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Uridine-cytidine kinase 2, a potential chemotherapeutic target for cancer therapy: The role of natural products in targeting UCK2 enzyme activity

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Ribonucleosides phosphorylation by uridine-cytidine kinase 2 (UCK2) is an important step for the biosynthesis of ribonucleotides required in cancer proliferation via alternative salvage pathway. Uridine-cytidine kinase 2 (UCK 2) is an enzyme that is abnormally expressed in tumour cell growth and therefore implicated in all types of cancers. Due to the selective expression of UCK 2 in cancer cells, inhibition of this key enzyme necessitates the discovery of its potential inhibitors for cancer chemotherapy. Cytotoxic ribonucleoside analogues that target UCK2 enzyme are currently being investigated in clinical trials useful for cancer treatment. The nucleoside analogues inhibit cancer progression via interference with DNA and RNA synthesis, either by competitive inhibition of RNA polymerases or by intercalation into DNA and RNA of cancer cells. This is well achieved through UCK2-dependant phosphorylation of these nucleoside analogues. Whilst findings have clearly shown these antimetabolites to inhibit cancer development in clinical development, the aftermath toxic side effects nevertheless remain worrisome. Alternatively, natural bioactive compounds with complex chemical structures have the ability to inhibit the enzyme's catalytic activity. In this respect, pharmacological activities of few natural anticancer agents currently used in the market, however, specifically inhibit human enzymes, particularly those involved in the biochemical pathways. However, natural bioactive compounds capable of inhibiting the UCK2 enzyme in particular are not being explored as potential anticancer drugs useful for treatment. Therefore, effective natural anticancer drugs that target UCK2, specifically require urgent attention.

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