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Therapeutic and adverse effects of chronic oral intake of Mucuna pruriens seed extracts or L-DOPA methyl ester in 6-hydroxydopamine lesioned rats

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Introduction
L-DOPA, or 3-O-methyldopa, is the most effective pharmacological agent in the treatment of Parkinson's Disease (PD) as a dopamine-replacement therapy. Chronic use of L-DOPA is frequently linked to adverse effects (dyskinesias) (Lundblad et al 2002). Seeds of the legume Mucuna pruriens (MP) are a rich source of L-DOPA and preparations of MP seed extracts have been shown to have neuroprotective effects in animal models of PD (Singhal et al 2003).

Aims
Seeds of the legume Mucuna pruriens (MP) are a rich source of L-DOPA and preparations of MP seed extracts have been shown to have neuroprotective effects in animal models of PD (Singhal et al 2003).

Method and materials
Animal model: adult male Sprague-Dawley rats of either sex (180-250 g) obtained from Kolon. Animals were maintained in accordance with the guidelines described in the Danish Animal Care Act of 1992 (KFAL 2000).

Dose of 6-Hydroxydopamine: A unilateral 6-hydroxydopamine (6-OHDA) lesion was created by unilateral injection (3 µl/µl) of 6-OHDA (15 µg/µl; Sigma) into the left lateral ventricle of anesthetized rats. The 6-OHDA solution was prepared in ascorbic acid and benserazide was added to prevent DA degradation (15 mg benserazide/kg, for ip administration or 1 mg benserazide/ml for oral administration).

Drug preparations: Seeds of Mucuna pruriens were milled, and the lipophilic fraction was extracted with hexane (MP-hex), the methanol fraction with methanol (MP-MeOH), and the aqueous fraction with water.

Drug intake via drinking water: Solutions were normalized to specific L-DOPA concentrations. MP hexane extract was administered via the drinking water. Blood sampling and DOPA assay: Solutions were normalized to specific L-DOPA concentrations. MP hexane extract was administered via the drinking water. Blood sampling and DOPA assay: Solutions were normalized to specific L-DOPA concentrations. MP hexane extract was administered via the drinking water.

Animal mode
In this study, an animal model for PD, the acute, dose-dependent testing and adverse effects of chronic oral intake of L-DOPA methyl ester (LDME) and MP-MeOH extract are observed (Seeds of the legume Mucuna pruriens (MP) are a rich source of L-DOPA and preparations of MP seed extracts have been shown to have neuroprotective effects in animal models of PD (Singhal et al 2003)).

Discussion and conclusions
Chronic treatment with LDME, MP-MeOH or MP-MeOH+hexane showed no significant differences in therapeutic and adverse effects. MP-MeOH and MP-MeOH+hexane showed the strongest therapeutic effects which were achieved with 6 mg DOPA/kg for MP-MeOH treated rats, but in LDME-treated rats the dose caused severe PD-animals suffering from normal body tone. Oral treatment via the drinking water caused large variations in plasma DOPA levels between morning and afternoon, but stable average plasma levels in LDME- and MP-MeOH-treated rats. A weak relation (r=0.47, p<0.01) was observed between the average amount of DOPA intake and the averaged body weight.

Acknowledgement
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References
Jørgensen, Monica, Lars Porskaer Christensen and Jan Bernt Gramsbergen, 2008. "Seeds of the legume Mucuna pruriens (MP) showed significant higher AFs scores with increasing dose (mg/kg, p<0.001) with no difference between LDME and MP-MeOH preparations. AIMs were observed even at low dose (2 mg/kg) in both groups. The highest dose effect was achieved with 6 mg DOPA/kg for MP-MeOH treated rats, but in LDME-treated rats this dose caused severe PD-animals suffering from normal body tone.

Figure 1: Acute observed AIMs after administration of LDME or MP-MeOH preparations (ip adm.), showed significant differences in therapeutic and adverse effects. The highest dose effect was achieved with 6 mg DOPA/kg for MP-MeOH treated rats, but in LDME-treated rats this dose caused severe PD-animals suffering from normal body tone.