

# Why disulfiram is not a panacea?

Boris Cvek<sup>1</sup>

<sup>1</sup>Palacky University Olomouc

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## Abstract

It is well-known fact that some drugs and drug candidates are remarkably “promiscuous” molecules. That means they bind to many various targets. Especially confusing is the case of disulfiram, an old drug used in alcohol aversion therapy.

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It is well-known fact that some drugs and drug candidates are remarkably “promiscuous” molecules. That means they bind to many various targets. Especially confusing is the case of disulfiram, an old drug used in alcohol aversion therapy.

Disulfiram is a highly reactive molecule which almost does not exist in the body after ingestion (and is metabolized after a few minutes in the blood). The therapeutic effect of the drug in alcoholics is caused by its metabolites which inhibit aldehyde dehydrogenase in human organism. Disulfiram easily creates S-S bonds with thiols and chelates metals (Eneanya, Bianchine, Duran, Andresen, 1981).

A lot of scientific literature has been published describing disulfiram ability to target various proteins in cancer (Cvek, 2011). For example, according to widely held assumption disulfiram can suppress cancer via inhibition of aldehyde dehydrogenase in cancer cells, although its metabolite while inhibiting the enzyme in cancer cells is not able – in contrast to disulfiram in copper containing medium – to kill the cells (Skrott et al., 2019).

Judging according to published scientific literature, disulfiram seems to be promising treatment for conditions as distinct as Alzheimer’s disease (Reinhardt et al., 2018), obesity (Bernier et al., 2020), tuberculosis (Dalecki et al. 2015), lyme borreliosis (Potula et al., 2020), and even for current pandemic. Indeed, two recent studies in Nature and Nature Immunology suggest that disulfiram could treat covid-19 (Jin et al., 2020) and sepsis (Hu et al., 2020), respectively.

The reactivity of the “promiscuous” drug pretends it is a panacea. Obviously, it is not. Meaningful biomedical research focused on disulfiram should identify the active compound, i.e. a disulfiram metabolite, in vivo and demonstrate coherence of both in vitro (the experiments with the disulfiram metabolite) and in vivo data (Skrott et al., 2017). Almost all published work on disulfiram ability to treat various maladies, including the two recent studies in Nature and Nature Immunology, fail to do so.

Boris Cvek (cvekb@seznam.cz)

Olomouc University Social Health Institute (OUSHI), Czech Republic

ORCID: <http://orcid.org/0000-0001-8238-3890>

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