Biverkningarna är överdrivna [Tea tree oil – adverse events exaggerated]

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Letter to the Editor,

Ahlin and colleagues make an important point in their article discussing herbal remedies [1]; namely that such remedies are not inherently harmless by virtue of their natural origins. Despite the widespread belief that this is so [2-4], they may cause adverse effects just as conventional medicines may.

The authors aimed to describe the prevalence of contact dermatitis caused by topically applied complementary and alternative medicines (CAM) approved by the Swedish Medical Products Agency. On this basis, four topical herbal products were included in the paper. These were tea tree oil, Herstat, Oleum salvum and Efabene. Their inclusion criteria were studies published in English or Swedish in which at least 20 participants were patch tested. For propolis, papers were limited to those in which the test concentration was 10%. The studies presented included series of self-selected participants, investigator-selected patients and consecutive patients attending specialist clinics.

A number of studies meeting these criteria were omitted from their article including studies in which the prevalence of contact allergy to tea tree oil ranged from 0.3-2.7% [5-9]. Other studies omitted from their review include data on the prevalence of contact allergy to propolis (1.9%) [10], peppermint oil (0.64-5%) [11, 12] and eucalyptus oil (0.25-1.8%) [12, 13]. Like Ahlin and colleagues, we could find no studies on the prevalence of contact allergy to cajeput oil.

In addition to the omission of studies containing relevant data, the prevalence of contact allergy for tea tree oil was mistakenly reported as ranging from 0-26% with work by Brenan *et al*. [14] cited as the source of the upper limit. In that study, 50 female patients presenting at a Dermogynaecology Clinic were semi-randomly selected for patch testing with 55 allergens, not including tea tree oil. Table 6 and text in the Results section of the Brenan *et al*. paper indicate that 13 of those 50 patients (26%) were also tested with tea tree oil (5% in paraffin) and none was positive (0/13). If data from this study were to be included in a

summary of the prevalence of contact allergy to tea tree oil, then the prevalence would be 0%.

The next highest prevalence of contact allergy for tea tree oil included in their paper was 11% reported by Southwell and colleagues [15]. The purpose of that work was not to determine the prevalence of contact allergy to tea tree oil but to determine the skin irritancy of varying concentrations of both pure 1,8-cineole and tea tree oils containing varying concentrations of 1,8-cineole. At the time the work was conducted the optimum concentration of 1,8-cineole in tea tree oil was a contentious issue and 1,8-cineole was regarded by some, incorrectly, as a skin irritant or as the component of tea tree oil largely responsible for allergic reactions [16]. The study participants were chosen from a list of willing volunteers used by the Skin and Cancer Foundation (Darlinghurst, NSW Australia) rather than a series of consecutive patients presenting to dermatologists or other specialists. It is well known that the prevalence of positive reactions in consecutive patch test patients is not comparable to the prevalence when only selected patients are tested; the prevalence in the latter group would be expected to be higher [12].

Ahlin and colleagues do point out in their penultimate paragraph that comparison between studies is difficult because of a lack of explanation of the reasons for presentation and testing. However, the comparisons have already been made and the conclusions drawn and in most cases sufficient information was available to make comparison pointless.

Apart from it being inappropriate to compare or combine data from the study of Southwell *et al*. [15] with data from series of consecutive patients attending dermatology or specialist centres, the oil samples used in the work were chosen because of their different 1,8-cineole concentrations and several did not meet the compositional requirements for tea tree oil applicable at the time [17]. Furthermore, some were aged oils up to 8 years old (Southwell, unpublished data). As such, it is likely that they contained peroxides, now thought to be largely responsible for adverse skin reactions to tea tree oil [18].

The inadvertent use of aged oil raises another issue, the use of oxidised tea tree oil in patch testing procedures. Oil oxidises as it ages and this process may be influenced by light, aeration and heat. As oil ages the composition changes and a number of peroxides are formed [18]. These are known skin sensitisers. The choice of whether to use fresh or aged oil for patch testing has arisen from time to time [19]. It appears that aged oil is more likely to provoke a positive patch test result than fresh oil [18]. Tea tree oil contained in well-formulated products, many containing anti-oxidants, would not be expected to oxidise significantly and would therefore produce less contact allergy than aged, oxidised oil, a point conceded by Ahlin and colleagues. Consequently, it seems rational to include details about the oxidation status of oils in reports on the prevalence of contact allergy to tea tree oil. While the use of aged oil in patch tests strikes us as counter-intuitive, if done, this important detail should be included in publications.

To further their case that herbal products may be involved in serious adverse reactions, a point we would not dispute, Ahlin and colleagues discuss a study which examined the incidence of adverse event reports related to the use of CAM [20]. They state that 11 people died in Sweden as a result of the use of herbal remedies over the period 1987-2000. This is not strictly correct. Over the course of those 20 years, there were 778 reports of adverse events related to the use of CAM, including herbal remedies, to the Swedish Medical Products Agency [20]. CAM-related events represented 1.2% of a total of 64 493 reports submitted to the Agency. The outcome of the adverse reaction in 11 of the 778 cases was death and in 5 of those cases the link between the adverse reaction and the CAM was regarded as at least possible using WHO criteria. The role of CAM in 4 of the remaining 6 cases was less certain, and in 2 cases there was no information available to make a judgement [20; Haag, pers. comm.]. Reports regarding tea tree oil comprised 5.2% (41/778) of those about CAM and the oil ranked 8th in terms of the number of CAM adverse event reports received. Although Ahlin and colleagues never implied otherwise, it is important to point out that no cases with a fatal outcome were known to involve tea tree oil, Herstat, Oleum salvum or Efabene.

Finally, in their discussion Ahlin and colleagues comment on the remarkably high frequency of contact allergy to herbal remedies (0-26%). If true, this would indeed be remarkable. However, the figure of 26% given for tea tree oil is incorrect and may be dismissed. The next highest figure of 11%, also for tea tree oil, would be regarded by many as out of context and unsuitable for comparison with the other figures. The remaining figures reported for tea tree oil (0-4.3%) and the other topical herbal products (0-6.4%) are all lower and tea tree oil is not the highest. In summary, the omissions, errors and misinterpretations contained in the article serve as a timely reminder that great care must be taken when reviewing data to ensure that no mistakes are inadvertently made or perpetuated and that only reasonable conclusions are drawn.

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The full text (in Swedish) is available at:
http://www.lakartidningen.se/07engine.php?articleId=18503

The original article (in Swedish) by Ahlin et al. (2011) is available at:
http://ltarkiv.lakartidningen.se/2011/temp/pda39894.pdf

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