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## Interactions of the Herbicides EPTC and EPTC plus R-25788 with Ozone and Antioxidants in Corn

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In greenhouse studies, the potential interactions of the herbicide EPTC (*S*-ethyl dipropylthiocarbamate) with ozone ( $O_3$ ) or the antioxidants piperonyl butoxide and *n*-propyl gallate on corn (*Zea mays* L., "Pioneer 3780") were investigated in the presence or absence of the herbicide antidote R-25788 (*N,N*-diallyl-2,2-dichloroacetamide). Commercial formulations of EPTC (EPTAM) or EPTC plus R-25788 (ERADICANE) were incorporated into the soil at 4.5, 5.6, and 6.7 kg/ha, and they were evaluated against 0.2 and 0.3 ppm of  $O_3$  or against 4.5, 6.7, and 9.0 kg/ha of soil applications of the two antioxidants. The interactive effects between selected treatment combinations of EPTC plus R-25788 and ozone or the two antioxidants were highly synergistic. In the absence of R-25788, the interactive effects of EPTC with  $O_3$  or the two antioxidants were additive, although EPTC at 6.7 kg/ha combined with some rates of piperonyl butoxide interacted synergistically. The implications of these findings as to the potential mode of action of the antidote R-25788 are discussed.

Preplant incorporated applications of the herbicide EPTC (*S*-ethyl dipropylthiocarbamate) at rates of 3.4-4.5 kg/ha are effective in controlling many annual grass weeds in corn and in other crops (Mullison, 1979). In addition, EPTC at higher rates (6.7 kg/ha) is very effective in managing certain tough-to-control perennial weeds such as quack grass [*Agropyron repens* (L.) Beauv.] and yellow nut sedge (*Cyperus esculentus* L.) or in suppressing Johnson grass [*Sorghum halepense* (L.) Pers.] (Mullison, 1979). However, at these rates, EPTC is commonly injurious to corn (Burnside et al., 1971; Burt and Akinsorotan, 1976; Burt and Buzio, 1979; Chang et al., 1972; Martin and Burnside, 1982; Meggitt et al., 1972; Rains and Fletchall, 1971). The phytotoxicity of EPTC to corn is greatly reduced with the use of selected herbicide antidotes such as R-25788 (*N,N*-diallyl-2,2-dichloroacetamide) (Chang et al., 1972; Martin and Burnside, 1982; Meggitt et al., 1972; Pallos et al., 1975; Rains and Fletchall, 1971). Currently, in the United States, all EPTC used for weed control in corn is exclusively formulated as a prepackaged mixture of the herbicide EPTC and the antidote R-25788 in a 12:1 ratio. This formulation is marketed under the trade name ERADICANE. Use of the antidote R-25788 does not reduce the toxicity of EPTC to other crop or weed species (Stephenson and Chang, 1978).

The exact mechanism(s) by which R-25788 counteracts the toxicity of EPTC to corn are not very well understood at the present time. Extensive research on the mode of the antidotal action of R-25788 has resulted in a plethora of proposed mechanisms, none of which is unequivocally accepted. Among the mechanisms proposed, two that have attracted considerable attention are those proposing either a counteraction of EPTC phytotoxicity by R-25788

through a competitive inhibition at some common site within the protected plant (Ezra and Gressel, 1982; Ezra et al., 1982; Görög et al., 1982; Leavitt and Penner, 1979a; Stephenson et al., 1978, 1979; Wilkinson and Smith, 1975) or an increase in the rate of metabolic detoxication of EPTC caused by the antidote R-25788 (Carringer et al., 1978; Kömives and Dutka, 1980; Lay and Casida, 1976; Leavitt and Penner, 1979b; Renneberg et al., 1982).

Air pollutants such as ozone ( $O_3$ ) have been reported to interact with several agricultural practices including chemical weed control (Rich, 1975). During the past decade, studies have shown that  $O_3$  may interact with selected herbicides on certain plant species, thereby modifying either the overall plant response to these herbicides (Carney et al., 1973; Reilly and Moore, 1982; Sung and Moore, 1979) or the metabolism of herbicides in fumigated plants (Hodgson et al., 1973, 1974; Hodgson and Hoffer, 1977a,b). In addition to air pollutants, insecticide synergists such as piperonyl butoxide [ $\alpha$ -[2-(2-butoxyethoxy)ethoxy]-4,5-(methylenedioxy)-2-propyltoluene] or other antioxidant compounds have also been reported to interact synergistically with selected herbicides on crop plants (Kömives and Dutka, 1980; Rubin et al., 1980).

The objectives of the present study were to evaluate any potential interactions between the herbicide EPTC and the air pollutant ozone ( $O_3$ ) or the antioxidants piperonyl butoxide and propyl gallate on corn in the presence or absence of the herbicide antidote R-25788 and then to explain possible relationships between these interactions and the responses they evoke.

### MATERIALS AND METHODS

**Chemicals.** The herbicides and antioxidant compounds used in the present study were obtained from the following sources: EPTC (formulated EPTAM herbicide) and EPTC plus R-25788 (formulated ERADICANE herbicide) were kindly provided by Stauffer Chemical Co., Westport, CT. Piperonyl butoxide was purchased from Pflanz and

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Table I. Shoot Dry Weights of Corn Seedlings Grown in Soil Treated with the Herbicide EPTC or EPTC plus R-25788 and Exposed to the Air Pollutant Ozone<sup>a</sup>

herbicide rate, kg/ha	type of response	ozone concentration, ppm <sup>b</sup>		
		0	0.2	0.3
<b>EPTC</b>				
0.0	observed <sup>c</sup>	1.82 ± 0.16	1.75 ± 0.11	1.89 ± 0.16
4.5	observed	1.49 ± 0.14	1.46 ± 0.11	1.62 ± 0.12
	expected <sup>d</sup>		(1.42)	(1.56)
5.6	observed	1.32 ± 0.10	1.15 ± 0.13	1.17 ± 0.07
	expected		(1.25)	(1.39)
6.7	observed	0.94 ± 0.17	0.74 ± 0.15	0.86 ± 0.11
	expected		(0.87)	(1.01)
<b>EPTC plus R-25788<sup>e</sup></b>				
0.0	observed	1.85 ± 0.13	1.71 ± 0.18	1.80 ± 0.05
4.5	observed	1.62 ± 0.10	1.47 ± 0.10	1.43 ± 0.10
	expected		(1.48)	(1.57)
5.6	observed	1.59 ± 0.09	1.41 ± 0.08	1.20* ± 0.08
	expected		(1.42)	(1.51)
6.7	observed	1.50 ± 0.13	1.38 ± 0.10	0.91** ± 0.14
	expected		(1.36)	(1.45)

<sup>a</sup> Data are expressed in grams and represent dry matter accumulations of corn seedlings during a 21-day period. <sup>b</sup> Six-hour exposure for 2 consecutive days when seedlings were 1 week old. <sup>c</sup> Mean weight values are from four replications ± standard error of each mean. Asterisks indicate significant interactions at the 5% (\*) and 1% (\*\*) levels of probability as determined by *F* values for each combination treatment calculated for 2-by-2 comparisons of the observed response for that treatment with the observed responses for the control and the separate levels of EPTC ± R-25788 and O<sub>3</sub> involved. <sup>d</sup> Expected values in parentheses were calculated by assuming no interactions (see Materials and Methods). <sup>e</sup> Formulated commercial mixture of 0.8 kg/L EPTC plus 0.07 kg/L R-25788.

Bauer, Inc., Stamford, CT. Propyl gallate was purchased from Sigma Chemical Co., St. Louis, MO. Ozone was generated by a laboratory ozonator.

**Plant Material and Chemical Application.** Corn (*Zea mays* L., "Pioneer 3780") plants were grown from seed in a 2:2:1 (v/v/v) mixture of potting medium (Weblite, Weblite Corp., Blue Ridge, VA), vermiculite, and peat, three plants per 473-mL plastic cup, under greenhouse conditions. A controlled-release N-P-K fertilizer (14-14-14) was added to the mixture to supplement nutrient levels. EPTC or EPTC plus R-25788 and piperonyl butoxide or propyl gallate were sprayed sequentially with a link-belt sprayer at 205.9 kPa in 935 L/ha spray volume on the soil surface, and then they were incorporated by mixing into the top 5 cm of soil in each cup before planting of corn seeds. EPTC or EPTC plus R-25788 were applied at 0, 4.5, 5.6, and 6.7 kg/ha, and the antioxidants piperonyl butoxide and propyl gallate were applied at 0, 4.5, 6.7, and 9.0 kg/ha. After treatment of the soil mixture with the chemicals and planting of the seeds, the cups were placed in a greenhouse with a 14-h photoperiod, 65 ± 5% relative humidity, and a day/night temperature of 29 °C/22 °C. All cups were watered from overhead to the soil surface as required.

**Fumigation of Corn Seedlings with O<sub>3</sub>.** One or two days after their emergence, corn seedlings grown in cups whose soil had been treated or not treated with EPTC or EPTC plus R-25788 were fumigated with O<sub>3</sub>. At this stage, corn seedlings were approximately 1 week old (from time of planting) and their average height was 7–9 cm. These seedlings were fumigated with O<sub>3</sub> for 6 h between 1000 and 1600 EST for 2 consecutive days in three continuously stirred tank reactors (CSTR) as previously described by Heck et al. (1978). Seedlings in the first chamber were exposed only to charcoal-filtered air (0 ppm of O<sub>3</sub>). Seedlings in the other two chambers were exposed to 0.2 and 0.3 ppm of O<sub>3</sub>, respectively. Ozone was generated by an UV ozone generator (Laboratory ozonator, Model T-408, Welsbach Ozone Systems Corp., Philadelphia, PA), and concentrations within the chambers were monitored with a chemiluminescent ozone analyzer (Model 8002, Bendix Process Institute Division, Lewisburg, WV). Ozone concentrations were maintained within ±0.01 ppm of de-

sired levels. The O<sub>3</sub> monitor was calibrated every 2 weeks with an automated ozone calibrator (Photocal 3000, Columbia Scientific Industries, Austin, TX). The relative humidity in all CSTR chambers was maintained at 65 ± 5% by means of a steam generator (Automatic Steam Products Corp., Long Island, NY), and the chamber air temperature was 30 ± 2 °C. After fumigation with O<sub>3</sub>, the corn seedlings were maintained in a charcoal-filtered greenhouse with a 29 °C/22 °C day/night temperature, 65 ± 5% relative humidity, and a 14-h photoperiod.

**Data Collection and Statistical Analysis.** Twenty-one days after planting (herbicide–ozone interactions) or 30 days after planting (herbicide–antioxidant interactions) corn seedling shoots were harvested, dried in a forced-air oven at 50 °C for 48 h, and weighed. Data presented are the means of two experiments with two replications and three subreplications in each experiment and are expressed as the average shoot dry weight per plant. These data were analyzed for variance as a four-by-three (herbicide by ozone) or as a four-by-four (herbicide by antioxidant) factorial experiment in a completely randomized design (Steel and Torrie, 1980). The standard errors of the observed mean responses were calculated. Statistically significant interactions for each treatment combination between herbicides and ozone or antioxidants were identified by the use of *F* tests for a two-by-two comparison of that treatment with the control and the separate levels of each herbicide and ozone or antioxidant involved, as has been described by Nash (1981). In addition, the expected responses for each treatment combination were calculated assuming no interactions (additive model) by subtracting the observed response of the control from the sum of the observed responses of the separate level of each herbicide and ozone or antioxidant involved (Steel and Torrie, 1980). For example, in Table I, the expected response of corn seedlings to the combined treatment of EPTC at 4.5 kg/ha and O<sub>3</sub> at 0.2 ppm was calculated as follows: (1.49 + 1.75) – 1.82 = 1.42. In Tables I–III the expected responses for each treatment combination are given in parentheses. The expected responses for each treatment combination, calculated in the aforementioned way, were then compared to the observed responses for the same combination treatment. When an observed value exceeds its respective

Table II. Shoot Dry Weights of Corn Seedlings Grown in Soil Treated with Combinations of the Herbicides EPTC or EPTC plus R-25788 and the Antioxidant Piperonyl Butoxide<sup>a</sup>

herbicide rate, kg/ha	type of response	piperonyl butoxide, kg/ha			
		0	4.5	6.7	9.0
<b>EPTC</b>					
0.0	observed <sup>b</sup>	3.07 ± 0.11	3.31 ± 0.19	3.20 ± 0.16	3.02 ± 0.37
4.5	observed	2.65 ± 0.19	2.95 ± 0.17	2.62 ± 0.19	2.40 ± 0.29
	expected <sup>c</sup>		(2.89)	(2.78)	(2.60)
5.6	observed	2.05 ± 0.35	2.40 ± 0.08	2.12 ± 0.34	1.77 ± 0.07
	expected		(2.29)	(2.18)	(2.00)
6.7	observed	1.27 ± 0.23	1.37 ± 0.11	0.82** ± 0.10	0.77** ± 0.13
	expected		(1.51)	(1.40)	(1.22)
<b>EPTC plus R-25788<sup>d</sup></b>					
0.0	observed	3.47 ± 0.33	3.77 ± 0.29	3.67 ± 0.09	3.47 ± 0.25
4.5	observed	3.20 ± 0.18	3.55 ± 0.25	2.95** ± 0.09	2.75* ± 0.13
	expected		(3.50)	(3.40)	(3.20)
5.6	observed	3.00 ± 0.15	3.02 ± 0.20	2.87** ± 0.11	2.50* ± 0.19
	expected		(3.30)	(3.20)	(3.00)
6.7	observed	2.77 ± 0.06	2.65* ± 0.22	2.42** ± 0.05	2.15** ± 0.09
	expected		(3.07)	(2.97)	(2.77)

<sup>a</sup> Data are expressed in grams and represent dry matter accumulation of corn seedlings during a 30-day period. <sup>b</sup> Mean weight values are from four replications ± standard error of each mean. Asterisks indicate significant interactions at the 5% (\*) and 1% (\*\*) levels of probability as determined by *F* values for each combination treatment calculated for 2-by-2 comparisons of the observed response of that treatment with the observed responses for the control and the separate levels of EPTC ± R-25788 and piperonyl butoxide involved. <sup>c</sup> Expected values in parentheses were calculated by assuming no interactions (see Materials and Methods). <sup>d</sup> Formulated commercial mixture of 0.8 kg/L EPTC plus 0.07 kg/L R-25788.

Table III. Shoot Dry Weights of Corn Seedlings Grown in Soil Treated with Combination of the Herbicides EPTC or EPTC plus R-25788 and the Antioxidant Propyl Gallate<sup>a</sup>

herbicide rate, kg/ha	type of response	propyl gallate, kg/ha			
		0	4.5	6.7	9.0
<b>EPTC</b>					
0.0	observed <sup>b</sup>	3.07 ± 0.11	3.20 ± 0.18	3.15 ± 0.38	3.17 ± 0.17
4.5	observed	2.65 ± 0.19	2.90 ± 0.40	2.80 ± 0.29	2.80 ± 0.21
	expected <sup>c</sup>		(2.78)	(2.73)	(2.75)
5.6	observed	2.05 ± 0.34	2.27 ± 0.28	2.35 ± 0.21	2.27 ± 0.06
	expected		(2.18)	(2.13)	(2.15)
6.7	observed	1.27 ± 0.23	1.27 ± 0.28	1.30 ± 0.20	1.05 ± 0.21
	expected		(1.40)	(1.35)	(1.37)
<b>EPTC plus R-25788<sup>d</sup></b>					
0.0	observed	3.47 ± 0.33	3.60 ± 0.21	3.62 ± 0.42	3.51 ± 0.13
4.5	observed	3.20 ± 0.18	3.00 ± 0.20	3.15 ± 0.25	3.00 ± 0.24
	expected		(3.33)	(3.35)	(3.24)
5.6	observed	3.00 ± 0.15	2.63* ± 0.19	2.65* ± 0.15	2.50* ± 0.24
	expected		(3.13)	(3.15)	(3.04)
6.7	observed	2.77 ± 0.06	2.50* ± 0.20	2.27** ± 0.09	2.12** ± 0.05
	expected		(2.90)	(2.92)	(2.81)

<sup>a</sup> Data are expressed in grams and represent dry matter accumulations of corn seedlings during a 30-day period. <sup>b</sup> Mean weight values are from four replications ± standard error of each mean. Asterisks indicate significant interactions at the 5% (\*) and 1% (\*\*) levels of probability as determined by *F* values for each combination treatment calculated for 2-by-2 comparisons of the observed response for that treatment with the observed responses for the control and the separate levels of EPTC ± R-25788 and propyl gallate involved. <sup>c</sup> Expected values in parentheses were calculated by assuming no interactions (see Materials and Methods). <sup>d</sup> Formulated commercial mixture of 0.8 kg/L EPTC plus 0.07 kg/L R-25788.

expected value, antagonism is indicated. When an observed value is less than its respective expected value, synergism is indicated. Finally, when observed and expected values are similar, the interactive effect is additive. In the ensuing discussion, differences between observed and expected responses for each treatment combination are viewed as biologically important only when the observed response for a given treatment combination between the herbicides and ozone or antioxidants was significant by the *F* test. In all other cases, differences between observed and expected responses are not viewed as biologically important, and the interactive effects are characterized as additive.

## RESULTS AND DISCUSSION

Data in Tables I-III indicate that EPTC, applied alone at rates of 4.5, 5.6, and 6.7 kg/ha, significantly reduced the dry matter accumulation of corn seedlings. Injured corn seedlings were characterized by stunted and twisted leaves,

failure of the second and higher order leaves to unroll properly from the coleoptile, a dark green color, and stimulated stem growth. These symptoms of EPTC injury to corn have been described also by other investigators (Donald et al., 1979). Inclusion of the herbicide antidote R-25788 in the formulation of the herbicide EPTC improved considerably the dry weights of corn seedlings treated with EPTC at rates as high as 6.7 kg/ha (Tables I-III) and alleviated the aforementioned symptoms of EPTC injury to corn. Although the dry weights of corn seedlings treated with EPTC in the presence of the antidote R-25788 were not as good as those of the untreated controls, they did not indicate severe injury. A slight injury of corn seedlings treated with EPTC plus R-25788 at planting or at 2-4 weeks after planting has been reported also by Burt and Buzio (1979). However, other investigators (Martin and Burnside, 1982) have shown that at the end of the growing season, yields of corn plants treated at planting with EPTC plus R-25788 were equal or even

better than those of untreated controls.

Exposure of corn seedlings to 0.2 or 0.3 ppm of O<sub>3</sub> for two 6-h periods did not adversely affect their dry matter accumulations (Table I). In addition, no visible symptoms of ozone injury to corn seedlings were evident following their fumigation with 0.2 or 0.3 ppm of O<sub>3</sub>. In the absence of the antidote R-25788, the interactive effects between EPTC and O<sub>3</sub> on corn seedlings appeared to be additive. However, when the protectant R-25788 was included in the formulation of EPTC, exposure of corn seedlings to 0.3 ppm of O<sub>3</sub> was found to interact significantly with 5.6 and 6.7 kg/ha of herbicide EPTC plus R-25788. New leaves of corn seedlings treated with these combinations of EPTC plus R-25788 and O<sub>3</sub> were stunted and twisted, indicating that the greatest corn injury observed was due to the herbicide EPTC rather than to O<sub>3</sub>. However, failure of corn leaves to properly unroll from the coleoptile—a typical symptom of EPTC injury to corn—was not observed. This was not surprising since fumigation of corn seedlings with O<sub>3</sub> was conducted after their coleoptiles had penetrated the soil surface and the first leaves had unrolled properly because of the protective effect of the antidote R-25788 that was applied together with the herbicide EPTC. Use of the *F* test and comparisons between the observed and expected responses for these combination treatments of O<sub>3</sub> and EPTC plus R-25788 indicated that these interactions were highly synergistic (Table I). The interactive effects between all rates of EPTC plus R-25788 and O<sub>3</sub> at 0.2 ppm as well as the interaction between 4.5 kg/ha EPTC plus R-25788 and 0.3 ppm of O<sub>3</sub> were additive (Table I).

Individual soil applications of the antioxidants piperonyl butoxide and propyl gallate at rates as high as 9.0 kg/ha did not reduce the dry weights of corn seedlings (Tables II and III). Growth responses of corn seedlings grown in soil treated with combinations of the herbicide EPTC at 4.5 or 5.6 kg/ha and all rates of piperonyl butoxide were indicative of additive effects. However, EPTC at 6.7 kg/ha interacted synergistically with 6.7 and 9.0 kg/ha piperonyl butoxide on corn seedlings (Table II). In the presence of the antidote R-25788, the synergism between piperonyl butoxide and the herbicide EPTC was much more pronounced. Data in Table II show that piperonyl butoxide at 4.5 kg/ha synergized the effects of 6.7 kg/ha EPTC plus R-25788 to corn, while piperonyl butoxide at 6.7 and 9.0 kg/ha accentuated the effects of all rates of EPTC plus R-25788 used in this study. In the absence of the antidote R-25788, the interactive effects between EPTC and propyl gallate were additive (Table III). When R-25788 was included in the formulation of EPTC, all rates of propyl gallate interacted synergistically with the higher rates (5.6 and 6.7 kg/ha) of EPTC plus R-25788 (Table III).

The results of this study indicate that fumigation with O<sub>3</sub> or soil applications of the antioxidants piperonyl butoxide and propyl gallate can synergize the effects of the herbicide EPTC plus R-25788 to corn seedlings. Since, in the absence of the antidote R-25788, the interactive effects between O<sub>3</sub> or the two antioxidants and EPTC were generally additive, it is possible that fumigation with O<sub>3</sub> or treatments with piperonyl butoxide and propyl gallate could interfere with the protective action of the antidote R-25788 against EPTC injury to corn. The antidotal activity of R-25788 against EPTC injury to corn is believed to be the result of an increase in the rate of the metabolic detoxication of the herbicide EPTC induced by the antidote. The major pathway of the metabolic degradation of EPTC in corn involves first an oxidation reaction that converts EPTC to its sulfoxide or sulfone and then a conjugation reaction of the EPTC sulfoxide with gluta-

thione (GSH) (Lay et al., 1975). Early investigations by Casida and co-workers (Lay et al., 1975; Lay and Casida, 1976; Hubbel and Casida, 1977) emphasized that conjugation of EPTC sulfoxide with GSH was the most important step in the metabolic degradation of this herbicide in corn and proposed that R-25788 protects corn by increasing the level of GSH in corn as well as the rate of the conjugation of EPTC sulfoxide to GSH. Recent studies by Kömives and Dutka (1980) and Leavitt and Penner (1979b), however, demonstrated that the sulfoxidation step of EPTC metabolism in corn is as important as the conjugation of the EPTC sulfoxide with GSH and suggested that R-25788 may protect corn from EPTC injury by increasing the rate of EPTC sulfoxidation in corn.

The sulfoxidation of EPTC in plant or mammalian systems is believed to be mediated by a group of hemo-proteins known collectively as mixed-function oxidases (Hubbell and Casida, 1977). Mixed-function oxidases use molecular oxygen as an obligatory substrate (Sato and Omura, 1978) and are involved in the metabolic detoxication of numerous herbicides in plants or in other living systems (Hatzios and Penner, 1982). Ozone is a very strong oxidant that can readily react with a variety of substances found within living systems (Heath, 1980). Rubin et al. (1980) reported recently that replacement of molecular oxygen by O<sub>3</sub> may cause an abnormal function of mixed-function oxidases of plants exposed to this air pollutant. Antioxidants are chemicals that prevent the reactions of organic materials with molecular oxygen. Because of that, the activity of mixed-function oxidase enzymes is readily inhibited by several antioxidant compounds such as piperonyl butoxide and SKF-525A (Hodgson and Tate, 1976). The antioxidant propyl gallate is a well-known inhibitor of lipoxygenase-mediated O<sub>2</sub> uptake in germinating seeds (Parrish and Leopold, 1978; Siedow and Girvin, 1980). Some of these antioxidant compounds are used today as insecticide synergists (Wilkinson, 1976). Recently, Kömives and Dutka (1980) reported that the insecticide synergists and mixed-function oxidase inhibitors piperonyl butoxide and SKF-525A synergized the action of the herbicide EPTC on corn. Similarly, tebuthiuron [*N*-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-*N,N'*-dimethylurea], a herbicide bearing some structural similarity to the insecticide synergists and mixed-function oxidase inhibitors 1,2,3-benzothiadiazoles, has been reported to synergize the activity of the herbicide EPTC plus R-25788 on corn (Hatzios, 1981). Piperonyl butoxide and propyl gallate have been also reported to act as synergists of other selected herbicides on corn and soybeans (Rubin et al., 1980). Unlike earlier reports by Casida et al. (1974, 1975), EPTC is phytotoxic itself and its toxic action on corn is not due to the action of EPTC sulfone or of the EPTC sulfoxide (Kömives and Dutka, 1980). On the other hand, conversion of EPTC to its sulfoxide or sulfone is an essential requirement for the subsequent conjugation of this herbicide with GSH (Horvath and Pulay, 1980). Therefore, an abnormal function of the mixed-function oxidase enzymes that sulfoxidize EPTC in corn, brought about by treatments with O<sub>3</sub> or antioxidant compounds, could result in a reduced rate of EPTC detoxication through sulfoxidation and subsequent conjugation with GSH. Thus, the synergistic interactions between the herbicide EPTC plus R-25788 and O<sub>3</sub> or the two antioxidants that were observed in the present study, could be explained by postulating that treatments with O<sub>3</sub> and the two antioxidants (piperonyl butoxide and propyl gallate) antagonized the stimulatory effect of the antidote R-25788 on the mixed-

function oxidases that sulfoxidize EPTC in corn. However, further and more detailed studies will be needed to validate such a hypothesis.

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**Registry No.** EPTC, 759-94-4; O<sub>3</sub>, 10028-15-6; piperonyl butoxide, 51-03-6; propyl gallate, 121-79-9; R-25788, 37764-25-3.

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