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

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Thesis submitted to the Faculty of the Virginia Polytechnic institute & State University in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

in

Veterinary Medical Sciences

APPROVED

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March 1998
Blacksburg, Virginia

Keywords: Toxicology, Organophosphate, Neuropathy, Promotion

ABSTRACT

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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, ellicitated 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.

ACKNOWLEDGMENTS

First and foremost, I would like to dedicate this work to my parents and immediate family members, with whom I have been blessed. Without their unconditional love, understanding and support, I would not have completed this program and become the person I am. They taught me to persevere and never give up. For these reasons, I thank them infinitely.

I would like to sincerely acknowledge the generous assistance provided by the following technicians: Linda Correll, Ginny Viers, Kristel Fuhrman, Kathy Lowe, and Sandy Perkins. These persons participated actively in this project, sharing their experience, knowledge and skills, which were very important in my scientific development. Without their tremendous help, this study would not have been possible. I would like to thank Rehana Durrani since her time and patience allowed me to include additional and important data to my research. I would also like to thank all members of the reprographic team, including Don Massey, Terry Lawrence, Jerry Baber, and Havah Dinnel for their generous assistance regarding the Figures in this work, and also for all the reprographic material they allowed me to use.

I would like to particularly thank the members of my committee, Dr. Bernard S. Jortner, Dr. Marion F. Ehrich, and Dr. Karen D. Inzana , whom were greatly supportive of my work throughout my graduate program. Dr. Jortner's willingness to teach me patiently the art of pathology was above and beyond the call of duty. I could always rely on his kindness and understanding. He always put my interests as a graduate student above his own, making time to answer all my questions thoroughly, and to help me in all aspects of

my graduate studies. The tremendous amount of knowledge I acquired during this program reflect the importance he attributes to each of his graduate students. Dr. Ehrich showed me the true meaning of friendship. The energy and enthusiasm she displays towards her work and the work of her graduate students were my source of motivation. Her constant encouragement gave me the strength to persevere. She taught me how to see the positive aspects in everything and everyone. Her generosity and kindness have no limits.

I also would like to acknowledge the financial support I had to perform my research. This work was partially supported by USDA Hatch funds. Additional funding including a graduate stipend, was provided by Virginia - Maryland Regional College of Veterinary Medicine.

Finally, I would like to sincerely thank my piano teacher, Monique Pomerleau, who always believed in me and my talent. Always reaching for perfection, the love she has for her students, and her complete devotion to music will always be my major source of inspiration, no matter which path I choose to follow in my life.

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