S33-6 Antiviral evaluation of natural products and their application to viral diseases

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The limited efficacy and significant clinical toxicity of combination interferon and ribavirin therapy have generated strong interest in developing novel inhibitors of hepatitis C virus (HCV) replication. Recently, a growing understanding of the structure and function of critical viral enzymes and the development of HCV replicons have accelerated the development of highly specific candidate antiviral agents. In the life cycle of HCV, enveloped virions bind to and penetrate into host cell using viral envelope glycoproteins. In the cytoplasm, the viral RNA genome serves as mRNA, and produces viral proteins as a long polyprotein that is cleaved by both host and viral proteases. Progeny virions assemble by budding into ER/Golgi apparatus, where the glycoproteins maturate, and are released at the cell surface.

All stages of replication cycle from the attachment of virus to the release of progeny should be antiviral targets. We have searched for antiviral candidates from natural resources for about 20 years. So far, we have found several classes of compounds with unique antiviral action. Among them, anionic substances interfere with virus attachment and/or entry, several substances inhibit the maturation of virus-specific glycoproteins, low molecules can inhibit the virus release from infected cells, glycerol derivatives reduce the pathogenicity of virus, and some compounds exert virucidal action that impairs the ability of virus to infect host cells. These substances might be worthy to be evaluated as novel anti-HCV agents by using HCV replication systems in cultured cell lines.