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Applicator Exposure to Maleic Hydrazide (MH) in Flue-Cured Tobacco[1]

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MH (1,2-dihydro-3,6-pyridazinedione) is the active ingredient of the systemic sucker control products available for use on tobacco in the United States. The acute oral LD50's to rats of technical MH and the potassium salt formulation (K-MH) are 5,000 and 14,145 mg/kg, respectively (Weed Science Society of America 1983). In response to reports of potential or suspected carcinogenicity and oncogenicity, the U.S. Environmental Protection Agency (EPA) issued a Rebuttable Presumption Against Registration (RPAR) (Johnson 1977).

In the field, two groups of workers, the applicators and harvesters, are exposed to MH. The degree of this exposure is unknown. This study was conducted to generate data on the exposure of applicators to MH through inhalation and dermal contact during application of MH to flue-cured tobacco.

MATERIALS AND METHODS

Seven applicators, one each on four research stations operated by N.C. State University and the N.C. Department of Agriculture and three owners or operators of private farms in North Carolina, applied K-MH (Royal MH-30) at 2.5 kg/ha to tobacco using commonly accepted agricultural practices. Exposure times to MH ranged from 1.75 to 5.5 h. The applicators wore socks, boots or shoes, hats, trousers, and short-sleeved, knit, white cotton shirts. Willson Respirator No. 2D Dustite model equipped with gauze and a cellulose filter pad (7 cm in diameter) was worn during application (Durham and Wolfe 1962). Absorbent pads (10.2 cm square) made of alpha cellulose, as described by Durham and Wolfe (1962), were attached to workers by tape and (or) safety pins at the chest, back, thighs, and calves. Absorbent pads sewn to elastic wrist bands were worn on the forearms.

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The volunteers applied MH to tobacco at recommended rates (2.5 kg a.i./ha) with standard equipment. High-clearance tractors were used on the research stations, and conventional farm tractors (low) were used on the private farms. With high-clearance sprayers the operator rode above the tobacco and the spray nozzles. With low sprayers the operator rode between the rows of tobacco in a skip-row and at the same level or below the level of the spray nozzles.

A urine void was collected immediately before application of MH. Total urine was collected for the 36-h period beginning with initial exposure to MH, with sample collection times of 0 to 6, 6 to 12, 12 to 24, and 24 to 36 h.

All samples were returned to the laboratory in insulated boxes. Respiratory and absorbent pads were frozen at -20°C until analysis. Urine samples were refrigerated until volumes were recorded, and then 100-mL aliquots of urine samples were frozen until analysis.

Various methods were evaluated for analysis of MH. The gas chromatographic procedure (Haeberer et al. 1978) was tried with little success The spectrophotometric method (Lane 1964) was modified which made possible the measurement of 3 µg in spiked samples. All samples were analyzed by this modified procedure.

The absorbent pads were trimmed to 8.9 x 8.9 cm. One half of each respiratory and of each absorbent pad were extracted in a Soxhlet apparatus with 150 mL of methanol for 4 h. The extract was taken to dryness on a rotary flash evaporator at 40°C. The residue was then transferred to a special MH distillation flask with a total of 50 mL of 70% NaOH. Five grams of 30-mesh zinc and 0.5 g of ferrous chloride were added and distillation begun. The distillate was collected in a 50-mL centrifuge tube containing 4 mL of 1 N H_2SO_4. The distillate was filtered through a medium porosity sintered-glass funnel, reduced to about 6 mL on a hot plate, then transferred with 1-mL water rinses to a 10-mL volumetric flask containing 2 mL of 2% p-dimethylaminobenzaldehyde in 1 N H_2SO_4. All other particulars of the method remained unchanged from those of Lane (1964).

Urine samples were analyzed by essentially the same procedure. Forty grams of NaOH were dissolved in 75 mL of urine; the solution was then transferred to the distillation flask with 2-mL water rinses. The remainder of the procedure was described above.

RESULTS AND DISCUSSION

The exposure rates, expressed as micrograms per hour, for various parts of the body are given in Table 1. Calculations were made following procedures outlined in Davis (1980). Applicators using equipment which allows them to ride above the spray boom were subjected to less spray drift than those riding at a level of or partially below the boom. Exposure on the chest-back area was five times greater when treatments were made with conventional farm tractors. The exposure to the arm and thigh areas of applicators on low tractors was about twice that for applicators on high-clearance tractors. The exposure to the shin area of the "low" applicators was about 25 times that of the "high" applicators, with MH levels ranging from 109 to 11,600 µg/h and from 76 to 312 µg/h, respectively. Areas of greatest exposure were the thighs and shins for the "high" and "low" applicators, respectively.

Table 1. MH exposure rates at various positions on applicators.

Location on body	Tractor type High-clearance (µg/h)	Low (µg/h)
Chest-back	105	518
Forearm	175	324
Thigh	711	1629
Shin	171	4332
Respirator	0.74	10

The rate of respiratory exposure was also expressed in micrograms per hour. Applicator position relative to the spray boom greatly influenced the amount of MH potentially inhaled. The level of MH inhaled by conventional tractor drivers was 13 times greater than that for applicators using high-clearance tractors (Table 1).

Considerable variation was encountered with the analysis of the urine samples. An unknown substance(s) was distilled along with the hydrazine and reacted with the reagents to produce color in some samples. In spite of this problem, all of the urine samples were still analyzed. The results are given in Table 2. According to Mays et al. (1968), 65% of the MH administered as a single oral

Table 2. MH in urine samples taken at specific intervals.

Sampling period (h)	Tractor type High-clearance (ppm)	Low (ppm)
0	0.03	<0.03
0-6	0.18	<0.03
6-12	0.26	0.07
12-24	0.07	0.06
24-36	0.06	<0.03

dose to rats was excreted in the urine in 12 h. Most of this was excreted as the parent compound although 6 to 8% was in an unidentified conjugate. In this study excretion was greatest during the 6 to 12-h period after initial exposure.

The type of equipment used to apply MH can reduce the amount of exposure. High-clearance equipment places the applicator ahead of and at least partially above the spray boom thus reducing exposure.

It is unlikely that applicators are at risk using either type of equipment. Exposure rates did not approach the estimated acute toxicity levels. No additional precautions are needed to reduce MH exposure to applicators.

In the "Determination Concluding the Rebuttable Presumption Against Registration," MH, MH-diethanolamine salt (DEA-MH), and K-MH were returned to the normal registration (Johnson 1983). The data reported in this paper were used by the EPA in making this final determination.

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