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Martin Seed and Raymond Agius

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LETTER

Further corroboration of the asthmagenicity of 5-aminosalicylic acid

Sastre *et al* described a case of occupational asthma caused by a novel low molecular weight (LMW) respiratory sensitiser, 5-aminosalicylic acid (5-ASA).¹ They concluded that the mechanism was probably not IgE-mediated because of a negative skin prick test and a late response to bronchial challenge testing with 5-ASA. They remarked, as is the case with several other LMW asthmagens, that the mechanism by which 5-ASA caused asthma is unknown.

Such uncertainty, and likely heterogeneity, in the pathophysiological mechanisms of asthma due to LMW chemicals is one of the reasons why no single in vitro or in vivo testing method has been developed for the prediction of asthmagenic potential. One way round this problem has been to utilise an 'in silico' approach that makes no a priori assumptions about pathophysiological mechanism. The development of such a quantitative structure–activity relationship (QSAR) model and its initial validation was published in a previous edition of *Occupational and Environmental Medicine*.² This assigns an asthma hazard index which is a value between zero and one, and the most recent validation³ has demonstrated that it has good global predictive value.

By entering the chemical structure of 5-ASA (figure 1) into this model, an 'asthma hazard index' of 0.82 was obtained indicating a high probability of asthmagenicity.

Novel LMW chemical causes of occupational asthma such as the one reported by Sastre *et al* appear only intermittently in the literature, but respiratory physicians have used this QSAR model to provide

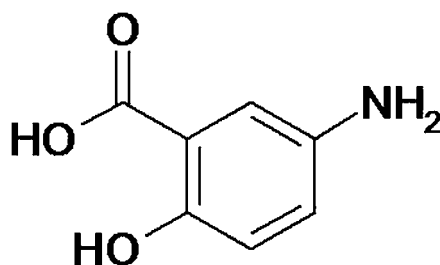


Figure 1 Chemical structure of 5-aminosalicylic acid (CAS RN 89-57-6).

corroborating evidence in the identification of a novel asthmagen.⁴ This model may also be of use when a clinician has diagnosed occupational asthma where the cause could be one of several LMW (organic) chemicals none of which are recognised respiratory sensitisers. By ranking the possible causes according to the QSAR generated asthma hazard index, it may be possible to prioritise the agent(s) with which the bronchial challenge testing can be performed. Further evaluation of the QSAR model for this purpose is planned and we would encourage respiratory and occupational physicians to utilise the model, which is freely available on the internet,⁵ for such purposes, and register their interest and observations by email with the undersigned.

Martin Seed, Raymond Agius

Centre for Occupational & Environmental Health, Health Sciences Group, School of Community Based Medicine, Faculty of Medical and Human Sciences, The University of Manchester, Manchester, UK

Correspondence to Martin Seed, Centre for Occupational & Environmental Health, Health Sciences Group, School of Community Based Medicine, Faculty of Medical and Human Sciences, The University of Manchester, Room C4.20, Ellen Wilkinson Building, Oxford Road, Manchester M13 9PL, UK; martin.seed@manchester.ac.uk

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Ethics approval In this letter, we encourage physicians to consider using a computer-based prediction model to help them investigate the cause of clinical cases of occupational asthma where a novel chemical sensitiser is suspected. The use of this asthma hazard prediction programme to assist physicians in their clinical investigation of such cases has been approved for a formal evaluation in the UK by the University of Manchester Committee on the Ethics of Research on Human Beings. The North West NHS Research Ethics Committee deemed such work to be more akin to service evaluation rather than research and hence did not require formal ethical approval. We therefore do not anticipate any new ethical issues arising from the contents of this letter.

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REFERENCES

1. Sastre J, del Potro MG, Aguado E, *et al*. Occupational asthma due to 5-aminosalicylic acid. *Occup Environ Med* 2010;**67**:798–9.
2. Jarvis J, Seed MJ, Elton RA, *et al*. Relationship between chemical structure and the occupational asthma hazard of low molecular weight organic compounds. *Occup Environ Med* 2005;**62**:243–50.
3. Seed MJ, Agius RM. Further validation of computer-based prediction of chemical asthma hazard. *Occup Med* 2010;**60**:115–20.
4. Moore VC, Manney S, Vellore AD, *et al*. Occupational asthma to gel flux containing dodecanedioic acid. *Allergy* 2009;**64**:1099–107.
5. The University of Manchester. Centre for Occupational and Environmental Health. Mechanisms of Occupational Asthma; Occupational asthma hazard prediction programme. <http://www.medicine.manchester.ac.uk/oeht/research/asthma/> (accessed Nov 2010).