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| <b>Thesis Title</b>                 | <b>Effects of pseudoephedrine on rat central dopaminergic system</b>                                |
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| <b>Degree</b>                       | <b>Master of Science (Neurosciences)</b>  |
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| <b>Date of Graduation</b>           | <b>28 April B.E. 2537 (1994)</b>  |

### **Abstract**

Pseudoephedrine (PSEU), which is commonly prescribed as a nasal decongestant, shows structural similarity to amphetamine, a well known psychomotor stimulant. The present study hypothesized that PSEU may have an effect on central nervous system by altering the dopaminergic system. To determine the correlation between neurochemical and behavioral changes caused by PSEU, the latter was administered to rats both acutely and chronically. Neurochemical data in both chronic and acute experiments was obtained by using an ion-pair high-performance liquid chromatographic method coupled with electrochemical detection.

Acute experiments were consisted of intraperitoneal injections of 80 mg/kg *d*-pseudoephedrine (*d*-PSEU). In order to determine the effect of *d*-PSEU on dopamine and its metabolites, all rats were killed 60 minute after injection, striatum and nucleus accumbens were dissected out, and monoamines, as well as, their metabolites were extracted by perchloric acid. PSEU caused an increase of DA and its metabolites in both areas, however a significant change was shown only in striatum. The time course effect of *d*-PSEU showed that the highest DA levels in both areas occurred 60 minute after drug administration. The DA levels in striatum were significantly different, whereas, in the nucleus accumbens they were not. The ED<sub>50</sub> value of

intraperitoneally administered *d*-PSEU on DA levels in striatum was 17 mg/kg. The observed increase in DA induced by PSEU could have been due to the release of DA from both "stored" and "newly synthesized" pools and/or inhibition of DA reuptake. The increase in the level of DOPAC increased linearly with the increase of DA indicating that monoamine oxidase activity was not affected by PSEU. The PSEU-induced increase of HVA could be accounted for the action of COMT on the increased level of DOPAC. Pseudoephedrine stimulation of DA release in the striatum would be consistent with the well-documented role of striatal projection neurons in mediating the adverse effect of this drug on extrapyramidal activity.

In the chronic experiment, water containing either no drugs, 0.01% *d*-amphetamine or 0.05% *d*-pseudoephedrine was for 1 hour everyday to negative control group, positive control group (AMPH group) and experimental group (PSEU group), respectively. Water intake, drug intake, food intake and body weight were measured. PSEU intake caused an initial decrease in food and water consumption. However within one week food consumption returned to control levels and remained at these levels for the remaining 3 weeks of the experiment. The final dose of PSEU intake was 25 mg/kg, which might not reach its oral ED<sub>50</sub>. When the data was analyzed as total weekly consumption it was observed that in the PSEU group, water was significantly lower than in control group in each week. Body weight did not change significantly. In contrast, in the AMPH group, body weight, food intake and water intake were significantly decreased throughout the experiment. On day 28, all rats were killed and brain areas (striatum and nucleus accumbens) were dissected to measure the level of dopamine and its metabolites. Chronic intake of PSEU caused no change in DA level possibly due to the depletion of dopamine storage in presynaptic site. However, chronic PSEU intake caused a significant decrease of HVA alone and both HVA and DOPAC in the striatum and nucleus accumbens, respectively.