

Original Article

Herbal Medicine for Cough: a Systematic Review and Meta-Analysis

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Appendix I. Characteristics of the included studies.

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
<i>Andrographis paniculata</i>									
1	Saxena, 2010	Common Cold /URTI, 18-60 years	2 groups 223 Pat.	KalmCold™ -Capsules (100 mg A.pan.) 1 capsule 2x/d (daily dose: 200mg A. pan.)	Placebo	5 days	<i>Prim. outcome:</i> Severity of symptoms assessed with a VAS (0-100) on day 1,3 and 5 of application	Significant improvement of overall severity of symptoms and sign. improvement of cough in KalmCold-group	6 Pat. with mild AEs
2	Cáceres, 1999	URTI, 25-50 years	2 groups 208	KanJang ® -Tablets (5mg Andrographolide) 4 Tab. 3x/d (daily dose: 400 - 20mg A. pan.)	Placebo-Tablets (Amylum solani)	5 days	<i>Prim. outcome:</i> Severity of symptoms assessed with a VAS ¹ on day 0,2 and 4 of application	KanJang is significantly superior to placebo in general; sign. improvement of the frequency of cough (p <0,001)	-
3	Melchior, 2000a	URTI 18-55 years	Pilot-Study n = 46	KanJang ®-Tablets (85mg Andr. pan.-extract) 3 x 4 Tab /d	Placebo	4-6 days	<i>Prim. outcome:</i> Improvement of diagnosis- and symptomsscores	No significant (p =0.08) improvement concerning the total symptom-scores, no improvement on cough	no AEs
4	Melchior, 2000b	URTI 18-55 years	Phase III-Study n = 180	KanJang ®-Tablets (85mg Andr. pan.-extract) 3 x 4 Tab /d	Placebo	3 days	<i>Prim. outcome:</i> Improvement of diagnosis- and symptomsscores	KanJang is significantly superior to placebo (p= 0.003 & 0.0006) ; cough-parameters have improved sign. in verum-group (cough frequency p= 0,004)	

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
5	Narimanian, 2005	acute bronchitis 18-54 years	3 groups n = 90 Pat.	1.) KanJang oral solution ® 2.) Echinacea-Preparation 30 ml 3x/d	Controlgroup: Bromhexine coated tablets (8mg)	6 days	<i>Prim. outcome:</i> Improvement of symptomscore assessed with a VAS ¹ on day 1-8 of application	<i>Prim. outcome:</i> Significant improvement of symptoms including cough (p< 0.001) by KanJang <i>Sec. outcome:</i> sign. fewer days of application nessecary in KanJang-group compared to Echinacea	no AEs
6	Thom, 1997	URTI, 18 – 40 years	2 groups n=60	KanJang ® oral-solution 15ml 3x/d	Placebo-Solution	5-10 days	<i>Prim. outcome:</i> severity of cough, frequency of cough, quality of sleep, load of sputum in respiratory tract system, nasal congestion, general disorders assessed with a VAS (0-10cm) on dyas 2,4 and 10 of application <i>Sec. outcome:</i> duration of treatment	<i>Prim. outcome:</i> Signif. improvement of symptoms especially between days 2 and 4 in KanJang-gropus; improvement of cough highly sign. <i>Sec. outcome:</i> sign. shorter duration of treatment in KanJang-group was needed	No AEs
Essential oils									
7	Matthys, 2000	acute bronchitis > 18 years	4 groups, n = 640	a) <i>Myrtol-group</i> 4 x 300 mg /d for 14 days b) <i>Cefuroxim-group</i> 2 x 250mg /d for 1-6 days c) <i>Ambroxol-group</i> 3 x 30mg /d for day 1-3, 2 x 30mg for day 4-14	4.) Placebo-group 4x 1Tab. /d for 14 days	28 days	<i>Prim. outcome:</i> examinations (week 1, 2, 3), daily change of symptoms, examination parameters, clinical symptoms, Overall efficacy, Changes in lung- function, Number of patients who were cured within 4 weeks	all interventional groups provide similiar results; for Myrtol: number of pat. with >4 coughing fits during the day decreased sign. , but Myrtol is not superior in comparison with the other interventional groups	131 cases of AEs, occurence similiar in all groups

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
8	Stafunsky, 1989	URTI 16 - 65 years	Two groups n = 40	Pinimenthol Oral N ® - capsules + 10 Min Inhalation with "Bad Emser Sole" daily	Placebo-capsules	10 days	<i>Prim. outcome:</i> lung-auscultation, sputum (secretion and consistency), dyspnoe and quality of coughing, Lung-function (VK, FEV1, FEV1%)	Signif. improvement in quality of cough (p<0.05) consistency of sputum, lungauscultation, less dyspnoe	-
9	Paul, 2010	URTI 2-11 years	three groups n = 138	Vicks VapoRub ®: apply on chest before going to bed, dosages: 2-5 years: 5ml, 6-11 years: 10ml	Vaseline OR No-Treatment	2 days	<i>Prim. outcome:</i> Changes in URTI-symptoms (including cough-parameters, rhinorrhoe, quality of sleep) assessed by parents (VRS) <i>Sec. outcome:</i> duration of illness, AEs	<i>Prim. Outcome:</i> signif. improvement of cough frequency and cough severity in VR-Group in comparison to No-treatment- group <i>Sec. outcome:</i> VR caused sign. more AEs compared to control-groups	(see outcome)
10	Gillissen, 2013	Acute bronchitis 18-83 years	Two groups N = 413	GeloMytrol ® forte 4 x 300 mg Myrtol/d for 14 days	Placebo	14 days	<i>Prim. Outcome:</i> ratio of the mean frequency of day-time □coughing fits on days D07- D09 to the baseline frequency on □D01 <i>Sec. Outcome:</i> for the daily day-time coughing fits, difficulty of coughing-up, sleep disturbance due to night- time coughing, and impairment of general wellbeing	<i>Prim. Outcome:</i> Sign. lower mean frequency of day-time coughing fits for days D07–D09 for treatment with Myrtol: mean change in coughing fits of 62.1 % (95 % CI: 57.6–66.6%) under Myrtol treatment compared to 49.8% (95% CI: 44.6–55.0 %) under placebo (p < 0.0001) <i>Sec. Outcome:</i> – a larger relative reduction in mean frequency of coughing	Mild AEs, no need to be treated

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
								<ul style="list-style-type: none"> fits ($p < 0.001$ and $p < 0.0001$), – a larger reduction in daily coughing fits ($p < 0.0001$) – the time to 50% reduction in coughing fits was shorter ($p = 0.0002$) – more patients achieved a condition without coughing fits ($p = 0.0012$) – it proved easier to cough up mucus during the day ($p = 0.0004$) – there was less sleep disturbance due to night-time coughing ($p = 0.0007$) 	
Bakumondoto									
11	Irifune, 2011	post-infectious cough 27 – 84 years	2 groups n = 20	Test-medication: TJ-29-Powder, 3g 3x/d Basic medication: Beta-2-Sympathomimeticum; additional medication: dextromethorphan hydrobromide (max. 3 x/d)	basic medication (+ additional medication)	14 days	Prim. outcome: Change of intensity of cough Sec. outcome: Quality of sleep	Prim. outcome: signif, improvement of intensity of cough Sec. outcome: no differences	AE: Palpitation and tremor of hands (ascribed to basic medication)
Echinacea									
12	Barrett, 2002	Common Cold	Two groups	Echinacea-capsules:	Placebo-Capsules	10 days	Prim. outcome:	no signif. differences	abdominal

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
		>18 years	n = 148	different Echinacea species, Thyme, Peppermint day 1: 4 Cap. 6x/d , >day 1:4 Cap. 3x/d , until being free of symptoms or max. 10 days			duration and severity of symptoms assessed with symptom-diary and VRS	between the two groups concerning duration of illness and severity of symptoms (including cough)	AE, similiar distribution
13	Bräuning, 1992	Common Cold 18-60 years	three groups n = 180	Two Echinacea-groups (oral solution) Group A: 450 mg/d Group B: 900 mg/d	Placebo	10 days	<i>Prim. outcome:</i> duration of illness, Improvement of symptoms and symptom-score (0-3 VRS) <i>Sec. outcome:</i> other parameters (new symptoms, blood count, ESR)	<i>Prim. outcome:</i> sign. improvement of symptomsscore in group b, → no signif. improvement of cough <i>Sec. outcome:</i> only group b provides significant results (headache, film of tongue, inflamed nose)	some respiratory AEs (cough, bronchitis)
14	O'Neil, 2008	URTI 18-65 years	Two groups n = 90	Echinacea-Capsules (300 mg) 3 Cap. 2x/d	Placebo-Capsules (300 mg parsley)	8 weeks	<i>Prim. outcome:</i> number of days with symptoms assessed with weekly telephone-interviews	No signif. differences between the two groups including cough	no serious AEs
15	Yale, 2004	Common Cold 18-62 years	Two groups n = 128	Echinacea – Capsule (100mg), 1 Capsule 3x/d	Placebo	max. 2 weeks	<i>Prim. outcome:</i> Change in Symptomscre	no significant differences (including cough) between the two groups	no serious AEs, GI- AEs, similiar distribution in both groups
16	Cohen, 2004	URTI 1-5 years	Four groups Verum- and Placebogroup s according to age-cohort	"Chizukit"-oral solution: 50 mg/ml Echinacea, 10 mg/ml Vit. C according to age: 1-3 y.: 5ml 2x/d, 4-5 y.: 7,5ml 2x/d	Placebo-oral solution	12 weeks	<i>Prim. outcome:</i> number of: episodes of illness, days of illness, children with >1 episode of illness, duration of symptoms	<i>Prim. outcome:</i> advantages of verum in number of: episodes of illness, days of illness, and duration of illness	mild GI-AEs, similiar in both groups

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
			n = 328				<i>Sec. outcome:</i> days of fever, usage of antipyretics or antibiotics, number of visits at the doctor, absence of kindergarden, rhinitis, daily+nightly cough	<i>Sec. outcome:</i> significant improvement in all parameters; → nighttime cough improves significantly (p=0.03), also daytime cough improves but does not reach stat. significance	
17	Goel, 2004	Common Cold 18-65 years	Two groups n = 128	Echinacea-oral solution 1st day: 4 ml 10x/d; >1st day: 4ml 4x/d	Placebo-oral solution,	one week	<i>Prim. outcome:</i> Change in Total Daily Symptom Score (TDSS) <i>Sec. outcome:</i> Change of single symptoms included in TDSS, duration of symptoms, response rate	<i>Prim. outcome:</i> signif. improvement of TDSS in verum-group No signif. improvement for cough (p<0,30) <i>Sec. outcome:</i> others improved signif.	mild GI-AE, itchy and irritated skin, similiar in both groups
18	Schulten, 2001	Common Cold >18 years	Two groups n = 80	Echinacea-oral solution "EC31J0", E. purpurea Intake: 2x /d for 10 days	Placebo-oral solution Intake analogue to verum	10 days	<i>Prim. outcome:</i> number of days of illness & pat. with complete disease pattern of common cold, duration of illness, area-under- the-curve of summarized symptomsscore <i>Sec. outcome:</i> area-under-curve of single symptoms, proportion of pat. developing the compl. disease pattern in first five days	<i>Prim. outcome:</i> no signif. superior results for improv. of cough in verumgroup; sign. advantages for verum- group in number of days of illness, less pat. with complete disease pattern, smaller area-under-the-curve of summarized symptomsscore	few & mild AEs, similiar in both groups
19	Sperber, 2004	induced viral Common Cold	Two groups n = 48 Pat.	Echinacea-oral solution ("EchinaGuard") 2,5 ml 3x/d for 14 days (7	Placebo-oral solution	one month	<i>Prim. outcome:</i> number of induced common colds (assessed by titer of	<i>Prim. outcome:</i> no significant differences	no serious AE, similiar in both

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
		18-65 years		days before and after virus - noculation)			antibodies, virus-titer in nasal secretion, symptom-score)	between both groups → no signif. differences for treatment of cough in both groups	groups
Ivy, Primrose, Thyme									
20	Kemmerich, 2007	acute bronchitis > 18 years	Two groups n = 362	Thyme-Primrose-Preparation (Bronchipret® -Tablets) 1 Tab. 3x/d	Placebo-Tab.	11 days	<i>Prim. outcome:</i> change in daily cough- frequency <i>Sec. outcome:</i> efficiency on frequency of cough, general efficiency (change of BSS)	<i>Prim. outcome:</i> → signif. reduction of frequency of cough in verumgroup (p < 0,0001 on day 9) <i>Sec. outcome:</i> signif. reduction concerning AUC in verumgroup (p < 0,0001); shorter time until frequency of cough reduces 50%; significant improvement of BSS in verumgroup and of general efficiency	only few, mild AEs
21	Kemmerich, 2006	acute bronchitis > 18 years	Two groups n = 363	Bronchipret®-oral solution, 5,4ml 3x/d	Placebo-oral solution	max. 15 days	<i>Prim. outcome:</i> change of frequency of cough (on days 7-9) <i>Sec. outcome:</i> efficiency on frequency of cough (by AUC of symptom scores, time until frequency of cough reduced about 50%, relative reduction related to average frequency of cough); general efficiency (response rate, change in BSS, ability to	<i>Prim. outcome:</i> singificant improvment of cough-frequency in verumgroup (p < 0,0001) <i>Sec. outcome:</i> signif. improvement in verumgroup on day 9 for cough frequency; time until 50%-reduction of cough-frequency is two days shorter in verumgroup;	few, mild AEs, similiar in both groups

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
							cough up sputum, sleep quality, general well-being)	sign. better general efficiency in verumgroup	
22	Cwientzek, 2011	acute bronchitis 2-86 years	Two groups n = 590	Two Ivy-preparations: 1. Hedelix ®-drops 2. Prospan®-drops	no controll-/ placebo-intervention	7 days	<i>Prim. outcome:</i> Improvement of BSS, global efficiency, tolerability, body temperature, ability to go to work	no significant differences between both groups (including cough)	no serious AEs
23	Kurth, 1978	URTI, allergic cough > 18 years	Two groups n = 113	Mintetten ®-Dragees Intake is individually, adopted to severity of symptoms	Plazebo-Dragee with fruit flavour	14-18 days	<i>Prim. outcome:</i> secretolysis, relieve of allergic cough assessed by investigational doctor	<i>Prim. outcome:</i> significant improvement of secretolysis and relieve of allergic cough (p<1%)	few, mild AEs
<i>Pelargonium sidoides</i>									
24	Matthys, 2010a	acute bronchitis >18 years	4 Groups n = 404	Three Pelargonium sid.-groups in different dosages: → 30mg, 60 mg, 90 mg; 3x/d	Placebo	one week	<i>Prim. outcome:</i> Change of BSS <i>Sec. outcome:</i> number of pat. with BSS < 3 on day 7 (1) & of pat. with a reduction of 7 in 7 days(2), combination of 1 + 2, start effect of medicine, intake of paracetamol, change of individual symptoms of BSS & of general symptoms, general health-status & QoL, time of inability to go to work, contendedness with medication	<i>Prim. outcome:</i> significant improvement of BSS (including cough) in all three dose-groups in comparison to placebo; highest dosage-groups provides best results <i>Sec. outcome:</i> significant improvement in all parameters	no serious AEs
25	Matthys, 2010b			as above			<i>Prim. outcome:</i> EQ-5D (EuroQoL- 5	<i>Prim. outcome:</i> EQ-5D und EQ VAS:	no serious AEs

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
							Dimensions), SF-12 (Health survey, short form-12) , EQ VAS (actual health-based quality of life), patients' diary about health-status, IMOS (= Integrative Medicine Outcome Scale), IMPSS (=Intergrative Medicine Patient Satisfaction Scale)	Significant improvement in verumgroup; SF-12: signif. improvement in Verumgroup; patients' diary: in all verumgroups superior results in comp. to placebo; more physical detractions in placebo-group; IMOS und IMPSS: sign. improvemnt on day 7 comp. to placebo	
26	Kamin, 2010a	acute bronchitis 6-18 years	Four groups n = 399	Three Pelargonium sid.- groups: 30mg, 60mg, 90mg	Placebo-Tab.	one week	<i>Prim. outcome:</i> change in BSS <i>Sec. outcome:</i> number of pat. with BSS <3 on day 7 & of pat. with a reduction of 7 in 7 days, combination of both, beginning of effect of medication, change of individual and general symptoms, status of health, duration of inability to go to kindergarden/school, IMOS, IMPSS	<i>Prim. outcome:</i> significant improvement in BSS in verumgroup, → signif. dose-dependent improvement of cough (p<0.0001) <i>Sec. outcome:</i> signif. improvement in 60mg- and 90mg-groups for all parameters, better results in 90mg-group	no serious AEs, more GI-AE
27	Kamin, 2010b	acute bronchitis 1-18 years	Two groups n = 200	Pelargonium sidoides (oral solution) dosage depending on age	Placebo (oral solution)	one week	<i>Prim. outcome:</i> Change of BSS <i>Sec. outcome:</i> response rate, start of effect of treatment, change of individual symptoms of BSS & of general symptoms, status of health, absence in kindergarden, effect of treatment (IMOS) &	<i>Prim. outcome:</i> improvement in BSS in Verumgroup → signif. improvement of cough <i>Sec. outcome:</i> signif. improvement in response rate, earlier start of effect of treatment, all parameters (except for the	27,5% AEs (mild) in total, (Verum 30,1%, Placebo 24,7%);

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
							contendness (IMPSS)	status of health)	
28	Matthys, 2007	acute bronchitis >18 years	Two groups n = 198	Pelargonium sidoides (oral solution)	Placebo	one week	<i>Prim. outcome:</i> change in BSS on day 7 <i>Sec. outcome:</i> general symptoms of infection, contendness with treatment (IMPSS), efficiency of treatment (IMOS)	<i>Prim. outcome:</i> signif. improvement of BSS (including cough) on day 7 in verumgroup <i>Sec. outcome:</i> greater efficiancy & satisfaction in verumgroup, signif. improvement of individual symptoms of BSS and general symptoms	no serious AEs
29	Chuchalin, 2005	acute bronchitis >18 years	Two groups n = 124	EPs 7630 (oral solution), 30 drops 3x/d (=4,5ml/d)	Placebo (oral solution)	one week	<i>Prim. outcome:</i> Change of BSS (on day 7) <i>Sec. outcome:</i> number of pat. with BSS <5 & of pat. with reduction of 5 points in BSS in 7 days, beginning of effect of medicine, intake of paracetamol, change of individual symptoms, status of health, QoL (SF-12 Health Survey, EQ-5D), treatment effect (IMOS), contendness with treatment (IMPSS)	<i>Prim. outcome:</i> signif. improvement of BSS (including cough) in verumgroup on day 7 <i>Sec. outcome:</i> signif. imrpovements in all parameters	no serious AEs
30	Matthys, 2003	acute bronchitis > 18 years	Two groups n = 468	EPs-7630 (oral solution), 30drops 3x/d	Placebo -solution	one week	<i>Prim. outcome:</i> Change in BSS <i>Sec. outcome:</i> number of pat. with BSS <3 (1)	<i>Prim. outcome:</i> signif. improvement of BSS in verumgroup (Verum 5,9 ± 2,9 vs Placebo 3,2 ± 4,1, p<0,0001	no serious AEs, mostly GI-AEs

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
							& of pat. with reduction of BSS >7 (2), combination of 1 + 2, IMOS, time until effect of medicine begins, Intake of Paracetamol, change of individual symptoms of BSS, status of health assessed by EQ-5D, contentness assessed (IMPSS)	<i>Sec. outcome:</i> signif. improvement in all parameters concerning BSS,	
31	Matthys, 2008	acute bronchitis >18 years	Two groups n = 217	Eps 7630 (oral solution), 30 drops 3x/d	Placebo-oral solution	one week	<i>Prim. outcome:</i> Change in BSS on day 7 <i>Sec. outcome:</i> evaluation of symptoms of infection, number of pat. unable leaving bed, intake of paracetamol, health associated QoL (SF-12 Health Survey, EQ-5D), effect of treatment (IMOS), contentness with treatment (IMPSS)	<i>Prim. outcome:</i> signif. improvement of BSS (especially for cough) in verumgroup <i>Sec. outcome:</i> signif. improvement in all symptoms (including cough)	no serious AEs, similiar in both groups
32	Lizogub, 2007	Common Cold 18-55 years	Two interventional and two control-groups n = 207	EPs 7630 (oral solution), 30 drops 3x/d for 10 days OR 60 drops 3x/d for 10 days	Placebo	10 days	<i>Prim. outcome:</i> Sum of Symptom intensity differences (SSID) of cold intensity score (CIS) from day 0 to dya 5 (including cough) <i>Sec. outcome:</i> change of individual symptoms of CIS, change of other symptoms of common cold, ability to go to work, level of activity, general	<i>Prim. outcome:</i> signif. improvement of SSID and CIS (including cough) in verumgroup <i>Sec. outcome:</i> signif. improvement of some symptoms (NOT incl. cough); signif. improvment of ability to work & level of activity, greater response-	no serious AEs, similiar in both groups

	Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
							well-being, health-related QoL (EQ-5D), time until set-up of effect, IMOS and IMPSS	rates in verumgroup, earlier Beginn of effect of treatment, & satisfaction	
33	Blochin, 1999	acute bronchitis 5-14 years	Two groups n = 30	Umckaloabo® (oral solution)	Acetylcystein – Granules	one week	<i>Prim. outcome:</i> Change of BSS <i>Sec. outcome:</i> change of general symptoms (control-visits on day 3 and 7)	<i>Prim. outcome:</i> no signif. differences in change of BSS (including cough) in both groups <i>Sec. outcome:</i> no signif. differences	-
34	Kamin, 2012	Acute bronchitis 1-18 years	Two groups N = 220	Umckaloabo ® (oral solution) 1-6 yo.:3 x 10 drops 6-12 yo.: 3 x 20 drops 12-18 yo.: 3 x 30 drops	Placebo	One week	<i>Prim. Outcome:</i> change in the BSS total score from day 0 to day 7 <i>Sec. Outcome:</i> Crit. 1: response rate defined as BSS total score of <3 points at day 7 Crit. 2: decrease in BSS total score by at least 4 points from day 0 to day 7 Crit. 3: BSS total score <3 at day 7 combined with a decrease in BSS total score by at least 4 points from day 0 to day 7 Further: – change of the individual symptoms of the BSS – onset of treatment effect, – health status	<i>Prim. Outcome:</i> BSS total score decreased by 4.4 1 1.6 points in the EPs 7630 group compared to a decrease of 2.9 1 1.4 points in the placebo group (P < 0.0001) <i>Sec. Outcome:</i> The response rate at day 7 according to all three response criteria was considerably higher in the active treatment group as compared to the placebo group (criterion 1, 81.1% vs 37.6%; crite- rion 2, 73.9% vs 36.7%; criterion 3, 64.9% vs 24.8%; P < 0.0001 each) Further: – individual symptoms	Three AEs occured, no further treatment needed

Author, Year	Diagnosis Age	number of groups number of patients	Intervention medication, dosage, frequency, duration	Controllintervention medication, dosage, frequency, duration	time of data acquisition	Outcomeparameters	Results	adverse events
						<ul style="list-style-type: none"> - quality of life of patients - Satisfaction with treatment - duration of bed rest - ability to attend kindergarten, school or work 	<ul style="list-style-type: none"> - 'coughing' and 'pulmonary rales at auscultation' P < 0.0001 - onset of effect occurred significantly earlier in the EPs 7630 group as compared with the placebo group (P < 0.0001) - satisfaction of patients was significantly better in the EPs 7630 group as compared to the placebo group (P < 0.0001) - health status, quality of life and bed rest advantages for verum but not significant 	

Short forms:

VAS = Visuel Analogue Scale

VRS = Verbal rating scale

TDSS = Total daily Symptom Score

BSS = Bronchitis Sseverity Score; includes 5 Symptoms of bronchitis: 1) Cough, 2) Sputum, 3) Rhonchi / Rassels, 4) (chest-)pain while coughing, 5) Dyspnoe; assessed with verbal rating scale: 0:absent, 1: mild, 2: moderate, 3: severe, 4: very severe

SSS = Sinusitis Severity Score includes 6 Symptoms: 1) headache, 2) pain in sinus, 3) pain in sinus, which increases under pressure or leaning forth, 4) purulent nasal congestion, 5) nasal secretion, 6) eitriges Nasensekret sichtbar im mittleren Meatus oder hinterer Abfluss von eitrigem Nasensekret; assessed with verbal rating scale: "0" – not present, "4" – very severe

Appendix II. Risk of bias of the included studies.

Author, year	Bias			Performance-Bias:				Attrition-Bias:		Reporting-Bias:	Detection-Bias::		Total: (max. 12) ^a
	Adequate Randomisation-Strategy	Adequate blinded allocation/assignment	Comparable Baseline-Characteristics	Adequate Blinding of Patients	Adequate Blinding of Investigators	Comparable or no Co-Interventions	Acceptable Compliance	Acceptable drop-out-rates	Use of an Intention-to-treat-Analysis	no selective Reporting of Outcome-Parameters	Adequate Blinding of detection	Comparable time of detection	
Andrographis paniculata / KanJang													
Saxena, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Yes ¹	Yes	10
Cáceres, 1999	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	9
Melchior, 2000a	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	9
Melchior, 2000b	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	10
Narimanian, 2005	Unclear	Yes	Yes	No	No	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	7
Thom, 1997	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Ätherische Kräuter													

Bias Author, year	Selection-Bias:			Performance-Bias:				Attrition-Bias:		Reporting-Bias:	Detection-Bias::		Total: (max. 12) ^a
	Adequate Randomisation-Strategy	Adequate blinded allocation/assignment	Comparable Baseline-Characteristics	Adequate Blinding of Patients	Adequate Blinding of Investigators	Comparable or no Co-Interventions	Acceptable Compliance	Acceptable drop-out-rates	Use of an Intention-to-treat-Analysis	no selective Reporting of Outcome-Parameters	Adequate Blinding of detection	Comparable time of detection	
Matthys, 2000	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	7
Stafunsky, 1989	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Unclear	Yes	3
Paul, 2010	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	7
Gillissen, 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	11
Bakumondoto													
Irifune, 2011	Unclear	No	Yes	Unclear	Unclear	No	Unclear	No	No	Yes	Unclear	Yes	3
Echinacea													
Barrett, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
O'Neil, 2008	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Yes	Yes	Yes	9
Yale, 2004	Unclear	Yes	Yes	Yes	Unclear	Yes	Unclear	Unclear	No	No	Yes	Yes	6
Cohen, 2004	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	No	No	Yes	Yes	Yes	9
Goel, 2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12

Author, year	Selection-Bias:			Performance-Bias:				Attrition-Bias:		Reporting-Bias:	Detection-Bias::		Total: (max. 12) ^a
	Adequate Randomisation-Strategy	Adequate blinded allocation/assignment	Comparable Baseline-Characteristics	Adequate Blinding of Patients	Adequate Blinding of Investigators	Comparable or no Co-Interventions	Acceptable Compliance	Acceptable drop-out-rates	Use of an Intention-to-treat-Analysis	no selective Reporting of Outcome-Parameters	Adequate Blinding of detection	Comparable time of detection	
Schulten, 2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
Bräuning, 1992	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	No	Yes	Unclear	Yes	3
Sperber, 2004	Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	No	Yes	Yes	Yes	7
Efeu, Primel, Thymian													
Kemmerich, 2007	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Cwientzek, 2011	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	9
Kemmerich, 2006	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Kurth, 1978	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	Yes	No	Yes	Unclear	Yes	8
Pelargonium sidoides													
Matthys, 2010a	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
Kamin, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
Matthys, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	10

Author, year	Selection-Bias:			Performance-Bias:				Attrition-Bias:		Reporting-Bias:	Detection-Bias::		Total: (max. 12) ^a
	Adequate Randomisation-Strategy	Adequate blinded allocation/assignment	Comparable Baseline-Characteristics	Adequate Blinding of Patients	Adequate Blinding of Investigators	Comparable or no Co-Interventions	Acceptable Compliance	Acceptable drop-out-rates	Use of an Intention-to-treat-Analysis	no selective Reporting of Outcome-Parameters	Adequate Blinding of detection	Comparable time of detection	
Chuchalin, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	11
Matthys, 2008	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	No	Yes	Yes	9
Lizogub, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	11
Kamin, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	11
Blochin, 1999	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	9
Matthys 2010	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	5
Matthys 2003	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	10
Kamin, 2012	Yes	Yes	Yes	Yes	Yes	Yes	unclear	Yes	YES	Yes	Yes	Yes	11

^ahigh numbers mean low risk of bias

Appendix III. Excluded studies.

Wrong intervention:

[1-10]

Chinese herbs:

[11-30]

No RCT:

[31-50]

Inappropriate etiology:

[51-77]

Other:

[78-101]

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