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Antiestrogenic Potential of Turmeric Rhizomes Extract to Decrease Weight and Uterine Diameters on Rats

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ABSTRACT

Turmeric (Curcuma longa L.) as an antiestrogenic can inhibit the hypothalamic-pituitary axis so that estrogen secretion is disturbed and affects the weight and diameter of the uterus. This study was conducted to examine the effect of turmeric extract (Curcuma longa L.) on weight and uterine diameters of female white rats (Rattus norvegicus) Sprague Dawley strain. Twenty-eight female rats were divided into four groups. Group C as a control (given H_2O), T1 (given 250mg/ Kg BW turmeric extract + 1ml H_2O), T2 (given 500mg/ Kg BW turmeric extract + 1ml H_2O), and T4 (given 1000mg/ Kg BW turmeric extract + 1ml H_2O). Turmeric extract was given daily for five days. The result showed that giving 250mg/Kg BW and 1000mg/Kg BW of turmeric extract significantly decrease weight and uterine diameters of female rats. In the conclusion, turmeric extract can decrease weight and uterine diameters and showing antiestrogenic potential in female rats.

Key words: *Turmeric rhizome, Antiestrogenic, Curcumin, Rat*

INTRODUCTION

The biggest problem that is often experienced by almost every developing country, especially in Indonesia, is an increase in population growth that is very fast and uncontrolled. Indonesia ranks fourth as one of the world's largest population contributors [1]. Family Planning is a program organized by the government to control the rate of population growth. One of the family planning programs is contraception for married couples [2]. However, the contraceptive used has many side effects such as dizziness, fatigue, bleeding, weight gain, hypertension, and menstrual cycle disorders. Therefore, researchers continue to research to find contraceptives that are effective, safe, comfortable, without side effects, reversible and do not interfere with the menstrual cycle [3].

The use of traditional medicinal plants has the advantage that it is easy to obtain, cheap, has a low level of toxicity, and does not cause side effects [4-7]. One of the traditional plants that can be used as a contraceptive is turmeric (*Curcuma longa* L.). The main content of curcumin in turmeric rhizomes has an antiestrogenic effect because it can inhibit the pituitary and hypothalamus so which can decrease secretion of estrogen hormone [8].

Estrogen is a hormone that controls the reproductive system. Estrogen can affect cell proliferation in the reproductive organs, one of which is the uterus. In the uterus, the endometrium layer is very responsive to changes in estrogen. The endometrium is composed of epithelial cells and stromal cells, when cell proliferation occurs, it will stimulate an increase in the number of epithelial cells and stromal cells than increase the vascularization of the spiral arteries that supply blood to the endometrium and increase the thickness of the endometrium [9]. Endometrial thickness is a major factor affecting weight and uterine diameters [10]. Curcumin

has an antiestrogenic activity which can decrease the endometrial thickness and lead to decreased implantation ability [11]. Based on the explanation above, it is important to research the effect of turmeric extract as an antiestrogenic in reducing testicular weight and diameter of female rats.

MATERIALS AND METHODS

Plant extract

The ethanol extract of turmeric was prepared using the maceration method. 500 g of turmeric powder dissolved in 8 liters of 96% ethanol. Then, the maceration results are filtered and evaporated using a vacuum rotary evaporator at temperatures 50-60 ºC [12].

Animals and treatment

Twenty-eight females rats aged 8-12 weeks with a weight of 120-160 g were obtained from Animal Vet Laboratorium Service Bogor, Indonesia which was then divided into 4 treatment groups. Group C as a control (given H_2O), T1 (given 250 mg/ kg BW turmeric extract + 1 ml H_2O), T2 (given 500mg/ Kg BW turmeric extract + 1 ml H_2O), and T4 (given 1000 mg/ kg BW turmeric extract + 1 ml H_2O). All treatment is given orally using stomach sonde once daily for 5 days. The specimen stomach was opened for the uterus to be taken. The cut uterus was fixed with formalin buffer 10% in the bottle. Then, taken to the Laboratory of Anatomical Pathology, Faculty of Medicine, the University of Lampung to make histological preparations. All of the research procedures were done with the approval and supervision of the Health Research Ethical Commission Faculty of Medicine University of Lampung No. 3048/UN26.18/PP.05.02.00/2019.

Study parameters

Parameters observed in the study were the development of uterine histology including weight and uterine diameters of the rat uterus (*Rattus norvegicus*) after given turmeric rhizome extract (*Curcuma longa* L.).

Statistical analysis

The data were analyzed using SPSS with an analysis bivariate test. Then, the data were analyzed using the Shapiro-Wilk normality test statistic for the number of example ≤50. If the results of the normality test were normally distributed and the variation of the data was homogeneous, it will be followed by a parametric test, namely the One Way Anova test. Then, if there was a significant diversity, the data will be tested further using the Least Significant Difference (LSD) test at the 5% real level.

RESULTS AND DISCUSSION

The effect of turmeric rhizome extract on the weight and diameters of the uterus are shown in **Table 1**. Uterine weight of rats given 250 mg/kg BW and 1000 mg/kg BW turmeric rhizome extract was significantly lower compared to the control group (p <0.024). The diameters of rats given turmeric extract were significantly lower compared to the control group (p <0.000). The rats were given 500 mg/kg BW turmeric rhizome extract was significantly higher compared to the control group which affected the weight and diameters of the uterus.

Table 1. Effect of Turmeric rhizome extract on weight and uterine diameters of rats

Treatments	Parameters (mean±SD)	
	Uterine weight (g)	Uterine diameters (µm)
C (control)	0,78 ± 0,17^{ab}	2897,60 ± 296,59^{ab}
T1 (250 mg)	0,59 ± 0,23^{a}	2740,28 ± 364,20^{c}
T2 (500mg)	0,85 ±0,12^{b}	3031,19 ± 174,37^{b}
T3 (1000mg)	0,67 ±0,04^{c}	2385,97 ± 113,35^{ac}
p	0.024	0.000

Note: Numbers followed by the same letter indicate no significant difference at the 5% level, the Post Hoc LSD (Least Significance Different) test.

In this study, the histological picture of rats given and those not given turmeric rhizome extract in **Figure 1**.

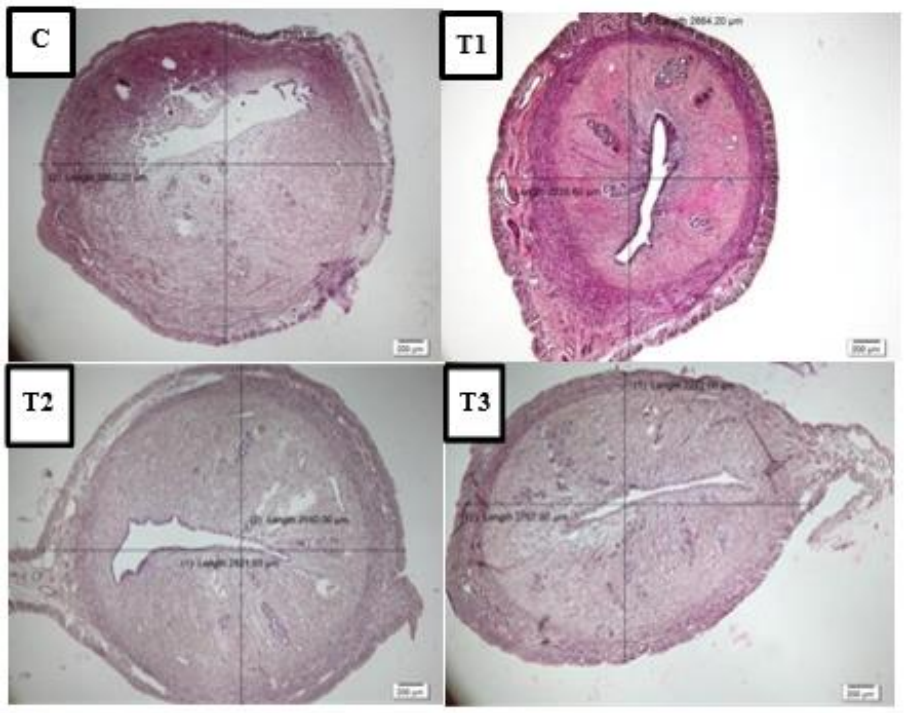

Figure 1. Histology of Uterus Mice given and not given turmeric extract (Curcuma longa L.) Description:
C= Control;
T1 = Treatment 1; T2 = Treatment 2; T3= Treatment 3. With a 4 x 10 magnification light microscope, staining Hematoxylin – Eosin.

Based on the results, there was a decrease in uterine weight due to given 250 mg/kg BW and 1000 mg/kg BW turmeric extract meanwhile at 500 mg/kg BW of turmeric rhizome extract increased compared to the control group. Turmeric was one of the traditional plant used for a contraceptive. The main component in turmeric rhizome extract is Curcumin. Curcumin can reduce the production of estrogen and progesterone, and one of the organs that were strongly influenced by the hormones estrogen and progesterone was the endometrium. Therefore the decrease in estrogen and progesterone levels in pregnancy caused the disturbances during pregnancy. Increased levels of estradiol (an estrogen derivative) corresponded to the increase in endometrial thickness. This was supported by Purwanti's (2009) study which shown that giving curcumin to Rattus norvegicus reduced endometrial thickness [13].

The decrease in uterine thickness directly proportional to the decreased in uterine weight, this was closely related to one of the uterine linings that were very responsive to changes in the hormone estrogen, namely the endometrium. Therefore, the decrease in the thickness of the endometrium caused the affection of the diameter of the uterus and impacted the decreasing uterine weight. In accordance with the research by Pratiwi (2018), giving turmeric extract (*Curcuma longa* L.) to female white mice reduced the thickness of the endometrium of rats [14]. The decrease in endometrial thickness caused implantation inhibition which leads to a decreased number of implants, which caused infertility in an organism [15].

Estrogen has an important role in the female reproductive organs, estrogen has 2 types of receptors, namely alpha receptors (REα) and beta β receptors (REβ). Alpha receptors are found in the uterus, adrenal glands, pituitary, epididymis, testes, and kidneys, and beta receptors are found high in the ovaries, bladder, brain, bones, prostate, and lungs [16]. Estrogen in the body works by binding to target cells and changing the conformation of estrogen receptors so that this hormone was able to stimulate proliferation and increased endometrial thickness [17]. The increase in uterine weight in line with the increase in uterine diameter. The increase in endometrial thickness was also caused by a hypoxic process that increased the amount of mRNA to encode VEGF, when VEGF coding occurs again, angiogenesis occurred again and increased the permeability and vasodilation of blood vessels. Curcumin caused hypoxia due to the inhibiting mechanism of COX-2 (Cyclooxygenase-2) which inhibited the epithelial cell proliferation, stimulated apoptosis, and inhibited angiogenesis [18]. VEGF was the main trigger for cyclic angiogenesis in the endometrium of women who are not pregnant and hypoxia was a strong stimulus for the formation of new blood vessels. The increase in VEGF occurs because the stromal and gland cells were deprived of oxygen, this condition caused hypoxia and increased the volume to encode VEGR,

this hypoxic process was controlled by HIF1 (Hypoxia Inducible Factor 1) which works to regulate the number of genes as a cellular response to hypoxia experienced [19].

The results also showed that giving 250 mg/kg BW turmeric rhizome extract and 1000 mg/kg BW decreased the uterine diameters of rats. This was caused by curcumin. Curcumin contains phytoestrogens which have an estrogen-like effect at low doses (estrogenic) and inhibit estrogen in high conditions (antiestrogenic). When estrogen levels are high, phytoestrogens bound the estrogen receptors even though their binding capacity was weak compared to estrogen. This condition caused the bond between estrogen and its receptors to be blocked which caused antiestrogenic effects. But when estrogen levels decrease in the body, phytoestrogens will become dominant and bind to estrogen receptors, causing an estrogenic effect [20]. This leads to decreasing uterine diameter.

After puberty, the production of secreted estrogen will double under the control of the hypothalamus-pituitary. The development of the genital organs will also continue to increase with increasing age. The most influential reproductive organs on estrogen are endometrium because estrogen can cause proliferation in the endometrial stroma which supported the development of the ovum during implantation. Apart from estrogen, the hormone that can affect the female reproductive organs was progesterone. The effect of progesterone on the uterus increased secretory changes in the endometrium of the uterus and prepared the uterus to accept the fertilized ovum. Progesterone can also reduce the frequency and intensity of uterine contractions thereby preventing the release of the implanted ovum [21].

Curcumin has the potential to be anti-fertility because curcumin can reduce the expression of the ERβ (Estrogen Receptor β) gene and estrogen in granulosa cells induced by FSH and LH hormones, decreased Erβ (Estrogen Receptor β) and estrogen result in interference with estrogen action. Disruption in the work of estrogen inhibited the steroidogenesis and folliculogenesis processes which resulted in the disruption of cell differentiation, FSH (Follicle Stimulating Hormone) mechanism, estrogen synthesis, LHR (Luteinizing Hormone Receptor), and FSHR (Follicle Stimulating Hormone Receptor) expression [22].

CONCLUSION

In conclusion, extract of turmeric rhizome (*Curcuma longa* L.) at 250 mg/kg BW and 1000 mg/kg BW can decrease the weight and diameters of the uterus and showed antiestrogenic potential in female rats (*Rattus norvegicus*) Sprague Dawley strain.

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CONFLICT OF INTEREST : None

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