Endocrine Disruptors and Essential Oils

22nd March 2018

On the 17th March 2018 a press release was published on the Endocrine Society webpage titled "**Chemicals in lavender and tea tree oil appear to be hormone disruptors**". This is available from: https://www.endocrine.org/news-room/2018/chemicals-in-lavender-and-tea-tree-oil-appear-to-be-hormone-disruptors.

This has generated wide interest on-line and in the press and morphed into dozens of other articles with more sensationalist titles: "**Essential oils in hygiene products may make boys grow breasts**" (https://www.newscientist.com/article/2163978-essential-oils-in-hygiene-products-may-make-boys-grow-breasts/) is one; other titles used are "**Lavender and tea tree oil can cause a male bust**" and "**Lavender and tea tree oil could give men 'MOOBS'**" to name just two.

The lead author of this study, J Tyler Ramsey, is research fellow at the National Institute of Environmental Health Sciences. He gave a 6 minute presentation as part of a news conference on Monday 19th March 2019 at ENDO 2018, the Endocrine Society's 100th annual meeting in Chicago which is available from: http://endowebcasting.com/endo/archives/endo18-1.php (commences at 10:30).

The actual study is not yet available and it is not known when it will be published; this is unfortunate because the very brief presentation gives no answers to some critically important questions and raises a question about the difference between good science journalism and 'clickbait': "E*ssential oils in hygiene products makes boys grow breasts*" and the many other similar titles can be considered pure clickbait; delivery of the topic in this manner is likely to have been designed solely with this in mind rather than with a concern for good science journalism.

Despite the lack of detail available, the abstract and presentation do provide some tantalising clues from the authors: They write '*Clinical studies have shown a linkage between prepubertal gynecomastia and Lavender Oil (LO) or Tea Tree Oil (TTO) commodities when used regularly.....our previous study demonstrated that these act as hormonal mimics through estrogen receptor alpha (ERα) and the androgen receptor (AR).'*

This is likely referring to the 2007 article in the New England Medical Journal [1] by Henley *et al* where the authors (including KS Korach, a co-author of the current study) provided 3 case studies and some *in vitro* work to demonstrate that TTO and LO cause gynecomastia.

There is nothing new here and there have been several articles published in response to this including Robert Tisserand [2] who pointed out that '*The shampoo was said to contain "very low concentrations" of tea tree oil, and the content in the hair gel was "virtually undetectable". Lavender oil concentration was not checked.*" and "*The in vitro evidence shows weak but definite endocrine disrupting effects for both lavender and tea tree oils. The second case was the only one in which tea tree oil was involved. Tea tree oil was tested because it was deemed to be "chemically similar" to lavender oil. However, apart from the fact that both are essential oils, they have very little in common chemically.'*

In a later publication on this subject Carson *et al* [3] reaffirm Tisserand's statements and also suggest that '*…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 maybe 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 xeno-estrogenic 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. This needs testing and it is worth noting that Henley et al. used polystyrene plates (Korach K, personal communication).*'

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This latest study by Ramsey *et al* looked at the impact of 8 chemicals on cells in a petri dish; these were chosen as they are the main constituents of both TTO and LO. Of the eight tested, four are common to TTO & LO (**1,8-cineole, terpinen-4-ol, limonene, α-terpineol**), two are common to LO (**linalyl acetate, linalool** = 90%+ of LO) and two others (**α-terpinene, ϒ-terpinene**) are common to TTO and a host of other essential oils as are the other six compounds.

Ramsey *et al* found that (in their as yet unknown) test system these eight compounds are endocrine disrupting chemicals (EDC's). Without the study details it is impossible to comment on factors such as the concentrations and reagents used, test systems and detail on treatment of the cells used both before and during the testing to name only a few.

In the press release on the Endocrine Society webpage a statement '*All eight chemicals demonstrated varying estrogenic and/or anti-androgenic properties, with some showing high or little to no activity, the investigators reported*'. The statement "*…little to no activity* ...'appears to be at odds with the sweeping statement by Ramsey that '*…our study has identified eight components of LO and TTO as endocrine disruptor chemicals (EDC's)'*. Until the study is published it is not possible to assess the veracity of this.

A key question here is the type of test system used. Were disposable plastic (96 well or other) laboratory equipment utilised and if so were potential contaminants from the plastics monitored and taken into account?

Recent unpublished research led by CF Carson and conducted at the University of Western Australia's School of Chemistry and Biochemistry have found that that these essential oils at low concentration (0.025% TTO and 0.025% LO) can enhance the amount of polystyrene-derived styrene oligomers extracted from the plasticware by up to 10,000-fold. Oligomer by-products formed in the manufacture of polystyrene have exhibited estrogenic activity *in vitro*. There is also evidence that the solvent properties of essential oils and their constituents significantly enhance leaching of potentially estrogenic compounds from plasticware including plasticisers such as di-2-ethylhexyl phthalate (DHEP) and Bisphenol A (BPA). Both of these were coincidentally reported as EDC's in the same news conference at ENDO 2018.

Ramsey concluded in his presentation that:

- *Lavender and tea tree oil components possess EDC's of varying magnitude that are estrogenic and anti-androgenic; thereby potentially contributing to the onset of prepubertal gynecomastia.*
- *The selected eight chemicals tested were found to be in at least 62/93 other essential oils, indicating they contain EDC's.*

If this is indeed the case then reverting to Carson *et al* the same question they posed must be asked:

> *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, beverages, 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.*

Hundreds of years of use of essential oils by countless thousands of people with beneficial effects to the consumer cannot be outweighed by a small number of case studies with tenuous links to some essential oils.

Essential oils comprise hundreds of organic compounds, as acknowledged by Ramsey, and it is accepted that these combinations of compounds work synergistically. To investigate only eight of the hundreds of compounds found in LO and TTO (and the other 62 essential oils that contain these compounds) in isolation begs the question: why? The answer to this is likely to because first they are far easier to do and

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second, and most importantly, approval and funding are easier to obtain. Does an easier route provide the right answer? Not always.

Studies that have been done on single constituent soy isoflavones on cells in a petri dish are a case in point: Many of these compounds, when in an *in vitro* setting, act as phytoestrogens in mammals. This should be of real concern to anyone with hormone positive breast cancer; however population studies on people who consume large quantities of soy based products show they have lower rates of breast cancer; additionally better survival rates have been recorded for those on a high soy diet [4].

There are several other questions that need to be fully addressed; unfortunately answers to these are not going to be available until the study is published and even then may go unanswered:

1. Politano *et al* (http://journals.sagepub.com/doi/abs/10.1177/1091581812472209) described a percutaneous uterotrophic bioassay in immature female rats and concluded '*lavender oil, at dosages of 20 or 100 mg/kg, was not active in the rat uterotrophic assay and gave no evidence of estrogenic activity*'. How does this study by Politano *et al* reconcile with the findings in this study?
2. An *in vitro* system differs significantly from common *in vivo* use patterns for most essential oils; the dermal barrier in humans prevents almost all of the 8 compounds listed from entering the bloodstream. Data on the percutaneous adsorption of TTO and LO is available, was any attempt made to address this factor?
3. If tea tree oil and lavender oil are estrogenic why was this study not conducted with the whole oil? Testing of individual components on cells *in vitro* cannot be realistically compared to the use of the whole oil in either an *in vitro* or an *in vivo* situation.
4. Was any consideration given to parallel *in vitro* testing where known doses of each compound are applied to volunteers followed by analysis of blood and/or urine for the presence of these compounds or their metabolites?
5. Thousands of tonnes, indeed hundreds of thousands if all citrus products are included, of essential oils and the compounds found in them are ubiquitously ingested by and applied to humans and other animals in products such as foods, beverages, personal care products and pharmaceutical agents. The fact is that 62 of 93 other essential oils examined by Ramsey *et al* contain at least one of the eight compounds tested and if these are indeed confirmed as EDC's why has the phenomenon of gynecomastia or premature thelarche not been seen more often?

Finally one of the compounds targeted (limonene) is usually, if not always, present in citrus extracts (juice, pulp etc) as well as in the whole fruit. If limonene is, as claimed, an EDC then responsible scientific reporting should also flag any product containing a citrus extract, especially if packaged or stored in plastic if the Carson *et al* hypothesis is true, in the same way that LO & TTO have been targeted.

Why then was a similar warning to consumers prepared along the lines of the press release "**Chemicals in lavender and tea tree oil appear to be hormone disruptors**" for citrus and citrus based products? The same is, to a lesser extent, true of the other seven compounds tested.

Is it reasonable to assume that the media have been manipulated into using 'clickbait' to publicise both this study and the conference where the findings were presented two days later?

References

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2. Tisserand R. Neither lavender oil nor tea tree oil can be linked to breast growth in young boys; 2008. Available from: http://www.roberttisserand.com/articles/TeaTreeAndLavenderNotLinkedToGynecomastia.pdf
3. Carson, C. F., Tisserand, R., & Larkman, T. (2014). Lack of evidence that essential oils affect puberty. Reproductive Toxicology, 44, 50–51.
4. Douglas CC, Johnson SA, Arjmandi BH. Soy and its isoflavones: the truth behind the science in breast cancer. Anticancer Agents Med Chem. 2013 Oct; 13(8):1178-87.

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