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Liver and kidney damage induced by 4-aminopyridine in a repeated dose (28 days) oral toxicity study in rats

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4-Aminopyridine (4-AP) is an orphan drug indicated for the treatment of neuromuscular disorders. There is a great controversy around the use of this drug because of its narrow safety index and because a large number of adverse effects have been reported. Moreover, it was shown to induce cell death in different cell lines, being reported mainly apoptosis and necrosis as the principal pathways of cell death mediated by blockage of K channels or the Na, K-ATPase, but until now it was not described in vivo cell death induced by 4-aminipyridine. To provide new sub chronic toxicity data and specifically, evaluate if 4-AP (2, 4 and 10 mg/kg) is able to induce in vivo cell death process and the main pathways related to it, a repeated dose (28 days) oral toxicity study, at therapeutic range of doses, was conducted in rats. The anatomical pathology, the biochemical and hematological parameters were analyzed. The leucocytes number, the lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) enzymatic activity were increased at all dose but the erythrocytes number, the hemoglobin concentration, the alkaline phosphatase (FAL) and alanine aminotransferase (ALT) enzymatic activity were increased only at highest dose studied. However, glucose levels decreased at all doses. The biochemical results are indicative of hepatic damage. The anatomy pathology studies showed cell death only on liver and kidney. The present work shows for the first time in vivo cell death on liver and kidney.

Biography

Javier Del Pino received his PharmD degree at the University Complutense University of Madrid in 2004. He has two Masters in Sciences 2009 and 2010. He specialized in neurotoxicology and neurodevelopmental toxicology and received his PhD in Toxicology in 2009. In 2010 he worked in Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was Associated Researcher at University of Massachusetts (UMASS) working in Sandra Petersen´s Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2012, he got a position as Assistant Professor of Toxicology at the Complutense University of Madrid.

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