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L35 ANSWER 80 OF 191 CA COPYRIGHT 1997 ACS
AN 127:14333 CA
TI p53 Gene ***mutation*** pattern in rat liver ***tumors*** induced by vinyl chloride 75-01-4
AU Barbin, Alain; Froment, Olivier; Boivin, Sandra; Marion, Marie-Jeanne; Belpoggi, Fiorella; Maltoni, Cesare; Montesano, Ruggero
CS IARC, 150, Cours Albert Thomas, Lyon, 69372, Fr.
SO Cancer Res. (1997), 57(9), 1695-1698
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB Vinyl chloride (VC) induces angiosarcomas of the liver (ASL) and hepatocellular ***carcinomas*** (HCCs) in humans and rodents. The authors examd. the presence of p53 gene ***mutations*** in ASL and HCC induced by VC in Sprague Dawley rats; 25 ASL and eight HCCs were analyzed for point ***mutations*** in exons 5-8, using PCR amplification, single-strand conformation polymorphism anal., and direct DNA sequencing. ***Mutations*** were found in 11 (44%) of the ASL and in 1 HCC. A 12-base pair deletion was found in one ***tumor*** ; all others were base-pair substitutions. Nine of the point ***mutations*** were obsd. at A:T base pairs (5 A:T .fwdarw. T:A; 2 A:T .fwdarw. G:C, and 2 A:T .fwdarw. C:G), and of three G:C .fwdarw. A:T transitions, only one was at a CpG site. In ASL, four ***mutations*** were found in exon 5, two in exon 6, and six in exon 7; the base-pair substitution found in one HCC was in exon 8. One ASL exhibited two point ***mutations*** , including a silent one. Two ASL exhibited the same ***mutation*** in codon 203 and two other samples in codon 253. Codon 235 was mutated in three ASL. Thus, p53 is often mutated in ASL induced by VC in rats, and as obsd. in ASL in humans exposed to VC, the majority of the missense ***mutations*** involved A:T base pairs. The characteristic patterns of ***mutations*** found suggest that a common mechanism operates in VC-induced p53 ***mutagenesis*** in both species; and these ***mutations*** are consistent with the formation of DNA etheno adducts by VC in the liver. The A:T .fwdarw. T:A transversion obsd. in the first nucleotide of codon 253 in two rat ASL is equiv. to the A:T .fwdarw. T:A transversion characterized previously in codon 255 in one human ASL assocd. with VC exposure.

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L35 ANSWER 132 OF 195 CA COPYRIGHT 1997 ACS
AN 127:125685 CA
TI Evaluation of alternative methods for establishing safe levels of occupational exposure to **vinyl halides**
AU **Storm, Jan E.**; Rozman, Karl K.
CS Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, KS, 66160-7417, USA
SO **Regul. Toxicol. Pharmacol. (1997), 25(3), 240-255**
CODEN: RTOPDW; ISSN: 0273-2300
PB Academic
DT Journal
LA English

75-01-4

AB The facts that redn. of occupational **vinyl chloride** exposures to levels within or below the 0.5-5 ppm range has so far been successful in eliminating vinyl chloride-induced liver angiosarcoma and that humans appear to be less sensitive to the carcinogenic effect of vinyl chloride than rats offered an opportunity to verify or dispute risk assessment extrapolation models used, and proposed, by the U.S. EPA. Safe occupational vinyl chloride exposures were defined as levels assocd. with an incidence of one angiosarcoma in 100,000 exposed workers, detd. from rat bioassay data using default no-threshold (linearized multistage model and benchmark dose approach with linear extrapolation) and threshold (NOEL/LOEL and benchmark dose uncertainty factor approaches) models, and then compared against the likely protective range of 0.5-5 ppm. Safe levels derived using either no-threshold model are equiv. and are two to three orders of magnitude below the 0.5-5 ppm range. Safe levels derived using either threshold model, when applying uncertainty factors which reflect equal or less sensitivity in humans compared to rats, fall within the 0.5-5 ppm range. Similar results were obtained for vinyl bromide and vinyl fluoride. These results undermine the U.S. EPA default assumption of no-threshold for vinyl halides as well as for other DNA-reactive carcinogens while simultaneously supporting the notion that a practical threshold exists. They further suggest that when threshold models are appropriate, the default assumption of greater sensitivity in humans compared to rats should be carefully evaluated.

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L35 ANSWER 39 OF 195 CA COPYRIGHT 1997 ACS
AN 127:139544 CA
TI Quantitative assessment of the ***health*** risk induced by occupational inhalation exposure to vinyl chloride in production plants in Poland 75-01-4
AU Szymczak, Wieslaw
CS Z Zakladu Epidemiologii Srodowiskowej, Inst. Medycyny Pracy Jerzego Nofera Lodzi, Lodz, 90-950, Pol.
SO Med. Pr. (1997), 48(2), 153-159
CODEN: MEPAAX; ISSN: 0465-5893
PB Instytut Medycyny Pracy
DT Journal
LA Polish
AB Vinyl chloride is classified by the IARC in group I - human carcinogens. In Poland occupational exposure to vinyl chloride is found among workers employed in many branches of industry, among others in the industry of vinyl chloride synthesis and polymn. as well as in the plastics, foot ware, rubber, pharmaceutical and metallurgical industries. Concns. obsd. range from the noon-determinable level to 90 mg/m3, at the MAC value equal to 5 mg/m3. ***Neoplasm*** of liver is a major carcinogenic effect of vinyl chloride. Hence, the ***health*** assessment focused on this crit. risk. Four different linear dose-response models, developed by several authors and based on results of different ***epidemiol*** . studies, were used to characterize the extent of ***cancer*** risk depending on the level of vinyl chloride concns. The estd. risk related to a forty-year employment under exposure equal to MAC values (5 mg/m3) fell within the range from 2.9.cntdot.10-4 to 2.6.cntdot.10-3. As the figures depict it did not exceed the acceptable level (10-3).