like superoxide dismutase, catalase, in ovary and uterus of control and experimental mice were showed in Table 1 and 2. The levels of these enzymes in ovary and uterus are significantly depleted ($P<0.01$) in the nicotine induced group compared to normal control group. Treatment with herbal drug *Curcuma aromatica* showed significant increase of those enzymes in group 3 treated animals when compared to group 2. No alterations in the levels of these enzymes in group 4 when compared to group 1. But the levels of LPO showed increased in nicotine induced Group. Treatment with herbal showed significant increase in group 3 animals when compared to group 2. No variation in the levels of these enzymes in group 4 when compared to group 1.

Nicotine is a highly addictive alkaloid induced oxidative stress both *in vivo* and in *vitro*.[11] In the present study, the effects of nicotine in the rat ovary were detected by antioxidant measurement. It was shown that *Curcuma aromatica* reversed the adverse effects of nicotine in rat ovaries ant uterus. The maintenance of high redox potential is a prerequisite for assuring the reproductive system functions in a healthy organism.[12]

Lipid peroxidation was induced by nicotine in the uterus and the ovary. The lipid peroxidation in nicotine treated rats was accompanied by depletion of antioxidant enzyme. It has been reported that the nicotine disrupts the mitochondrial respiratory chain leading to an increase generations of super oxide ions and hydrogen peroxide.[13] Superoxide anion and hydrogen peroxide are the main sources of the nicotine induced free radical generation and depletion of the cellular antioxidant.[14] Glutathione being an important cellular reductant involves in protection against free radicals, peroxides and toxic compounds. GPx decomposes excess hydro peroxides including hydrogen peroxide (H_2O_2).[15] Decreased level of GPx also

confirms that nicotine challenges the cell defense mechanism and disrupts antioxidative activities.[16]

The ameliorative effect of curcumin is due to its scavenging or neutralizing free radicals activities that inhibits peroxidation of membrane lipids and maintains cell membrane interiority and functions. *Curcuma aromatica* provided antioxidant activity on the rat tissues by increasing the levels of SOD, CAT, GPx and GST thus reducing MDA in the tissues of the ovary and uterus.

Table 1 Effect of nicotine and *curcuma aromatica* on antioxidant enzymes in ovary

Parameter	Group I	Group II	Group III	Group IV
LPO	1.6±0.08	3.4±0.15**	2.23±0.05	1.8±0.08
SOD	5.87 ±0.28	3.53 ±0.04**	4.93 ±0.10**	5.8 ±0.27*
CATALASE	6.35±0.08	3.54±0.21**	4.23±0.10*	6.75±0.09
GPx	30.77±0.3	25.5±0.46**	27.8±0.61*	29.3±0.3
GST	9.42±0.07	7.49±0.04**	8.68±0.17*	9.4±0.14

Values are Mean ± S.E. ** = P < 0.01,* = P < 0.05

LPO n moles of MDA/mg protein

SOD-units/mg protein

Catalase µ moles of H2o2 decomposed/min/mg protein

GPx (nmoles of GSH oxidized/min /mg protein)

GST (µ moles of CDNB conjugate formed/min /mg protein)

Table 2 Effect of nicotine and *curcuma aromatica* on antioxidant enzymes in uterus

Parameter	Group I	Group II	Group III	Group IV
LPO	0.63 ±0.08	2.9±0.3**	1.75±0.23*	0.82±0.08
SOD	3.24±0.14	1.67±0.10**	2.50±0.03**	3.5±0.09
CATALASE	1.6±0.079	0.8±0.08**	1.3±0.04*	1.50±0.11
GPx	25.9±0.17	21.9±0.27**	24.04±0.21*	25.01±0.8
GST	4.6±0.06	3.9±0.04**	4.3±0.17*	4.6±0.04

Values are Mean ± S.E. ** = P < 0.01,* = P < 0.05

LPO n moles of MDA/mg protein

SOD-units/mg protein

Catalase µ moles of H2o2 decomposed/min/mg protein

GPx (nmoles of GSH oxidized/min /mg protein)

GST (µ moles of CDNB conjugate formed/min /mg protein)

CONCLUSION

The present study reported the beneficial effects of *Curcuma aromatica* on ovarian toxicity induced by nicotine induction.

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