Healthcare Provider Resource

CCNM | Patterson Institute for Integrative Oncology Research

THE CENTRE FOR HEALTH INNOVATION

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General information

diabetes, hypercholesterolemia, certain heart conditions, and cancer (6).

Pharmacokinetics

DCA is a small water soluble molecule of 150 Da, allowing it to achieve 100% bioavailability when given either orally or intravenously (6). When given orally, DCA is readily absorbed in the gastrointestinal tract and less than 1% of the total given dose is excreted in the urine (5, 8, 9). Metabolism of DCA occurs in the liver and follows a simple one compartment pharmacokinetic model (5, 6, 9, 10).

ROS Production

By relying heavily upon cytoplasmic aerobic glycolysis for energy, cancer cells are able to avoid the production of reactive oxygen species (ROS) via mitochondrial oxidative phosphorylation (20, 23, 24). DCA triggers the remodeling of mitochondrial metabolism, opening transition pores and increasing the levels of pro-apoptotic ROS through the activation of caspases (20, 21, 23). High levels of ROS (such as H_2O_2) can inhibit tumour growth and result in apoptosis (7).

Release of Mitochondrial Calcium

The lack of mitochondrial oxidative phosphorylation in cancer cells facilitates an increase in intracellular calcium (Ca++), resulting in an increase of proliferative transcription factors (25). Increased intracellular Ca++ is responsible for activating ornithine decarboxylase, the rate limiting enzyme in DNA synthesis, as well as the anti-apoptotic nuclear factor of activated T lymphocytes (6, 25, 26). DCA causes a decrease in intracellular calcium, potentiating apoptosis in cancer cells and inhibiting proliferation (25, 26).

Mitochondrial K^+ Channel Axis

Cancer cells exhibit down regulation of the potassium (K+) channel Kv1.5 by decreasing the tonic efflux of K+ down its intracellular/extracellular gradient (7). K+ exerts a tonic inhibitory effect on caspases, and K+ channel inhibition suppresses apoptosis in cancer cells. DCA activates mitochondrial Kv channels in cancer cells, promoting apoptosis.

Cancer stem cells

Although less well established, there is some evidence that DCA may be able to reduce stemness and induce differentiation in cancer stem cells through many of the same mechanisms already described, including shifting cells to oxidative metabolism (1

Preclinical evidence related to effectiveness

Preclinical studies have demonstrated an anticancer effect of DCA in many cancer cell lines in vitro and in vivo, including glioblastoma (7, 27), colon (28, 29), breast (30, 31), prostate (22), ovarian (32), endometrial (26), cervical (33), lung (34), leukemia (35), and renal (36) cancer cells. One study in noncancerous cells and six cancer cell lines from various cancer types exposed cells to DCA at increasing concentrations (37). High levels of cell death were observed in five of the cancerous cell lines initially; however, three of the lines had subsequent delayed cell death at later stages. Two of the noncancerous cell lines also died when treated with DCA, and at the highest concentrations, all cell lines showed high rates of death. This study demonstrates that noncancerous cells may not be resistant to DCA. There are also some preclinical studies which have produced mixed results or failed to show an anticancer effect of DCA, including one in colon cancer (25).

Clinical Evidence related to effectiveness

One randomized controlled trial, five single-arm clinical trials and two

able to function and perform her work activities. Her survival time since diagnosis was one year and seven months.

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