Kurkumin meningkatkan sensitivitas sel kanker payudara terhadap tamoksifen melalui penghambatan ekspresi p-glikoprotein dan breast cancer resistance protein = Curcumin increased breast cancer cells sensitivity to tamoxifen through inhibition of p-glycoprotein and breast cancer resistance protein expression

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Abstrak

ABSTRAK
Penurunan sensitivitas hingga resistensi terhadap tamoksifen sering terjadi dalam pengobatan kanker payudara jangka panjang. Salah satu penyebab utamanya adalah peningkatan ekspresi transporter efluks P-glikoprotein (P-gp) dan Breast Cancer Resistance Protein (BCRP). Kurkumin diketahui sebagai penghambat P-gp dan BCRP. Pemberian kurkumin pada sel yang telah menurun sensitivitasnya terhadap tamoksifen diharapkan mampu meningkatkan sensitivitas sel kanker payudara terhadap tamoksifen melalui penghambatan kedua transporter tersebut.
Metode
Sel MCF-7 dipaparkan tamoksifen 1 µM selama 10 pasasi (sel MCF-7(T)), kemudian dianalisis perubahan sensitivitas sel terhadap tamoksifen melalui viabilitas sel dan ekspresi mRNA P-gp dan BCRP. Pada sel MCF-7(T), kurkumin diberikan dalam dosis 5, 10, dan 20 µM dengan atau tanpa tamoksifen selama 5 hari dan dianalisis viabilitas sel dan ekspresi mRNA P-gp dan BCRP pada hari ke-2 dan 5. Sebagai kontrol positif, verapamil 50 µM digunakan sebagai penghambat P-gp, ritonavir 15 µM dan nelfinavir 15 µM sebagai penghambat BCRP.
Hasil
Setelah diberikan tamoksifen 1 µM selama 10 pasasi (44 hari), sel MCF-7(T) menurun sensitivitasnya terhadap tamoksifen yang dibuktikan dengan terjadinya pergeseran CC50 sebesar 32,08 kali, peningkatan viabilitas sel sebesar 106,4%, dan peningkatan ekspresi mRNA P-gp dan BCRP sebesar 10,82 kali dan 4,04 kali. Pemberian kurkumin dengan atau tanpa tamoksifen selama 5 hari dapat menurunkan viabilitas sel dan ekspresi mRNA P-gp dan BCRP ($p < 0,05$).Kesimpulan
Kurkumin meningkatkan sensitivitas sel MCF-7(T) terhadap tamoksifen yang ditandai dengan penurunan viabilitas sel dan ekspresi mRNA P-gp dan BCRP. Peningkatan sensitivitas tersebut diduga terjadi melalui penghambatan ekspresi mRNA P-gp dan BCRP oleh kurkumin.
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ABSTRACT
Background
Decrease of sensitivity or resistance to tamoxifen occurs after long-term treatment in breast cancer. One of the major factor in tamoxifen resistance is overexpression

of efflux transporter P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP). Curcumin has been known as inhibitor of P-gp and BCRP. The addition of curcumin to tamoxifen resistant cells is expected to increase the sensitivity of breast cancer cells to tamoxifen.

Methods

MCF-7 breast cancer cell line was exposed with tamoxifen 1 µM for 10 passage (MCF-7(T)), then cell viability and mRNA expression of P-gp and BCRP were analyzed. To the MCF-7(T) cells, curcumin of 5, 10, dan 20 µM with or without tamoxifen was given for 5 days and cell viability and mRNA expression of P-gp and BCRP were analyzed on day 2 and 5. As positive control, verapamil 50 µM was used as P-gp inhibitor, ritonavir 15 µM and nelfinavir 15 µM were used as BCRP inhibitor.

Results

The administration of tamoxifen 1 µM for 10 passage (44 days), caused a decreased of MCF-7(T) cells sensitivity to the drug, with 32,08 times reduction in CC50 towards tamoxifen, increased of cell viability of 106,4%, and increased mRNA expression of P-gp and BCRP mRNA of 10,82 and 4,04 fold, respectively. The administration of curcumin with or without tamoxifen for 5 days reduced cell viability and the mRNA expression of P-gp mRNA and BCRP ($p < 0,05$).Conclusion

Curcumin increased MCF-7(T) sensitivity to tamoxifen, characterized by decreased of cell viability and mRNA expression of P-gp and BCRP. Increased of sensitivity was estimated at least in part through inhibition of P-gp and BCRP mRNA expression by curcumin.