au=mitchell

7/3/1
DIALOG(R)File 161:Occ.Saf.& Hth.
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0129034 NIOSH-00168608
Effects of Phthalic Acid Esters on the Liver and Thyroid
Hinton, R. H., F. E. Mitchell, A. Mann, D. Chescoe, S. C. Price, A. Nunn, P. Grasso, and J. W. Bridges
Environmental Health Perspectives, Vol. 70, pages 195-210, 91 references December 1986 CODEN: EVHPAZ

7/3/2
DIALOG(R)File 161:Occ.Saf.& Hth.
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0125273 NIOSH-00164589
Effects of Mono (2-Ethylhexyl) Phthalate and Its Straight Chain Analogues Mono-n-hexylphthalate and Mono-n-octyl Phthalate on Lipid Metabolism in Isolated Hepatocytes
Mitchell, F. E., J. W. Bridges, and R. H. Hinton
Biochemical Pharmacology, Vol. 35, No. 17, pages 2941-2947, 25 references September 1, 1986 CODEN: BCPCA6

7/3/3
DIALOG(R)File 161:Occ.Saf.& Hth.
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0123778 NIOSH-00161224
Comparison Of The Short-Term Effects Of Di(2-Ethylhexyl) Phthalate, Di(n-hexyl) Phthalate, And Di(n-octyl) Phthalate In Rats
Mann, A. H., S. C. Price, F. E. Mitchell, P. Grasso, R. H. Hinton, and J. W. Bridges
Toxicology and Applied Pharmacology, Vol. 77, No. 1, pages 116-132, 39 references January 1985 CODEN: TXAPA9

7/3/4
DIALOG(R)File 161:Occ.Saf.& Hth.
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0117434 NIOSH-00155756
Time And Dose-Response Study Of The Effects On Rats Of The Plasticizer Di(2-ethylhexyl) Phthalate
Mitchell, F. E., S. C. Price, R. H. Hinton, P. Grasso, and J. W. Bridges
Toxicology and Applied Pharmacology, Vol. 81, No. 3, pages 371-392, 33 references December 1985 CODEN: TXAPA9

FE MITCHELL

1/5/1 (Item 1 from file: 156)
DIALOG(R)File 156:Toxline(R)
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02788289 Subfile: TOXBIB-78-251864
Effects of 4-ipomeanol, a product from mold-damaged sweet potatoes, on the bovine lung.
Doster AR; Mitchell FE; Farrell RL; Wilson BJ
Source: Vet Pathol; VOL 15, ISS 3, 1978, P367-75 ISSN: 0300-9858
Coden: XBQ
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 7812
Cattle given intraruminal administration of 4-ipomeanol, a furanoterpenoid originally obtained from sweet potatoes infected with Fusarium solani (F. javanicum), developed a respiratory syndrome clinically and histologically indistinguishable from atypical interstitial pneumonia. There were edema and emphysema in the lungs and mediastinum. The maximum nonlethal oral dose of 4-ipomeanol was estimated to be between 7.5 and 9 mg/kg of body weight.
Tags: Animal; Female
Descriptors/Keywords: *Pneumonia, Atypical Interstitial, of Cattle --Chemically Induced--CI; *Terpenes--Toxicity--TO; *Vegetables; Cattle; Furans--Toxicity--TO; Fusarium; Lung--Pathology--PA; Pneumonia, Atypical Interstitial, of Cattle--Pathology--PA

1/5/2 (Item 2 from file: 156)
DIALOG(R)File 156:Toxline(R)
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02636214 Subfile: HEEP-72-07644
Atypical interstitial pneumonia in cattle fed moldy sweet potatoes.
PECKHAM JC; MITCHELL FE; JONES O H JR; DOUPNIK B JR
Source: J AM VET MED ASSOC; 160 (2). 1972 169-172 Coden: JAVMA
Language: UNSPECIFIED
Journal Announcement: 7312
HEEP COPYRIGHT: BIOL ABS. Sixty-nine adult cattle in a herd of 275 died after being fed moldy cull sweet potato (Ipomoea batatas) roots. Clinical signs and necropsy findings were characteristic of atypical interstitial pneumonia. The disease was experimentally reproduced in cattle by oral administration of homogenized sweet potato cultures infested with Fusarium solani (F. javanicum) isolated from the moldy sweet potatoes fed the herd.

1/5/3 (Item 3 from file: 156)
DIALOG(R)File 156:Toxline(R)
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02633093 Subfile: PPBIB-03380
Atypical interstitial pneumonia in cattle fed moldy sweet potatoes.
Peckham JC; Mitchell FE; Jones OH Jr; Doupnik B Jr
Source: J Am Vet Med Assoc, Vol. 160, 2, p. 169-172, 1972
Language: UNSPECIFIED
Journal Announcement: 8709
Sixty-nine adult cattle in a herd of 275 died after being fed moldy cull sweet potato (Ipomoea batatas) roots. Clinical signs and necropsy findings were characteristic of atypical interstitial pneumonia. The disease was experimentally reproduced in cattle by oral administration of homogenized sweet potato cultures infested with Fusarium solani (F. javanicum) isolated from the moldy sweet potatoes fed the herd.
Descriptors/Keywords: Case report; Experimental exposure; Georgia; United states; Chicken; Swine; Fusarium solani; Fungi; Ipomoea batatas; Convolvulaceae; Lung; Respiratory; Dyspnea; Hyperpnea; Emphysema; Pulmonary edema; Congestion; Death; Weight loss

1/5/4 (Item 4 from file: 156)
DIALOG(R)File 156:Toxline(R)
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02489378 Subfile: TOXBIB-72-157884
Atypical interstitial pneumonia in cattle fed moldy sweet potatoes.
Peckham JC; Mitchell FE; Jones OH Jr; Doupnik B Jr
Source: J Am Vet Med Assoc; VOL 160, ISS 2, 1972, P169-72 ISSN: 0003-1488 Coden: HAV
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 7208
Tags: Animal; Female; Male
Descriptors/Keywords: *Animal Feed; *Fusarium; *Pneumonia, Atypical Interstitial, of Cattle--Etiology--ET; *Vegetables; Cattle; Cattle Diseases --Etiology--ET; Food Poisoning--Etiology--ET; Food Poisoning--Veterinary --VE; Mycotoxins; Pneumonia, Atypical Interstitial, of Cattle--Pathology --PA

1/5/5 (Item 5 from file: 156)
DIALOG(R)File 156:Toxline(R)
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02342199 Subfile: ETIC-14943
TOXICOPATHOLOGIC AND PHARMACOLOGIC PROPERTIES OF PIPERACETAZINE,A POTENT TRANQUILIZING AGENT
WEAVER LC; MITCHELL FE; KERLEY TL
Source: TOXICOL APPL PHARMACOL 5:49-60,1963 Coden: TXAPA
Language: UNSPECIFIED
Document Type: JOURNAL
Journal Announcement: 9103

Descriptors/Keywords: CANIS FAMILIARIS; MAMMAL, DOG; VIABILITY, FERTILITY AND MORTALITY; 2-ACETYL-10-(3(-4-(BETA-HYDROYETHYL)-PIPERIDINO)PROPYL)-PHENOTHIAZINE

1/5/6 (Item 6 from file: 156)
DIALOG(R)File 156:Toxline(R)
(c) format only 1995 Knight-Ridder Info. All rts. reserv.

01810309 Subfile: BIOSIS-86-35785
EFFECTS OF MONO-2-ETHYLHEXYLPHTHALATE AND ITS STRAIGHT CHAIN ANALOGUES MONO-N-HEXYLPHTHALATE AND MONO-N-OCTYLPHTHALATE ON LIPID METABOLISM IN ISOLATED HEPATOCYTES
MITCHELL FE; BRIDGES JW; HINTON RH
Source: BIOCHEM PHARMACOL; 35 (17). 1986. 2941-2948. Coden: BCPCA
Language: ENGLISH
Journal Announcement: 8612
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT CLOFIBRIC-ACID METABOLIC-DRUG CARCINOGEN CARCINOGENESIS ALLOSTERIC REGULATION NUTRITIONAL STATE
Tags: COMPARATIVE STUDY
Descriptors/Keywords: Cytology and Cytochemistry-Animal; Comparative Biochemistry, General; Biochemical Studies-General; Biochemical Studies-Proteins, Peptides and Amino Acids; Biochemical Studies-Lipids; Biochemical Studies-Sterols and Steroids; Enzymes-Physiological Studies; Metabolism-Lipids; Metabolism-Sterols and Steroids; Metabolism-Proteins, Peptides and Amino Acids; Nutrition-General Studies, Nutritional Status and Methods; Nutrition-General Dietary Studies; Digestive System-Pathology; Pharmacology-Drug Metabolism; Metabolic Stimulators; Toxicology-General; Methods and Experimental; Neoplasms and Neoplastic Agents-Carcinogens and Carcinogenesis ; Tissue Culture, Apparatus, Methods and Media; Muridae; *CARCINOGENS; ANIMALS; CYTOLOGY; HISTOCYTOCHEMISTRY; BIOCHEMISTRY; BIOCHEMISTRY; AMINO ACIDS; PEPTIDES; PROTEINS; LIPIDS; STEROIDS; STEROLS; ENZYMES--Physiology--PH; LIPIDS--Metabolism--ME; STEROIDS--Metabolism--ME; STEROLS--Metabolism--ME; AMINO ACIDS--Metabolism--ME; PEPTIDES--Metabolism--ME; PROTEINS--Metabolism--ME; NUTRITION; NUTRITIONAL STATUS; DIET SURVEYS ; DIET; DIGESTIVE SYSTEM DISEASES--Pathology--PA; DIGESTIVE SYSTEM --Pathology--PA; DRUGS--Metabolism--ME; POISONING; ANIMALS, LABORATORY; MURIDAE
CAS Registry No.: 24539-57-9; 5393-19-1; 4376-20-9; 882-09-7

1/5/7 (Item 7 from file: 156)
DIALOG(R)File 156:Toxline(R)
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01540782 Subfile: TOXBIB-86-097848
Time and dose-response study of the effects on rats of the plasticizer di(2-ethylhexyl) phthalate.
Mitchell FE; Price SC; Hinton RH; Grasso P; Bridges JW
Source: Toxicol Appl Pharmacol; VOL 81, ISS 3 Pt 1, 1985, P371-92 ISSN: 0041-008X Coden: VWO
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8604

Groups of male and groups of female Wistar albino rats were administered diets containing sufficient di(2-ethylhexyl) phthalate (DEHP) to ensure intakes of either 1000, 200, or 50 mg/kg/day. Four rats from each experimental group and six control rats of the same sex were killed 3, 7, 14, and 28 days and 9 months after commencement of treatment. At all time points the major abdominal organs were removed and subjected to histological examination. A more extensive necropsy was performed on those rats killed after 9 months of treatment. At all time points the livers of the rats were subjected to extensive histologic, electron microscopic, and biochemical examination. Changes could be grouped according to their time course. Two early and transient alterations were noticed. First, there were morphologic changes in the bile canaliculi of male rats treated with 1000 mg/kg/day of DEHP. Second, there was a burst of mitosis immediately after the start of administration of the compound. The time course of this mitotic burst varied; the increase in mitosis was greatest at 3 days in rats treated with 1000 mg/kg/day of DEHP and was smaller but more prolonged in rats treated with 200 or 50 mg/kg/day. Other changes, namely, a midzonal to periportal accumulation of fat, induction of peroxisomal enzymes, and induction of the P-450 isoenzyme also developed rapidly but were sustained throughout the study. The maximal change was usually attained within 7 days of commencement of treatment. More slowly developing changes were hypertrophy of the hepatocytes, centrilobular loss of glycogen, and a fall in glucose-6-phosphatase activity. Here maximal changes were not attained until 28 days after commencement of treatment. These three effects were clearly observed in rats treated with 200 or 1000 mg/kg/day of DEHP but were only marginally altered in rats treated with 50 mg/kg/day. Finally accumulation of lipid-loaded lysosomes assessed by light and electron microscopy and by assay of beta-galactosidase activity was only apparent in rats treated with DEHP for 9 months with 200 or 1000 mg/kg/day of DEHP. Changes in female rats were qualitatively similar to those observed in male rats. The alterations were, however, less pronounced than in male rats treated with an equal dose of DEHP and the degree of liver enlargement was much less because, although the initial hyperplasia was clearly apparent, there was a much smaller degree of hypertrophy.

Tags: Animal; Female; Male; Support, Non-U.S. Gov't

Descriptors/Keywords: *Diethylhexyl Phthalate--Toxicity--TO; *Liver--Drug Effects--DE; *Phthalic Acids--Toxicity--TO; Administration, Oral; Body Weight--Drug Effects--DE; Catalase--Metabolism--ME; Cytochrome P-450 --Pharmacology--PD; DNA--Biosynthesis--BI; Glycerolphosphate Dehydrogenase --Metabolism--ME; Hepatomegaly--Chemically Induced--CI; Liver--Enzymology --EN; Liver--Ultrastructure--UL; Liver Neoplasms--Chemically Induced--CI; Liver Neoplasms--Metabolism--ME; Neoplasms, Experimental --Chemically Induced--CI; Neoplasms, Experimental--Metabolism--ME; * Palmitoyl-CoA Hydrolase--Metabolism--ME; Rats; Rats, Inbred Strains; Sex Factors

CAS Registry No.: 0 (Phthalic Acids); 117-81-7 (Diethylhexyl Phthalate); 9007-49-2 (DNA); 9035-51-2 (Cytochrome P-450)

Enzyme No.: EC 1.1.- (Glycerolphosphate Dehydrogenase); EC 1.11.1.6 (Catalase); EC 3.1.2.2 (Palmitoyl-CoA Hydrolase)

1/5/8 (Item 8 from file: 156)
DIALOG(R)File 156:Toxline(R)

01444179 Subfile: TOXBIB-87-161718
Effects of phthalic acid esters on the liver and thyroid.
Hinton RH; Mitchell FE; Mann A; Chescoe D; Price SC; Nunn A; Grasso P; Bridges JW
Source: Environ Health Perspect; VOL 70, 1986, P195-210 ISSN: 0091-6765 Coden: EIO
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8707
The effects, over periods from 3 days to 9 months of administration, of diets containing di-2-ethylhexyl phthalate are very similar to those observed in rats administered diets containing hypolipidemic drugs such as clofibrate. Changes occur in a characteristic order commencing with alterations in the distribution of lipid within the liver, quickly followed by proliferation of hepatic peroxisomes and induction of the specialized P-450 isoenzyme(s) catalyzing omega oxidation of fatty acids. There follows a phase of mild liver damage indicated by induction of glucose-6-phosphatase activity and a loss of glycogen, eventually leading to the formation of enlarged lysosomes through autophagy and the accumulation of lipofuscin. Associated changes are found in the kidney and thyroid. The renal changes are limited to the proximal convoluted tubules and are generally similar to changes found in the liver. The effects on the thyroid are more marked. Although the levels of thyroxine in plasma fail to about half normal values, serum triiodothyronine remains close to normal values while the appearance of the thyroid varies, very marked hyperactivity being noted 7 days after commencement of treatment, this is less marked at 14 days, but even after 9 months treatment there is clear cut evidence for hyperactivity with colloid changes which indicate this has persisted for some time. Straight chain analogs of di-2-ethylhexyl phthalate, di-n-hexyl phthalate and di-n-oxtyl phthalate differ entirely in their short-term effects on the liver and kidney but have similar effects on the thyroid. The short-term in vivo hepatic effects of the three phthalate esters can be reproduced in hepatocytes in tissue culture. All three phthalate esters, as well as clofibrate, have early marked effects on the metabolism of fatty acids in isolated hepatocytes. The nature of these changes is such as to increase storage of lipid in the liver. A hypothesis is presented to explain the progress from these initial metabolic effects to the final formation of liver tumors.
Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't
Descriptors/Keywords: *Liver--Pathology--PA; *Phthalic Acids--Toxicity --TO; *Thyroid Gland--Pathology--PA; Cells, Cultured; Kidney--Drug Effects --DE; Kidney--Pathology--PA; Liver--Drug Effects--DE; Liver--Metabolism --ME; Rats; Rats, Inbred Strains; Structure-Activity Relationship; Thyroid Gland--Drug Effects--DE; Thyroid Gland--Metabolism--ME
CAS Registry No.: 0 (Phthalic Acids)

1/5/9 (Item 9 from file: 156)
DIALOG(R)File 156:Toxline(R)

01435802 Subfile: TOXBIB-87-019946

Time and dose study on the response of rats to the hypolipidaemic drug fenofibrate.

Price SC; Hinton RH; Mitchell FE; Hall DE; Grasso P; Blane GF; Bridges JW

Source: Toxicology; VOL 41, ISS 2, 1986, P169-91 ISSN: 0300-483X
Coden: VWR
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8701

Groups of male Wistar albino rats were administered diets containing sufficient fenofibrate to ensure intakes of either 200, 60 or 13 mg/kg/day or sufficient clofibrate to ensure an intake of 400 mg/kg/day. Four rats from each experimental group and 6 control rats were killed, 3, 7, 14 and 28 days, 8, 12 and 20 weeks and 6, 9, 12 and 18 months after commencement of treatment. At all time points livers were subjected to histological, electron microscopic and biochemical examination, the other major abdominal organs were removed for histological examination. A more extensive necropsy was carried out on rats killed after 12 and 18 months. The major alterations were observed in the liver, although there were also morphological changes in the thyroid, pancreas and kidney after prolonged treatment. The hepatic changes followed a distinct time course. Within 24 h of offering diets containing the compounds to the rats there was accumulation of small droplets of lipid, induction of peroxisomal enzymes and of the specific cytochrome P-450 catalysing omega-hydroxylation of fatty acids and an increase in the number of mitotic figures. More slowly developing changes were loss from the centrilobular zone of fat, glycogen and of glucose 6-phosphatase activity. Here maximal changes were observed after 14 days of treatment. A still more slowly developing change was accumulation of enlarged lipid-loaded lysosomes, which was maximal at 26 weeks, accompanied by the development of lipofuscin bodies. Finally, in animals treated for 12 months or more there was evidence for increasing cell turnover as indicated by an increased number of mitotic figures, more dark cells and induction of serum alanine transaminase. The last 2 groups of changes were not observed in rats treated with 13 mg/kg/day of fenofibrate. In general the degree of change in rats treated with 400 mg/kg/day of clofibrate was similar to those found in rats treated with 60 mg/kg/day of fenofibrate.

Tags: Animal; Male; Support, Non-U.S. Gov't
Descriptors/Keywords: *Antilipemic Agents--Toxicity--TO; *Liver --Drug Effects--DE; *Procetofen--Toxicity--TO; *Propionates--Toxicity--TO; Clofibrate--Toxicity--TO; Cytochrome P-450--Analysis--AN; Dose-Response Relationship, Drug; Endoplasmic Reticulum--Drug Effects--DE; Kidney--Drug Effects--DE; Lipids--Metabolism--ME; Liver--Metabolism--ME; Liver --Pathology--PA; Lysosomes--Drug Effects--DE; Microbodies--Drug Effects--DE ; Rats; Rats, Inbred Strains; Time Factors
CAS Registry No.: 0 (Antilipemic Agents); 0 (Propionates); 49562-28-9 (Procetofen); 637-07-0 (Clofibrate); 9035-51-2 (Cytochrome P-450)

1/5/10 (Item 10 from file: 156)
DIALOG(R)File 156:Toxline(R)

01432709 Subfile: TOXBIB-86-295900

Effects of mono (2-ethylhexyl) phthalate and its straight chain analogues mono-n-hexylphthalate and mono-n-octyl phthalate on lipid metabolism in isolated hepatocytes.

Mitchell FE; Bridges JW; Hinton RH

Source: Biochem Pharmacol; VOL 35, ISS 17, 1986, P2941-7 ISSN: 0006-2952 Coden: 9Z4

Language: ENGLISH

Document Type: JOURNAL ARTICLE

Journal Announcement: 8611

In cultured hepatocytes, as in vivo, mono-2-ethylhexyl phthalate (MEHP) and its straight chain analogues mono-n-hexyl phthalate (MnHP) and mono-n-octyl phthalate (MnOP) each cause accumulation of lipid but only MEHP produces significant induction of peroxisomal fatty acid oxidizing enzymes. To elucidate the mechanisms underlying this lipid accumulation we investigated the effects of these phthalates and the drug clofibric acid on fatty acid metabolism in suspensions of isolated hepatocytes. The effects were found to be markedly dependent on the nutritional state of the animals from which the hepatocytes were isolated. In hepatocytes isolated from animals fasted overnight, or animals fed ab libitum but killed at approximately 2.30 p.m., MEHP, MnHP, MnOP and clofibric acid each caused a marked rapid stimulation of fatty acid oxidation and the synthesis of triglycerides in hepatocytes when incubated in Hanks saline. Export of very low density lipoprotein (VLDL) from the cells was either unchanged or somewhat reduced. In contrast, in hepatocytes isolated from rats fed ad libitum but killed at approximately 9.30 a.m. MEHP and clofibric acid did not alter fatty acid oxidation or triglyceride synthesis, while MnOP and MnHP increased triglyceride synthesis but decreased fatty acid oxidation. The effects of fasting were largely abolished by incubations of the cells in a complete tissue culture medium (Liebowitz L-15). The results suggest that MEHP and its straight chain analogues can, either as the free acid or the CoA ester, mimic the action of fatty acids in the allosteric regulation of fatty acid metabolism.

Tags: Animal; Male; Support, Non-U.S. Gov't

Descriptors/Keywords: *Diethylhexyl Phthalate--Toxicity--TO; *Lipids --Metabolism--ME; *Liver--Metabolism--ME; *Phthalic Acids--Toxicity--TO; Cells, Cultured; Clofibrate--Pharmacology--PD; Diethylhexyl Phthalate --Analogs and Derivatives--AA; Lipoproteins--Biosynthesis--BI; Liver--Drug Effects--DE; Microbodies--Drug Effects--DE; Microbodies--Metabolism--ME; Oxidation-Reduction; Palmitic Acids--Metabolism--ME; Rats; Rats, Inbred Strains; Triglycerides--Metabolism--ME

CAS Registry No.: 0 (Lipoproteins); 0 (Palmitic Acids); 0 (Phthalic Acids); 0 (Triglycerides); 117-81-7 (Diethylhexyl Phthalate); 24539-57-9 (mono-n-hexyl phthalate); 4376-20-9 (mono-(2-ethylhexyl)phthalate); 5393-19-1 (mono-n-octyl phthalate); 57-10-3 (palmitic acid); 637-07-0 (Clofibrate)

1/5/11 (Item 11 from file: 156)
DIALOG(R)File 156:Toxline(R)
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01393485 Subfile: TOXBIB-85-091246
Comparison of the short-term effects of di(2-ethylhexyl) phthalate, di(n-hexyl) phthalate, and di(n-octyl) phthalate in rats.
Mann AH; Price SC; Mitchell FE; Grasso P; Hinton RH; Bridges JW
Source: Toxicol Appl Pharmacol; VOL 77, ISS 1, 1985, P116-32 ISSN: 0041-008X Coden: VWO
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8504
This study compares changes in the livers of rats treated with di(2-ethylhexyl) phthalate (DEHP) and its straight-chain analogs di(n-hexyl) phthalate (DnHP) and di(n-octyl phthalate (DnOP). Groups of rats were fed diets containing 20,000 ppm of one of these compounds. Subgroups were killed after 3, 10, and 21 days, and the livers were examined by histological, cytological, and biochemical methods. The results show considerable differences between the effects of the branched-chain phthalate ester DEHP and its straight-chain analogs. The major effects on the liver following administration of diets containing DEHP were midzonal and periportal accumulation of small droplets of lipid, hepatomegaly accompanied by an initial burst of mitosis, proliferation of hepatic peroxisomes and of smooth endoplasmic reticulum accompanied by induction of peroxisomal fatty acid oxidation, damage to the peroxisomal membranes as evidenced by increased leakage of catalase to the cytosol, and centrilobular loss of glycogen and falls in glucose-6-phosphatase activity and in low-molecular-weight reducing agents. In contrast, diets containing DnHP or DnOP induced accumulation of large droplets of fat around central veins leading, by 10 days, to mild centrilobular necrosis and a very slight induction of one peroxisomal enzyme and an increase in liver weight, but no significant changes in any other parameters which were affected by DEHP.
Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Descriptors/Keywords: *Diethylhexyl Phthalate--Pharmacology--PD; *Liver --Drug Effects--DE; *Phthalic Acids--Pharmacology--PD; Administration, Oral ; Body Weight--Drug Effects--DE; Eating--Drug Effects--DE; Liver --Enzymology--EN; Liver--Pathology--PA; Organ Weight--Drug Effects--DE; Rats; Rats, Inbred Strains; Structure-Activity Relationship; Testis--Drug Effects--DE
CAS Registry No.: 0 (Phthalic Acids); 117-81-7 (Diethylhexyl Phthalate); 117-84-0 (di-n-octyl phthalate); 84-75-3 (di-n-hexyl phthalate)

1/5/12 (Item 12 from file: 156)
DIALOG(R)File 156:Toxline(R)
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01272945 Subfile: HEEP-85-07125
Comparison of the short-term effects of di(2-ethylhexyl)phthalate, di(n-hexyl)phthalate and di(n-octyl)phthalate in rats.
MANN AH; PRICE SC; MITCHELL FE; GRASSO P; HINTON RH; BRIDGES JW
Robens Institute of Industrial and Environmental Health and Safety,

University of Surrey, Guildford, Surrey GU2 5XH, United Kingdom.
Source: TOXICOL APPL PHARMACOL; 77 (1). 1985. 116-132. Coden: TXAPA
Language: ENGLISH
Journal Announcement: 8506
HEEP COPYRIGHT: BIOL ABS. Changes in the livers of rats treated with di(2-ethylhexyl) phthalate (DEHP) and its straightchain analogs di(n-hexyl)phthalate (DnHP) and di(n-octylphthalate (DnOP) were compared. Groups of rats were fed diets containing 20,000 ppm of each compound. Subgroups were killed after 3, 10 and 21 days, and the livers were examined by histological, cytological and biochemical methods. The results showed considerable differences between the effects of the branched-chain phthalate ester DEHP and its stra containing DEHP were midzonal and periportal accumulation of small droplets of lipid, hepatomegaly accompanied by an initial burst of mitosis, proliferation of hepatic peroxisomes and of smooth endoplasmic reticulum accompanied by induction of p roxisomal fatty acid oxidation, damage to the peroxisomal membranes as evidenced by increased leakage of catalase to the cytosol and centrilobular loss of glycogen and falls in glucose-6-phosphatase activity and in low MW reducing agents. Diets containing DnHP or DnOP induced accumulation of large droplets of fat around central veins leading, by 10 days, to mild centrilobular necrosis and a slight induction of 1 peroxisomal enzyme and an increase in liver weight, but no significant changes in any other parameters which were affected by DEHP.
CAS Registry No.: 117-84-0; 117-81-7; 84-75-3

1/5/13 (Item 13 from file: 156)
DIALOG(R)File 156:Toxline(R)

01100581 Subfile: TOXBIB-82-119752
Response of gray foxes to modified live-virus canine distemper vaccines.
Halbrooks RD; Swango LJ; Schnurrenberger PR; Mitchell FE; Hill EP
Source: J Am Vet Med Assoc; VOL 179, ISS 11, 1981, P1170-4 ISSN: 0003-1488 Coden: HAV
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8206
Ten gray foxes seronegative for canine distemper virus were vaccinated with 1 of 3 commercial modified live-virus canine distemper vaccines. Of 5 foxes receiving vaccine A (chicken tissue culture origin), 4 developed significant titers (greater than or equal to 1:100) of neutralizing antibody to canine distemper virus and remained clinically normal after vaccination. Two of 3 foxes vaccinated with vaccine B (canine cell line origin) and both foxes receiving vaccine C (canine cell line origin) died of vaccine-induced distemper. Five unvaccinated control foxes died of distemper after a known occasion for contact transmission of virus from a fox vaccinated with vaccine B. The results suggested that the chicken tissue culture origin modified live-virus canine distemper vaccine is probably safe for normal adult gray foxes, whereas the canine cell origin vaccines are hazardous. The results of this study tended to corroborate anecdotal experiences of veterinarians who have observed that gray foxes fr quently die from distemper soon after vaccination with modified live-virus canine distemper vaccines.

Tags: Animal; Support, Non-U.S. Gov't
Descriptors/Keywords: *Distemper--Etiology--ET; *Distemper Virus, Canine --Immunology--IM; *Foxes--Immunology--IM; *Viral Vaccines--Adverse Effects --AE; Dogs; Vaccines, Attenuated--Adverse Effects--AE
CAS Registry No.: 0 (Vaccines, Attenuated); 0 (Viral Vaccines)

1/5/14 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit(R)

00713316 89374079 MEDL/89374079
THE PHOSPHORYLATION OF PROTEIN KINASE C AS A POTENTIAL MEASURE OF ACTIVATION
Mitchell FE; Marais RM; Parker PJ
Ludwig Institute for Cancer Research (Middlesex Hospital/University College Branch), London, U.K.
Biochem J; 261(1):131-6 1989 ISSN 0264-6021 Journal Code: 9YO
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8911
Subfile: X; L; M
As a means of determining the role of protein kinase C in the signal transduction from novel growth factors and hormones, we investigated the effects of well-characterized agents on the phosphorylation state of protein kinase C itself. These studies show that agents that stimulate protein kinase C either directly (phorbol esters) or indirectly through phosphatidylinositol breakdown (platelet-derived growth factor) induce an increase in the phosphorylation state of the kinase. By contrast, epidermal growth factor, which does not stimulate protein kinase C in fibroblasts, does not increase the phosphorylation state of protein kinase C, but leads to a decrease. The data suggest that the phosphorylation state of protein kinase C is dynamically controlled and can be used to provide evidence of protein kinase C activation.
Tags: Human
Major Descriptors: *Protein Kinase C--Metabolism--ME
Minor Descriptors: Cells, Cultured; Enzyme Activation; Epidermal Growth Factor-Urogastrone; Fibroblasts--Enzymology--EN; Phosphorylation; Platelet-Derived Growth Factor; Tetradecanoylphorbol Acetate
CAS Registry No.: 0 (Platelet-Derived Growth Factor); 16561-29-8 (Tetradecanoylphorbol Acetate); 62229-50-9 (Epidermal Growth Factor-Urogastrone)
Enzyme No.: EC 2.7.1.- (Protein Kinase C)

1/5/15 (Item 2 from file: 159)
DIALOG(R)Fil 159:Cancerlit(R)

00545071 87161718 MEDL/87161718
EFFECTS OF PHTHALIC ACID ESTERS ON THE LIVER AND THYROID
Hinton RH; Mitchell FE; Mann A; Chescoe D; Price SC; Nunn A; Grasso P; Bridges JW
Robens Institute of Industrial and Environmental Health, University of Surrey, Guildford, UK.
Environ Health Perspect; 70:195-210 1986 ISSN 0091-6765 Journal Code: EIO
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8706
Subfile: L; M
The effects, over periods from 3 days to 9 months of administration, of diets containing di-2-ethylhexyl phthalate are very similar to those observed in rats administered diets containing hypolipidemic drugs such as clofibrate. Changes occur in a characteristic order commencing with alterations in the distribution of lipid within the liver, quickly followed by proliferation of hepatic peroxisomes and induction of the specialized P-450 isoenzyme(s) catalyzing omega oxidation of fatty acids. There follows a phase of mild liver damage indicated by induction of glucose-6-phosphatase activity and a loss of glycogen, eventually leading to the formation of enlarged lysosomes through autophagy and the accumulation of lipofuscin. Associated changes are found in the kidney and thyroid. The renal changes are limited to the proximal convoluted tubules and are generally similar to changes found in the liver. The effects on the thyroid are more marked. Although the levels of thyroxine in plasma fall to about half normal values, serum triiodothyronine remains close to normal values while the appearance of the thyroid varies, very marked hyperactivity being noted 7 days after commencement of treatment, this is less marked at 14 days, but even after 9 months treatment there is clear cut evidence for hyperactivity with colloid changes which indicate this has persisted for some time. Straight chain analogs of di-2-ethylhexyl phthalate, di-n-hexyl phthalate and di-n-oxtyl phthalate differ entirely in their short-term effects on the liver and kidney but have similar effects on the thyroid. The short-term in vivo hepatic effects of the three phthalate esters can be reproduced in hepatocytes in tissue culture. All thre phthalate esters, as well as clofibrate, have early marked effects on the metabolism of fatty acids in isolated hepatocytes. The nature of these changes is such as to increase storage of lipid in the liver. A hypothesis is presented to explain the progress from these initial metabolic effects to the final formation of liver tumors.
Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't
Major Descriptors: *Liver--Pathology--PA; *Phthalic Acids--Toxicity--TO; *Thyroid Gland--Pathology--PA
Minor Descriptors: Cells, Cultured; Kidney--Drug Effects--DE; Kidney --Pathology--PA; Liver--Drug Effects--DE; Liver--Metabolism--ME; Rats; Rats, Inbred Strains; Structure-Activity Relationship; Thyroid Gland--Drug Effects--DE; Thyroid Gland--Metabolism--ME
CAS Registry No.: 0 (Phthalic Acids)

1/5/16 (Item 3 from file: 159)
DIALOG(R)File 159:Cancerlit(R)

00484211 86097848 MEDL/86097848
TIME AND DOSE-RESPONSE STUDY OF THE EFFECTS ON RATS OF THE PLASTICIZER DI(2-ETHYLHEXYL) PHTHALATE
Mitchell FE; Price SC; Hinton RH; Grasso P; Bridges JW
Robens Institute of Industrial and Environmental Health and Safety, University of Surrey, Guildford, United Kingdom.
Toxicol Appl Pharmacol; 81(3 Pt 1):371-92 1985 ISSN 0041-008X
Journal Code: VWO
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 8603
Subfile: X; L; M
Groups of male and groups of female Wistar albino rats were administered diets containing sufficient di(2-ethylhexyl) phthalate (DEHP) to ensure intakes of either 1000, 200, or 50 mg/kg/day. Four rats from each experimental group and six control rats of the same sex were killed 3, 7, 14, and 28 days and 9 months after commencement of treatment. At all time points the major abdominal organs were removed and subjected to histological examination. A more extensive necropsy was performed on those rats killed after 9 months of treatment. At all time points the livers of the rats were subjected to extensive histologic, electron microscopic, and biochemical examination. Changes could be grouped according to their time course. Two early and transient alterations were noticed. First, there were morphologic changes in the bile canaliculi of male rats treated with 1000 mg/kg/day of DEHP. Second, there was a burst of mitosis immediately after the start of administration of the compound. The time course of this mitotic burst varied; the increase in mitosis was greatest at 3 days in rats treated with 1000 mg/kg/day of DEHP and was smaller but more prolonged in rats treated with 200 or 50 mg/kg/day. Other changes, namely, a midzonal to periportal accumulation of fat, induction of peroxisomal enzymes, and induction of the P-450 isoenzyme also developed rapidly but were sustained throughout the study. The maximal change was usually attained within 7 days of commencement of treatment. More slowly developing changes were hypertrophy of the hepatocytes, centrilobular loss of glycogen, and a fall in glucose-6-phosphatase activity. Here maximal changes were not attained until 28 days after commencement of treatment. These three effects were clearly observed in rats treated with 200 or 1000 mg/kg/day of DEHP but were only marginally altered in rats treated with 50 mg/kg/day. Finally accumulation of lipid-loaded lysosomes assessed by light and electron microscopy and by assay of beta-galactosidase activity was only apparent in rats treated with DEHP for 9 months with 200 or 1000 mg/kg/day of DEHP. Changes in female rats were qualitatively similar to those observed in male rats. The alterations were, however, less pronounced than in male rats treated with an equal dose of DEHP and the degree of liver enlargement was much less because, although the initial hyperplasia was clearly apparent, there was a much smaller degree of hypertrophy.
Tags: Animal; Female; Male; Support, Non-U.S. Gov't
Major Descriptors: *Diethylhexyl Phthalate--Toxicity--TO; *Liver--Drug Effects--DE; *Phthalic Acids--Toxicity--TO
Minor Descriptors: Administration, Oral; Body Weight--Drug Effects--DE;

Catalase--Metabolism--ME; Cytochrome P-450--Pharmacology--PD; DNA --Biosynthesis--BI; Glycerolphosphate Dehydrogenase--Metabolism--ME; Hepatomegaly--Chemically Induced--CI; Liver--Enzymology--EN; Liver --Ultrastructure--UL; Liver Neoplasms--Chemically Induced--CI; Liver Neoplasms--Metabolism--ME; Neoplasms, Experimental--Chemically Induced--CI; Neoplasms, Experimental--Metabolism--ME; Palmitoyl-CoA Hydrolase --Metabolism--ME; Rats; Rats, Inbred Strains; Sex Factors

CAS Registry No.: 0 (Phthalic Acids); 117-81-7 (Diethylhexyl Phthalate); 9007-49-2 (DNA); 9035-51-2 (Cytochrome P-450)

Enzyme No.: EC 1.1.- (Glycerolphosphate Dehydrogenase); EC 1.11.1.6 (Catalase); EC 3.1.2.2 (Palmitoyl-CoA Hydrolase)

1/5/17 (Item 4 from file: 159)
DIALOG(R)File 159:Cancerlit(R)

00080456 75703187 CARC/75703187

METABOLISM OF 2,4-TOLUENEDIAMINE IN THE RAT.

Grantham PH; Glinsukon T; Mohan LC; Benjamin T; Roller PP; Mitchell FE; Weisburger EK

Carcinogen Metabolism and Toxicology Branch, Natl. Cancer Inst., Bethesda, Md.

Toxicol Appl Pharmacol; 33(1):179 1975 ISSN 0041-008X

Languages: ENGLISH

Document Type: JOURNAL ARTICLE

Journal Announcement: 7604

2,4-Toluenediamine, a polyurethane intermediate, has induced hepatocellular carcinomas in rats. During a metabolism study with **14 C-labeled 2,4-toluenediamine in male Fischer rats, the excretion was followed up to 120 hr after an ip dose. Within 24 hr 81% of the **14 C was recovered (73% in urine, 8% in feces). By 120 hr, 98.6% was excreted (76.4% in urine, 22.2% in feces). Fractionation of urinary metabolites revealed that 21% of the dose was unconjugated metabolites; 7.5% glucuronic acid conjugates; 10% acid-hydrolyzable conjugates; and 30% water-soluble metabolites. The major unconjugated metabolites were indentified by mass sp ctrometry, thin layer chromatography and gas liquid chromatography, as 4-acetylamino-2-aminotoluene 5.2% of dose; 2,4-diacetylaminotoluene 1.4%, and 4-acetylamino-2-aminobenzoic acid 4.4%. The glucuronide fraction contained four major metabolites, one of which has been identified as 4-acetylamino-2-aminobenzoic acid. The radioactivity in blood and plasma reached a peak 1 hr after an ip dose of 2,4-toluenediamine, decreased rapidly through 7 hr and gradually through 48 hr. Tissue concentrations were greatest in kidney and liver, and much less in spleen, heart, testis, and brain. Radioactivity was bound to nuclear DNA, to RNA, and to microsomal and soluble protein of liver.