EFEK EKSTRAK ETANOLIK DAUN SIRSAK (*Annona muricata Linn*) TERHADAP AKTIVITAS PROLIFERASI, EKSPRESI p53 EPITEL LIDAH DAN FREKUENSI MIKRONUKLEUS MUKOSA BUKAL TIKUS GALUR *Sprague Dawley* YANG DIINDUKSI 7,12 DIMETILBENZ(α)ANTRASENA

INTISARI

Polycyclic aromatic hydrocarbon merupakan salah satu kelompok karsinogen terbesar di lingkungan. Senyawa ini dapat ditemukan dalam polutan udara maupun makanan. 7,12-Dimetillbez(α)antransena merupakan senyawa golongan PAH yang mempunyai potensi karsinogenik. Sirsak merupakan tanaman yang dapat tumbuh baik di indonesia. Daun sirsak mengandung flavonoid dan *acetogenin* yang diduga mempunyai potensi kemopreventif dan aktivitas antikanker. Tujuan penelitian ini adalah mengkaji efek pemberian ekstrak etanolik daun sirsak terhadap aktivitas proliferasi, ekspresi p53 sel epitel lidah dan frekuensi mikronukleus mukosa bukal tikus yang diinduksi DMBA.

Dua puluh empat tikus *Sprague Dawley* jantan berumur 5 minggu dengan berat badan 49-89 g dibagi dalam enam kelompok. Dorsum lidah tikus kelompok I-III diinduksi DMBA secara topikal tiga kali seminggu selama 16 minggu, kelompok II dan III tidak hanya diinduksi DMBA, tetapi juga diberi ekstrak etanolik daun sirsak 100 dan 200 mg/kg BB selama 18 minggu, kelompok IV diberi ekstrak etanolik daun sirsak 200 mg/kg BB, kelompok V diberi DMSO 1% dan kelompok VI tidak diberi perlakuan. Setelah minggu ke-18, s*wab* mukosa bukal dilakukan untuk uji mikronukleus dan dicat dengan *Feulgen-Rossenbeck*. Selanjutnya tikus dinekropsi dan dieksisi lidahnya untuk diproses secara histologis dan dicat dengan AgNOR untuk mengetahui aktivitas proliferasi serta imunohistokimia untuk mengetahui ekspresi p53.

Hasil penelitian menunjukkan bahwa ekstrak etanolik daun sirsak 100 dan 200 mg/kg BB mempunyai efek menurunkan progresivitas karsinogenesis mulut yang dibuktikan dengan penurunan derajat lesi displasia pada kelompok yang diinduksi DMBA dan diberi ekstrak. Dari analisis data menggunakan *one way ANOVA* diikuti dengan *Tukey* HSD menunjukkan bahwa aktivitas proliferasi kelompok II (0,89±0,06) dan kelompok III (0,76±0,05) berbeda signifikan dengan kelompok I (1,41±0,24). Ekspresi p53 kelompok II (20±1,29) dan kelompok III (17±1,26) berbeda signifikan dengan kelompok I (25±0,82). Frekuensi mikronukleus kelompok II (13±0,82) dan kelompok III (12±0,96) berbeda signifikan dengan kelompok I (24±1,71). Dari penelitian ini dapat disimpulkan bahwa ekstrak etanolik daun sirsak dapat menurunkan progresivitas karsinogenesis mulut melalui penurunan aktivitas proliferasi, ekspresi p53 sel epitel lidah dan frekuensi mikronukleus mukosa bukal.

Kata kunci: DMBA, ekstrak etanol daun sirsak, aktivitas proliferasi, ekspresi p53, frekuensi mikronukleus

THE EFFECTS OF SOURSOP LEAVES (*Annona muricata linn*) ETHANOLIC EXTRACT ON PROLIFERATION ACTIVITY, p53 EXPRESSION OF TONGUE EPITHELIUM AND MICRONUCLEUS FREQUENCY OF BUCCAL MUCOSA EPITHELIUM OF *Sprague dawley* RATS INDUCED BY 7,12-DIMETILBENZ(α)ANTHRACENE

ABSTRACT

Polycyclic aromatic hydrocarbon is one of the largest group of carcinogen in the environment. These compound can be found in air pollutants and food. 7,12-Dimetillbez(α)antransena is a compound of PAH class that has carcinogenic potency. Soursop is a plant that can grow well in Indonesia. Soursop leaves contain flavonoid and *acetogenin* that assumed having chemopreventive potency and anticancer activity.The aim of this study was to assess the effects of soursop leaves ethanolic extract toward proliferation activity, p53 expression of the epithelial cells of the tongue and micronucleus frequency of DMBA-induced lingual mucosa of rat.

Twenty-four Sprague Dawley rats aged 5 weeks, weighed 49-89 g were divided into six groups. The lingual dorsum of group I-III were induced by DMBA topically three times a week for 16 weeks, group II and III not only induced by DMBA, but also given soursop leaves ethanolic extract of 100 and 200 mg/kg body weight for 18 weeks, group IV was given soursop leaves ethanolic extract 200 mg/kg body weight, group V was given DMSO 1% and group VI was given no treatment. After the 18th week, buccal mucosa swab for micronucleus test was conducted and stained with Feulgen-Rossenbeck method. Furthermore, rats were necropsized and their tongue were excised for AgNOR staining to determine the proliferation activity and for immunohistochemical staining to determine the expression of p53.

The results showed that soursop leaves ethanolic extract of 100 and 200 mg/kg body weight had lowering effect toward the oral carcinogenesis progression as indicated by decreasing the level of dysplastic lesions on group that has been induced by DMBA and given the extract. Data analysis using one-way ANOVA followed by Tukey HSD showed that the proliferation activity of group II (0.89 ± 0.06) and III (0.76 ± 0.05) were significantly different from group I (1.41 ± 0, 24). The p53 expression of group II (20 ± 1.29) and III (17 ± 1.26) were significantly different from group I (25 ± 0.82). The micronucleus frequency of group II (13 ± 0.82) and group III(12 ± 0.96) were significantly different from group I (24 ± 1.71). It can be concluded that the soursop leaves ethanolic extract decreases oral carcinogenesis progression through reduction of proliferative activity and p53 expression of the tongue epithelial cells as well as micronucleus frequency of buccal mucosa.

Keywords: DMBA, soursop leaves ethanolic extract, proliferation activity, p53 expression, micronucleus frequency.