

Efficacy of Systemic and Contact Fungicide Mixtures in Controlling Late Blight in Potatoes

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ABSTRACT

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A single foliar spray of either metalaxyl, fosetyl AI, mancozeb, fentin acetate, folpet, chlorothalonil, captafol, or one of a mixture of them was applied to potted potato plants (cv. Alpha) 1 day before inoculating with either a metalaxyl-sensitive (MS) or -resistant (MR) field isolate of *Phytophthora infestans*. Systemic and contact fungicidal mixtures were far more effective in controlling both MS and MR isolates than individual

components at corresponding concentrations combined. No such increased efficacy was exerted by mixtures of metalaxyl and fosetyl AI, nor by mixtures of mancozeb and fentin acetate. It is hypothesized that any two fungicides that differ in mode of action and in stage of fungal growth that they affect will exhibit increased control efficacy of late blight in potato.

Additional key words: chemical control, fungicide interaction, oomycetes.

Studies on the joint action of pesticides in agriculture were conducted as early as 50 years ago (1,2,13,19). With insect control, attention was mainly focused on increasing insecticide efficacy by mixing a relatively inexpensive, less toxic ingredient with an expensive toxic compound (11). For plant disease control, various mixtures of contact fungicides were used mainly to achieve synergy and to broaden the spectrum of activity (19). In recent years, particularly after single-site systemic fungicides were developed and because of the high risk of fungal resistance in using them, prepackaged mixtures of systemic and contact fungicides were formulated. Such mixtures are expected to delay the buildup of resistant fungal strains (12). The producers of systemic fungicides, such as metalaxyl, sell them as products combined with contact fungicides for the control of foliage pathogens, such as *Phytophthora infestans* (Mont.) DeBary in potatoes. In spite of the availability of such prepackaged mixtures, limited data exist concerning the performance of such mixtures compared with their single components. Recent studies in our laboratory showed that a foliar spray of metalaxyl-mancozeb mixtures provided much better control of downy mildew (*Pseudoperonospora cubensis*) in cucumbers than either metalaxyl or mancozeb alone. This was true

under both growth chamber and field conditions when either metalaxyl-sensitive (MS) or -resistant (MR) isolates were used for inoculation (17). Synergistic interactions between fungicides with different modes of action were demonstrated by Gisi et al in vitro with *Phytophthora cactorum* and *P. cinnamomi* and in vivo with *P. infestans* on tomato and *Plasmopara viticola* on grape leaves (7,8).

There is voluminous literature on the theory of drug joint action (1,2,6,9,13-15,20-22) and on the experimental methodology for calculating their joint action (2,6,9,13,14,21). The expected efficacy of mixtures is often calculated with the aid of the Wadley formula (21,22), which hypothesizes an independent similar joint action between ingredients. Transformed dose-response curves (with at least five points on each) of the mixtures and of their components are experimentally obtained, and the ratio between the expected and the observed efficacy of the mixtures (in terms of concentration) indicates the type of interaction occurring between the ingredients (synergism, antagonism, additivity).

Another approach is based on Abbott's formula (6) in which the difference in control efficacy (in terms of percentage of mortality) of a mixture relative to its ingredients is calculated (2,19) based on the hypothesis that the ingredients act independently, but with overlapping. Any deviation from this hypothesis indicates an interaction. With this approach, dose-response curves are not required.

Our data demonstrate that the efficacy of mixtures of metalaxyl or fosetyl AI with contact fungicides in controlling late blight in potatoes is much greater than predicted by the hypothesis of

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independent action. A preliminary report on some of these observations was published (16).

MATERIALS AND METHODS

Plant material. All experiments were conducted with the potato (*Solanum tuberosum* L.) cultivar Alpha. Tubers (about 170 g per tuber) were sown in 2-L pots filled with sandy loam, vermiculite, and peat (1:1:1, v/v) and were grown in the greenhouse (19–28 C). The five to six shoots (100–125 leaflets per shoot) that were in each pot 6–7 wks after sowing were used for each inoculation test.

Fungal isolates. MS and MR isolates of *P. infestans* were collected from blighted potato fields in Israel during 1984 and 1985. Identification of isolates is given in Table 1. Isolates were maintained and propagated on detached potato leaflets floating on water in petri dishes.

Fungicides and fungicide application. Metalaxyl (25WP) and fosetyl A1 80WP (Alette) were the systemic fungicides used. The contact fungicides were mancozeb 80WP, fentin acetate 60WP, folpet 75WP, chlorothalonil 50EC (Bravo 500), and captafol 48EC. All fungicides were suspended in water and sprayed 24 hr before inoculation. Sprays were applied to initial runoff on upper leaf surfaces with the aid of a hand garden sprayer (about 10 ml per shoot).

Inoculation. Sporangial suspensions in cold (4 C), double-distilled water (about 500 sporangia per milliliter) of the appropriate isolate were inoculated onto the upper leaf surfaces of the plants with the aid of a glass atomizer. Inoculated plants were

TABLE 1. Isolates of *Phytophthora infestans* used in this study

Isolate	Location	Collection date	Treatment	Cultivar
MS19	Ramat-Hakovesh	Feb. 84	Not treated	Alpha
MS49	Bet-Kama	Dec. 84	Not treated	Alpha
MS58	Tira	Jan. 85	Not treated	Alpha
MS60	Zofit	Feb. 85	Ridomil-mancozeb	Alpha
MR29	Raanana	Feb. 84	Ridomil-mancozeb	Alpha
MR52	Gevuloth	Nov. 84	Ridomil-mancozeb	Mirka
MR53	Aza	Nov. 84	Ridomil-mancozeb	Spunta

TABLE 2. Efficacy of metalaxyl and fosetyl A1 in controlling late blight in potatoes incited by metalaxyl-sensitive (MS) and -resistant (MR) isolates of *Phytophthora infestans*^a

Fungicide ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^b			
	MS49	MS58	MR52	MR53
Metalaxyl				
6.25	17 \pm 3 a	26 \pm 8 a
12.5	22 \pm 5 a	47 \pm 7 b
25	55 \pm 8 b	75 \pm 4 c
50	...	100 d
125	100 c	...	0 a	5 \pm 4 a
250	22 \pm 9 b	15 \pm 8 b
500	39 \pm 8 c	16 \pm 7 b
1,000	44 \pm 5 c	24 \pm 9 c
Fosetyl A1				
50	13 \pm 5 a
100	21 \pm 8 a	27 \pm 9 a	0 a	...
200	45 \pm 8 b	45 \pm 6 b	5 \pm 5 a	...
250	1 \pm 1 a
300	...	74 \pm 7 c
400	90 \pm 1 c	100 d	7 \pm 7 a	...
500	3 \pm 2 a
1,000	5 \pm 4 a
2,000	10 \pm 7 a

^a Isolates MS58 and MR52 were used for testing mixtures with all contact fungicides except captafol. Isolates MS49 and MR53 were used for testing mixtures with captafol.

^b Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

kept in a moist atmosphere (18 C, darkness) for about 20 hr to ensure infection and then transferred to growth cabinets (20 \pm 1 C, 12 hr of light per day, about 120 $\mu\text{E}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$) for symptom production.

TABLE 3. Efficacy of five contact fungicides in controlling late blight in potatoes incited by metalaxyl-sensitive (MS) and -resistant (MR) isolates of *Phytophthora infestans*^a

Fungicide ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^b	
	MS	MR
Mancozeb		
10	10 \pm 6 ab	3 \pm 4 ab
20	37 \pm 7 d	11 \pm 9 bc
40	50 \pm 6 f	44 \pm 4 e
80	100 i	100 h
Fentin acetate		
5	16 \pm 10 b	12 \pm 9 bc
10	47 \pm 7 ef	31 \pm 8 d
15	60 \pm 5 g	54 \pm 8 f
20	100 i	100 h
Folpet		
3.12	5 \pm 8 a	6 \pm 6 ab
6.25	26 \pm 6 c	26 \pm 9 d
12.5	51 \pm 7 de	44 \pm 6 e
25	100 i	100 h
Chlorothalonil		
5	15 \pm 9 b	17 \pm 8 c
10	56 \pm 6 gf	58 \pm 6 f
15	73 \pm 4 h	76 \pm 7 g
20	100 i	100 h
Captafol		
2.5	15 \pm 8 b	12 \pm 6 bc
5	32 \pm 9 cd	39 \pm 9 d
10	48 \pm 8 ef	45 \pm 8 e
20	80 \pm 3 h	79 \pm 4 g
25	100 i	100 h

^a MS58 and MR52 were used except for captafol with which MS49 and MR53 were used.

^b Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

TABLE 4. Efficacy of metalaxyl mixtures with contact fungicides in controlling late blight in potatoes incited by a metalaxyl-sensitive isolate (MS58) of *Phytophthora infestans*

Mixture ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^a		
	Observed	Expected	Ratio ^b
Metalaxyl + mancozeb			
6.25 + 10	92 \pm 2 b	33	2.78
12.5 + 20	98 \pm 1 d	61	1.60
25.0 + 40	100 e	87	1.15
Metalaxyl + fentin acetate			
6.25 + 5	96 \pm 2 c	38	2.52
12.5 + 10	98 \pm 2 de	72	1.36
25.0 + 15	100 e	90	1.11
Metalaxyl + folpet			
6.25 + 3.12	87 \pm 3 a	30	2.90
12.5 + 6.25	94 \pm 1 c	61	1.54
25.0 + 12.5	100 e	88	1.13
Metalaxyl + chlorothalonil			
6.25 + 5	90 \pm 3 b	37	2.43
12.5 + 10	97 \pm 1 d	77	1.26
25.0 + 15	100 e	87	1.15
Metalaxyl + captafol			
6.25 + 2.5	91 \pm 1 b	29	3.13
12.5 + 5	100 e	47	2.12
25.0 + 10	100 c	77	1.29

^a Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

^b Expected control efficacy was calculated with data from Tables 2 and 3 using the Abbott formula (6).

Disease assessment. Disease incidence was determined 7 days after inoculation. The number of leaflets infected of the total number of leaflets inoculated was counted for each shoot and expressed as percentage of leaflets infected. Leaflets showing a hypersensitive response (lesions less than 2 mm) were considered healthy.

Calculation of increased efficacy of mixtures. The ratio between percentage of observed control efficacy (OCE) and percentage of expected control efficacy (ECE) of a mixture was defined as the increased control efficacy (ICE). $ICE = OCE/ECE$. ECE was calculated using Abbott's formula (6):

$$ECE = C + S - C.S/100$$

TABLE 5. Efficacy of metalaxyl mixtures with contact fungicides in controlling late blight in potatoes incited by a metalaxyl-resistant isolate (MR52) of *Phytophthora infestans*

Mixture ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^a		
	Observed	Expected	Ratio
Metalaxyl + mancozeb			
125 + 10	75 ± 5 a	3	25.0
250 + 20	88 ± 2 cd	31	2.83
500 + 40	100 f	66	1.51
Metalaxyl + fentin acetate			
125 + 5	80 ± 4 b	12	6.66
250 + 10	91 ± 3 cd	46	1.97
500 + 15	100 f	72	1.38
Metalaxyl + folpet			
125 + 3.12	78 ± 4 ab	6	13.0
250 + 6.25	93 ± 2 e	42	2.21
500 + 12.5	100 f	66	1.51
Metalaxyl + chlorothalonil			
125 + 5	76 ± 6 ab	17	4.47
250 + 10	87 ± 3 c	67	1.29
500 + 15	100 f	85	1.17
Metalaxyl + captafol			
125 + 2.5	92 ± 1 ed	16	5.75
250 + 5	100 f	48	2.08
500 + 10	100 f	54	1.85

^a Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

TABLE 6. Efficacy of fosetyl AI mixtures with contact fungicides in controlling late blight in potatoes incited by a metalaxyl-sensitive isolate (MS58) of *Phytophthora infestans*

Mixture ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^a		
	Observed	Expected	Ratio
Fosetyl AI + mancozeb			
100 + 10	86 ± 3 c	34	2.52
200 + 20	94 ± 2 d	60	1.56
300 + 40	100 e	87	1.15
Fosetyl AI + fentin acetate			
100 + 5	87 ± 4 c	39	2.23
200 + 10	95 ± 1 d	71	1.33
300 + 15	100 e	90	1.11
Fosetyl AI + folpet			
100 + 3.12	80 ± 4 b	35	2.28
200 + 6.25	88 ± 3 c	59	1.49
300 + 12.5	100 e	87	1.15
Fosetyl AI + chlorothalonil			
100 + 5	86 ± 4 c	38	2.26
200 + 10	95 ± 1 d	76	1.26
300 + 15	100 e	90	1.11
Fosetyl AI + captafol			
50 + 2.5	75 ± 5 a	26	2.88
100 + 5	100 e	54	1.85
200 + 10	100 e	71	1.40

^a Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

in which C and S represent percentage of disease control exerted by the contact and the systemic fungicide, respectively. ICE expresses the efficacy of the mixture relative to the combined efficacies of its two components. An ICE value of 1 suggests no interaction between the components. In this case, the control efficacy of the mixture is equal to the sum of the partial control efficacies of its components minus a correction factor due to overlapping between

TABLE 7. Efficacy of fosetyl AI mixtures with contact fungicides in controlling late blight in potatoes incited by a metalaxyl-resistant isolate (MR52) of *Phytophthora infestans*

Mixture ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD) ^a		
	Observed	Expected	Ratio
Fosetyl AI + mancozeb			
100 + 10	71 ± 5 b	3	23.66
200 + 20	83 ± 4 c	15	5.53
400 + 40	92 ± 3 d	48	1.91
Fosetyl AI + fentin acetate			
100 + 5	73 ± 6 b	12	6.08
200 + 10	84 ± 3 c	34	2.47
400 + 15	93 ± 2 d	57	1.63
Fosetyl AI + folpet			
100 + 3.12	85 ± 6 b	6	12.50
200 + 6.25	86 ± 4 c	29	2.96
400 + 12.5	95 ± 2 de	47	2.02
Fosetyl AI + chlorothalonil			
100 + 5	72 ± 5 b	17	4.23
200 + 10	84 ± 4 c	60	1.40
400 + 15	92 ± 2 d	77	1.19
Fosetyl AI + captafol			
250 + 2.5	49 ± 8 a	12	4.08
500 + 5	85 ± 4 c	41	2.07
1,000 + 10	100 e	47	2.12

^a Different letters following figures in vertical columns indicate significant difference at 5% level ($n = 5$) by Duncan's multiple range test. Percentage leaflets infected in control, fungicide-free, plants ranged between 93 and 100%.

TABLE 8. The relationship between fungicidal component concentrations and observed control efficacy (OCE) of late blight in potatoes incited by metalaxyl-sensitive and -resistant isolates of *Phytophthora infestans*

Metalaxyl		Mancozeb		Metalaxyl + mancozeb		Ratio ^d	
$\mu\text{g/ml}^h$	OCE ^c	$\mu\text{g/ml}$	OCE	$\mu\text{g/ml}$	OCE		
Metalaxyl-sensitive isolate (MS19) ^a							
0	0	a	
0.312	2 ± 2 a	1.25	0	0.312 + 1.25	35 ± 8 b	17.50	
0.625	4 ± 2 a	2.5	2 ± 3 a	0.625 + 2.5	52 ± 7 c	10.00	
1.25	5 ± 4 a	5	5 ± 3 a	1.25 + 5	66 ± 3 d	8.80	
2.5	10 ± 8 a	10	9 ± 5 a	2.5 + 10	76 ± 4 d	4.44	
5	24 ± 9 b	15	24 ± 9 b	5 + 15	94 ± 2 e	1.79	
10	49 ± 9 c	25	50 ± 6 c	10 + 25	100 f	1.34	
15	90 ± 1 e	40	90 ± 3 e	15 + 40	100 f	1.01	
30	100 f	50	100 f	30 + 50	100 f	1.00	
Metalaxyl-resistant isolate (MR29)							
0	0	a	
25	0	a	1.25	1 ± 1 a	25 + 1.25	28 ± 6 b	28.00
50	0	a	2.5	2 ± 3 a	50 + 2.5	46 ± 9 c	23.00
100	5 ± 3 a	5	3 ± 3 a	100 + 5	56 ± 6 cd	7.13	
...	...	10	4 ± 4 a	100 + 10	64 ± 5 de	7.27	
125	9 ± 4 a	15	11 ± 3 a	125 + 15	74 ± 4 e	3.89	
...	...	20	25 ± 10 b	250 + 20	92 ± 2 f	2.13	
250	24 ± 9 b	25	33 ± 8 b	250 + 25	96 ± 1 f	1.95	
500	49 ± 6 c	30	51 ± 5 c	500 + 30	100 g	1.33	
1,000	75 ± 6 e	35	75 ± 5 e	1,000 + 30	100 g	1.06	
2,000	90 ± 2 f	40	89 ± 3 f	2,000 + 40	100 g	1.01	

^a Duncan's multiple range test applies both vertically and horizontally for each isolate separately.

^b Active ingredient.

^c OCE = Observed control efficacy in percentages ± SD of the mean ($n = 5$).

^d Ratio between observed and expected control efficacies. The expected efficacy was calculated with the aid of Abbott's formula.

TABLE 9. Efficacy of metalaxyl, fosetyl AI, and their mixtures in controlling late blight in potatoes incited by metalaxyl-sensitive and -resistant isolates of *Phytophthora infestans*

Metalaxyl-sensitive isolate (MS60)				Metalaxyl-resistant isolate (MR53)			
Metalaxyl ($\mu\text{g a.i./ml}$)	Fosetyl AI ($\mu\text{g a.i./ml}$)	OCE ^a	Ratio ^b	Metalaxyl ($\mu\text{g a.i./ml}$)	Fosetyl AI ($\mu\text{g a.i./ml}$)	OCE	Ratio
0	0	0 a	...	0	0	0 a	...
6.25	0	22 \pm 9 b	...	125	0	10 \pm 8 ab	...
12.5	0	75 \pm 5 e	...	250	0	21 \pm 9 cd	...
0	100	31 \pm 10 c	...	0	250	6 \pm 9 ab	...
0	200	71 \pm 3 e	...	0	500	11 \pm 6 bc	...
6.25	100	44 \pm 7 c	0.95	125	250	11 \pm 10 bc	0.75
6.25	200	75 \pm 5 e	0.97	125	500	21 \pm 10 cd	1.05
12.5	100	84 \pm 5 f	1.01	250	250	23 \pm 8 d	0.90
12.5	200	90 \pm 3 f	0.97	250	500	31 \pm 7 d	1.16

^aOCE = Observed control efficacy in percentages \pm SD of the mean.

^bRatio between observed and expected control efficacies. The expected efficacy was calculated with the aid of Abbott's formula.

the fungicides. ICE values smaller than 1 suggest an antagonistic interaction between the components, and ICE values greater than 1 suggest synergistic interaction between the components.

RESULTS

The efficacy of metalaxyl and fosetyl AI in controlling MS and MR isolates of the fungus is given in Table 2. Although isolates MS49 and MS58 were fully controlled by metalaxyl of 125 and 50 $\mu\text{g a.i.}$ per milliliter, respectively, isolates MR52 and MR53 were only partially affected by metalaxyl of 1,000 $\mu\text{g a.i.}$ per milliliter. Fosetyl AI effectively controlled the MS isolates, but not the MR isolates, at 400 $\mu\text{g a.i.}$ per milliliter (18). The efficacy of five contact fungicides is given in Table 3. Complete control of MS and MR isolates was achieved by mancozeb, fentin acetate, folpet, chlorothalonil, and captafol at 80, 20, 25, 20, and 25 $\mu\text{g a.i.}$ per milliliter, respectively. Mixtures of metalaxyl (Tables 4 and 5) or of fosetyl AI (Tables 6 and 7) with any one of the five contact fungicides exhibited a much increased efficacy in controlling the MS and the MR isolates. The relative increase in control efficacy of MS isolates ranged between 1.11 and 3.13 for metalaxyl mixtures and 1.11 and 2.88 for fosetyl AI mixtures, whereas that of MR isolates ranged between 1.17 and 25.0 for metalaxyl mixtures and between 1.19 and 23.66 for fosetyl AI mixtures. In all cases, diluted mixtures exhibited higher ratio (ICE) values than concentrated mixtures did, due to the very low efficacy of their components when used alone.

The inverse relationship between mixture (metalaxyl and mancozeb) concentration and ICE value is given in detail in Table 8. Metalaxyl at 0.312–1.25 $\mu\text{g a.i.}$ per milliliter and mancozeb at 1.25–5 $\mu\text{g a.i.}$ per milliliter had a negligible control efficacy (0–5%) on isolate MS19 when used alone. When mixed together, efficacy ranged between 35 and 66%. These efficacies were 8.8–17.5 times higher than the expected sum efficacies of the single components. Responses were similar with the MR29 isolate, but with higher concentrations of metalaxyl (25–100 $\mu\text{g a.i.}$ per milliliter). Here again, ICE values were higher for the MR than for the MS isolate.

Other results indicated that no interaction occurred between metalaxyl and fosetyl AI (Table 9) or between mancozeb and fentin acetate (Table 10).

DISCUSSION

Fungicidal mixtures have at least three advantages over single-fungicide formulations, namely higher cost/benefit ratio due to synergistic action between components of the mixture, reduced buildup of subpopulations resistant to the site-specific component of the mixture, and simultaneous action against more than one target organism, each sensitive to one or both components of the mixture. A mixture may bear one, two, or all three advantages.

The monocycle disease programs in this study with one fungal pathogen provide no information on the first two advantages but give a clear indication on the third advantage.

TABLE 10. Efficacy of mancozeb-fentin acetate mixtures in controlling late blight in potatoes incited by a metalaxyl-sensitive isolate (MS60) of *Phytophthora infestans*

Mancozeb ($\mu\text{g a.i./ml}$)	Fentin acetate ($\mu\text{g a.i./ml}$)	Control efficacy (% + SD)		
		Observed	Expected	Ratio ^a
0	0	0 a		
5	0	9 \pm 4 b		
10	0	20 \pm 9 c		
20	0	45 \pm 6 gef		
0	5	21 \pm 9 c		
0	10	43 \pm 7 ef		
0	20	100 j		
5	5	30 \pm 8 d	28	1.06
5	10	51 \pm 6 gf	48	1.05
5	20	100 j
10	5	39 \pm 6 e	37	1.05
10	10	52 \pm 7 g	55	0.94
10	20	100 j
20	5	61 \pm 7 h	57	1.07
20	10	75 \pm 5 i	69	1.08
20	20	100 j

^aRatio between observed and expected control efficacies was calculated with the aid of Abbott's formula.

Metalaxyl or fosetyl AI combinations with any one of the five contact fungicides used were far more efficient in controlling either MS or MR isolates of *P. infestans*. Mixtures of a systemic and a contact fungicide, each inefficient in controlling the disease when used singly, exerted in some cases 23–25 times higher control efficacy than expected. However, no increased control efficacy was obtained when mixtures of metalaxyl and fosetyl AI or mancozeb and fentin acetate were used.

The MR isolates used in this study were resistant (to various extents) to either metalaxyl or fosetyl AI (18). However, these isolates were efficiently controlled when either metalaxyl or fosetyl AI were combined with any contact fungicide. The relative increase in control efficacy (ICE) of mixtures was consistently higher toward MR than MS isolates, in spite of their lower efficacy per unit weight of active ingredient, thus confirming our previous findings with *P. cubensis* (17).

Preliminary experiments in our laboratory indicate that a short-period exposure of sporangia of *P. cubensis* and *P. infestans* to mancozeb increased their sensitivity to metalaxyl (B. Bashan, Y. Levy, and Y. Cohen, unpublished). This, together with the data provided here, may suggest that the fungus weakened at germination by a contact fungicide is finally killed by a normally sublethal dose of the systemic compound that affects mycelial development. Our data suggest that synergistic interaction occurred between fungicides that differ in their mode of action, mode of uptake and translocation, and effect on pathogenesis. Although the contact fungicides primarily affect sporangial and cyst germination of *P. infestans*, the systemics affect

postinfectious stages in pathogenesis. Although the contact fungicides inhibit respiration (nonspecifically for all except fenitrothion, which inhibits oxidative phosphorylation [10]), metalaxyl inhibits RNA polymerase activity (4) and fosetyl Al may act indirectly through the host (3) or directly on the fungus in an unknown manner (5). Our data do not indicate whether fungicides should differ in all three respects for synergy to occur. Our finding that two contact fungicides, or two systemics, do not interact synergistically, suggests that different modes of action, together with differential effect on pathogenesis, are both required for synergy to occur.

The practical implication of this study is that prepackaged mixtures of fungicides should be formulated to achieve maximal disease control per unit weight of active ingredient. The contribution of such mixtures in avoiding the buildup of resistant genotype awaits long-term field studies.

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