

PATENT SPECIFICATION

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(72) Inventor JOSEPH F. SCHWER



(54) FUNGICIDAL FORMULATIONS

(71) We, LILLY INDUSTRIES LIMITED, a British Company of Lilly House, Hanover Square, London, W1R 0PA, formerly of Henrietta House, Henrietta Place, London, W1, England, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

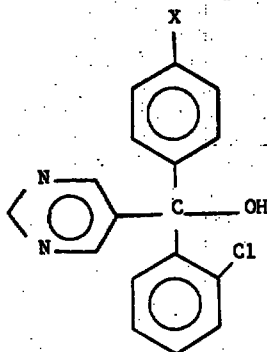
The present invention relates to a method of treating fungal infections of cultivated plants, especially cereals and cucurbits, to a novel fungicidal combination useful in such treatment, to fungicidal formulations containing said novel combinations and to a method of preparing said fungicidal formulations.

Many plants of economic and decorative importance are damaged annually by various types of fungi. Because of the financial losses involved, a great deal of research has been done in an attempt to find methods and substances for the control of these deleterious fungi.

U.S. Patent No. 3,887,708 describes the use of various α, α - disubstituted - 5 - pyrimidinemethanes and methanols, including α - (2 - chlorophenyl) - α - (4 - chlorophenyl) - 5 - pyrimidinemethanol and α - (2 - chlorophenyl) - α - (4 - fluorophenyl) - 5 - pyrimidinemethanol, as plant fungicides. 2,4,5,6 - Tetrachloro - 1,3 - dicyanobenzene also known as tetrachloroisophthalonitrile and as chlorothalonil, is described in U.S. Patents Nos. 3,290,353 and 3,331,735 as being active as a plant fungicide.

It has now been discovered that when either of the pyrimidine methanols specifically mentioned above is used in combination with 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene a surprising synergistic effect is obtained in the treatment of fungal infections of cultivated plants.

According to the present invention therefore there is provided a fungicidal combination of 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I)



(I)

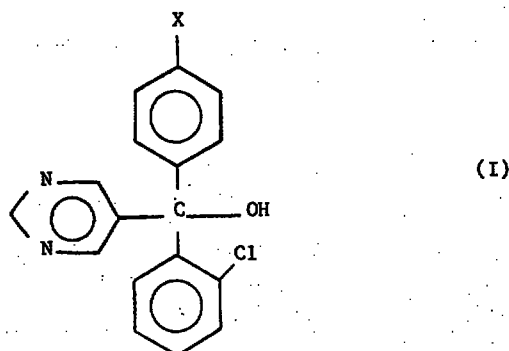
where X is chlorine or fluorine.

2,4,5,6 - Tetrachloro - 1,3 - dicyanobenzene (hereinafter abbreviated to ("DCB")) can be prepared by the process described in U.S. Patent Specification No. 3,290,353 or 3,331,735 and the pyrimidine methanols of formula (I) may be prepared by the process described in U.K. Patent Specification No. 1,218,632.

The novel combination of the present invention is surprisingly effective in controlling or combatting fungal infections such as mildew and septoria in

cultivated plants, especially cereals and cucurbits. Specifically, the combination is especially active against the following plant pathogens — *Erysiphe graminis*, *Septoria nodorum*, *Puccinia recondita*, *Fusarium nivale*, *Puccinia glumarum* and *Pseudoperonospora cubensis*.

The invention therefore also provides a method of treating fungal infections of cultivated plants comprising administering a combination of 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I)



where X is chlorine or fluorine, to the cultivated plants after crop emergence but before harvest.

The frequency and duration of treatment is determined by the severity of the actual or expected fungal infection. The components of the combination may be applied sequentially or simultaneously to the crop to be treated.

The pyrimidine methanol is preferably applied in an amount of from 5 to 100 g per hectare, advantageously 20 to 100 g per hectare, whereas the DCB is preferably applied in an amount of from 60 to 2000 g per hectare, advantageously 500 to 2000 g per hectare. Preferred by weight ratios of the pyrimidine methanol to DCB are therefore in the range from 1:400 to 1.6:1. In the treatment of fungal infections such as *Puccinia recondita* in cereals particularly advantageously weight ratios of pyrimidine methanol to DCB have been found to be in the range of from 1:10 to 1.6:1. In the treatment of fungal infections such as *Pseudoperonospora cubensis* in cucurbits particularly advantageous by weight ratios of pyrimidine methanol to DCB have been found to be in the range of from 1:400 to 1:20.

The novel combination of the invention is advantageously used in the form of a fungicidal formulation comprising DCB and a pyrimidine methanol of formula I as defined above in association with a non-phytotoxic inert carrier therefor. Such a fungicidal formulation is also provided by this invention.

The invention further includes a method of preparing a fungicidal formulation, which method comprises bringing DCB and a pyrimidine methanol of formula I as defined above into association with a non-phytotoxic inert carrier.

The combination of DCB and either of the pyrimidine methanols of formula I as defined above is found to be synergistic in the control of wheat leaf rust caused by *Puccinia recondita* and of downy mildew caused by *Pseudoperonospora cubensis*.

In order to determine that the fungicidal effect obtained by combining a pyrimidinmethanol of formula I as defined above and DCB is synergistic, as compared to the percent control of the fungus accomplished by the two substances applied alone, the formula developed by S. R. Colby, *Weeds*, 15, 20—22 (1967) is used. As is well-known to those working in the field of plant science, if the value obtained by use of the Colby equation is less than the percent control produced by application of the combination, in this case, of DCB and a pyrimidinmethanol of formula I as defined above then synergism is considered to have occurred between the two active ingredients in their effect on the fungi.

The fungicidal formulations of the invention preferably comprise from 5 to 90% by weight of active ingredients and will usually be in the form of a wettable powder or dust, or an aqueous suspension.

Wettable powders or dusts comprise an intimate mixture of the active ingredients, one or more inert carriers and appropriate surfactants. The inert carrier may be chosen from the attapulgite clays, the montmorillonite clays, the diatomaceous earths, kaolins, micas, talcs and purified silicates. Effective surfactants may be found among the sulfonated lignins, the naphthalene sulfonates and condensed naphthalene sulfonates, the alkyl succinates, the alkylbenzene

sulfonates, the alkyl sulfates and nonionic surfactants such as ethylene oxide adducts of phenol. Illustrative of wettable powders falling within the scope of the invention are those having the following compositions:

Wettable Powders

		% by weight	
5	Pyrimidine methanol	0.25 to 10	5
	DCB	25 to 80	
	Surfactant(s)	0 to 10	
	Dispersing agent	0 to 10	
10	Anticaking agent	0 to 10	10
	Inerts	to 100	

Aqueous suspensions comprise the active ingredients suspended in water together with any desired surfactants, thickening agents, antifreezing agents or preservatives. Suitable surfactants may be chosen from those mentioned above in connection with wettable powders. Thickening agents, if used, are normally chosen from appropriate cellulose materials and natural gum whilst glycols will generally be used when an anti-freezing agent is required. Preservatives may be chosen from a wide range of materials such as the various paraben antibacterials, phenol, *o*-chlorocresol, phenyl mercuric nitrate and formaldehyde. Illustrative of aqueous suspensions falling within the scope of the invention are those having the following composition:

Aqueous Suspensions (Flowable)

		% by weight	
25	Pyrimidine methanol	0.2 to 8	25
	DCB	20 to 60	
	Surfactant(s)	0 to 15	
	Thickening agent	0 to 3	
	Anti-freezing agent	0 to 20	
	Preservative	0 to 1	
30	Antifoaming agent	0 to 0.5	30
	Water	to 100	

Whilst the foregoing general examples will adequately demonstrate to those skilled in the art the types of concentrate compositions of use in the present invention, the following non-limiting specific examples are given to further illustrate the invention. In these examples, CCPM represent the compound α - (2 - chlorophenyl) - α - (4 - chlorophenyl) - 5 - pyrimidine methanol and CFPM represents the compound α - (2 - chlorophenyl) - α - (4 - fluorophenyl) - 5 - pyrimidine methanol. Examples 1 and 2 illustrate embodiments of wettable powder in accordance with the invention whereas Examples 3 and 4 are concerned with aqueous suspensions.

EXAMPLE 1

	CFPM	2	
	DCB	60	
45	Ethoxylated nonyl phenol	4	45
	Sodium lignin sulphonate	3	
	Silica	6	
	Kaolin	25	

The active ingredients CFPM and DCB are milled and then blended with the other ingredients in conventional mixing equipment. The blend is then milled in a fluid energy mill to a size range of from 1 to 10 microns and finally the mixture is reblended and deaerated prior to being packaged.

Similarly, the following concentrate was prepared:

EXAMPLE 2

55	CCPM	2.5	55
	DCB	50	
	Sodium alkyl succinate	3	
	Sodium lignin sulphonate	3	
	Talc	41.5	

EXAMPLE 3

	% by weight
CFPM	2
DCB	50
Sodium naphthalene sulphonate	3
Gum arabic	1
Propylene glycol	10
<i>o</i> -chlorocresol	0.3
Water	to 100

Both active ingredients, size reduced by conventional means, if necessary, are dispersed in water containing the surfactant system, preservative and part of the thickening agent. The particle size of both components is further reduced by liquid milling, the balance of the thickening agent added, allowed to hydrate and the product diluted to volume with water.

Similarly, the following aqueous suspension was prepared:

EXAMPLE 4

	% by weight
CCPM	1
DCB	50
Ethoxylated nonyl phenol	2.0
Xanthan gum	0.2
Emulsion silicone	0.1
Water	to 100

The synergistic effect of combining DCB and the pyrimidinemethanols of formula I as defined above is demonstrated by the following tests.

Test 1

The efficacy of combinations of DCB and α - (2 - chlorophenyl) - α - (4 - chlorophenyl) - 5 - pyrimidine methanol (hereinafter referred to as fenarimol) for the control of wheat leaf rust (*Puccinia recondita*) was determined in the greenhouse, using concentrations of fenarimol of 10, 20 or 40 ppm. in combination with 25, 50 or 100 ppm. of DCB. Fenarimol was also evaluated alone at 10, 20 or 40 ppm., and DCB was also evaluated alone at 25, 50 and 100 ppm. of active ingredient.

The fenarimol was formulated as a 1 lb/gal. emulsifiable concentrate (1 EC), and the DCB as a 75% wettable powder (75 WP). The treatment solutions were prepared by dilution of the fenarimol 1 EC or the DCB 75 WP with tap water to the necessary concentrations.

Wheat plants of the variety Monon were grown in plastic pots, each pot containing approximately 50 wheat plants. Each treatment was sprayed on the plants in two plastic pots at the time the plants were seven days old, spraying continuing until runoff occurred. After drying, the plants were inoculated with spores of the wheat rust fungus and the pots and plants were placed in a moist chamber for about 40 hours and then moved to the greenhouse for development of the disease.

Two weeks after the plants were placed in the greenhouse, they were examined visually to determine the percent disease incidence and this figure was converted to percent disease control. The results appear in Table 1, which follows.

TABLE 1

Treatments	PPM	Percent Control of Wheat Leaf Rust DCB			
		0	25	50	100
Fenarimol	0	0 ^{1/2}	36	45	84
	10	40	91	100	100
	20	77	100	100	100
	40	92	92	100	100

^{1/2}Percent disease incidence in untreated control.

(17)

Test 2

Following the same procedure as described in Test 1 the efficacy of combinations of α - (2 - chlorophenyl) - α - (4 - fluorophenyl) - 5 - pyrimidinemethanol (hereinafter referred to as nuarimol) and DCB for the control of *Puccinia recondita* was determined in the greenhouse, using concentrations of nuarimol of 10, 20 or 40 ppm. in combination with 25, 50 or 100 ppm. chlorothalonil. The nuarimol was also evaluated alone at concentrations of 10, 20 or 40 ppm., active ingredient, and DCB was also evaluated alone at concentrations of 25, 50 or 100 ppm. active ingredient.

The formulations of the test compounds, alone and in combination, were prepared in the same manner as in Test 1, using tap water as the diluent, the nuarimol containing formulations being prepared from an emulsifiable concentrate containing 0.75 lb/gallon of nuarimol (0.75 EC).

The test wheat plants, variety Monon, were prepared and treated with the test chemicals in the same manner as described in Test 1 and then inoculated with spores of the wheat rust fungus as described in Test 1. Controls consisted of plants treated with the solvent alone.

Two weeks after the plants were placed in the greenhouse, they were examined visually to determine the percent disease incidence and this figure was converted to percent disease control. The results appear in Table 2, which follows.

TABLE 2

Percent Control of
Wheat Leaf Rust DCB

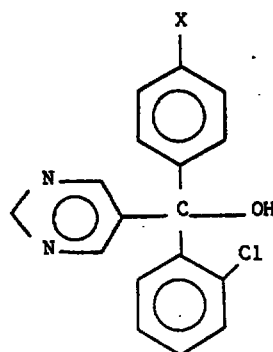
Treatments	PPM	0	25	50	100
Nuairimol	0	(1) ^{1/2}	36	45	84
	10	4	81	93	100
	20	44	100	100	100
	40	79	—*	100	100

^{1/2}Percent disease incidence in untreated control.

* Not run.

WHAT WE CLAIM IS:—

1. A fungicidal combination of 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I).



(I)

where X is chlorine or fluorine.

2. A fungicidal formulation comprising 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I) as defined in Claim 1 in association with a non-phytotoxic inert carrier therefor.

3. A fungicidal combination or formulation according to Claim 1 or 2, wherein the by weight ratio of the pyrimidine methanol to the 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene is in the range from 1:400 to 1.6:1.

4. A method of preparing a fungicidal formulation, which method comprises bringing 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I)



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Test 2

Following the same procedure as described in Test 1 the efficacy of combinations of α - (2 - chlorophenyl) - α - (4 - fluorophenyl) - 5 - pyrimidinemethanol (hereinafter referred to as nuarimol) and DCB for the control of *Puccinia recondita* was determined in the greenhouse, using concentrations of nuarimol of 10, 20 or 40 ppm. in combination with 25, 50 or 100 ppm. chlorothalonil. The nuarimol was also evaluated alone at concentrations of 10, 20 or 40 ppm., active ingredient, and DCB was also evaluated alone at concentrations of 25, 50 or 100 ppm. active ingredient.

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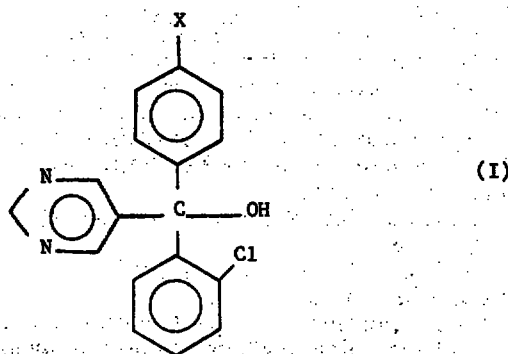
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Nuairimol	0	0 ^{1/2}	36	45	84
	10	4	81	93	100
	20	44	100	100	100
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^{1/2}Percent disease incidence in untreated control.

* Not run.

WHAT WE CLAIM IS:—

1. A fungicidal combination of 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I).



where X is chlorine or fluorine.

2. A fungicidal formulation comprising 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I) as defined in Claim 1 in association with a non-phytotoxic inert carrier therefor.

3. A fungicidal combination or formulation according to Claim 1 or 2, wherein the by weight ratio of the pyrimidine methanol to the 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene is in the range from 1:400 to 1.6:1.

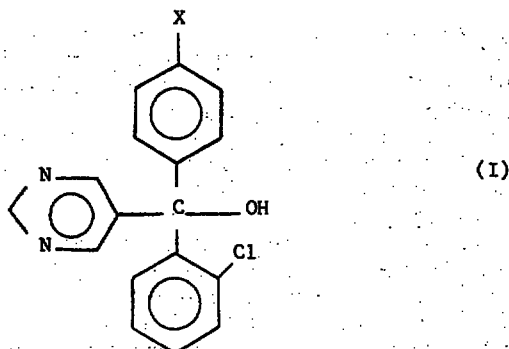
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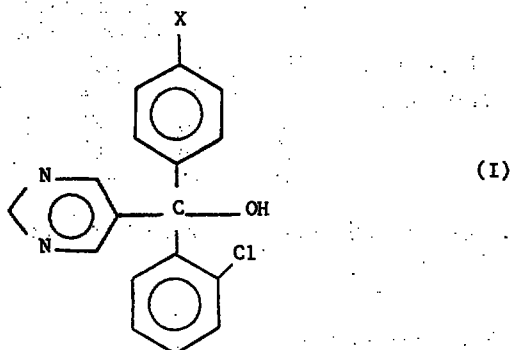
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wherein X is chlorine or fluorine into association with a non-phytotoxic inert carrier.

5. A method according to Claim 4, wherein the by weight ratio of the pyrimidine methanol to the 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene is in the range from 1:400 to 1.6:1.

6. A method of treating fungal infections of cultivated plants comprising administering a combination of 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene and a pyrimidine methanol of formula (I)



where X is chlorine or fluorine, to the cultivated plants after crop emergence but before harvest.

7. A method according to Claim 6 which comprises applying to the cultivated plants a fungicidal formulation in accordance with Claim 2.

8. A method according to Claim 6 or 7 of treating fungal infections, such as *puccinia recondita*, in cereals which comprises applying the said combination or formulation to the cereal after crop emergence but before harvest.

9. A method according to any one of Claims 6 to 8, wherein the by weight ratio of the pyrimidine methanol to the 2,4,5,6 - tetrachloro - 1,3 - dicyanobenzene is in the range from 1:400 to 1.6:1.

10. A fungicidal formulation according to Claim 2 substantially as hereinbefore described.

11. A fungicidal formulation according to Claim 2 substantially as hereinbefore described in any one of the Examples.

12. A method according to Claim 4 substantially as hereinbefore described.

13. A method according to Claim 4 substantially as hereinbefore described in any one of the Examples.

14. A method according to Claim 6 substantially as hereinbefore described.

15. A method according to Claim 6 substantially as hereinbefore described in any one of the Tests.

K. W. H. McVEY,
Chartered Patent Agent,
Erl Wood Manor,
Windlesham,
Surrey, England,
Agent for the Applicants.