

# VU Research Portal

## No aspirin in red wine

Janssen, P.L.T.M.K.; Katan, M.B.; Hollman, P.C.H.; Venema, D.P.

### **published in**

Lancet  
1994

### **DOI (link to publisher)**

[10.1016/S0140-6736\(94\)92258-6](https://doi.org/10.1016/S0140-6736(94)92258-6)

### **document version**

Publisher's PDF, also known as Version of record

### [Link to publication in VU Research Portal](#)

### **citation for published version (APA)**

Janssen, P. L. T. M. K., Katan, M. B., Hollman, P. C. H., & Venema, D. P. (1994). No aspirin in red wine. *Lancet*, 344(8924), 762. [https://doi.org/10.1016/S0140-6736\(94\)92258-6](https://doi.org/10.1016/S0140-6736(94)92258-6)

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- 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 the publication in the public portal

### **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.

### **E-mail address:**

[vuresearchportal.ub@vu.nl](mailto:vuresearchportal.ub@vu.nl)

## Lack of voltage-dependent anion channel in human mitochondrial myopathies

SIR—In several hundreds of patients with a mitochondrial myopathy an enzyme defect in mitochondrial energy metabolism is identified. However, in a substantial number of subjects no enzyme defect can be detected, although diminished substrate oxidation and ATP production rates are found in their muscle *in vitro*. The hypothesis, that in this group of patients proteins for transport of various ions and substrates across mitochondrial membranes might be affected, led us to study these transport proteins more systematically. Among 40 investigated patients, 1 was found with a diminished content of the voltage-dependent anion channel (VDAC or human porin).

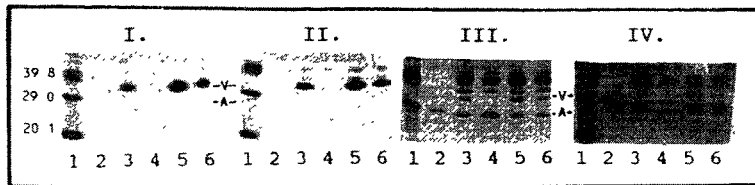


Figure: Immunoblots with VDAC and ANT antisera

Samples of muscle 600 g supernatants from patient (lanes 4) and 3 controls (lanes 3, 5, 6) were dissolved in sodium dodecylsulphate and loaded on polyacrylamide gels (10–15% gradient), together with biotinylated molecular weight markers (lanes 1: 39.8, 29.0, 20.1 kDa) and purified ANT (lanes 2: 29 kDa). All lanes of controls and patient contained 100 mU cytochrome c oxidase (the patient's muscle had normal cytochrome c oxidase activity). After electrophoresis (Phast System, Pharmacia-LKB, Woerden, Netherlands) proteins were electroblotted to nitrocellulose. Immunolabelling of the proteins was done with 4 different antibodies: human B-lymphocyte VDAC monoclonal antibodies from 2 different cell lines (mAb-No 4 in panel I and mAb-No 6 in panel II),<sup>1</sup> anti-bovine heart VDAC<sup>2</sup> (panel III), and anti-C-terminal bovine heart ANT<sup>3</sup> (panel IV). Immunodetection was done applying the Biotin-ECL method (Amersham International, UK).

The patient was born at term from non-consanguineous parents. He had dysmorphism, hypotonia, respiration and feeding problems, and seizures. He was treated for hypothyroidism. Because of lactic acidosis a quadriceps muscle biopsy specimen was taken at the age of 2 years. Decreased rates of pyruvate and malate oxidation and of ATP production were found. The content of the membrane transport proteins VDAC and ATP/ADP translocator (ANT) were estimated immunochemically. The amount of VDAC protein (35 kDa, marked by -v- in figure) appeared to be clearly decreased, with use of monoclonal anti-N-terminal human VDAC (figure; panels I, II), and polyclonal anti-bovine-heart VDAC (panel III) antibodies. The ANT content (29 kDa, marked by -A-) appeared to be slightly reduced. The polyclonal antiserum also reacted with other supernatant proteins (panel III). In this panel the VDAC deficiency of the patient was additionally confirmed: apart from the VDAC protein the amounts of all proteins, including ANT, were similar to those in controls.

To our knowledge, this case is the first in which a lack of VDAC protein has been shown in human pathology. The detailed function of VDAC is still under investigation. VDAC is a pore-forming protein in the outer mitochondrial membrane, which at low transmembrane voltage is open for anions such as phosphate, chloride, and adenine nucleotides. At higher transmembrane voltage or in the presence of VDAC-modulating proteins VDAC can function as a selective channel for cations and uncharged molecules.<sup>4</sup> These features make VDAC likely to play a regulatory role in mitochondrial energy metabolism.<sup>5</sup> The lack of VDAC might cause a bottleneck in the outer membrane

of the patient's muscle mitochondria with respect to ADP and/or inorganic phosphate transport inwards, or ATP transport outwards, thereby disturbing energy metabolism.

Marjan Huizing, Wim Ruitenbeek, Friedrich P Thinnies, Vito DePinto

Department of Paediatrics, University Hospital Nijmegen, PO Box 9101, NL-6500, Nijmegen, Netherlands; Max Planck Institut für Experimentelle Medizin, Göttingen, Germany; and Università di Bari, Bari, Italy

- 1 Babel D, Walter G, Götz H, et al. Studies on human porin, VI: production and characterization of eight monoclonal mouse antibodies against the human VDAC "Porin 31 HL" and their application for histological studies in human skeletal muscle. *Biol Chem Hoppe Seyler* 1991; **372**: 1027–34.
- 2 DePinto V, Prezioso G, Thinnies F, Link TA, Palmieri F. Peptide specific antibodies and proteases as probes of the transmembrane topology of the bovine heart mitochondrial porin. *Biochemistry* 1991; **30**: 10191–200.
- 3 Brandolin G, Boulay F, Dalbon P, Vignais PV. Orientation of the N-terminal region of the membrane-bound ADP/ATP carrier protein explored by antipeptide antibodies and an arginine-specific endoprotease: evidence that the accessibility of the N-terminal residues depends on the conformational state of the carrier. *Biochemistry* 1989; **28**: 1093–100.
- 4 Mannella CA. The 'ins' and 'outs' of mitochondrial membrane channels. *Trends Biochem Sci* 1992; **17**: 315–20.
- 5 Liu MY, Colombini M. Regulation of mitochondrial respiration by controlling the permeability of the outer membrane through the mitochondrial channel, VDAC. *Biochim Biophys Acta* 1992; **1098**: 255–60.

## No aspirin in red wine

SIR—Muller and Fugelsang (June 4, p 1428) suggest that wine is a good source of salicylic acid and that this may explain a preventive effect in cardiovascular diseases. We measured salicylic and acetylsalicylic acid in red Bordeaux wines (Rineau 1993, Lavergne 1993, and Mondetour, 1992) with high-performance liquid chromatography and a highly specific fluorescence detection method. The method was validated by varying extraction conditions, mainly extraction solvents and extraction time. In red wine we found 0.7 mg salicylic acid per litre and no acetylsalicylic acid (detection limit 0.025 mg/L). Thus, by contrast with Muller and Fugelsang we found negligible amounts of (acetyl)salicylic acid in wine. Even if wine did contain larger amounts of salicylic acid this would not be expected to affect cardiovascular risk. Salicylic acid and dihydroxybenzoic acids do not affect thromboxane B<sub>2</sub> formation and platelet aggregation; this specifically requires acetylsalicylate (aspirin), which inactivates cyclo-oxygenase by irreversible acetylation.<sup>1</sup>

Supported by a PhD fellowship from the Wageningen Agricultural University, and grants from the Netherland Heart Foundation (93084) and the Netherlands Foundation for Nutrition and Health Research.

P L T M K Janssen, M B Katan, P C H Hollman, D P Venema  
Department of Human Nutrition, Agricultural University, 6703 HD, Wageningen, Netherlands; and State Institute for Quality Control of Agricultural Products (RIKILT-DLO), Wageningen

- 1 Roth GJ, Calverley DC. Aspirin, platelets, and thrombosis: theory and practice. *Blood* 1994; **83**: 885–98.

## CORRECTION

Effect of simvastatin on coronary atheroma—In figure 1 of the article by MAAS investigators (3 Sept, p 633), the indicators for placebo and simvastatin were incorrect. Placebo is represented by open circles connected by solid lines and simvastatin by filled circles connected by interrupted lines.