S33-5 Search for HCV Invasion Inhibitory Principles from Medicinal Plants

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Hepatitis C virus (HCV) is the most important causative agent of posttransfusion infecting more than 200 million people worldwide. HCV infection becomes chronic in most cases and may eventually result in hepatitis, liver cirrhosis, and hepatocellular carcinoma. In spite of highly vigorous and extensive research in this field, a highly effective treatment is not yet available. The mainstay of anti-HCV therapy, interferon (IFN) along with ribavirin leads, at best, to viral clearance for about 40-50% of patients infected HCV. Therefore, exploration for new anti-HCV principles has been needed urgently. However, absence of an efficient cell culture system to replicate HCV has prevented this trial over a long period. Recently, Matsuura *et al.* established a model virus encoding two envelope glycoproteins (E1 and E2) responsible for receptor binding to virus invasion as well as secretory alkaline phosphatase (SEAP).

This circumstance prompted us to engage in search for unprecedented HCV invasion inhibitors from medicinal plants. Bioassay guided separation of the extracts from *Rosa rugosa* Thunb., *Oenothera erythrosepala*, and Ephedrae Herba disclosed three principles as HCV invasion inhibitors. As for the principle from *R. rugosa* Thunb., the crucial portion for biological potency was elucidated through structure-activity relationship of naturally occurring congeners and synthesized analogs. In addition, all bioactive ingredients were shown to antagonize receptors on hepatocytes to result in inhibition for virus invasion.