Sterol Inhibitors: What do they do?

By Michael Semler

Within the last decade, Golf Course Superintendents have been introduced, on a widespread basis, to a relatively new class of fungicides — the sterol-inhibitors. They are a welcome addition to our arsenal for battling turfgrass diseases and will give us another alternative to rotate into our disease control programs. I hope to shed some light on the subject matter involved, including information on what sterols are, their role in eukaryotic organisms and how the sterol-inhibitor fungicides help prevent disease.

The sterol-inhibitors are a unique class of fungicides with several characteristics which differentiate them from other systemics. They are the largest group of compounds with the same mode of action and they are a diverse group of compounds with respect to their chemical structures. Although they are quite different structurally, their antifungal spectra are similar.

Sterols are required for growth and reproduction by eukaryotic organisms. Although a complete understanding of the functions of sterols in the cells has not been achieved, their importance in membrane structure and function, and their role in sexual reproduction has been partially exposed.

Sterol biosynthesis is one aspect of general lipid metabolism in which acetate, the basic starting chemical unit, is transformed thru a series of reactions into squalene. The cyclization of squalene to the first sterol intermediate, lanosterol, is the first step in a series of complex reactions leading to the synthesis of ergosterol, the major sterol in the cell membranes of the higher fungi.

The biosynthesis of sterols occurs in the smooth portion of the endoplasmic reticulum. The endoplasmic reticulum functions as a communication system in the cell and also as a means for channeling materials — such as proteins and lipids — to different parts of the cell.

Figure #1 gives an illustration of the general pathway of ergosterol biosynthesis in fungi. Many of these steps have not been completely elucidated and the precise steps may vary with different species of fungi.

Various assays and analyses on the toxic actions of the sterol inhibitors on fungi have revealed certain characteristics. The general characteristics of the fungi are: "they fail to inhibit spore germination or initial cell growth and dry weight increase; they alter cell morphology, causing abnormal growth patterns, swollen hypahe, and/or excessive hyphal branching; and the accumulation of free fatty acids and sterol intermediates in the cell. They have no immediate effects on respiratory metabolism or macromolecule syntheses."[1]

These characteristics are produced by an interference in the sterol biosynthetic pathway caused by an accumulation of the sterol inhibiting fungicide. The results are the inhibition of ergosterol synthesis and the accumulation of some sterol intermediates. The primary action site of these fungicides in sterol synthesis is the c-14 demethylation. (Figure 1, reactions 1 and 2).

With the inhibition of ergosterol by C-14 demethylation, marked accumulations of some sterol intermediates is noted, namely, lanosterol, obtusifolial and 14 α methyl 8,24(28)—ergostadienol. This accumulation indicates that only specific aspects of sterol synthesis are inhibited. It also suggests the failure of some control mechanism governing sterol biosynthesis, and that in normal cells some end product gives feedback to stop the synthesis. When the mechanism is absent, synthesis continues on a limited basis and an excessive amount of intermediates collect.

Even though ergosterol biosynthesis is quite sensitive to inhibition by these toxicants, mycelial growth and various aspects of metabolism are only slightly affected for a short time after the synthesis of ergosterol is prevented. The levels of ergosterol do not decline rapidly after synthesis stops. However, once the ergosterol level is depleted, an interference in membrane synthesis occurs, growth inhibition, and changes in metabolism and morphology are noted.

In the synthesis from squalene to ergosterol, sterol carrier proteins bind the water insoluble intermediates, enabling enzymatic conversion and then the transfer of the sterol of intercellular sites. "It has been suggested that the inhibitions of sterol biosynthesis bind to the carrier proteins and prevent enzyme interactions with the sterol carrier protein — sterol complex."[1]

The ultimate toxicity undoubtedly results from the lack of proper sterols for membrane synthesis. Although the sterol-inhibitor fungicide structures vary considerably, their seemingly similar modes of action probably result from their movement in the cell by the endoplasmic reticulum, where they inhibit sterol synthesis and possibly other synthesis as well.

Many of us realize the growth retarding effects the sterol-inhibitors exhibit on turfgrass. The slight greening and plant growth retarding is due to the effect the fungicides have on the plant growth regulator — gibberellin. This is due to the similarities that exist between the initial stages of gibberellin synthesis and of sterol synthesis, both of which involve portions of the isoprenoid pathway. Also, many of the cyclizations and oxidations that occur in the latter stages of sterol synthesis are similar to those in gibberellin synthesis.

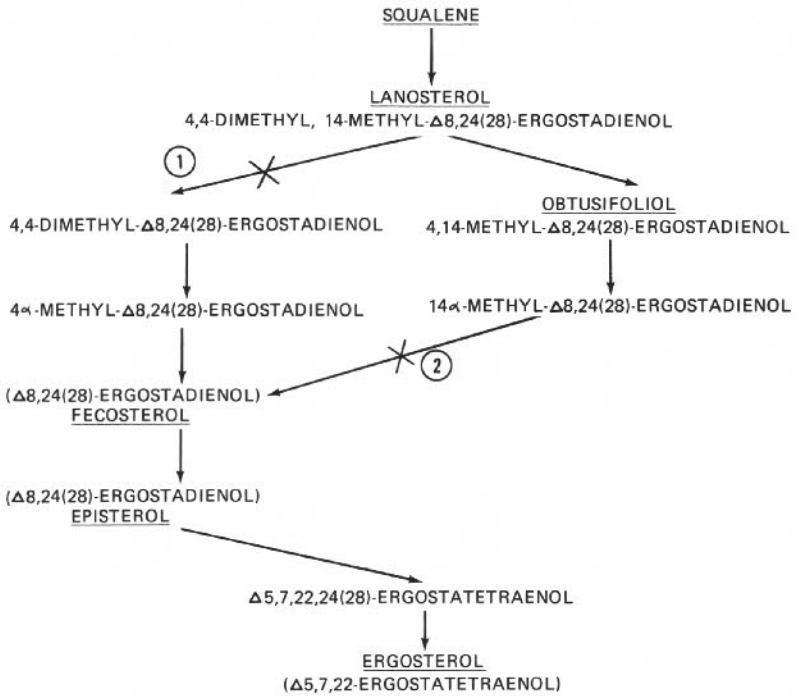
It appears the inhibition of gibberellin or sterol synthesis could involve one another through membrane function. Sterols are an important part of membrane structure and gibberellins effect the membrane properties. However, the relationship between these two is not entirely understood.

Much of the research on the roles of ergosterol in the higher fungi is still going on because their func-

1. Malcolm R. Siegel, 1981. Sterol Inhibiting Fungicides: Effects on Sterol Biosynthesis and Sites of Action. Plant Disease. 65:986-989.

Sterol Inhibitors — continued

tion is only partially understood at this time. This article has only covered the generalities involved for a few reasons; one is that the organic chemistry involved is quite technical and may cause more confusion than necessary, the second is that I did not intend this to be a be-all or end-all on the subject matter. If you are like me, there was always some confusion as to how the sterol inhibitors really worked. I hope I have given some enlightment on the subject without causing confusion.



LETTERS

In the last issue of the Badger Broadcast, our lead article was entitled **"Who's in Charge Here?" A Case for the General Manager Concept**. This concept is not only supported and promoted by CMAA but also by NCA.

Since this article came out, the Wisconsin Golf Course Superintendents (or Managers) Association had an editorial in their "Grass Roots" publication responding to our article. After reading it, I felt like the bully on the block picking on all the small guys that couldn't defend themselves.

First of all, I feel that the General Manager concept is a good one and I for one support it whole-heartedly, but I also realize that the G.M. concept does not apply to all clubs; all clubs are not the same, for a large city club, athletic club, yacht club and your larger country clubs you have, in most instances, a General Manager.

Our colleagues, the Golf Course Superintendent (Manager) have this dreadful idea that if a club initiates the G.M. concept that the golf course budget would be slashed in favor of more kitchen equipment or dining room chairs, etc. Can you imagine what the golfing members would do to that G.M. if that was the case; which we all know it isn't. A G.M. is not going to tell the Superintendent how to cut the fairways or greens or how to design a sandtrap, we didn't go to college for that and the Superintendent didn't go to college to write up a 12-course gourmet dinner. We all have our own expertise.

So what's the big problem? Everyone is hired to do a job, to work with the committees and the Board and let the members enjoy the golf and dining. So whether it's a Club Manager, or General Manager or Golf Course Superintendent or Golf Course Manager, the most important thing is working together as a team and not as rivals.

To me, friendship is more important than titles, so let's get on with it and let the members enjoy the fruits of our labor.

Bernd U. Sturm, CCM
President, Wisconsin Badger
Chapter, Club Managers
Association of America

Editor's Note: Even the best of friends sometimes have disagreements, Bernie. You missed several of my points about the ***Perspectives*** *article:*

1) The NCA didn't qualify their remarks about general managers by indicating they'd best have a place, using your words, "in a large city club, athletic club, yacht club and your larger country clubs." They put ***all*** *clubs under their notion. My remarks were directed toward the vast number of* ***average*** *golf clubs where most of us work. The NCA and CMAA are promoting this idea here, as well as for the clubs you mention.*

2) The GM is a "false title" in many of the instances where it is used, usually by the man who is only the clubhouse manager. I can give you, right off the top of my head, a number of clubs where the clubhouse manager uses the title GM and yet has absolutely nothing to do with the golf course or the golf shop operation. This is worse than self-promotion, deception or insecurity — it is childish and silly.

3) You haven't told me what's so wrong with the triumvirate system or where the GM concept will save money or improve services, a key point in my position.

You don't need to worry about feeling like a bully. We are fully capable of defending ourselves and our positions. Should this foolish idea become the "new wave," you'll find many golf course managers moving in and filling these jobs. We are, however, most interested in promoting ideas that are good for golf and good for golf clubs, and I repeat: "The GM concept is high fantasy. It's an idea whose time hasn't come and probably won't. It's a bad idea that won't be instituted, no matter how often it is brought to the table. It doesn't need to be revised, or refined or resurrected; it needs to be buried." MSM