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Activity of the Fungicide JS399-19 Against Fusarium Head Blight of Wheat and the Risk of Resistance

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Abstract

This report reviews the characteristics of JS399-19, a novel cyanoacrylate fungicide. JS399-19 strongly inhibits the mycelial growth of the fungal plant pathogens of the genus *Fusarium* and exhibits great potential in controlling Fusarium head blight (FHB) on wheat and other cereals. The mode of action of JS399-19 is evidently different from that of benzimidazole (for example, carbendazim) and other sort of fungicides, making it a possible replacement for carbendazim in China to manage carbendazim-resistant subpopulations of *Fusarium graminearum* and *F. asiaticum*. JS399-19 has excellent protective and curative activity against these pathogens. Incorrect use of this fungicide, however, is likely to select for resistance. Among JS399-19-resistant mutants of *F. asiaticum* induced in the laboratory, the resistant level of mutants was high and the phenotype of resistance against JS399-19 was conferred by a major gene by genetic analysis. The fitness of laboratory-induced JS399-19-resistant mutants of *F. asiaticum* was nearly equal to that of their parents. JS399-19 lacks cross resistance with other sort fungicides. To control FHB with JS399-19 and to delay the development of the fungicide-resistance, farmers should use tank mixtures containing JS399-19 and carbendazim, metconazole, tebuconazole, or prothioconazole.

Key words: fungicide JS399-19, cyanoacrylate fungicide, Fusarium head blight, activity, resistance risk

INTRODUCTION

The fungicide JS399-19 (development code number) is a novel cyanoacrylate fungicide that was developed and patented by the Jiangsu Branch of National Pesticide Research & Development South Center of China in 1998. The chemical name of JS399-19 is 2-cyano-3-amino-3-phenylancryic acetate (Fig. 1). Its molecular formula is $C_{12}H_{12}N_2O_2$ and its molecular weight is 216.23. It is soluble in chloroform, acetone, and dimethylsulfoxide but is unsoluble in ether or toluene. Pure JS399-19 powder is white or primrose yellow with a melting point of 117 to 119°C (Lang and Ni 2007).

According to previous studies, this new fungicide, which was recently introduced to the market, exhibits specific activity against fungal plant pathogens of the genus *Fusarium*. JS399-19 strongly interfered with mycelial growth and showed great potential in controlling Fusarium head blight (FHB) on wheat and other cereals (Li *et al*. 2008). FHB, which is mainly caused by *Fusarium graminearum* and *F. asiaticum* (formerly known as *F. graminearum*) in China, is one of the most economically important diseases worldwide (Bai and Shaner 1994; McMullen *et al*. 1997; Chen *et al*. 2008; Yin *et al*. 2009). In China, FHB generally occurs in the middle and lower reaches of the Yangtze River, in the Huaihe River valley, and in the Eastern coastal region

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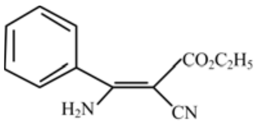

Fig. 1 Chemical structure of the fungicide JS399-19 (Chen *et al*. 2008).

(Chen *et al*. 2008), where it reduces grain quality because of the production of deoxynivalenol (DON), nivalenol (NIV), zearalenone (ZEN), and other mycotoxins harmful to humans and animals (Snijders 1990; Carter *et al*. 2002; Stoyan *et al*. 2003; Semaškienė *et al*. 2006). The fungicide carbendazim, which has been widely used to control FHB for more than 30 years, is no longer effective against this disease because carbendazim resistance is now common in *F. asiaticum* populations in China (Zhou *et al*. 1994a, b; Zhou and Wang 2001; Wang and Zhou 2002).

The new fungicide JS399-19 was registered in China for FHB control and was first marketed in China in 2007. The results of recent studies showed that control of FHB was better with the JS399-19 than with carbendazim in a field where carbendazim had been extensively used for decades but had increasingly failed to control the disease (Li *et al*. 2008). This paper reviews the characteristics of JS399-19, including its physical and chemical properties, anti-fungal spectrum, activity, systemic translocation in wheat plants, and its risk of resistance.

ANTI-FUNGAL SPECTRUM

The anti-fungal properties of JS399-19 were tested against 12 economically important plant pathogens (Li *et al*. 2008). This compound strongly inhibited the mycelial growth of *F. asiaticum*, *F. moniliforme* and *F. oxysporum* with EC_{50} values of 0.14, 0.46 and 3.57 μg mL^{-1}, respectively. However, it exhibited little or no activity against mycelial growth of nine other fungal pathogens (Table 1). These results indicate that the anti-fungal activity of JS399-19 is specific to pathogens of *Fusarium* species.

BIOACTIVITY AGAINST *F. asiaticum*

JS399-19 had the same inhibitory effect on mycelial growth of carbendazim-sensitive and carbendazim-resistant isolates (Table 2). The average EC_{50} values for JS399-19 were (0.11±0.01) μg mL^{-1} for carbendazim-sensitive (S) isolates and (0.12±0.02) μg mL^{-1} for carbendazim-resistant isolates (R), and these values were not significantly different (P<0.05) (Li and Zhou 2006). In contrast, the average EC_{50} for carbendazim against wild-type isolates was (0.61±0.03) μg mL^{-1}. This indicates that the activity of JS399-19 is about five times higher than that of carbendazim and that there is little probability for cross-resistance between JS399-19 and carbendazim.

Table 1 Toxicity of JS399-19 against twelve economically important agricultural fungal plant pathogens (Li *et al*. 2008)

Pathogens	Regression equation	EC_{50} (μg mL^{-1})	R[1)]
Fusarium asiaticum	Y=2.188X+6.860	0.14	0.987
F. moniliforme	Y=1.626X+5.550	0.46	0.935
F. oxysporum	Y=1.299X+4.282	3.57	0.975
Colletotrichum capsici	Y=2.175X+1.847	28.16	0.992
Dothiorella gregaria	Y=1.865X+2.018	39.69	0.997
Sclerotinia sclerotiorum	Y=2.864X-0.321	72.07	0.996
Botrytis cinerea	Y=2.166X+0.974	72.19	0.979
Pyricularia grisea	Y=2.288X+0.682	77.08	0.991
Phytophthora capsici	Y=2.390X+0.108	111.41	0.997
Alternaria solani	Y=3.107X-1.410	133.29	0.983
Xanthomonas oxyzae	Y=2.090X+1.633	40.78	0.965
Pseudoperonospora cubensis	Y=2.231X+2.506	12.74	0.925
Blumeiria graminis	-	>1 000.00	-

1) Correlation coefficient between concentration and inhibition.

The baseline sensitivity of *F. asiaticum* to JS399-19 (i.e., the sensitivity of isolates without the history of exposure to the fungicide) has been established. The EC_{50} values for JS399-19 (based on inhibition of mycelial growth) of three wild-type *F. asiaticum* populations from three regions where JS399-19 has been never used (Tongzhou, Jiangsu Province; Jiaxing, Zhejiang Province; and Shanghai, China) ranged from 0.06 to 0.13, 0.07 to 0.17, and 0.06 to 0.16 μg mL^{-1}, respectivel y; the mean EC_{50} values for the three regions were (0.10±0.05), (0.11±0.04), and (0.11±0.04) μg mL^{-1}, respectively (Chen *et al*. 2008). Each of the three baseline sensitivity curves was unimodal over a sensitive range.

Previous studies also indicated that JS399-19 inhibited not only conidial germination, but also germ tube growth, although more than 90% spores could germinate after 12 h on water agar (WA) media amended with JS399-19. Cells were swollen and malformed, and germ tubes were inhibited and contorted on WA amended with 50 and 100 μg mL^{-1} JS399-19 (Fig. 2) (Li and Zhou 2006; Chen *et al*. 2007b).