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SUPERINTENDENCIA DE INDUSTRIA Y CO

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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Referencia: Expediente No. 07.029.888

Solicitud de Patente de Invención titulada: "Mezclas fungicidas de derivados de tiofeno".

Solicitante: E.I. DuPont De Nemours and Company

RESPUESTA AL OFICIO NOTIFICADO POR FIJACIÓN EN LISTA NO. 137
DEL 08 DE ABRIL DE 2011, OFICIO NO. 06121 (ART 46 BÚSQUEDA DE
ANTERIORIDADES)

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad en referencia, doy respuesta al oficio emanado por ese Despacho dentro del término legal:

Presentación de los documentos requeridos de conformidad al artículo 46 de la Decisión 486.

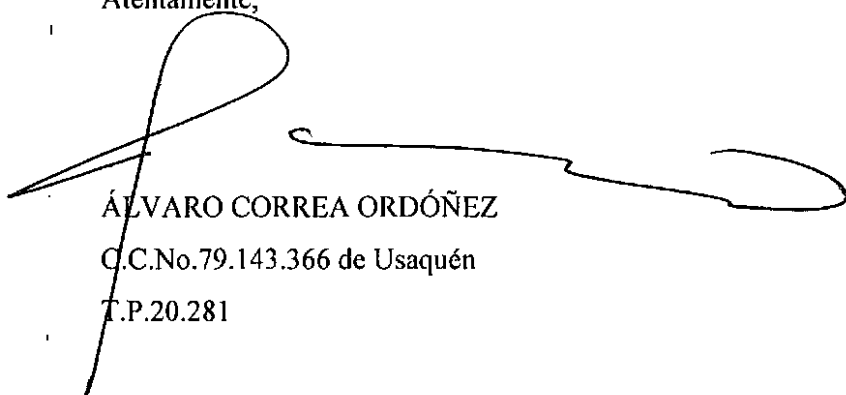
Presento copia completa del siguiente documento:

- 1) TOMIYA, K; YANASE, Y: "MTF-753: a novel fungicide" CONGRESS PROCEEDINGS-BCPC INTERNATIONAL CONGRESS: CROP SCIENCE &

TECNOLOGY, GLASGOW, UNITED KINGDOM, NOV. 10-12, 2003, vol 1,
2003, pages 99-104, XP009060687 Bracknell, UK.

En virtud de lo anterior, solicito se proceda con el análisis de patentabilidad para la
invención que se tramita en este expediente.

Atentamente,



ÁLVARO CORREA ORDÓÑEZ
C.C.No.79.143.366 de Usaquén
T.P.20.281

Anexos: Cópia de la publicación Yomiya, K; XP009060687.

MTF-753: a novel fungicide

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ABSTRACT

MTF-753, (RS)-N-[2-(1,3-dimethylbutyl)thiophen-3-yl]-1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide is a novel fungicide which belongs to carboxamide family. It is well known that early carboxamide fungicides have an activity against rust and *Rhizoctonia* diseases, but MTF-753 shows a remarkable activity against not only these diseases but also grey mold, powdery mildew and apple scab. Its mode of action is different from the other fungicides used to control these diseases. Here, we briefly describe how MTF-753 was discovered and also show its chemical and biological properties.

INTRODUCTION

It has been well known that carboxamide type fungicides such as carboxin have activity against rust and *Rhizoctonia* diseases, but BC-723, discovered by Mitsubishi Chemical Corporation and a type of benzamide derivatives, has an activity against grey mold (*Botrytis cinerea*). We had paid attention to the fact that *N*-phenyl benzamide compounds, which were a type of benzamide derivatives, had a weak, but broad-spectrum activity against pathogenic fungi. After long research, we found a novel carboxamide derivative which contained two heteroaromatic rings and had a high fungicidal activity, and found the fact that branched alkyl substitution on the heteroaromatic ring on the amino part of the carboxamide played an important role to expand its anti-fungal spectrum. After intensive research, we finally discovered MTF-753 that was classified as a carboxamide fungicide and it has a pyrazole unit and a thiophen ring.

Here we show the chemical and physical properties, the biological profile, and the toxicological and environmental behavior of MTF-753.

CHEMICAL AND PHYSICAL PROPERTIES

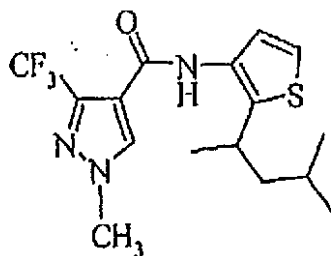
Code number:

MTF-753

Common name:

penthioapyrad (ISO proposed)

Structural formula:



AF 003000007

Chemical name: (RS)-N-[2-(1,3-dimethylbutyl)thiophen-3-yl]-1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide
 CAS RN: [183675-82-3]
 Empirical Formula: C₁₆H₂₀F₃N₃OS
 Molecular Weight: 359.42
 Appearance: white powder
 Vapor pressure: 6.43 x 10⁻⁶ Pa at 25°C
 Solubility in water: 7.53 mg/litre at 20°C

FORMULATIONS

MTF-753 is formulated as a 20% SC and a 15 % SC, both show good compatibility with conventional crop protection products

HUMAN SAFETY

Acute oral LD ₅₀	Rat (male/female)	>2,000 mg/kg
Acute dermal LD ₅₀	Rat (male/female)	>2,000 mg/kg
Acute inhalation LC ₅₀ (4 h)	Rat (male/female)	>5,669 mg/kg
Eye irritation	Rabbit	Slight-irritant
Skin irritation	Rabbit	Negative
Skin sensitisation	Rabbit	Negative
Mutagenicity	Ames test	Negative
	Chromosomal aberration	Negative

ENVIRONMENTAL SAFETY

Carp LC ₅₀ (96 h)	1.17 ppm
Daphnia LC ₅₀ (24 h)	40 ppm
Algae EC ₅₀ (growth rate 72 h)	2.72 ppm

BIOLOGICAL PROPERTIES

Laboratory evaluation

MTF-753 has fungicidal activity against various species of fungi. The activity of MTF-753 is shown in Table 1.

Table 1 Anti-fungal activity of MTF-753 on agar medium

Fungi	MIC (mg/litre)	Fungi	MIC (mg/litre)
<i>Alternaria mali</i>	15	<i>Monilinia mali</i>	3
<i>Alternaria solani</i>	3	<i>Monilinia fructicola</i>	5
<i>Botrytis cinerea</i>	4	<i>Mycosphaerella melonis</i>	2
<i>Botrytis squamosa</i>	9	<i>Mycovellosiella natrasii</i>	10
<i>Cercospora beticola</i>	>50	<i>Phomopsis</i> sp	84
<i>Colletotrichum acutatum</i>	8	<i>Pyricularia oryzae</i>	7
<i>Corticium rolfsii</i>	7	<i>Rhizoctonia solani</i>	50
<i>Diplocarpon rosae</i>	105	<i>Sclerotinia sclerotiorum</i>	8
<i>Elsinoe ampelina</i>	40	<i>Ustilago maydis</i>	<0.4
<i>Fulvia fulva</i>	8	<i>Venturia inaequalis</i>	14
<i>Glomerella cingulata</i>	13	<i>Microdochium nivale</i>	35

Efficacy against resistant fungi

Table 2. Activity of MTF-753 against various resistant strains of *Botrytis cinerea*

Compound	S HR HR ¹	HR S S	HR MR HR	RAP ²
Thiophanate-methyl	-	+++	+++	NT ³
Procymidone	+++	-	+++	NT
Diethofencarb	+++	-	+++	NT
Mepanipyrim	NT	NT	NT	+++
MTF-753	-	-	-	-

Growth on Potato dextrose agar media where - indicates no growth of pathogen; +++ indicates good growth

¹ This strain is susceptible to benzimidazoles, highly resistant to dicarboximides and diethofencarb. MR designates moderate resistant.

² Resistant strain to anilinopyrimidine compounds

³ NT = Not tested

Table 3. Activity of MTF-753 against resistant *Venturia inaequalis*

Compound	Susceptible strain	Resistant strain to DMIs	Resistant to strobilurins
Fenarimol	-	+	-
Azoxystrobin	-	-	+++
MTF-753	-	-	-

Growth on Potato dextrose agar media where - indicated no growth of pathogen, + indicates slight growth of pathogen and +++ indicates good growth of pathogen.

Inhibitory test against mitochondrial complex II

Mitochondria were isolated from mycelia of *Rhizoctonia solani*, *Botrytis cinerea*, and *Fusarium oxysporum*. Succinate dehydrogenase activity was assayed spectrophotometrically and the results are listed in Table 4 expressed as I_{50} (50% inhibition).

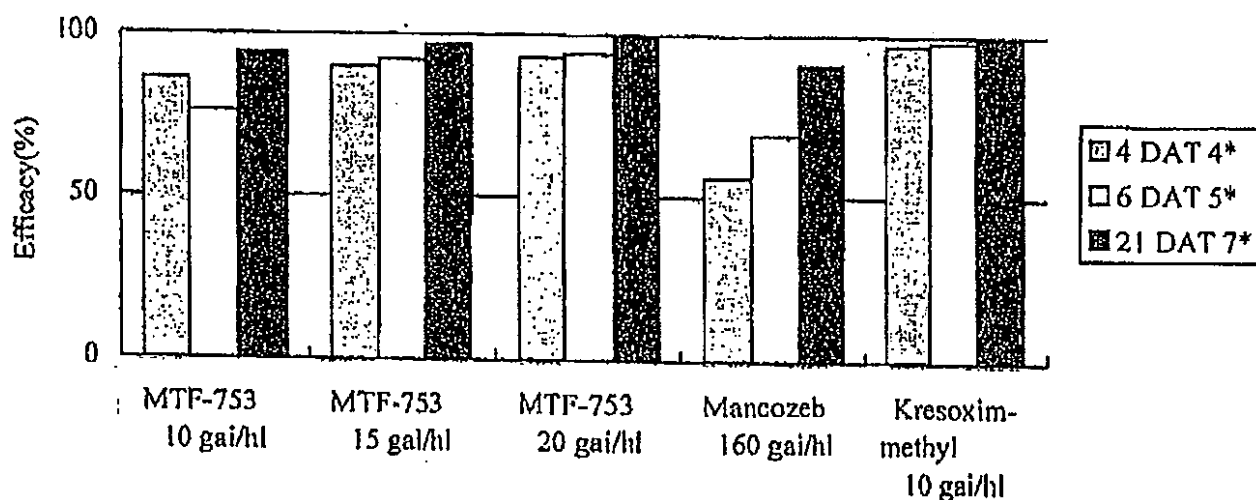
Table 4. Enzyme inhibition activity of MTF-753 as indicated by I_{50} (n.mol)

Compound	<i>Rhizoctonia solani</i>	<i>Botrytis cinerea</i>	<i>Fusarium oxysporum</i>
Flutranil	372	<8000	800-2000
MTF-753	50	14	4-8

Field evaluation

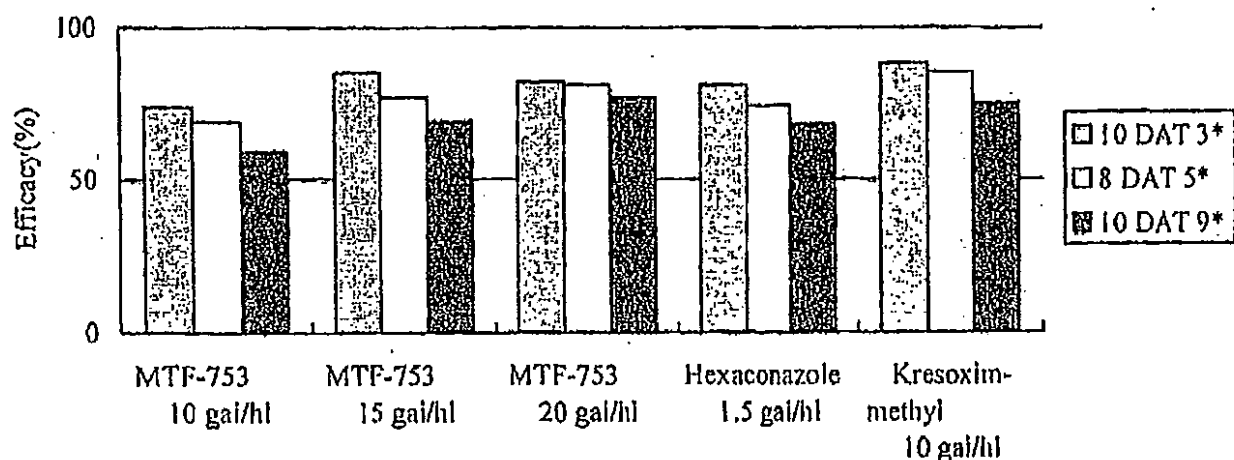
Many field trials were carried out in vegetable and fruit crops.

MTF-753 was proven to be highly active against apple scab (*Venturia inaequalis*, Figure 1) and powdery mildew (*Podosphaera leucotricha*, Figure 2) at 100-200 g ai/hl in comparison with other commercial standards. Also MTF-753 showed a good effect on grape grey mold at 100 ppm (Figure 3) and on powdery mildew in cucumber at 25 ppm (Figure 4).



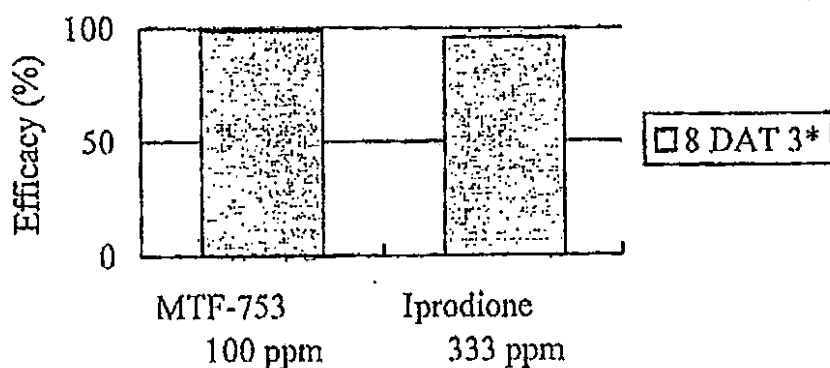
*4 DAT 4 = assessment date 4 days after the 4th treatment

Figure 1. Efficacy of MTF-753 15% SC against apple scab - foliar application (France, 2002)



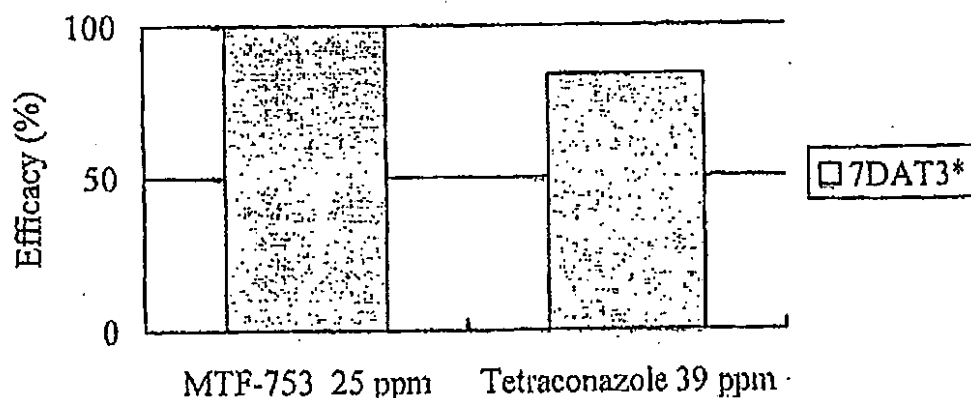
*10 DAT 3 = assessment date 10 days after the 3rd treatment

Figure 2. Foliar efficacy of MTF-753 against apple powdery mildew (France, 2002)



*8 DAT 3 = assessment date 8 days after the 3rd treatment

Figure 3. Efficacy of MTF-753 20% SC against grape grey mold - foliar application (Japan, 2002)



*7 DAT 3 = assessment date, 7 days after the 3rd treatment

Figure 4. Efficacy of MTF-753 20%SC against cucumber powdery mildew - foliar application (Japan, 2001)

CONCLUSION

From laboratory and field tests, MTF-753 showed good efficacy against a wide range of fungal pathogens. In field trials, MTF-753 gave an excellent activity against scab, grey mold and powdery mildew.

ACKNOWLEDGEMENTS

We thank Dr. Miyoshi of the Department of Applied Life Science, Kyoto Univ. for the study of the mode of action of MTF-753, and to Dr. Ishii of National Institute of Agro-Environmental Sciences for work on the resistant fungi.

REFERENCE

Miyoshi H; Yamashita A; Hatano T; Iwamura H (1996). Inhibitory test against mitochondrial complex II, *Journal of Biochemistry*, 120(2), 377-384.