

ABSTRACT

Ethanol Extract of *Physalis minima* Linn Effect on c-Myc, p53 wild type, Apaf-1 Protein Expression, Mitosis and Apoptosis Cell Count in Breast Cancer

Experimental Study on Wistar-rat

Physalis minima Linn, widely available in various regions in Indonesia and has been used traditionally as anticancer agent. Ethanol extract of *Physalis minima* Linn contains some active steroid compound known as physalins, that shows cytotoxic effects on breast cancer cell lines : MCF-7, MDA-MB 231, and several other cancer cells. Ethanol extract of *Physalis minima* Linn also contains other active compound like flavonoid, poliphenol, chlorogenic acid, tannin, vitamin C and glucose etc. Until now there is no accurate data of the ethanol extract of *Physalis minima* Linn effect on breast cancer *in vivo*. The aims of this study was to clarify the effect of ethanol extract of *Physalis minima* Linn on the c-Myc, p53 wild-type, Apaf-1 protein expression, mitosis and apoptosis count on Wistar-rat breast cancer induced *N-nitrosomethylurea*.

An experimental research was performed using female Wistar-rat as animal models. Animal models were divided into 5 groups (n=8). K0 group without induction, while K1, P1, P2, and P3 groups were induced with *N-nitrosomethylurea* 50 mg/kg body weight, subcutaneous injection at mammary area, once a week for 5 times. At week 15, P1, P2 and P3 groups were administered with ethanol extract of *Physalis minima* Linn, per oral, 100, 250 and 400 mg/kg body weight, everyday for 4 weeks. At week 20, the termination was done, and breast cancer induced *N-nitrosomethylurea* was removed for preparations of the slides. The changes in c-Myc, p53 wild-type, Apaf-1 protein expression, mitosis and apoptosis count in all groups were examined and analyzed using *multivariate analysis of variance (MANOVA)*, SPSS 17 for Windows, SPSS Inc. USA (p : 0.05).

The result indicates that ethanol extract of *Physalis minima* Linn has anticancer effect on Wistar-rat breast cancer induced *N-nitrosomethylurea* (*in vivo*). Ethanol extract of *Physalis minima* Linn 100 mg/kg body weight effectively increased p53 *wild-type*, Apaf-1 protein expression, and apoptosis count, but it is not effective in reducing c-Myc protein expression and mitosis count. The dose of 250 mg/kg body weight of ethanol extract of *Physalis minima* Linn was effectively lowered c-Myc protein expression and mitosis count; increased p53 *wild-type*, Apaf-1 expression, and apoptosis count. The dose of 400 mg/kg body weight of ethanol extract of *Physalis minima* Linn was effectively lowered c-Myc protein expression and mitosis count; increased p53 *wild-type*, Apaf-1 expression, and apoptosis count, but it was not more effective than 250 mg/kg body weight, in lowering c-Myc protein expression and mitosis count, as well as in increasing Apaf-1 protein expression. Correlation analysis shown there was strong correlation between c-Myc protein expression and mitosis count (r : +0,707; P<0,001), p53 *wild type* and apoptosis cell count (r : + 0,858; P<0,001), also Apaf-1 and apoptosis cell count (r : + 0,922; P<0,001).

The conclusions of this study is the ethanol extract of *Physalis minima* Linn has anticancer effect on Wistar-rat breast cancer induced *N-nitrosomethylurea*, inhibits cancer cell growth by lowering c-Myc protein expression, increasing the p53 *wild type* and Apaf-1 protein expression, lowering mitosis count and increasing apoptosis count. Apoptotic induction is more dominant than mitosis inhibition.

Keyword: *Physalis minima* Linn, Wistar-rat breast cancer induced *N-nitrosomethylurea*, c-Myc, p53 *wild type*, Apaf-1, mitosis, apoptosis