

Metformin for Cancer Treatment?

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Metformin, a biguanide, is a well-known and safe pre-diabetic drug that works by decreasing glucose production by liver and decreasing peripheral glucose uptake [1]. Although famous as the initial line of therapy for diabetes mellitus type 2, it also has other benefits. Metformin may improve fertility [2] and reduce weight and cholesterol [3]. It is also used for several other diseases such as Polycystic Ovarian Syndrome (PCOS) [2]. Although inexpensive and readily available, metformin has been known to have major adverse effects including lactic acidosis, diarrhea and headache. Studies are currently exploring the role of metformin in the treatment of wide range of cancers such as breast cancer, endometrial cancer, prostate cancer and colorectal cancer [4]

The primary mechanism of action of metformin in diabetic patients is to activate adenosine 5-mono-phosphate-activated protein kinase (AMPK) that inhibits gluconeogenesis. This potential mechanism is being studied in many cancer trials where metformin activates AMPK that further works by inhibiting the mammalian target of the rapamycin (mTOR) signalling pathway of cancer cells [5, 6]. Hence, metformin plays a dual role of inhibiting growth and proliferation of cancer cells by targeting mTOR pathway and by restricting glucose required by the cells to grow. Metformin may inhibit another pathway; mitochondrial complex I (NADH dehydrogenase) activity, and hence cellular respiration of cancer cells [7]. Early studies have shown that a combination of conventional chemotherapy drugs with metformin helped to kill the cancer stem cells, thus preventing relapse of cancer disease [8]. In contrast, a recent study suggests that metformin's action in activating AMPK in cancer may actually promote cancer growth further confusing the picture [9]. It is no surprise that the results of many clinical trials have been inconclusive and contradicting. Ongoing research will likely clarify the proposed role of metformin in the treatment and prevention of cancer

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