The Very-Long-Chain Fatty Acid Synthase Is Inhibited by Chloroacetamides

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The first elongation step to form very-long-chain fatty acids (VLCFAs) is catalyzed by the VLCFA-synthase. CoA-activated fatty acids react with malonyl-CoA to condense a C2-unit. As shown with recombinant enzyme this reaction is specifically inhibited by chloroacetamide herbicides. The inhibition is alleviated when the inhibitor (*e.g.* metazachlor) is incubated together with adequate concentrations of the substrate (*e.g.* oleoyl-CoA). Malonyl-CoA has no influence. However, once a chloroacetamide has been tightly bound to the synthase after an appropriate time it cannot be displaced anymore by the substrate. In contrast, oleoyl-CoA, is easily removed from the synthase by metazachlor. The irreversible binding of the chloroacetamides and their competition with the substrate explains the very low half-inhibition values of 10^{-8} M and below. Chiral chloroacetamides like metolachlor or dimethenamid give identical results. However, only the (*S*)-enantiomers are active.

Key words: Fatty Acid Elongation, Recombinant VLCFA-Synthase, Tight-Inhibitor Binding