

## Research Article

# The Effect of *Hydrocotyle sibthorpioides* Lam. Extracts on *In Vitro* Dengue Replication

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**Objective.** To investigate the potential effect of *Hydrocotyle sibthorpioides* Lam. (*H. sibthorpioides*) extracts against *in vitro* dengue viral replication. **Methods.** The cytotoxicity of *H. sibthorpioides* was evaluated using a cell viability assay. Cells were pre- and posttreated with water and methanol extracts of *H. sibthorpioides*, and the viral inhibitory effect was investigated by observing the morphological changes, which were further confirmed by plaque assay. **Results.** The methanolic extract cytotoxicity was higher in Vero and C6/36 cells than the cytotoxicity of the water extract. Preincubation of the cells with *H. sibthorpioides* extract showed nonexistent to mild prophylactic effects. The posttreatment of Vero cells with *H. sibthorpioides* methanolic extract presented higher antidengue activities when compared with the water extract. Surprisingly, posttreatment of C6/36 cells resulted in an enhancement of viral replication. **Conclusion.** *H. sibthorpioides* had variable effects on dengue viral replication, depending on the treatment, cell lines, and solvent types. This study provides important novel insights on the phytomedicinal properties of *H. sibthorpioides* extracts on dengue virus.

## 1. Introduction

Dengue virus (DENV) is a mosquito-borne member of the Flaviviridae family and is transmitted through the bites of *Aedes aegypti* and *Aedes albopictus* female mosquitoes. Four different serotypes of DENV exist, namely, dengue serotypes 1, 2, 3, and 4 [1]. Infection with one of the serotypes may be asymptomatic but commonly results in a flu-like illness termed dengue fever, ranging to more severe forms, such as dengue hemorrhagic fever or dengue shock syndrome. The incidence of dengue has grown dramatically in the world in recent decades. It has been reported that over 2.5 billion people are now at risk for dengue infection [2]. In Malaysia, a 277% increase in cases was reported in early 2014 compared with the same period in 2013 [3]. The present treatments for patients with dengue fever tend to be more supportive than curative. Treatments include bed rest, fluid replacement, and

antipyretic agents. At best, prevention lies in proper mosquito control.

Asia, with its rich flora and fauna, is one of the most promising regions for the discovery of novel biologically active substances. A large and ever-expanding global population has expressed its preference towards natural products in treating and preventing medical problems [4]. *H. sibthorpioides* is a widespread uncultivated perennial herb that holds an important place in Chinese herbal medicine. Chinese people of the Hakka ethnic group use it to treat several diseases, including adenolymphitis, herpes zoster and cholecystitis. It also has some folkloric uses in the treatment of several other minor illnesses including fever and edema, in detoxication and for soothing throat pain [5]. In addition, it has been shown to act as an antidiuretic and is effective, when applied externally, for skin tumors and in enhancing phagocytic activity and immune function [6].