A Method For Treating Manganese Toxicity In A Subject

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INVENTORS

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OTHER INFORMATION

KEYWORDS

manganese, manganism, SLC30A10, HIF, prolyl hydroxylase inhibitor, parkinsonism, small molecule inhibitor, daprodustat, desidustat, enarodustat, molidustat, roxadustat, vadadustat, manganese homeostasis

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System
  - Disease: Genetic Diseases and Dysmorphic Syndromes
  - Therapeutics

RELATED CASES

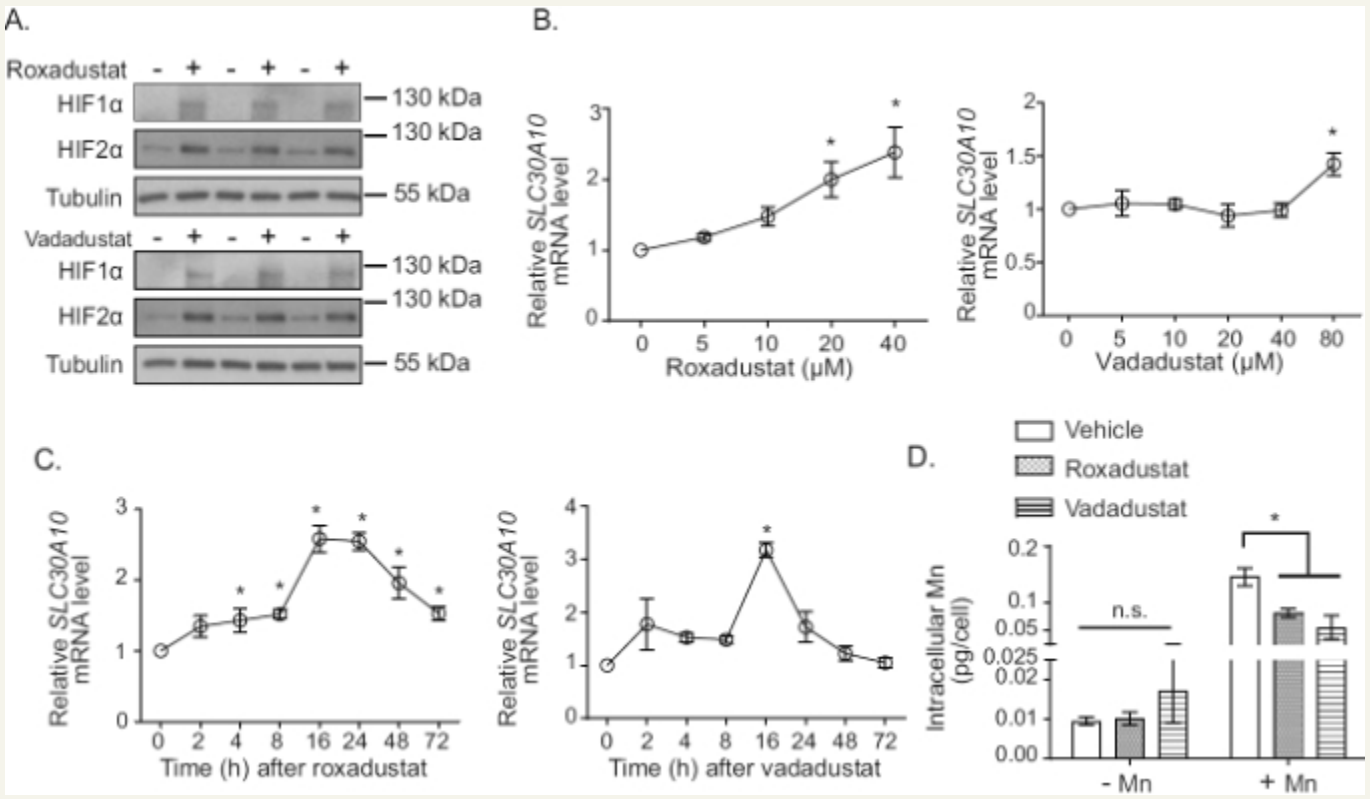
2022-802-0

BACKGROUND

Manganese (Mn) is an essential metal that must be maintained at levels within a narrow physiological range in cells and organisms to avoid deficiency or toxicity. Humans can be exposed to elevated manganese levels from occupational sources (e.g., welding) or environmental sources (e.g., drinking water). Elevated manganese levels cause manganese to accumulate in the brain, inducing neurotoxicity that can manifest as parkinsonism. Thus, manganese toxicity is a public health concern and developing ways to treat it is crucial. Based on elucidative manganese homeostasis studies, a UC Santa Cruz researcher, in collaboration with researchers at University of Texas at Austin, has developed methods for treating manganese toxicity.

TECHNOLOGY DESCRIPTION

The methods include treating manganese toxicity with hypoxia inducible factor (HIF) prolyl hydroxylase inhibitors, such as Roxadustat. The methods are based on the discovery, among others, that upregulating the manganese transporter SLC30A10 increases manganese excretion and protects against manganese toxicity. HIF-1 and HIF-2 proteins are thought to increase SLC30A10 expression. Normally, prolyl hydroxylases target the HIF-α subunits of HIF proteins so that the HIF-α subunits can ultimately be degraded. By administering HIF prolyl hydroxylase inhibitors to a subject, prolyl hydroxylation of HIF-α subunits is inhibited, and HIF-α subunits are stabilized. HIF protein levels then increase, which upregulates SLC30A10, which in turn protects against manganese toxicity.



APPLICATIONS

- treating manganese toxicity
- treating manganese-induced parkinsonism

ADVANTAGES

- repurposes existing prolyl hydroxylase inhibitors

INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Published Application	20230101768	03/30/2023	2022-802

Additional Patent Pending

RELATED MATERIALS

▶ Up-regulation of the manganese transporter SLC30A10 by hypoxia-inducible factors defines a homeostatic response to manganese toxicity - 08/26/2021

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