

ABSTRACT

Hypoglycin-A is a toxic, non-proteinogenic amino acid of considerable biochemical interest. It is obtained from the fruit of Blighia sapida K., and is the causative factor of the Jamaican "vomiting sickness". The toxicity of hypoglycin-A is attributed to the formation of a metabolite methylenecyclopropaneacetic acid which inhibits the oxidation of long-chain fatty acids. Hypoglycin-A induced in pregnant rats a significantly high incidence of congenital abnormalities and resorption. It did not reduce the fertility in mice, malformations were absent and only a small increase in resorption sites was observed after the administration of large doses. Hypoglycin-A administered to pregnant rabbits resulted in a high incidence of foetal resorption and overall stunting. Injected into the yolk sac of 24 and 48 hour chick embryos, hypoglycin-A was not teratogenic. Leucine, administered to pregnant rats simultaneously with hypoglycin-A, afforded no protection against the teratogenic action of hypoglycin-A. Leucine was shown to be highly teratogenic and exaggerated the teratogenicity of hypoglycin-A. Simultaneous administration of riboflavin and hypoglycin-A to preg-

nant rats reduced the occurrence of congenital abnormalities. Inhibition of long-chain fatty acid oxidation may represent a basic cellular mechanism involved in the teratogenicity of hypoglycin-A, because of its influence on oxidative phosphorylation and the electron transport system. Reversal of the hypoglycin-induced teratogenic effects by riboflavin, suggests that inhibition of the acyl dehydrogenase flavin-dependent-oxidation reaction, occurring during the degradation of fatty acids, is the site of action of hypoglycin-A.