Pharmacology and Toxicology

Screening of Peruvian Ethnobotanicals for 5HT1a and 5HT2a Receptor Binding Activity [MAS]

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Late in 1995, plants of ethnobotanical importance were collected in southeastern Peru. Many of these plants have been used by natives for treatment of headache. Since headache, especially migraine, is thought to involve serotonergic mechanisms, we have started to screen crude 70% ethanol extracts for *in vitro* receptor binding activity in two systems, 5HT1a and 5HT2a. About two dozen specimens have been examined. Only three of these specimens have significant activity at 5HTla receptors, but nearly half of the specimens demonstrate substantial binding activity at 5HT2a receptors. As quantified by displacement of tritiated ketanserin, three specimens give approximately 90% binding at 1/100 dilution of the crude extract. These samples have also been tested for concentration-dependent binding and are considered to be lead samples at this time. Protocols for identification of active principles from these high priority samples involve standard solvent partitioning followed by HPLC fractionation. HPLC fractions are then retested pharmacologically. The single highest priority plant, *Petiveria alliacea*, has shown outstanding activity following fractionation. The long-term goal of this work is to develop superior anti-migraine drugs.

Differential Activation of C6 Glioma Protein Kinase C Isoforms by a Phorbol Ester and Trimethyltin [MAS]

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Trimethyltin (TMT) is a potent neurotoxin that produces delayed, irreversible damage. Damage is usually not evident for 48 hours. Activation of Protein Kinase C (PKC) has been implicated in the neurotoxicity produced by TMT. In a neuronal cell line, TMT causes translocation and activation of PKC within 30 minutes. We used a rat C6 glioma cell line to determine the ability of PKC to translocate in the presence of phorbol 1 2-myristate 1 3-acetate (PMA) or TMT. Further studies were conducted to differentiate specific isozyme involvement. Isoforms were separated by gel electrophoresis and identified by Western blotting with specific monoclonal antibodies. We have identified the presence of the α, β, γ, δ, ε, θ, ζ, λ, and μ isozymes

in our C6 cell line. These isozymes of PKC were evaluated on their responses to PMA and TMT exposure. All of the cPKC and nPKC isoforms translocated to the cell membrane following PMA exposure. The aPKC isozymes were not translocated by this treatment. TMT exposure for up to 1 hour did not translocate any of the PKC isoforms. PKCs α, δ, and ζ were also evaluated after 24 hours of treatment with PMA and TMT. PKCs a and d had down-regulated with the PMA treatment, while no translocation was detected with TMT treatment on any isoform.

Assessment of Cardiovascular Risk in a Pharmaceutical Sciences Laboratory Course [MAS]

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The current study assessed blood lipid levels in pharmacy students by 4 methods. The measurements were made by a commercial laboratory, by the O-T-C product Advanced Care ™, by the Cholestech ™ LDX Auto-Analyzer System, and by Sigma Kits #352-20 and #352-5 for total cholesterol and HDL fraction, respectively. The possibility that the lipid profiles of male and female pharmacy students might differ from each other and from the general population was also explored. All methods of determining blood total cholesterol and other lipid fractions were comparable and observed differences were attributed to gender. Male pharmacy students (N= 88) had total cholesterol levels of 185.84 ± 1.17 mg/dL which did not differ from those of female students (N= 84) which were 185.60 ± 0.73 mg/dL. Female pharmacy students (N= 77) had higher HDL-C levels (59.64 ± 0.78 mg/dL) than did males (44.47 ± 0.46 mg/dL). Because female students had greater HDL-C levels than their male peers, they also had lower cardiovascular risk ratios defined as the ratio of total cholesterol to HDL-C. Female students (N= 54) also had lower blood triglyceride levels (120.05 ± 6.74 mg/dL) than those (163.6 ± 3.00 mg/dL) of males (N= 55). Our conclusions are that the methods of measuring blood lipids are comparable, that female pharmacy students have a better cardiovascular lipid profile than their male counterparts, and that both groups have a better cardiovascular lipid profile than the general U. S. population.