

**Conclusions:** Pulmonary exposure to MWCNT large was associated with increased incidence and severity of morphological liver lesions as compared with exposure to MWCNT small.

**PRENATAL DEVELOPMENTAL TOXICITY STUDIES OF RODENTS AND NON-RODENTS PERFORMED IN THE INSTITUTE OF INDUSTRIAL ORGANIC CHEMISTRY IN PSZCZYNA – RECORDED CHANGES**

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**Introduction:** Prenatal developmental toxicity studies are performed in order to evaluate the influence of tested items on pregnant females and developing fetuses and their potential to induce structural and functional abnormalities in fetuses as well as increases in their mortality.

**Materials and Methods:** The studies were performed on rats and rabbits. In each study there were three treated groups and one control group of pregnant females. Pregnant females were treated from the 5th to the 19th day of gestation for rats, and from the 6th to the 27th day of gestation for rabbits. Clinical signs, body mass and food consumption were controlled. All females were subjected to caesarean section. The fetuses were examined for deformations of the body and the skeletons of the fetuses were evaluated.

**Results:** The following changes were noted in rat fetuses: statistically significant increase in average weight of fetuses, weight of placenta and lengths of fetuses in treated groups, supranumerary digits (polydactylia), lack of digits and wavy ribs. The following changes were noted in rabbits: increased number of resorptions, statistically significant lower average number of ossification points in the metacarpus, seven digits (polydactylia) affecting the forelimb digits and conjoined fetuses.

**Conclusions:** The following changes, polydactylia in rats, conjoined fetuses and polydactylia in rabbits, provided evidence of a teratogenic effect. Conducting this type of studies on two species makes it possible to confirm the non-random character of the observed changes and to facilitate determination of potential risk to man.

**EFFECTS OF TRIHALOMETHANES ON LIVER MITOCHONDRIA**

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**Introduction:** Trihalomethanes (THMs), namely dibromochloromethane (DBCM) and bromodichloromethane (BDCM), are disinfection byproducts of chlorinated water. This experiment aimed to evaluate the mitochondrial dysfunction induced by THMs at low levels in a mouse model.

**Materials and Methods:** Experimental procedures were in accordance with European Directive 2010/63/EU. Forty-two male ICR mice were divided randomly into four experimental groups: DBCM exposed ( $n = 11$ ), BDCM exposed ( $n = 11$ ), methanol exposed ( $n = 11$ ) and control ( $n = 9$ ). Animals received DBCM, BDCM

and methanol, each at a concentration of 117 $\mu$ g/kg, once daily, by gavage, for a total of four administrations. Methanol was used as a vehicle for DBCM and BDCM. Animals from the control group only received water. Animals were killed 4 weeks after administration. Liver mitochondria were isolated and the mitochondrial respiratory activity (RCR), membrane potential ( $\Delta\Psi$ ), bioenergetic activity and oxidative stress were measured.

**Results:** During the experimental protocol, 12 animals died and were excluded from the study. RCR and  $\Delta\Psi$  were lower in DBCM-, BDCM- and methanol-exposed animals than in control group ( $P < 0.05$ ). Concerning mitochondrial bioenergetic activity, succinate dehydrogenase and ATP synthase activity was lower in DBCM- and BDCM-exposed groups. However, cytochrome c oxidase activity was only lower in the DBCM-exposed group ( $P < 0.05$ ). Concerning oxidative stress, the activity of superoxide dismutase and catalase was increased by DBCM, BDCM and methanol. Glutathione transferase activity was significantly increased in both DBCM and BDCM groups ( $P < 0.05$ ).

**EXPERIMENTAL GLIOBLASTOMA IN THE FISHER RAT MODEL: TREATMENT WITH A BIOCOMPATIBLE SYSTEM AS CARRIER OF METHOTREXATE**

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**Introduction:** Anticancer drug delivery through solid lipid nanoparticles (SLNs) to the brain parenchyma for the treatment of glioblastoma may represent a valid strategy aiming to overcome the blood–brain barrier. The aim of the present study was to report the in-vivo effects of SLNs loaded with methotrexate (SLN-MTX) in the treatment of glioblastoma in the Fisher rat model.

**Materials and Methods:** SLN-MTX biodistribution was evaluated in 12 rats, 30 min after an intravenous injection. Twelve rats implanted with the F98 glioma cell line into the caudate nucleus area were used to study tumour growth. Animals were imaged in a high field (7T) MRI scanner at postoperative days 7, 9 and 11. The MRI protocol included a T-w SE sequence before and after administration of a contrast medium. At postoperative days 7 and 9, six animals were treated intravenously with SLN-MTX. At day 11, all rats were killed and submitted for a complete necropsy examination with further histological and immunohistochemical investigations.

**Results:** The biodistribution showed a minimal increase of drug concentration in the brain. Tumour volumes (days 7, 9 and 11) were calculated by the MRI scanner. The growth curves appear to indicate a slowing of tumour growth in treated animals compared with controls rats, although this was not significant. Histological examination of the brains confirmed the presence of tumour masses characterized by an increased mitotic index and variable degrees of apoptosis, necrosis, vascular proliferation and glial reaction.

**Conclusions:** Preliminary data suggest a potential therapeutic effect of SLN-MTX. Additional histopathological investigations are in progress to confirm this hypothesis.