

ENHANCEMENT OF ANTI-HEPATITIS C VIRUS ACTIVITY BY THE COMBINATION OF CHALEPIN FROM *RUTA ANGUSTIFOLIA* AND CURRENT ANTIVIRAL DRUGS

Tutik Sri Wahyuni^{1,2}, Adita Ayu Permanasari²; Aty Widyawaruyanti¹, Achmad Fuad Hafid^{1,2}, Hiroyuki Fuchino³, Nobuo Kawahara³ and Hak Hotta⁴

¹Department of Pharmacognocny and Phytochemistry, Faculty of Pharmacy,

²Institute of Tropical Disease, Airlangga University, Surabaya, Indonesia;

³Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation, Tsukuba, Ibaraki; ⁴Faculty of Clinical Nutrition and Dietetics, Konan Women's University, Kobe, Japan

Abstract. Hepatitis C virus (HCV) infection is a serious disease, which chronically infects 71 million people worldwide. Currently oral interferon (IFN)-free regimen usage involving a combination of direct-acting antiviral agents (DAAs) is capable of providing a sustained virologic response (SVR) of >90%. However, a number of DAA-resistant HCV strains have emerged and many patients do not have access to this therapy owing to its high cost. Combination drug therapy is one strategy for lowering cost and improving effectiveness of antiviral therapy. Chalepin from *Ruta angustifolia* is known to exhibit strong anti-hepatitis C activity. Anti-HCV efficacies of combinations of chalepin and current antiviral drugs, namely, cyclosporine A (CsA), daclatasvir (DCV), IFN- α , ribavirin (RBV), simeprevir (SMV), and telaprevir (TVR) were measured by treating HCV-infected cells *in vitro*. Chalepin enhanced anti-HCV activities of CsA, DCV, IFN- α , RBV, SMV, and TVR with a synergistic combination index of <1. The results suggest drug combinations that include chalepin should be considered when developing alternative and complementary medicine as anti-HCV agents.

Keywords: *Ruta angustifolia*, chalepin, combination drug treatment, direct-acting antiviral, Hepatitis C virus

Correspondence: Tutik Sri Wahyuni, Department of Pharmacognocny and Phytochemistry, Faculty of Pharmacy, Airlangga University, Surabaya 60115, Indonesia.

Tel: +62 81241437599

E-mail: tutik-s-w@ff.unair.ac.id