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Dose- and time-dependent therapeutic and adverse effects of *Mucuna pruriens* extracts in the 6-OHDA rat model of Parkinson’s disease

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**Introduction**

In traditional Ayurvedic Indian medicine, preparations of *Mucuna pruriens* seeds (fig. 1) are used in the treatment of Parkinson’s disease (PD). It has been suggested that *Mucuna* preparations may possess some clinical advantages over conventional, synthetic L-DOPA/carbidopa preparations, including a rapid onset of action and longer on time without concomitant increase in dyskinesias (Katzenschlager et al. 2004, Kasture et al. 2009, Liu et al. 2010). Alcoholic extracts of MP seeds are rich in L-DOPA, but other, as yet unknown compounds may contribute to its therapeutic effects.

**Objectives**

In 6-hydroxydopamine (6-OHDA) lesioned rats we determined:

1. Therapeutically effective doses of a methanol extract of *Mucuna pruriens* seeds and of (synthetic) L-DOPA with or without additives.
2. Abnormal involuntary movements (AIMs) during chronic treatment at therapeutically effective doses.
3. Dose-dependent effects of *Mucuna* extract and L-DOPA in the presence of benserazide (peripheral decarboxylase inhibitor).
4. Effects of a *Mucuna* preparation lacking L-DOPA.

**Materials and Methods**

Twenty-four 6-hydroxydopamine (6-OHDA) lesioned rats were used (Sprague Dawley, males, 8-9 g 6-OHDA free base in 2 μl saline, 0.1% ascorbic acid stereotaxically injected into left medial forebrain bundle) all displaying significant contralateral forelimb akinesia and amphetamine-induced rotations 3-5 weeks post-surgery.

Ten rats were assigned to a chronic “dose-finding” study (series M1, two periods of 4 weeks treatment) and 14 rats assigned to a comparative study of therapeutic and adverse effects of chronic *Mucuna* versus L-DOPA treatments without additives (series M2-D2, 4 daily injections in week 1, 5 injections in week 2 and 7 injections in week 3).

After a wash-out period of 4 weeks the latter group of 14 rats was used to study effects of *Mucuna* and L-DOPA in the presence of benserazide and of *Mucuna* extract lacking L-DOPA.

Forelimb akinesia, therapeutic and adverse effects (i.e. abnormal involuntary movements, AIMs) of different target treatments were assessed using the cylinder test, recorded on video and rated on a scale from 0-6 (Lundblad et al. 2002).

*Mucuna* extracts containing ca. 20% L-DOPA (dry weight extract) were prepared by preparative HPLC. *Mucuna* or L-DOPA preparations were solubilized in saline, 1% ascorbic acid and mass spectrometry to ensure reproducible quality. A Mucuna extract lacking the major constituent L-DOPA was prepared by preparative HPLC. *Mucuna* or L-DOPA preparations were solubilized in saline, 1% ascorbic acid and administered i.p. in a volume up to 12.5 ml/kg. Benserazide was used at a dose of 15 mg/kg.

Rats were killed and brains dissected one week after the last *Mucuna* or L-DOPA injection. Dopamine and 5-hydroxytryptamine (5-HT) levels in ipsilateral and contralateral striatum were determined by HPLC with electrochemical detection (Gramsbergen et al. 2002).

**Results**

Therapeutic dose finding: *Mucuna* without benserazide

Therapeutic effect chronic treatment

Adverse effects

Conclusions:

• Chronic *Mucuna* treatments induced a sustained motor improvement that took days to build up and lasted for 3-4 days after cessation of treatment, i.e. similar to the long duration response of L-DOPA treatment. Determination of the lowest, therapeutically effective doses required therefore repeated dosing.

• *Mucuna* extract was more effective than synthetic L-DOPA at equivalent L-DOPA doses of 12.5-25 mg/kg ip. However, chronic treatment with these doses of *Mucuna* extract caused also more severe AIBs (predominantly ballistic, but also axial and orofacial dyskinesias) than L-DOPA alone.

• Co-treatments with benserazide in *Mucuna* or L-DOPA-sensitized rats, did not reveal differences in therapeutic or adverse effects of *Mucuna* or L-DOPA.

• *Mucuna* extract lacking L-DOPA did not show any therapeutic effect. This study in 6-OHDA lesioned rats did not reveal clinical benefits of *Mucuna* treatment over conventional L-DOPA therapy.

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**References**
