# Dithiocarbamates

*Fungicides*

## Background Information

Dithiocarbamates (DTCs) are a class of fungicides that have been in widespread agriculture use, including tobacco, for many years to control both seedbed and field disease, including blue mould. The basic structure of DTC is shown in Figure 1. They are analogous to the carbamates except oxygen is replaced with sulphur.

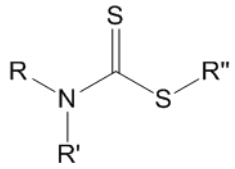



**Figure 1.** Basic DTC structure

DTCs can be broadly divided into two subgroups: ***N,N-dimethyldithiocarbamates*** (DMDCs) and ***ethylenebis-(dithiocarbamates)*** (EBDCs). Examples of DMDCs include Ferbam, Thiram and Ziram. The EBDCs generally possess the same DTC structure (Figure 2) and exist as complexes with different metal ions, e.g. manganese (Maneb), zinc (Zineb), manganese & zinc (Mancozeb), and sodium (Nabam). EBDCs can decompose through heating, photolytically or metabolically to form the degradation product ethylene thiourea (ETU). DMDCs do not form ETU.

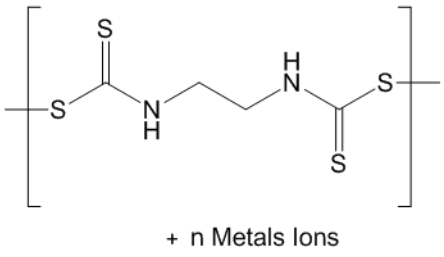



**Figure 2.** General EBDC structure

DTCs present a low toxicity, but the metabolites and degradation products of EBDCs, ethylene thiourea, affect the thyroid, and furthermore, neurotoxic effects have also been observed. Because of their chelating properties, DTCs inhibit enzymes containing Cu, Fe, Zn, or thiol groups [1]. Ferbam, Maneb, Thiram, Zineb and Ziram have all been considered by the International Agency for Research on Cancer (IARC) and have been classified as Group 3 agents – "not classifiable as to their carcinogenicity to humans" [2].

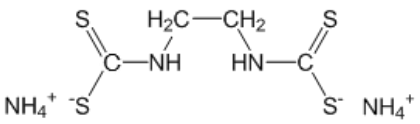
In countries where fungal diseases such as blue mould are a persistent problem in the field throughout the growing season, the use of DTCs fungicides can be an essential part of the season-long disease management strategy and in keeping with good agricultural practice (GAP) as a means of ensuring crop quality and economic viability for the producer. Under high disease pressure residues of DTCs slightly above the specified guidance residue level (GRL) can be observed. In countries where there is not a field fungal disease problem the use of fungicides is not necessary, and there should be no residues detected. Consistent with GAP, DTCs must be used only according to label instructions to combat fungal diseases in the seedbed and in the field [3].

DTCs are one of the few agrochemical residues that are generally not analyzed as their individual residues. Under certain analytical conditions, all DTCs release carbon disulfide ($CS_2$). The current residue definition of DTCs for compliance with maximum residue levels, at national levels, is total residues arising from the use of any or each DTC that is typically analyzed. The current CORESTA GRL for DTCs, expressed as $CS_2$, is 5 ppm [3].

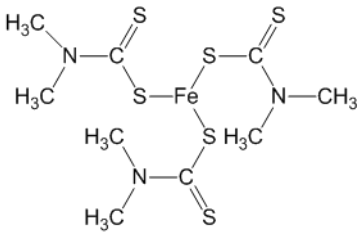
DTCs are registered for use on tobacco in various countries with Mancozeb being the most widely used:

**Table 1.** Main countries where DTCs are registered for use on tobacco

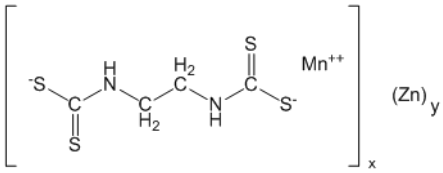
| Country | Amobam | Ferbam | Mancozeb | Maneb | Metiram | Nabam | Polycarbamate | Propineb | Thiram | Zineb | Ziram |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Argentina | | • | • | | • | | | | | • | |
| Brazil | | | • | | | | | • | | | • |
| Bulgaria | | | • | | • | | | | | • | |
| Canada | | • | • | | | | | | | | |
| Chile | | • | • | | | | | | | | |
| China | | | • | | • | | | • | • | • | |
| Colombia | | | • | | | | | • | | | |
| Cuba | | | • | • | | | | • | | • | |
| France | | | • | • | | | | | | | |
| Germany | | | • | • | | | | | | | |
| Greece | | | • | • | | | | • | • | | |
| India | | | • | | | | | | | • | |
| Indonesia | | | • | | | | | • | • | • | |
| Italy | | | • | • | • | | | • | • | | |
| Jamaica | | | • | | | | | | | | |
| Japan | • | | | | | | • | | • | | |
| Kenya | | | • | | | | | | • | | |
| Malaysia | | | • | • | | | | • | | | |
| Mexico | | | • | | | | | | | • | |
| Morocco | | | | • | | | | • | | | |
| Paraguay | | | • | | | | | | | | |
| Philippines | | | • | • | | | | | | | |
| Poland | | | • | | | | | | | | |
| Serbia | | | • | | | | | | | | |
| South Africa | | | • | | | | | | | • | |
| Spain | | | • | • | | | | | | | |
| Switzerland | | | • | • | | | | | | • | |
| Tunisia | | | • | • | | | | | | | |
| Turkey | | | • | • | • | | | | • | | |
| USA | | • | | | | | | | | | |
| Vietnam | | | • | | | | | • | | • | |
| Zimbabwe | | | • | | | | | | | | |



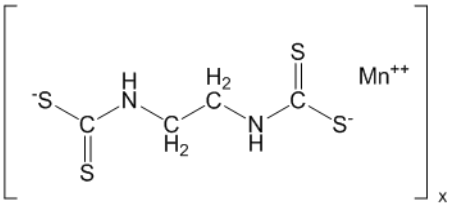
**Amobam**



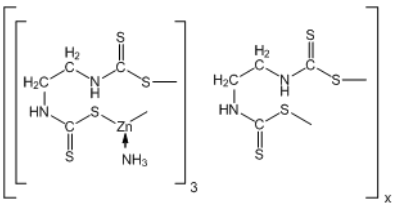
**Ferbam**



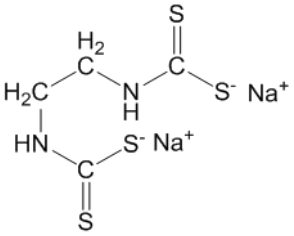
**Mancozeb**



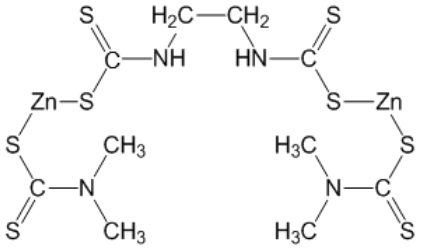
**Maneb**



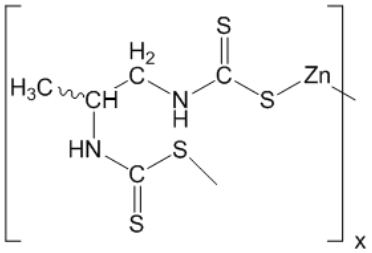
**Metiram**



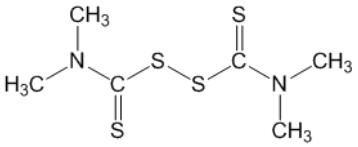
**Nabam**



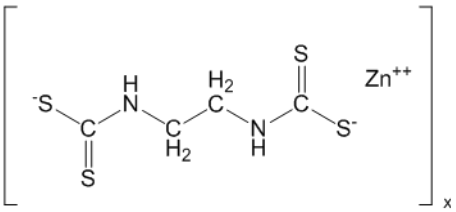
**Polycarbamate**



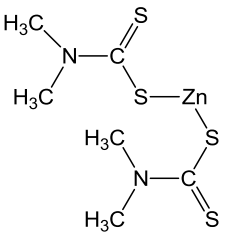
**Propineb**



**Thiram**



**Zineb**



**Ziram**

**Figure 3.** Individual DTC structures

**Table 2.** Individual DTC properties [4,5]

| Compound | CAS RN | MW | Formula | Solubility | Stability |
|---|---|---|---|---|---|
| Amobam | 3566-10-7 | 246.44 | $C_4H_{14}N_4S_4$ | Soluble in water. Slightly soluble in acetone and ethanol; insoluble in benzene. | |
| Ferbam | 14484-64-1 | 416.5 | $C_9H_{18}FeN_3S_6$ | Water 130 mg/L at room temperature; soluble in common organic solvents with high dielectric constant (e.g. chloroform, pyridine, acetonitrile and acetone). | Decomposes on exposure to moisture, heat, and on prolonged storage. |
| Mancozeb | 8018-01-7 *(formerly 8065-67-5)* | 271.2 per monomer unit | $[C_4H_6MnN_2S_4]_xZn_y$ A coordination complex of maneb and zinc | Water 6 mg/L at 25 °C; essentially insoluble in most organic solvents. | Stable under normal, dry storage conditions. Slowly decomposed by heat and moisture. Half-life for aqueous hydrolysis of 10 mg/L suspended in distilled water: pH 5 (36 hours); pH 7 (55 hours); pH 9 (16 hours). |
| Maneb | 12427-38-2 | 265.3 | $C_4H_6MnN_2S_4$ | Practically insoluble in water and common organic solvents. Soluble in chelating agents (e.g. the sodium salt of ethylenediamine-tetraacetic acid [EDTA]) with the formation of complexes. | Stable to light. Decomposes on prolonged exposure to air or moisture. Half-life for aqueous hydrolysis is < 24 hours (at pH 5, 7 or 9). |
| Metiram | 9006-42-4 *(at least ten former numbers)* | $(1088.7)_x$ | $[C_{16}H_{33}N_{11}S_{16}Zn_3]_x$ | Practically insoluble in water and organic solvents. Soluble in pyridine (with decomposition). | Stable at 30 °C; slowly decomposed by light. Half-life for aqueous hydrolysis is < 24 hours (at pH 7). |
| Nabam | 142-59-6 | 256.3 | $C_4H_6N_2Na_2S_4$ | Water 200 g/L at room temperature; insoluble in common organic solvents. | Decomposed by light, moisture and heat. Stable as an aqueous solution. |
| Polycarbamate | 64440-88-6 | 581.58 | $C_{10}H_{18}N_4S_8Zn_2$ | | |
| Propineb | 12071-83-9 *(monomer);* 9016-72-2 *(homopolymer);* *(formerly 31530-30-0)* | 289.8 *(theoretical monomer)* | $[C_5H_8N_2S_4Zn]_x$ | Water <0.01 g/L at 20 °C. In toluene, hexane, dichloromethane <0.1 g/L. | Stable when dry. Decomposed by moisture, and in acidic and alkaline media. |
| Thiram | 137-26-8 | 240.4 | $C_6H_{12}N_2S_4$ | Water 18 mg/L at room temperature; in hexane 0.04, dichloromethane 170, toluene 18, and isopropanol 0.7 (all in g/L at 20 °C). | Decomposed in acid media. Some deterioration on prolonged exposure to heat, air or moisture. |
| Zineb | 12122-67-7 | 275.8 | $C_4H_6N_2S_4Zn$ | Water 10 mg/L at room temperature. Practically insoluble in common organic solvents. Soluble in certain chelating agents (e.g. salts of EDTA). | Unstable to light, moisture and heat on prolonged storage. |
| Ziram | 137-30-4 | 305.8 | $C_6H_{12}N_2S_4Zn$ | Water < 19 mg/L at 20 °C. Acetone 2.88, methanol 0.22, toluene 2.33, n-hexane 0.07 (all in g/L at 20 °C). | Half-life for aqueous hydrolysis is < 18 hours (at pH 7). |

## Sample Extraction and Analysis

The extraction and analysis of intact DTC is complex due to their insolubility in most solvents, their ability to form strong complexes with a variety of metal ions, and their instability, which is affected by oxygen, moisture, temperature, pH and even other tobacco constituents [1,6,7]. Since most of the DTCs have been in use in agriculture for more than 60 years, a variety of methods have been developed for the analysis of their residues in different substrates; these methods have been reviewed [8]. Many of these methods are based on acid hydrolysis of DTCs in the presence of stannous chloride, as proposed by Keppel [9], and analysis of the evolved $CS_2$ (Figure 4) is carried out by different analytical techniques.

Many modifications of the original method have also been reported with regard to sample pretreatment, conditions of acid hydrolysis, and trapping and analysis of released $CS_2$, with the aim of reducing the time and complications of Keppel's method.

In some recent methods sample preparation is carried out in closed vials in heated water baths or ovens. Microwave-assisted extraction based method for analysis of DTCs in tobacco also was published [10]. The evolved $CS_2$ is analyzed by headspace gas chromatography (GC) [1,11-13]; alternatively $CS_2$ trapped into an organic solvent is analyzed either by GC [11,14] or by flow injection and colorimetric quantification of $CS_2$ as a copper complex [15].

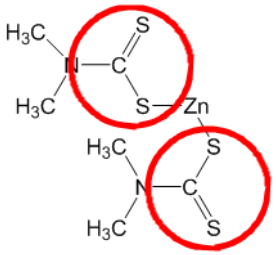



**Figure 4.** Ziram – 1 mole of Ziram generates two moles of $CS_2$

Analytical methods for the determination of DTC residues usually involve the degradation of the DTC to $CS_2$ by acid hydrolysis and subsequent determination of the resulting $CS_2$ by spectrophotometry [16,17] or GC using headspace analysis [18-20]. Meanwhile methods employing high-performance liquid chromatography have been reported [21-23].

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