Effects of the C1 domain-targeted PKC modulator HMI-1a3 on the viability of colon cancer cells in culture

Ilari M E Tarvainen, Rebecca Nunn, Maria H Jaentti, Virpi Talman, Raimo K Tuominen

Drug Research Program, Division of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, University of Helsinki, Finland

Protein kinase C (PKC) is a family of Ser/Thr kinases with 10 isoforms identified in humans. PKC plays a role in the control of fundamental cellular processes such as proliferation, induction of apoptosis, motility and differentiation, and has been implicated in variety of diseases ranging from cancer and neurological disorders to cardiovascular diseases. PKC is therefore an attractive and potential target for therapeutic intervention. A recent discovery identifying PKC as a tumour suppressor rather than a tumour promoter as previously thought, has called for a re-think regarding the therapeutic approaches. PKC activation as opposed to inhibition is expected to be beneficial in treating some forms of cancer. Our group has developed a new line of PKC modulating agents based on the structure of isophthalic acid, with promising cytotoxic activity against human cervical and prostate cancer cell lines. In this study, we investigated the effects of our compound in different colon cancer cell lines. In COLO 205, HT-29 and Caco-2 colon cancer cell lines, the lead isophthalate derivative HMI-1a3 reduced cell viability in the MTT assay, without causing necrosis in the LDH assay. These results further validate research into HMI-1a3 as a potential anti-cancer agent against various tumour types.