

## INTISARI

Agen kemoterapi doksorubisin memiliki berbagai efek, salah satunya yaitu dapat menginduksi peningkatan level *reactive oxygen species* (ROS) intraseluler termasuk pada sel normal. Akumulasi radikal bebas yang berlebih dapat menyebabkan terjadinya kerusakan DNA. Minyak biji pala (*Myristica fragrans*) mengandung senyawa terpenoid yang memiliki aktivitas antioksidan yang dapat menghambat penuaan sel. Penelitian ini bertujuan untuk mengeksplorasi minyak atsiri dari pala (MP) sebagai agen *anti-senescence* pada sel ginjal yang diinduksi doksorubisin dan prediksi target molekulernya. MP diperoleh dengan distilasi uap air dan diperoleh kandungan senyawanya berdasarkan hasil GC-MS yaitu sabinene (34,87%), terpinolen (24,63%), safrol (11,67%),  $\alpha$ -terpinen (8,60%),  $\beta$ -pinen (8,46%), dan  $\alpha$ -pinen (3,38%). Prediksi target molekuler dilakukan menggunakan studi bioinformatika. Sebanyak 16 gen dianalisis fungsi fisiologisnya dan diketahui dalam respon seluler pada stres oksidatif dan respon seluler pada stres kimiawi. CASP3 merupakan gen target yang paling potensial senyawa dalam MP yang berperan pada kejadian nefrotoksik akibat pemberian doksorubisin. *Trypan blue exclusion assay* digunakan untuk menguji sitotoksik tunggal MP dengan parameter IC<sub>50</sub> pada sel Vero. Sel Vero digunakan sebagai model sel normal ginjal dalam penelitian ini. MP bersifat sitotoksik lemah dengan nilai IC<sub>50</sub> sebesar 267  $\mu$ g/mL. Uji aktivitas *anti-senescence* dilakukan menggunakan *SA- $\beta$ -Gal assay* dan diketahui MP mampu menurunkan jumlah sel Vero yang *senescence* akibat pemberian doksorubisin. Oleh karena itu, minyak biji pala berpotensi sebagai agen *anti-senescence* pada sel ginjal akibat pemberian doksorubisin.

**Kata Kunci :** Pala (*Myristica fragrans*), *senescence*, ginjal, target molekuler

## **ABSTRACT**

Doxorubicin chemotherapy agent has various effects, one of which is to induce an increase in intracellular reactive oxygen species (ROS) levels, including in normal cells. Excessive accumulation of free radicals can cause DNA damage. Nutmeg seed oil (*Myristica fragrans*) contains terpenoid compounds that have antioxidant activity that can inhibit cell aging. This study aims to explore essential oil from nutmeg (MP) as an anti-senescence agent which is induced by doxorubicin in kidney cells to predict its molecular target. MP was obtained by steam distillation and obtained its compound content based on GC-MS results, namely sabinene (34.87%), terpinolene (24.63%), safrole (11.67%),  $\alpha$ -terpinene (8,60%),  $\beta$ -pinene (8,46%), dan  $\alpha$ -pinene (3,38%). Prediction of molecular targets was carried out using bioinformatics studies. A total of 16 genes were analyzed for their physiological function and are known to be involved in cellular responses to oxidative stress and cellular responses to chemical stress. CASP3 is the most potential target gene for compounds in MP that play a role in nephrotoxicity due to doxorubicin administration. Trypan blue exclusion assay was used to test single cytotoxic MP with parameter IC<sub>50</sub> in Vero cells. Vero cells were used as a normal kidney cell model in this study. MP is weak cytotoxic with an IC<sub>50</sub> value of 267  $\mu$ g/mL. The anti-senescence activity test was carried out using the SA- $\beta$ -Gal assay and it was found that MP was able to reduce the number of Vero cells that were senescent due to doxorubicin administration. Therefore, nutmeg seed oil has the potential as an anti-senescence agent in kidney cells due to doxorubicin administration.

**Keywords:** Nutmeg (*Myristica fragrans*), senescence, kidney, molecular target