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Gesellschaft Deutscher Chemiker

GDCh-Advisory Committee
on Existing Chemicals of
Environmental Relevance (BUA)

Butylated Hydroxytoluene

(2,6-Bis(1,1-dimethylethyl)-4-methylphenol)

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(February 1991)

S. Hirzel
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on Existing Chemicals of Environmental Relevance (BUA)

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Foreword

The German Chemicals Act (Chemikaliengesetz - ChemG) of 1980 stipulates that certain existing chemicals must be reported to the competent authority, if they exhibit properties which indicate that they may be hazardous, either alone or in combination with other substances.
In the summer of 1982, an Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) was set up by the German Chemical Society (Gesellschaft Deutscher Chemiker - GDCh). It brings together representatives from the scientific community, the chemical industry and the governmental authorities. This Advisory Committee is responsible for elaborating appropriate solutions for substances of relevance for health and the environment on the basis of voluntary measures. It selects and examines existing chemicals from the aforementioned angles. The testing and evaluation are based on scientific criteria alone.
It was, therefore, necessary to develop priority setting procedures. In a first phase reports were only prepared for priority chemicals. Within the framework of a first priority setting procedure, chemicals were compiled from several priority lists and 135 chemicals were selected for detailed substance reports.
In a second priority setting procedure the survey of the German Chemical Industry Association (VCI) on all substances with a production volume of more than 10 tons per year was used as a starting list. Since this survey covered 4,600 chemicals, BUA decided to process the corresponding list in several stages. The first stage included approx. 1,050 substances with a production volume of more than 1,000 tons per year.
Detailed reports are drawn up on chemicals suspected of having a hazard potential and abridged reports on those presenting only a minor hazard potential, according to the current state of knowledge.
The detailed BUA reports take in both the published literature and data from industry. If data for the evaluation of the chemicals are not available, additional studies are recommended and the results are published as updates to the reports. The reports serve as a basis for the instigation of administrative measures, when there are indications of risks to health or the environment.

Tübingen, May 1993

Ernst Bayer
Chairman of the Advisory Committee
on Existing Chemicals
of Environmental Relevance

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BUA Report on Butylated Hydroxytoluene

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Summary and conclusions

Ecological aspects

Occurrence and distribution in the compartments

In 1989 approximately 18,000 tonnes of butylated hydroxytoluene (BHT) were produced in the European Community. In West Germany butylated hydroxytoluene has been assigned to the > 1,000 tonnes/year category in the Verband der Chemischen Industrie (VCI, Association of the German Chemical Industry) high production volume chemicals list. Consumption is estimated at about 1,500 - 1,600 t/a.

Butylated hydroxytoluene is used as a stabilizer in the production of plastics and rubber, and as an antioxidant for plastic and rubber articles, adhesives, mineral oil products, cosmetics, animal feed and foodstuffs.

During manufacturing there are emissions as exhaust gas (no quantification possible) and waste water (in the range of kg), during industrial use one can expect emissions mainly as exhaust gas, in a minor rate with waste water and by solid waste. As there are insufficient data, they cannot be quantified. The quantitatively most significant entry into the environment one can estimate to occur after migration of butylated hydroxytoluene onto the surface of articles containing butylated hydroxytoluene, mostly as volatilization. There are no data for the amount of stabilizer released and the time needed for this process. It has been estimated that 40 t/a of butylated hydroxytoluene are released into the environment through tyre wear.

In the 1970s, before waste water treatment plants were built, concentrations of butylated hydroxytoluene ranging from n.a. to 0.014 mg/l were recorded in surface water in West Germany. Measurements taken at workplaces in the

butylated hydroxytoluene production and processing industries in 1985 showed air concentrations ranging from n.a. to 2.7 mg/m³.

Butylated hydroxytoluene can pass directly into the human body and animal organisms when used as an additive in animal feed or foodstuffs, or indirectly via migration from plastics. The substance may also be absorbed from cosmetics (e.g. lipsticks, skin creams or toothpaste) which have been stabilized with butylated hydroxytoluene or into which butylated hydroxytoluene has migrated from packing material made of plastics. In several analyses of human fat tissue (Americans, British, Japanese) concentrations of butylated hydroxytoluene from 0.02 to 3.19 mg/kg were measured.

More recent data on the occurrence of butylated hydroxytoluene in the different compartments are not available.

Degradation

Degradation tests with activated sludge (with and without adaptation) showed a degradation rate < 10 %.

Further degradation tests with activated sewage sludge and with soil were carried out with ^{14}C-labelled butylated hydroxytoluene.
Butylated hydroxytoluene is metabolized rapidly in soil. After 24 days about 95 % had been degraded, with complete biodegradation accounting for between 20 and 29 %. Degradation seems to consist of more than ten stages. The degradation of butylated hydroxytoluene by activated sludge is dependent on the proportion of substrate concentration to activated sludge and on the incubation period. Half-lives of 3.4 and 7 days were recorded for proportions of 0.3 and 30 mg/l substrate to 100 mg/l activated sludge.

Butylated hydroxytoluene was observed to undergo photodegradation in water. After eight days a degradation rate of 42 % was recorded.

A calculation based on the model designed by Atkinson suggests that the substance has a half-life of about 17 hours in the troposphere where it undergoes photochemical oxidative degradation.

Bioaccumulation

Measured data on the bioaccumulation potential of butylated hydroxytoluene are available only for the aquatic environment. ^{14}C-labelled butylated hydroxytoluene was added to soil in a model ecosystem; the highest BCFs were recorded in the initial weeks of the four-week trial period. The BCFs were lower for fish (carp, 15 - 25) than for daphnia (73), algae (98) or snails (125).

Bioconcentration factors of butylated hydroxytoluene in man have been calculated for Japan, the USA and the United Kingdom. They range from 0.30 to 0.98 calculated on body fat.

Accordingly, it is unlikely that a considerable amount would accumulate via the food chain. These experiments and calculations do not corroborate conclusions from either the recorded log P_{OW} of 5.1 or of certain calculated values.

Ecotoxicology

The available data on the effect of butylated hydroxytoluene all refer to aquatic organisms. Some of the concentrations recorded are only conclusive to a limited extent as they are greater than the solubility of butylated hydroxytoluene in water (≤ 1 mg/l).

Daphnia proved to be the most sensitive test organisms and were found on the water surface after a brief period of exposure to concentrations of 0.2 mg/l and above. A three-week period of exposure to 0.5 mg/l caused a 60 % reduction in the reproduction rate and a high mortality rate among adult daphnia. Rainbow trouts were exposed on a longer-term basis to feed containing butylated hydroxytoluene (0.12 % in feed). This resulted in a significant reduction in the relative liver weight and in the proportion of acid soluble SH groups in the post-mitochondrial supernatant of homogenized liver. It also caused the induction of microsomal liver enzymes.

Toxicology

Butylated hydroxytoluene accumulates predominantly in fatty tissue and, to a lesser extent, in the liver following long-term administration. Two main metabolic pathways have been identified:

1) Oxidation of the methyl group fixed directly to the ring and

2) Oxidation of one or both of the tertiary butyl substituents.

Oxidation at the aromatic ring and conjugation with glucuronic acid and glutathion also occur. Marked enterohepatic circulation has been described in the rat; this probably also occurs in man. Approximately 66 % of the compound is excreted in the urine.

Butylated hydroxytoluene is of low acute oral toxicity with LD_{50} values of approx. 2000 mg/kg body weight in the rat and mouse. The considerable differences in sensitivity displayed by various strains of mouse following intraperitoneal administration have been explained in terms of metabolic differences of genetic origin. Oral administration of lethal doses to mice produces weight loss, dyspnoea, enlarged lungs with pulmonary oedema and haemorrhage, and in isolated cases haemorrhage into the intestinal lumen. Histological changes have been observed at doses of 40 mg/kg body weight and above. Acute oral administration to rats also leads to internal haemorrhage as a result of inhibition of coagulation factors.

Butylated hydroxytoluene has a slighthy irritant effect on rabbit skin and eye and shows no sensitizing effect in guinea-pigs. In man, on the other hand, indications to cases of contact dermatitis have been reported.

Repeated administration of butylated hydroxytoluene (≥ 25 mg/kg body weight/day for 26 days) causes impaired function of and histological changes in the liver, kidneys and thyroid and impaired coagulation of the blood. Body weight gain is reduced and enzyme induction occurs in the liver. One week of oral administration of 15 mg/kg body weight/day is sufficient to bring about a reduction of the prothrombin index in the rat.

Longer-term administration of butylated hydroxytoluene (approx. 450 mg/kg body weight/day) leads to lung and liver lesions in the mouse accompanied by biliary duct hyperplasia and reduced body weight gain.

Butylated hydroxytoluene has been investigated extensively for genotoxicity. Isolated positive results from *in vitro* mutagenicity studies are contrasted by numerous *in vitro* and *in vivo* tests which have produced negative results. The overall data do not give rise to any founded suspicion that butylated hydroxytoluene has mutagenic properties.

The results of carcinogenicity testing with butylated hydroxytoluene are contradictory. Long-term feeding studies in mice have indicated an increase in lung, ovary and lachrymal gland tumours which is not dose-dependent. Pituitary adenomas developed in rats. However, other studies have produced no indication of a tumorigenic effect in rats and mice. In a two-generation feeding study, male and female rats displayed an increased incidence of liver tumours at doses of 100 and 250 mg/kg body weight/ day; mortality differed in the treatment and control groups. Mice fed 39 or 390 mg/kg body weight/day for 10 months showed an increased incidence of liver tumours in male animals. Administration of 3486 mg/kg body weight/day for two years also caused liver tumours in male mice. However, the doses stated in this study should be appraised critically in comparison with the results of other studies and, in particular, in view of the methodology used.

Butylated hydroxytoluene has a tumour-promoting action *in vivo* and *in vitro*; the extent of this action is dependent on the dose and length of treatment with butylated hydroxytoluene and the nature and dose of the carcinogen. Affected organs include rat liver, colon, thyroid gland, oesophagus, urinary bladder and pancreas, and mouse lung.

The available reproductive toxicology investigations contain contradictory results. There are no indications that the compound has teratogenic properties at non-maternotoxic doses.

Butylated hydroxytoluene had an immunosuppressive action in one *in vitro* study. There are indications that the compound sensitizes human skin.

On the other hand, however, butylated hydroxytoluene in combination with various other compounds has occasionally displayed antimutagenic, anticarcinogenic and antipromoting properties and, in some studies, has prolonged the lifetime of the animals. These effects are probably due at least partly to the general mode of action of antioxidants (e.g. their radical-scavenging action).

Recommendations

Ecotoxicology

We recommend systematic analysis of the occurrence of BHT in surface water as it is not possible to quantify immissions since measurements from the hydrosphere are not available.

We also recommend investigating the volatility of BHT from a representative range of plastics.

Toxicology

All the major toxicological end points have been investigated for butylated hydroxytoluene, and the available results enable the toxicological profile of the compound to be evaluated. Investigations are currently being carried out at the Robens Institute (Guildford, England) on behalf of the European BHT Manufacturers Association (EBMA; a subgroup of CEFIC) into the role of hepatocellular damage in the chronic rat toxicity of butylated hydroxytoluene. However, the Final Report is not expected until 1994.