Hepatitis C virus infects about 3% of world’s population. Progress in molecular biology and better knowledge of hepatitis C virus life cycle contribute to the development of specifically targeted antiviral therapies for HCV. This new treatment also targets the internal ribosome entry site (IRES), which is highly conserved and therefore an attractive target for intervention. In addition, inhibition of IRES function could disable the propagation of the virus early in the HCV life cycle. Novel therapeutics are aimed both at the HCV IRES structure and its nucleotide sequence. Small molecules and synthetic nucleic acids, e.g. antisense oligonucleotides and ribozymes, have been tested as potential therapeutic substances. In this paper particular attention is paid to small molecules interacting with HCV IRES.