



## ABSTRAK

### Pengaruh Kurkumin terhadap Reseptor Estrogen- $\alpha$ , Reseptor Progesteron, COX-2, VEGF dan Ketebalan Endometrium pada Fase Proestrus dan Fase Diestrus *Rattus norvegicus* strain Wistar

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**Latar Belakang:** Ketebalan endometrium mempengaruhi keberhasilan implantasi. Ketebalan endometrium dipengaruhi oleh proliferasi sel, desidualisasi sel stroma dan angiogenesis. Estrogen dan progesteron bekerja pada endometrium dengan berikatan pada reseptor. Estrogen memacu proliferasi sel dan angiogenesis, progesteron mempengaruhi desidualisasi. COX-2 dan VEGF merupakan faktor penting yang mempengaruhi angiogenesis. Kurkumin diketahui sebagai antifertilitas, tetapi aksi kerja terhadap endometrium dan perbedaan fase belum diteliti. Penelitian ini ingin mengkaji pengaruh kurkumin terhadap reseptor estrogen- $\alpha$ , reseptor progesteron, COX-2, VEGF dan ketebalan endometrium pada fase proliferasi dan sekresi.

**Metode:** Hewan coba *Rattus norvegicus* strain Wistar betina berumur 8-12 minggu, BB 110-150 gram sebanyak 48 ekor dan dibagi menjadi 2 kelompok: fase proestrus (proliferasi) dan fase diestrus (sekresi), tiap kelompok dibagi 4 sub-kelompok: kontrol (tanpa perlakuan), perlakuan dengan kurkumin 100 mg/kgBB, kurkumin 150 mg/kgBB dan kurkumin 200 mg/kgBB diberikan selama satu siklus estrus. Parameter estrogen- $\alpha$  dan reseptor progesteron diukur dengan menggunakan metode PCR dari sampel jaringan uterus, parameter COX-2 dan VEGF diukur dengan ELISA dari sampel serum darah, serta ketebalan endometrium dengan pewarnaan *Hematoxylin Eosin* dari jaringan uterus. Analisis statistik dengan SPSS menggunakan uji ANOVA dilanjutkan *post hoc LSD*, dengan  $p<0,05$ .

**Hasil:** Kurkumin pada kelompok fase proestrus meningkatkan ekspresi reseptor estrogen- $\alpha$  (dosis 100 mg/kgBB, dosis 150 mg/kgBB dan 200 mg/kgBB), meningkatkan ekspresi reseptor progesteron (dosis 200 mg/kgBB), serta menurunkan VEGF (dosis 100 mg/kgBB), sedangkan COX-2 dan ketebalan endometrium tidak berbeda. Kurkumin pada kelompok fase diestrus tidak mempengaruhi ekspresi estrogen- $\alpha$ , reseptor progesteron, COX-2, VEGF, serta ketebalan endometrium.

**Kesimpulan:** Kurkumin meningkatkan ekspresi reseptor estrogen- $\alpha$ , ekspresi reseptor progesteron pada fase proliferasi, menurunkan VEGF pada fase proliferasi. Kurkumin tidak mempengaruhi ekspresi reseptor estrogen- $\alpha$ , ekspresi reseptor progesteron, COX-2, VEGF, serta ketebalan endometrium pada fase sekresi.

**Kata kunci:** kurkumin, reseptor estrogen- $\alpha$ , reseptor progesteron, COX-2, VEGF, ketebalan endometrium



## ABSTRACT

### **Effect of Curcumin on Estrogen Receptors- $\alpha$ , Progesterone Receptors, COX-2, VEGF and Endometrial Thickness in the Proestrus and Diestrus Phases of Wistar Rats**

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**Background:** Endometrial thickness affects successful implantation. Endometrial thickness is influenced by cell proliferation, stromal cell decidualization, and angiogenesis. Estrogen and progesterone act on the endometrium by binding to receptors and are very dynamic depending on the menstrual cycle. Estrogen stimulates cell proliferation and angiogenesis, progesterone affects decidualization. COX-2 and VEGF are important factors in angiogenesis. Curcumin is known as an antifertility agent, but its action on the endometrium and its phase has not been studied. This study aims to analyze the effects of curcumin on estrogen receptors- $\alpha$ , progesterone receptors, COX-2, VEGF, and endometrial thickness in the proliferative and secretory phases.

**Methods:** Forty-eight female Wistar rats aged 8-12 weeks, weight 110-150 grams, were divided into 2 groups: proestrus phase (proliferation) and diestrus phase (secretory), each group was divided into 4 sub-groups: control (without treatment), 100 mg/kgBW curcumin, 150 mg/kgBW curcumin and 200 mg/kgBW curcumin were given in one estrous cycle. Estrogen- $\alpha$  and progesterone receptors were measured by PCR method using uterine tissue samples, COX-2 and VEGF were measured by ELISA using serum blood samples, and endometrial thickness by Hematoxylin Eosin staining using uterine tissue samples. Statistical analysis was done with SPSS using ANOVA followed by post hoc LSD, with  $p<0.05$ .

**Results:** Curcumin in the proestrus phase increased estrogen receptors- $\alpha$  expression (100 mg/kgBW, 150 mg/kgBW, and 200 mg/kgBW), increased progesterone receptors expression (200 mg/kgBW), and decreased VEGF (100 mg/kgBW). COX-2 and endometrial thickness are statistically not significant. Curcumin in the diestrus phase group has no effect on the expression of estrogen- $\alpha$ , progesterone receptors, COX-2, VEGF, and endometrial thickness.

**Conclusion:** Curcumin increases estrogen receptors- $\alpha$  expression and progesterone receptors expression in the proliferative phase, and decreases VEGF in the proliferative phase. Curcumin has no effect on estrogen receptors- $\alpha$  expression, progesterone receptors expression, COX-2, VEGF, and endometrial thickness in the secretory phase.

**Keywords:** curcumin, estrogen receptor- $\alpha$ , progesterone receptor, COX-2, VEGF, endometrial thickness