Efek heptil galat dan oktil galat sebagai anti inflamasi pada kultur sel endometriosis : studi pada jalur inflamasi il-1b, cox-2, tgf-b dan il-10 = The effects heptyl galate dan octyl galate as anti inflammation on endometriosis cell culture: studies on the inflammatory pathways il 1b, cox-2, tgf-b and il-10

Fajar Sulistya Utami, author

Abstrak

ABSTRAK
Latar belakang. Potensi terjadinya kekambuhan paska pengobatan endometriosis dengan terapi hormonal dan pembedahan konservatif masih terjadi sekitar 11-32 dalam waktu 1-5 tahun. Salah satu faktor pemicunya adalah proses inflamasi kronik yang merangsang peningkatan sitokin proinflamasi dalam rongga peritoneum, sehingga perlu pengembangan terapi baru. Heptil galat dan oktil galat merupakan senyawa turunan asam galat yang berpotensi menekan proliferasi beberapa jenis sel kanker. Penelitian kami sebelumnya membuktikan oktil galat dapat menekan ekspresi mRNA NFkB yang merupakan faktor transkripsi aktivasi jalur proinflamasi, serta dapat menekan proliferasi sel endometriosis in vitro. Saat ini kami ingin menganalisis aktivitas heptil galat dan oktil galat terhadap protein target NFkB melalui teknik insilico docking dan efeknya terhadap regulasi sitokin proinflamasi IL-1, COX-2, TGF-1 dan IL-10 pada kultur primer sel endometriosis.
Metode. In silico docking heptil galat dan oktil galat terhadap protein target NFkB melalui teknik bioinformatika. Sel endometriosis dari jaringan primer pasien diisolasi secara enzimatis dan dikultur, kemudian diberi perlakuan heptil dan oktil galat dengan 2 macam dosis (51,2 μg/mL dan 102,4 μg/mL) selama 48 jam, dilanjutkan induksi LPS 10 ng/mL selama 24 jam. Kelompok kontrol positif hanya diinduksi LPS tanpa perlakuan, dan kontrol negatif tanpa perlakuan dan LPS. Regulasi inflamasi dinilai dari tingkat kadar sitokin IL-1, COX-2, TGF-1 dan IL-10 dengan teknik ELISA.
Hasil. Analisis in-silico docking protein NFkB menunjukan nilai ikatan energi oktil galat lebih tinggi (-7,98 kkal/mol) dibandingkan heptil galat (-7,68 kkal/mol) dan asam galat (-7,66 kkal/mol). Terjadi penurunan kadar sitokin COX-2 secara signifikan ($p<0,03$) pada kelompok perlakuan dibandingkan dengan kontrol positif, begitu juga dengan sitokin IL-1 dan IL-10 cenderung menurun ($p>0,05$). Sedangkan kadar sitokin TGF-1 mengalami kenaikan pada kelompok perlakuan dibandingkan kontrol positif meskipun kurang bermakna secara statistik ($p>0,05$).
Kesimpulan. Melalui jalur NF-kB sebagai regulator inflamasi, baik oktil galat dan heptil galat terbukti dapat menekan produksi sitokin proinflamasi COX2 dan IL-1 serta meningkatkan sitokin TGF-1 dan menurunkan sitokin IL-10 sehingga berpotensi sebagai bahan terapi tambahan pada endometriosis.
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ABSTRACT
Background: The potential for relapse post endometriosis treatment with hormonal therapy and conservative surgery still occurs around 11-32 within 1-5 years. One of the trigger factors is a chronic inflammatory process that stimulates an increase proinflammatory cytokines in the peritoneal cavity, so needed the development of new therapies. Heptyl galate and octyl galate are gallic acid derivatives which have the potential to suppress the proliferation of several types cancer cells. Our previous research proved that octyl galate can suppress the expression of NFkB mRNA which is a proinflammatory activation transcription factor, and can suppress endometriosis cell proliferation in vitro. We currently want to analyze the activity of heptyl galates and octyl galates against the NFκB target protein through in-silico docking techniques and their effects on the regulation of proinflammatory cytokines IL-1, COX-2, TGF-1 and IL-10 in primary cultures of endometriosis cells.
Method: In silico docking heptyl and octyl galates against the NFkB target proteins through bioinformatics techniques. Endometriosis cells from primary tissue were enzymatically isolated and cultured, then given heptyl and octyl gallate treatment with 2 doses (51.2 μg/mL and 102,4 μg/mL) for 48 hours, continued induction of 10 ng / mL LPS for 24 hours. The positive control group only induced LPS without treatment, and negative treatment without treatment and LPS. Inflammatory regulation was assessed from levels of cytokines IL-1, COX-2, TGF-1 dan IL-10 with ELISA techniques.
Results: In-silico docking analysis of the NFkB gene showed higher energy bonding values in octyl galate (-7,98 kcal / mol) than heptyl galate (-7,68 kcal / mol) and gallic acid (-7,66 kcal / mol). Significantly decreased levels of COX-2 cytokine ($p < 0,03$) in the treatment group compared with positive controls, so also the cytokines of IL-1 and IL-10 tended to decrease ($p > 0,05$). Whereas the levels of cytokine TGF-1 experienced an increase in the treatment group compared to the positive control although it was less statistically significant ($p > 0,05$).
Conclusion: Through the NFkB pathway as an inflammatory regulator, both octyl galates and heptyl galates have been shown to suppress the production of proinflammatory cytokines COX2 and IL-1, as well as increase TGF-1 cytokines and reduce IL-10 cytokines so that they have the potential to be additional therapeutic agents in endometriosis.