PESTICIDE CONTROL: THE METHOD OF MICHEL WITH AN EMPHASIS ON QUALITY CONTROL[MAS]

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The use of pesticides, especially organophosphate pesticides, causes different adverse effects in human applicators. Most of the symptoms are due to inhibition of the enzyme cholinesterase. There are several methods that are used to determine these drops in cholinesterase levels. The Montana Department of Health and Environmental Sciences uses a modification of the Method of Michel that measures change in pH of human plasma samples to determine cholinesterase levels. During the 1994 field application season, two new quality control sessions were added to ensure more accurate results and these proved to be helpful. However, this study suggests additional changes including the involvement of more applicators. The program, if run correctly, could protect the health of many Montana pesticide applicators.

EFFECTS OF TRIMETHYLTIN ON C6 GLIOMAX[MAS]

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Trimethyltin (TMT) is a potent neurotoxin. Symptoms manifest in 48 hours. The rat C6 glioma cell line was used as a glial cell model of TMT toxicity. Three indices: morphological change, cytotoxicity, and generation of reactive oxygen species (ROS) were investigated. Morphological changes were observed over a 72 hr period with 2.5 mM and 5 mM TMT showing changes at 48 hrs and 24 hrs respectively. These changes involved cell swelling, loss of processes, and loss of adhesion to culture flasks. Concentrations of 5mM and higher of TMT showed time and concentration dependent increases in cytotoxicity up to 72 hrs. A concentration of 5 mM TMT increased the intracellular levels of ROS by 24 hours, but 2.5 mM TMT did not produce any increase in ROS after 72 hours. A cytotoxic concentration of TMT (5 mM and higher) produced morphological changes and increased ROS at times prior to detectable cytotoxicity. Trimethyltin also produced morphological changes at times and concentrations that did not increase ROS and were not cytotoxic.

Relating Autogenic Biofeedback-Assisted Relaxation and Migraine Treatment[MAS]

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This study attempts to establish autogenic biofeedback training as a possible non-pharmaceutical treatment for migraine. The approach is to show that both autogenic training and prescribed medications share a common effect upon the autonomic nervous system. Since the abnormal biphasic event of vasoconstriction followed by vasodilation is recognized as the precursor of a migraine episode, both treatments should alter the activity of the vascular system. Hand temperature is directly related to peripheral blood flow, and given that peripheral circulation is controlled entirely by the autonomic nervous system, a change in hand temperature can be used as a convenient indicator of the state of the system. It is therefore proposed that if hand temperature is decreased in both forms of treatment, both treatments share a common effect on the autonomic system. The work is designed to be completed in two phases: 1) In conjunction with normal medication procedure at a medical clinic, hand temperature changes are monitored by a registered nurse; and 2) volunteer female high school students will be monitored for hand temperature while participating in Autogenic Biofeedback Training. The training involves listening to a formatted relaxation and imagery tape which utilizes abdominal breathing, autogenic phrases and general relaxation techniques.

Serotonergic Receptor Binding of the Natural Product Parthenolide [MAS]

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Serotonin (5-HT) receptors are thought to play roles in the pathology of migraine headache. Of the multiple 5-HT receptor subtypes known, 5-HT1 and 5-HT2 receptors are targets for the acute and prophylactic treatment of migraine, respectively. In this preliminary study, 5-HTla and 5-HT2 receptors were utilized as targets for parthenolide, a major component of European Feverfew. Feverfew has been successfully used as a folk remedy for migraine, and has been shown to be a clinically relevant treatment in controlled studies. The 5-HTla receptors from rabbit brain were labeled with the specific agonist, [^{3}H]-8-OH-DPAT. While known 5-HTla agents such as spiroxatrine and buspirone displace this agonist in a concentration-dependent fashion, parthenolide is without activity. Rabbit and rat brain 5HT2 receptors were labeled with the antagonist, [^{3}H]-ketanserin. Methysergide and mesulergine displace this binding in a fashion consistent with published potencies. Parthenolide also displaces ketanserin binding in a concentration-dependent fashion, but weakly (IC_{50} of about 0.1 mM). A crude,

highly polar extract of Feverfew was shown to be capable of displacing ketanserin, suggesting that some component other than the non-polar parthenolide may be the active agent. Identification of the pharmacological sites of action for Feverfew awaits further investigation.

5-HT1a Receptors: A Comparison of Ligand Binding in Rabbit, Rat, and Human [MAS]

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Serotonin (5-HT) exerts its actions through a group of receptors in the central nervous system. These receptors have been characterized pharmacologically and are classified into seven subtypes. One of the first subtypes identified, 5-HT1, is represented by five divisions (5HT1a,b,d,e,f). 5HT1a has been analyzed in several mammalian species including rabbit, rat, and human; it has never been fully characterized in rabbit. The current study compares the characteristics of the 5HT1a receptor in rabbit brain to those in rat and human. A selective agonist, 8-OH-DPAT, is at 5HT1a and is used in the characterization of this receptor. [^{3}H]-8-OH-DPAT binding was analyzed in rabbit and rat brain and in Chinese hamster ovary (CHO) cells transfected with clonal cDNA for the human 5-HT1a receptor (gift from John Raymond, Duke). Specific, saturable binding was observed with Kd values of 1. 1, 0.8, and 0.6nM for the rabbit, rat, and human receptor, respectively. To further investigate the receptor, displacement studies were conducted in which drugs with known activity (i.e. buspirone, propranolol) competed for binding with [^{3}H]-8OHDPAT. Ki values for each of the competing drugs were similar across the three species. These results suggest that the 5-HT1a receptor in the rabbit brain shows comparable characteristics to that in rat and human.