THE EFFECTS OF DIETARY DDT ON PLASMA LEVELS OF CALCIUM AND MAGNESIUM IN RATS

by

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B. S., University of Iowa, 1971

A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE UNIVERSITY

Manhattan, Kansas

1974

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STATEMENT OF PROBLEM

The effects of dietary DDT (2,2-bis-(p-chlorophenyl)-1,1,1-trichloroethane) on the plasma calcium and magnesium levels in rats were evaluated in an attempt to clarify the mechanism of poisoning. Both the total ion and the ultrafiltrable (free and complexed) ion were measured.

INTRODUCTION

Rationale for the study

Since the discovery in 1939 of the effectiveness of DDT as an insecticide researchers have been attempting to establish how DDT works. Although much more information is available today the question is still unanswered. Some of this information is presented and related to a research project to study the effect of DDT on blood levels of calcium and magnesium.

Mullins (1955) and Gunther, Blinn, Carman, and Metcalf (1954) proposed that DDT possessed insecticidal action because of its structural properties. Using this idea Holan (1969) reasoned that if DDT had the proper steric properties to fit in the nerve membrane-pore channel, then other molecules of similar steric properties should also be effective insecticides. Holan was successful in using the structural theory to synthesize new pesticides.

Evidence for formation of two charge-transfer complexes of DDT with components of cockroach nerve was presented by O'Brien and Matsumura (1964). Matsumura, Bratkowski, and Patil (1969) definitely identified a complex but were unable to establish that it was of the charge-transfer type.

The work reviewed above was all done on insects. Barnola, Camejo, and Villegas (1971) used squid and human material to establish that DDT accumulates in the plasma membranes of nerve fibers. The membrane lipids provide an appropriate medium for the interaction of DDT with membrane proteins. Spectral evidence for a complex between DDT and nerve membrane proteins in the presence of membrane lipids was presented.

DDT alters the observed electrical activity of nerve. Gordon and Welsh (1948) reported repetitive firing and spontaneous activity from DDT-poisoned nerve in the crayfish. This effect could be inhibited by calcium or magnesium ions.

Other workers have found that DDT delays the process turning off the peak transient (sodium) current and inhibits the steady-state (potassium) current in voltage clamped axons. Narahashi (1967) used lobster nerve and Hille (1968) used frog nerve. Hille further reported that a fraction of the sodium channels remained open for a longer time than normal following depolarization. Barnola, et al. (1971) suggested that changes in the sodium current may be due to the effect on potassium. The observation of Matsumura (1966) that cockroach nerve poisoned by DDT has an increased ability to take up sodium or to lose potassium is surely related to the observed electrical characteristics.

Based on a rather large body of evidence, some of which will be presented, Matsumura, et al. (1969) suggested that the nerve enzyme adenosine triphosphatase (ATPase) might actually be the site of DDT attack. This suggestion is based on the close correlation between ATPase inhibition by DDT and nerve symptoms of DDT poisoning.

Two kinds of ATPase are of concern and have been identified (S. Puskin, Berl, E. Puskin and Clarke, 1968). Both kinds are dependent upon the presence of certain ionic species. One requires Na^{+}, K^{+}, and Mg^{++} and is referred to as the Na-K-Mg type. The other requires Ca^{++} or Mg^{++}.

The two types of ATPase have been associated with different functions. The Na-K-Mg type is assigned a governing role in cation transport across the cell membrane (Germain and Proulx, 1965 and Skou, 1965). Kadota, Mori, and Imaizumi (1967) have found the Ca-Mg type in the synaptic vesicle fraction and Germain and Proulx (1965) suggested that it may be involved in the release of acetylcholine.

DDT definitely inhibits ATPase. Matsumura, et al. (1969) found inhibition of the Na-K-Mg type in rat brain. Koch (1969) and Koch, Cutkomp, and Do (1969) reported inhibition of both types of ATPase in cockroach, honey bee and rabbit