NEUROPATHOLOGIC EFFECTS OF PHENYL METHYL SULFONYL FLUORIDE (PMSF)-INDUCED PROMOTION AND PROTECTION IN ORGANOPHOSPHORUS ESTER-INDUCED DELAYED NEUROPATHY (OPIDN) IN HENS.

By

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ABSTRACT

NEUROPATHOLOGIC EFFECTS OF PHENYLMETHYLSULFONYL FLUORIDE (PMSF)-INDUCED PROMOTION AND PROTECTION IN ORGANOPHOSPHORUS ESTER-INDUCED DELAYED NEUROPATHY (OPIDN) IN HENS.

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The serine/cysteine protease inhibitor phenylmethylsulfonyl fluoride (PMSF) has been used both to promote and to protect against neuropathic events of organophosphorus-induced delayed neuropathy (OPIDN) in hens (Lotti et al., 1991; Veronesi et al., 1985; Pope and Padilla, 1990; Pope et al., 1993). This study expands upon this work by correlating clinical and neuropathological findings in these modifications of OPIDN. To provide appropriate models of OPIDN, single phenyl saligenin phosphate (PSP) dosages of 0.5, 1.0, or 2.5 mg/kg were administered to adult hens. PMSF (90 mg/kg) was given either 4 hours after or 12 hours prior to PSP administration. Clinical signs and pathologic changes in the biventer cervicis nerve (El-Fawal et al., 1988) were monitored. PSP alone, 2.5 mg/kg, elicitated severe OPIDN (terminal clinical score 7.5 ± 1.0 [0-8 scale]; neuropathology score 2.7 ± 0.3 [0-4 scale, based on myelinated fiber degeneration]). PMSF given 12 hours prior to PSP gave complete protection (clinical and neuropathology scores of 0; p<0.0001). Signs and lesions of OPIDN were absent following 0.5 mg/kg PSP alone, but PMSF given 4 hours after PSP potentiated its neurotoxic effects (clinical score 4.0 ± 0.0; neuropathology score 3.5 ± 0.3; p<0.0001). At the time of sacrifice, there was a correlation (r = 0.61) between the clinical score on the last day of observation and the neuropathology scores (p<0.0001). This study demonstrates that the intensity of peripheral nerve myelinated fiber degeneration correlates with clinical deficits in PMSF-induced potentiation and protection in OPIDN.
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Dear God,

Give me the faith to accept the things I can not change,

The strength to change the things I can,

And the wisdom to know the difference.
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ABBREVIATIONS

ACh: Acetylcholine
AChE: Acetylcholinesterase
ANOVA: Analysis of variance
ATPase: Adenosine triphosphatase
CR: Cross section
BPAU: Parabromophenylacetylurea
CS: Clinical score
DFP: Diisopropyl-fluorophosphate
DNA: Diribonucleotide acid
EPN: O’-ethyl-O-p-nitrophenyl phenylphosphonothioate
Epot: Equilibrium potential
EPSP: Excitatory post - synaptic potential
GLM: General linear models
I: Immersion fixation
IPSP: Inhibitory post - synaptic potential
KD: Kilodalton
MANOVA: Multivariate analysis of variance
MAP: Microtubule - associate protein
mRNA: Messenger ribonucleic acid
N: Nitrogen
NAD: Neuroaxonal dystrophy
NTE: Neurotoxic esterase or neuropathy target esterase
NTF: Nerve fiber teasing technique
O: Oxygen
OCD: Ornithine decarboxylase
OP: Organophosphorus
OPIDN: Organophosphorus-induced delayed neuropathy
P: Phosphorous
pf: perfusion fixation
p: statistical probability
PMSF: Phenyl methane sulfonyl fluoride
Pscore: Pathological score
Pscoret: Pathological score with teased fibers
PSP: Phenyl saligenin phosphate
rRNA: Ribosomal ribonucleic acid
S: Sulfur
SER: Smooth endoplasmic reticulum
Stat: Statistic
Stdev or SD: Standard deviation
TOCP: Tri-o-cresyl phosphate
TOTP: Tri-o-tolyl phosphate
TPP: Tri-phenyl phosphite
US EPA: United States Environmental Protection Agency
VP: Voltage potential
% nor F: Percentage of normal fibers
% deg F: Percentage of degenerated fibers