photographs and in figure 8.17, the shy-natured girls are posing as though they are doing some work and the only person (a woman but not a child) actually working in that photograph is facing away from the camera. The gem industry in India has taken proper care to avoid child labour. Moreover, the type of labour in this industry needs a considerable expertise that *only an experienced adult can provide*. The photographs have been published unintentionally and should not be misinterpreted as projecting 'child labour in India'. The Gem and Jewellery Export Promotion Council and Ministry of Commerce in India have taken stern action against child labour involved in this industry. At least as far as my knowledge goes child labour does not exist in the gem cutting industry in India.

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Srote features

A few years back we had received your permission to reproduce articles from *Current Science* in our feature service. We are happy to inform you that we have, since then, reproduced a number of general articles from *Current Science* and these have been well received in Hindi newspapers.

Through this letter, we would like to request the authors of your esteemed journal to contribute to *Srote* (स्रोत) *features* service. *Srote features* is a project sponsored by the National Council of Science & Technology Communication and actualized by 'Eklavya', a voluntary organization working in the field of education. *Srote features* is focused on S&T issues, especially the issues at STS interface. It is dispatched every week to around 150 Hindi newspapers. *Srote* has been published over the last 12 years and its acceptance amongst newspapers is established.

We try to feed authentic S&T information to newspapers, especially small and medium ones. However, not many authors write. We would like the authors to contribute articles (around 1500 to 2000 words) on topics of their choice and of general interest. Even if they write in English, *Srote* will get them translated.

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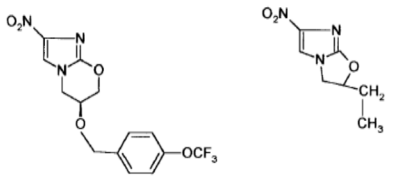
Nitrobicyclicimidazoles with potent antitubercular activity

I wish to offer some remarks on the article entitled 'A new broad-spectrum antitubercular drug on the horizon' by Pawan Sharma[1]. The properties of PA-824 (**1**) and the thoroughness of the investigation do deserve to be highlighted, although I wonder whether the use of the term 'broad spectrum' is justified, since the activity of **1** according to the authors is highly specific for the *Mycobacterium tuberculosis* (*MTB*) complex and is moderate or negligible against Mycobacteria outside the *MTB* complex (*M. avium*, *M. smegmatis* and *M. fortuitum*)[2].

I like to use this forum more to introduce the anti TB activity of nitroimidazooxazole, CGI 17341 (**2**) (ref. 7 in the article) which we had synthesized at Ciba-Geigy Research Centre in 1984 and which we first published in 1989 (ref. 3). **2** was about equiactive with isoniazid and rifampicin H 37 Rv *in vitro*. In an *in vivo* mouse model with *M. bovis* infection, **2** was more than half as active as rifampicin. In a subsequent publication[4] which Sharma's article does not refer to, we had shown that **2** was highly active *in vitro* against strains of *MTB* resistant to isoniazid, rifampicin, ethambutol and streptomycin. It was moderately active against *M. kansai*, *M. scrofulaceum* and *M. gordonae* but inactive against *M. avium*, *M. fortuitum* and *M. intracellurare*. Interestingly the *MIC* of **2** against *MTB* strain 437Rv was independent of the pH of the medium in the range of 5.6 to 6.8 like rifampicin, whereas those of isoniazid and ciprofloxacin were increased 4 to 6 times at the lower pH in this range. In an *in vivo* model of *MTB* infection in mice, **2** was highly active with a potency of about 50% of isoniazid and rifampicin. Stover *et al.*[2] have acknowledged our two publications in their paper in *Nature* as well as in their patents.



1 PA-824 **2** CGI 17341

2 was mutagenic in the standard Ame's test while **1** is reported by Stover

et al.[2] to be nonmutagenic (data not shown). It remains to be seen whether the test systems are comparable. However the mutagenicity of **2** need not have prevented its further development since nitroimidazoles are known to be mutagenic, but drugs like metronidazole have not shown any adverse properties related to this trait in more than three decades of clinical use[5]. Moreover the relevance of Ame's test is a matter of continuous debate. In terms of the novelty of the structure for anti TB activity, high *in vitro* activity, including that against drug-resistant strains and *in vivo* potency, **2** could have been taken up for further development, but due to a combination of several unfortunate circumstances which I have described elsewhere[6], Ciba-Geigy did not pursue this despite an expression of interest from WHO. In this context, I invite the readers to refer to a publication of WHO's Tropical Diseases Research Group wherein one of the disincentives to anti TB research has been mentioned as the miniscule size of the anti TB market at less than US $ 150 million per annum, compared to the total world pharma market of over US $ 300 billion, while the cost of developing a new drug has been placed at US $ 300 to 500 million.

Sharma's article repeats two factual errors found in the publication of Stover *et al.*[2] on **1**. The molecule is a nitroimidazo-oxazine and *not* a nitroimidazopyran, thus embarassingly questioning the appropriateness of the acronym NAP! It also repeats the statement that no new drug with novel mechanism of action against the tubercular bacillus has appeared in the last three decades. This is questionable since antibacterial quinolones like ofloxacin and sparfloxacin with inhibitory action on topoisomerase II have recently found clinical use in the treatment of TB, while macrolides like clairthromycin and azithromycin are also under investigation as components of multidrug anti TB therapy[7].

Further, the oxazolidinone U-100480 (ref. 8), a close analogue of the recently introduced antibacterial drug, linezolid, has probably entered clinical trials as an anti TB drug. The oxazolidinones are reported to act by very early inhibition of protein synthesis prior to chain initiation. I had written a letter to *Nature* pointing out these errors, but did not have the pleasure of publication in the prestigious journal even sideways! I resist the temptation to ascribe it to the geography of my genesis and concede that *Nature* publishes more momentous matters!

Lastly, Stover *et al.*[2] mention a test against nonreplicating *MTB* in an anaerobic culture model wherein metronidazole, **1** and **2** are active, the first two more than the last. Referring to this, Sharma has opined that people with latent TB (and they constitute one-third of the entire human population!) are largely responsible for the high incidence of the disease and hence **1** holds strong promise of cutting down the incidence to a very significant extent. This activity has been known for metronidazole since 1994 (ref. 9). I wonder whether any of your readers can comment on the appropriateness or worthwhileness of adding this popular antiprotozoal–antianaerobic drug to the existing multi-drug therapy of TB.

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