INTISARI

Agen antivirus dibutuhkan sebagai upaya pengendalian kasus infeksi SARS-CoV-2 sehingga laju infeksi dapat ditekan. Hesperetin diketahui memiliki aktivitas antivirus yang berpotensi menghambat infeksi virus SARS-CoV-2. Penelitian ini bertujuan mempelajari potensi antivirus dari hesperetin melalui penghambatan *viral cellular entry* menggunakan model *pseudovirus.* Hesperetin diuji dengan uji [3-(4,5dimethylthiazol- 2-yl)-2,5-diphenyltetrazolium bromide] (MTT) untuk menentukan konsentrasi non sitotoksik. Hesperetin konsentrasi <100 µM menunjukkan hasil tidak toksik pada model sel 293T dengan persen viabilitas sel >70%. *Angiotensin Converting Enzyme 2* (ACE2) dan *Transmembrane protease serine*2 (TMPRSS2) adalah reseptor yang berperan pada mekanisme masuknya virus SARS- CoV-2. Ekspresi ACE2 dianalisis dengan *immunofluorescence staining* yang ditandai ekspresi Alexa-594 pada sel 293T. Model sel yang digunakan pada uji *entry inhibitor* adalah 293T yang ditransfeksi plasmid ACE2 dan TMPRSS2. Pseudovirus SARS-CoV-2 merupakan rekayasa rVSV-ΔG/G*-GFP-Spike yang inkompeten. Persen sel terinfeksi dilakukan untuk menilai potensi hesperetin menghambat *pseudovirus* SARS-CoV-2. Nilai persen sel terinfeksi secara berturut-turut pada kontrol, hesperetin 10 µM, dan hesperetin 100 µM adalah 43,07%; 18,25%; dan 15,83%. Keseluruhan hasil dianalisis menggunakan One Way Anova Bonferroni ($p<0,05$). Perlakuan hesperetin konsentrasi 10 dan 100 µM memiliki potensi inhibitor yangsignifikan dibanding kontrol. Hesperetin berpotensi dikembangkan sebagai antivirus dengan target spesifik melalui penghambatan entri virus yang difasilitasi reseptor ACE2 dan TMPRSS2.

Kata kunci: SARS-CoV-2, viral entry inhibitor, antivirus, Hesperetin

ABSTRACT

Antiviral agents are needed as an effort to control cases of SARS-CoV-2 infection so that the rate of infection can be reduced. Hesperetin is known to have antiviral activity that has the potential to inhibit infection with the SARS-CoV-2 virus. This study aims to study the antiviral potential of hesperetin through inhibition of viral cellular entry using a pseudovirus model. Hesperetin was tested by [3-(4,5dimethylthiazol- 2-yl)-2,5-diphenyltetrazolium bromide] (MTT) test to determine the non-cytotoxic concentration. Hesperetin concentration <100 µM showed non-toxic results in the 293T cell model with a percent cell viability of >70%. Angiotensin Converting Enzyme 2 (ACE2) and Transmembrane protease serine 2 (TMPRSS2) are receptors that play a role in the entry mechanism of the SARS-CoV-2 virus. ACE2 expression was analyzed by immunofluorescence staining which marked Alexa-594 expression on 293T cells. The cell model used in the entry inhibitor test was 293T transfected with ACE2 and TMPRSS2 plasmids. The SARS-CoV-2 pseudovirus is an incompetent engineered rVSV-ΔG/G-GFP-Spike. The percentage of infected cells was carried out to assess the potential of hesperetin to inhibit the SARS-CoV-2 pseudovirus. The percentage value of infected cells respectively in control, 10 µM hesperetin, and 100 µM hesperetin was 43.07%; 18.25%; and 15.83%. All results were analyzed using Bonferroni's One Way Anova ($p<0.05$). The hesperetin treatment with concentrations of 10 and 100 µM had significant inhibitory potency compared to the controls. Hesperetin has the potential to be developed as a specific target antiviral through inhibition of viral entry facilitated by ACE2 and TMPRSS2 receptors.*

Keywords: SARS-CoV-2, viral entry inhibitor, antiviral, Hesperetin