PROJECT NO Y-68-135
REPORT NO

64

YOUNGER LABORATORIES

Biochemists . Pharmacologists . . . Analysts

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Certificate of Analysis

January 22nd, 1969

SUBJECT -

Toxicological Investigation Of: Pydraul 312 (MCS-312) OB-116021

Monsanto Sample Number 172

Monsanto Project Number Y-68-135

Y-68-135
1/22/69

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats, Mixed Sex)

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino male and female rats.

After the approximate Minimum Lethal Dose was determined, groups of male and female rats were fed in increasing doses at increments of 0.2 fractional log intervals at four levels designed to blanket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to a modification of the method of E. J. de Beer.

Observations were made for toxic symptoms and the viscera of the animals that succumbed were examined macroscopically.

The data are shown in Table I.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits.

The treated areas were covered with plastic strips and the animals held in wooden stocks for periods up to twenty-four hours, after which time they were assigned to individual cages.

Observations were made for toxic symptoms and the viscera of the animals that succumbed were examined macroscopically.

The data are shown in Table II.

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EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits, Mixed Sex)

The undiluted compound was applied to the clipped, intact skin of albino male and female rabbits and removed after twenty-four hours. The application was covered with plastic strips to retard evaporation and avoid contamination.

Observations were made over a period of several days for irritation.

The data, scored according to the method of Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Rabbits, Mixed Sex)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino male and female rabbits and observations made over a period of several days for inflammation.

The eyes were rinsed with warm isotonic saline solution after twenty-four hours.

The data, scored according to the method of Draize, et al, are shown in Table IV.

SUMMARY -

Pydrawl 312 (MCS-312) 08-11602)

A) Oral LD_{50} (Rats, Mixed Sex)

The Oral LD_{50} for male and female rats was placed at >5330 milligrams per kilogram with lower and upper limits of 4430 to 6390 milligrams per kilogram.

The compound was classed as practically non-toxic by oral ingestion in male and female rats.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 3160 milligrams per kilogram and less than 5010 milligrams per kilogram.

The compound was classed as slightly toxic by skin absorption in male and female rabbits.

C) Skin Irritation (Rabbits, Mixed Sex)

The compound was classed as a mild irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 2.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

The compound was classed as a slight eye irritant in male and female rabbits.

The average maximum score was 8.6 out of a possible 110 in one hour.

TOURISME LABORATORIES

BY: MELVIN D. BIRCH

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TABLE I

THE ORAL LD_{50} OF

'Hydrasl 312 (HCS 312) CB-116021' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	230	2,510	Survived
2- Male	240	2,510	Survived
3- Female	225	2,510	Survived
4- Male	255	2,510	Survived
5- Female	190	2,510	Survived
6- Male	230	3,980	Died
7- Female	205	3,980	Survived
8- Male	245	3,980	Survived
9- Female	225	3,980	Survived
10- Male	235	3,980	Survived
11- Female	210	6,310	Survived
12- Male	240	6,310	Died
13- Female	210	6,310	Survived
14- Male	255	6,310	Died
15- Female	230	6,310	Died
16- Male	230	10,000	Died
17- Female	225	10,000	Died
18- Male	235	10,000	Died
19- Female	220	10,000	Died
20- Male	255	10,000	Died

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 5330 milligrams per kilogram with lower and upper limits of 4430 to 6390 milligrams per kilogram.

The compound was classed as practically non-toxic by oral ingestion in male and female rats.

Survival time was two to four days with most deaths occurring within two to three days.

Toxic symptoms included slight tremors in two to six hours, loss of appetite, lethargy, and collapse.

At autopsy there was inflammation of the gastrointestinal mucosa and renal, liver, and pulmonary hyperemia by macroscopic examination.

TABLE II

THE MINIMUM LETHAL DOSE OF 'Pydrenal 312 (MCS 312) OR-116021'
BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Female	2.3	794	+ 0.1	Survived
2 - Male	2.4	1260	+ 0.2	Survived
3 - Female	1.9	2000	+ 0.1	Survived
4 - Male	2.4	3160	+ 0.1	Survived
5 - Female	2.1	5010	- 0.1	Died -- 8 Days
6 - Male	2.2	7940	- 0.2	Died -- 6 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 3160 milligrams per kilogram and less than 5010 milligrams per kilogram.

The compound was classed as slightly toxic by skin absorption in male and female rabbits.

Survival time was six to eight days.

Toxic symptoms included reduced activity and appetite followed by weakness and collapse.

At autopsy there was liver discoloration and pulmonary congestion macroscopically.

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF

'Pydraul 312 (MCS-312) OM-116021'

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	0	2	2	1	0	0
2 - Female	0	3	3	2	0	0
3 - Male	0	3	3	1	0	0
Average	0.0	2.6	2.6	1.3	0.0	0.0

DISCUSSION -

The compound was classed as a mild irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 2.6 out of a possible 8 in twenty-four hours.

No skin changes were noted in one hour.
Moderate to marked erythema with no edema was recorded in twenty-four hours. Gradual improvement was noted in seventy-two hours and all animals received a score of zero in five days.

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TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF
'Pydraul 312 (MGS-312) OB-116021'

Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Female	8	2	2	0	0	0
2 - Male	10	4	2	0	0	[illegible]
3 - Female	8	2	2	0	0	0
Average	8.6	2.6	2.0	0.0	0.0	0.0

DISCUSSION -

The compound was classed as a slight eye irritant in male and female rabbits. The average maximum score was 8.6 out of a possible 110 in one hour.

There was blinking and mild lacrimation immediately following application.

In one hour there was marked redness of the lids and moderate lacrimation. Lacrimation had ceased and redness reduced to mild in twenty-four hours. There was no discernible corneal dullness.
Redness had reduced to very slight in forty-eight hours on two animals and disappeared completely on the third.
All animals received a score of zero within seventy-two hours.

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