

New generation of drugs protecting against neurotoxic industrial chemicals

Chlorpyrifos and parathion, pesticides widely used in agriculture, belong to the family of the organophosphorus compound (OP), the same family than the nervous agents sarin [GB)] and soman [GD]. Whereas acrylamide (ACR) is mainly used in the industry, organic mercury (MeHg) is used in both industry and agriculture. Different reports show that acute exposure to high doses of these three compounds results in neurotoxic syndromes with high morbidity and/or mortality. Neurotoxic agricultural or industrial chemicals (neuroTICs) represent a significant military and terrorist threat for NATO countries, because both troops and civilian population can be exposed to high doses of these compounds if they are used in improvised explosive devices or after contaminating food or water. Despite the risk, no effective medical countermeasures to fight against most of neurotoxic syndromes are currently available. To improve the current medical countermeasures against neurotoxic chemicals a good knowledge of the molecular pathways involved in the pathophysiology of each syndrome is needed. This information is already available for OPs, ACR and MeHg, so it has been possible to identify neuroinflammation, oxidative stress and apoptosis as new potential therapeutic targets. N-acetylcysteine-amide (NAC-amide or AD4) and thioredoxin-mimetic (TXM) peptides are blood-brain barrier (BBB) permeable drugs specifically developed for reducing inflammation, oxidative stress and apoptosis in the central nervous system (CNS). Moreover, considering the electrophile-scavenging activity of these drugs, they should be able to decrease the bioavailability of electrophile neurotoxicants, including ACR and MeHg. However, there is currently no information about the therapeutic potential of these drugs for the treatment of acute neurotoxic syndromes.

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