LIFE: International Journal of Health and Life-Sciences
ISSN 2454-5872

Rashmi Wardhan, 2016

Volume 2 Issue 2, pp. 55-70

Year of Publication: 2016

DOI- http://dx.doi.org/10.20319/lijhls.2016.22.5570

This paper can be cited as: Wardhan, R. (2016). Carcinogenic and Organo Toxic Compounds in Milk. LIFE: International Journal of Health and Life-Sciences, 2(2), 55-70.

CARCINOGENIC AND ORGANO TOXIC COMPOUNDS IN MILK

Rashmi Wardhan
Department of Biochemistry, Shivaji College, University of Delhi, Delhi-110027, India
rashmiwardhan56@gmail.com

Abstract

Milk Adulteration has been a serious health issue since the last few decades because of increasing population, industrialization and urbanization of cities like Delhi. Milk is a major diet component for every individual, from infant to adult. Consumption of adulterated milk may cause serious developmental disorders in children. The aim of the present study is to analyse various toxic substance in milk samples collected from different zones of Delhi Capital Region by GC-MS. We observed 41 toxic compounds with varied degree of toxicity like Benzene and related compounds, phthalates and plasticizers, pesticide degradative products and Savoring agents in the samples. These compounds are reported to have ecotoxic, carcinogenic, mutagenic and organotoxic properties. The presence of such toxic substances may not show immediate effects but might cause a serious threat later in the life.

Keywords

Carcinogenic; Mutagenic; Pesticides; Organotoxic; Phthalates; Plasticizers; Eco toxic

1. Introduction

Milk and milk products are generally considered as complete food for human consumption especially for infants and children because of proteins, fats and minerals (Kholif et al, 1994, Abou Arab, 1996). The presence of any adulterant in milk may affect the food chain at all levels and this could be a major health concern. These toxic compounds as adulterants could have several effect on human body such as reproductive toxicity, reduced sperm counts in semen, childhood cancer and neurological dysfunction (Dalvie et al, 2004, Ribas-Fito et al, 2003, Wigle, 2003). The toxic compounds on the basis of their structure and physiological function may be divided into four categories: Pesticides, Plasticizers, Genotoxic compounds and Organotoxic compounds with delayed toxicity.

Pesticides like DDT (dichloro diphenyl trichloro ethane) persist in environment through agriculture waste. Their accumulation leads to long term toxic affects like birth defects, endocrine disruption (US NTP, 2007 & Wigle, 2003), especially reproductive hormones disruption and cancer (Foster et al, 2000). These pesticides also affects steroid hormone synthesis and thyroid hormone levels in the body that results in heart diseases, damage to nervous and reproductive system. The contamination of the milk with pesticides has been reported in the samples from different parts of the world (Abdou et al, 1983, Ashnagar et al 2009, Losada et al, 1996, Maitre et al 1994). The human breast milk also shows pesticide contamination within the range from 0.1 mg/L - 26 mg/L (Srivastava & Patel, 1990).

Phthalates, another class of adulterants in milk and food samples come under the category of plasticizers, which provides sturdiness and softness to plastics. Phthalates are usually dialkyl or alkyl aryl ester of 1, 2 benzene dicarboxylic acids. These chemicals may intoxicate the food chain and are transferred at various levels. Being lipophilic in nature, these compounds tend to cluster in lipid part of the food. Since all the dairy products are enriched in different types of lipids, they have more possibility to get contaminated by this class of adulterant. The common types of phthalates are diethyl phthalate (DEP), dimethyl tetraphthalate, butylbenzyl phthalate and dibutyl phthalate. Milk and dairy products contribute for 17.2 % to 27.6% phthalates to the total dietary exposure (Clark & Mackay, 2003). These phthalates are investigated to affect endocrine system and cause general developmental abnormalities like skeletal malformation and increased fetal death in experimental studies

(ATSDR, 2002, , ATSDR, 1995, ATSDR, 1997 b, Wigle, 2003). These compounds majorly affect male primarily testes development, caused decreased anogenital distance and other effects (Swan et al, 2005). Neonates are commonly affected by phthalates toxicity because their exposure to plastics in feeding bottles, nipples etc.Genotoxic compounds like Benzene and benzene derivatives may enter human body by inhalation, oral ingestion and dermal route. They are metabolized to phenol, hydroquinone andcatechols. Addition of a single oxygen atom by cytochrome P450 converts benzene ring to benzene oxide primarily in liver. It might rearrange itself to phenol or converted to dihydro-diol intermediates by epoxide hydrolase or converted to catechol by dehydrogenase (http://www.crios.be/Benzene/toxicology.htm). Second oxygen and hydroxyl group addition forms Hydroquinone from these compounds. Benzene and its metabolites are reported to be cytotoxic, induce chromosome aberrations and affect nuclear morphology. While Catechol delays sister chromatid exchange and cell cycle, benzene induce chromatids, chromosome gaps , deletion mutation (Morimoto & Sheldon, 1980), other benzo compounds like nonylphenol and octylphenol shows estrogenic, hematological and general effects in living organisms (Satyanarayan 2011, Bennie 1999).Milk adulteration is a common practice in Indian cities. With the upcoming reports of different class of adulterants observed in milk samples like urea, cane sugar, ammonium salts, formalin, detergents, hydrogen peroxides and pesticides in the samples collected from different cities of India (Singuluri et al, 2014, Nath et al 2013). Delhi is an alarming case in concern. Due to increased migration of human population and urbanization in Delhi, there is increase in demands of food products. To meet these demands, there is definite milk transport chain from cows to consumers which have multiple halts of contamination. Therefore, there is a need for public survey to access the level of adulteration and contamination of milk samples in the Delhi Capital Region. For this purpose, several milk samples were collected from different zones of Delhi to check the presence of pesticides and other contaminants in the milk to determine the bio safety aspect of the marketed milk.

2. Material and Methods

Collection of Samples: Milk Samples were collected from different Dairies of North, South, East, West and Central zones of Delhi. Samples were pooled zone wise and processed further for analysis.

Extraction of contaminants from Milk for multi-residue analysis by Gas Chromatography and Mass Spectroscopy: Milk sample (15 ml) was mixed with 40 ml n-Hexane and 40 ml of acetone [1:1, v/v] of HPLC grade in glass stoppered cylinder and shaken vigorously. The mixture was allowed to stand until the clear separation of two layers. The upper organic phase and lowerphase were separately collected. The organic phase was passed through anhydrous sodium sulphate and C-Fluorocil in 3:2 ratios in a 300 mm long and 18 mm diameter chromatographic column, which was obstructed by glass wool preconditioned with n-hexane and acetone mix. After step 1, the contents were further eluted with n-Hexane and acetone. The collected aliquot was analysed by GC/MS [GCMS-QP2010 plus] (Modified method of Ribeiro & Ribeiro, 2010). GC-MS analyses were carried out on GC-MS [GCMS-QP2010 Plus] system equipped with a quantitative analysis by SIM mode detector. A VF-5 ms column of 30 m length, 0.25 mm diameter, and 0.25 urn film thickness was used. The oven was programmed as follows: an initial temperature 100 °C , injection temperature 250 °C .Flow control mode linear , Pressure 95.5 kpa, total flow 16.3 ml/min , column flow 1.21 ml/ min, linear velocity 40.9 cm/sec, purge flow 3ml/min, split ratio 10. Ion source 230 °C, interface temperature 260 °C and solvent cut time 2.50 min .GC-MS was performed at JNU centre, New Delhi.

3. Results

GC-MS analysis of the milk samples resulted in detection of different organic compounds which includes fatty acids, phytohormones, flavoring agents, derivative of penicillic acid, terpenes and toxic compounds (Supplementary Table 1-4). However no typical pesticides like DDT, Malathion, parathion etc. was detected in the collected milk samples. But measurable quantities of several organic compounds with different extent of toxicity were found in the samples. These compounds are classified according to their toxic effects on human beings such as genotoxic, phthalates and plasticizers and other suspected compounds according to their structure and functional groups [Table 1, Table2]. Total percentage of the toxic

compounds per milk sample was observed to be 32.81%. Amongst these compounds, the estimate of the Genotoxic compounds like Benzo-compounds were 3.9% and Phenolic compounds were 2.57% and observed in all the samples collected from different zones of Delhi Capital Region. Phthalates and Plasticizers were observed to be 19.33% and in maximum amounts in all the samples. Henicosyl compound like Henicosane and Henicosyl Heptafluro phosphate were observed at the concentration of 0.53%, and also present in all the samples. Ethylene Brassylate at 0.30% concentration observed only in the samples collected from south zone of Delhi. Terpinol and itsderivatives at a concentration of 0.40% observed in the samples collected from central, north, south and west Delhi region. Glycidyl stearate at a concentration of 0.22% observed in a sample collected from central region of Delhi. Octa tricontyl penta fluoro propionate at 0.09% concentration observed in the samples collected from only north zone of Delhi Region. Compounds like 3-chloro propionic acid heptadecyl ester, Benzene, (4-chloro butyl) and triphenyl phosphoric acid ester which are pesticide intermediates were observed at concentration of 0.13% and detected in the samples from different zones of Delhi Capital Region.

Table 1: *Toxic substances observed in milk samples through GC MS*

S. No.	Name of the Compound	Effect
1	CYCLOHEXENE, 1-METHYL-4-Q-METHYLETHENYL	Suspected liver toxicant, kidney toxicant, neurotoxicant, respiratory toxicant, and immunotoxicant Carcinogenic in rats
2	BENZENE, (4-CHLOROBUTYL)	Pesticide degradative product, cause general genotoxicity

3	BENZENE, (1-ETHYLNONYL)	Induce chromosomal abbretions
4	BENZENE, (1- PENTYLHEPTYL)	Induce chromosomal abbretions
5	1,2-BENZENEDICARBOXYLIC ACID, BIS (2-METHYLPROPYL)	Mild Mutagen, endocrine disrupters
6	1,2-BENZENEDIC CARBOXYLIC ACID	Genotoxic
7	BENZEMETHANOL,ALPHA.,ALPHA-DIPHENYL	Ecotoxic, Acute toxicity to invertebrate and fish
8	BENZENEMETH ANOL,. ALPHA.,. ALPHA. -DIMETHYL	Irritant to the skin, eyes, nose, throat, and upper respiratory tract
9	ACETIC ACID 2 PHENYL ETHYL ESTER	Mild genotoxic
10	BENZENAMINE ,N-PHENYL	Genotoxic
11	BENZO METHANOL	Genotoxic and organotoxic
12	PHENOL,4-(1,1,3,3-TETRAMETHYLBUTYL)	Endocrine disrupter
13	4-NONYLPHENOL	Environment toxic, cause anemia, increases bilirubin content

14	PHENOL, 3,5-BIS (1,1-DIMETHYL)	Toxic to aquatic animals The acute toxicity is low by the oral route and moderate by the dermal route to human acute toxicity is low by the oral route and moderate by the dermal route to human
15	BICYCLO[4.1.0]HEPT-3-ENE, 3,7,7-TRIMETHYL	Induce hypersensitivity and cause chronic lung function impairment
16	3-CYCLOHEXEN-l-OL, 4-METHYL-l-(l –METHYLETHYL	Organotoxic
17	d-LIMOLENE	Nausea, vomiting, and diarrhea in dose dependent manner
18	4-METHYL-3-OXO-1-CYCLOHEXENYL 2-METHYLPRO	Nausea, vomiting, and diarrhea in dose dependent manner
19	OXALIC ACID, 2-ETHYLHEXYL OCTADECYL ESTER	Plasticizer, inhibitory roles on the calcium signaling coupled with human AchR
20	OXALIC ACID, DECYL NEOPENTYL ESTER	Plasticizer

21	OXALIC ACID, NEOPENTYL UNDECYL ESTER	Plasticizer
22	OXALIC ACID, NEOPENTYL NONLYL ESTER	Plasticizer
23	ETHYLENE BRASSYLATE	Skin irritant, Ingradient of pesticide Rentikol
24	PHOSPHORIC ACID, TRIPHENYL ESTER	Pesticide synthesis intermediate damage nerves, kidney
25	BICYCLO [4.1 0] HEPT-3-ENE, 3,7,7-TRIMETHYL	Highly toxic to aquatic organism
26	BICYCLO [4.1 0] HEPT-3-ENE, 3,7,7-TRIMETHYL	Highly toxic to aquatic organism
27	PHENOL, NONYL	Environment toxic, cause anemia, increases bilirubin content.
28	3 , CHLORO PROPIONIC ACID,HEPTA DECYL ESTER	Degradative product of polythene
29	BUTANOIC ACID, 1,2,3-PROPANETRIYL ESTER	Plasticizer
30	BUTYRIC ACID, 3-TRIDECYL ESTER	Plasticizer
31	BUTYRIC ACID, 3-PENTADECYL ESTER	

		Plasticizer
32	2,2,4-TRIMETHYL 1,3 PANTANE DIOL DIISOBUTYRATE	Plasticizer
33	2-BUTEN-L-ONE, 1,3-DIPHENYL	Plasticizer
34	TRIBUTYL ACETYL CITRATE	Plasticizer
35	1,2-BENZENEDICARBOXYLIC ACID, DIISODECYL EST	Plasticizer
36	OCTA TRIACONTYL PENTA FLUORO PROPIONATE	Used as lubricant in synthesis of PVC Masaru Higuchi et al 1977
37	2-ETHYLBUTYRIC ACID, 2,4,4-TRIMETHYLPENTYL ESTER	Fragrance ingredient
38	2-ETHYL BUTYRIC ACID,3-METHYL PENT-2-YL ESTER	Fragrance ingredient
39	2H-PYRAN-2-ONE, 6-HEPTYLTETRAHYDRO-	Flavoring agent
40	HENEICOSYL HEPTAFLURO BUTYRATE	

		Insect pheromone

4. Discussion

India is one of the largest milk producer as well as consumer in the world. Total milk consumption in the Delhi Capital Region is more than 70 lakh litre per day. Milk is a major food for infants and children and hence the adulteration of the milk with toxic compounds is very alarming. Adulteration could occur at any stage from fodder of animals to delivery of milk at all ports of value chain. There are already published reports from different parts of the world where the milk samples are contaminated with pesticides having carcinogenic effects and phthalates which have plasticizing toxicity (Nath et al, 2013, Fierens et al, 2012). In the present study, we observed different class of toxic compounds which are ecotoxic, carcinogenic; interfering compounds in the normal physiology of organs in human beings and plasticizers [Table 1], Compounds like Cyclohexene, 1 methyl, 4(1-methylethenyl) can cause abdominal burning, nausea, vomiting, diarrhea, dysuria, hematuria, unconsciousness, shallow respiration, and convulsions on ingestion.(www.toxipedia.org/). Terpinol and derivatives like cyclohexan, 3-cyclohexan-1-ol, 4 methyl-1-methyl ethyl belongs to terpenoid family which causes CNS depression if ingested in large amounts (www.chemwatch.net). Chlorinated benzene compounds are toxic which cause liver and kidney dysfunction (Bryant 1993, Meek et al 1994 a, b). Ethylene Brassylate is a member of the fragrance structural group macrocyclic lactone and lactide derivatives. It causes adverse effects to aquatic organisms (Me Ginty et al, 2011). In humans, it causes irritation in mucous membrane of upper respiratory tract. It is also used as an ingredient of Rentokil, a pesticide used in U.K (www.rentokil-initial.com). Phthalates and plasticizers are generally used to strengthen the PVC products. Compounds like 4-Methyl-3oxo-1 Cyclo Hexyl 2, Methyl Propyl or Methyl Isobutyrate ketone is generally found in spray paint and shows peripheral neuropathy (AuBuchon et al 1979). Phosphoric acid triphenyl is a plasticizer and degradative product of pesticide, cause skin allergy, may affect liver and kidney (http://www.state.nj.us/health/eoh/odosweb/). High and repeated exposure may damage nerves causing paralysis. Alkyl derivative of oxalic acid are also used as plasticizers which have toxic effects (http://www.nicans.gov.au). Other suspected toxic compounds like

Heneicosane is an oviposition attractant pheromone of larval origin in *Aedes aegypti* mosquito (Mendki et al 2000). According to TCI America material safety Data sheet, SO366, Glycidal stereate is amutagen and cause skin and eye irritation. 2H-pyran-2-one tetrahydra-6-nonyl is long chain alkyl phenol and might be inhibitor of long chain fatty acid metabolism and can cause contact allergy. Phenyl acetic acid esters are mutagenic and genotoxic *in vivo.* Phenylethyl alcohol cause low order of reproductive toxicity (Groundschober, 1977). These compounds observed in the milk samples through GC-MS analysis are not the conventional metabolites of animal physiology. Such compounds present at the different concentrations in the milk samples might be carcinogenic, hormone disrupters and organ interfering. Daily consumption of such adulterated milk can lead to slow poisoning effect by such compounds which can't be diagnosed immediately and has later on effects. In future, further research is needed to determine the toxic concentration of these contaminants in milk.

References

Abdou, S.M., Abd-El-Gawad, A. A., Abo-El Amaiem, E. & El-Alfy, M.B. (1983). Effect ofsome organochloride insecticide on some species of bacteria used in the dairy industry.Egyptian Journal of Dairy Science, 11, 205.

Abou-Arab, A. A. K. (1996). Fate of some pollutants in various papers fed to lactating buffaloes and their effect on the milk. Journal of Agricultural Science MansouraUniversity, 21, 1385-1395.

Ashnagar, A., Gharib Naseri, N. & Cheraghi Farmad, M. (2009). Determination of organochloride pesticides residues in cow's milk marketed in Ahwaz city of Iran. International Journal of PharmTech Research, 1, 247-251.

ATSDR(2002) , Phthalates - Environmental Protection Agency www.epa.gov/teach/chem_summ/phthalates_summary.pdf

ATSDR, 1995. Toxicological profile ,Diethyl phthalate.www.atsdr.cdc.gov/toxprofiles/tp69-p.pdf

ATSDR, 1997b. Agency for Toxic Substances and Disease Registry. Health guidelines comparison values. 1997

AuBuchon, J., Robin, H.I. & Viseskul, C. (1979). Peripheral Neuropathy after exposure to methyl isobutyl ketone in spray paint. Lancet, 2, 363-364.

Bennie, D. (1999). Review of the environmental occurrence of alkyl phenols and alkyl phenol ethoxylates. Water Quality Research, Journal Of Canada. 34, 79-122.

Benzene Toxicology: http://www.crios.be/Benzene/toxicology.html

BICYCLO [4.1.0]HEPT-3-ENE, 3,7,7-TRIMETHYL or Carene ,Guide Chem.CAS 13466-78- 9, MSDS.

Bryant, J.G. (1993) Chlorinated benzenes. IN: Kroschwitz, J.I. & Howe-Grant, (Eds). The Kirk Othmer Encyclopedia of Chemical Technology, Fourth Edition, Wiley-Interscience,N.Y., 6: 87-100.

Clark, K., Cousin, IT. & Mackay, D. (2003). Assessment of critical exposure pathways. In: Staples, C.A. (Ed.), The Handbook of Environmental Chemistry: Phthalate Esters. Springer, Berlin, Germany, 227-262.

Cyclohexene, 1 methyl4(1 methylethenyl), (4R). Toxipedia. (www.toxipedia.org/pages/viewpage. action?pageId=60171

Dalvie, M. A. , Myers, J. E. , Thompson, M. L. , Robins, T. G. , Dyer, S. , Riebow, J., Molekwa, J. , Jeebhay, M., Millar, R. & Kruger, P. (2004). The Long-Term Effects of DDT Expo- sure on Semen, Fertility, and Sexual Function of Malaria Vector control Workers in Limpopo Province. South African Environmental Research, 96, 1-8.doi: 10.1016/j.envres.2003.09.002

Ethylene brassylate, http://www.matrixscientific.com/media/msds.

Ethylene Brassylate , RENTOKIL CLOTHES MOTH KILLER CASSETTE SDS No. 1135 - EN - GB Issue : 3 28 : 04 : 2014,http:// www http://www.rentokil-initial.com.

Fierens, T., Servaes, K., Van Holgerbeke, M., Greerts, L., De Henauw S., Sioen, I, & Vanermen, G. (2012). Analysis of phthalates in food products and packaging materials soldon the Belgian market. Food and Chemical Toxicology, 50, 2575-2583.

Foster, P.M.D., Cattley, R.C., & Mylchreest, E. (2000) Effect of Di -n-butyl phthalate (DBP) on male reproductive development in the rat: Implications for human risk assessment. Food and Chemical Toxicology, 38, s97-s99.

Grundschober, F. (1977). Toxicological assessment of flavoring esters. Toxicology, 8, 387-390.

Higuchi, M., Ohnishi, H. & Yagihara, H. (1974). Lubricants for thermoplastic resins such as polyvinylchloride. Patent Filed Dec. 27, 1971, Ser. No. 212,787 Claims priority, application Japan, Dec. 30, 1970. Patent number 3817900, United States Patent Office,Patented June 18, 1974.

Human Health Tier II: Assessment for Oxalic acid soluble salts (http://www.nicans. gov.au)

Kholif, A.M., S. Abo El- Nor, A. A. K. Abou-Arab & H.A. El-Alamy (1994). Effect of spraying diazinon to control the external parasites on the productive performance of dairy animals. I. Yield and composition of buffalo's and Friesian cow's milks. Egyptian Journal of Dairy Science, 22, 145-154.

Losada, A.N., Fernandez, N., Dioz, M.J., Teran, M.T., Garcia, J.J. & Sierra, M. (1996). Organochlorine pesticides in bovine milk from Leon (Spain). The Science of the Total Environment, 181, 133-135.

Maitre, ML, Sierra, P., Lenardon, A., Enrique, S. & Marino, F. (1994). Pesticide residue levels in Argentinian pasteurized milk. The Science of Total Environment, 155, 105-108.

Mc Ginty,D., Letizia,C.S. & Ap, A.M. §(2011). Fragrence material review on 11-oxo hexadecanolide.food and chemical toxicology, 49 Suppl 2:S163-167. doi:10.1016/j.fct.2011.07.016.Epub2011 Jul23.

Meek, M.E., Giddings, M. & Gomes, R. (1994a). Monochlorobenzene: Evaluation of risks to health from environmental exposure in Canada. Environmental Carcinogenesis andEcotoxicology Reviews. 12, 409-415.

Meek, M.E., Giddings, M. & Gomes, R. (1994b). 1, 2-Dichlorobenzene: Evaluation of risks to health from environmental exposure in Canada. Environmental, Carcinogenesis and Ecotoxicology Reviews.12, 269-273.

Mendki, M.J., Ganeshan, K., Shriprakash, Suryanarayan, M.V.S; Malhotra, R.C, Rao, K.M, & Vaidyanathanswami, R. (2000). Heneicosane is an oviposotion attractant pheromone of larval origin in Aedes aegypti mosquito. Current Science, 78, 1295-1296.

Morimoto, Kanehisa & Wolff , Sheldon (1980),Increase of chromatid exchanges anperturbations of cell division kinetics in human Lymphocytes by benzene metabolites.Cancer Research, 40, 1189-1193.

Nath, A., Vendan, S. E., Priyanka, Singh, J.K., Singh, C.K., & Kumar, S. (2013). Carcinogenic pesticides residue detection in cow milk and water samples from Patna, India. Current Trends in Biotechnology and Chemical Research, 3, 1-7.

Nonphyenol and Nnonylphenol Ethoxylates Action Plan .U.S. Enivronmental Protection Agency (EPA) August 2010. Accessed 9/22/2011.

Ribas-Fito, N. , Cardo, E., Sala, M. , de Muga, M. E. , Ma- zon, C, Verdu, A.,Kogevinas, M., Grimalt, O. J. & Sunyer, J. (2003). Breastfeeding, Exposure to Organochlorine Compounds and Neurodevelopment in Infants. Pediatrics, 111, 580-585.doi:10.1542/peds.lll.5.e580.

Ribeiro, A.C. & Ribeiro, S. D. A. (2010). Specialty Products Made from Goat Milk. Small Ruminant Research, 89, 225-233. doi: 10.1016/j.smallrumres.2009.12.048.

Sangale, M. K., Shahnawaz Mohd, & B Ade, A. (2012). A Review on Biodegradation of Polythene, The Microbial Approach. Journal of Bioremediation and Biodegradation , 3 , 1 - 9.http://dx.doi.org/10.4172/2155-6199.1000164.

Satyanarayan S. K., Chokkalingam, K., Mathan, R., & Grummit, T. (2011b). Toxicity studies of nonylphenol and octylphenol: hormonal, hematological and biochemical effect in *Clarias gariepinus.* Journal of Applied Toxicology, 31:752-756 (doi 10.1002/jat.l629).

Singuri, H. & Sukumaran M.K. (2014). Milk Adulteration in Hyderabad, India-A Comparative Study on the Levels of Different Adulterants present in Milk. Journal of Chromatography Separation Techniques, 5, 1-3. (http://dx.doi.org/10.4172/2157-7064.10002121

Srivastava, U.K. & Patel, N.T. (1990). Pesticide Industry in India. Oxford and IBH Publishing Company Ltd., New Delhi.

Swan S.H., Main K.M., Liu F., Stewart S.L., Kruse R.L., Calafat A.M., Mao C.S., Redmon J.B., Ternand, C.L., Sullivan, S. & Teague, J.L. (2005). The Study for Future Families Research Team: Decrease in anogenital distance among male infants with prenatalphthalate exposure: Environmental Health Perspectives, 113, 1056-1061.

Terpinol and derivatives, Santa Cruez Biotechnology. Inc,(www.chemwatch.net).

Toxicology and Carcinogenesis Studies of d-Limonene in F344/N Rats and B6C3F1 Mice Gavage Studies (National Toxicology Program Technical report series number 347, CAS No. 5989275). US Department of Health and Human Services.

Triphenyl Phosphate : http://www.state.nj.us/health/eoh/odosweb

3,3,5-trimethylcyclohexan-1 –one Sub-chronictoxicity (90-day): oralhttp ://echa. europa. eu/about-us. TSCA Chemical Inventory (2005). Stearic Acid Glycidyl ester S0366.

U.S.National Toxicology program, Center for the Evaluation of Risks to Human Reproduction. 2007" NTP-CERHR Reports and Monographs. http ://cerhr. niehs. nih. gov/reports/index. html.

U.S. Agency for Toxic Substances and Disease Registry (ATSDR) (2002) ToxicologicalProfile for Di(2-Ethylhexyl)phthalate (DEHP). http ://www. atsdr. cdc. gov/toxprofiles/tp9. html.

U.S. Environmental Protection Agency Ground Water and Drinking Water(2002). Technical Fact Sheet on: Di (2-Ethylhexyl) phthalate (DEHP). http://www.epa.gov/safewater/dwh/t-soc/dehp.html.

U.S. Agency for Toxic Substances and Disease Registry (1995). Toxicological Profile for Diethyl Phthalate. http://www.atsdr.cdc.gov/toxprofiles/tp73.html.

U.S. Agency for Toxic Substances and Disease Registry (1997a). Toxicological Profile for Di-n-Butyl Phthalate. http://www.atsdr.cdc. gov/toxprofiles/tp 135.html.

U.S. Agency for Toxic Substances and Disease Registry (1997b). Toxicological Profile for

Di-nOctylphthalate (DNOP). http://www.atsdr.cdc.gov/toxprofiles/tp95.html.

Wigle, D. T. (2003). Hormonally Active Agents. In Wiggle, D.T. Child Health and the Environment. Oxford, Oxford University press, Inc