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Synthesis and characterization of a systemic fungicide 5, 6-dihydro-2-methyl-1, 4-oxathiin-3-caboxanlido(Vitavax)

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ABSTRACT

blight on corn and wheat. It is very often used in combination with other fungicides such as Thiram or captan.Carboxin (alternative name Uniroyal D735, DCMO), was discovered and developed by Uniroyal International Division of Uniroyal Inc.USA under the trade name Vitavax.Chemically it is 5,6-dihydro-2-methyl-1,4- oxathiin-3-caboxanlido with the formula $C_{12}H_{13}NSO_2$ and molecular weight 235. The activity of fungicides is intimately related to its chemical structure. Knowledge about the chemical structure of a chemical is useful for the synthesis of new compounds with more specific actions and fewer adverse reactions, to increase/decrease the duration of action of the original drug or to get a more potent compound, to restrict the action to a specific system of the body and to reduce the adverse reactions, toxicity and other disadvantages associated. We can understand the basic chemical groups responsible for drug action[1]. Recently it has been observed that some of the fungicides are loosing their effects. So analogous compounds can be designed as substitute, if their structures are known. A rational approach to test these fungicides is to know the three dimensional structure of these compounds and macromolecular receptor sites as well as their molecular complex.

KEYWORDS

X-ray crystallography;
Infrared spectra;
Systemic fungicides.

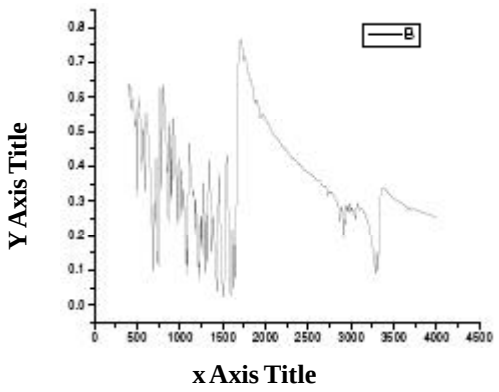
INTRODUCTION

Fungicides are the important class of chemicals used widely for the protection of crops. A systemic fungicide is defined as systemic fungi toxic compound that controls a fungus pathogen remote from the point of application and that can be detected or identified[2]. These compounds are absorbed by the plant and get trans located within it, thus providing protection as well as eradicating already established infection. Carboxin is a white solid having 2 crystal structures (in solution these crystal structures revert to one and biological tests have shown no difference in their activity)It has a faint odour and is non- volatile. Its melting points are 91.5-92.50^{0}C (A form) and 98.0-100^{0}C (B form). The solubility per 100g in water, methanol, dimethyl sulfoxide, ethanol, acetone and benzene is 0.017,21,150,11,60 and 15 respectively. The systemic fungicide Carboxin (5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide) inhibited oxidation of succinate by membranes prepared from *Micrococcus denitrificans*, the K_i being 16μM. Oxycarboxin (5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide-4,4-dioxide), F831 (5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide-4-oxide), and another succinate oxidize inhibitor, 4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione (TTB) were less effective inhibitors of

succinate oxidation by membranes of *M.denitrificans* [3]. Oxidation of other substrates (nicotinamide adenine dinucleotide, reduced form, d-lactate, l-lactate, malate, and d,l-α-hydroxybutyrate) was inhibited to a lesser degree by Carboxin, and format oxidation was entirely resistant[4]. With all substrates tested, Oxycarboxin, the dioxide analogue of carboxin, was less effective than carboxin. Carboxin also inhibited dichlorophenol indophenols (DCIP) reductase activities by these membranes in a manner both qualitatively and quantitatively similar to the inhibition of oxidation of the various substrates[5]. The inhibition of DCIP reductase activities by TTB was qualitatively similar to carboxin, but TTB was a less effective inhibitor with all substrates tested[6]. The inhibition of DCIP reductase by carboxin could be relieved by phenazine methosulfate with all substrates except d-lactate[7]. Only slight inhibition of d-lactate-stimulated uptake of [^{14}C] glycine by these membrane vesicles was seen with carboxin[8]. Uptake of [^{14}C] glycine could be stimulated to varying degrees with the other substrates tested, but in no case did carboxin cause significant inhibition[9]. Membranes isolated from *M.denitrificans* are a useful system for investigating the mechanism of inhibition of electron transport function by carboxin, and the use of this system for evaluations of carboxin and its metabolites is suggested[10].

EXPERIMENTAL

The X-ray diffraction pattern (XRD) using Philips PW3040/60 X-ray powder diffractometer is obtained with Ni-filtered Cu Kα radiation (λ=1.54A°) having voltage 40kV and current 100mA[11]. The infrared absorption spectra of the sample and complexes are measured at room temperature.. Crystallization of Vitavax is done by slow evaporation from a solution of cyclohaxenone at 282°K temp.The crystals obtained are white and rectangular in shape. The density of the crystal is determined by floatation method at room temp.The Crystal is placed in RD bottle with carbon tetrachloride. Benzene is added to the solution until the crystal floated in the middle of the mixture. Thus the crystal and solution are of same density and the density of solution is measured with Pyknometer. For determination of structure of the crystal VAX machine using SHELXS-97[12] is used. In the beginning all the non-



hydrogen atom'. are located The coordinates thus obtained are fed to SHELXL-97[13] for refinement vitavax.

IR spectra

The IR spectra of all samples are performed at field between 4000–300 cm^{-1}, along with tentative assignments. The infrared spectral, data of legend show a very strong band at 1673 cm^{-1} which may be attributed to ν(C=O) stretching vibration on complexation a band at 1673 cm^{-1} has shifted to lower region 1685-1581 cm^{-1} showing carbonyl oxygen are involved in coordination. This is clear evidence for coordination by carbonyl oxygen. The band due to ν(NH) shift to lower wave number side by about 20-30 cm^{-1} in all and this band becomes weak in complexes suggesting the coordination of nitrogen of ν(NH) group. In addition, ν(C=N) mode may be coupled with ν(C=S) and ν (NO_2) to give intense band, they were observed at (1565-1494) cm^{-1} , (1249-1128) cm^{-1} and (1534-1527,1335-1328) cm^{-1}[14].

Carboxin is rapidly degraded to carboxin sulfoxide in soil. After seven days, 95% of the parent was gone and the sulfoxide represented 31 to 45% of the amount applied[14]. Minor products formed were carboxin sulfone, hydroxy carboxin and CO_2. Carboxin does not readily absorb to soil (adsorption coefficient less than one). Both parent and sulfoxide are very mobile and could possibly leach to groundwater(2).In water, carboxin oxidizes to the sulfoxide and sulfone within seven days(2)[15]. This happens both under ultraviolet

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light and in the dark(5).Although the distribution pattern of the parent and sulfoxide metabolite vary, carboxin is systemic in all species of plants studied(5). Plants grown from treated seed had no carboxin present six weeks after emergence. The carboxin sulfoxide found in plants can be either from the soil or oxidation within the plant[16].

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