

## EDITOR'S NOTE

# 2-Aminoethylnitrate: earlier investigation as a drug was missed by recent authors due to changes in nomenclature

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*Editor in Chief, British Journal of Pharmacology***Linked Article**

This Editor's Note accompanies correspondence by Uppu and Daiber. To view the letter by Uppu visit <http://dx.doi.org/10.1111/bph.12146>. To view the letter by Daiber visit <http://dx.doi.org/10.1111/bph.12147>.

Drugs or compounds that are tested as potential drugs can be known by several different names. We have all scratched our heads a bit trying to chase a drug name through the literature. We now publish a letter drawing attention to a paper in BJP whose title starts off with 'A new class of organic nitrates:' (Schuhmacher *et al.*, 2009) and which had an accompanying Commentary entitled 'Aminoethyl nitrate – the novel super nitrate?' (Bauersachs, 2009). The Letter writer, Miss Satvika Uppu, an undergraduate student at Louisiana State University, points out that this chemical, known by a different name, had been tested for such an effect fifty years ago (Batterman and Mouratoff, 1963).

We now publish her letter together with a response from the paper's authors. We will also publish their response as a correction to the paper.

As a Pharmacological journal, BJP's 'Author Guidelines' ([http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1476-5381/homepage/ForAuthors.html](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1476-5381/homepage/ForAuthors.html)) state that 'Drug names should be International Non-proprietary Names (INN). See website <http://mednet.who.int> for a full list. If a drug has no INN, its full chemical name must be used (for nomenclature rules, see Handbook for Chemical Society Authors (London, Chemical Society – <http://rsc.org>) or its structural formula given'. This was all in order in the paper in question and a search in the RSC site does lead back to the old names. So the authors of the recent BJP paper should have found and mentioned the papers cited by Miss Uppu, but, as they explain, this was understandable.

The compound aminoethyl nitrate was investigated for its vasodilator and anti-anginal properties around 1960 and, particular formulations, was given two names: itramin tosylate or Nilatil (which was trademarked). In the light of this, the title of the paper 'A new class of organic nitrates . . .' seems inappropriate.

The reason that this early work was missed may relate to the fact that no one cited it. The original paper by Batterman and Mouratoff (1963) does not seem to have been cited at all, and the one by Kinnard *et al.* (1964) was cited once, by Fremont (1967), and that seems not to have been cited. However, Miss Uppu found them so it was possible! Alerted by her detective work, I found another couple of papers, one earlier (Ehrenberger, 1960), one later (Takenaka and Umeda, 1976), than the ones she found.

Of course, the recent paper in BJP provides new information on mechanisms of action. In the 1960s, there was little knowledge of the mechanism of action of nitrates. It was in the late 1970s that Furchgott and Zawadzki (1980) discovered that NO was released from vascular endothelium and that led to a great amount of work on the mechanisms of nitrates which donate NO. I am quite sure that there was no intention to deceive as Miss Uppu implies. We all miss things sometimes.

**References**

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Schuhmacher S, Schulz E, Oelze M, König A, Roegler C, Lange K *et al.* (2009). A new class of organic nitrates: investigations on

bioactivation, tolerance and cross-tolerance phenomena. *Br J Pharmacol* 158: 510–520.

Takenaka F, Umeda T (1976). Effect of propranolol, itramin tosylate and dipyridamole on myocardial phosphate metabolism in anoxic perfused rat hearts. *Arch Int Pharmacodyn Ther* 222: 45–54.

## LETTERS TO THE EDITOR

# 2-Aminoethylnitrate: pharmacological uses rediscovered and claimed as original

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I am writing regarding an article I read recently which was published in your journal. The article, entitled 'A new class of organic nitrates: investigations on bioactivation, tolerance and cross-tolerance phenomena' was published by Schuhmacher *et al.* (2009). I happened to see this article while working as an undergraduate student researcher in a chemistry/biochemistry laboratory. The article presents the mononitrate compound 2-aminoethylnitrate as a modern marvel in the treatment of endothelial dysfunction that leads to cardiovascular disease(s). I was asked to synthesize this compound and as per my aspiration to understand the details and purpose of my assignment, I delved into a search for some useful references. During this process, I stumbled upon an article dating back to 1963 titled Anginal syndrome: Treatment with a long-acting nitrate (itramin tosylate) published by Batterman and Mouratoff (1963). This article addressed the use of 2-aminoethylnitrate in its p-toluenesulfonate salt form for the treatment of anginal syndrome. Not only had this idea been discussed in this article, but a number of clinical trials had also been performed relaying successful results. Also, some of the observations were confirmed by Kinnard *et al.*, (1964). I found it quite intriguing that nearly the same information is presented in the article by Schuhmacher *et al.* (2009) who failed to mention, acknowledge or cite the earlier works which were published more than 40 years before their article. Upon discovering this, I brought this information to my mentor's attention who encouraged me to write to the editor to raise awareness of the issue. I was later surprised to also find a supportive and encouraging commentary written by Bauersachs (2009) in

the same issue of British Journal of Pharmacology (BJP). Understandably, there was an attempt of undue, instant promotion of the use of 2-aminoethylnitrate as a modern breakthrough in which BJP became an inadvertent partner. I am concerned about the reputation of BJP and also the fact that this type of percolation of scientific errors must stop before they become a dogma and therefore have taken the initiative to bring this to your attention.

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### Linked Article

This letter is responded to by Daiber, pp. 951–952 of this issue. To view the letter visit <http://dx.doi.org/10.1111/bph.12147> These letters are accompanied by an Editor's Note on pp. 949–950 of this issue. To view visit <http://dx.doi.org/10.1111/bph.12148>

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