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

Gramsbergen, Jan Bert; Jørgensen, Monica; Christensen, Lars Porskjær

Published in:
Journal of Neurochemistry

Publication date:
2011

Document version
Final published version

Citation for published version (APA):

Terms of use
This work is brought to you by the University of Southern Denmark through the SDU Research Portal.
Unless otherwise specified it has been shared according to the terms for self-archiving.
If no other license is stated, these terms apply:

- You may download this work for personal use only.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying this open access version

If you believe that this document breaches copyright please contact us providing details and we will investigate your claim.
Please direct all enquiries to puresupport@bib.sdu.dk

Download date: 30. Jan. 2020
Dose- and time-dependent therapeutic and adverse effects of Mucuna pruriens extract in the 6-OHDA rat model of Parkinson's disease

Jan Bert Gramsbergen1, Monica Jørgensen1 and Lars Parajkar Christensen1

1Institute of Molecular Medicine, Institute of Chemical Engineering, Biotechnology and Environmental Technology, University of Southern Denmark, Odense, Denmark

E-mail: jan.bertram@idSilkeborg.sdu.dk

Introduction

In traditional Ayurvedic Indian medicine, preparations of Mucuna pruriens seeds 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-term benefit without concomitant increases in dyskinesias. Katzenschlager et al. (2004), Kasture et al. (1995) and Liu et al. (2010) have recently reported that Mucuna extracts are rich in L-DOPA, but other, as yet unknown compounds may contribute to its therapeutic effects.

Objectives

• In 6-OHDA-induced parkinsonian rats, we determined:
  1. Therapeutically effective doses of a methanol extract of Mucuna pruriens seeds and of (synthetic) L-DOPA 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-six 6-OHDA-lesioned rats (Sprague Dawley, males, 6-8 weeks old) were used for this study. All rats were housed individually and kept on a 12h-light/12h-dark cycle with ad libitum access to food and water. Upon sacrifice, animals were perfused with saline followed by 4% paraformaldehyde. Brains were removed and post-fixed in 4% paraformaldehyde. Sagittal sections were cut at 40 µm on a cryostat and stained with cresyl violet.

Results

1. Therapeutically effective doses of a methanol extract of Mucuna pruriens seeds and of (synthetic) L-DOPA without additives.

   (Figure 1) These results show that the therapeutic effects of Mucuna extract are dose-dependent and that the therapeutic window is considerably larger than for L-DOPA. The therapeutic window for Mucuna extract is between 2.5 and 20 mg/kg, while for L-DOPA, the therapeutic window is between 5 and 10 mg/kg.

2. Abnormal involuntary movements (AIMs) during chronic treatment at therapeutically effective doses.

   (Figure 2) These results show that Mucuna extract treatment caused AIMs, while L-DOPA treatment did not. This suggests that Mucuna extract may have adverse effects that are not seen with L-DOPA.

3. Dose-dependent effects of Mucuna extract and L-DOPA in the presence of benserazide (peripheral decarboxylase inhibitor).

   (Figure 3) These results show that the dose-dependent effects of Mucuna extract are attenuated by benserazide, while L-DOPA effects are not affected. This suggests that the adverse effects of Mucuna extract are mediated by peripheral decarboxylases.

4. Effects of a Mucuna preparation lacking L-DOPA.

   (Figure 4) These results show that a Mucuna preparation lacking L-DOPA does not have the same therapeutic effects as Mucuna extract with L-DOPA, indicating that L-DOPA contributes to the therapeutic effects of Mucuna extract.

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. Deformation 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.

• However, chronic treatment with these doses of Mucuna extract caused also more severe AIMs (predominantly dystonias, but also axial and orofacial dystonias) than L-DOPA alone.

• Co-treatments with benserazide in Mucuna or L-DOPA-sensitized rats, did not reveal new 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.

Acknowledgements

This work is supported by Industriekoncern Danmark and Forma.(8421).

References


Acknowledgements

This work is supported by Industriekoncern Danmark and Forma.(8421).