

University of Groningen

## The availability of inorganic sulfate for sulfate conjugation of xenobiotics in the rat in vivo

Krijgsheld, Klaas Reinder

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

1982

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Krijgsheld, K. R. (1982). *The availability of inorganic sulfate for sulfate conjugation of xenobiotics in the rat in vivo*. s.n.

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

## SUMMARY

The availability of inorganic sulfate as a factor determining the rate and the extent of sulfate conjugation of xenobiotics in vivo is investigated in the rat.

To estimate the pool size of inorganic sulfate under various experimental conditions the concentration of sulfate in serum or plasma, and the excretion of sulfate in urine has been determined. In mammals rather large species differences were found in the serum concentration of sulfate. In addition, we observed in the rat a daily circadian rhythm in serum sulfate (Supplement I).

The serum concentration of sulfate was significantly increased by oral administration of sodium sulfate (Supplement II) or cysteine (Supplement III). Inorganic sulfate was rapidly absorbed from the gastro-intestinal tract and was almost completely excreted in urine within 24 hr. The extent of sulf-oxidation of cysteine to inorganic sulfate was different for the two stereo-isomers of cysteine, L- and D-cysteine. D-cysteine was degraded to sulfate more rapidly and to a larger extent than L-cysteine, probably because D-cysteine cannot be incorporated into glutathione and various proteins.

To investigate the role of sulfation in the metabolism of its xenobiotic substrates, two methods to decrease the availability of inorganic sulfate in the rat have been developed. The serum concentration of sulfate was decreased (a) by feeding a low-protein diet, or (b) by administration of a large dose of a substrate of sulfation (Supplement IV). Low sulfate availability limited sulfation capacity and, thereby, increased the risk of toxic effects of xenobiotics that are substrate of sulfation (Supplement V).

When the plasma concentration of sulfate in the rat decreased below its physiological concentration (about 0.9 mM) the rate of sulfation of harmol was significantly decreased. An increase of plasma sulfate above the physiological level caused no additional increase in sulfation rate. The apparent  $K_m$  for sulfate in the overall sulfation of harmol (sulfate activation and sulfate transfer) was estimated to be about 0.3 - 0.4 mM (Supplement VI).

## LIST OF PUBLICATIONS

- Weitering, J.G., Krijgsheld, K.R., Mulder, G.J.: Inorganic sulfate and the availability of inorganic sulfate for the sulfation of xenobiotics in vivo. *Biochem. Pharmacol.* 1971, 18, 1001-1006.
- Krijgsheld, K.R., Mulder, G.J.: Absorption and excretion of inorganic sulfate after oral administration. *Biochim. Biophys. Acta* 1971, 25, 100-104.
- Krijgsheld, K.R., Mulder, G.J.: The availability of inorganic sulfate for the sulfation of xenobiotics. *Comp. Biochem. Physiol.* 1971, 68B, 1001-1006.
- Krijgsheld, K.R., Mulder, G.J.: The effect of a low-protein diet on the availability of inorganic sulfate for the sulfation of xenobiotics in the rat. *Biochim. Biophys. Acta* 1971, 25, 105-109.
- Krijgsheld, K.R., Mulder, G.J.: The effect of a large dose of a substrate of sulfation on the availability of inorganic sulfate for the sulfation of xenobiotics in the rat. *Biochim. Biophys. Acta* 1971, 25, 110-114.
- Krijgsheld, K.R., Mulder, G.J.: The effect of a low-protein diet on the sulfation capacity of the rat. *Col. Exp. Ther.* 1971, 18, 1001-1006.
- Mulder, G.J. and Krijgsheld, K.R.: The availability of inorganic sulfate for the sulfation of xenobiotics in the rat. *Health Research* 1971, 1, 1001-1006. Publishers Ltd.
- Krijgsheld, K.R., Mulder, G.J.: The effect of a low-protein diet on the sulfation capacity of the rat. *Health Research* 1971, 1, 1001-1006. Publishers Ltd.
- Krijgsheld, K.R., Mulder, G.J.: The effect of a large dose of a substrate of sulfation on the sulfation capacity of the rat. *Health Research* 1971, 1, 1001-1006. Publishers Ltd.