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Original Article | [Published: 16 January 2009](#)

# Molecular hydrogen alleviates nephrotoxicity induced by an anti-cancer drug cisplatin without compromising anti-tumor activity in mice

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*Cancer Chemotherapy and Pharmacology* **64**, 753–761 (2009)

**1888** Accesses | **136** Citations | **7** Altmetric | [Metrics](#)

## Abstract

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### Purpose

Cisplatin is a widely used anti-cancer drug in the treatment of a wide range of tumors; however, its application is limited by nephrotoxicity, which is affected by oxidative stress. We have reported that molecular hydrogen (H<sub>2</sub>) acts as an efficient antioxidant (Ohsawa et al. in *Nat Med* 13:688–694, 2007). Here we show that hydrogen efficiently mitigates the side effects of cisplatin by reducing oxidative stress.

## Methods

Mice were administered cisplatin followed by inhaling hydrogen gas (1% H<sub>2</sub> in air). Furthermore, instead of inhaling hydrogen gas, we examined whether drinking water containing hydrogen (hydrogen water; 0.8 mM H<sub>2</sub> in water) is applicable by examining oxidative stress, mortality, and body-weight loss. Nephrotoxicity was assessed by morphological changes, serum creatinine and blood urea nitrogen (BUN) levels.

## Results

Inhalation of hydrogen gas improved mortality and body-weight loss caused by cisplatin, and alleviated nephrotoxicity. Hydrogen was detected in blood when hydrogen water was placed in the stomach of a rat. Consuming hydrogen water ad libitum also reduced oxidative stress, mortality, and body-weight loss induced by cisplatin in mice. Hydrogen water improved metamorphosis accompanying decreased apoptosis in the kidney, and nephrotoxicity as assessed by serum creatinine and BUN levels. Despite its protective effects against cisplatin-induced toxicity, hydrogen did not impair anti-tumor activity of cisplatin against cancer cell lines in vitro and tumor-bearing mice in vivo.

## Conclusion

Hydrogen has potential for improving the quality of life of patients during chemotherapy by efficiently

mitigating the side effects of cisplatin.

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## Acknowledgments

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We thank Blue Mercury Inc. (Tokyo, Japan) for the generous gift of hydrogen water. This work was supported by grant from the Ministry of Education, Culture, Sports, Science and Technology of Japan (19659331, S. O. and 20500723 to N. N.-K.).

## Conflict of interest statement

Dr. Ohta is a director of Mito Co. Ltd. (Kawasaki, Japan), and a scientific adviser to Blue Mercury Inc. (Tokyo, Japan). Blue Mercury Inc. supplied the fresh hydrogen water used in this study and has donated a research division to our institute.

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Cite this article

Nakashima-Kamimura, N., Mori, T., Ohsawa, I. *et al.*

Molecular hydrogen alleviates nephrotoxicity induced by an anti-cancer drug cisplatin without compromising anti-tumor activity in mice. *Cancer Chemother Pharmacol* **64**, 753–761 (2009). <https://doi.org/10.1007/s00280-008-0924-2>

Received

24 September  
2008

Accepted

30 December  
2008

Published

16 January 2009

Issue Date

September 2009

DOI

<https://doi.org/10.1007/s00280-008-0924-2>

Keywords

**Antioxidant**

**Cisplatin**

**Dihydrogen**

**Oxidative stress**

**Side effect**