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## Promising natural compounds for treatment of Hepatitis C virus and its complications

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As many as 200 million people worldwide are infected with hepatitis C virus (HCV) and more than 350,000 people die yearly from hepatitis C-related diseases (WHO, June 2011). There is no preventive vaccine available for HCV due to its highly mutable nature evidenced by the presence of more than 50 subtypes of HCV. In the present study, the water extract of the leaves of the wild Egyptian artichoke (WEA) (Cynara cardunculus L. var. sylvestris (Lam.) Fiori) showed improvement of HCV infection symptoms through the clinical investigation of WEA extract on some infected Egyptian patients. The results showed outstanding activity against HCV and its complications such as ascites and jaundice by measuring the PCR, and liver functions such as ALT, and AST. The phytochemistry of the WEA extract and its subsequent evaluation of inhibition capacity in vitro using cell-culture derived HCV resulted in the identification of two potent sesquiterpene lactones showing in vitro activity against all genotypes. Their structural elucidation was done by extensive spectroscopic tools such as NMR and HR-MS spectroscopy. The absolute configuration was determined by TDDFT ECD calculations and comparison with the experimental CD spectra. Cynaropicrin and grosheimol showed EC50 at 1.03 µM, and 1.27 µM, by using a luciferase-carrying reporter virus. Time-of-addition experiments revealed that these compounds inhibited HCV virus at a time-point during entry. Finally, the results showed that compounds cynaropicrin and grosheimol inhibited HCV particles from genotypes 1a, 1b, 2b, 3a, 4a, 5a, 6a and 7a indicating that these compounds inhibit HCV cell entry independently of viral genotype or subtype. Most important is that compound cynaropicrin can inhibit HCV through many important mechanisms: cell-entry inhibitor, inhibition of cell to cell coinfection, antihyperlipedemic and antitumor activities. There is a plenty of publications confirmed that cynaropicrin is a very promising drug as antitumor agent.

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