The FASEB Journal express article 10.1096/fj.00-0685fje. Published online June 8, 2001.

Characterization of α-casozepine, a tryptic peptide from bovine α_{s1}-casein with benzodiazepine-like activity

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ABSTRACT

Caseins are a known source of biologically active peptides. In this study, we have shown evidence of a novel anxiolytic activity in a tryptic hydrolysate of bovine α_{s1}-casein. Injection of 3 mg/kg of this hydrolysate significantly reduced the epileptic symptoms caused by pentylenetetrazole in rats. Anxiety reduction was also observed when the hydrolysate was tested in the elevated plus-maze and in the conditioned defensive burying rat models. Peptides isolated from the hydrolysate were examined for their affinity for the γ-amino-butyric acid (GABA) type A receptor. Only one peptide, named α-casozepine, corresponding to the 91–100 fragment from bovine α_{s1}-casein, expressed affinity for $GABA_A$ receptor. *In vitro*, the peptide had 10,000 less affinity for the benzodiazepine site of the $GABA_A$ than did diazepam. However, in the conditioned defensive burying paradigm it was 10-fold more efficient than diazepam. The difference observed between the *in vitro* and *in vivo* activity of α-casozepine could not been explained by an action via the peripheral-type benzodiazepine receptor; α-casozepine had no affinity for this receptor. The α-casozepine amino acid sequence could be related to the carboxy-terminal sequence of the polypeptide diazepam binding inhibitor, an endogenous ligand of the central $GABA_A$ and peripheral-type benzodiazepine receptors.

Keywords: milk • casein peptide • anxiolysis • anticonvulsant • diazepam binding inhibitor