

TOXICOLOGY OF SYNTHETIC FUELS - A MINI REVIEW

Raymond Poon and Ih Chu
Bureau of Chemical Hazards,
Health Canada, Ottawa, Canada

Recent analytical and toxicological studies on synthetic fuels have confirmed previous observations that higher boiling fractions and blends are more toxic. It has also been reported that toxic effects of synfuels are related to the polycyclic aromatic hydrocarbon (PAH) content, including nitrogen containing and polar PAHs. Although carcinogenicity and mutagenicity are the main health concern of higher boiling synthetic fuels, the systemic toxicity (effects on liver, blood, bone marrow, thymus and thyroid) should not be overlooked. The marked thymic atrophy and perturbation of immune cells of PAH treated animals suggest that these fractions are immuno-suppressive. The lower-boiling fractions possess relatively weak carcinogenicity, mutagenicity and systemic toxicity, but their dermal irritant effects are still of concern in occupational settings. In the fractions and blends studied, the benzo(a)pyrene level is an indicator of their PAH content and hence toxicity. However, it is also clear that different composition of PAH mixtures in the high boiling fractions produce interactive effects that results in complex toxic and biochemical manifestations. The purpose of this article is to review recent mammalian toxicity data of various synfuels, and to shed some light on their potential human health hazards.

CARCINOGENICITY AND MUTAGENICITY

Early epidemiological studies showed that workers involving in the production of coal gas had a significantly higher rate of bladder and lung cancer (Doll et al., 1972), and those in the production of shale oils had a higher incidence of skin and scrotum cancer (Costello, 1979; Purde and Etlin, 1980). Reviews conducted by the International Agency for Research on Cancer concluded that shale oils were human carcinogen (IARC 1985), and exposure to "older" coal-gasification processes was carcinogenic to humans (IARC 1984). Workers in coal liquefaction plants were also reported to have a higher incidence of skin cancer (Shepard, 1981). A large body of evidence indicated that coal-derived synthetic fuels (Reilly and Renne, 1988; McKee et al., 1995; for review see Chu et al., 1994) and shale oils (Holland et al., 1981) were carcinogenic in animal studies and mutagenic in bacterial bioassays. In general, the middle and high boiling streams were more tumorigenic. More recent studies on coal coprocessing products and bitumen derived products also indicated that the middle and high-boiling fractions were more mutagenic (Table 1) (Otson and Peake, 1993).

SUBCHRONIC TOXICITY

Although carcinogenicity and mutagenicity are the main health concern of high-boiling synthetic fuels, their subchronic toxicity data are also required for health risk assessment. Table 2 summarizes the data from animal studies that provide no-observed-adverse-effect levels (NOAELs) for the fuels tested. It can be seen that the major target organs are liver, blood, bone marrow, thymus and thyroid. The effects on hematological disorders, and on the liver, consisting principally of hepatomegaly and microsomal enzyme induction were reported (Chu et al., 1988, 1992, 1994; Poon et al., 1994, 1996). The higher boiling fractions were more toxic and had NOAELs of less than 8 mg/kg/day. In contrast, petroleum derived unleaded gasoline and Fuel Oil no. 1 were less toxic, with NOAELs of greater than 250 mg/kg/day (Table 2).

EFFECTS ON THE SKIN

While the lowest boiling distillates showed the weakest tumor induction and systemic effects, they were shown to be a strong skin irritant. For example, shale-oil derived distillates, jet fuels (Holland et al., 1981; ATSDR, 1995), and the light gas oil fraction of bitumen upgrading products (Poon et al., 1994) produced severe skin lesions in rats. Feuston (1994) suggested that the skin irritation was associated with 2-ring aromatics, which were found to be most abundant in the low-boiling fractions. Chemical-induced skin phototoxicity appears to be a major concern for high-boiling distillates and bottom fractions. McKee and Maibach (1985) reported that EDS liquids with boiling points above 200°C produced skin phototoxic effects in guinea pigs. In a survey of workers at a pilot coal liquefaction plant, Driscoll et al., (1995) noted that self-reported photosensitivity reactions were strongly associated with dermal exposure to the solvents containing bottom fractions of coal liquids. Paint that contained bitumen was considered to be the cause of an outbreak of skin phototoxicity and ocular symptoms in workers in a dockyard (Davies, 1996). Coal tar and its products have been known to cause photosensitive skin reactions (Gould et al., 1995). PAHs in coal tar and bitumens, such as acridine, pyrene, and phenanthrene were reported to be potent phototoxins (Gendimenico and Kochevar, 1984; Davies, 1996). These compounds are also present in the high-boiling fractions

(Table 1).

EFFECTS ON IMMUNE FUNCTIONS

Studies with laboratory animals showed that high-boiling coal liquefaction products (Springer et al., 1986), high-boiling coal co-processing products, and medium- and high-boiling bitumen upgrading products (Chu et al., 1992; Poon et al., 1994) produced thymic atrophy. Because the thymus is an essential organ for the normal development of immunological functions in early life, these observations suggest that treatment with higher-boiling fuels may compromise the immune system. In contrast to a paucity of immunotoxicity data on synthetic fuels, these effects of PAHs were well documented (reviewed in Ward et al., 1985; Davila et al., 1997). In addition to benzo(a)pyrene, other PAHs such as phenanthrene and fluoranthene, which are widely present in synthetic fuels, were also found to have immunosuppressive effects (Davila et al., 1996; Yamaguchi et al., 1996; Tsien et al., 1997). Recent surveys of coke-oven workers exposed to PAHs revealed significant changes in their immune functions (Szczeklik et al., 1994; Winker et al., 1996).

COMPLEX MIXTURES

It is generally accepted that the toxicities of higher boiling synthetic fuels are predominantly related to their high PAH level, and the benzo[a]pyrene content is often used as an indicator of the total PAHs in synfuels (Table 3). However, it would be an oversimplification to solely rely on the benzo[a]pyrene level as the predictor of toxicity because different fuels have different PAH compositions, and various chemicals in the mixtures may exert individual and interactive effects. For example, individual PAHs were reported to exert an interactive effect on the mutagenicity of the other hydrocarbon components coexisted in the mixtures (Hermann, 1981). Neutral PAHs were associated with skin carcinogenicity while nitroaromatic and other polar aromatic compounds appeared to be potent mutagen (Otson and Peake, 1993; McKee et al., 1995). Hydrotreatment is known to substantially reduce the carcinogenicity, mutagenicity and acute toxicity of various synthetic fuels (Holland et al., 1981; McKee and Lewis 1987). However, detail studies on the effect of hydrotreatment on the PAH composition are still lacking.

SUMMARY

Prolonged exposure to synthetic fuels produces a broad range of systemic effects which include carcinogenicity, growth suppression, biochemical changes, anemia and other hematological disorders. Bone marrow, liver, kidney, thymus and skin are target organs affected by treatment. The effects are more severe with heavy distillates, and distillates containing N-PAHs are more biologically active. Although there is limited information on the occupational effects of synthetic fuels, experience in the health effects of workers in petroleum industry and coke-oven operations can serve as a guide in the implementation of industrial hygiene programs for synthetic fuel operations. These include engineering controls, personal monitoring, hygiene practices and medical surveillance.

REFERENCES

- ATSDR. Agency for Toxic Substances and Disease Registry. Toxicological Profile for "Jet Fuels (JP4 and JP7)". 1995, U.S. Department of Health and Human Services. Atlanta, Georgia.
- Beck, L.S., Hepler, D.I., and Hansen, K.L., 1983, The acute toxicology of selected petroleum hydrocarbons. In: MacFarland H.N., Holdsworth, L.E., MacGregor J.A., et al., eds. Proceedings on the 1st Symposium on the toxicology of petroleum hydrocarbons. Washington, DC: American Petroleum Institute. May 1982. 1-12.
- Chu, I., Villeneuve, D.C., Cote, M., Secours, V., Otson, R., and Valli, V.E., J. Toxicol. Environ. Health. 25:509-525, 1988.
- Chu, I., Suzuki, C.A.M., Villeneuve, D.C., and Valli, V.E., Fundam. Appl. Toxicol. 19:246-257, 1992.
- Chu, I., Villeneuve, D.C., and Rousseaux, C.G., J. Appl. Toxicol. 14: 241-256, 1994.
- Costello, J., Environ. Health Perspect. 30:205-208, 1979.
- Cruzan, G., Low, L.K., Cox, G.E., Meeks, J.R., Mackerer, C.R., Craig, P.H., Singer, E.J., and Mehlman, M.A., Toxicol. Ind. Health. 2:429-444, 1986.

- Davies, M.G., *Cont. Dermatitis*. 35:188-189, 1996.
- Davila, D.R., Romero, D.L., and Burchiel, S.W., *Toxicol. Appl. Pharmacol.* 139: 333-341, 1996.
- Davila, D.R., Mounho, B.J., And Burchiel, S.W., *Toxicol Ecotoxicol. News/Review*. 4:5-9, 1997.
- Doll, R., Vessey, M.P., Beasley, R.W.R., Buckley, A.R., Fear, E.C., Fisher, R.E.W., Gammon, E.J., Gunn, W., Hughes, G.O., Lee, K., and Norman-Smith, B., *Br. J. Med.* 29:394-406, 1972.
- Driscoll, T., Mandryk, J., Corvalan, C., Nurminen, M., Hull, B., Rogers, A., Yeung, P., Hollo, C., Ruck, E., and Leigh, J. *Occup. Med.* 45:239-246, 1995.
- Feuston, M.H., Low, L.K., Hamilton, C.E., and Mackerer, C.R., *Fund. Appl. Toxicol.* 22:622-630, 1994.
- Gendimenico, G.J., and Kochevar, I.E., *Toxicol. Appl. Pharmacol.* 76: 374-382, 1984.
- Gould, J.W., Mercurio, M.G., and Elmets, C.A., *J. Am Acad. Dermatol.* 33:551-573, 1995.
- Griest, W.H., Guerin, M.R., Yeatts, L.B., and Clark, B.R. 1981. Sample management and chemical characterization of the PARAH/O/SOHIO/U.S. Navy crude and refined shale oil suite. In: Griest W.H., Guerin, M.R., and Coffin, D.L. eds. *Health Effects Investigation of Oil Shale Development*. Ann Arbor Science, Ann Arbor, Michigan. 1981. P. 27-44.
- Hermann, M., *Mut. Res.* 90:399-409, 1981.
- Holland, J.M., Gibson, L.C., Whittaker, M.J., and Stephens, T.J. 1981. Chronic dermal toxicity of Paraho shale oil and distillates. In: Griest, W.H., Guerin, M.R., Coffin, D.L. (Eds): *Health Effects Investigation of Oil Shale Development*. Ann Arbor Science, Ann Arbor, Michigan, pp 97-116.
- IARC 1984. International Agency for Research on Cancer Monograph no. 34. Polynuclear Aromatic Compounds, Part 3, Industrial exposures. World Health Organization. Lyon, France.
- IARC 1985. International Agency for Research on Cancer Monograph no. 35. Polynuclear Aromatic Compounds, Part 4, Bitumens, Coal-tars and Derived Products, Shale-oils and Soots. World Health Organization. Lyon, France.
- McKee R.H., and Maibach, H.I., *Cont. Dermatitis*. 13:72-79, 1985.
- McKee, R.H., and Lewis, S.C., *Can. J. Physiol. Pharmacol.* 65:1793-1797, 1987.
- McKee, R.H., Traul, K.A., and Przygoda, R.T., *J. Appl. Toxicol.* 15: 159-165, 1995.
- NTP. 1986. National toxicological program technical report series no. 310: Toxicology and carcinogenesis studies of marine diesel fuels and JP-5 navy fuel in B6C3F1 mice (dermal studies). Research Triangle Park, NC: National Toxicology Program/National Institute of Health. NIH publication no. 86-2566.
- Otson, R., and Peake, E. 1993. Characterization of bitumen upgrading and coprocessing products. In: P. Garrigues and M. Lamotte (eds.), *Polycyclic Aromatic Compounds. Synthesis, Properties, Analytical Measurements, Occurrence and Biological Effects*. PAH XIII, Gordon and Breach, Langhorn, PA.
- Peake, E. 1990. Characterization of coal coprocessing products. The toxicology of heavy distillates. A final report to the Health Protection Branch, Department of National Health and Welfare, Ottawa, Canada.
- Poon, R., Chu, I., Villeneuve, D.C., and Valli, V.E., *Fundam. Appl. Toxicol.* 23:237-250, 1994.
- Poon, R., Chu, I., Davis, H., Yagminas, A.P. and Valli, V.E., *Toxicology*. 109:129-146, 1996.
- Purde, M., and Etlin, S. 1980. Cancer cases among workers in the Estonian oil shale processing industry. In: Rom, W.N. and Archer, V.E.(eds.) *Health Implications of New Energy Technologies*, Ann Arbor Science, Ann Arbor, Michigan, pp. 527-528.
- Rao, T.K., Allen, B.E., Ramsey, D.W., Epler, J.L., Rubin, B., Guerin, M.R., and Clark, B.R., *Mutat.*

Res. 84:29-39, 1981.

Reilly, C.A., and Renne, R.A. 1988. Toxicological effects of coal-based synfuels. In: Gray, R.H., Drucker, H., Massey, M.J. (eds.). *Toxicology of Coal Conversion Processing*. John Wiley & Sons, New York, p.57-245.

Shepard, H., *J. Soc. Occup. Med.* 31:9-15, 1981.

Szczeklik, A., Szczeklik, J., Galuszka, Z., Musial, J., Kolarzyk, E., and Targosz, D., *Environ. Health Perspect.* 102:302-304, 1994.

Springer, D.L., Miller, R.A., Weimer, W.C., Ragan, H.A., Buschbom, R.L., and Mahlum, D.D., *Toxicol. Appl. Pharmacol.* 82:112-131, 1986.

Tomkins, B.A., Kubota, H., Griest, W.H., Caton, J.E., Clark, B.R., and Guerin, M.R., *Anal. Chem.* 52:1331-1334, 1980.

Tomkins, B.A., Reagan, R.R., Caton, J.E., and Griest, W.H., *Anal. Chem.* 53:1213-1217, 1981.

Tsien, A., Diaz-Sanchez, D., Ma, J., and Saxon, A., *Toxicol. Appl. Pharmacol.* 142:256-263, 1997.

Ward, E.C., Murray, M.J., and Dean, J.H. 1985. Immunotoxicity of nonhalogenated polycyclic aromatic hydrocarbons. In: *immunotoxicology and immunopharmacology* (J.H. Dean, M. I. Luster, A.E. Munson and H. Amos, Eds.). pp. 291-300. Raven Press, New York.

Winker, N., Tuschl, H., Kovac, R., and Weber, E., *J. Appl. Toxicol.* 17:23-29, 1996.

Yamaguchi, K., Near, R., Shneider, A., Cui, H., Ju, S-T., and Sherr, D.H., *Toxicol. Appl. Pharmacol.* 139:144-152, 1996.

Table 1. Mutagenicity (Salmonella test) of synthetic fuels.

Material tested	Without S-9	With S-9	Reference
<u>Coal Liquefaction Products</u>			
Hydrotreated naphtha (<200°C)	NT	-	McKee et al., 1995
EDS ¹ process, RS-I (200-427°C)	NT	+	McKee et al., 1995
EDS process, RS-II (200-427°C)	NT	+	McKee et al., 1995
Pittsburgh Energy Technology Center	NT	+	Ran et al., 1995
COED pyrolysis process	NT	+	Rao et al., 1995
<u>Coal Coprocessing Products</u>			
CANMET LGO (< 243°C)	-	-	Otson and Peake, 1993
CANMET HGO I (243-409°C)	-	+	Otson and Peake, 1993
CANMET HGO II (387-521°C)	+	+	Otson and Peake, 1993
<u>Bitumen Upgrading Products</u>			
CANMET LGO (200-315°C)	-	-	Otson and Peake, 1993
CANMET HGO I (315-415°C)	-	+	Otson and Peake, 1993
CANMET HGO II (415-525°C)	+	+	Otson and Peake, 1993

¹Abbreviations: EDS, a direct liquefaction process that utilizes an "in stream" catalytic hydrotreatment process; RS, recycle solvent; COED, Char-oil Energy Development liquid; CANMET, Canadian Centre for Mineral and Energy Technology; LGO, light gas oil; HGO, Heavy gas oil; NT (Not tested)

Table 2. Systemic toxicity of synthetic fuels via percutaneous administration.

Synthetic fuel	Animal/Length of Exposure	Target organ	NOAEL ^a (mg/kg/day)	Reference
<u>Gasoline (unleaded)</u>	Rabbits/2 weeks	Liver, blood, skin	590	Beck et al., 1983
<u>Fuel oil No. 1</u>	Mice/13 weeks	Blood	250	NTP 1986
<u>Clarified slurry oil</u>	Rats/13 weeks	Liver, thymus, bone marrow	<8	Cruzan et al., 1986
<u>Coal liquefaction products</u>				
CANMET HGO-I (154-378°C)	Rats/13 weeks	Liver, blood, bone marrow	<50	Chu et al., 1988
<u>Coal coprocessing products</u>				
CANMET HGO-II (387-521°C)	Rats/13 weeks	Liver, blood, thymus, thyroid, bone marrow	<8	Chu et al., 1992
<u>Bitumen upgrading products</u>				
CANMET LGO (200-315°C)	Rats/4 weeks	Bone marrow, skin	25	Poon et al., 1994
CANMET HGO-I (315-415°C)	Rats/4 weeks	Liver, blood, bone marrow, thymus	<25	
CANMET HGO-II (415-525°C)	Rats/4 weeks	Liver, blood, bone marrow, thymus	<25	
CANMET HGO-II (415-525°C)	Rats/13 weeks	Liver, blood, bone marrow, thymus, thyroid	<8	Poon et al., 1996

^a NOAEL = no-observed-adverse-effect-level

Table 3. Benzo(a)pyrene content in petroleum and synthetic fuels.

Synthetic fuel	Benzo(a)pyrene (µg/g)	Reference
<u>Jet Fuel JP5 (from shale oil)</u>	ND ¹	Griest et al., 1981
<u>Petroleum (crude)</u>	2.8-3.7	IARC 1985
<u>Shale oil (SRM 1580 certified)</u>	3.3-192	IARC 1985
<u>Coal liquefaction products</u>		
Coal derived fuel oil	82	Tomkins et al., 1980
NBS Coal liquid oil	179	Tomkins et al., 1981
Coal-II heavy distillate, 288-454°C	550	Springer et al., 1986
<u>Coal coprocessing products</u>		
HGO I, 315-435°C	211	Otson and Peake, 1993; Peak, 1990
<u>Bitumen upgrading products</u>		
LGO, 200-315°C	6.5	Otson and Peake, 1993; Peak, 1990
HGO I, 315-415°C	23	
HGO II, 415-525°C	590	

¹ ND - non-detectable