

ABSTRAK

KAJIAN BIOLOGI MOLEKULER EKSPRESI P53, CYCLIN D1 DAN BAX PADA KANKER PAYUDARA CELL LINE T47D SETELAH PEMBERIAN MUCOXIN

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Mucosin merupakan salah satu jenis asetogenin yang diisolasi dari daun *Rollinia mucosa* yang dapat dijadikan sebagai agen anti tumor, diduga bekerja dengan cara menghambat proliferasi dan meningkatkan apoptosis, dan berperan meningkatkan ekspresi *p53* dan *Bax* serta menurunkan ekspresi *cyclin D1*. Tujuan penelitian ini adalah mengkaji ekspresi gen *p53*, *Bax* dan *cyclin D1* pada kanker payudara *cell line* T47D setelah pemberian *mucosin*.

Penelitian ini adalah penelitian eksperimental dengan sampel *cell line* T47D yang dibagi berdasar kelompok jam 0, 24, 48 dan 72 jam . dan masing-masing kelompok jam dengan kontrol dan pemberian *mucosin* $0,1 \times 10^{-3}$ $\mu\text{g/ml}$; $0,5 \times 10^{-3}$ $\mu\text{g/ml}$; 1×10^{-3} $\mu\text{g/ml}$; 5×10^{-3} $\mu\text{g/ml}$; 10×10^{-3} $\mu\text{g/ml}$, dilakukan 3 kali pengulangan. Ekspresi gen *p53*, *Bax* dan *cyclin D1* diperiksa menggunakan RT-PCR, ekspresi protein *p53*, *Bax* dan *cyclin D1* diperiksa menggunakan teknik imunohistokimia dan nilai apoptosis dan proliferasi diperiksa menggunakan metode *flow cytometry*. Data diuji statistik menggunakan uji *Anova*, *Kruskal Wallis*, *Mann Whitney*, regresi linier sederhana dan regresi linier berganda.

Hasil penelitian menunjukkan terdapat penurunan nilai proliferasi dan peningkatan nilai apoptosis dengan meningkatnya dosis dan waktu pemaparan *mucosin*. Hasil uji *Kruskal Wallis* pada pemeriksaan proliferasi pada 0, 24, 48 dan 72 jam didapatkan nilai $p=0,007$; $0,009$; $0,006$ dan $0,006$. Hasil uji *Kruskal Wallis* pada pemeriksaan apoptosis pada 0, 24, 48 dan 72 jam didapatkan nilai $p=0,008$; $0,012$; $0,005$ dan $0,005$. Terdapat pengaruh *mucosin* terhadap ekspresi *p53*, *cyclin D1* dan *Bax* pada *cell line* T47D. Hasil uji *Kruskal Wallis* dan *Anova* ekspresi *p53* pada 0, 24, 48 dan 72 jam didapatkan nilai $p=0,0001$; $0,008$; $0,0001$ dan $0,005$. Hasil uji *Kruskal Wallis* dan *Anova* ekspresi *cyclin D1* pada 0, 24, 48 dan 72 jam didapatkan nilai $p=0,0001$; $0,0001$; $0,0001$ dan $0,006$. Hasil uji *Kruskal Wallis* dan *Anova* ekspresi *Bax* pada 0, 24, 48 dan 72 jam didapatkan nilai $p=0,007$; $0,011$; $0,0001$ dan $0,012$. Hasil uji regresi linier sederhana ekspresi *p53* dengan nilai proliferasi didapatkan nilai $p=0,0001$, R^2 $0,085$ dengan korelasi negatif ($-0,675$); ekspresi *cyclin D1* dengan proliferasi nilai $p=0,0001$, R^2 $0,534$, dengan korelasi positif ($0,240$); ekspresi *p53* dengan nilai apoptosis didapatkan nilai $p=0,0001$, R^2 $0,664$, dengan korelasi positif ($0,202$); ekspresi *Bax* dengan apoptosis dengan nilai $P=0,0001$ dengan korelasi positif; Hasil analisis regresi linier berganda ekspresi gen *p53* dengan ekspresi gen *Bax* dan gen *cyclin D1* didapatkan nilai $p=0,004$.

Simpulan, terdapat pengaruh *mucosin* terhadap ekspresi *p53*, *cyclin D1* dan *Bax* serta proliferasi dan apoptosis pada *cell line* T47D. *Mucosin* dapat menurunkan proliferasi yang disebabkan penurunan *cyclin D1* dan meningkatkan apoptosis yang dimediasi oleh *p53*.

Kata kunci: Apoptosis, *Bax*, *Cyclin D1*, *Mucosin*, *P53*, Proliferasi, T47D.

ABSTRACT

STUDY OF MOLECULAR BIOLOGY THE EXPRESSION OF P53, CYCLIN D1 AND BAX IN BREAST CANCER CELL LINE T47D AFTER TREATMENT OF MUCOXIN

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Mucosin is one of acetogenin which is isolated from leaves of *Rollinia mucosa*, can be used as an anti-tumor agent, believed to work by inhibiting proliferation and increase apoptosis, and served to increase the expression of p53 and Bax and decreased expression of cyclin D1. The aim of this research is to identify mucosin effect on the expression of genes p53, Bax and cyclin D1 in breast cancer cell line T47D.

This study was analytic with cross sectional approach, and purely experimental which is done on 72 groups. Samples were divided into 2 groups, one group were not given mucosin, and the test group were given mucosin 1×10^{-3} $\mu\text{g/ml}$; 0.5×10^{-3} $\mu\text{g/ml}$; 1×10^{-3} $\mu\text{g/ml}$; 5×10^{-3} $\mu\text{g/ml}$; 10×10^{-3} $\mu\text{g/ml}$, performed 3 repetitions examination. Expression of p53, Bax and cyclin D1 gene were examined using RT-PCR, protein expression of p53, Bax and cyclin D1 were examined using immunohistochemical techniques and the value of apoptosis and proliferation checked using flow cytometry. Samples examined at 0, 24, 48 and 72 hour after exposure mucosin, compared with controls. Data were tested statistically using *Anova*, Kruskal Wallis, Mann Whitney, simple linear regression and multiple linear regression.

Result show there is an impairment of proliferation and increase in apoptosis values with increasing dose and exposure time of mucosin. Kruskal Wallis test results in proliferation examination at 0, 24, 48 and 72 hours, obtained p value=0.007, 0.009, 0.006 and 0.006. Kruskal Wallis test results in apoptosis examination at 0, 24, 48 and 72 hours, obtained p value=0.008, 0.012, 0.005 and 0.005. There are differences in the expression of p53, cyclin D1 and Bax in cell line T47D were given mucosin compared with those not given mucosin. Results of Kruskal Wallis and *Anova* test in p53 expression at 0, 24, 48 and 72 hours, obtained p value=0.000, 0.008, 0.000 and 0.005. Results of Kruskal Wallis and *Anova* test in cyclin D1 expression at 0, 24, 48 and 72 hours, obtained p value = 0.0001, 0.0001, 0.0001 and 0.006. Results of Kruskal Wallis and *Anova* test in Bax expression at 0, 24, 48 and 72 hours, obtained p value=0.007, 0.011, 0.0001 and 0.012. There is a relationship between p53 expression with the value of proliferation and apoptosis in cell line T47D were given mucosin. Result of simple regression analysis of p53 expression with apoptosis value, obtained p value=0.000 with the positive correlation. Result of simple regression analysis of p53 expression with proliferation value, obtained p value = 0.000 with a negative correlation. There is effect of p53 expression in Bax and cyclin D1 expression. Results of multiple linear regression analysis of p53 expression with Bax and cyclin D1 expression, obtained p value=0.004.

Conclusions, There are differences in the expression of p53, cyclin D1 and Bax in cell line T47D given mucosin with control. There is a relationship between the expression of p53, cyclin D1 and Bax with proliferation and apoptosis cell line T47D. There is effect of p53 expression on the expression of cyclin D1 and Bax.

Key word: Apoptosis, Bax, Cyclin D1, Mucosin, P53, Proliferation, T47D.