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Efficacy and safety of phytotherapy and anthroposophic medicine in bronchial asthma: A systematic review

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ABSTRACT

Background: Bronchial asthma is a highly prevalent health condition associated with low quality of life and high economic costs. Treatments from traditional, complementary and integrative medicine (TCIM) are commonly used by individuals with bronchial asthma. However, a synthesis of the evidence on plant-derived medications is lacking.

Objective: This review aims to systematically summarize the evidence on the efficacy, effectiveness and safety of European/Western phytotherapy (PT) and medications from anthroposophic medicine (AM) in individuals with bronchial asthma.

Methods: Four electronic databases and additional references were screened for clinical trials published between 1990 and 2023. The findings of the included studies were qualitatively synthesized and study quality was assessed.

Results: Of 23 included studies, 19 examined European/Western PT and four investigated AM medications. Nine studies of sufficient quality reported beneficial effects of various plants (e.g., Nigella sativa) on asthma symptoms, pulmonary function and immunological parameters. The medications were considered safe in studies that reported on safety.

Conclusion: This systematic review suggests several medications from European/Western PT and AM that may be beneficial and appear to be safe in the treatment of bronchial asthma. However, further rigorous studies are needed to provide evidence-based guidance on add-on treatment options for individuals with bronchial asthma.

1. Introduction

Bronchial asthma is one of the major non-communicable health conditions, affecting about 5–8 % of the European population [1,2]. The condition is characterized by chronic inflammation and narrowing of the airways due to an allergic reaction to certain substances in the environment (e.g., pollen, dust mites, nuts), a non-allergic reaction caused by other stimuli (e.g., physical exertion, infection, drugs), or a combination of both. Typical symptoms include breathlessness up to life-threatening shortness of breath, chest tightness, wheezing and coughing. Bronchial asthma is associated with low quality of life and high economic costs due to reduced productivity at work or school, for example [3,4]. Current guideline recommendations include pharmaceuticals, namely anti-inflammatory corticosteroids and sympathomimetic bronchodilators, that can control asthma symptoms and help individuals with bronchial asthma to participate in daily life [5]. Additionally, interventions from traditional, complementary and integrative medicine (TCIM) are commonly used by individuals with bronchial asthma [6–8], although they are not currently included in the clinical guidelines. As some individuals have concerns about the potential side effects of conventional medicine, especially during long-term use for chronic cases, and a small number of patients do not tolerate pharmaceuticals [9,10], interventions from TCIM may offer an additional treatment option.

Phytotherapy (PT), as one field of TCIM, may be beneficial in the treatment of bronchial asthma. PT aims to treat or prevent a health condition by using whole plants or parts of plants (e.g., leaves, roots, seeds, fruits), including exudates derived from plants (e.g., gum). Different preparations (e.g., extracts, distillates) are applied internally (e.g., capsules), externally (e.g., ointment), or as inhalation therapy. Modern PT focuses on a biomedical understanding of the mode of action of plants [11]. Accordingly, plants or their preparations consist of a mixture of multi-substances that lead to a range of effects. Many medical systems around the world use or have used plants for healing purposes.

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This systematic review focuses on European/Western PT, which has been defined as medications from plants that are either grown and/or monographed by the expert commissions on PT in Europe (i.e., Committee on Herbal Medicinal Products (HMPC); Comission E (1978-1995)). Current evidence from *in vitro* and *in vivo* studies suggests that a variety of plants have immunomodulatory, anti-inflammatory and bronchodilatory effects [12,13]. Considering the significant role of these properties in bronchial asthma [14], this systematic review focuses on all plants that have been studied in individuals with bronchial asthma.

Plants are also utilized in anthroposophic medicine (AM), a whole medical system developed in the 1920s [15]. AM combines conventional medicine with the concepts and methods from anthroposophy. Medications from AM are prescribed based on an individual's needs and combined with other treatments from AM, such as art therapy or eurythmy therapy. Unlike PT, medications from AM are not just derived from plants but also from minerals and animal products. In AM the human organism, down to the separate organs, is structured in three functional systems, namely the nervous-sensory, the rhythmic and the metabolic-limb system [16]. In the case of bronchial asthma, respiration is part of the rhythmical system and the lung itself comprises the three functional systems. An imbalance in these systems can lead to disease. Therefore, AM medications support an individual's self-regulatory processes to restore a balance of these systems [15,17]. Additionally, the mode of action on biochemical levels can also be described. For example, research on animal models showed that specific plants used in AM, e.g., *Citrus limonis*, have anti-allergic effects [18]. It might therefore also be efficacious in treating bronchial asthma in humans.

Although there is some evidence about plants used in European/Western PT and AM, a synthesis of current evidence on the effect of plant-derived medications in individuals with bronchial asthma is lacking. Existing systematic reviews are mostly outdated or summarize evidence of non-Western PT [19–21]. Therefore, this review aims to systematically summarize the evidence on the efficacy, effectiveness and safety of European/Western PT and medications from AM in individuals with bronchial asthma. Additionally, this review seeks to assess the quality of the evidence, identify research gaps and provide guidance for future research and clinical practice.

2. Methods

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22]. The review protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42023412488).

2.1. Data sources and search strategy

Separated searches were conducted for interventions from European/Western PT and AM. Studies were primarily identified through searches in three electronic databases, i.e., Ovid Medline, Ovid Embase and Ovid AMED (last searches April 2023). For studies from AM, the database Anthromedics was additionally searched. The search strategy was designed based on the two concepts of the research question: population (i.e., bronchial asthma) and intervention (i.e., European/Western PT or AM). A building block approach was used to create blocks including subject headings and free text search terms for each concept. In addition, a filter was applied to exclude animal studies. The search strategy was created in Ovid Medline and adapted to each database. Details on the search strategy are provided in the Supplementary Fig. S1 and S2. References and citations of included studies, drawn from the Scopus database, were screened to identify additional studies.

2.2. Study selection

Studies were included if they met the following criteria: (1) published in English or German as original research in a peer-reviewed journal from January 1, 1990, onward, (2) clinical trial of any study design (to capture the full range of evidence), (3) involved humans of any age with bronchial asthma (i.e., diagnosis by a physician), (4) included an intervention of European/Western PT (i.e., full-extract of plant(s) grown or monographed in Europe) or AM (i.e., any medication from AM, including as part of a multimodal AM treatment), (5) reported any outcome that was assessed with a validated instrument (e.g., asthma symptoms questionnaires, spirometry to measure pulmonary function, or blood measures for immunological parameters). Excluded were isolated pure substances or components derived from plants (e.g., isolated curcumin), as these are not classified by the HMPC as PT.

Following the selection criteria, two reviewers independently screened titles and abstracts for eligibility and retrieved full texts of potentially eligible studies. Articles from additional reference searches were screened for eligibility by the first author and full texts of potential eligible studies were screened by a second reviewer. Any disagreement was resolved by consensus following discussion or consultation with a third reviewer.

2.3. Data extraction

The following information was extracted by two authors using a predefined form: study characteristics (i.e., first author, year of publication, country of origin, study design, categories of asthma medications), participants (i.e., number, mean age, female gender) and intervention (i.e., plant(s) studied, medication name, dosage, duration of the intervention, intervention as add-on therapy or only PT/AM, type of control group, adverse events (AEs)). The results of the included studies were extracted and summarized qualitatively. The main findings were summarized for studies that were rated to be of sufficient quality. The results were categorized into three domains: asthma symptoms/control, pulmonary function, and immunological parameters. Pre-to post-intervention effects were classified as beneficial (significant improvement in the intervention group), zero (no group difference), or non-beneficial (favoring the control group). Given the limited number of studies that investigated interventions of the same plant on the same outcome measurement, a meta-analysis was not feasible.

2.4. Quality assessment

Study quality was evaluated by two independent reviewers using the integrated quality criteria for the review of multiple study designs (ICROMS) tool [23]. The assessment consisted of general questions (criteria) and questions specific to each study design. General questions included, e.g., clear aims of the research, bias in reporting or ethical considerations. Study design-specific questions included, e.g., bias in sampling, between-group differences at baseline, or blinding for randomized controlled trials (RCTs). Each question had to be answered by yes (2), unclear (1) or no (0). Depending on the study design, a different minimum and maximum score applied (i.e., RCT: min. = 22, max. = 32; non-controlled before after (NCBA): min. = 22, max. = 30; Cohort: min. = 18, max. = 26). A study was rated as being of sufficient or insufficient quality if the score is above or below the minimum score, respectively.

3. Results

3.1. Study selection

Figs. 1 and 2 present the selection process separately for European/Western PT and AM. In total 5398 and 128 records for PT and AM, respectively, were identified through searches in Medline (PT: 1658; AM: 24), Embase (PT: 3466; AM: 45), AMED (PT: 274; AM: 24) and Anthromedics (AM: 35). After removing 1458 (PT) and 36 duplicates (AM), another 3899 (PT) and 79 records (AM) were excluded based on title and abstract screening. Of these, 24 articles from PT were excluded

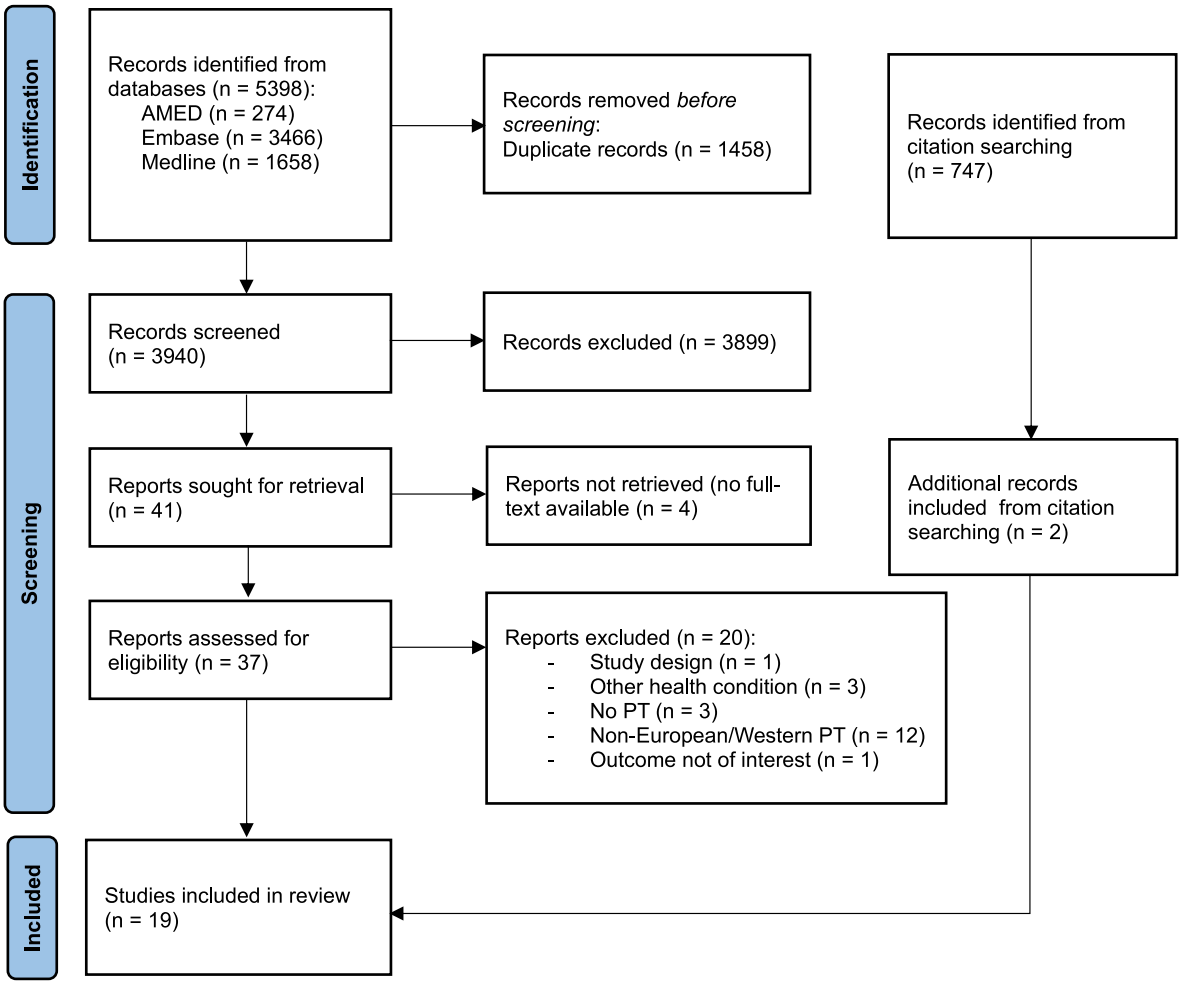

Fig. 1. Selection process of included studies from European/Western PT.

after full-text screening, mainly because of non-European/Western PT (n = 12). For AM, nine articles were excluded after full-text screening, primarily because the study population consisted of health conditions other than bronchial asthma (n = 4). In addition, two studies for PT were identified through additional reference search, resulting in a final set of 19 studies for PT and four studies for AM.

3.2. Study characteristics

The main characteristics of included studies are presented in Table 1. All included studies investigated pre-to post-intervention effects and none of them included further follow-up measurements.

For European/Western PT (No. 1–19), most of the studies were conducted in Iran (n = 8), followed by Germany (n = 3). An RCT design was used by all studies, except for two studies using an NCBA design. Of the RCTs, placebo (n = 13), active control (n = 3) and treatment as usual (n = 1) were used as control. The sample size ranged from 13 to 95. The average age of the participants was between 14 and 54 years. Four studies partially or exclusively included children or adolescents. The most studied plant was *Nigella sativa* (n = 5), followed by *Crocus sativus* L., *Pinus maritima, Curcuma longa* L. and *Petasites hybridus* (n = 2 each). Other plants studied were *Hedera helix, Punica granatum, Plantago major* and P*runus dulcis, Portulaca oleracea* L., *Origanum majorana* and *Lactuca sativa* and *Glycyrrhiza glabra* (n = 1 each). All preparations were applied internally, primarily as capsules (n = 13). Interventions were conducted for a single experiment up to six months, most frequently over four weeks (n = 6). Eleven studies assessed AEs, none of which were serious or differed between intervention and control groups. Based on the quality assessment, nine studies were rated to be of sufficient quality (Supplementary Table S3).

Four studies investigated the effect of AM medications (No. 20–23). Of these, two studies were based on the same sample (No. 22 and 23). The included studies were conducted in Germany, the Netherlands and Georgia. A cohort study design (n = 2) and an NCBA design (n = 2) were used by the included studies. The sample size was 92, 90 and 38. Participants were 3–70 years old (range) and 53.0 % were women (reported by one study). Individually prescribed AM medications were used from various plants, respectively substances. The choice of medication and dosage was individually tailored to a person's needs. Preparations were provided internally as globules, drops, injections, or ampoules for inhalation, or as external applications. Interventions lasted between five weeks and twelve months. One study reported AEs, which was a reaction at the injection site in one participant. None of the included studies were rated as being of sufficient quality (Supplementary Table S4).

3.3. Results from qualitative synthesis

3.3.1. European/Western PT

Table 2 presents a qualitative synthesis of reported results from European/Western PT studies that were rated of sufficient quality (n = 9). Study results are presented along the different plants studied and refer to post-intervention effects.

The most studied plant was *Nigella sativa* (black cumin; n = 5) provided as oil or whole seeds. Two of the five studies were of sufficient quality. Both of these reported beneficial between-group effects on asthma control, measured as the average level of symptom control. In

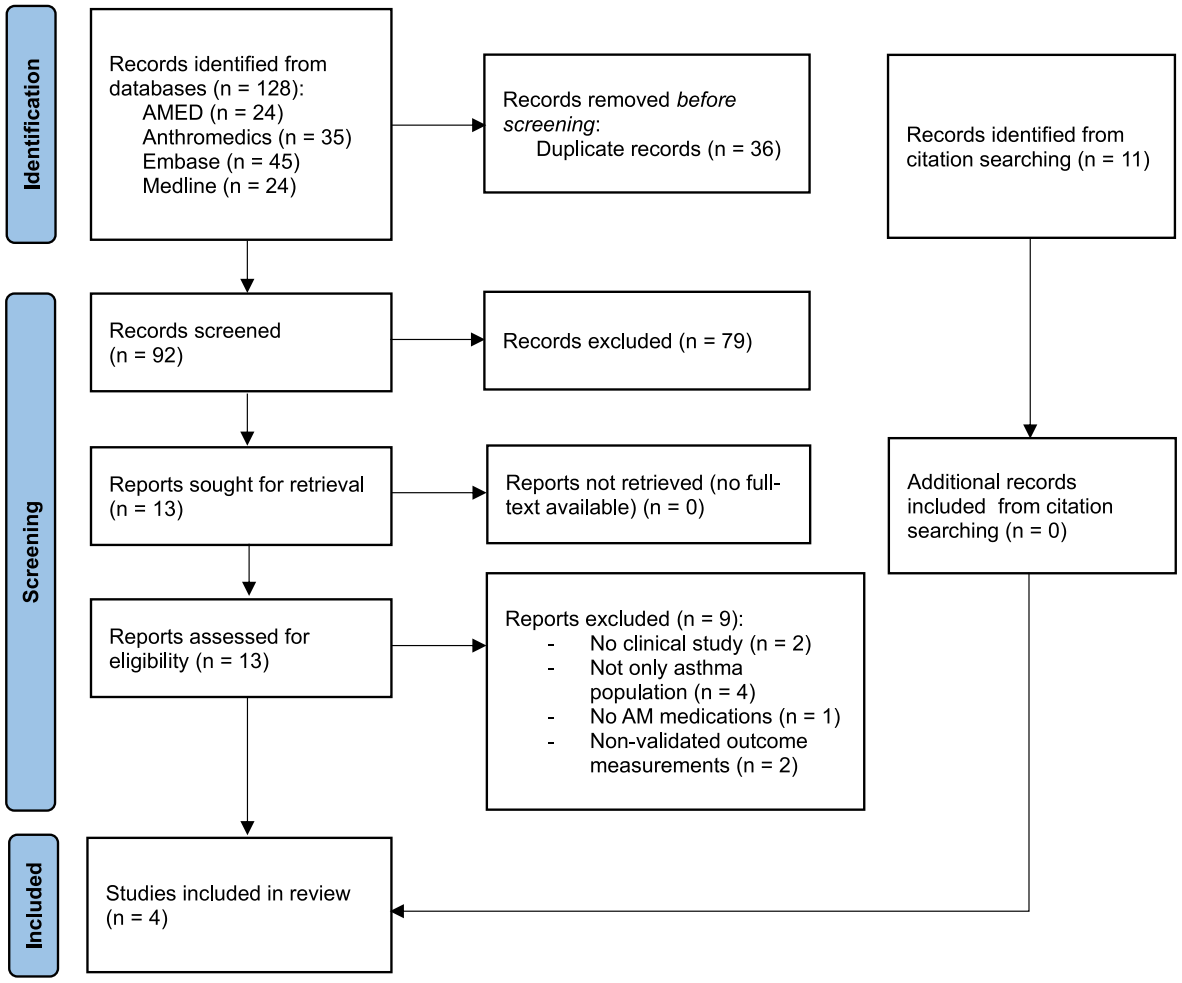

Fig. 2. Selection process of included studies from AM.

addition, study no. 10 reported a significant reduction in eosinophil counts compared to placebo but no significant differences in immunoglobulin E (IgE), a marker for allergic responsiveness, between groups. Study no. 17 showed beneficial between-group effects of *Nigella sativa* on pulmonary function, i.e., peak expiratory flow (PEF) variability. Furthermore, study no. 17 reported lower amounts of cytokines and lower fractional exhaled nitric oxide (FeNO), a biomarker for indicating the level of inflammation in the airways, within the intervention group.

Crocus sativus L. (saffron; stigma) was examined by two studies, both of sufficient quality. These studies showed that saffron extract led to beneficial effects on asthma symptoms (e.g., shortness of breath, limitations in activities), pulmonary function and immunological parameters (i.e., serum levels of different proteins) compared to placebo. Additionally, study no. 19 reported beneficial effects on asthma severity within the intervention group. However, no significant between-group differences were shown.

Pinus maritima (maritime pine; bark) was studied twice, with one study being of sufficient quality. It showed that pine bark extract led to improvements in pulmonary function (i.e., PEF), asthma symptoms and control, and an immunological parameter (i.e., urinary leukotriene) within the intervention group. Between-group effects were not analyzed.

Curcuma longa L. (turmeric; roots) was investigated by two studies, one of which was of sufficient quality. This study reported beneficial effects on some asthma control parameters (i.e., nighttime awakenings, use of adrenergic bronchodilators and disease control) between the intervention and the control group. No significant improvements were found in pulmonary function (i.e., forced expiratory volume in 1 s (FEV1)), neither between groups nor within the intervention group.

Petasites hybridus (butterbur; roots) has been studied by one study that was of sufficient quality. This study reported beneficial between-group effects on pulmonary function (i.e., bronchial hyperresponsiveness) and the inflammatory marker exhaled nitric oxide (eNO), but not on other pulmonary functions, i.e., FEV1, forced expiratory flow (FEF25–75) and PEF. Potential improvements within the intervention group were not provided in this study.

Hedera helix (ivy; leaves) was investigated by one study of sufficient quality. Beneficial between-group effects were reported for pulmonary functions (i.e., FEV1, maximal expiratory flow (MEF75-25)). No significant improvements were observed in asthma control, FeNO and asthma quality of life within the intervention group.

Punica granatum (pomegranate; seeds) was explored in one study of sufficient quality. It showed that Punica granatum extract led to beneficial effects on all asthma symptoms, except for asthma medication use, and on immunological parameters (i.e., eosinophils; neutrophils) compared to placebo. Beneficial within-group effects were reported for all outcome measures.

3.3.2. Medications from AM

Table 3 shows plants and substances used in studies investigating AM medications. *Nicotiana tabacum* was used in all four included studies. Three studies prescribed *Argentum/Echinacea* and *Citrus limonis/Cydonia oblonga* (Gencydo®, provided as injection or inhalation therapy). Other substances used in two studies were *Cuprum aceticum*, Levico water (i.e., specific mineral water) and oak bark. Wala and Weleda were the main manufacturers of the prescribed AM medications.

The effect of AM medications on bronchial asthma was investigated

Table 1
Descriptive summary of studies from PT (no. 1–19) and AM (no. 20–23) included in this systematic review.

No.	First author, year of publication	Country	Study design	Sample size at baseline	Mean age (SD), yrs	Female gender (%)	Intervention characteristics				Adverse events (AEs)	Sufficient quality (total/min score)
							Plant(s)/component	Preparation/drug (concentration)	Dosage and no. Of sessions, period	Type of control		
1	Abidi, 2014 [24]	India	RCT[1,3,5-7]	60	31.6 (2.0)	50.0	*Curcuma longa* L./roots	Caps/CUR- 500 (500 mg curcumin)*	1 caps twice daily, 30 days	TAU	No sign. Difference between groups. Most reported AE was headache.	No (15/22)
2	Anushiravani, 2020 [25]	Iran	NCBA[8]	28	54.7 (11.2)	75.0	*Plantago major*/seeds; *Prunus dulcis*/gum	Sachet to drink with water (2 g seeds and 3 g gum powder)*	1 sachet 3 times daily, 4 weeks	–	n/a. Four participants withdrew due to joint pain and stomach discomfort.	No (14/22)
3	Boskabady, 2007 [26]	Iran	RCT[db,1-5]	29	41.8 (13.7)	79.3	*Nigella sativa*/seeds	Boiled extract (oil; 0.1 g%)*	15 ml/kg daily, 3 months	PL	n/a	No (17/22)
4	Boskabady, 2010 [27]	Iran	RCT[db, xovr (4 trials),9]	15	42.8 (11.4)	66.7	*Nigella sativa*/seeds	Boiled extract (oil; 200 mg/ml)	50 and 100 mg/kg once, max. 2 weeks	AC (theophylline; salbutamol)	n/a	No (18/22)
5	Danesch, 2004 [28]	DE	NCBA[8]	80[n = 16 children]	35.3 (nr)	55.5	*Petasites hybridus*/roots	Caps/Petadolex® (50 mg)*	1 caps 3 times[adults] or 1–2 times[children] daily, 2–4 months	–	Seven participants reported AEs, two treated for allergic rhinitis and dyspnoea.	No (10/22)
6	Hosseini, 2001 [29]	Iran	RCT[db, xovr,8]	26	32 (nr)	54.6	*Pinus maritima*/bark	Caps/Pycnogenol®*	1 to max. 200 mg daily, 4 weeks for each trial	PL	No AEs related to the drug. One participant had gastrointestinal problems.	No (17/22)
7	Hosseini, 2018 [30] †	Iran	RCT[tb,8]	76	41.0 (9.9)	40.0	*Crocus sativus* L./stigma	Caps (50 mg extract)*	1 caps twice daily, 8 weeks	PL	No serious AEs. Few minor feelings of warming up.	Yes (25/22)
8	Hosseini, 2023 [31]	Iran	RCT[db,10]	64	38.4 (11.9)	48.8	*Punica granatum*/seeds	Caps (250 mg extract)	1 caps twice daily, 8 weeks	PL	n/a	Yes (25/22)
9	Kalus, 2003 (Study 1) [32]	DE	RCT[db,10]	63[incl. children]	nr	nr	*Nigella sativa*/seeds	Caps/Immerfit® (oil; 500 mg)	1 caps 3 times daily, 8 weeks	PL	One child reported gastrointestinal problems.	No (15/22)
10	Koshak, 2017 [33]	Saudi Arabia	RCT[db,1,3,6]	80	40.5 (14.0)	58.5	*Nigella sativa*/seeds	Caps/Cuminmar® (oil; 500 mg)*	1 caps twice daily, 4 weeks	PL	No difference between groups. Three participants reported stomach upset, headache, and insomnia.	Yes (22/22)
11	Lau, 2004 [34]	USA	RCT[db,3,6]	60[children only]	14 (nr)	41.7	*Pinus maritima*/bark	Caps/Pycnogenol®*	0.5 mg/kg daily in two dosages, 3 months	PL	No AEs associated with the drug.	Yes (23/22)
12	Lee, 2004 [35]	UK	RCT[db, xovr,1]	16	45 (nr)	43.8	*Petasites hybridus*/roots	Caps/Petaforce® (25 mg)*	1 caps twice daily, 1 week each trial	PL	n/a	Yes (23/22)
13	Malek, 2004 [36]	Iran	RCT[xovr (3 trials),8]	13	48.5 (15.0)	69.2	*Portulaca oleracea* L./leaves	Boiled extract (5 %)*	0.25 ml/kg once, single experiment	AC (theophylline; salbutamol)	n/a	No (21/22)
14	Manarin, 2019 [37]	Brazil	RCT[db,8]	34	12.0 (3.4)	36.0	*Curcuma longa* L./roots	Caps (250 mg; 13 mg curcumin)*	30 mg/kg daily, 6 months	PL	One AE reported in intervention group (nausea).	Yes (24/22)
15	Mohamed, 2008 [38]	Egypt	RCT[8]	30	42.6 (1.8)	50.0	*Origanum majorana*/seeds; *Lactuca sativa*/seeds	Oil (ns)*	2 drops majoran[Group1] or 5 ml lettuce[Group2] once daily, 2 months	TAU	n/a	No (15/22)
16	Sadek, 2020 [39]	Egypt	RCT[1,3]	95	nr	51.9	*Glycyrrhiza glabra*/roots	Caps (500 mg aqueous extract)*	1 caps twice[Group1] or 3 times[Group2] daily, 4 weeks	PL	n/a	No (21/22)
17	Salem, 2017 [40]	Saudi Arabia	RCT[sb,1]	76	38.0 (12.4)	65.7	*Nigella sativa*/seeds	Caps (whole seeds)*	0.5 g[Group1] or 1 g[Group2] twice daily, 3 months	PL	No AEs reported in both groups.	Yes (26/22)
18	Zeil, 2014 [41]	DE	RCT[db, xovr,1]	30[children only]	nr	43.3	*Hedera helix*/leaves	Syrup/Prospan® (5 ml/35 mg extract)*	5 ml twice daily, 4 weeks each trial	PL	nr	Yes (26/22)
19	Zilaee, 2019 [42] †	Iran	RCT[db,10]	76	41.0 (9.9)	40.0	*Crocus sativus* L./stigma	Caps (50 mg extract)	1 caps twice daily, 8 weeks	PL	No serious AEs. Few minor feelings of warming up.	Yes (26/22)

(*continued on next page*)

Table 1 (*continued*)

No.	First author, year of publication	Country	Study design	Sample size at baseline	Mean age (SD), yrs	Female gender (%)	Intervention characteristics			Type of control	Adverse events (AEs)	Sufficient quality (total/min score)
							Plant(s)/component	Preparation/drug (concentration)	Dosage and no. Of sessions, period			
20	Andriashvili, 2007 [43]	GA	CS[8]	92 children only	nr (range 3–15)	nr	Various	Globules/drops/ampoules for inhalation*	Individually prescribed, 5–6 weeks	TAU	n/a	No (7/18)
21	Ecker, 2009 [44]	NL, DE	CS[retrospective,8]	38 children only	nr (range 7–13)	nr	Various	ns/external applications*	Individually prescribed, min.12 months	TAU	n/a	No (10/18)
22	Hamre, 2009 [45] †	DE	NCB[8]	90[n=36 children]	29.5 (19.5)	53.0	Various	Drops/injections/others ns*	Individually prescribed, 12–26 weeks (median: 17 weeks)	–	One AEs due to AM medication reported (injection-site reaction).	No (18/22)
23	Hamre, 2013 [46] †	DE	NCBA[8]	90[n=36 children,6]	nr (range 2–70)	nr	Various	Drops/injections/others ns	Individually prescribed, ns	–	nr for asthma (see study no. 22).	No (18/22)

Note. Unless stated otherwise, adults were the main participants of included studies. Plant(s) are listed using their pharmacopeial name. None of the included studies had a follow-up measurement. Abbreviations: AC = active control; caps = capsule; CS = cohort study; db = double-blind; n/a = not assessed; nr = not reported; NCBA = non-controlled before-after; PL = placebo; RCT = randomized controlled trial; sb = single-blind; SD = standard deviation; TAU = treatment as usual; tb = triple-blind; xovr = cross-over design; yrs = years. † No. 7 and 19, and no. 22 and 23 used the same sample. The following numbers represent the categories of asthma medications used during the study: [1] = inhaled corticosteroids (e.g. Budesonide, Fluticasone); [2] = oral corticosteroids; [3] = inhaled β2-agonists (e.g., Formoterol); [4] = oral β2-agonists; [5] = Theophylline/Xanthine derivatives, [6] = Leukotriene receptor antagonists (e.g. Montulekast), [7] = Antihistamines, [8] = asthma medication used but not further specified, [9] = asthma medication not allowed, [10] = not specified/known, * = intervention as add-on therapy to PT/AM.

within a multimodal AM intervention in all included studies. For example, in study no. 22, one to 22 % of participants received eurythmy therapy, art therapy and/or rhythmical massage besides medication. The authors reported improvements in asthma severity, symptoms and quality of life at 12- and 24-month follow-up compared to baseline. In the follow-up study no. 23, lower asthma severity was reported at four-year follow-up compared to baseline. Two studies compared AM interventions with conventional medicine. Study no. 20 and no. 21 showed lower use of conventional asthma medicine (e.g., corticosteroids) in the AM group compared to the conventional medicine group. No between-group differences were found in asthma symptoms (i.e., frequency of asthma attacks) in study no. 21 or in pulmonary function in study no. 20.

4. Discussion

In this systematic review, clinical trials investigating European/Western PT or medications from AM in individuals with bronchial asthma were systematically summarized. Overall, a broad set of plants and substances have been studied in bronchial asthma. Findings from qualitative synthesis of European/Western PT studies showed beneficial effects of *Nigella sativa* (black cumin), *Crocus sativus* L. (saffron), *Pinus maritima* (maritime pine), *Curcuma longa* L. (turmeric) and *Punica granatum* (pomegranate) on asthma symptoms compared to placebo. Further, beneficial effects on immunological parameters were found for black cumin, *Petasites hybridus* (butterbur) and pomegranate. Also, turmeric, saffron, pine and *Hedera helix* (ivy) had beneficial effects on pulmonary function. Findings from AM studies suggest improvements in asthma symptoms, severity and quality of life after individually prescribed AM treatment. However, the limited quality of the AM studies needs to be considered when interpreting the results.

The beneficial effects of European/Western PT on inflammatory parameters, pulmonary function and asthma symptoms may be explained by the anti-asthmatic properties of plants. Evidence from *in vitro* and animal studies shows that plants identified in this review have immunomodulating and/or anti-inflammatory and/or bronchodilatory effects [47–53]. For example, the beneficial effects of ivy leaf extract on pulmonary function can be explained by the secretolytical and broncholytical properties of saponins contained in ivy, particularly alpha-hederin [54,55]. In addition, anti-inflammatory properties of preparations from black cumin [56], pine bark [52], butterbur [53], or pomegranate [49] are shown in reported improvements in immunological and inflammatory parameters (i.e., eosinophils and neutrophils, cytokines and FeNO). Comparable to conventional medicine, the anti-inflammatory and bronchodilatory effects of plants lead to less swollen airways and relaxation of bronchial muscles. These effects may be reflected in the reported improvements in asthma symptoms, such as reduced shortness of breath, fewer asthma attacks and fewer nocturnal awakenings. However, included studies did not always find beneficial effects on all outcome measurements investigated. The duration of the intervention and dosage of the herbal preparation may have an impact on potential improvements. Dose-dependent effects of black cumin were observed in study no. 17. Thus, the inflammatory marker FeNO was improved in the low-dose group but not in the high-dose group; the reverse was found for the immunological parameter IgE, a marker for allergic responsiveness. Overall, the findings of included studies showed that specific plants used in European/Western PT may be beneficial in the treatment of bronchial asthma.

Findings from studies investigating AM medications were heterogeneous, especially regarding intervention and results. In general, AM medications were the primary intervention of a multimodal AM treatment. Since various medications were prescribed in different combinations and dosages, the observed effects cannot be ascribed to a specific medication. Nevertheless, certain medications possibly contributed to the reported improvements in asthma symptoms and severity in studies no. 22 and 23. For example, Gencydo® manufactured from *Citrus limonis*

Table 2
Main results from European/Western PT studies of sufficient quality (n = 9).

Plant(s)/ component	Studies of sufficient quality/total	Study design (type of control group)	Pre- to post-intervention differences in primary and secondary outcomes measures		Safety	
			Within European/Western PT group	Between intervention and control group	AEs in intervention group (yes/no)	Diff. between groups (yes/no)
Nigella sativa/oil; seeds	2 (no. 10, no. 17)/5	2 RCTs (PL)	no. 10 ***Beneficial:*** nr ***Zero:*** nr	***Beneficial:*** asthma symptoms (ACT total score), pulmonary function (FEV1 in subgroup with baseline FEV1 % <80 %), immunological parameter (peripheral blood eosinophils) ***Zero:*** pulmonary function (FEV1, peak expiratory flow overall group), immunological parameter (serum IgE[10]).	Yes: stomach upset, headache and insomnia.	No
			no. 17 ***Beneficial***: asthma symptoms (ACT total score in both groups); pulmonary functions (PEF variability, FEF25-75, FEV1 in high dose group; PEF variability in low dose group), immunological parameters (cytokine IFN-γ in both groups; FeNO in low-dose group; IFN-γ and IgE in high-dose group). ***Zero***: immunological parameters (cytokines IL-4, IL-10, IL-17A, eotaxins in both groups).	***Beneficial:*** asthma symptoms (ACT total score in both groups), pulmonary function (PEF variability in both groups); immunological parameter (IFN-γ[1] in both groups). ***Zero:*** pulmonary function (FEF25-75, FEV1), immunological parameter (cytokines IL-4, IL-10, IL-17A, eotaxins, FeNO, IgE).	No: no AEs reported.	Yes: fewer exacerbations in the intervention group.
Crocus sativus L./ stigma	2 (no. 7, no. 19)/2 †	2 RCTs (PL)	no. 7 ***Beneficial:*** pulmonary functions (FEV1, FVC, FEV1/FVC ratio, FEF25–75), immunological parameter (hs-CRP). ***Zero:*** immunological parameter (anti-HSP 70)	***Beneficial:*** pulmonary function (FEV1, FVC, FEV1/FVC ratio, FEF25–75 %), immunological parameter (hs-CRP, anti-HSP 70) ***Zero:*** - ***Beneficial:*** asthma symptoms (shortness of breath, inhaler use, activity limitation, nighttime awakenings). ***Zero:*** asthma severity, immunological parameters (eosinophils, basophils).	Yes: minor feelings of warming up.	Yes
			no. 19 ***Beneficial:*** asthma symptoms (day/night shortness of breath, inhaler use, night wakening, activity limitation), immunological parameters (eosinophils, basophils). ***Zero:*** asthma severity.	***Beneficial:*** asthma symptoms (shortness of breath, inhaler use, activity limitation, nighttime awakenings). ***Zero:*** asthma severity, immunological parameters (eosinophils, basophils).	Yes: minor feelings of warming up (in both groups).	No
Pinus maritima/ bark	1 (no. 11)/2	RCT (PL)	***Beneficial:*** asthma symptoms, use of rescue inhaler, pulmonary function (PEF), immunological parameter (leukotriene C4/D4/E4). ***Zero:***	***Beneficial:*** no statistical comparisons between groups described. ***Zero:***	No AEs reported.	–
Curcuma longa L./ roots	1 (no. 14)/2	RCT (PL)	***Beneficial:*** asthma control (frequency of symptoms, nighttime awakenings, activity limitation, bronchodilators use, disease control). ***Zero:*** pulmonary function (FEV1).	***Beneficial:*** asthma control (nighttime awakenings, bronchodilators use, disease control). ***Zero:*** asthma control (frequency of symptoms, activity limitation); pulmonary function (FEV1).	Yes: one participant reported nausea	nr
Petasites hybridus/ roots	1 (no. 12)/2	RCT (PL)	*Not reported*	***Beneficial:*** pulmonary function (bronchial hyper-responsiveness, FeNO); inflammatory parameters (eosinophils). ***Zero:*** pulmonary function (FEV1, FEF25–75, PEF).	n/a	n/a
Hedera helix/ leaves	1 (no. 18)/1	RCT (PL)	***Beneficial:*** pulmonary function before bronchodilation (FEV1, MEF75-25). ***Zero:*** asthma control, asthma quality of life*	***Beneficial:*** ***Zero:*** asthma control, asthma quality of life, pulmonary function before bronchodilation (FEV1, MEF75-25)*	nr	nr
Punica granatum/ seeds	1 (no. 8)/1	RCT (PL)	***Beneficial:*** asthma symptoms (day-and-night breath shortness, activity limitation), immunological parameters (eosinophils, basophils, neutrophils). ***Zero:*** asthma symptoms (asthma spray use).	***Beneficial:*** asthma symptoms (day-and-night breath shortness, activity limitation), immunological parameters (neutrophils). ***Zero:*** asthma symptoms (asthma spray use), immunological parameters (basophils, eosinophils).	n/a	n/a

Note. Results are presented for all outcome measures, separated by the categories asthma symptoms/control, pulmonary function, and immunological parameters. Beneficial effects indicate significant pre-to post-intervention improvements in the intervention group (i.e., European/Western PT), with 'beneficial' defined as statistically significant improvement ($p < 0.05$); zero effects state no group differences; non-beneficial effects favor the control group. Abbreviations: ACT = asthma control test; AEs = adverse events; eNO = exhaled nitric oxide; FeNO = fractional eNO; FEF25-75 = forced expiratory flow 25–75 %; FEV1 = forced expiratory volume

in 1 s; FVC = force vital capacity; IgE = immunoglobulin E; MEF75-25 = maximal expiratory flow at 75-25 %; nr = not reported; n/a = not assessed; PEF = peak expiratory flow; PL = placebo; VC = vital capacity. † Based on the same study population, * results only reported for primary outcome measures.

Table 3
Substances, medication name and preparations used in AM studies (n = 4).

Plant(s)/ substance(s)	Medication name, preparation		
	Study no. 20	Study no. 21	Study no. 22 and 23 †
Nicotiana tabacum	Wala Nicotiana comp., globules Weleda Tabacum cupro culta, drops	ns	Weleda Tabacum cupro culta, drops
Cuprum aceticum	Wala Cuprum aceticum comp., ampoules for inhalation	ns	–
Levico water	Weleda Levico D3, ampoules Wala Levico comp., globules	ns	–
Oak bark	Weleda Quercus D6, drops	ns	–
Argentum/ Echinacea	Weleda Argentum/ Echinacea, ampoules	–	Weleda *Argentum/ Echinacea*, ns
Citrus limonis/ Cydonia oblonga	Gencydo®, ampoules for inhalation	–	Gencydo®, injections
Others	Wala Bronchi/ Plantago, globules Weleda Veronica D6, drops Weleda Pneumodoron I and II, ns	Mustard flour, ext. appl. Ginger, ext. appl. Lavender, ext. appl.	Heracleum mantegazzianum, ns Quartz, ns Tartarus stibiatus, ns

Note. The list refers to the reported medications. It is not exhaustive regarding all medications used. Abbreviations: ns = not specified; ext. appl. = external applications † Same study population.

(lemon juice) and an aqueous extract from *Cydonia oblonga* (quince) has a potential anti-inflammatory effect, which could be beneficial in bronchial asthma. *In vitro* studies have demonstrated that Gencydo® can inhibit substances from immune cells and suppress specific inflammatory proteins, similarly to antihistamines [18,57]. The potential benefits of Citrus/Cydonia were first recognized in the 1920s from an anthroposophic perspective and can now be explored with the modern molecular understanding. A similar path holds true for medications from PT, which were first used traditionally and investigated at a later stage. Another plant that was used in the included AM studies was *Nicotiana tabacum*. From the perspective of AM, *Nicotiana tabacum* can harmonize the rhythmical system, which includes the lung, by supporting bronchial smooth muscle relaxation [58]. Two studies (no. 20, no. 21) investigating the effect of AM on pulmonary function reported fewer improvements compared to conventional medicine. However, the authors emphasize potential measurement errors influencing pulmonary function results. In general, the findings for AM medications need to be interpreted carefully given the limited quality of the included studies.

4.1. Strengths and limitations

This is the first systematic review providing a comprehensive overview of all plants studied in European/Western PT and AM. Most of the included studies were RCTs, considered the gold standard for testing intervention effects. The broad range of plants studied provides a basis for clinical implications and further investigations. Nevertheless, several limitations should be considered when interpreting the findings of this review. First, included studies on European/Western PT and AM were heterogeneous in various respects, such as study population, plants studied or intervention duration and dosage, making it difficult to reach an overall conclusion about their efficacy and effectiveness. The generalizability of the results is further limited as half of the included studies were based on a small sample size. Besides, the absence of safety measures in some studies presents a challenge in forming judgments regarding the safety of European/Western PT and AM. Furthermore, insufficient study quality was indicated based on the quality assessment in about half of the included studies, with bias in reporting and lack of rigorous data analysis emerging as the main reasons for insufficient quality. Older studies in particular did not address limitations of their research and/or did not report specific manufacturing processes, as now required by the CONSORT statement for herbal interventions [59]. Also, in some studies, specific efficacy measures were not reported, making it impossible to draw conclusion about the magnitude of the effect. Lastly, as a range of different outcome measurements were used in the included studies and thus a general close and a meta-analysis for specific outcome parameters was not feasible.

4.2. Implications

This systematic review supports physicians and pharmacists in advising individuals with bronchial asthma about additional treatment options from European/Western PT and AM. Given that TCIM is commonly used by individuals with bronchial asthma [6,7], scientifically based recommendations are needed. Findings from this review suggest several plants that may be beneficial in bronchial asthma. This could be particularly useful for individuals with severe bronchial asthma who wish to enhance asthma control further or reduce consumption of conventional medication, for example. One benefit of herbal preparations is their composition as multi-substance mixtures, allowing them to affect various parameters. For example, extracts derived from ivy leaves exhibit both immunomodulatory and bronchodilatory properties. Isolated pure substances may also offer beneficial effects and could be explored as supplemental therapy in asthma treatment [60]. Furthermore, the results of this review showed that European/Western PT seems to be safe. The combination of multiple substances in herbal preparations usually minimizes potential side effects, though this varies depending on the dosage. Also, potential herb-drug interactions need to be considered when prescribing medication from European/Western PT or AM (for further information see ESCOP website). To ensure safety, European/Western PT or AM medications should be integrated as add-on therapy into conventional treatment, with dosage adjusted according to the treatment effect and severity of asthma.

Future research may consider verifying the reported beneficial effects based on current quality standards and larger sample sizes to increase confidence in results. Precise information about the manufacture and standardized manufacturing processes of herbal preparations would increase the reliability of results. In this regard, information about the bioavailability of certain preparations should be included. Evidence shows, for instance, that the clinical efficacy of turmeric preparations can vary based on how it is metabolized in the gastrointestinal tract [61]. Further studies may also compare different dosages of herbal preparations, as done by study no. 17, to detect any dose-dependent effects. In this context, thorough evaluations of AEs are advised to identify interventions that are both effective and safe. Future research could gain valuable insights from conducting follow-up measurements to assess the long-term effects and safety profiles of these interventions. In this context, it could be valuable to further examine exacerbations and comorbidities over time. Additionally, studies should aim to generate evidence across different age groups to ensure the relevance of the findings to broader populations. It would also be valuable to investigate the effect of European/Western PT or AM as an add-on therapy to conventional medicine more in detail, as most of the RCTs included in this systematic review primarily compared European/-Western PT with placebo. Finally, establishing recommendations on

outcome measures for clinical studies conducted in bronchial asthma, including clinically useful biomarkers [62], quality of life, and cost-effectiveness, would allow for better comparison of results and interventions of different studies.

5. Conclusion

The findings of this systematic review suggest certain plant-derived medications from European/Western PT and AM to have beneficial effects on asthma symptoms, pulmonary function and inflammatory parameters in individuals with bronchial asthma. Further rigorous studies are needed to test and explore the reported beneficial effects. Still, this systematic review provides an overview for clinicians in advising individuals with bronchial asthma on potentially effective add-on treatment options from plant-derived medication.

CRediT authorship contribution statement

Céline Braunwalder: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Jana Ertl:** Writing – review & editing, Conceptualization. **Matteo Wullschleger:** Writing – review & editing, Methodology, Conceptualization. **Eliane Timm:** Methodology, Formal analysis. **Ursula Wolf:** Writing – review & editing, Conceptualization.

Data availability statement

All data relevant to the study are included in the article.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: This work was financially supported by the grant SAGST P14441 and the Swiss Medical association FMH. The funder had no role in the design, data collection, data analysis, and reporting of this study. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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