بسم الله الرحمن الرحيم

HOSSAM MAGHRABY

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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لم ترد بالأصل

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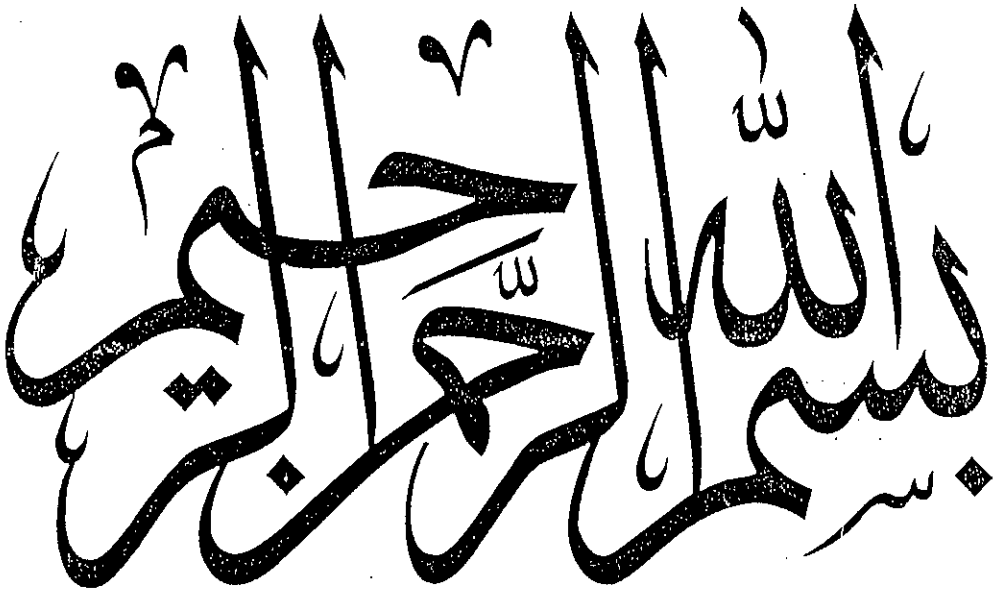
بسم الله الرحمن الرحيم

Histological and Histochemical Study of the Effect of Chlorpyrifos on the Myocardium and the Coronary Arteries of Albino Rats and the Possible Protective Effect of Ascorbic Acid

Thesis

Submitted to The Faculty of Medicine – University of Alexandria
in partial fulfillment of the requirements for the degree of

Master of Histology

By

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Thank to Allah

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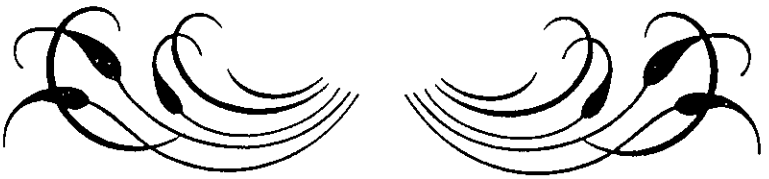

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INTRODUCTION

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Pesticides are unusual among environmental pollutants in that they are used deliberately for the purpose of killing some forms of life. They are highly selective, destroying target organisms while leaving nontarget organisms unharmed.[1]

In considering the use of pesticides, the benefits must be weighed against the risk to human health and enviromental quality. Among the benefits of pesticides are control of vector borne diseases, increased agricultural productivity, and control of urban pests.[1]

Organophosphorus (OP) insecticides are among the most widely used synthetic chemicals for the control of agricultural and domestic insect pests.

The use of this class of chemistry has resulted in world wide increases in food and fibre production, and the control of major disease carrying vectors and structure damaging insect pests.[2,3]

Organophosphates (Ops) have achieved great popularity because of their effectiveness as insecticides and their lack of persistence in the environment. Because of their unstable chemical structure, they disintegrate into harmless radicals within days of application.[2]

During World War II, the United States used large quantities of DDT to control vector borne disease, such as typhus and malaria, to which US troops were exposed. After the war, DDT use became widespread in agriculture, public health and house holds.[3]

There is increasing concern that exposure to the organophosphates insecticides as chlorpyrifos may cause adverse health effects in humans, suggesting that children and adults have been routinely exposed to this compound in the enviroment.[4]

The organophosphates are closely related family of chemicals varying in structure, potency, and latency of onset of symptoms. This latent period varies with route of administration, degree of exposure, fat solubility affinity of the substance to be endogenously hydrolyzed, affinity to the cholinesterase active site, inherent toxicity of the particular organophosphates, and whether the toxin is direct acting or must first undergo conversion to an active metabolite.[5]

Chemistry, absorption, metabolism and mode of action of chlorpyrifos:

Organophosphates are a heterogeneous group of compound that are composed of a phosphoric acid derivative with two organic side chains and an additional side chain that can be a cynaide, thiocyanate, halid, phosphate, phenoxy, thiophenoxy, or carboxylate group.[1]

Chemical name is 0.0-diethyl-0- (3,5,6-tri-chloro–2-pyridyl) phosphorothioate. It has the empirical formula CO_1 H_{11} C_{l3} NO_3 PS and a moleculr weight of 350.75. The pure material forms white crystals with a mild mercaptan odor. It is stable under normal storage conditions.[6]

Absorption

Organophosphates compounds may be absorbed virtually by any route such as trans-dermal, trans-conjunctival, through the pulmonary tree, or across the gastrointestinal mucosa,and, rarely through direct injection.[5]

Mechanism of action

Each organophosphate has a different affinity for the histidine-serine esteratic subsite on the acetylcholinesterase molecule. This determines how strongly the organophosphate is bound to each site. The degree of the affinity as well as the route of absorption, the amount of metabolism, amount of blood flow, and the active site concentration all determine which signs and symptoms will predominate.[5]

The mechanism of action of chloropyrifos or its active metabolities is the inhibition of acetylcholinesterase (AchE), located in the synapses of somatic autonomic nerves and CNS. When biologically activated organophosphates [Ops] react covalently with AchE in the synapses resulting in a build up of acetyl choline (Ach) in the synaptic cleft and in the vicinity of Ach receptor. This, in turn, causes repetitive firing of