

Consumption of medicinal plants and herbal medicines by children and adolescents with chronic conditions: a survey in a tertiary-care outpatient clinic

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ABSTRACT

Objectives: Medicinal plants and herbal medicines are widely used worldwide. However, patients with chronic health conditions or their caregivers do not often disclose these practices to their healthcare providers, leading to potentially severe interactions with current treatments, especially in children. We aimed to describe the prevalence of the use of medicinal plants and herbal medicines by children and adolescents with chronic health conditions and whether their physicians were informed about it. **Methods:** We conducted a cross-sectional electronic survey on parents and caregivers of children and adolescents with chronic health conditions seen at a university, tertiary-care pediatric outpatient clinic. The common names of the plants cited by respondents were reviewed and Latin names of the species were provided whenever possible. **Results:** From 20,213 text messages sent in May and June 2021, 521 valid responses were obtained. The prevalence of the use of medicinal plants and herbal medicines was 34.6%, most without a medical prescription (self-medication), and few physicians (4.0%) were aware of it. The five most used species were: *Mentha spicata* L. (mint), *Foeniculum vulgare* Mill. (fennel), "cidreira" (a common name possibly corresponding to *Cymbopogon citratus* (DC.) Stapf, *Melissa officinalis* L. or *Lippia alba* (Mill.) N.E. Br. ex Britton & Wilson, P.), *Matricaria chamomilla* L. (German chamomile), and *Plectranthus barbatus* Andrews (boldo). **Conclusions:** The prevalence of the use of medicinal plants and herbal medicines by children and adolescents with chronic health conditions in a tertiary-care outpatient clinic was 34.6%, and only a few physicians were aware of it.

Keywords: Plants medicinal, Herbal medicine, Phytotherapy, Pediatrics, Chronic disease.

RESUMO

Objetivos: Plantas medicinais e seus derivados são amplamente utilizados no mundo todo. Entretanto, pacientes com condições crônicas de saúde ou seus cuidadores frequentemente não informam essas práticas para seus profissionais de saúde, levando a interações potencialmente graves com os demais tratamentos, especialmente em crianças. Nós objetivamos descrever a prevalência do uso de plantas medicinais e derivados por crianças e adolescentes com condições crônicas de saúde, e se seus médicos foram informados sobre isto. **Métodos:** Levantamento eletrônico transversal junto a pais e cuidadores de crianças e adolescentes com condições crônicas de saúde atendidos em um serviço ambulatorial pediátrico universitário terciário. Os nomes comuns das plantas citadas pelos participantes foram revisados e os nomes latinos das espécies foram identificados, sempre que possível. **Resultados:** De 20.213 mensagens de texto enviadas em maio e junho de 2021, 521 respostas válidas foram obtidas. A prevalência de utilização de plantas medicinais e derivados foi de 34,6%, sendo a maioria sem prescrição médica (automedicação), e poucos médicos (4,0%) estavam cientes disto. As cinco plantas mais comumente utilizadas foram: *Mentha spicata* L. (hortelã), *Foeniculum vulgare* Mill. (funcho), "cidreira" (possivelmente correspondendo a *Cymbopogon citratus* (DC.) Stapf, *Melissa officinalis* L. ou *Lippia alba* (Mill.) N.E. Br. ex Britton & Wilson, P.), *Matricaria chamomilla* L. (camomila) e *Plectranthus barbatus* Andrews (boldo nacional). **Conclusões:** A prevalência de uso de plantas medicinais e derivados por crianças e adolescentes com condições crônicas de saúde em um serviço ambulatorial pediátrico terciário foi de 34,6%, com grande potencial para interações, e somente poucos médicos estavam cientes disto.

Palavras-Chave: Plantas medicinais, Medicina herbária, Fitoterapia, Pediatria, Doença crônica.

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INTRODUCTION

According to the World Health Organization (WHO), most people worldwide rely on complementary and alternative medicine (CAM), including medicinal plants and herbal medicines, as their primary source of healthcare or as adjuvants to current treatments for their health problems. Moreover, patients with specific chronic health conditions are more likely to use CAM and herbal medicines¹.

There is a common belief that natural products are always harmless, leading to self-medication and excessive consumption. On the contrary, these products can be contaminated with microorganisms or pesticides, be of poor quality, or the species itself may be dangerous or cause serious adverse events. For example, herbal-drug interactions can increase or decrease the plasma concentrations of drugs, unpredictably affecting their efficacy and/or toxicity². This is especially concerning in patients with complex, chronic health conditions, who often continuously use one or more drugs. Nonetheless, patients and their caregivers often do not report the use of these products to their healthcare providers (physicians, nurses, and others)³.

Brazil has a solid cultural background in the use of medicinal plants, with multi-ethnic cultural influences from Native Americans, Africans, and Europeans. There are reports on the frequent use of medicinal plants in children of a Brazilian school⁴ and a general pediatric outpatient clinic. However, to the best of our knowledge, there are no reports on the use of medicinal plants in children with chronic health conditions in Brazil.

This study aimed at describing the use of medicinal plants and herbal medicines by children and adolescents with chronic health conditions attending the outpatient clinics of a university, tertiary-care Brazilian hospital, including the commonly used species and the frequency of use.

PATIENTS AND METHODS

This was a cross-sectional, online open survey on parents and caregivers of children and adolescents with chronic health conditions attending a university, tertiary-care Brazilian pediatric hospital (HC Criança, Hospital das Clínicas, Ribeirão Preto Medical School,

University of São Paulo). The study was designed according to The Checklist for Reporting Results of Internet E-Surveys (CHERRIES)⁵. This study was approved by the local institutional review board (Research Ethics Committee, Ribeirão Preto Medical School, University of São Paulo, Brazil, CAAE 42780821.7.0000.5440). All participants received an electronic informed consent form and agreed to participate before answering the questionnaire.

Parents and caregivers of all patients younger than 18 years seen in HC Criança were eligible. Invitations to answer the questionnaire (SMS, short message service) were sent to all the phone numbers registered in the electronic medical records, with a clickable URL leading to the online consent form. After reading the consent form, they could choose to participate or not. They were included if they agreed to participate, and they could request their exclusion from the study anytime. No incentives were offered.

The consent form and the questionnaire were built in the Research Electronic Data Capture (REDCap) tool (<https://projectredcap.org>), using a responsive design that allowed respondents to fill out the questionnaire on smartphones or computers. This tool allows efficient data collection, data safety, and exports to the main statistical packages⁶. Briefly, there were questions on the use of medicinal plants or herbal medicines, type, species, or brand names, along with their dosages, indications, origin, perceived efficacy, side effects, adverse reactions, and who prescribed or recommended the product (21 items, 3 pages). All items had a non-response option (not applicable or rather not say). Respondents were able to review their responses before submitting them. Partial responses were analyzed.

Two researchers reviewed the plant common names in the answers and matched them with the corresponding scientific names whenever possible. The Latin names were checked in Tropicos (<https://www.tropicos.org/home>).

Sample size calculation

Approximately 32,000 patients are seen at HC Criança yearly. Considering a response rate of 10%, we anticipated obtaining 3,200 answers. Besides, considering an estimated prevalence of the use of herbal medicines of 50%, a minimum of

376 answers would be needed for a representative sample with 80% power and 5% significance. If the actual prevalence is lower (20%), 1,403 answers are needed to be a representative sample.

Statistical analysis

Results were expressed in means (standard deviations), median (interquartile ranges), or frequencies (percentages).

RESULTS

From a total of 20,213 SMSs sent in May and June 2021, 710 answers were obtained (3.5% response rate), and 521 agreed to participate (73.4% of respondents). The demographic characteristics of the children and adolescents are depicted in Table 1.

Table 1

Demographic characteristics of the patients whose parents or caregivers participated in the study (n=521).

Characteristic	Result
Sex	
<i>Male</i>	295 (56.6%)
<i>Female</i>	224 (43.0%)
<i>Rather not say</i>	2 (0.4%)
Age group (years)	
0-4	124 (27.4%)
5-9	136 (30.0%)
10-14	118 (26.0%)
15-19	58 (12.8%)
20-24	12 (2.7%)
25-29	5 (1.1%)
Ethnicity	
<i>White</i>	323 (62.5%)
<i>Brown</i>	148 (28.6%)
<i>Black</i>	40 (7.7%)
<i>Asian</i>	0
<i>Native</i>	0
<i>Rather not say</i>	6 (1.2%)
Main caregiver	
<i>Mother</i>	445 (85.6%)
<i>Grandparent</i>	46 (8.9%)

<i>Father</i>	13 (2.4%)
<i>Older brother or sister</i>	7 (1.3%)
<i>Uncle or aunt</i>	5 (0.9%)
<i>Other</i>	5 (0.9%)
Monthly income (USD)	
≤ 200	125 (34.9%)
201-1900	211 (58.9%)
901-1800	15 (4.2%)
1801-2700	4 (1.1%)
2701-3600	2 (0.6%)
≥ 3601	1 (0.3%)

Legend: USD, United States of America dollars.

The patients were followed up in different medical specialties, mostly Neurology, Endocrinology, and General Pediatrics (Table 2).

Table 2

Medical specialties following up the patients whose parents or caregivers participated in the study (n=521).

Medical specialty	N	%
Neurology	129	24,8%
Endocrinology	71	13,6%
Pediatrics	68	13,0%
Ophthalmology	47	9,0%
Cardiology	45	8,6%
Ear, nose, and throat	38	7,3%
Immunology	35	6,7%
Allergology	32	6,1%
Psychiatry	31	5,9%
Gastroenterology	27	5,2%
Pulmonology	23	4,4%
Pediatric surgery	22	4,2%
Nephrology	20	3,8%
Gynecology	12	2,3%
Hematology	12	2,3%
Neonatology	12	2,3%
Infectious diseases	11	2,1%
Oncology	8	1,5%
Hepatology	6	1,1%
Obesity	3	0,6%
Other	74	14,2%

The use of medicinal plants or herbal medicines (previous or current) was reported by 180 (34.6%) parents or caregivers. They also reported that only 4.0% of physicians asked about the use of CAM, whereas 2.9% of physicians prescribed or recommended such treatments. Among participants reporting the use of herbal medicines, these products were obtained mostly from relatives, neighbors, or friends or were grown at home (Table 3).

Table 3

Origin of the herbal products used (n=175).

Origin	N	%
From relatives, neighbors, or friends	68	38.9%
Home garden	59	33.7%
Pharmacy	54	30.9%
Natural products store	38	21.7%
Grocery stores or supermarkets	24	13.7%
Other	16	9.1%
Local farmers	15	8,57%
Traditional healers	3	1,71%

The five main plant species reported were: *Mentha spicata* L. (mint), *Foeniculum vulgare* Mill. (fennel), "cidreira" (a common name possibly corresponding to *Cymbopogon citratus* (DC.) Stapf, *Melissa officinalis* L. or *Lippia alba* (Mill.) N.E. Br. ex Britton & Wilson, P.), *Matricaria chamomilla* L. (German chamomile), and *Plectranthus barbatus* Andrews (boldo) (Table 4).

The main forms of use were as teas (infusions, decoctions, or macerations), and the main indications were: cold and flu; anxiety, irritability, and restlessness; productive cough; insomnia; colic, dyspepsia, diarrhea, or constipation; inflammatory conditions; immune-boosting; headaches; skin ulcers; and worms.

When asked about the perceived efficacy of herbal medicines, 54.8% of parents and caregivers reported significant benefit, 24% partial benefit, and only 1% lack of benefit (20.2% missing or unsure) (Table 5). None of the participants reported side effects or adverse events.

DISCUSSION

In this survey, we found that one-third (34.6%) of children and adolescents with chronic health conditions attending a pediatric tertiary care

outpatient clinic have used or currently use medicinal plants and herbal medicines. Moreover, only a few physicians (4%) questioned the patients and their parents or caregivers about this. This means that most children were given herbal medicines without the supervision of a healthcare professional, that is, self-medication. Moreover, parents and caregivers reported they obtained the medicines from relatives, neighbors, friends, their home gardens, pharmacies (without a prescription), or natural products stores.

The use of medicinal plants and herbal medicines by adult patients has been described in several countries with different incomes⁷. In children, the scenario is not different: there are reports on the use of CAM, including herbal products, by pediatric patients with a broad range of chronic health conditions, such as inflammatory bowel disease (IBD) (22-84%)⁸, cancer (6-91%)⁹, liver and gastrointestinal diseases (49%)¹⁰, food allergy (8.4%)¹¹, chronic viral hepatitis (46%)¹², and atopic dermatitis (42.5%)¹³, among others. This is consistent with what we found that patients seen by different medical specialties do use herbal medicines. Also, like in our study, most of these patients use herbal medicines without the supervision of a healthcare professional. This scenario is better in some countries, such as Germany, in which nearly half of the herbal products are prescribed to children by their medical doctors¹⁴.

The prevalence of CAM use does not seem to differ in developed versus developing countries. The prevalence of CAM use among Australian children within the previous 12 months was 73.8%, whereas herbal medicines were 38.8% of these practices¹⁵. In Nigerian children living in the Turkish Republic of Northern Cyprus, the prevalence of CAM use was 68% (55.9% herbal medicines) within the preceding 12 months¹⁶. Among children and adolescents attending the general pediatric outpatient department of two German university children's hospitals and the practice of two general pediatricians, herbal products were used by 85.5% of them¹⁷. In Italy, the prevalence of CAM use in children was 48.3% (at least once in life) and 38,1% (during the previous year)¹⁸. A survey in two Canadian pediatric hospitals assessed the prevalence and patterns of CAM use in ten subspecialty clinics. CAM use was more frequent in the western (71%) than in the central hospital (42%)¹⁹.

Children without chronic health conditions also use herbal medicines worldwide. In a systematic

Table 4

Main medicinal plants mentioned by participants (with at least five citations), their pharmaceutical forms, and main indications (n=521).

Species	Citations	Pharmaceutical forms	Indications
<i>Mentha spicata</i> L.	89	infusion*, syrup, essential oil, topic preparation†	Cold and flu, sore throat, stuffy nose, gastrointestinal complaints (colic, vomiting, dyspepsia), headache, cough, anxiety, and worms.
<i>Foeniculum vulgare</i> Mill.	50	infusion, tincture, syrup, essential oil	Colic, constipation, cold and flu, insomnia, insect bites, wounds, anxiety, and inflammation.
Cidreira*	48	infusion, syrup	Insomnia, cold and flu, colic, dyspepsia, anxiety, and as a diuretic.
<i>Matricaria chamomilla</i> L.	46	infusion, tincture, syrup, essential oil, topic preparation, capsule [§]	Insomnia, colic, teething, allergy, anxiety, and inflammation.
<i>Plectranthus barbatus</i> Andrews	39	infusion, syrup	Dyspepsia, epigastric pain, headache, and liver conditions.
<i>Mikania</i> spp	30	infusion, syrup	Cold and flu, sore throat, stuffy nose, asthma, and cough.
<i>Melissa officinalis</i> L.	21	infusion, tincture, capsule	Anxiety and insomnia.
<i>Mentha pulegium</i> L.	18	infusion, syrup, topic preparation	Cold and flu, epigastric pain, dyspepsia, colic, immune-boosting, anxiety, cough.
<i>Dysphania ambrosioides</i> (L.) Mosyakin & Clemants	15	infusion, tincture, syrup, topic preparation	Cold and flu, colic, cough, worms, and inflammation.
<i>Rosmarinus officinalis</i> L.	14	infusion	Anxiety, headache, allergy, and inflammation.
<i>Zingiber officinale</i> Roscoe	13	infusion, syrup	Cold and flu, sore throat, ear pain, allergy, inflammation, and immune boosting.
<i>Cymbopogon citratus</i> (DC.) Stapf.	12	infusion, essential oil	Cold and flu, insomnia, and anxiety.
<i>Passiflora</i> spp	11	infusion, tincture, syrup, capsule	Insomnia, irritability, and anxiety.
<i>Cinnamomum</i> spp	9	infusion, syrup	Cold and flu, cough, pain, and urolithiasis.
<i>Cotyledon orbiculata</i> L.	9	tincture, essential oil, topic preparation	Ear pain, epigastric pain, diarrhea, diaper rash, burns, and wounds.
<i>Ocimum basilicum</i> L.	9	infusion, syrup	Cold and flu, headache, anxiety, and cough.
<i>Aloe vera</i> (L.) Burm. f.	8	syrup, topic preparation	Wounds.
<i>Ocimum</i> spp	8	infusion	Cold, flu, and cough.
<i>Curcuma longa</i> L.	7	infusion, capsule	Inflammation, constipation, immune boosting, and dyspepsia.
<i>Pereskia aculeata</i> Mill	7	raw (fresh or dry) material	Anemia, low platelet count, malnutrition, cough, and impaired vision.
<i>Allium sativum</i> L.	6	infusion, syrup	Cold and flu, cough, immune boosting, and inflammation.
<i>Citrus × latifolia</i> Tanaka ex Q. Jiménez	6	infusion	Cold and flu and inflammation.
<i>Baccharis trimera</i> (Less.) DC.	5	infusion, capsule	Digestive complaints.

<i>Lavandula angustifolia</i> Mill.	5	essential oil	Anxiety and insomnia.
<i>Pelargonium sidoides</i> DC.	5	tincture, capsule	Cold and flu, cough, and immune boosting.
<i>Psidium guajava</i> L.	5	infusion	Colic and diarrhea.
<i>Punica granatum</i> L.	5	infusion, syrup	Sore throat and anemia.
<i>Ruta graveolens</i> L.	5	infusion, tincture	Epigastric pain, and conjunctivitis.
Other ^{††}	135	all the above	

[†] Includes infusion, decoction, and maceration.

^{††} Includes ointments, creams, and gels.

[‡] May refer to different species, including *Cymbopogon citratus* (DC.) Stapf., *Melissa officinalis* L., and *Lippia alba* (Mill.) N.E. Br. ex Britton & Wilson, P.

[§] Includes capsules with powdered plant material, dry extract, soft extract, or tablets with dry extract.

^{||} Includes *Citrus sinensis* (L.) Osbeck, *Copaifera* spp, *Mentha × piperita* L., *Arnica montana* L. OR *Solidago chilensis* Meyen, *Ilex paraguariensis* A. St.-Hil., *Artemisia absinthium* L., *Alternanthera brasiliana* (L.) Kuntze, *Myristica fragrans* Houtt., *Hedera helix* L., *Ageratum conyzoides* L., *Coriandrum sativum* L., *Maytenus officinalis* Mabb., *Equisetum hyemale* L., *Echinacea* spp, *Eucalyptus globulus* Labill., *Achyrocline satureioides* DC., *Commiphora leptophloeos* (Mart.) J.B. Gillett, *Phyllanthus* spp, *Costus* spp, *Dioscorea* spp, *Rosa alba* L., *Camellia sinensis* (L.) Kuntze, *Amburana* spp, *Xanthosoma sagittifolium* (L.) Schott, *Petroselinum crispum* (Mill.) Fuss, *Hypericum perforatum* L., *Pterodon emarginatus* Vogel, *Cinnamomum camphora* (L.) J. Presl, *Syzygium aromaticum* (L.) Merr. & L.M. Perry, *Sambucus australis* Cham. & Schtdl., *Cucurbita pepo* L., *Annona muricata* L., *Hymenaea courbaril* L., *Boswellia* spp, *Cassia angustifolia* Vahl, *Cenostigma pyramidale* (Tul.) Gagnon & G.P. Lewis, *Ricinus communis* L., *Justicia pectoralis* Jacq., *Origanum vulgare* L., *Kalanchoe pinnata* (Lam.) Pers., *Carapa guianensis* Aubl., *Cichorium intybus* L., *Bauhinia forficata* Link, *Linum usitatissimum* L., *Beta vulgaris* L., *Malva sylvestris* L., *Bidens pilosa* L., *Apium graveolens* L., Tamarine® (*Cassia fistula* L. plus *Senna alexandrina* Mill.), *Cinchona* spp, *Syzygium cumini* (L.) Skeels, *Erythrina mulungu* Mart. ex Benth., *Brassica oleracea* L., *Apuleia ferrea* (Mart.) Baill., *Peumus boldus* Molina, *Salvia officinalis* L., *Plantago major* L., *Silybum marianum* (L.) Gaertn., *Polygonum* spp, *Solanum melongena* L., *Herreria* spp OR *Smilax* spp, *Capsicum* spp, *Pyrostegia venusta* (Ker Gawl.) Miers, *Musa × paradisiaca* L., *Hibiscus sabdariffa* L., *Allium cepa* L., *Cymbopogon nardus* (L.) Rendle, *Citrus* spp, *Cocos nucifera* L., *Aristolochia* spp, *Solanum cernuum* Vell., *Achillea millefolium* L., *Solanum tuberosum* L., *Citrus reticulata* Blanco, *Cynara cardunculus* L., *Moringa oleifera* Lam., *Thuja occidentalis* L., *Valeriana officinalis* L., *Ginkgo biloba* L., *Zea mays* L., *Gossypium* spp, *Abelmoschus esculentus* (L.) Moench, and *Hamamelis virginiana* L..

Table 5

Perceived benefit of the use of medicinal plants and herbal medicines by children and adolescents with chronic health conditions (with at least five citations, n=521).

Species	Citations	Significant benefit	Partial benefit	No benefit	Unsure	Missing	No side effects	Unsure about side effects
<i>Mentha spicata</i> L.	89	50 (56.2%)	24 (27%)	-	1 (1.1%)	14 (15.7%)	71 (79.8%)	4 (4.5%)
<i>Foeniculum vulgare</i> Mill.	50	24 (48%)	15 (30%)	-	-	11 (22%)	39 (78%)	-
Cidreira*	48	26 (54.2%)	12 (25%)	-	3 (6.2%)	7 (14.6%)	40 (83.3%)	1 (2.1%)
<i>Matricaria chamomilla</i> L.	46	28 (60.9%)	11 (23.9%)	-	-	7 (15.2%)	38 (82.6%)	1 (2.2%)
<i>Plectranthus barbatus</i> Andrews	39	18 (46.1%)	12 (30.8%)	-	3 (7.7%)	6 (15.4%)	31 (79.5%)	2 (5.1%)
<i>Mikania</i> spp	30	25 (83.3%)	2 (6.7%)	-	1 (3.3%)	2 (6.7%)	27 (90%)	1 (3.3%)
<i>Melissa officinalis</i> L.	21	13 (61.9%)	3 (14.3%)	-	1 (4.8%)	4 (19%)	16 (76.2%)	1 (4.8%)
<i>Mentha pulegium</i> L.	18	10 (55.6%)	3 (16.7%)	-	1 (5.5%)	4 (22.2%)	13 (72.3%)	1 (5.5%)
<i>Dysphania ambrosioides</i> (L.) Mosyakin & Clemants	15	3 (20%)	8 (53.3%)	-	1 (6.7%)	3 (20%)	11 (73.3%)	1 (6.7%)
<i>Rosmarinus officinalis</i> L.	14	7 (50%)	3 (21.4%)	-	-	4 (28.6%)	10 (71.4%)	-

<i>Zingiber officinale</i> Roscoe	13	7 (53.8%)	3 (23.1%)	-	1 (7.7%)	2 (15.4%)	9 (69.2%)	2 (15.4%)
<i>Cymbopogon</i> <i>citratus</i> (DC.) Stapf.	12	6 (50%)	2 (16.7%)	-	-	4 (33.3%)	7 (58.4%)	1 (8.3%)
<i>Passiflora</i> spp	11	4 (36.4%)	4 (36.4%)	1 (9.0%)	-	2 (18.2%)	9 (81.8%)	-
<i>Cinnamomum</i> spp	9	4 (44.5%)	2 (22.2%)	-	1 (11.1%)	2 (22.2%)	6 (66.7%)	1 (11.1%)
<i>Cotyledon orbiculata</i> L.	9	6 (66.7%)	2 (22.2%)	-	-	1 (11.1%)	8 (88.9%)	-
<i>Ocimum basilicum</i> L.	9	4 (44.5%)	2 (22.2%)	1 (11.1%)	-	2 (22.2%)	7 (77.8%)	-
<i>Aloe vera</i> (L.) Burm. f.	8	7 (87.5%)	1 (12.5%)	-	-	-	8 (100%)	-
<i>Ocimum</i> spp	8	4 (50%)	2 (25%)	-	-	2 (25%)	6 (75%)	-
<i>Curcuma longa</i> L.	7	4 (57.1%)	-	-	1 (14.3%)	2 (28.6%)	5 (71.4%)	-
<i>Pereskia aculeata</i> Mill	7	5 (71.4%)	-	-	-	2 (28.6%)	5 (71.4%)	-
<i>Allium sativum</i> L.	6	3 (50%)	2 (33.3%)	-	-	1 (16.7%)	5 (83.3%)	-
<i>Citrus × latifolia</i> Tanaka ex Q. Jiménez	6	5 (83.3%)	-	-	-	1 (16.7%)	5 (83.3%)	-
<i>Baccharis trimera</i> (Less.) DC.	5	2 (40%)	-	1 (20%)	-	2 (40%)	2 (40%)	1 (20%)
<i>Lavandula</i> <i>angustifolia</i> Mill.	5	2 (40%)	3 (60%)	-	-	-	5 (100%)	-
<i>Pelargonium</i> <i>sidoides</i> DC.	5	5 (100%)	-	-	-	-	5 (100%)	-
<i>Psidium guajava</i> L.	5	4 (80%)	-	-	-	1 (20%)	4 (80%)	-
<i>Punica granatum</i> L.	5	1 (20%)	3 (60%)	-	-	1 (20%)	3 (60%)	1 (20%)
<i>Ruta graveolens</i> L.	5	-	2 (40%)	1 (20%)	-	2 (40%)	3 (60%)	-
Total	505	277 (54.8%)	121 (24%)	5 (1%)	13 (2.6%)	89 (17.6%)	400 (79.2%)	16 (3.2%)

* May refer to different species, including *Cymbopogon citratus* (DC.) Stapf., *Melissa officinalis* L., and *Lippia alba* (Mill.) N.E. Br. ex Britton & Wilson, P.

review, the use of CAM by children and adolescents without chronic health conditions from 19 countries ranged from 10.9 to 87.6% for lifetime use and from 8 to 48.5% for current use. The countries with higher rates of herbal medicine use were Germany, Turkey, and Brazil, ranging between 0.8-85.5% (lifetime) and 2.2-8.9% (current)²⁰.

This practice is also common among hospitalized patients or those scheduled for surgery. In hospitalized children in Israel, the prevalence of current CAM use was 54.3%²¹. CAM use in children presenting for surgery in five geographically diverse centers in the USA was 3.5% within two weeks before surgery²². In another study in the US, 6.4% of children

were currently taking an herbal preparation while presenting for ambulatory anesthesia and surgery²³.

The reasons why people around the world use herbal medicines and other forms of CAM include low cost, cultural reasons, and lack of access to health services¹. Motivations for the use of CAM in other studies include disease severity, concern for adverse effects of conventional medicines⁸, intention to cure the disease, symptomatic relief, and support of ongoing use of conventional therapy⁹. In our study, parents and caregivers reported low-complexity symptoms as indications for the herbal products, such as cold and flu, dyspepsia, colic, and anxiety. Accordingly, the main indications for herbal

medicines in children from Germany were coughs and colds¹⁴.

Noticeably, parents and caregivers usually do not disclose their use of CAMs to physicians or nurses^{12,15,16,21}. One explanation for this behavior is that parents and caregivers do not always feel comfortable discussing CAM with their healthcare providers¹⁹. Another explanation is that physicians do not question their patients regarding the use of CAM. In our study, only 4% of parents reported that their doctors did so.

The use of medicinal plants and their derivatives is not inherently bad, and most people worldwide do it. In otherwise healthy people, these products are unlikely to produce serious adverse events, given adequate doses are used. We do not intend to discourage the use of herbal medicines. The problem arises when patients with chronic health conditions, often using more than one drug for their treatment. Herbal products can interact with many conventional drugs through synergism or antagonism, although antagonism is rarely reported in the literature. Herbal products can also stimulate or inhibit cytochrome P450 (CYP450) enzymes, increasing or decreasing the half-life of drugs metabolized by CYP450, such as oral hypoglycemics, antibiotics, and antiepileptic drugs²⁴. A list of drugs with the greatest potential to interact with herbal products include benzodiazepines, corticosteroids, cyclosporine, digoxin, diuretics, hypoglycemics, iron, levothyroxine, non-steroidal anti-inflammatory drugs, monoamine oxidase (MAO) inhibitors, phenobarbital, phenytoin, spironolactone, and warfarin²⁵. This is concerning since about 40% of the patients in this study had neurological or endocrinological diseases and are very likely to use drugs in that list.

The major group of patients in our sample was seen in the pediatric neurology specialty. Although we did not collect information on the drugs the patients were receiving, pediatric patients with neurologic conditions frequently use antiepileptic drugs (AED), such as valproate, carbamazepine, benzodiazepines (clobazam, lorazepam), phenytoin, and barbiturates (phenobarbital)²⁶. There are reports of severe adverse events and death caused by interactions between herbal products and AED^{27,28}.

In patients with cancer, most antineoplastic drugs are metabolized in the liver through CYP450 enzymes. Among the main CYP enzymes that metabolize anticancer drugs (CYP3A4, CYP2D6,

CYP2C9, and CYP2C19)²⁹, herbal products have great potential to interact with CYP3A4 and CYP2C9 affecting the pharmacokinetics of bortezomib, busulfan, cyclophosphamide, dasatinib, ciclosporin, dexamethasone, docetaxel, doxorubicin, erlotinib, etoposide, everolimus, gefitinib, ifosfamide, irinotecan, imatinib, lapatinib, methylprednisolone, nilotinib, paclitaxel, prednisone, prednisolone, sirolimus, sorafenib, sunitinib, tacrolimus, tamoxifen, temsirolimus, and tretinoin²⁹.

Concerning the most used species by our patients [mint, fennel, "cidreira" (possibly lemon balm or lemongrass), German chamomile, and boldo], fennel should be avoided by people with hyperestrogenism and can interact with ciprofloxacin³⁰; mint can cause respiratory depression or laryngeal spasm in young infants because of menthol or trigger seizures because of pulegone³¹; chamomile can interact with anticoagulants and decrease iron absorption³²; lemon balm can disrupt TSH-stimulated adenylate cyclase activity³³, whereas boldo can potentiate the effects of barbiturates on the central nervous system and interact with metronidazole, disulfiram, antihypertensives, digoxin, and thyroid modulators³⁴.

On the other hand, herbal medicines should not always be seen as prejudicial. If used properly, they can be useful in a wide range of clinical situations. For example, *Centella asiatica* (L.) Urb. (Apiaceae) has the potential to improve the therapeutical efficacy of AED, such as valproate and phenytoin, through pharmacokinetic potentiation³⁵. Another example is *Echinacea* spp (Asteraceae), which can be safely used to prevent and shorten respiratory tract infections and reduce antibiotic use in children³⁶.

Healthcare providers must be aware that a significant proportion of their patients use herbal medicines and other natural products, and it is also important to ask which ones, when, how often, how much, and what are the possible interactions with the current treatment. However, physicians and other healthcare providers do not feel comfortable about their patients using CAM, possibly because of misconceptions about it and because there usually is no formal education in CAM and herbal medicine in medical schools³⁷. If properly trained, healthcare professionals could also educate their patients regarding the rational use of herbal medicines so they did not need to rely on information found on

the Internet or from relatives and friends^{16,21}, as we found in our study.

Policymakers, researchers, and faculty members should include herbal medicine in the curricula of medical schools and universities with undergraduate courses in the health professions, as suggested by WHO¹.

A limitation of this study was the report of common names of the plants. Although experienced researchers matched these names with the corresponding scientific names, common names sometimes can correspond to different species. In addition, these families may have been incorrectly naming the species they use. Using the wrong species may result in no benefit but, more importantly, can cause mild to severe adverse reactions. This is especially true when different species are morphologically similar or have the same common name. Only an ethnobotanical study could address this limitation.

In our study, parents and caregivers consistently reported perceived benefits of herbal medicines to their children and reported no side effects or adverse events. This might not be completely true since people who like or believe in CAM are more likely to have participated in the survey, which is another limitation of our study. Therefore, our findings cannot be generalized to a broader population without caution. Nevertheless, even if the actual proportion of patients using herbal medicines is lower, some patients are at risk of interactions with their treatments, side effects, and adverse events, and healthcare providers are not aware of this.

In conclusion, the prevalence of the use of herbal medicines in children and adolescents with chronic health conditions seen in our pediatric hospital was 34.6%, mostly without a medical prescription (self-medication), and few of their physicians were aware of that.

REFERENCES

1. WHO. WHO Traditional Medicine Strategy: 2014-2023. Geneva: World Health Organization; 2013. 78 p.
2. Izzo AA, Ernst E. Interactions Between Herbal Medicines and Prescribed Drugs [Internet]. 2009 Sep;69(13):1777-98. Available from: <http://link.springer.com/10.2165/11317010-000000000-00000>
3. Marlière LDP, Ribeiro AQ, Brandão M das GL, Klein CH, Acúrcio F de A. Utilização de fitoterápicos por idosos: resultados de um inquérito domiciliar em Belo Horizonte (MG), Brasil. Rev Bras Farmacogn [Internet]. 2008 Dec;18:754-60. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-695X2008000500021&lng=pt&nrm=iso&tlng=pt
4. Motta AO, Lima DCS, Vale CR. Survey on the use of medicinal plants in a elementary school at Goiania - GO [Portuguese]. Rev da Univ Val do Rio Verde [Internet]. 2016;14(1):629-46. Available from: <http://www.periodicos.unincor.br/index.php/revistaunincor/article/view/2613>
5. Eysenbach G. Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res [Internet]. 2004 Sep 29;6(3):e34. Available from: <http://www.jmir.org/2004/3/e34/>
6. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inf [Internet]. 2009;42(2):377-81. Available from: <http://dx.doi.org/10.1016/j.jbi.2008.08.010>
7. Dergal JM, Gold JL, Laxer DA, Lee MSW, Binns MA, Lanctt KL, et al. Potential Interactions between Herbal Medicines and Conventional Drug Therapies Used by Older Adults Attending a Memory Clinic. Drugs Aging [Internet]. 2002;19(11):879-86. Available from: <http://link.springer.com/10.2165/00002512-200219110-00005>
8. Phatak UP, Alper A, Pashankar DS. Complementary and Alternative Medicine Use in Children With Inflammatory Bowel Disease. J Pediatr Gastroenterol Nutr [Internet]. 2019 Feb;68(2):157-60. Available from: <https://journals.lww.com/00005176-201902000-00002>
9. Bishop FL, Prescott P, Chan YK, Saville J, von Elm E, Lewith GT. Prevalence of Complementary Medicine Use in Pediatric Cancer: A Systematic Review. Pediatrics [Internet]. 2010 Apr 1;125(4):768-76. Available from: <http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2009-1775>
10. Mosavat SH, Heydari M, Hashempur MH, Dehghani SM. Use of complementary and alternative medicine among paediatric patients with hepatogastrointestinal diseases. East Mediterr Heal J [Internet]. 2018 Oct 1;24(10):1018-25. Available from: http://applications.emro.who.int/emhj/v24/10/EMHJ_2018_24_10_1018_1025.pdf
11. Nakano T, Shimojo N, Okamoto Y, Ebisawa M, Kurihara K, Hoshioka A, et al. The Use of Complementary and Alternative Medicine by Pediatric Food-Allergic Patients in Japan. Int Arch Allergy Immunol [Internet]. 2012;159(4):410-5. Available from: <https://www.karger.com/Article/FullText/338936>
12. Erlichman J, Salam A, Haber BA. Use of Complementary and Alternative Medicine in Pediatric Chronic Viral Hepatitis. J Pediatr Gastroenterol Nutr [Internet]. 2010 Apr;50(4):417-21. Available from: <https://journals.lww.com/00005176-201004000-00014>

13. Hughes R, Ward D, Tobin AM, Keegan K, Kirby B. The Use of Alternative Medicine in Pediatric Patients with Atopic Dermatitis. *Pediatr Dermatol* [Internet]. 2007 Mar;24(2):118–20. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1525-1470.2007.00355.x>
14. Du Y, Wolf I-K, Zhuang W, Bodemann S, Knöss W, Knopf H. Use of herbal medicinal products among children and adolescents in Germany. *BMC Complement Altern Med* [Internet]. 2014 Dec 2;14(1):218. Available from: <https://bmccomplementalternmed.biomedcentral.com/articles/10.1186/1472-6882-14-218>
15. Frawley JE, Anheyer D, Davidson S, Jackson D. Prevalence and characteristics of complementary and alternative medicine use by Australian children. *J Paediatr Child Health* [Internet]. 2017 Aug;53(8):782–7. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/jpc.13555>
16. Christopher G, Ozturk C. The prevalence and determinants of complementary medicine use for nigerian children in the Turkish Republic of Northern Cyprus. *Niger J Clin Pract* [Internet]. 2020;23(8):1053. Available from: <http://www.njconline.com/text.asp?2020/23/8/1053/291844>
17. Hümer M, Scheller G, Kapellen T, Gebauer C, Schmidt H, Kiess W. Phytotherapie in der Kinderheilkunde. *DMW - Dtsch Medizinische Wochenschrift* [Internet]. 2010 May 5;135(19):959–64. Available from: <http://www.thieme-connect.de/DOI/DOI?10.1055/s-0030-1253683>
18. Stampini V, Bortoluzzi S, Allara E, Amadori R, Surico D, Prodám F, et al. The use of Complementary and Alternative Medicine (CAM) among Italian children: A cross-sectional survey. *Complement Ther Med* [Internet]. 2019 Dec;47:102184. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0965229919306004>
19. Adams D, Dagenais S, Clifford T, Baydala L, King WJ, Hervas-Malo M, et al. Complementary and Alternative Medicine Use by Pediatric Specialty Outpatients. *Pediatrics* [Internet]. 2013 Feb 1;131(2):225–32. Available from: <http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2012-1220>
20. Italia S, Wolfenstetter SB, Teuner CM. Patterns of Complementary and Alternative Medicine (CAM) use in children: a systematic review. *Eur J Pediatr* [Internet]. 2014 Nov 30;173(11):1413–28. Available from: <http://link.springer.com/10.1007/s00431-014-2300-z>
21. Oren-Amit A, Berkovitch M, Bahat H, Goldman M, Kozar E, Ziv-Baran T, et al. Complementary and alternative medicine among hospitalized pediatric patients. *Complement Ther Med* [Internet]. 2017 Apr;31:49–52. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0965229916301352>
22. Everett LL, Birmingham PK, Williams GD, Randall Brenn B, Shapiro JH. Herbal and homeopathic medication use in pediatric surgical patients. *Pediatr Anesth* [Internet]. 2005 Jun;15(6):455–60. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1460-9592.2005.01487.x>
23. Crowe S, Lyons B. Herbal medicine use by children presenting for ambulatory anesthesia and surgery. *Pediatr Anesth* [Internet]. 2004 Nov;14(11):916–9. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1460-9592.2004.01353.x>
24. Sharma AK, Kapoor VK, Kaur G. Herb–drug interactions: a mechanistic approach. *Drug Chem Toxicol* [Internet]. 2020 Mar 12;0(0):1–10. Available from: <https://doi.org/10.1080/01480545.2020.1738454>
25. Miller LG. Herbal Medicinals: Selected Clinical Considerations Focusing on Known or Potential Drug-Herb Interactions. *Arch Intern Med* [Internet]. 1998 Nov 9;158(20):2200. Available from: <http://archinte.jamanetwork.com/article.aspx?doi=10.1001/archinte.158.20.2200>
26. Bhatt KM, Malhotra SD, Patel KP, Patel VJ. Drug utilization in pediatric neurology outpatient department: A prospective study at a tertiary care teaching hospital. *J Basic Clin Pharm* [Internet]. 2014;5(3):68. Available from: <http://www.jbclinpharm.org/text.asp?2014/5/3/68/139729>
27. Kupiec T, Raj V. Fatal seizures due to potential herb–drug interactions with Ginkgo biloba. *J Anal Toxicol*. 2005;29(7):755–8.
28. Yamada-Takeda M, Patel A, Fenton G. Energy Drink-Induced Breakthrough Seizure in a Patient on Valproic Acid—Considering Herbal Safety in Epilepsy. *J Pharm Pract*. 2019;32(5):485–7.
29. Haidar C, Jeha S. Drug interactions in childhood cancer. *Lancet Oncol* [Internet]. 2011;12(1):92–9. Available from: [http://dx.doi.org/10.1016/S1470-2045\(10\)70105-4](http://dx.doi.org/10.1016/S1470-2045(10)70105-4)
30. Micromedex [Internet]. Fennel [Internet]. *AltMedDex*. 2017 [cited 2017 Apr 30]. Available from: <http://psbe.ufrn.br/>
31. Mahendran G, Verma SK, Rahman L-U. The traditional uses, phytochemistry and pharmacology of spearmint (*Mentha spicata* L.): A review. *J Ethnopharmacol* [Internet]. 2021 Oct;278:114266. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0378874121004931>
32. Newall CA, Anderson LA, Phillipson JD. *Herbal Medicines: A Guide for Health-Care Professionals*. London: The Pharmaceutical Press; 1996.
33. Santini F, Vitti P, Ceccarini G, Mammoli C, Rosellini V, Pelosini C, et al. In vitro assay of thyroid disruptors affecting TSH-stimulated adenylate cyclase activity. *J Endocrinol Invest*. 2003;26(10):950–5.
34. Brasil. *Formulário de Fitoterápicos da Farmacopeia Brasileira*. 2ª. Brasília: Agência Nacional de Vigilância Sanitária (ANVISA); 2021. 223 p.
35. Kumar R, Arora R, Sarangi SC, Ganeshan N S, Agarwal A, Kaleekal T, et al. Pharmacodynamic and pharmacokinetic interactions of hydroalcoholic leaf extract of *Centella asiatica* with valproate and phenytoin in experimental models of epilepsy in rats. *J Ethnopharmacol* [Internet].

- 2021;270(June 2020):113784. Available from: <https://doi.org/10.1016/j.jep.2021.113784>
36. Ogal M, Johnston SL, Klein P, Schoop R. Echinacea reduces antibiotic usage in children through respiratory tract infection prevention: a randomized, blinded, controlled clinical trial. *Eur J Med Res* [Internet]. 2021;26(1):1–9. Available from: <https://doi.org/10.1186/s40001-021-00499-6>
37. Carmona F, Pereira AMSAMS. Herbal medicines: old and new concepts, truths and misunderstandings. *Brazilian J Pharmacogn* [Internet]. 2013 Apr [cited 2014 Jun 6];23(2):379–85. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-695X2013000200026&lng=en&nrm=iso&tlng=en

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Declaration

The database that originated the article is available upon request to the corresponding author.

Conflict of interest

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