The role of azole fungicides in safeguarding food safety and security

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We need all the tools we can get to feed a growing world (including fungicides)

Double world food production by 2050

Becoming more and more difficult just to hold our own, much less double it.

Major challenges are loss of crop land to soil degradation and urbanization, climate change, water depletion, scarcity of key inputs, politics and wars, etc.

Why the huge increase in fungicide use?

- 1. Low cost (generics such as tebuconazole)
- 2. New diseases emerging or diseases spread to new areas (ex. Soybean rust)
- 3. Higher value commodities
- 4. "Plant health" uses to increase yield apart from controlling disease

US Precipitation Map

(Water = food production AND fungal diseases)



Fungicides are an ESSENTIAL input – Peanut as a case study

("Not just a bigger cow, but a live cow")

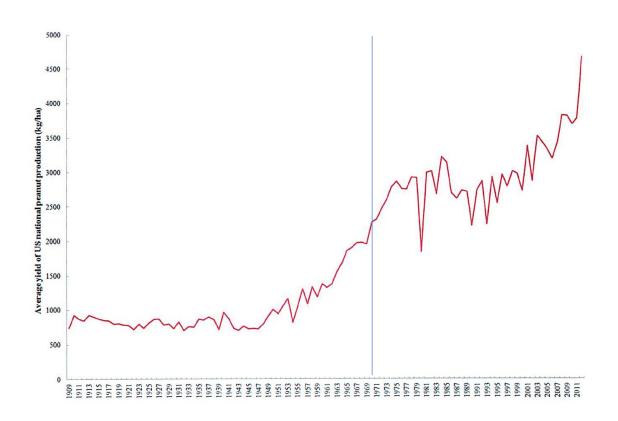




Sprayed with fungicides 5-8 times annually, even with IPM (Crop rotation, etc.)

Yield per hectare for US peanut for past 100 years

(Highest in the world)



Slide courtesy of Dr. Corley Holbrook

Huge advances in white mold fungicides in the last 35 years

Terraclor 10G – 112 kg/ha (25-30% control)

Tebuconazole – 0.2 kg/ha (75% control and excellent on leaf spot)





Sterol Biosynthesis Inhibitors (SBIs)

- Broad spectrum of activity even reduce some toxins such as deoxynivalenol (DON), cause of enormous losses in small grains
- Varying systemicity and post-infection activity
- Relatively cheap, especially older ones like tebuconazole that are now generic
- <u>Labeled on a wide range of crops (roughly 1/3 of global fungicide market)</u>

Sterol Biosynthesis Inhibitors (Four Subclasses)

- I. Demethylation inhibitors (DMIs)
- II. Amines or morpholines
- III. Hydroxyanilides
- IV. Squalene-epoxidase inhibitors (pharmacological use only)

DMIs in Agriculture

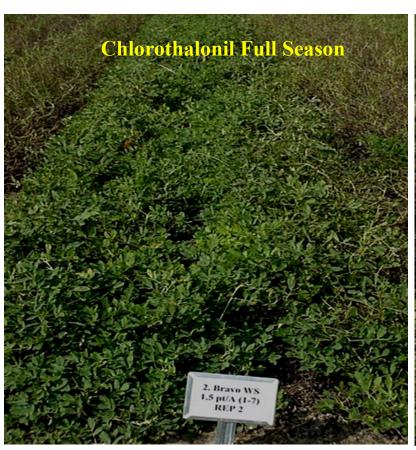
- 36 fungicides inhibit C14 demethylase
- Numerous cases of resistance, but seldom complete loss of efficacy due to quantitative or stepwise polygenic resistance, backshift due to fitness costs, etc.
- Multiple documented mechanisms of resistance, but newer generation DMI's are often more active

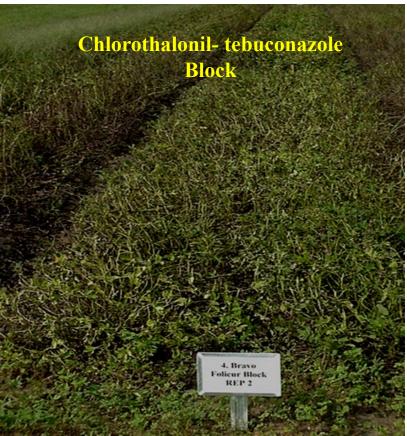
The Rise (and Fall) of Fungicides for Peanut Leaf Spots

Fungicide Class (FRAC #)	Active Ingredients	Single site?	Introduction and <u>Time</u> to Resistance?
Benzimidazoles (1)	Benomyl	Yes	1970s, several years
Multisite (Y)	Chlorothalonil	No	<u>1970s, NEVER</u>
DMIs (3)	Propiconazole, Tebuconazole, Fenbuconazole, etc.	Yes	<u>1980's, about 10</u> <u>years</u>
Qols (11)	Azoxystrobin, Kresoxim methyl, etc.	Yes	1990's, about 10 years
SDHIs (7)	Fluxapyroxad, Pydiflumetofen, etc.	Yes	2000's, ???

Tebuconazole (Folicur)

(In 1994 it was amazing. By 2005 it was gone!)





Heat and drought are increasing issues with *Aspergillus* spp.

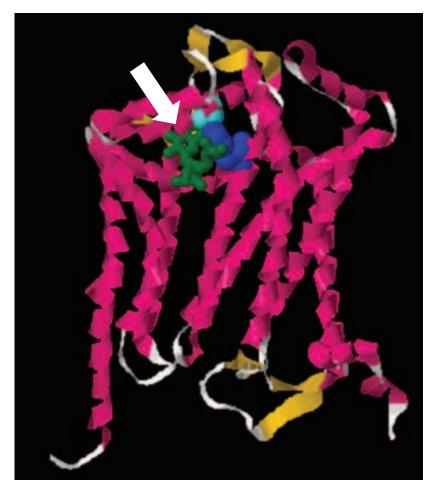


Both *A. flavus and A. niger* both now have resistance to Qol fungicides

In 2020 the peanut industry changed to seed trt fungicides w/ SDHI's and azoles

Quinone outside inhibitors

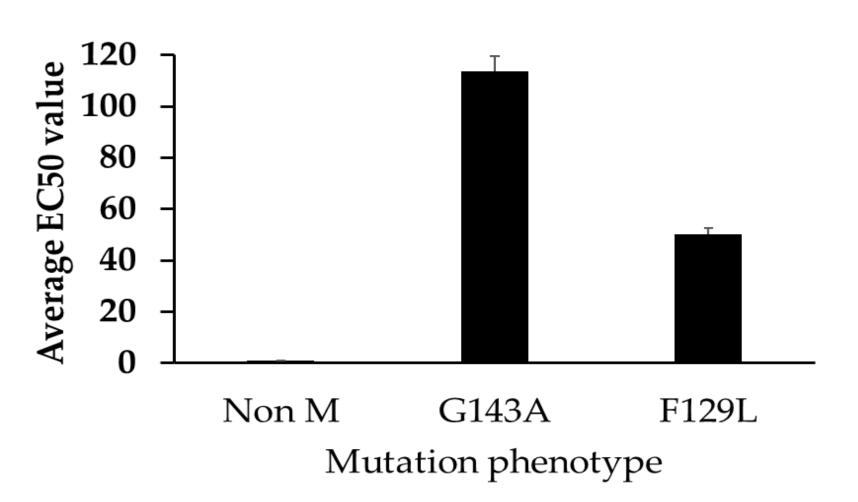
- Inhibit respiration within cytochrome b
- Single site mode of action, ie. High Risk
- Multiple point mutations confer different levels of resistance from partial to immunity



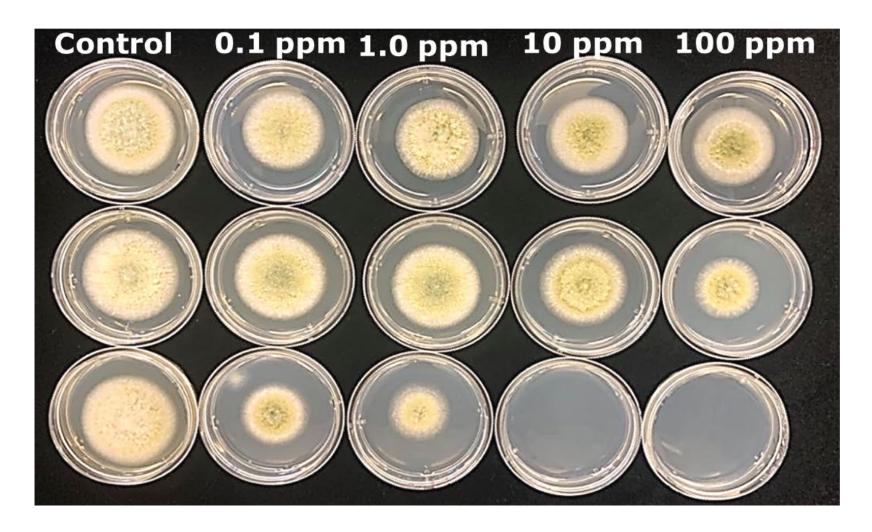
(Fernández-Ortuño et al. 2010)

Two mutations in mitochondrial CYTB gene confer Qol resistance

(Ali et al., 2021)



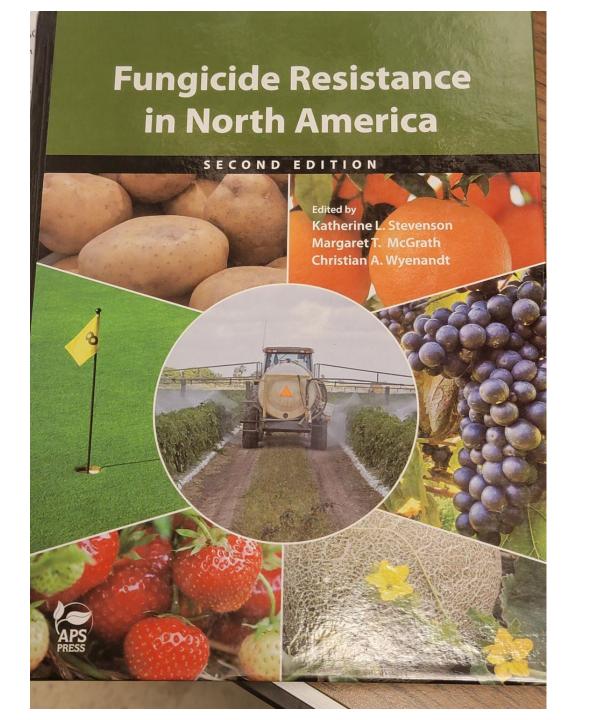
A. flavus sensitivity to azoxystrobin



❖ Photo by Dr. Emran Ali, Molecular Diagnostic Lab, UGA, Tifton.

Summary

- DMI's are wounded but not dead still making very valuable contributions
- Resistance is a HUGE threat. Every class of fungicide lost to resistance makes it harder to preserve those remaining
- The loss of older multisite products will dramatically accelerate this process!
- Any new approaches to plant disease
 management will reduce selection pressure on
 fungicides and prolong life of existing products



Thank you for your attention!



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