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The relationship between lavender and tea tree essential oils and pediatric endocrine disorders: A systematic review of the literature

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ABSTRACT

Objectives: Essential oils are common ingredients in personal care products, little is known about the effects of chronic exposure to these ingredients in human health. It has been suggested that these two essential oils cause prepubertal gynecomastia and premature thelarche in children. The purpose of this study was to systematically review the evidence related to the proposed link between these essential oils and endocrine disruption

Methods: This study sought to investigate the proposed link between LEO and TTEO and endocrine disrupting outcomes by identifying and evaluating the clinical evidence regarding this topic. Studies qualified if the participants included prepubertal children who have experienced either prepubertal gynecomastia or premature thelarche. The Case Series Critical Appraisal Tool (CSCAT) was used to identify the reliability of the identified case series. The potential for evidence of causality was evaluated using the tool proposed by Murad.

Results: A total of four manuscripts were identified, describing a total of eleven cases reported to have experienced both the exposure and the outcome. Reporting of inclusion, demographic data, clinical data, and the potential for causality was found to be insufficient. This study did not find evidence to support the claim that tea tree essential oil is related to endocrine disruption in children, and little to no evidence to substantiate the proposed link between lavender essential oil and endocrine disruption in children.

Conclusion: Because this potential link remains a concern among pediatric care providers and parents, epidemiological research to address the proposed link is needed.

1. Introduction

Essential oils are common ingredients in personal care products. These ingredients are often thought to be safer than synthetic fragrances because they are extracted from botanical sources. Lavender (*Lavandula* spp.) and tea tree (*Melaleuca alternifolia*) are two of the most commonly used essential oil ingredients. Tea tree essential oil was valued at $31 million in the US in 2018, according to industry market reports, and the global lavender oil market is expected to top $124 million by 2024.[1,2]

Despite this widespread prevalence of exposure, little is known about the effects of chronic exposure to these ingredients in human health. It has been suggested that these two essential oils cause prepubertal gynecomastia and premature thelarche in children.[3] The same report has identified linalool in lavender as well as the shared phytochemicals α-terpineol and 4-terpinenol as demonstrating both anti-androgenic and estrogenic activity when tested *in vitro*.

1.1. Rationale

These two essential oils were first identified as potential endocrine disruptors in prepubertal children in a 2007 report of three cases of prepubertal gynecomastia, accompanied by an *in vitro* study.[4] Additional cases of essential oil exposure and endocrine disrupting outcomes have since been documented.[5] As a result, health professionals have issued warnings regarding the use of products which contain lavender essential oil (LEO) and tea tree essential oil (TTEO).

Both LEO and TTEO are commonly utilized for integrative health treatments. Lavender has been found to relieve anxiety and to provide anti-inflammatory and antimicrobial benefits.[6–11] A standardized lavender preparation, Silexan, is the active ingredient in a dietary supplement shown to be an effective treatment for mild to moderate anxiety.[12] The potential for this LEO preparation to interact with oral contraceptives was investigated and it was determined that internal use of lavender oil does not affect estrogen and progesterone levels.[13]

LEO has also been evaluated for its potential to influence estrogen levels in peri-menopausal women and for the potential for estrogenic

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activity in rats. The oil was inhaled in a study evaluating salivary estrogen levels in peri-menopausal women and researchers concluded that it does not have an effect on estrogen levels.[14] Similarly, in animal tests, the oil was not found to have any affect on estrogen levels in rats.[15] These results are consistent with laboratory analyses. When multiple essential oils were tested for potential estrogenic activity, LEO was one of the only two oils to exhibit little to no estrogenic activity.[16]

TTEO is used in integrative health for its antibacterial, antifungal, and antiprotozoal actions. It has been found to be an effective treatment for acne, head lice, and other dermatological concerns.[17–19] When evaluated as a treatment for skin conditions in children, no adverse effects have been reported.[20] Similarly, in a study evaluating common ingredients in personal care products, researchers found that TTEO demonstrates anti-estrogen activity.[21]

There are conflicting reports in the scientific literature regarding the potential for LEO and TTEO to exhibit estrogen-like or anti-androgen actions. The purpose of this study was to systematically review the evidence related to the proposed link between TTEO and LEO with outcomes related to endocrine disruption, including prepubertal gynecomastia and premature thelarche.

1.2. Objectives

This study sought to investigate the proposed link between LEO and TTEO and endocrine disrupting outcomes by identifying and evaluating the clinical evidence regarding this topic. To ensure a comprehensive review, all epidemiological studies available in the published literature were included. Studies qualified if the participants included prepubertal children who have experienced either prepubertal gynecomastia or premature thelarche.

2. Methods

2.1. Protocol & registration

The study protocol has been submitted to PROSPERO for registration, ID #152302.

2.2. Eligibility criteria

To be included in the search, the exposure was required to be any form of LEO or TTEO-related botanical fragrance (including essential oil, isolated chemicals extracted from botanicals, synthetic fragrances, and botanical extracts), and the outcome was prepubertal gynecomastia and/or premature thelarche.

To gather all available research, no time restrictions were applied and no restrictions were placed on research methodology. Case-control studies, cohort studies, cross-sectional studies, case studies, and case series were all included. Letters to the editor, opinion articles, and other articles were excluded if they did not include one of the previously referenced methodologies. Articles must be published in a peer reviewed journal in the English language.

2.3. Information sources

A comprehensive search was conducted using ScienceDirect, Google Scholar, PubMed, and EBSCO. The search took place between December 2018 and June 2019. Prior to analysis, a follow-up search was conducted in September 2019. During the follow-up search, one additional paper was identified and included.

2.4. Search

The search included all possible combinations of the following terms: lavender oil, lavender essential oil, tea tree oil, tea tree essential oil, *Lavandula angustifolia*, *Melaleuca alternifolia*, prepubertal gynecomastia, premature thelarche, endocrine disruption, endocrine disrupting chemical, essential oil, aromatherapy, precocious puberty, breast growth, prepubertal, children, safety, cross sectional, case control, case study, and cohort.

2.5. Study selection

The initial search involved screening each abstract for inclusion. Potential manuscripts were further evaluated through a full text analysis. A secondary search using author affiliations was conducted on ScienceDirect and PubMed. Those searches consisted of searching each author name to identify potentially related research. References contained within the included manuscripts were also reviewed in the search for potential studies.

2.6. Data collection process

Three authors independently extracted data from the identified case series using a data extraction sheet. These findings were compared for consistency. Inter-rater reliability was found to be high, with only three areas requiring further discussion. This discussion addressed the ambiguity regarding the region and/or nationality of participating children, and the lack of specificity within the reports regarding exposure to the suspected endocrine disrupting chemicals (EDCs).

Authors extracted data regarding the patients, the proposed essential oil exposure, and the clinical outcomes. Patient data extraction included age, sex, race, nationality, household region, year of case, and rationale for selection of participants such as inclusion/exclusion criteria.

Clinical data included height, weight, BMI, diagnostic method, comorbidities, presence of alternate causal factors, diet, additional treatments, duration of symptoms, Tanner stage of pubic hair, size of breast tissue, presence of body odor, testicular volume (where applicable), hormone testing status, and follow-up duration. Exposure data included the product associated with the exposure, the method of exposure, duration of exposure, frequency of exposure, and method of confirmation regarding the child's exposure to LEO and TTEO.

2.7. Risk of bias within and across studies

This review did not identify any case-control, cross sectional, or cohort studies which met the inclusion criteria. All identified articles describe case series, so the tools used to assess bias within and across studies were specific to case reports.

The Case Series Critical Appraisal Tool (CSCAT) was used to identify the reliability of the identified case series.[22] The potential for evidence of causality was evaluated using the tool proposed by Murad.[23] Constructs of the Murad tool which assessed outcomes already identified in the CSCAT were omitted.

Collectively, these two tools provide a comprehensive assessment of the risk of bias within the included studies, the strength of evidence presented within these studies, and the overall methodological quality reflected in the existing literature on this proposed relationship.

2.8. Summary of measures

Because research studies were not identified for this analysis and the available case series had neither consecutive nor complete inclusion of participants, no statistical analyses were appropriate with the available data. Descriptive statistics of the cases, where possible, are reflected.

3. Results

3.1. Study selection

The search for studies produced a total of 191 manuscripts. After

Table 1
Studies Analyzed.

Study Name	Pub Year	Methodology	Number of Participants
Henley, 2007	2007	case series	3
Diaz, 2016	2016	case series	3
Linklater, 2015	2015	case study	1
Ramsey, 2019	2019	case series	4

screening abstracts, 11 articles were retrieved. After evaluating the full text, 5 manuscripts remained, and during data extraction one additional manuscript was excluded.

Case-control, cohort, and cross-sectional studies were not identified in this search. One medical office review and four case series were identified. Upon full manuscript evaluation, the medical office review did not describe or utilize any research methodology, nor did it reference IRB authorization or informed consent from patients.[24] The article provided a total count of diagnosed cases in a given timeframe. As a result, there was no evidence to analyze. This left a total of four manuscripts in the final analysis.[25–28]

A total of 11 cases were described in the four manuscripts. None of the studies conducted any statistical analyses or utilized any comparison groups for evaluation.

3.2. Studies

All 11 cases are reported to have experienced both the exposure and the outcome (See Table 1: Studies Analyzed)

3.3. Results of individual studies

3.3.1. Patient descriptions and inclusion

Rationale for patient inclusion was unclear from the reports. Consecutive or complete inclusion of participants was neither noted nor implied. Overall, methodological reliability regarding participant inclusion was poor.

Demographic data are important for evaluating generalizability, and are of particular importance when a case study or series implies causation or seeks to identify a potential environmental risk. This allows providers to identify at-risk populations. The cases included in this review did not provide key demographic variables such as race and nationality, nor did they identify the year in which the cases occurred (See Table 2: Demographic Data).

The age of each patient was supplied. Mean age of the cases was 7 years 2.4 months (SD 2 years, 10.2 months; range 14 months - 10 years, 1 month) or 8 years 5.9 months for males (SD 1 year, 11.7 months; range 4 years, 5 months to 10 years, 1 month) and 5 years 1 month for females (SD 3 years, 1.7 months; range 14 months to 7 years, 9 months).

A diagnosis of prepubertal gynecomastia or premature thelarche requires confirming that the child is not pubertal. By definition, if the child has started puberty, these outcomes are no longer “prepubertal” or “premature.” Traditionally, the minimum age for pubertal symptoms to be considered normal is 8 years for females and 9 years for males within the United States.[29] However, many experts have questioned the continued accuracy of this figure in recent years due to documented decreases in the mean age of the onset of puberty.

A two-phase cross sectional study published in 2009 found that the mean age females reached Tanner breast stage 2 decreased by approximately 1 year between the first cohort of 1991–1993 and the follow-up group in 2004-2006..[30]. Kaplowitz & Bloch concluded in 2016 that the cut-off may not need to be reduced, but that the, “majority (of patients referred to endocrinologists for breast growth before age of 8) will not have true endocrine pathology but represent the lower end of the new normal range for sexual maturation”.[31]

Four male cases were 9 years or older, placing them in the pubertal age range. These reports did not indicate why males within the pubertal age range were considered to be prepubertal. Because gynecomastia is a common occurrence among pubertal males, with incidence rates of approximately 50 %, a case of prepubertal gynecomastia requires confirming that the child is indeed prepubertal.[32]

Race is unknown for all 11 cases. Onset of puberty varies dramatically by racial and ethnic background. Recent studies demonstrate that 22–23 % of black females reach Tanner breast stage 2 at 7 − 8 years old, compared with 15 % of Mexican American females and 10 % of white females.[33,34] Two of the four females described in these cases were in the 7 − 8 year age range, so the extent to which these cases were abnormal is unclear.

Other demographic variables, such as family income, parental education level, nationality, and geographic region of the cases were not included in the case studies. Socioeconomic status is also known to play a role in the timing of puberty.[35] Factors such as parental educational attainment and family income are linked to earlier onset of puberty.[36,37]

These data would have provided opportunity to compare these cases to similar populations to either evaluate other potential factors associated with the outcome. Such analysis was not possible due to a lack of data.

3.3.2. Measurement instruments

Breast tissue was diagnosed through a physical exam. Resolution of the condition was evaluated through the same process, but only in some cases. Follow up for one case occurred through communication with the family, and others were examined by the primary care provider, rather than the specialist, for follow-up. Due to differences in measurement of breast tissue, patient age at follow-up, and the potential for inter-rater reliability to be low, the validity and reliability of this method of measurement is low.

3.3.3. Clinical data

Clinical data for these cases was extracted to evaluate alternate causal factors and to further identify the population at risk. There is an

Table 2
Demographic Data.

Author / Case	Age	Sex	Race	Nationality	Region	Time Period
Henley Case 1	4y 5m	M	–	–	–	–
Henley Case 2	10y 1 m	M	–	–	–	–
Henley Case 3	7y 10 m	M	–	–	–	–
Diaz Case 1	9y 7m	M	–	–	Miami	–
Diaz Case 2	9y 9m	M	–	Cuban immigrant	Miami	–
Diaz Case 3	9y 4 m	M	–	Second Generation Immigrant	Miami	–
Linklater	14 m	F	–	–	–	–
Ramsey Case 1	7y 6m	F	–	–	–	–
Ramsey Case 2	3y 11 m	F	–	–	–	–
Ramsey Case 3	7y 9m	F		–	–	–
Ramsey Case 4	7y 11 m	M	–	–	–	–

Table 3
Clinical Information.

Author / Case	Height	Weight	BMI	Comorbidities	Diet	Other Interventions
Henley Case 1	97 %	75-90 %	–	–	no soy	–
Henley Case 2	> 97 %	> 97 %	21.1	adrenarche (persisted after resolution)	no soy	–
Henley Case 3	75-90 %	50 %	–	–	no soy	–
Diaz Case 1	“short stature”	–	–	none	–	–
Diaz Case 2	“correspond to genetic potential”	–	–	none	–	–
Diaz Case 3	97 %	–	–	large for gestational age	–	–
Linklater	75 %	15 %	–	none	–	–
Ramsey Case 1	“normal"	“normal"	–	none	–	–
Ramsey Case 2	–	–	–	none	–	–
Ramsey Case 3	“normal"	"normal"	–	uterine enlargement	–	–
Ramsey Case 4	“above the percentiles that correspond to his age”	“above the percentiles that correspond to his age”	95 %	ADHD & Speech Delay	–	–

established link between BMI and the onset of puberty, with children who are overweight achieving puberty approximately 6 months earlier than children with a healthy BMI.[38] Similarly, early signs puberty may also be related to diet and clinical co-morbidities.[39–43]

Few of these details were available in the reported cases (See Table 3: Clinical Information). Height and weight were reported in nonspecific terms such as “normal” or “75-95 %.” The Henley cases screened for soy intake but did not look at overall diet. All but two cases discussed co-morbidities (Table 4).

3.3.4. Ascertainment & causality

While establishing correlation is not possible within case studies or case series, a case series should identify and provide data regarding confirmation of the suspected exposure if the purpose of the manuscript is to propose a potentially causal link.

The studies included in this review varied in the level of exposure confirmation conducted (See Table 5: Exposure). Some cases relied exclusively on parental recall of ingredient lists, while others conducted laboratory analysis of the product in question to search for ingredients that may be EDCs. This produces an extensive variation in the potential for causality. While parental recall of product exposure may be reliable, parents are not typically expected to accurately recall specific ingredients from within their child’s personal care products.

Exposure method also varied dramatically among the cases. All 11 cases involved the suspected use of LEO, while only one involved the suspected use of TTOE. The most common exposure was a cologne (“violet water”), found in 4 (36 %) of the cases. The second case in the Ramsey report (2019) lists an exposure that contains lavender botanical extract rather than the essential oil. The manuscript does not state a rationale for classifying this substance as an essential oil containing product. One exposure occurred through inhalation in a classroom, and the rest were exposed through personal care products, such as shampoo or hair care.

Frequency of exposure was also highly variable. Some cases did not document duration and/or frequency of exposure, while others used vague terminology such as “becoming more frequent,” and “since early childhood” to refer to frequency and duration, respectively. When it was documented, frequency ranged from intermittent to daily, and duration ranged from “since infancy” to “shortly before.” Given that the purpose of these reports is to propose potential for a casual relationship between the exposure and the outcomes, the lack of specificity regarding duration and exposure limits generalizability and leaves practitioners unable to make informed decisions in clinical practice.

Furthermore, absorption of volatile botanical ingredients from wash-off and airborne exposure in sufficient quantities to disrupt the endocrine system is a phenomenon which has not been previously reported in the literature. Previous work has established that the chemicals in LEO and TTEO which are suspected EDCs demonstrate significant variability in absorption rates from topical products.[44] When these chemicals are diluted in a topical vehicle, such as a skincare product, or emulsified, the potential for absorption is reduced.

A proposed mechanism of action by which a shampoo ingredient or an aromatic presence in a room may be absorbed in sufficient quantities to cause breast growth was not suggested in any of the case reports.

3.3.5. Alternative explanations

One of the requirements for establishing causation is to eliminate alternative explanations for the outcome. While case series are unable to provide sufficient evidence to establish causation, case studies which propose a causal link should identify and evaluate potential alternative causes.

Most of the authors identified potential co-morbidities and

Table 4
Symptoms.

Author / Case	Duration of Symptom	Pubic Tanner Stage	Body Odor	Testicular Volume	Left Breast	Right Breast	Lab tests
Henley Case 1	3.5 - 4 months total	1	–	3ml	2.5 × 2.5	2.5 × 2.5	Normal
Henley Case 2	–	2	–	3ml	3.5 × 4	x	high testosterone & DHEA
Henley Case 3	1 m	1	–	3ml	correspond with Tanner stage 2	correspond with Tanner stage 2	high estriol
Diaz Case 1	–	1	Y	2ml	x	2 × 2 cm	Normal
Diaz Case 2	1y	1	Y	2ml	x	5 × 6 cm	Normal
Diaz Case 3	past 3 years	1	–	2ml	2 × 2	4 × 4	Normal
Linklater	from 6 months	none	–	N/A	up to 3 cm	up to 3 cm	Mildly Elevated
Ramsey Case 1	“since age 6″	1	–	N/A	4 × 3	x	Normal
Ramsey Case 2	"since age 1″	1	–	N/A	x	3.3 × 2.8	No Evaluation Discussed
Ramsey Case 3	–	1	–	N/A	“Tanner stage 2″	x	No Evaluation Discussed
Ramsey Case 4	“since 4 years of age”	–	–	1 ml	4 × 4	4 × 4	Normal

Table 5
Exposure.

Author / Case	Exposure	Exposure to LO Confirmed	Other Exposures Identified	Exposure Duration	Exposure Frequency	Follow up Duration
Henley Case 1	unidentified healing balm	Ingredient List	Y, none	"shortly before"	–	"several months after 4 m"
Henley Case 2	unidentified styling gel / shampoo	Ingredient List	Y, none	–	daily	9 months
Henley Case 3	lav scented soap / intermittent use of lav scented lotion	No	Y, none	–	intermittent use	"a few months" - according to patient's family
Diaz Case 1	unidentified shampoo	No	unidentified	"approx1 year"	–	4 m
Diaz Case 2	agua de violetas	Tested	unidentified	since childhood	intermittent / "becoming more frequent"	"soon after"
Diaz Case 3	agua de violetas	Tested	unidentified	since childhood	–	4 m
Linklater	wipes, shampoo, body wash, cream, lotion	Ingredient List	unidentified	–	daily	"immediately"
Ramsey Case 1	Mi Tesoro Agua de Violetas	Tested	unidentified	"since early childhood"	"frequent"	6m
Ramsey Case 2	Baby Magic Calming Baby Bath	No	unidentified	"since infancy"	–	6m
Ramsey Case 3	unknown diffuser	No	unidentified	"1 year" - not clear calendar or school year	"all day"	3m
Ramsey Case 4	Crusellas Violet Water	Tested	unidentified	"since infancy"	daily	6m

laboratory tests for genetic conditions. However, only Henley reported ruling out potential alternative causes. Multiple endocrine disrupting chemicals have been identified in the environment. Certain drugs, diets, and environmental exposures can produce sufficient activity to result in these outcomes.[45] Whether these cases included known risk factors, such as long term consumption of soy products or drug exposure during pregnancy, is not clear.

Because most cases of prepubertal gynecomastia and premature thelarche are considered to be idiopathic and resolve spontaneously, the potential that these outcomes are unrelated to the exposure is significant.[46] Furthermore, many of the children were no longer prepubertal when resolution was noted. Because progression of puberty was not monitored, it is not possible to determine from the existing reports if these children were prepubertal at the time of the onset of symptoms.

4. Discussion

The existing body of evidence is insufficient to confirm the proposed link between LEO, TTEO, and endocrine disruption in children. With the possible exception of reversibility, none of the Bradford Hill criteria for causation are met through the current evidence. Aside from the presence of case reports, the only human research in the literature concludes that these two essential oils do not exhibit endocrine disrupting activity when used in integrative health and as an ingredient in personal care products.

4.1. Tea tree essential oil and endocrine disruption

This systematic review found no evidence that tea tree essential oil exposure is related to endocrine disrupting outcomes such as prepubertal gynecomastia and premature thelarche. Only one of the case studies involved the suspected use of TTOE and the exposure was confirmed through parental recall of the product's ingredients. Previous findings support the conclusion that TTEO has anti-estrogen activity, which further decreases the likelihood that a causal relationship exists.[47]

Based on the evidence identified in this report, the proposed association between tea tree essential oil and prepubertal gynecomastia / premature thelarche is highly speculative and clinically unlikely. Future prepubertal gynecomastia case reports should evaluate other potential causes which are better substantiated through the literature.

4.2. Lavender essential oil and endocrine disruption

Lavender was a proposed causal agent in all 11 cases. However, confirmation of exposure to lavender essential oil was inconsistent across the studies. Six of the eleven case studies did not identify the product which is said to contain lavender essential oil. One of the case studies (Case 2, Ramsey, 2019) incorrectly identifies Baby Magic Calming Baby Wash as a lavender essential oil-containing product. Without confirmation of the presence of this ingredient in the products in question, it is not clear whether these proposed links are related to essential oils, synthetic fragrances, some other ingredient, or some other exposure altogether.

While some form of lavender-related ingredient appears to exist in all of these products, the chemical composition of the ingredients varies substantially. While pediatric epidemiological studies are not available for review, previous work has concluded that LEO does not have an estrogenic effect in adults.[48,49] Therefore, other shared ingredients in the products in question should be evaluated as potential causal factors.

4.3. Limitations

Because sufficient data were not provided in the reports, statistical analysis of the patients was not possible. There are also limits to the

generalizability of this review. Without demographic and socio-economic data regarding the cases, the current evidence does not allow conclusions to be made regarding which population(s) may be at risk. Authors of case studies have indicated these cases are more prevalent among hispanic populations, but this statement lacks context and data.[50]

4.4. Recommendations

This review finds no epidemiological evidence that TTEO is capable of causing prepubertal gynecomastia or premature thelarche in children, and little to no evidence that LEO is a likely causal agent. It should be emphasized that a lack of evidence of harm cannot be interpreted as evidence of safety. These cases raise important questions about the safety of routine exposure to personal care product ingredients, such as essential oils, that have yet to be investigated through scientific evaluation. This leaves a substantial gap in knowledge regarding the safety, or lack thereof, of these common household products.

Epidemiological studies are urgently needed to identify the incidence of endocrine disruption outcomes in pediatric populations with documented exposure to lavender essential oil. The use of essential oils has increased in prevalence in recent years, yet these cases remain extremely rare. Any causal relationship that may exist between these oils and endocrine disrupting outcomes likely involves some level of genetic or environmental predisposition. Future research, including any future case studies, should report demographic details of the patients so that the risk factors that contribute to that association can also be identified.

5. Conclusions

This systematic review finds that tea tree essential oil is not related to documented cases of endocrine disruption in children, and that there is little to no evidence to substantiate the proposed link between lavender essential oil and endocrine disruption in children. Because this potential link remains a concern among pediatric care providers and parents, epidemiological research to address the proposed link is needed.

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Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2019.102288.

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