CASWELL FILE # 159

002310

Data Evaluation Record

Study Type: Mutagenic

Study Title: Effects of Cysteine and a Liver Metabolic Activation System on the Activities of Mutagenic Pesticides. Moriya, M., K. Kato, and Y. Shirasu. 1978 Mutation Research, 57 259-263.

MRID No.: none

Captafol TOX. Chem. No. 828
Captan TOX. Chem. No. 159
Folpet TOX. Chem. No. 464

Reviewed by: William R. Schneider, Ph.D. 7/23/84
Toxicology Branch
Hazard Evaluation Division. (TS-769)

Secondary Review'd as part of Captafol registration Standard

Study Classification: Adequate: Reverse mutations induced in Escherichia coli WP2 hcr and Salmonella typhimurium TA1535 by captan, captafol and folpet are greatly reduced or eliminated by preincubation of captan with rat liver homogenate, rat blood, or cysteine.

Test Materials: Captafol, Captan, and Folpet Technicals: "Standard material obtainable in Japan". Purity not stated. Obtained from Agricultural Chemical Inspection Station of the Ministry of Agriculture and Forestry (Kodaira, Tokyo).

Organisms used: Escherichia coli WP2 hcr and Salmonella typhimurium TA1535

Materials and Methods:

The materials were prepared and the assay was conducted according to the method described by Ames, et. al., 1975. Before adding the soft agar, the test chemicals were pre-incubated 10 minutes with 0.5 ml of: S-9 fraction of rat liver homogenate without cofactors, S-9 mixture with standard cofactors, 20mM cysteine, or rat blood dilured twice with phosphate buffer. A second experiment was performed preincubating the pesticide with 0, 0.5, 1.0, 2.5, and 5 umole of cysteine/umole of pesticide. All plates were done in duplicate.

Results: (as reported)

Pesticide	Concentration (uM/plate)	Organism	Revertants /plate, pre-incubated with: H_2O	S9 mix	S9 fraction	Cysteine	Blood
Captan	0.15	WP2 hcr	3200	30	111	19	32
		TA 1535	268	6	31	4	6
Captafol	0.15	WP2 hcr	158	31	24	31	21
Folpet	0.15	WP2 hcr	1320	50	60	21	19
		TA 1535	219	8	35	6	14
Negative control	-	WP2 hcr	<30				
		TA 1535	<17				

Effect of Pre-incubation with Cysteine on E. coli WP2 hcr

Pesticide	Concertration (umole/plate)	Revertants/plate preincubated with cysteine (uM/uM pesticide) 0	0.5	1.0	2.5	5.0
Captan	0.15	2900	2580	1660	183	10
Captafol	0.15	117	120	137	91	11
Folpet	0.15	1700	1190	732	18	8
Negative Control		<30				

Discussion:

The authors showed that pre-incubation of these pesticides with rat liver S-9 microsomal fraction (with or without the cofactors necessary for full activity), rat blood, or cysteine greatly reduced or eliminated the mutagenicity when tested with E. coli WP2 hcr and S. typhimurium TA 1535. A dose response reduction in mutagenicity was seen with increasing concentrations of cysteine in the pre-incubation mixture. The authors concluded that the activity is " rapidly destroyed by compounds that contain the sulfhydryl groups rather than by metabolism".

This study was well conducted and is adequate to use for regulatory purposes.

002310

Data Evaluation Record

Study Type: Mutagenic

Study Title: Sister-Chromatid Exchanges and Chromosomal Aberrations in Cultured Chinese Hamster Cells Treated With Pesticides Positive in Microbial Reversion Assays. Tezuka, H., N. Ando, R. Suzuki, M. Terahata, M. Moriya, and Y. Shirasu; 1980, Mutation Research 78, 177-191.

MRID No.: none

Captafol TOX. Chem. No. 828
Captan TOX. Chem. No. 159

Reviewed by: William R. Schneider, Ph.D. William R. Schneider 7/12/84
Toxicology Branch
Hazard Evaluation Division (TS-769)

Study Classification: Adequate: Captafol and captan induced sister chromatid exchanges (SCE's) and chromosome aberrations in chinese hamster V79 cells in culture.

Test Materials: Captafol Technical, purity >98.0%, obtained from Wako Pure Chemicals Co. Ltd., Japan. Vehicle: DMSO
Captan Technical, purity 99.9%, obtained from Nishio Industry Co. Ltd., Japan. Vehicle: DMSO

Cell culture used: Chinese hamster V79 cell line cloned for a stable karyotype of 22 chromosomes.

Metabolic Activation: None used.

Materials and Methods:

Cultures of the cells were incubated 26.5 hours with the test substance and 2uM 5-Bromodeoxyuridine (BrdUrd). Duplicate cultures were used at each level. At each of five dose levels, for each chemical, 50 metaphases were counted for SCE's and 100 metaphases were scored for chromosome aberrations. For the DMSO vehicle controls, 200 cells were counted for SCE's, and 400 were scored for chromosome aberrations.

Results:

Chemical	Concentration ($\times 10^{-6}$M)	SCE's/cell	% cells with chromosome aberrations (excluding gaps)
DMSO -		4.7	3.5
Captan	6	6.6	1.0
	15	11.2	4.0
	30	15.0	7.0
	45	21.1	23.0
	60	24.9	28.0
Captafol	2	8.8	2.0
	5	15.7	3.0
	10	28.6	24.0
	15	38.2	28.0
	20	45.3	48.0

At the high dose level for captan, the following aberrations from cells with 9 or less aberrations were reported: 14 chromatid gaps, 3 isochromatid gaps, 11 chromatid breaks, 10 isochromatid breaks, 18 chromatid exchanges, and 1 chromosome aberration. In addition, 13 cells had 10 or more aberrations.

At the high dose level for captafol, the following aberrations from cells with 9 or less aberrations were reported: 5 chromatid gaps, 8 chromatid breaks, 7 isochromatid breaks, and 5 chromatid exchanges. In addition, 24 cells had 10 or more aberrations.

Discussion:

This study was performed in an adequate manner and was sufficiently well reported to show that both captan and captafol induce sister chromatid exchanges and chromosome aberrations in chinese hamster V79 cells in culture.

Captan Lowest Effect Level (LEL) for SCE's:	1.5×10^{-5}M
Captafol LEL for SCE's:	5.0×10^{-6}M
Captan LEL for chromosome aberrations:	4.5×10^{-5}M
Captafol LEL for chromosome aberrations:	1.0×10^{-5}M