

杀菌剂毒理学

杀菌剂毒理学分论

酞酰亚胺类（三氯甲硫基类）杀菌剂作用机制

- 三氯甲硫基类杀菌剂主要有两个品种：克菌丹(captan)、灭菌丹(folpet)
- 影响丙酮酸的脱羧作用，使之不能进入三羧循环。
- 抑制 α -酮戊二酸脱氢酶系的活性，阻断三羧酸循环。

铜、汞制剂

- 破坏菌体细胞膜，膜的通透性发生变化，使一些金属离子，主要是 K^+ 向细胞膜外渗透，而菌体内糖酵解过程中最重要的磷酸果糖激酶的活性是由 K^+ 来活化的。

硫磺 (Sulphur) 作用

- 硫对已糖激酶也有抑制作用。

硫代氨基甲酸酯类杀菌剂的作用机制

- 硫代氨基甲酸酯类包括乙撑双二硫代氨基甲酸盐，即“代森”类，二甲基二硫代氨基甲酸类“福美”类
- (1) 破坏C₀ASH，从而影响脂肪酸的氧化。

如代森锌:又如福美双，亦又类似反应：

辅酶A被瓦解后直接影响了脂肪酸的 β -氧化，丙酮酸脱氢酶系、 α -酮戊二酸脱氢酶系的活性受到抑制，因为这些酶系中必须要有辅酶A的参与。

(2) 抑制以铜、铁等为辅基的酶的活性。

硫代氨基甲酸酯类杀菌剂可和铁、铜等形成螯合物可使酶失去活性。

如在三羧酸循环中，柠檬酸经顺乌头酸到异柠檬酸必须要有乌头酸酶的参与，而乌头酸酶的辅基含有高铁，代森类、福美类杀菌剂和铁形成螯合物使乌头酸酶失活，三羧酸循环中断。

取代苯类杀菌剂的作用机制

- 取代苯类杀菌剂以百菌清(chlorothalonil)为代表, 还有diclroan和dichlone, 其主要作用机制在于和含—SH的酶反应, 抑制了含—SH基团酶的活性, 特别是磷酸甘油醛脱氢酶的活性。
- Vincent和Sisler认为百菌清也和含—SH的谷胱甘肽反应, 破坏了谷胱甘肽。众所周知, 谷胱甘肽在菌体内对外源物的解毒反应中有主要作用。Barak和Edgington在抗性机理研究中发现, 抗百菌清菌株中的谷胱甘肽含量远远高于敏感菌标, 这也是百菌清作用于谷胱甘肽的一个证据。

羧酰苯胺类杀菌剂作用机制

- 羧酰苯胺类，以氧硫杂环二烯为主，还有噻吩、噻唑、呋喃、吡唑、苯基等衍生物，代表品种有羧锈灵(carboxin)、氧化羧锈灵(oxycarboxin)、邻酰胺(mebenil)、氟酰胺(flutolanil)、furametper、triflumazid等。这些杀菌剂的主要作用部位是线粒体呼吸电子传递链中从琥珀酸到辅酶Q之间的氧化还原体系，即复合体Ⅱ。复合体Ⅱ是由黄酶Ⅱ(FAD)为辅酶的黄素蛋白、非血红素铁硫蛋白及其他结合蛋白组成的。
- 羧锈灵和复合体Ⅱ的活性中心——非血红素铁硫蛋白结合，从而阻断了电子向辅酶Q的传递(图5—17)。氟酰胺等杀菌剂也作用于复合体Ⅱ，但这些杀菌剂的结合部位既不是黄素蛋白，也不是非血红素铁硫蛋白这两个主要的亚单位，而是结合于一种固膜蛋白，嵌入铁硫蛋白和辅酶Q之间，阻止电子传递。

甲氧丙烯酸酯类杀菌剂的作用机制

- Strobilurin A . B是Anke和Oberwinkler(1977)从担子菌中分离的天然抗菌活性物质。近年来以Strobilurin A为先导化合物，开发出一类新型杀菌剂——甲氧丙烯酸酯类，代表品种有ICIA5504和BAS490F。甲氧丙烯酸酯类杀菌剂同样抑制了病原菌线粒体呼吸电子传递链中电子的传递，其作用部位是复合体Ⅲ(即细胞色素b和细胞色素C1复合体)。据研究，甲氧丙烯酸酯类杀菌剂就通过和复合体Ⅲ中的活性部位结合而抑制了线粒体的电子传递。
此外，抗菌素抗霉素A(antimycin A)和杀菌剂杀枯净(phenazine, 5-氧吩嗪)也是作用于复合体Ⅲ。

重氮磺酸盐类杀菌剂

- 敌克松(dexon)为重氮磺酸盐类杀菌剂，主要用于防治烟草黑胫病、小麦腥黑穗病、白菜软腐病及水稻烂秧。敌克松作用于复合体工，阻断了辅酶 I (NAD) 和黄酶 I (FMN) 之间的电子传递：
FMN(磷酸核黄素)中具有异咯嗪环结构，敌克松可能和这种异咯嗪环组成了一个稳定的复合物，从而使FMN失去传递电子的功能

- 氟啶胺 (fluazinam) 近年来投入欧洲市场，主要用于防治马铃薯晚疫病。据研究，氟啶胺是一种强有力的解偶联剂，破坏氧化磷酸化，推测是分子中的氨基基团的质子化和质子化作用引起的。此外，五氯硝基苯 (terrachlor) 也是解偶联剂。

有机磷杀菌剂的作用机制

- 有机磷杀菌剂以异稻瘟净(IBP)和克瘟散(edifenphos)为代表，主要用于防治水稻稻瘟病。关于有机磷杀菌剂的作用机制，20世纪70年代认为是干扰了病原菌细胞壁几丁质的合成，20世纪80年以后人们倾向于认为这类杀菌剂主要是抑制了卵磷脂的合成而破坏了细胞质膜的结构。卵磷脂(磷脂酰胆碱)是细胞质膜最重要的组分，其生物合成途径如图所示。
- 卵磷脂的合成必需要有磷脂酰乙醇胺甲基转移酶的参与。异稻瘟净的作用机制主要是抑制磷脂酰乙醇胺甲基转移酶的活性，阻断了卵磷脂合成。

嘧啶胺类杀菌剂作用机制

- 嘧菌胺等杀菌剂的作用机制主要有两种解释：
 - 一是抑制细胞壁降解酶的分泌。
 - 二是干扰甲硫氨酸(蛋氨酸)的生物合成。

苯基酰胺类杀菌剂的作用机制

- 苯基酰胺类杀菌剂至少包括4类：酰基丙氨酸类、丁内酯类、硫代丁内酯类和恶唑烷酮类，其中以酰基丙氨酸类（以甲霜灵为代表）、恶唑烷酮类（以恶霜灵为代表）最重要。这类杀菌剂广泛用于藻菌纲病害（如霜霉病）的防治。关于苯基酰胺类的作用机理，一般认为是抑制了病原菌中核酸的生物合成，主要是RNA的合成。

苯并咪唑类杀菌剂作用机制

- 苯并咪唑类杀菌剂，苯来特、多菌灵和甲基硫菌灵等杀菌剂主要影响菌体内微管的形成而影响了细胞分裂

Part I: Protective Fungicides

- 1. Lime-sulfur (石硫合剂)



Lime-sulfur: A fungicide used to control a variety of diseases

- Lime-sulfur was originally developed in 1851 by Grison who was the head gardener at the vegetable houses in Versailles, France. In 1886, lime-sulfur was used to control peach leaf curl in California.

Lime-sulfur: A fungicide used to control a variety of diseases

- Sulfur is the only ingredient in the mix that is toxic to pathogens. Once taken up by the fungus, sulfur disrupts the transfer of electrons causing the reduction of sulfur to hydrogen sulfide (H_2S), which is toxic to most cellular proteins.

Lime-sulfur: A fungicide used to control a variety of diseases

- Sulfur itself is also toxic to certain plant species and is capable of causing a phytotoxic reaction. As a result, lime has been added to the mix to reduce the phytotoxicity of sulfur. The more lime added to the mix the less phytotoxic. In general, lime is considered a "safener" for the plant.

Bordeaux Mixture(波尔多液)

- Bordeaux mixture is an outstanding fungicide and bactericide that has been used to control some diseases. The ability of Bordeaux mixture to weather the fall, winter, and spring rains and to adhere to plants makes it an excellent choice for a winter fungicide. The application of Bordeaux during hot weather may cause yellowing and leaf drop.

Bordeaux Mixture(波尔多液)

- Bordeaux mixture fungicide consisting of cupric sulfate and lime in water. Its fungicidal activity is associated with the slow formation of copper compounds, the ultimate toxicant being the cupric ion.
- Bordeaux mixture achieves its effect by means of the copper ions (Cu^{2+}) of the mixture. These ions affect enzymes in the fungal spores in such a way as to prevent germination. This means that Bordeaux mixture must be used proactively, before the fungal disease has struck.

Bordeaux Mixture(波尔多液)

- It originated in France in 1885 and was widely used for spraying orchards, crops, and treating seeds until 1930.

Bordeaux Mixture(波尔多液)

- It originated in France in 1885 and was widely used for spraying orchards, dusting crops, and treating seeds until 1930. Since it was found that Bordeaux mixture frequently caused russetting of fruit, injured the leaves, and led to premature defoliation, it has been generally replaced by solutions made with powdered fixed copper.

Thiram (福美双)

- Thiram was one of the first fungicides used in agriculture.
- It has been used to control a variety of fungal disease of plants.
- Trade and Other Names: Common names include thiram (U.S.), thiuram (Japan).

Thiram (福美双)

- Thiram is a dimethyl dithiocarbamate compound used as a fungicide to prevent crop damage in the field and to protect harvested crops from deterioration in storage or transport. Thiram is also used as a seed protectant and to protect fruit, vegetable, ornamental, and turf crops from a variety of fungal diseases.

Thiram (福美双)

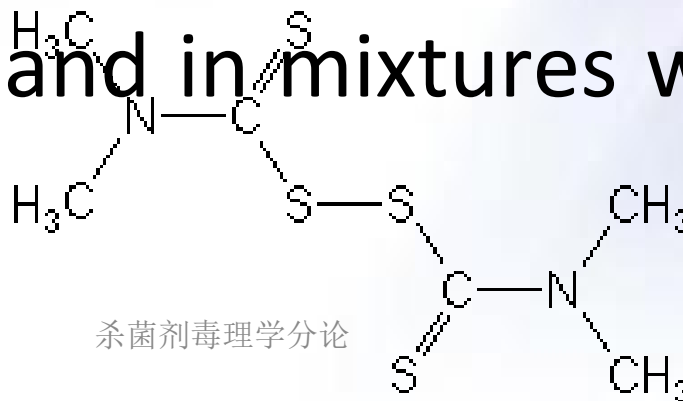
- Thiram has been used in the treatment of human scabies, as a sunscreen, and as a bactericide applied directly to the skin or incorporated into soap.

Thiram (福美双)

- Regulatory Status: Thiram is registered as a General Use Pesticide (GUP) by the U.S. Environmental Protection Agency (EPA). It is classified as toxicity class III - slightly toxic . Pesticide products containing thiram bear the Signal Word CAUTION on the product label.

Thiram (福美双)

- Chemical Class: dimethyl dithiocarbamate (二甲基二硫代氨基甲酸酯)
- Formulation: Thiram is available as dust, wettable powder, water dispersible granules, and water suspension formulations, and in mixtures with other fungicides.

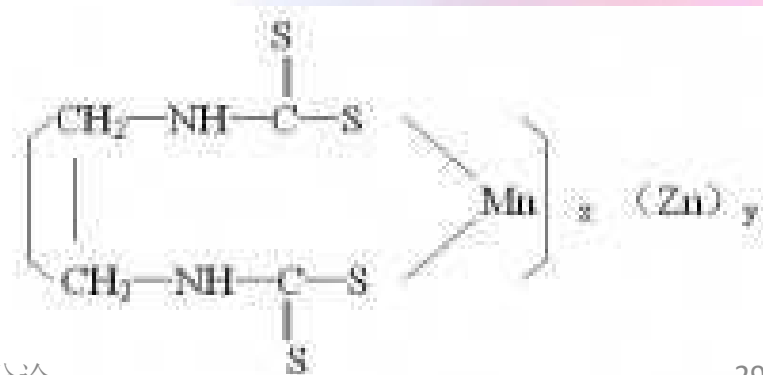


Thiram (福美双)

- Mode of action:
- Thiram is inhibitory agent . Their biochemical mode of action are thought to involve inhibition of some specific site in respiration.
- Thiram---respiration---tricarboxylic acid cycle

Manozeb (代森锰锌)

- Chemical Class: ethylene(bis) dithiocarbamate (乙撑二硫代氨基甲酸盐)
- Mancozeb is a polymeric complex of manganese and zinc ethylenebis-(dithiocarbamate)



Manozeb (代森锰锌)

- Trade and Other Names: Trade names include Dithane, Mancozeb, Manzeb.
- Regulatory Status: Mancozeb is a practically nontoxic in EPA toxicity class IV - practically nontoxic. It is registered as a General Use Pesticide (GUP). Labels for products containing mancozeb must bear the Signal Word CAUTION.

Manozeb (代森锰锌)

- Mancozeb is used to protect many fruit, vegetable, nut and field crops against a wide spectrum of fungal diseases, including potato blight (马铃薯晚疫病), leaf spot, scab (on apples and pears), and rust (on roses). It is also used for seed treatment of cotton, potatoes, corn, sorghum, peanuts, tomatoes, flax, and cereal grains.

Manozeb (代森锰锌)

- It is used as a protective fungicide (to prevent fungal growth) and in foliar and seed treatments to control a wide range of pathogens in field crops, fruits, ornamentals and vegetables.
- 作用机理:抑制丙酮酸的氧化.

Chlorothalonil (百菌清)

- Chlorothalonil is a broad-spectrum organochlorine fungicide used to control fungi that threaten vegetables, trees, small fruits, turf, ornamentals, and other agricultural crops.
- Chlorothalonil is a non-systemic foliar fungicide.

Chlorothalonil (百菌清)

- **Regulatory Status:** Chlorothalonil is classified as a General Use Pesticide (GUP) by the U.S. -EPA. It is classified as toxicity class II - moderately toxic, due to its potential for eye irritation. Chlorothalonil containing products have a range of Signal Words, including **WARNING, CAUTION, and DANGER.**

Chlorothalonil (百菌清)

- Toxicological Characteristics
- Technical chlorothalonil is a severe eye irritant, moderately toxic via inhalation, and of low toxicity via oral and dermal exposures.

Chlorothalonil (百菌清)

- Mechanism of pesticidal action:
- The mode of action of chlorothalonil involves its reaction with thiol groups of the pathogenic fungi's enzyme systems.

Chlorothalonil (百菌清)

- Mechanism of pesticidal action:
- In control of mildew in paints, it conjugates and depletes thiols from germinating fungal cell, leading to disruption of glycolysis and energy production, fungistasis, and fungicidal action.

Chlorothalonil (百菌清)

- Chlorothalonil has a multiple site mode of action, making the development of resistance much less likely. No resistance has been confirmed to date, making chlorothalonil an excellent component of a resistance management strategy.

Chlorothalonil (百菌清)

- Chronic toxicology and oncogenicity
- A two-year dietary study caused forestomach tumors in female mice, attributed to local gastric mucosal (粘膜) irritation.
- No evidence of carcinogenicity was found.

Vinclozolin (农利灵, 乙烯菌核利)

- Vinclozolin is a protectant non-systemic fungicide that is used both pre and post-harvest on fruits, vegetables and ornamental plants for the control of several species of fungi.
- It was first introduced by BASF in Germany in 1976 and is sold under a number of trade names including Ronilan and Flotilla.

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