Discovery of highly potent anti-HCV with new core scaffolds and new conformational aspects

NS5A is a dimeric protein and an interesting target to inhibit the replication of HCV. Reported here are two series of symmetric molecules with the scaffolds of 4,4’-(buta-1,3-diyn-1,4-diyl) dianiline core- and 3,3’-(buta-1,3-diyn-1,4-diyl) dianiline core, connected to a L/D-proline moiety and capped with the methyl, ethyl, butyl, isobutyl and benzyl carbamate of L/D-valine, L/D-leucine and L-isoleucine amino acids. The compounds showed inhibitory effect on the replication of HCV genotype 1b in vitro with EC50s in the low picomolar range and SI50s of several orders of magnitude. Also, some of the compounds showed pan-genotypic activity. Higher activities were associated with compounds showing curving of the core scaffolds that leads to better fit and interaction with the desired target.

Biography

Ashraf H Abadi has completed his PhD from the College of Pharmacy, University of Florida, USA and Cairo University. He is the Head of Pharmaceutical Chemistry Department, Faculty of Pharmacy and Biotechnology, German University in Cairo and former Dean of the Faculty. He has published more than 80 papers in reputed journals; 7 patents and has been serving as an Editorial Board Member and Reviewer of reputed international pharmaceutical sciences journals.

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