Silatecan AR-67

National Cancer Institute

Source

National Cancer Institute. Silatecan AR-67. NCI Thesaurus. Code C64618.

A synthetic, highly lipophilic derivative of camptothecin, with potential antineoplastic and radiosensitizing activities. 7-tert-butyldimethylsilyl-10-hydroxycamptothecin binds to and stabilizes the topoisomerase I-DNA covalent complex. This inhibits the religation of topoisomerase I-mediated single-stranded DNA breaks and produces lethal double-stranded DNA breaks when encountered by the DNA replication machinery, thereby inhibiting DNA replication and inducing apoptosis. Camptothecin readily undergoes hydrolysis at physiological pH, changing its conformation from the active lactone structure to an inactive carboxylate form. Modifications on the E ring of camptothecin prevent binding of human serum albumin, which prefers the inactive carboxylate form, thereby enhancing the stability of the active lactone structure and resulting in prolonged agent activity. In addition, this agent sensitizes tumor cells toward radiation treatment.