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DIALOG File 154: MEDLINE _ 85-92/FEB (9202)

chang d in various brain regions. It is concluded that this investigation failed to reveal overt toluene-induced CNS-neurotoxicity, however, certain irreversible effects were found which further add to the accumulating evidence of the chronic CNS-neurotoxicity of toluene.

07912002 92050002

Neurotoxicity of ammonia and fatty acids: differential inhibition of mitochondrial dehydrogenases by ammonia and fatty acyl coenzyme A derivatives.

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N urochem Res (UNITED STATES) Jul 1991, 16 (7) p795-803, ISSN 0364-3190 Journal Code: NX9

Contract/Grant No.: NS 24592; DK 16739

Languages: ENGLISH

Document type: JOURNAL ARTICLE

In several metabolic encephalopathies, hyperammonemia and rganic acidemia are consistently found. Ammonia and fatty acids (FAs) are neurotoxic: previous workers have shown that mmonia and FAs can act singly, in combination, or synergistically, in inducing coma in experimental animals. Howev r, the biochemical mechanisms underlying the neurotoxicity of ammonia and FAs have not been fully elucidated. FAs are normally converted to their corresponding CoA derivatives (CoAs) once they enter cells and it is known th t these fatty acyl CoAs can alter intermediary metabolism. Th pres nt study was initiated to determine the effects of ammonia and fatty acyl CoAs on brain mitochondrial d hydrogenases. At a pathophysiological level (2 mM), ammonia is a potent inhibitor of brain mitochondrial alpha-ketoglutarate dehydrogenase complex (KGDHC). Only at toxicological levels (10-20 mM) does ammonia inhibit brain mitochondrial NAD(+)- and NADP(+)- linked isocitrate d hydrog nase (NAD-ICDH, NADP-ICDH), and NAD(+)-linked malate dehydrogenase (MDH) and liver mitochondrial NAD-ICDH. Butyryl- (BCoA), octanoyl- (OCoA), and palmitoyl (PCoA) CoA were potent inhibitors f brain mitochondrial KGDHC, with IC50 values of 11, 20, and 25 microM, respectively; moreover, the inhibitory eff ct of fatty acyl CoAs and ammonia were additive. At levels of 250 microM or higher, both OCoA (IC50 = 1.15 mM) and PCoA (IC50 = 470 microM) inhibit brain mitochondrial NADP-ICDH; only at higher levels (0.5-1 mM) does BCoA inhibit this enzyme (by 30-45%). Much less sensitive than KGDHC and NADP-ICDH, brain mitochondrial NAD-ICDH is only inhibited by 1 mM BCoA, OCoA, and PCoA by 22%, 35%, and 44%, respectively.(ABSTRACT TRUNCATED AT 250 WORDS)

ASI 00005024

07911433 92049433

The influence of solvent stress on MMS-induced genetic change in Saccharomyces cerevisiae.

Zimmermann FK; Rohlfs A

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Mutat Res (NETHERLANDS) Sep-Oct 1991, 250 (1-2) p239-49, ISSN 0027-5107 Journal Code: NNA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

MMS induced mitotic recombination but not mitotic chromosome loss when tested in pure form in strain D61.M of Saccharomyces cerevisiae, confirming previous results of Albertini (1991), whereas in Aspergillus nidulans it also induced chromosomal malsegregation in addition to mitotic recombination (Kafer, 1988). However, induction of mitotic chromosome loss was observed in combination with strong inducers of chromosom loss such as the aprotic polar solvents ethyl acetate and to a lesser extent methyl ethyl ketone but not with gamma-valerolactone and propionitrile. In addition to this, 4 solvents, dimethyl formamide, dimethyl sulfoxide, dioxane and pyridine, enhanced the MMS-induced mitotic recombination in strain D61.M. An enhancement of MMS-induced mitotic recombination and reverse mutation could be demonstrated for ethyl acetate and gamma-valerolactone in yeast strain D7.

75-01-4

07910879 92048879

[Vinyl chloride and hemangiosarcoma of the liver]

Vinylchlorid und Hamangiosarkom der Leber.

von Schonfeld J; Breuer N

Abteilung fur Gastroenterologie, Medizinischen Universitatsklinik Essen.

Med Klin (GERMANY) Sep 15 1991, 86 (9) p482-4, ISSN 0723-5003 Journal Code: M9K

Languages: GERMAN

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL (28 Refs.)

07910172 92048172

Inhibition of acetaminophen activation by ethanol and acetaldehyde in liver microsomes.

Sato C; Liu J; Miyakawa H; Nouchi T; Tanaka Y; Uchihara M; Marumo F

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Life Sci (ENGLAND) 1991, 49 (24) p1787-91, ISSN 0024-3205 Journal Code: L62

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Mechanisms of the inhibitory effect of ethanol on acetaminophen hepatotoxicity are controversial. We studi d the effects of ethanol and acetaldehyde, an oxidative m tabolite of ethanol, on NADPH-dependent acetaminophen-glutathione conjugate production in liver microsomes. Ethanol at concentrations as low as 2mM prevented the conjugate production noncompetitively. Acetaldehyde also inhibited acetaminophen-glutathione c njugate production at concentrations as l w as 0.1mM that is comparable with thos observ d in vivo after social drinking. Acetaldehyde may be

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