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Studies on antifertility effect of rhizome of *curcuma longa linn.*

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ABSTRACT:

Turmeric is used as a condiment and also as a herbal medicine in different kinds of illness. It is used by tribes as an antifertility and aborcifacient agent for a long period in different parts of India. Because of scarcity of research data regarding the effectiveness and mode of action of curcumin, the active principle present in turmeric, we undertake this research work to evaluate its antifertility effect. Control and curcumin treated albino rats were observed for ovulation by vaginal smear method. Ovarian weights were measured in control and curcumin treated rats for antigonadotrophic effect. Animals were scarified and histopathological examination of the ovaries and uteri were done. In the control group there was a normal oestrus cycle and ovaries, uteri also were normal. In curcumin treated group it was seen that there were absence of cornified epithelium in vaginal smear in all the rats which persist even after few days of withdrawn of the drug. And also there were no features of ovulation and ovaries showed cystic changes in histopathological examination. The result obtained from this study provide evidence that curcumin has antiovulatory effect probably by its antioestrogenic activity through suppression of negative feedback effect of estrogen on pituitary.

keywords*: Curcumin, contraceptives, antifertility, antiovulatory, antioestrogenic.*

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INTRODUCTION:

Births and deaths are two ends of life. Man can not prevent death but can prevent birth. However, with the advancement of modern medical science infant mortality rate has been declined and the average life expectancy is also increased. Progressive increase in birth rate as well as gradual decline in death rate cause a huge population burst in the world. So, the prevention of births forms the main basis of the various population control and family welfare programmes.

To prevent conception scientists have made attempts both on male and female counterparts. In male contraception, attempts are being made to find out suitable spermicidal agents. On the female side since conception consist of different stages like ovulation, fertilization of the ovum, implantation of the fertilized ovum and ultimate maturation of the foetus to term, which are more vulnerable to drug action. Therefore, an attempt to interfere fertilization has been directed mostly to affect these stages by various agents, claimed to be antiovulatory, anti-implantation, or abortifacient. Till date, steroidal pills and injections, IUDs, barrier methods, sterilization devices are available for contraception, but the changing life style and increasing population burden telling us that the ideal contraceptive is yet to be discovered. So, the

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scientists all over the globe are in search for ideal contraceptive.

Among the currently used methods, oral agents are the most popular and acceptable due to their simplicity of application. However, scientists as well as birth control pill user become suspicious about the rationale of these steroidal pills especially due to their side effects like thromboembolic manifestation, hypertension, liver disease, uterine and breast cancer.

The potential damage of long term use of hormones may be curtailed by use of nonsteroidal compounds. In India, centuries old confidence of rural population in herbal preparation makes a good ground for the use of plant products as contraceptives (1). Moreover, reports in current literatures regarding the antifertility action of some indigenous plants are quite encouraging (2).

One such plant, *Curcuma longa Linn.* (zingibercae) has been mentioned as a medicinal agent as early as 1600 B.C. in Rigveda. The rhizome of the plant, turmeric from which the active principle curcumin is obtained, has been consumed almost daily as condiments by the people of our country (3). On toxicity study it was found to be nontoxic with wide margin of safety (4). The rhizome of the plant Curcuma Longa was mentioned as contraceptive agent first by Kirtikar (5). But, after that the literatures on its antifertility property were scanty. In 1971, reversible antiovulatory(6) and anti-implantation (7) effect of curcumin were reported.

Being encouraged by these reports and considering that it is cheap, easily available, nonsteroidal, nontoxic even on prolonged use (8), it is thought worth to make an attempt to evaluate the possibility of curcumin as an antifertility agent and its mode of action. So, our experiment was aimed to find out the possible anitovulatory and antigonadotrophic effects as the basis of its antifertility action.

MATERIAL AND METHODS:

Curcuma longa is a tall herb belonging to the family of zingibercae of monocotyledons. The rhizomes are yellowish brown in colour.The powder of the rhizome is dark orange in colour known as turmeric yellow containing curcumin and altered starch grains (9). The yellow pigment curcumin (C21H20 06) is present 2% to 5% in different samples (10). Curcumin forms orange-yellow crystals, melting point 183^0C, insoluble in water and ether but soluble in alcohol and propylene glycolol (11). Powdered curcumin 200mg was dissolved in propylene glycol on slight worming and the volume was made upto 10 ml. Thus a standard propylene glycol solution 20mg/ml was prepared.

Antiovulatory effect:

For studying antiovulatory effect of curcumin albino rats were chosen as experimental animal. Twenty female vergin albino rats weighing 125g-150g were housed in cages for acclimatization in the laboratory environment for two weeks. The rats were provided with usual laboratory diet and water ad libitum (12). Each rat was thereafter allowed to complete at least five consecutive oestrus cycles and studied by vaginal smear method according to Burn(1950)(13). Vaginal smear was drawn by a sterile pipette from upper ¼ of vagina, stained by leishman stain and examined microscopically daily to determine the stages of the oestrus cycle by cytological features. Oestrus cycle consist of four phases- Oestrus (9-15 hrs.), Metoestrus (20hrs.), Dioestrus (60-70hrs.), and Pro-oestrus (12hrs.). Cytologically in rats oestrus or ovulatory phase is characterized by presence of almost 100% cornified cells, which are big cells with pyknotic nucleus in vaginal smear.

This ovulatory phase, also called sexual receptive phase appears every fourth to fifth day in rats. It was seen that all the rats had oestrus regularly in every 4^{th}

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to 5th day. After normal periodicity was established curcumin in propylene glycol was given to two groups of animals of six in each, in 25mg/kg and 50mg /kg doses respectively orally, daily for 10 consecutive days. Another group of six animals were given propylene glycol (vehicle) alone in a dose of 2.5 ml/kg of body weight orally for the same period of 10days. One animal from each group were sacrificed and histopathological studies of the ovaries and uterus carried out. Vaginal smears were taken from the remaining animals from the three groups daily for a period of 30 days including 10 days of medication and studied after staining and fixing as before.

Antigonadotrophic effect:

The antigonadotrophic activity of curcumin was studied on ovarian weight in unilateral ovariectomised female albino rats according to the method described by Fox et.al (14). The ovarian weight increases in control animal seven to fourteen days after removal of other ovary. This action is mediated by excess release of gonadotrophic hormones from the pituitary gland due to less suppression by oestrogen in unilateral ovariectomised rat. A decrease in ovarian weight in treated animals compare to the control group will indicate suppression of gonadotrophic hormones release. Twentyfour female albino rats weighing 150g to 180g were taken. They were studied for five consecutive normal oestrus cycles by vaginal smear methods, as describe earlier. Left sided ovariectomy were done in all the animal under light ether anesthesia. Ovaries which were taken out, and carefully dissected out from surrounding fatty tissue and dried by soaking in filter paper. The weight of each ovary was recorded against respective animal. Histological studies were carried out in all the ovaries to confirm the microscopical structure. The ovariectomised animals were then divided into four groups of six animals each. The first group served as control. In the second group propylene glycol was given orally for 10 consecutive days in a dose of 2.5 ml/kg of body weight. The third and fourth groups of animals were treated with curcumin in doses of 25mg and 50mg /kg body weight respectively orally for 10 consecutive days, considering the day of ovariectomy as day one. On the eleventh day, the remaining ovary was taken out under light ether anesthesia from all the animals, dissected clean, properly dried and their respective weights were recorded against each animal. The difference in weight, between the ovaries prior to and after treatment with drug were recorded and tabulated.

OBSERVATIONS AND RESULTS:

From the first study it is observed that in the control group of animals treated with propylene glycol which was used as a vehicle in the present experiment all the six animals manifested normal cyclical oestrus phase throughout the study period. But in curcumin treated 1st group (25mg/kg), normal cyclical oestrus phase was absent in all the six animals after 4.5 days on an average. With higher doses in 2nd group (50mg/kg) oestrus phase disappeared more quickly i. e within 3 days on an average. This oestrus suppressing effect of curcumin lasted for some peroid of drug treatment and even after discontinuation of the drug. In the group treated with 25mg/kg curcumin, oestrus suppressing effect lasts for about 10 to 14 days and in the 2nd group treated with 50mg/kg curcumin oestrus suppress for about 15 to 22 days. From the above observation it is seen that curcumin caused suppression of the oestrus phase in female albino rats in a dose dependent, reversible manner. Since oestrus phase in animal is a manifestation of ovulation, it may be presumed that suppression of oestrus phase in albino rats is due to suppression of ovulation, suggesting an antiovulatory effect of the drug in the experimental group of animals.

In the second study it is found that in the control group the weight of the remaining ovary increased

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considerably from 30.5+_2.03 mg to 85.80^{+}–2.38 mg in unilateral ovariectomised animal and corresponding increase was calculated to 181.4%. In the propylene glycol treated group there was also significant increase in the ovarian weight (179.8%) which was almost same as that of the control group. So, it may be seen that the vehicle propylene glycol alone had no significant effect on ovarian hypertrophy. In curcumin 25mg/kg treated group the increase in ovarian weight as observed was 33.8% which was significantly less than that of the control group. With higher doses of curcumin (50mg/kg) the increment of ovarian weight was even less i.e 16.3% suggesting a dose related reduction in ovarian hypertrophy in unilateral ovariectomised animals.

Since ovarian hypertrophy is known to be due to direct action of gonadotrophic hormone, it may be inferred that curcumin may possess antigonadotrophic effect.

Histological observations:

Histological examination of the uteri and ovaries were carried out in the curcumin treated groups of animals with an idea to substantiate the experimental findings. It is seen that there is no change of uterine structure in any animal. But the ovaries removed from curcumin treated animals showed presence of large cystic changes. Moreover , neither the ruptured graffian follicle nor any corpus luteum could be seen in any of the histological specimen in this group of animals, strongly suggesting failure of ovulation . This observation corroborates with our previous study , where it has been reported that the curcumin suppress the oestrus phase.

DISCUSSION:

In the present study, curcumin, the active principle obtained from rhizome of the plant , curcuma longa Linn has been studied for antiovulatory and antigonadotrophic effect to elucidate its antiantifertility effect. Ovulation in rat is known to be correlated with the appearance of oestrus phase, manifested by the presence of almost 100% cornified cells in the vaginal smear in every four to five days.

Curcumin in the present study was observed to cause persistent absence of cornified epithelium in the vaginal mucosa in the entire animal in a dose dependent reversible manner, suggesting a ovulation suppression effect.

This antiovulatory effect of curcumin was further confirmed by histological studies of the ovaries removed from the curcumin treated rats by the absence of ruptured graffian follicle and corpus luteum.

It is known that oestrus cycles are predominantly controlled by the anterior pituitary gland through FSH and LH secretion. FSH is responsible for early maturation of graffian follicles that FSH and LH together are responsible for their final maturation and a burst of LH secretion i.e LH surge, mediated by positive feed back effect of oestrogen is responsible for ovulation and their initial formation of corpus luteum Byskov et. al (15).

It is presumed that antiovulatory action of curcumin may be due to its antioestrogenic property preventing oestrogen induced LH surge.

Antigonadotrophic effect of curcumin was observed in unilateral ovariectomised rat and curcumin was observed to reduce hypertrophy of remaining ovary significantly in a dose dependent manner, as it caused only 33.8 and 16.3 percent hypertrophy in the doses of 25mg/kg and 50 mg/kg body weight respectively, in comparison to 181.4 per cent hypertrophy in control animals. This reduction of ovarian hypertrophy may be either due to less secretion of gonadotrophins at the level of pituitary or due to counteraction at the level of target organs can not be predicted by the present study.

Curcumin, on other hand has been reported to lower cholesterol level in rabbits and rats (16), since, it is presumed that reduction in cholesterol utilization for

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the synthesis of oestrogen may also be affected and possibly another facet of its antioestrogenic effect.

Curcumin may inhibit the oestrogen induced negative feedback effect on FSH either by occupying oestrogen receptors or by lowering oestrogen synthesis leading to increased release of FSH. Unopposed action of which on ovary is responsible for the cystic changes as observed in the present study. Another possibility of this cystic change is failure of rupture of the graffian follicle may lead to accumulation of fluid leading to the observed cystic changes.

CONCLUSIONS:

From the above discussion it may reasonably be concluded, that curcumin may be considered as a potential antifertility agent. The antifertility effect of curcumin appears to be possibly due to its antioestrogenic effect, either by blocking the oestrogen receptors or by diminished oestrogen synthesis due to diminished cholesterol metabolism or both.

REFERENCE:

1. United States Department of Agriculture. A treatise on medicinal plants used by Indian Tribes of Niveda : NewYork;1951.

2.Vopel, G., Gaisbaver, M. and Winkler, W., *Phytotherapie in der Praxis*. Deutscher Arzteverlag, Kolu, 1990, **74**.

3. Eigner, D. and Scholz, D., *Ferula asa-foetida* and *Curcuma longa* in traditional medicinal treatment and diet in Nepal. *J. Ethnopharmacol*., 1999, **67**, 1–6.

4. Ammon, H. P. T. and Wahl, M. A., Pharmacology of *Curcuma longa*. *Planta Med*., 1991, **57**, 1–7.

5. Kirtikar, Lalit Mohan Basu. Indian Medicinal Plant: Allahabad;1935

6. Sinha, M. Studies on the pharmacological actions of curcuma longa Linn. Thesis submitted for degree of doctor of Philosophy (Medical) of the university of Calcutta; 1971.

7. Garg, S.K. Curcumin as an anti-implantation agent. Indian J of Med.Research 1971;59: 1285.

8. Kiso, Y., Suzuki, Y., Watanabe, N., Oshima, Y. and Hikino, H., Antihepatotoxic principles of *Curcuma longa* rhizomes. *Planta Med*.,1983, **49**, 185–187.

9. Roughley, P. J. and Whiting, D. A., Experiments in the biosynthesis of curcumin. *J. Chem. Soc*., 1973, **20**, 2379–2388.

10. Kapoor, L. D., *Handbook of Ayurvedic Medicinal Plants*, CRC Press, Boca Raton, Florida, 1990

11. Araujo, C. A. C. and Leon, L. L., Biological activities of *Curcum longa* L. *Mem. Inst. Oswaldo Cruz*, 2001, **96**,723–728.

12. Ghosh, M.N. fundamentals of Experimental Pharmacology.2nd Ed. Calcutta: Scientific book agency; 1980

13. Burn,J. Biological Standardisation. New York : Oxford University Press ; 1950.

14. Fox B.W, Jacson, H. Evaluation of drug activities. London :Academic Press ; 1964.

15. Byskov ,A.G.,Jones.R.E. The Vertebrate Ovary. New York : Planum Press; 1978

16. Kamal-Eldin, A., Frank, J., Razdan, A., Tengblad, S., Basu, S. and Vessby, B., Effects of dietary phenolic compounds on tocopherol, cholesterol, and fatty acids in rats. *Lipids*, 2000, **35**, 427–435.