In the past, the well established role of Aldehyde dehydrogenase (ALDH) in alcohol metabolism has driven the research behind the discovery of ALDH inhibitors. Accumulation of acetaldehyde after ethanol consumption leads to the development of unpleasant physiological effects comprising facial flushing, nausea, and tachycardia. This condition, termed the alcohol flushing syndrome, commonly occurs in subjects possessing a genetic polymorphism that confers upon them reduced activity of ALDH2, the enzyme responsible for the efficient metabolism of acetaldehyde. This observation led to the initial development of selective ALDH2 inhibitors as antidipsotropic or alcohol-aversive agents [1)].

As our understanding of the roles played by the various ALDH isozymes in disease states continues to expand, the rationale for the development of selective inhibitors of the individual isozymes becomes more apparent. The availability of such inhibitors, at minimum, would permit verification of the putative roles of the isozymes. Optimally, such inhibitors would be used to treat disease states in which ALDH activity is implicated in their pathophysiology [2)].

1)
Keung WM. (2003) Anti-dipsotropic isoflavones: the potential therapeutic agents for alcohol dependence. Med Res Rev 23:669–696
2)
Hiltbrand E, Fournet G, Giliberto JP, Paret MJ, Chantepie J, Morel D, Goré J, Reichert U, Mehier H, Rochedix ME, et al. (2009) Synergetic bitherapy in mice with xenografts of human prostate cancer using a methional mimic (METLICO) and an aldehyde dehydrogenase 3 inhibitor (MATE): systemic intraperitoneal (IP) and targeted intra-tumoral (IT) administration. Curr Med Chem 16:1184–1191