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Effects of Neurotoxin 6-aminonicotinamide on Morphological and Biochemical Changes in Animal Tissues

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Effects of neurotoxin 6-aminonicotinamide(6-AN) on morphological and biochemical changes in animal tissues were investigated. 6-AN produced spongy-like numerous vacuoles in the posterior horn and the central region around the central canal of the spinal cord of hamster. In addition, the neuroglial cells such as astrocytes and oligodendrocytes were severely damaged and numerous vacuoles, swollen mitochondria and cisterna of rough endoplasmic reticulum were observed in damaged neuroglial cells. SDS-PAGE showed that 6-AN increased the level of 75 kDa spinal cord protein but caused the loss of 64.8 kDa protein. In pectoral muscle, the levels of 207.4 kDa and 32.1 kDa protein increased but that of 97.2 kD protein decreased. In testis, proteins of 125.4, 88.7, 69, 31.2, 19.1 and 17.4 kDa were missing, and the levels of 311.5, 75, 64, 54.1 and 53.2 kDa protein increased whereas those of 51.3, 42, 33, 27.2 and 22.6 kDa protein decreased. The specific activity of liver 6-phosphogluconate dehydrogenase markedly increased and that of spleen acetylcholinesterase reduced but intestine enzyme increased. Monoamine oxidase activity markedly decreased in the brain stem, cerebrum, kidney and liver.

In quail, 6-AN induced a new synthesis of prealbumin in plasma and also increased the levels of β-globulin but reduced the levels of γ-globulin. Plasma alkaline phosphatase and aspartate aminotransferase activities markedly decreased but those of creatine phosphokinase increased. Malic enzyme activity markedly decreased in pectoral muscle but reduced in liver. 6-Phosphogluconate dehydrogenase and lactate dehydrogenase activities decreased in liver. Glyceraldehyde-3-phosphate dehydrogenase decreased in liver and pectoral muscle and acetylcholinesterase increased in pectoral muscle. NAD glycohydrolase activity decreased in pectoral muscle.

In the hindlimb muscle, glyceraldehyde-3-phosphate dehydrogenase activity decreased but succinate dehydrogenase and glutathione reductase activities increased. Cytochrome c oxidase activity was not affected. SDS-PAGE showed that 6-AN appeared to

induce tentatively presumptive casein kinase 11 with a molecular mass of 32 kDa. N-terminal sequence of casein kinase 11 was determined to be N-Pro-Phe-Ser-Asn-Thr-His-Asn-His-Lys-Leu-Lys-Ser-Pro-Glu-Glu-Glu-Phe-Pro-C. RT-PCR analysis showed that casein kinase 11 has 650 bp. 2-D gel analysis showed that 6-AN induced the synthesis of new proteins with pI values of 4 and 6.8 but removed the protein with pI value of 7.2.

Overall results suggest that the metabolic actions of 6-AN are very specific for certain proteins or enzymes depending on tissues with the effect being the most pronounced in muscle tissues.