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Herbal Medicine in Pediatrics: A Systematic Review of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 March 2025 and was last updated on 30 March 2025.

INTRODUCTION

Review question / Objective To evaluate the effectiveness of herbal medicine in pediatric patients.

Rationale Herbal medicine has been used since ancient times for the treatment of a wide range of diseases and symptoms and are increasingly integrated into modern healthcare. It is utilized globally in both adult and pediatric populations, though its prevalence varies considerably across countries. In the United States, approximately 10 % of parents report administering herbal products to their children, compared to nearly 44 % in Turkey and over 85 % in Germany (Loman 2003; Ozturk und Karayagiz 2008; Hümer et al. 2010). The widespread use of herbal medicine is largely driven by the perception that it is natural and therefore inherently safe, alongside its broad therapeutic applications, low risk of adverse effects, and limited potential for drug interactions (Hümer et al. 2010).

The therapeutic use of herbal remedies refers to the treatment, prevention, and alleviation of diseases and symptoms using herbal components, including roots, leaves, and flowers. These plant-based components are used to produce various multi-component mixtures, such as essential oils, extracts, juices, minerals, or tincture. Monosubstances extracted from plants, such as digoxin, codeine, caffeine, morphine, and menthol, are not classified as phytotherapeutics (Kraft und März 2006).

Herbal medicinal products are widely recognized for their broad range of therapeutic effects, including anti-inflammatory properties, antiviral effects, mucosecretory benefits, and immunomodulatory functions (Gündling 2018). However, with a few expectations (such as milk thistle (Silybum marianum (L.) Gaertn), colchicum extract (Colchicum autumnale L.)) herbal medicinal prodructs are generally not used in emergency care nor as standalone treatments for severe diseases. Instead, they are primarily employed in the treatment of mild to moderate diseases or as adjunctive therapy (Schilcher und Kammerer 2016).

In a survey of children and adolescents, the most frequently reported indications for the use of herbal medicine included respiratory infections, gastrointestinal disorders, restlessness, dermatological conditions, allergies, teething discomfort, and immune system support (Hümer et al. 2010).

Despite the widespread use of herbal medicine, research on its efficacy in the treatment of children and adolescents remains insufficient. To date, only a limited number of systematic reviews have focused on specific indications within the pediatric population (Anheyer et al. 2018; Anheyer et al. 2017a; Anheyer et al. 2017b; Anheyer et al. 2024; Marquardt et al. 2014). However, no comprehensive systematic review has examined randomized controlled trials (RCTs) investigating the effectiveness of herbal medicine across all indications in pediatric patients. Therefore, this review aims to systematically assess evidence from RCTs on the effectiveness of herbal medicine, evaluating any relevant outcomes in comparison to no treatment, placebo, or conventional medication.

Condition being studied The study will focus on herbal medicine irrespective of the indication.

METHODS

Search strategy For literature search, search terms were created and modified upon requirements of other databases. As an example, the search term for PubMed is presented:

("Pediatrics"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh] OR "Adolescent"[Mesh] OR "Pediatric*"[Title/Abstract] OR "Child*"[Title/Abstract] OR "Infant*"[Title/Abstract] OR "Adolescent*"[Title/Abstract])

AND

("Plants, Medicinal"[Mesh] OR "Herb*"[Title/Abstract] OR Angelica[Mesh] OR Angelica[Title/Abstract] OR Iberogast[Supplementary Concept] OR Iberogast[Title/Abstract] OR "STW 5"[Title/Abstract] OR Pimpinella[Mesh] OR Pimpinella[Title/Abstract] OR Anise[Title/Abstract] OR Arnica[Mesh] OR Arnica[Title/Abstract] OR Retterspitz[Supplementary Concept] OR Euphrasia[Mesh] OR Euphrasia[Title/Abstract] OR Eyebright[Title/Abstract] OR Valeriana[Mesh] OR Valeriana[Title/Abstract] OR Valerian[Title/Abstract] OR Arctostaphylos[Mesh] OR Arctostaphylos[Title/Abstract] OR Bearberr*[Title/Abstract] OR Comfrey[Mesh] OR Comfrey[Title/Abstract] OR Comfrey[Title/Abstract] OR Traumaplant[Supplementary Concept] OR Traumaplant[Title/Abstract] OR Betula [Mesh] OR Betula[Title/Abstract] OR “Menyanthes trifoliate” [Title/Abstract] OR Solanum[Mesh] OR Solanum[Title/Abstract] OR Bittersweet[Title/Abstract] OR "bitter nightshade"[Title/Abstract] OR “Cinnamomum camphora"[Mesh] OR "Cinnamomum camphora"[Title/Abstract] OR camphor[Title/Abstract] OR Cinchona[Mesh] OR Cinchona[Title/Abstract] OR "China bark"[Title/Abstract] OR Hedera[Mesh] OR Hedera[Title/Abstract] OR Ivy[Title/Abstract] OR Bronchipret[Supplementary Concept] OR Bronchipret[Title/Abstract] OR Prospan[Supplementary Concept] OR Prospan[Title/Abstract] OR Althaea[Mesh] OR Althaea[Title/Abstract] OR "Marsh Mallow"[Title/Abstract] OR Imupret[Supplementary Concept] OR Imupret[Title/Abstract] OR Quercus[Mesh] OR Quercus[Title/Abstract] OR "Oak bark"[Title/Abstract] OR Verbena[Mesh] OR Verbena[Title/Abstract] OR Vervain[Title/Abstract] OR Gentiana[Mesh] OR Gentian*[Title/Abstract] OR Sinupret[Supplementary Concept] OR Sinupret[Title/Abstract] OR Eucalyptus[Mesh] OR Eucalyptus[Title/Abstract] OR Pinimenthol[Supplementary Concept] OR Pinimenthol[Title/Abstract] OR Gelomyrtol[Supplementary Concept] OR Gelomyrtol[Title/Abstract] OR Foeniculum[Mesh] OR Foeniculum[Title/Abstract] OR Fennel[Title/Abstract] OR Picea[Mesh] OR Picea[Title/Abstract] OR Spruce[Title/Abstract] OR Psyllium[Mesh] OR Psyllium[Title/Abstract] OR Plantago[Title/Abstract] OR Alchemilla[Mesh] OR Alchemilla[Title/Abstract] OR "Lady's Mantle"[Title/Abstract] OR Eugenia[Mesh] OR Eugenia[Title/Abstract] OR Clove[Title/Abstract] OR Solidago[Mesh] OR Solidag*[Title/Abstract] OR Goldenrod[Title/Abstract] OR Grindelia[Mesh] OR Grindelia[Title/Abstract] OR Gumweed[Title/Abstract] OR Ononis[Title/Abstract] OR Ononidis[Title/Abstract] OR Restharrow[Title/Abstract] OR "Vaccinium myrtillus extract"[Supplementary Concept] OR Vaccinium[Mesh] OR Vaccinium[Title/Abstract] OR Blueberr*[Title/Abstract] OR Capsella[Mesh] OR Capsella[Title/Abstract] OR Cress[Title/Abstract] OR Galeopsis[Title/Abstract] OR "Hemp nettle"[Title/Abstract] OR “Sambucus nigra”[Mesh] OR "Sambucus nigra"[Title/Abstract] OR Sinupret[Supplementary Concept] OR Humulus[Mesh] OR Humulus[Title/Abstract] OR Kytta[Title/Abstract] OR Tussilago[Mesh] OR Tussilago[Title/Abstract] OR Coltsfoot[Title/Abstract] OR Ginger[Mesh] OR Ginger[Title/Abstract] OR Zingiber[Title/Abstract] OR “Cetraria islandica”[Title/Abstract] OR “Icelandic moss”[Title/Abstract] OR Hypericum[Mesh] OR Hypericum[Title/Abstract] OR "St. John's Wort"[Title/Abstract] OR Tropaeolum[Mesh] OR

Tropaeolum[Title/Abstract] OR "angocin Anti-Infekt N"[Supplementary Concept] OR Angocin[Title/Abstract] OR "Anti-Infekt N"[Title/Abstract] OR Nasturtium[Title/Abstract] OR Matricaria[Mesh] OR Matricaria[Title/Abstract] OR Chamomile[Title/Abstract] OR Kamillosan[Supplementary Concept] OR Kamillosan[Title/Abstract] OR Kamillosan Liquidum [Supplementary Concept] OR Kamillosan Liquidum[Title/Abstract] OR Pinus[Mesh] OR Pinus[Title/Abstract] OR Pine[Title/Abstract] OR Coriandrum[Mesh] OR Coriandrum[Title/Abstract] OR Coriander[Title/Abstract] OR Carum[Mesh] OR Carum[Title/Abstract] OR Caraway[Title/Abstract] OR Lavandula[Mesh] OR Lavendula[Title/Abstract] OR Lavender[Title/Abstract] OR Thuja[Mesh] OR Thuja[Title/Abstract] OR Cedar[Title/Abstract] OR Esberitox[Supplementary Concept] OR Esberitox[Title/Abstract] OR Flax[Mesh] OR Flax[Title/Abstract] OR Tilia[Mesh] OR Tilia[Title/Abstract] OR Taraxacum[Mesh] OR Taraxacum[Title/Abstract] OR Dandelion[Title/Abstract] OR "Oenothera biennis"[Mesh] OR "Oenothera biennis"[Title/Abstract] OR "evening primrose"[Title/Abstract] OR Efamol[Supplementary Concept] OR Efamol[Title/Abstract] OR Malva[Mesh] OR Malva[Title/Abstract] OR “Milk Thistle”[Mesh] OR “Milk Thistle”[Title/Abstract] OR Thistle[Title/Abstract] OR Filipendula[Mesh] OR Filipendula[Title/Abstract] OR meadowsweet[Title/Abstract] OR Armoracia[Mesh] OR Armoracia[Title/Abstract] OR horseradish[Title/Abstract] OR Melissa[Mesh] OR Melissa[Title/Abstract] OR Commiphora[Mesh] OR Commiphora[Title/Abstract] OR myrrh[Title/Abstract] OR Myrtus[Mesh] OR Myrtus[Title/Abstract] OR Agrimonia[Mesh] OR Agrimonia[Title/Abstract] OR Orthosiphon[Mesh] OR Orthosiphon[Title/Abstract] OR Passiflora[Mesh] OR Passiflora[Title/Abstract] OR "Mentha piperita"[Mesh] OR "Mentha piperita"[Title/Abstract] OR peppermint[Title/Abstract] OR Pelargonium[Mesh] OR Pelargonium[Title/Abstract] OR "Balsanum Peruvianum"[Title/Abstract] OR "Balsam of Peru"[Title/Abstract] OR Citrus[Mesh] OR Citrus[Title/Abstract] OR "bitter orange"[Title/Abstract] OR Primula[Mesh] OR Primula[Title/Abstract] OR cowslip[Title/Abstract] OR "Thymus serpyllum"[Title/Abstract] OR "Wild Thyme"[Title/Abstract] OR Rheum[Mesh] OR "Rheum palmatum"[Title/Abstract] OR "Rhei radix"[Title/Abstract] OR Pieplant[Title/Abstract] OR "pyralvex berna"[Supplementary Concept] OR "pyralvex berna"[Title/Abstract] OR Calendula[Mesh] OR Calendula[Title/Abstract] OR Rosmarinus[Mesh] OR Rosmarinus[Title/Abstract] OR Rosemary[Title/Abstract] OR "Salvia officinalis"[Mesh] OR “Salvia officinalis”[Title/Abstract] OR Salvia[Title/Abstract] OR Sage[Title/Abstract] OR Rumex[Mesh] OR Rumex[Title/Abstract] OR Sorrel[Title/Abstract] OR Achillea[Mesh] OR Achillea[Title/Abstract] OR Yarrow[Title/Abstract] OR Equisetum[Mesh] OR Equisetum[Title/Abstract] OR horsetail[Title/Abstract] OR "Iberis amara"[Title/Abstract] OR "Bitter Candytuft"[Title/Abstract] OR Chelidonium[Mesh] OR Chelidonium[Title/Abstract] OR celandine[Title/Abstract] OR Echinacea[Mesh] OR Echinacea[Title/Abstract] OR echinacin[Supplementary Concept] OR echinacin[Title/Abstract] OR Drosera[Mesh] OR Drosera[Title/Abstract] OR sundew[Title/Abstract] OR "Plantago lanceolata"[Title/Abstract] OR Ribwort[Title/Abstract] OR "Viola tricolor"[Title/Abstract] OR Heartsease[Title/Abstract] OR Glycyrrhiza[Mesh] OR Glycyrrhiza[Title/Abstract] OR liquorice[Title/Abstract] OR Centaurium[Mesh] OR Centaurium[Title/Abstract] OR centaury[Title/Abstract] OR Melaleuca[Mesh] OR Melaleuca[Title/Abstract] OR "Thymus Plant"[Mesh] OR "Thymus Plant"[Title/Abstract] OR thyme[Title/Abstract] OR "Balsanum tolutanum"[Title/Abstract] OR "Tolu balsam"[Title/Abstract] OR Potentilla[Mesh] OR Potentilla[Title/Abstract] OR "Xysmalobium undulatum"[Title/Abstract] OR "Milk bush"[Title/Abstract] OR Milkwort[Title/Abstract] OR “Artemisia absinthium”[Mesh] OR “Artemisia absinthium”[Title/Abstract] OR Artemisia[Title/Abstract] OR wormwood[Title/Abstract] OR Salix[Mesh] OR Salix[Title/Abstract] OR Assalix[Supplementary Concept] OR Assalix[Title/Abstract] OR "willow bark"[Title/Abstract] OR Triticum[Mesh] OR Triticum[Title/Abstract] OR Verbascum[Mesh] OR Verbascum[Title/Abstract] OR mullein[Title/Abstract] OR Hamamelis[Mesh] OR Hamamelis[Title/Abstract] OR "Witch hazel"[Title/Abstract] OR “Cinnamomum zeylanicum”[Mesh] OR “Cinnamomum zeylanicum” [Title/Abstract] OR Cinnamon[Title/Abstract] OR Garlic[Mesh] OR Garlic*[Title/Abstract] OR “Allium sativum”[Title/Abstract] OR “Ginkgo biloba”[Mesh] OR “Ginkgo biloba”[Title/Abstract] OR “Vaccinium macrocarpon”[Mesh] OR “Vaccinium macrocarpon”[Title/Abstract])

AND

(“randomized controlled trial”[Publication Type] OR “controlled clinical trial”[Publication Type] OR randomized[Title/Abstract] OR randomised[Title/Abstract] OR randomly[Title/Abstract] OR random[Title/Abstract] OR placebo[Title/Abstract] OR group[Title/Abstract] OR blind[Title/Abstract] OR Trial[Title/Abstract]).

Participant or population Pediatric population aged from 0 to 18 years, with no restrictions regarding gender and ethnicity.

Intervention This review will include only studies investigating the treatment with herbal medicine. Traditional Chinese, Korean, Indian, and Kampo medicine will be excluded due to their frequently unclear compositions and the potential risk of heavy metal contamination. Furthermore, studies examining highly diluted herbal preparations will also be excluded.

Comparator 1. placebo 2. active control options (e.g. other herbs; treatment as usual).

Study designs to be included Only randomized controlled trials will be considered for inclusion.

Eligibility criteria
Inclusion:
- Age group 0-18 years
- topical or systemic herbal medicine
Exclusion:
- traditional Chinese medicine
- traditional Indian medicine
- traditional Korean medicine
- traditional Kampo medicine
- highly diluted / homeopathic preparations.

Information sources Electronic databases (cochrane, scopus, pubmed), contact with authors, trial registers.

Main outcome(s) Disease specific outcomes (e.g. SCORAD, duration of illness, ...).

Data management A literature manager (e.g. Zotero) will be used as software tool to manage literature and to record decision making. First titles, then abstracts, and further full texts will be screened for eligibility independently by two authors.
If disagreements appear, a third author will be consulted. Further disagreements will be discussed until consent is reached.
Data extraction will be done in Excel, statistical analyses will be done in R and R Studio.

Quality assessment / Risk of bias analysis The risk of bias analysis will be conducted using the Cochrane risk of bias tool 2.0. Two authors will assess all included studies independently for bias. In case of disagreements, a third author will be consulted. Any remaining disagreements will be resolved through discussion until consensus is reached.

Strategy of data synthesis If there are at least two studies available for a specific outcome, a combined analysis will be conducted. For continuous outcomes, standardized mean differences (SMD) will be calculated along with 95% confidence intervals (CI), using Hedges's correction for small study samples (Borenstein et al. 2009; Higgins et al. 2019). In cases where standard deviations are not available, they will be calculated from standard errors, confidence intervals, or t values. For dichotomous outcomes, odds ratios (OR) will be calculated with 95% CI (Borenstein et al. 2009; Higgins et al. 2019). If data is missing, an effort will be made to obtain it from the trial authors. A random effects model will be used, applying the inverse variance method for continuous outcomes and the Mantel-Haenszel method for dichotomous outcomes (Harrer et al. 2021). To enhance comparability, fixed effects model estimates will be added to the forest plots in case of non-significant heterogeneity. Furthermore, the Hartung-Knapp small-sample correction will be employed (Cornell et al. 2014). The presence of statistical heterogeneity between studies will be investigated using the I2 and τ2 statistics. If heterogeneity exists in the meta-analysis, subgroup analyses and meta-regression (if at least 10 studies can be included) will be conducted to explore possible reasons for heterogeneity (Harrer et al. 2021; Borenstein et al. 2009; Higgins et al. 2019).

Subgroup analysis Not planned.

Sensitivity analysis Sensitivity analyses will be conducted for studies with high risk of bias versus low risk of bias in respective domains.

Language restriction Studies published in English and German will be included in the review.

Country(ies) involved Deutschland.

Keywords complementary medicine, integrative medicine, pediatrics, herbal medicine, systematic review, children, adolescents.

Dissemination plans The review is intended to be published in a peer reviewed scientific journal.
Results of this review will be presented at scientific congresses.

Contributions of each author
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