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MSU Research on PBBs 1974-1979
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RESEARCH REPORT 372 FARM SCIENCE

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MSU Research on PBBs 1974 - 1979

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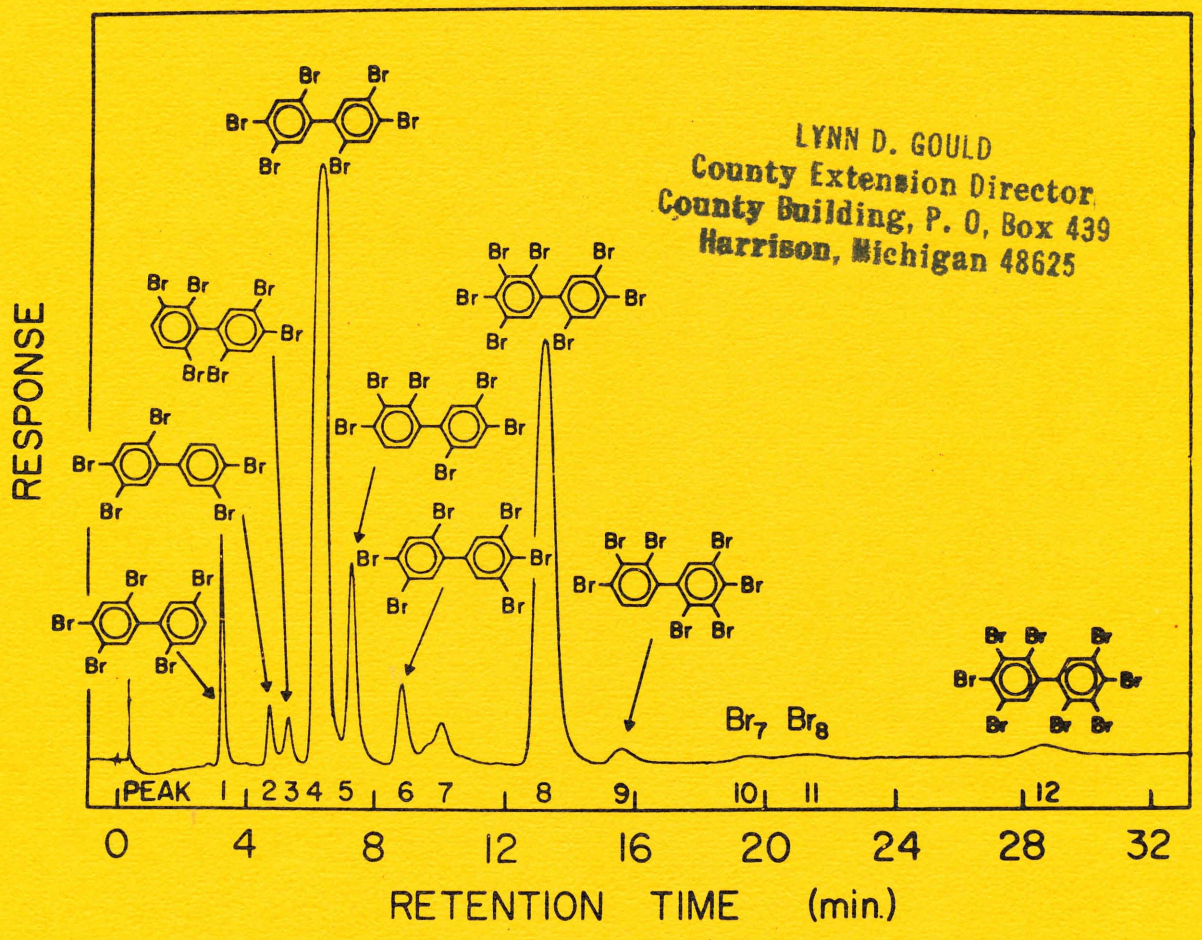

A gas chromatograph printout showing the individual PBB compounds found in fireMaster. Chemical models for each of the compounds are shown and associated with the individual "peaks" on the printout.

FOREWORD

This is the second in a series of Michigan Agricultural Experiment Station reports giving an update on available scientific information related to the PBB problem in Michigan.

The initial contamination of dairy cattle, due to a ration additive labeling accident, occurred in the late summer or fall of 1973. Identification of the feed contaminant was made in the spring of 1974. Following this disclosure, research on the PBB problem was initiated at Michigan State University.

The first general summary of this research was prepared for the public in May of 1976. This volume constitutes the second report to the citizens of Michigan. It is based upon careful scientific efforts of researchers in the following departments at Michigan State University:

Biochemistry
Crop and Soil Sciences
Dairy Science
Food Science and Human Nutrition
Large Animal Surgery and Medicine
Pathology
Pesticide Research Laboratory
Pharmacology
Poultry Science

A major scientific effort is now in progress to arrive at answers to questions of state and national concern which are posed by PBBs and other environmental contaminants. It is our hope that the results of scientific inquiry relating to food contamination and toxic chemicals in the environment will receive due consideration in future economic, regulatory and political decisions.

One result of the accidental PBB contamination in Michigan, as exemplified by the new MSU Environmental Toxicology Research Center, has been an aggressive action by the Michigan Agricultural Experiment Station, and Michigan State University, to exercise leadership in the resolution of problems relating to toxic chemicals in the environment. We believe that this leadership will help mitigate food contamination problems that may arise in the future.

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MSU Research on PBBs
1974 - 1979

INTRODUCTION

Ten to twenty 50-pound bags of polybrominated biphenyls (PBBs) were accidentally mixed in livestock feed in the summer or fall of 1973. The chemical mixture was apparently assumed to be magnesium oxide which is used to buffer high energy diets for dairy cattle. When rations containing PBBs were consumed by poultry and animals, the meat, milk and eggs became contaminated.

Early in May 1974, when the problem became known, MSU research teams were assembled to begin exhaustive laboratory tests involving dairy cattle, poultry, swine, beef cattle, and laboratory animals.

The following items are digested versions of some of the research results to come out of these MSU studies during the five-year period of 1974 to 1979.

NOTE: References in the text to "fireMaster" apply to either of the commercial mixes, since the active ingredients in both are identical. If interpretation of the results is dependent on knowing which one of the commercial mixtures was used in the study, the appropriate designation will be made. In general usage throughout the text the term "PBBs" will mean one of the fireMaster mixtures, unless otherwise noted.

DEFINITIONS

PBBs (polybrominated biphenyls) -- a class of stable, relatively inert chemicals, containing two or more bromine atoms within the molecular structure, that are widely used for fire resistant applications in both industrial and consumer products such as television cases and electronic circuits. PBBs are commonly incorporated in plastics as a fire retardant.

fireMaster BP-6 -- the registered trademark for an industrial fire retardant formulation of chemicals, primarily PBBs, manufactured by the Michigan Chemical Corp., St. Louis, Michigan. At least 11 distinct PBBs have been identified in fireMaster: two with five bromine atoms attached to the molecule; four with six bromine atoms; three with seven bromine atoms; and two with eight bromine atoms. The predominant PBB is one of the six bromine compounds known as 2,2' ,4,4' ,5,5'-hexabromobiphenyl. It makes up about 60 percent of the PBB content of fireMaster. The next most common PBB is 2,2' ,3,4,4' ,5,5'-heptabromobiphenyl which makes up 28 percent of the mixture.

fireMaster FF-1 -- identical to fireMaster BP-6 except for the addition of inert compounds (silicates) to improve flowability of the product. Also distributed by the Michigan Chemical Corp.

CHEMISTRY

Due to the wide variety of ways in which the key elements can be combined to make PBB molecules, there are 209 possible and distinct PBBs.

The chemical structures of most of the PBBs present in the Michigan contamination incident have been determined and conditions required for their metabolism have been outlined.

PBBs have been found to have a very stable chemistry in soils. They will not move in the environment unless the soil itself is moved by erosion or other physical means. Thus, areas of high contamination (manure piles, milk disposal sites, feedlots, etc.) should be managed to minimize soil erosion.

Sunlight can speed the natural breakdown of PBBs that are at, or very near, the surface of contaminated soils. The recorded photolysis (breakdown due to radiant energy of light) was seven times greater than the photolysis of polychlorinated biphenyls under the same conditions.

TOXICOLOGY

Enough is now known to classify PBBs as a subgroup of a family of known toxins. In general, they induce biochemical changes in the liver, they affect the immune system, and they cause a loss of body weight. These effects are also symptomatic of other halogenated aromatic hydrocarbons, like polychlorinated biphenyls (PCBs).

PBBs are toxic compounds when consumed at high levels. Death in laboratory animals due to massive doses of PBBs occurs in 14 to 21 days. This is a delayed reaction compared to other known toxic compounds. Death occurs after a significant weight loss. If the dose is below the fatal level, body weight will stabilize and the animal survives.

Like other similar halogenated aromatic hydrocarbon compounds, individual PBBs may be more toxic in one species than in others. This has been verified by research and means that it is hard to compare toxicity in laboratory animals to toxicity in humans or other animals.

It has been shown that there is a strict chemical requirement for toxicity -- the number and position of the bromine atoms on the molecule is critical to whether an individual PBB is toxic or not.

Unfortunately, only two minor PBB components of fireMaster are metabolized by laboratory animals at any appreciable rate, and these two would not be expected to be toxic. Two other minor components of the PBB mix are expected to be toxic, but only at high dosage rates.

After 16 weeks on diets containing 20 and 200 parts per million of PBBs, growing pigs showed the following symptoms when compared to pigs on an uncontaminated diet: slower growth rate and increased weight of liver, heart, kidneys and adrenal glands. No overt signs of toxicity were noted, however. Organ weights apparently return to normal after 14 weeks on an uncontaminated diet and normal growth rate resumes. In the one pig tested, conception, pregnancy and birth were normal.

Foreign chemicals in the diet cause the liver to produce one of two types of enzymes. One group of enzymes is produced in response to a large number of relatively nontoxic chemicals, such as barbituates. The other is produced in response to relatively toxic chemicals. When fireMaster is fed to laboratory animals both enzyme types are induced. Study of individual components of fireMaster indicate the two major PBBs in the mixture (accounting for about 88 percent of the PBBs present) are not toxic. One of the minor PBBs has been found to be toxic, but not overly toxic, and it does not account for all the toxicity observed in fireMaster. Another minor PBB should theoretically be toxic and tests are underway to confirm or deny this.

In experimental animals the liver shows little ability to break down and eliminate (by oxidation) the two major PBBs present in fireMaster PBB mixture that contaminated Michigan's food chain. The two compounds don't appear to be metabolically activated. PBB contamination may, however, increase the chances of cancer or birth defects caused by other aromatic hydrocarbons.

Exposure to PBBs has been shown to decrease the number of white blood cells produced by bone marrow and changed in the thymus. Mice fed 1, 10, and 100 ppm of PBBs in the diet showed lowered immune antibody responses. The responses were 80 percent, 30 percent, and 12 percent, respectively, of the immune responses (100 percent) of control mice not receiving PBBs. Thus, exposure to PBBs may decrease normal resistance to disease.

In lactating cows exposed to PBBs, about half of PBBs in their bodies will be eliminated every 60 days, on an average. PBB residues in the parts per million range are generally distributed in the body according to the amount of fat in the tissues -- the more fat, the higher the level of PBBs. Milk fat is the major means of eliminating PBBs from the bodies of cows.

In June of 1974, 33 cows that had received a high level of PBBs over a relatively short period of time were brought to MSU. It was estimated that the cows consumed 250 grams of PBBs over a two-week period or 30 to 40 milligrams of PBBs per kilogram of body weight per day for two weeks. In these cows feed consumption decreased, milk production decreased, skin lesions and loss of hair were apparent, metritis and retained placentas were frequent, there was difficulty calving, and calves were often weak. This group of cows was used to see if exposure to PBBs caused adverse effects in body tissues, toxicity in the fetus, and whether or not the rate of PBBs elimination from lactating cows could be increased. RESULTS: There were no significant tissue lesions nine months after exposure to high levels of PBBs that could be attributable to PBBs. Cows that were autopsied 11, 15, 17 and 19 months after exposure to PBBs did not contain tissue lesions either. When consumed at high levels, particularly in early gestation, fireMaster, or a contaminant in fireMaster, is fetotoxic. Treatment of cows with phenobarbital and vitamins resulted in slight increases in the amounts of PBBs excreted in the milk.

When foreign chemicals are introduced into the body, they cause drug metabolizing enzymes to be made by the liver in an effort to break down and eliminate the foreign compounds. In laboratory rats fed PBBs, dietary contamination of about 0.1 ppm does not cause enzyme increases. Higher levels of PBBs induce similar liver enzyme responses across several generations if the same contaminated diets are maintained.

Possible cancer causing properties of PBBs are being tested by a Swiss scientist who is collaborating with MSU. A standard carcinogen test is used in which the tested chemicals are painted on the skin of laboratory mice at repeated intervals. To date, no tumors have been observed in mice treated with either fireMaster or 2,4,5,2' ,4' ,5'-hexabromobiphenyl. Also, PBBs did not promote tumor formation when mice were pre-exposed to them and then treated with a chemical known to cause cancer in animals biochemically predisposed to the disease.

Feeding fireMaster to rats at levels up to 100 ppm in the ration for 60 days produced no change in growth or feed efficiency. Results of tests for kidney and liver function were in the normal range, as were red and white blood cell counts. All tissues studied were apparently normal except for the liver. After feeding fire-Master for 30 days, the livers of rats were increased in size at all feeding levels. At the lowest feeding level (1.0 ppm) no visible or microscopic lesions were detected, but the liver was still larger than normal. At higher levels of PBBs (10,100, and 500 ppm) the liver cells were swollen and more fat than normal was present. Electron microscope photographs of liver cells indicated an increase in the size of cell mitochondria at the lowest feeding level of PBBs, with degenerative changes appearing at the higher levels.

Tests with rats indicate that there are interrelationships between iodine levels in the diet and PBBs.

-- excess iodine and PBBs may cause vitamin A deficiency;
-- other interactive responses seen include:
   a) growth rates,
   b) liver size and function,
   c) abnormal bile ducts.

Treatment of growing and adult rats with PBBs produced the following results.

-- Weight gain was reduced after 90 days of exposure.
-- Enzyme activity in the kidneys was changed (a normal reaction to foreign chemicals) but no effect on kidney function was observed.

Young laboratory animals exposed to 100 ppm PBBs during fetal development and the period just after birth showed no adverse effects on the development of secondary sexual characteristics or the presence of birth defects. At 10 months after the exposure period ended, however, these animals still showed increased breakdown of male and female hormones in their bodies. This indicates that a potential exists for altering normal sexual development in animals exposed to PBBs during gestation and after birth.

Studies of rats fed the commercial PBB mixture fireMaster indicate that certain of the PBBs contained in the product are concentrated in the mother's milk and passed to the offspring. Direct evidence is not available, but it is believed that the PBBs concentrated in the mothers' milk were responsible for tissue changes observed in exposed pups.

Preliminary findings indicate that PBBs stimulate key chemical activities related to several basic cell functions, including immune reactions and cell growth and division. Implications of the observed activities (in rat lung tissues) are not clear.

Prior dietary exposure to PBBs made rats more susceptible to kidney and liver damage caused by chlorinated hydrocarbon solvents (chloroform, carbon tetrachloride, trichloroethylene, and trichloroethane). Lethal effects of chloroform and carbon-tetrachloride were also greater in PBB "sensitized" rats. Thus, long-term exposure to low concentrations of PBBs might "sensitize" humans to the toxic effects (possibly including cancer) of various other chemicals they were exposed to.

The following effects of PBBs were observed in pregnant and nursing rats (and their offspring) that were fed a diet containing 50 ppm of PBBs. Lactation did not significantly alter PBB concentrations except in mammary tissue. Newborn are apparently contaminated largely through the milk; placental transfer is much less important.

Tests of laying hens fed diets with various levels of PBBs (0.2, 1, 5, 25, 30, 45, 60, 90, 120, 125, 625, and 3125 ppm) show significant effects on production, hatchability, and viability of offspring on diets containing 45 ppm or more of PBBs. If contamination did not exceed 125 ppm, production and hatchability returned to normal 3 to 4 weeks after withdrawal of PBBs.

In egg laying hens, feed consumption is depressed by PBBs when they reach about 125 ppm in the diet. This level must be fed for several weeks before feed consumption drops, and then the decrease is very slight. At high levels (500 ppm) eating stops almost completely and death from starvation occurs. PBBs do not affect eggshell thickness, egg weight or egg fertility. Accumulation of PBBs in eggs is directly related to the amount of PBBs in the hen's diet. A constant level is reached when the yolk is fully formed in the ovary. This level is 1.5 times the amount of PBBs in the diet. On the experimental diets containing PBBs, nearly 60 percent of the daily intake of the PBBs went into the egg yolk. The remaining portion went into the hen's fat deposits, liver, muscles, or was excreted (about 10 percent of the daily intake was excreted). Tests indicate that laying hens exposed to 1.0 ppm of PBBs for 7 to 10 days need at least 90 days on a PBB-free diet before contamination levels in the eggs drop to .05 ppm or less.

PBBs fed to immature chickens at levels of 50 to 250 ppm resulted in:

-- depressed body weight due to lowered feed intake;
-- decreased weights of the comb and testes;
-- increased weights of the liver and thyroid;
-- decreased heart rate and a general anemic condition;
-- potential decrease in disease resistance (not verified) due to observed changes in immunological system organs.

For poultry, present information indicates that PBBs in excess of 30 ppm have drastic effects on the lymphatic organs which control disease immunity. When the PBBs are transmitted from the hen to the chick via the egg, however, the toxicity to the chick's immune system is reduced. This indicates that the passage through the adult hen alters the ratio of the various PBBs that are present in commercial PBB mixtures. When tested separately, the major PBB present in fireMaster did not cause decreases in hatchability or abnormalities in embryos and chicks. Thus, one or more of the PBBs present in fireMaster in lesser quantities is thought to be responsible for the negative effects.

Mink proved to be extremely sensitive to diets contaminated with PBBs. Levels of PBBs studied in the feeding trials included six dietary levels from 1 ppm to 15.625 ppm. Survival of newborn kits decreased on all contaminated diets. Mortality of adult mink occurred on all diets except the control (no PBBs) and the diet containing fireMaster at 1 ppm. No adults survived on the two diets with the highest contamination; 11.98 ppm and 15.625 ppm, respectively.

PBBs IN THE FOOD CHAIN

Little, if any, PBB is transferred from contaminated soils to plant tops -- feeds grown on contaminated soils won't recontaminate livestock. Root crops from high contaminated soils may contain PBBs, but much of the PBB would be removed by peeling.

Processing and cooking can alter the amount of PBBs in contaminated foods:

Processing of milk -- PBBs are concentrated in high-fat products. Spray-drying reduces the amount of PBBs in whole milk and skim milk. Pasteurization freeze-drying, aging of cheese and condensation have no effect.

Cooking of poultry -- pressure cooking removed from 36 percent to 53 percent of the PBBs present in chickens that had been fed contaminated diets.

SOURCES

Sources for the information contained in this publication include:

Michigan Science in Action, "MSU Research on PBBs," Michigan State University Agricultural Experiment Station, East Lansing, Michigan. May 1976.

Environmental Health Perspectives, "Polybrominated Biphenyls;" U.S. Department of Health, Education and Welfare; Public Health Service, National Institutes of Health, and National Institute of Environmental Health Sciences, Vol. 23, No. (NIH) 78-218. Government Printing Office, Washington, D.C., April 1978.

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