The infections produced by hepatitis B virus (HBV) and hepatitis C virus (HCV) are becoming the world’s leading cause of death. Chronic HBV infections produced by them can lead to cirrhosis, liver failure, and hepatocellular carcinoma. HCV infection is a major cause of liver failure and has been responsible for the majority of liver transplant.

So far only a few drugs have been approved by FDA for the treatment of HBV and HCV infections. For HBV infection, they include lamivudine, adefovir dipivoxil, and entacavir. Adefovir dipivoxil, an ester prodrug of PMEA (9-[2-(phosphonomethoxy)ethyl]adenine), has potent in vitro and in vivo activity against HBV. However, dose-limiting nephrotoxicity and its potential of releasing toxic formaldehyde and pivalic acid are its primary limitations. For HCV infection, interferon-α cytokine with antiviral activity, has been widely used. However, approximately 50% of patients with chronic hepatitis C caused by genotype 1 virus showed no virological response even after treatment with the most effective combination therapy to date, pegylated interferon-α-2a with synthetic guanosine nucleoside ravavirin. In addition, considerable side effects are associated with these treatments, resulting in limited patient compliance. Because of these reasons there is an urgent need to develop more effective HBV and HCV agents. It has therefore forced the medicinal chemists to design effective inhibitors of these viruses. The quantitative structure-activity relationship (QSAR) studies have been of great help in the design and development of drugs. Therefore, we have made an exhaustive QSAR study on some series of HBV and HCV inhibitors to provide the guidelines to develop potent anti-HBV and anti-HCV agents. The results and their implications are discussed in detail.