Failure of Ditiocarb (Diethyldithiocarbamate) Therapy: Was Diet the Reason?
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It was the exciting message for HIV patients that inexpensive drug ditiocarb (diethyldithiocarbamate) was able to suppress the disease progression in clinical trials published 20 years ago in Lancet [1, 2]. Moreover, subsequent study (available in JAMA) confirmed ditiocarb as a potent drug against opportunistic infections in patients with symptomatic HIV disease [3]. Of course, such findings stimulated a larger trial which was, however, fatal for ditiocarb therapy [4]. Ditiocarb had no positive effect on HIV patients. Even more, the authors ended their study as follows: “A remote hypothesis is that two different compounds might have been used in the various studies. Against this possibility are the facts that the production of ditiocarb has not changed, that the American and the present study overlapped in time, that the same batches of experimental drug were used and that the content of unused capsules was analyzed and found to be correct.” Nonetheless, the cause of the ditiocarb efficacy in the Lancet and the JAMA studies has never been elucidated (however, it is clear ditiocarb had no beneficial immunomodulatory effect in HIV patients [5]). Can we now, from our today knowledge find the mechanism of ditiocarb-mediated AIDS suppression and, consequently, by such hypothesis explain the discrepancy of the trials results? In my view, it is possible.

In fact, the drug in the body can react with dietary components, e.g. metal salts, thus the reaction product can display different chemical properties than the drug itself. Therefore, the patients can be treated by the same drug with different compounds in the body according to their diet. This is the case of disulfiram, diethyldithiocarbamate dimer and prospective anticancer drug [6], which requires in a starting clinical trial at US National Cancer Institute (ClinicalTrials.gov Identifier NCT00742911) copper supplementation to be effective enough. In turn, the diethyldithiocarbamate complexes with copper or zinc formed either by disulfiram or ditiocarb could be able to cure cancer as they are potent proteasome inhibitors [7, 8]. Given that proteasome inhibition seems to be a successful means to suppress HIV infection [9-11], diethyldithiocarbamate complexes produced in patients with elevated copper or zinc in their body could prevent the progression of disease in HIV infected patients. Such hypothesis should be easy to verify as disulfiram is an old drug [12] able to enter clinical trials [13] with zinc or copper gluconate supplementation. This could help to explain astonishing success of trials published in Lancet and JAMA about 20 years ago.

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