Social Europe

Recommendation from the Scientific Committee on Occupational Exposure Limits for pyrethrum

SCOEL/SUM/95

January 2003

European Commission

Table of Contents

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8 hour TWA	1 mg/m^3 (for pyrethrum purified from sensitising lactones)
STEL (15 min):	-
Additional classification	sensitiser (only if not fully purified)

Substance:

The term "pyrethrum" refers to a natural insecticide produced by certain species of the chrysanthemum plant and containing a variable mixture of pyrethrins, mainly cinerin I and II, jasmolin I and II, and pyrethrin I and II.

Usually, 25% of the mixture is made of pyrethrin, plus smaller amounts of the related cinerin and jasmolin.

The flowers of the plant are harvested shortly after blooming and are either dried and powdered or the oils within the flowers are extracted with solvents.

The resulting pyrethrin-containing extracts usually have an active ingredient content of about 30%, the remainder consisting of oleoresins containing glycoproteins and sesquiterpene lactones. These compounds are not usually present in the purified commercially available formulations.

Identification and Properties

CAS no.	8003-34-7 (for Pyrethrum)
Chemical group: chrysanthemumic acid ester.	
Molecular weight (for pyrethrin I)	328.4
Boiling point	146-150°C pyrethrin I 192-193°C pyrethrin II
Solubility	water insoluble; soluble in a range of organic solvents
Synonyms	Dalmatian insect flowers; pyrethrins; Pyrenone
Conversion factor	(for pyrethrin I) 1 mg/m^3 =0.074 ppm 1 ppm = 13.51 mg/m^3

After extraction with solvents, Pyrethrum is a viscous liquid or oil coloured from yellow to brown depending on its state of purity.

1. Occurrence and use

Pyrethrum compounds have been used primarily to control human lice and scabies, mosquitoes, cockroaches, beetles and flies. Some "pyrethrin dusts", used to control insects in horticultural crops, contain from 0.3% to 0.5% pyrethrins, and are used at rates of up to 50 lb/A. Other pyrethrin compounds may be used in grain storage and poultry pens and on dogs and cats to control lice and fleas.

The natural pyrethrins are contact poisons that quickly penetrate the nervous system of the insect.

Pyrethrins, generally combined with a synergist, piperonyl butoxide, are used in sprays and aerosols against a wide range of flying insects.

The most common pyrethrum formulations are the following:

Public health purposes: 0.2-0.4% in powder formulations; 0.2-0.4% dissolved in kerosene or petroleum distillate; 0.05-0.10% in solution, with additional agents, in kerosene as flying insects spray.

0.5-2% in shampoos for human and pet usage.

Household use

0.15-0.30% in powder formulations
0.015-1.2% in aerosol pressure packs
0.05-0.10% in sprays

2. Health effects

Irrespective of grade or the addition of solvents, the rat oral dose LD_{50} values for pyrethrin are in the range of 200 to 900-1000 mg/kg/bw. In contrast, the intravenous and intraperitoneal LD_{50} ranges between 1 and 10 mg/kg, depending on the animal species tested.

The very marked difference in the oral and intravenous toxicities of pyrethrins might be explained by a low rate of absorption from the gastrointestinal tract, very efficient destruction by the liver in first-pass metabolism, or a combination of the two (Hayes, 1982).

However, excretion data after oral administration of pyrethrin I to rats point to a considerable absorption via the gastrointestinal tract: 46% of orally administered ^{14}C-labelled pyrethrin -I (1 to 5 mg/kg/bw) to rats was recovered in the urine after 48 hours (Elliot et al., 1972).

This means that the difference in effect in mammals between oral and parental toxicities could be due to rapid metabolic degradation of active ingredients by hydrolysis and oxidation in the liver.

Pyrethrins have a very low dermal toxicity in rats and rabbits: dermal LD_{50} values in rabbits for pyrethrum extract (20% in petroleum distillate) ranged from 1100 to 3680 mg/kb/bw (Carpenter, 1950).

Studies in female guinea pigs demonstrated that refined pyrethrum extract used in aerosol fly killers did not evoke an allergic response even in sensitised animals. Pyrethrin I and II were also negative in these studies. This shows that pyrethrins themselves are not responsible for allergic responses to the crude pyrethrum extracts. It has therefore been argued that impurities (sesquiterpene lactones and glyconproteins) might be responsible for the allergenic properties of pyrethrum dusts (ACGIH, 1994).

Since 1965, the NOEL for limit settings has been based on the study by Lehman (Lehman, 1965): groups of 12 males and 12 females rats were fed natural pyrethrin at dietary levels of 0, 200, 1000 and 5000 ppm for 2 years (the daily dosage was therefore approximately 0, 10, 50 and 250 mg/kg.).

Based on long term dietary studies, WHO-FAO (WHO-FAO, 1975) concluded that no significant effects on the growth and survival of rats were seen when rats were fed a maximum dietary level of 5000 ppm for two years. Slight though definite liver damage, according to Lehman (1965), was seen at 1000 and 5000 ppm, but not at 200 ppm. Therefore, the NOEL may be identified at 200 ppm in the diet, equivalent to 10 mg/kg bw/day. This NOEL has been used to define the Acceptable Daily Intake of 0-0.04 mg/kg bw/day established by JMPR in 1974 (JMPR, 1972).

Injury to man from pyrethrum is frequently attributable to the allergenic properties of the formulations rather than to the direct toxicity of the active ingredient.

Contact dermatitis is by far the most common: the usual picture is a mild erythematous, vesicular dermatitis with papules and intense pruritus. Some individuals show manifestations of pyrethrum sensitivity similar to those seen in pollinosis. In some cases, asthma attacks have been observed (Ramirez, 1930). Some of the affected subjects had a previous history of asthma.

The above-mentioned sensitising effects are attributable to the contaminants present in the crude extracts.

Sensitivity to unrefined pyrethrum as judged by skin tests occurs in over 40% of persons who are sensitive to ragweed or who had shown positive reactions to unrefined pyrethrum extracts (Zucker, 1965; Ellenhorn, 1988). Formerly, contact allergy from pyrethrum was common and was caused by sensitising sesquiterpene lactones contained in the crude extract, derived from a chrysanthemum species. Today, the extraction and purification process is such that the active insecticidal principle present in modern mixtures should not contain any sensitising sesquiterpene lactone (Zenz C 1994); on the other hand, it should be mentioned that inadequately purified pyrethrins can cause severe allergic dermatitis and systemic allergic reactions. (The Merk Index, 1989).

Apparently, only one case of pneumonitis due to pyrethrins has been reported in a woman using 2 aerosol cans of pyrethrum-based insecticides in her house each week. A lung biopsy showed interstitial fibrosis with eosinophilic infiltration and aggregates of histiocytic cells. A pulmonary challenge test with the insecticide was positive as was a skin test with pyrethrum alone (Carlson and Villaveces, 1977).

Piperonyl butoxide inhibits mixed-function oxidase enzymes of the liver, which metabolise and combine with pyrethrins. Piperonyl butoxide is minimally toxic: the LD 50 in rat is 11.5 g/kg (Gosselin, et al, 1984) and 7.5 g/kg in cat and dog (Hayes, 1991). This is the reason why piperonyl butoxide is often combined with other insecticides. Its synergic activity can be elicited in acute toxicity studies carried out in insects as well as in mammals, but there is no evidence of a synergic effect for low dose administration (Kimbrough et al, 1968).

Recommendation

For the dried, powdered chrysanthemum flowers or the relatively crude solvent-extracted oil that can be derived initially from the flowers (containing oleoresins with glycoproteins and sesquiterpene lactones), SCOEL considered that skin and respiratory sensitisation are major health concerns. From the information available, SCOEL concluded that it was not possible to recommend a health-based limit value for these materials.

Nowadays, however, the commercially available insecticides have been purified to remove sensitising sesquiterpene lactones. For this purified "pyrethrum" (a mixture of pyrethrins I and II, cinerins I and II and jasmolins I and II), SCOEL considered that a limit value could be derived.

In a 2-year study in rats, slight liver damage was observed at oral doses of 50 and 250 mg/kg/day, with no effects at 10 mg/kg/day (Lehman, 1965). This NOAEL of 10 mg/kg/day was taken as a starting point for the derivation of a limit value. The NOAEL was obtained in an oral study and there is evidence that the toxicity of pyrethrins via the oral route is appreciably less than via parental routes (probably as a result of first-pass metabolism). Also, there is a general paucity of toxicological data on pyrethrum, including its individual constituents. Furthermore, no data on the consequences of long-term exposure in humans were available.

For these reasons, an uncertainty factor of 50 was applied to the oral NOAEL of 10 mg/kg/day, to derive a predicted no-effect level in humans of 0.2 mg/kg/day. This is equivalent to a daily inhalation exposure of 1.4 mg/m^3, assuming a body weight of 70 kg, an inhaled volume of air of 10 m^3 during a working day of 8 hours and absorption of 100% of the amount reaching the respiratory tract. Following the above logic, and assuming a preferred value, SCOEL recommended a limit value of 1 mg/m^3 for "pyrethrum" purified to remove sesquiterpene lactones.

At the level recommended, no measurement difficulties are foreseen.

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