A novel chemical suppressor of the growth, adhesion and migration of human pancreatic cancer cells

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The tumor aggressiveness is closely related to adhesion, migration and metastasis formation. In this regard, pancreatic cancer remains one of the most aggressive types of human cancers. Previously we have shown that calix[6]arene, a macrocyclic compound of phenolic units linked by methylene group at 2,6-positions, displayed a potent antileukemic action. Therefore, the aim of this study was to evaluate the influence of this compound on human pancreatic cancer cells (PANC-1). Calix[6]arene inhibited cells proliferation in a dose- and time-dependent, which IC$_{50}$ was estimated to be 17.9 µM after 24h treatment. Calix[6]arene influence on cells adhesion was assessed by plating and treatment of cells with the compound. Interestingly, this compound was able to abolish cell adhesion within 1 and half hour. Accordingly, by using slite assay, we also observed inhibition of cells migration with 10 µM calix[6]arene. The modulation of metabolic pathways by calix[6]arene was investigated by Western blot. It was observed that the antiproliferative action of this compound was due to inhibition of survival signaling pathways such as PI3K/AKT cascade and downregulation of retinoblastoma protein. The above mentioned is dysfunctional in several cancers including pancreatic, and in turn, remains the cell cycle activated. Besides, our findings revealed that calix[6]arene induces autophagy of pancreatic cells as indicated by augment LC3B protein expression and vacuole formation. Importantly, autophagy process induced by calix[6]arene culminated in cell death and it was not related with cellular resistance response. Our data strongly provide evidences that calix[6]arene appears as a potential candidate for overcoming pancreatic cancer aggressiveness.

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