The paralyzing effect of apo-β-erythroidine was similar to that observed after administration of benzimidazole

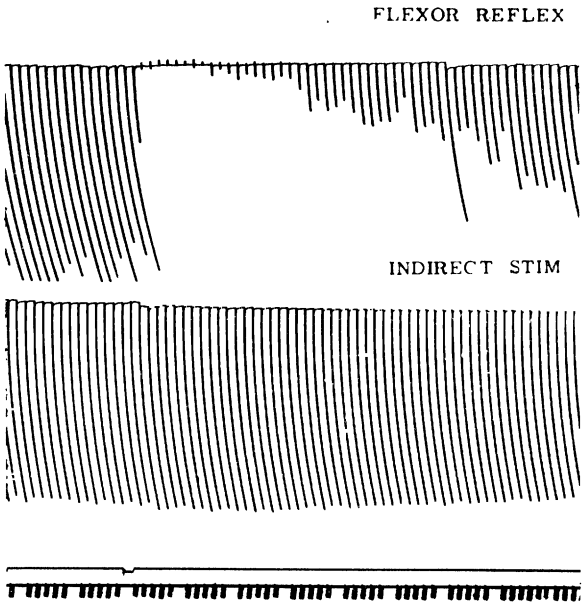

FIG. 1. Effect of apo-β-erythroidine on the flexor reflex and indirect excitability of the muscle. Tracing from above downwards: 1) flexor reflex; 2) stimulation of gastrocnemius muscle through its nerve; 3) signal line and 4) time at 10-sec intervals.

At the signal 20 mg of apo-β-erythroidine was injected into the external jugular vein.

(*9*), myanesin (*2*), and glyketal (*1*). It differed from these agents in producing paralysis of much longer duration. The mean duration of paralysis with doses of 180 mg per kg was 6 min for myanesin and 35 min for apo-β-erythroidine. After 250 mg per kg of apo-β-erythroidine paralysis lasted for several hours. Death after toxic doses of apo-β-erythroidine was due to respiratory arrest. In mice the mean lethal dose was more than twice as large as the mean paralyzing dose.

Analysis of the pharmacodynamic effects of apo-β-erythroidine in cats showed that the compound did not block transmission at the myoneural junction. It produced paralysis by a depressant effect on the central nervous system. Two neuronal spinal reflexes such as the knee jerk were not affected but multineuronal reflexes such as the flexor reflex were selectively depressed by small doses of the drug. This effect together with the lack of curare-like action of the compound is illustrated in Fig. 1.

The results indicate that apo-β-erythroidine has a selective depressant action on the interneurons. It resembles in this respect other interneuronal blocking agents (*1, 2, 9*). The fact that four chemically different substances produce similar central effects and act at the same site is of great interest. They are likely to act by blocking some important but as yet unknown mechanism of transmission in the central nervous system. None of these substances interferes with the action of acetylcholine as a transmitter of nervous impulses.

It has been suspected for some time that β-erythroidine, apart from its curare-like action, also possessed central depressant properties (*3, 10*). These two properties have been dissociated in apo-β-erythroidine, which lacks the peripheral action but still retains the central depressant properties of β-erythroidine.

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Surface Action in 2,4-D Sprays[1]

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A number of workers (*1–4*) have reported increased toxicity when various substances are added to sprays of 2,4-dichlorophenoxyacetic acid used as an herbicide. Preliminary results in the summer of 1947, extensively corroborated since, show that the toxicity of these sprays may be increased several fold by adding various surface-acting substances, and suggest that some previously reported results may have been due to similar effects.

Commercial soapless powders with a base of sodium lauryl sulfate have been used most extensively as sur-

TABLE 1

YIELDS OF FLAX SEED WHEN SPRAYED WITH 2,4-D, WITH OR WITHOUT A WETTING AGENT

Spray	Surface tension of spray		Yields in bu/acre*	
	2,4-D only	Plus ½% "D"	2,4-D only	Plus ½% "D"
Water	72 dynes	28 dynes	16.4	17.4
Na salt—½ lb	58	28	13.6	*5.4*
—¼ lb	57	28	18.5	*12.2*
—⅛ lb	57	28	16.2	14.6
Amine —½ lb	53	29	15.4	*6.1*
—¼ lb	51	29	15.2	*10.7*
—⅛ lb	52	29	15.7	12.8
Ester —½ lb	34.1	30	11.7	11.2
—¼ lb	35.0	30	13.5	...
—⅛ lb	35.7	30	16.4	15.1

* Least significant difference (5%), 3.29 bu/acre.

[1] Paper No. J1654, Iowa agric. Exp. Sta., Project 944.

face-acting compounds. The effects of adding ½% of one such preparation to various sprays used on flax at the rate of 10 gal per acre are shown in Table 1. The wetting agent alone had no effect, but when added to the sodium or amine salts of 2,4-D, the yields were reduced seriously at the heavier rates of 2,4-D. The appearance of the plots some 10 days after spraying suggested that the mixed sprays would be lethal, but the plants made enough late second growth to produce some seed. The wetting agent did not increase the toxicity of the ester formulation on flax, although in another experiment it did increase injury of corn. These plots were fairly free of weeds and all spray treatments reduced weed growth to an insignificant level.

TABLE 2

STALK REACTIONS AND YIELDS OF CORN SPRAYED WITH THE SODIUM SALT OF 2,4-D CONTAINING VARIOUS WETTING AGENTS

Wetting agent	Surface tension (dynes)	Stalk reaction score	Yield* bu/acre
None (check)	...	0.0	93.5
None (2,4-D)	51	0.7	94.5
"D"—¼%	29.3	4.0	97.0
"D"—½%	28.6	6.5	76.7
"D"—¾%	28.6	6.0	71.6
"D"—1%	28.9	7.8	53.8
"D"—2%	28.8	7.8	52.5
"V"—½%	29.9	6.2	81.3
"AO"—½%	28.6	5.5	64.5
"T"—½%	29.4	6.5	77.2
"TA"—½%	31.5	2.0	94.0

* Least significant difference (5%), 14.6 bu/acre.

Corn at the laying-by (10-leaf) stage was sprayed with the sodium salt (monohydrate) at ½ lb per acre in 47 gal water. The effects of various kinds and concentrations of wetting agents on plant reaction and yield are shown in Table 2. Yields again are in bushels per acre; stalk reaction is on a scale of 0 for no response to 10 for all the stalks twisted and bent nearly to the ground. All of the wetting agents except "TA" were approximately equal in giving a significant reduction in yield at ½%. "TA" was an experimental compound of a non-ionic type. In another experiment it was active on soybeans. Most of the surface-active compounds decreased the yield of corn by 10–15% when used alone because of the increased smut infection carried into the meristematic regions. The increased injury with increased percentages of agent "D" needs further investigation. It may represent direct toxicity at rates that reached 8 lb per acre, or it may mean more rapid surface action during the spraying operation. The wetting effect was identical whether the agent was mixed with the 2,4-D spray or applied to the leaves and allowed to dry before spraying with 2,4-D.

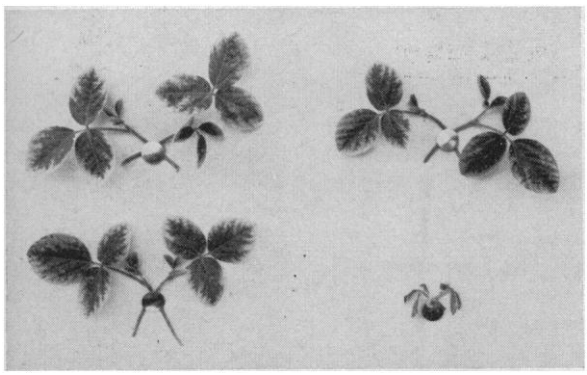

FIG. 1. New growth on sprayed soybean plants: upper left, water only; lower left, ½% "D"; upper right, 2,4-D, 500 ppm; lower right, 2,4-D + ½% "D."

The striking effect of a wetting agent in increasing the toxicity of 2,4-D on soybeans is shown in Fig. 1. The plants were wet with a 500-ppm solution of the sodium salt of 2,4-D, except for the growing point, which was covered with a waxed cap. The figure shows the new growth made in the week following spraying. Growing points, and most plants, died when the wetting agent was added, but recovered from the 2,4-D alone.

The toxicity of the sodium and amine salts of 2,4-D to corn, flax, and soybeans has been increased five or more times by adding about 1% of commercial non-soap wetting agents. Since several divergent types of agents have given the effect, it is probably not chemical in nature. Decreased surface tension and increased penetration of the sprays seem to be the probable answer, but it is not a simple relationship. A non-ionic wetting agent was ineffective on corn but active on soybeans. An ionic agent of the lauryl sulfate type gave increased response up to 2.0% of the agent in a dilute 2,4-D spray, even though the spray surface tension did not vary significantly after the first 0.05% of wetting agent was added.

The effect of the surface agent has been to increase the speed and severity of the plant reaction, but not necessarily to hasten death. No corn (moderately resistant) or flax (slightly resistant) plants have been killed by any of the treatments reported here. The effect on weeds is similar to the effect on crops. Resistant weeds show more injury but are not more readily killed. The main effect of the wetting agents, then, is to reduce the selective action of 2,4-D by which it is possible to kill susceptible weeds with little injury to resistant crops.

A special warning is necessary on this point because of the practice of using soap to reduce precipitation of amines in hard water. Excess soap gives results similar to those reported here. The new sequestering agents which prevent precipitation by tying up calcium insoluble acetates appear to be free of this objection.

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