

ABSTRACT**ANTIHEPATITIS C VIRUS ACTIVITY OF COMBINATION *Ruta angustifolia* L. LEAF ETHANOLEXTRACT WITH ANTIHEPATITIS C VIRUS DRUGS IN VITRO**

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Ruta angustifolia L. is a plant of rutaceae's family which has been traditionally used for jaundice. Previous study showed that ethanol extract of *R. angustifolia* inhibit hepatitis C virus against JFH1a virus on hepatocyte cell Huh7 with IC_{50} 3.0 ± 1.4 μ g/ml. In order to continue our study, ethanol extract of *R. angustifolia* combined with antihepatitis C virus drugs such as simeprevir, telaprevir, and ribavirin to determine the activities and synergistic or additive effects caused by these combinations. The results of the combination activity of extract *R. angustifolia* with simeprevir obtained the increasing of antihepatitis C virus activity which is showed a decreasing IC_{50} simeprevir, which is from 43.84 ± 0.96 nM (single treatment) to 19.70 ± 0.28 nM (combination) with a combination index value (CI) = 0.833. The combination of extract *R. angustifolia* with telaprevir decreased IC_{50} telaprevir from 10.48 ± 0.11 nM (single treatment) to 3.64 ± 0.07 nM (combination) and CI value = 0.677. Then a combination of extract *R. angustifolia* with ribavirin which can decrease IC_{50} ribavirin from 10.43 ± 0.18 μ g/ml (single treatment) to 2.80 ± 0.03 μ g/ml (combination) with CI value = 0.691. The Compusyn software possess a CI value <1, which means the three combinations have a synergistic effect. Toxicity analysis showed that the three combinations were not toxic to hepatocyte cells with percent viability cells higher than 90%. These results indicate that *R. angustifolia* has the potential to be used as a recommendation for combination therapy for antihepatitis C virus.

Keyword: *R. angustifolia* extract, combination therapy, and synergistic effect.