**TABLE 1** Hazard indices of common vitamin compounds

| Vitamin | Molecular mass Da | Hazard index |
|---|---|---|
| All-trans retinoic acid (A) | 300.44 | 0.9329 |
| Retinyl palmitate (A) | 524.88 | 0.9974 |
| beta-carotene (provitamin A) | 536.89 | 0.9970 |
| Ergocalciferol ($D_2$) | 396.66 | 0.9432 |
| Cholecalciferol ($D_3$) | 384.65 | 0.9355 |
| Tocopherol acetate (E) | 472.76 | 0.9036 |
| Naphthoquinone (K) | 158.16 | 0.1600 |
| Phylloquinone ($K_1$) | 116.16 | 0.1157 |
| Menaquinone ($K_2$) | 168.15 | 0.2958 |
| Menadione (Provitamin K) | 172.19 | 0.2044 |
| Thiamine ($B_1$) | 263.34 | 0.9400 |
| Thiamine hydrochloride ($B_1$) | 338.28 | 0.9469 |
| Thiamine mononitrate ($B_1$) | 329.38 | 0.9548 |
| Riboflavin ($B_2$) | 376.37 | 0.9987 |
| Niacin ($B_3$) | 123.11 | 0.9169 |
| Pantothenic acid ($B_5$) | 219.24 | 0.9896 |
| Pyridoxine ($B_6$) | 169.18 | 0.0963 |
| Pyridoxine hydrochloride ($B_6$) | 205.64 | 0.0948 |
| Biotin (H/$B_7$) | 244.31 | 0.9631 |
| Folic acid ($B_9$) | 441.41 | 1.0000 |
| Cyanocobalamin ($B_{12}$)# | 1355.37 | |
| Ascorbic acid (C) | 176.13 | 0.0196 |

#: high molecular weight unsuitable for quantitative structural activity relationship model.

spectator anion seems to alter the hazard index only marginally. Significant differences in asthmagenicity are not observed between the provitamin, the naturally occurring vitamin or its synthetic derivative used in industry. The positive predictive value of the QSAR for the identification of suspect chemical asthmagens is >50%. Even in the context of testing random chemicals for asthmagens, the QSAR has a negative predictive value of 100%; thus vitamins $B_6$, C and K are certainly nonasthmagens. The property of water or fat solubility, which forms the basis of the traditional classification of vitamins, does not seem to be a determinant of a vitamin's asthma hazard index. Skin sensitisers are typically more hydrophobic than respiratory sensitisers. Both water-soluble and fat-soluble vitamins are used as additives in the food industry. Exposure at work to both of the above classes of vitamin compounds may occur, resulting in respiratory and skin sensitisation of workers during the manufacturing process.

In the milk powder factory study, it is possible that many of the work-related symptoms were caused by exposure to the vitamin compounds added to the milk powder [1]. Vitamins are commonly used as fortifying agents in the food industry and their asthmagenic potential in the workplace needs to be recognised.

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**STATEMENT OF INTEREST**
None declared.

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*From the authors:*

We recently reported results of a cross-sectional study of 167 milk powder factory workers and 76 office workers from Thailand showing that production and packing workers exposed to relatively low concentrations of milk powder experienced significantly increased risk of nasal symptoms and breathlessness, had clearly increased risk of wheezing and asthma, and had reduced spirometry [1]. Workers who added a vitamin mixture to milk had significantly increased risk of skin symptoms, in addition to having increased risk of nasal symptoms and reduced lung function. A.D. Vellore and colleagues address the respiratory sensitisation potential of vitamins by applying a quantitative structure-activity relationship model developed by Jarvis *et al.* [2] for low molecular weight agents. Based on an asthma hazard index calculated by the model, they conclude that vitamins, apart from vitamins B6, C and K, have high potential asthmagenicity. A.D. Vellore and colleagues suggest that in our milk powder factory study, exposure to vitamin compounds might explain ''many of the work-related symptoms''. The latter conclusion seems to be based on the chemical structure of vitamins, one previous case report of occupational asthma related to exposure to thiamine in a cereal worker, and some misunderstandings concerning our study, which need to be corrected.

In our study of the milk powder factory, only 22 (13%) of 167 factory workers worked in the vitamin-adding area, where they had exposure to a mixture of vitamins, minerals and corn syrup [1]. All vitamin-adding workers also had exposure to milk powder, while the other 145 workers did not have significant exposure to the vitamin mixture. Thus, it is not possible that exposure to vitamins could explain a high proportion of the respiratory symptoms detected in our study. When looking at individual exposures in the factory, milk powder was most consistently related to respiratory symptoms and reduced lung function. What was unique to vitamin-adding staff was increased risk of skin symptoms, which was most likely related to their use of natural rubber latex gloves, although it cannot be excluded that some of the skin symptoms could be explained by vitamin exposure.

A.D. Vellore and colleagues also state that milk protein allergy is ''well recognised'' as a cause of occupational asthma, without giving any reference for this. However, we performed a systematic Medline database search and were not able to identify any previous study assessing the risk of respiratory effects in relation to inhalation of milk powder. We were only able to identify four case reports linking milk protein exposure to occupational asthma and/or occupational rhinitis [3–6], which we refer to in our article. After our milk powder factory study had appeared in the *European Respiratory Journal*, we were contacted by a German research group who have noted similar findings related to milk powder exposure (R. Jäckel, Berlin, Germany; personal communication). In our opinion, more studies are needed to address the respiratory effects related to inhalation of milk powder in occupational settings before any conclusions about the mechanisms can be made, although the symptom pattern in our study was compatible with hypersensitivity-type mechanisms (*i.e.* wheezing, breathlessness and nasal symptoms). Despite the uncertainty concerning the exact mechanisms, our results suggest that workers with milk powder exposure should get attention, for example in a form of surveillance of respiratory symptoms and spirometry. We also propose that respiratory symptoms in general should be inquired after, as asking specifically about work-related symptoms only in questionnaires may introduce misclassification, *i.e.* some workers may not be able to relate their symptoms to work by themselves, while others may over-report work-relatedness of symptoms for other reasons, such as stress at work (for which we adjusted our results).

Use of the quantitative structure-activity relationship modelling approach to assess potential asthmagenicity of chemicals based on their chemical (sub)structure [2] could be an interesting approach to screen chemicals as they are first introduced into occupational settings and to generate hypotheses about their potential to cause respiratory sensitisation. However, we believe that studies and/or observations in humans are needed before any definite conclusions can be made about the hazards related to a specific chemical in the workplace.

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## STATEMENT OF INTEREST

None declared.

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