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Title: Lack of evidence that essential oils affect puberty

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Dear Sir,

The review by Fisher and Eugster [1] due to be published in *Reproductive Toxicology* repeats the putative link between the essential oils of lavender and tea tree and breast development stating:

> *"Other examples of naturally occurring endocrine disruptors include lavender oil, tea tree oil and fennel, all of which have been linked to breast development in prepubertal children presumably due to estrogenic effects."*

Here the authors have referred to the 2007 paper by Henley *et al*. [2]. They have linked essential oils to endocrine disruption by referring to gynecomastia and/or to in vitro estrogenic activity, without also referring to other studies that suggest otherwise.

The review "summarizes the current understanding of the major environmental influences on pubertal timing, focusing on factors for which the most scientific evidence exists" [1]. Knowledge in the field is growing steadily and recently published data on lavender oil provide compelling evidence that lavender oil is not estrogenic [3]. In this study, lavender oil at dosages of 20 or 100 mg/kg was not active in a rat uterotrophic assay, the gold-standard in vivo assay, with no evidence of estrogenic activity shown.

While tea tree oil has not yet been tested in vivo, in a report on the oil by the European Commission's Scientific Committee on Consumer Products (now the Scientific Committee on Consumer Safety) [4], the committee commented:

"Since the hormonal active ingredients of Tea Tree Oil were shown not to penetrate the skin, the hypothesized correlation of the finding of 3 cases of gynecomastia to the topical use of Tea Tree Oil is considered implausible."

The implausibility of tea tree oil having any estrogenic effect is further supported by Tisserand's review [5] of the estrogenic activity of clary sage in which he notes that according to Anstead *et al*. [6] and Blair *et al*. [7] phenolic structure is important for estrogenicity, as is the presence of a second ring. This does not rule out other mechanisms of xenoestrogenic action such as metabolic activation [8-10] or epimutations after developmental exposure [11, 12]. However, none of this negates the fact that a putative link [2] has been made and is being overstated and perpetuated. Since the Henley et al. article was published, it has been cited more than 170 times (Google Scholar, accessed 16 Sep 2013) to reference the estrogenic or endocrine disrupting activity of lavender and/or tea tree oils without the benefit of additional data.

Case reports are a very useful means of identifying possible links between product exposure and detrimental biological effects. However, they are not definitive in their own right. The co-incidence of oil exposure and endocrine disruption, manifested as breast development, has not been demonstrated to be causal. The cause of the pre-pubertal gynecomastia has not been identified and tea tree and lavender oils have not been definitively identified as endocrine disrupting compounds. Both tea tree (*Melaleuca alternifolia*) and lavender (*Lavandula angustifolia*) oils have a long history of apparently safe use [13, 14].

Tisserand has previously postulated [15] that phthalates may have contributed to the endocrine effect noted by Henley *et al*. [2]. Tisserand [15] also noted:

> "*The composition of the essential oils tested is not given, nor is any other information about them, apart from the supplier. Since they do not appear to be organically grown, biocide content is a possibility*."

Since no compositional data on the lavender or tea tree oils was provided in the original paper [2], the presence or absence of xenoestrogenic contaminants such as plasticisers, pesticides or herbicides is unknown. Conclusions about the estrogenic activity of the oils are not possible without these data. The absence of tea tree oil exposure by two of the three reported cases [2] also argues against a causative role for tea tree oil and a number of publications questioned the purported link between gynecomastia and the two essential oils at the time [16-20].

Any link, casual or causal, between lavender or tea tree oil product use and the development of pre-pubertal gynecomastia has public health, regulatory, ecotoxicological and/or commercial consequences. It is worth considering that the chemical constituents of lavender and tea tree essential oils are not unique to those oils [21-23]. They are found in hundreds of other essential oils. If these two oils did possess estrogenic activity, then it is likely that other essential oils would also have estrogenic activity by virtue of the constituents they share with lavender and tea tree oil. Each year thousands of tonnes of essential oils are ubiquitously ingested by and applied to humans and other animals in products such as foods [24], beverages [25, 26], personal care products and pharmaceutical agents. Consequently, it is important that the nature of any link between essential oils and endocrine disruption be clarified. This may be achieved by continued research into the safety and efficacy of

the oils funded by industry and independent sources combined with ongoing surveillance of reports of adverse effects by industry and regulatory authorities.

Finally, a recent revisiting of the existing literature on the in vitro and in vivo estrogenic activity of essential oils has led one of the authors (CFC) to suggest an alternative hypothesis. It may be that a large proportion of the in vitro results suggesting that essential oils and/or their components are estrogenic, are false positive results. Commonly utilised disposable laboratory plasticware, such as the 96-well polystyrene plastic trays in which the tests for estrogenic activity are often performed, contains many xenoestrogenic compounds including phthalates and nonylphenols that may leach into the test system, especially in the presence of essential oils which have solvent properties. The use of disposable laboratory plasticware may be confounding the results, a phenomenon that has been reported in the past [27, 28]. This needs testing and it is worth noting that Henley *et al*. used polystyrene plates (Korach, K, Personal Communication).

Closing remarks go to Fisher and Eugster [1] who rightly point out that more research is “needed to address the question of what environmental factors affect puberty and how we can best eliminate relevant exposures with the goal of maximizing the health and well-being of today’s children and future generations to come.”

Disclosure Statement

In the past, CF Carson has received research grants and/or consulting fees from the Australian Government and/or from industry for research about essential oils. R

Tisserand is a shareholder of First Natural Brands, which owns Tisserand Aromatherapy. T Larkman is CEO of the Australian Tea Tree Industry Association (ATTIA Ltd), an Australian based not-for-profit organisation formed in 1986 as the peak body to promote and represent the interests of the Australian tea tree industry.

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