D.4 Herbal medicines

Overview of the PICO structure

Definition of the intervention	
WHO defines herbal medicines as herbs, herbal materials, herbal preparations and finished herbal products that contain, as active ingredients, parts of plants, or other plant materials, or combinations of both. For the purpose of this guideline, herbal medicines were restricted to plants or parts of plants used for medicinal purposes, administered orally (ingestion) or applied topically. This definition does not include plant substances, smoked individual chemicals derived from plants, or synthetic chemicals based on plant constituents.	
PICO question	
Population and subgroups	Community-dwelling adults (aged 20 years and over) experiencing chronic primary low back pain, with or without leg pain, including older people (aged 60 years and older). Subgroups: • Age (all adults and those aged 60 years and over) • Gender and/or sex • Presence of leg pain (radicular, non-radicular, mixed) • Race/ethnicity - studies of populations who were historically marginalized compared with studies of those who were not • Regional economic development - studies carried out in high-income countries compared with studies in low- to middle-income countries
Comparators	a) Placebo/sham b) No or minimal intervention, or where the effect of the intervention can be isolated c) Usual care

Web Annex D.D4: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Outcomes	Critical outcomes constructs (all adults) • Pain • Back-specific function/disability • General function/disability • Health-related quality of life • Psychosocial function • Social participation • Change in the use of medications • Adverse events (as reported in trials) Pain • Back-specific function/disability • General function/disability • Health-related quality of life • Psychosocial function • Adverse events (as reported in trials) • Change in the use of medications • Falls Critical outcomes constructs (older adults, aged ≥ 60 years)

Other Evidence-to-Decision (EtD) considerations across all herbal medicines

Summary of *values and preferences*	
All adults	**Older people**

No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	**# Review findings GRADE-CERQual Assessment of confidence** 7 Some participants adopted alternative forms of treatment (traditional or herbal medicines) as a part of their self-management approach when conventional treatments failed. Some viewed this as experimenting to find a solution. Often participants did not inform their health care provider about taking this type of treatment. LOW

Summary of *resource considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *equity and human rights considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *acceptability considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *feasibility considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of judgements

D.4.1 Topical Cayenne pepper [Capsicum frutescens]

Domain	**All adults**	**Older people**
Benefits	Moderate; small; uncertain	Moderate; small; uncertain
Harms	Moderate; small; uncertain	Moderate; small; uncertain
Balance benefits to harms	Probably favours cayenne pepper; probably does not favour cayenne pepper; neutral; uncertain	Probably favours cayenne pepper; probably does not favour cayenne pepper; neutral; uncertain
Overall certainty	Low	Low
Values and preferences	Possibly important uncertainty or variability; probably no important uncertainty or variability	Possibly important uncertainty or variability; probably no important uncertainty or variability
Resource considerations	Moderate costs; varies	Moderate costs; varies
Equity and human rights	No impact; uncertain; varies	No impact; uncertain; varies
Acceptability	Yes; varies	Yes; varies
Feasibility	Yes; probably yes; varies	Yes; probably yes; varies

D.4.2 Devil's claw [Harpagophytum procumbens]

Benefits	Small; trivial; uncertain	Small; trivial; uncertain

Harms	Uncertain	Uncertain
Balance benefits to harms	Probably does not favour Devil's claw; uncertain	Probably does not favour Devil's claw; uncertain
Overall certainty	Low; very low	Low; very low
Values and preferences	Possibly important uncertainty or variability; probably no important uncertainty or variability	Possibly important uncertainty or variability; probably no important uncertainty or variability
Resource considerations	Moderate; varies	Moderate; varies
Equity and human rights	No impact; uncertain; varies	No impact; uncertain; varies
Acceptability	Yes; varies	Yes; varies
Feasibility	Yes; probably yes; varies	Yes; probably yes; varies

D.4.3 White willow [Salix spp.]

Benefits	Uncertain	Uncertain
Harms	Uncertain	Uncertain
Balance benefits to harms	Uncertain	Uncertain
Overall certainty	Low; very low	Low; very low
Values and preferences	Possibly important uncertainty or variability; probably no important uncertainty or variability	Possibly important uncertainty or variability; probably no important uncertainty or variability
Resource considerations	Moderate; varies	Moderate; varies
Equity and human rights	No impact; uncertain; varies	No impact; uncertain; varies
Acceptability	Yes; varies	Yes; varies
Feasibility	Yes; probably yes; varies	Yes; probably yes; varies

D.4.4 Brazilian arnica [Solidago chilensis]

ETD process not completed based on GDG decision that too few trials contributed to the evidence base.

D.4.5 Ginger [Zingiber officinale Roscoe]

ETD process not completed based on GDG decision that too few trials contributed to the evidence base.

D.4.6 White lily [Lilium candidum]

ETD process not completed based on GDG decision that too few trials contributed to the evidence base.

D.4.7 Combination herbal compress [Zingiber cassumunar Roxb. rhizomes, Curcuma longa L. rhizomes, Cymbopogon citratus (DC.), Stapf leaves and leaf sheaths, Croton roxburghii N.P.Balakr. leaves, Tamarindus indica L. leaves, Citrus hystrix DC. peels, Blumea balsamifera (L.) DC. leaves, Vitex trifolia L. leaves and camphor]

ETD process not completed based on GDG decision that too few trials contributed to the evidence base.

D.4.8 Combination transdermal diffusional patch [Oleum thymi, Oleum limonis, Oleum nigra, Oleum rosmarini, Oleum chamomilla and Oleum lauri expressum]

ETD process not completed based on GDG decision that too few trials contributed to the evidence base.

Web Annex D.D4: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

GRADE Table 1. ***What are the benefits and harms of Cayenne pepper [Capsicum frutescens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared to placebo?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Capsicum frutescens	Placebo	Relative (95% CI)	Absolute (95% CI)		
Pain (reduction of >30% pain score) - short term												
3	randomized trials	serious[a]	not serious	not serious	Not serious	none	203/304 (66.8%)	146/307 (47.6%)	RR 1.40 (1.22 to 1.62)	**190 more per 1000** (from 105 more to 295 more)	⨁⨁⨁◯ Moderate	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Pain (reduction of >50% pain score) - short term												
3	randomized trials	serious[a]	not serious	not serious	Not serious	none	140/304 (46.1%)	76/307 (24.8%)	RR 1.85 (1.47 to 2.31)	**210 more per 1000** (from 116 more to 324 more)	⨁⨁⨁◯ Moderate	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Pain - intermediate term or long term – no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term, intermediate term or long term – no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse events												

Web Annex D.D4: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Capsicum frutescens	Placebo	Relative (95% CI)	Absolute (95% CI)		
3	randomized trials	serious[a]	not serious	not serious	serious[b]	none	36/304 (11.8%)	17/307 (5.5%)	RR 2.04 (1.19 to 3.51)	**58 more per 1000** (from 11 more to 139 more)	⨁⨁◯◯ Low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Serious adverse events: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Change in medication - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; RR: risk ratio

Explanations
a. Risk of bias downgraded by 1 level due to unclear or high risk of selection bias, attrition bias, reporting bias, similar groups at baseline, and compliance.
b. Imprecision downgraded by 1 level due to few events.

GRADE Table 2. ***What are the benefits and harms of Cayenne pepper [Capsicum frutescens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared to no intervention***?

No trials

GRADE Table 3. ***What are the benefits and harms of Cayenne pepper [Capsicum frutescens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared to usual care***?

No trials

GRADE Table 4. ***What are the benefits and harms of Devil's claw [Harpagophytum procumbens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with placebo?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	H.procumbens	Placebo	Relative (95% CI)	Absolute (95% CI)		
Pain - short term (reduction of at least 30% pain intensity)												
2	randomized trials	serious[a]	not serious	not serious	serious[b]	none	25/185 (13.5%)	4/121 (3.3%)	RR 3.73 (1.29 to 10.81)	**90 more per 1000** (from 10 more to 324 more)	⨁⨁◯◯ Low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Pain - intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term												
2	randomized trials	serious[a]	not serious[c]	not serious	very serious[d]	none	In Chrubasik 1996 (n=118) the relative median change in the intervention group was 20% (IQR 0; 35) and in the placebo group 8% (IQR -2; 23) (p=0.059). In Chrubasik 1999 (n=197) the relative median change in the low dose group was 21% (IQR 2; 34), the high dose group 18% (IQR 0; 40) and in the placebo group 21% (IQR 6; 34) (p=0.68).				⨁◯◯◯ Very low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Back-specific functional status - intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

Web Annex D.D4: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	H.procumbens	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adverse events												
2	randomized trials	serious[a]	serious[f]	not serious	very serious[g]	none	12/185 (6.5%)	11/121 (9.1%)	RR 1.08 (0.12 to 9.94)	**7 more per 1000** (from 80 fewer to 813 more)	⨁◯◯◯ Very low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Serious adverse events: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Change in medication - short term												
2	randomized trials	serious[a]	not serious[c]	serious[h]	very serious[e]	none	Chrubasik 1996 (n=118) reported that the intervention group consumed a mean (± SD) of 95 ± 157mg in the last three weeks of treatment while the placebo group consumed 102 ± 250mg (p=0.44). Chrubasik 1999 (n=197) reported the number of participants using Tramadol in week 4 was 13 in the placebo group; 5 in the low dose group, and 11 in the high dose group.					⨁◯◯◯ Very low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Change in medication - intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias downgraded by 1 level due to high or unclear risk of bias in random sequence generation, allocation concealment, incomplete outcome data, selective reporting, cointerventions, and compliance.

b. Imprecision downgraded by 1 level due to low number of events.
c. Inconsistency not assessed; no meta-analysis performed.
d. Imprecision downgraded by 2 levels, unable to pool data reported as relative median change from baseline and small sample size.
e. Imprecision downgraded by 2 levels, unable to pool data and small sample size. Tramadol provided by trial investigators as rescue medication, unclear what instructions to participants were.
f. Inconsistency downgraded by 1 level due to substantial heterogeneity (I^2 = 73%) not explained by subgroup analyses.
g. Imprecision downgraded by 2 levels due to wide confidence intervals that encompass a potential benefit, no effect, and a potential harm.
h. Indirectness downgraded 1 level because baseline consumption of medication not reported. Tramadol provided by trial investigators as a rescue medication.

GRADE Table 5. ***What are the benefits and harms of Devil's claw [Harpagophytum procumbens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with no intervention***?

No trials

GRADE Table 6. ***What are the benefits and harms of Devil's claw [Harpagophytum procumbens] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with usual care***?

No trials

GRADE Table 7. ***What are the benefits and harms of White willow [Salix spp.] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with placebo?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Salix spp.	Placebo	Relative (95% CI)	Absolute (95% CI)		
Pain - short term (reduction of at least 30% pain intensity)												
1	randomized trials	serious[a]	not serious[b]	not serious	serious[c]	none	42/140 (30.0%)	4/70 (5.7%)	RR 5.25 (1.96 to 14.05)	**243 more per 1000** (from 55 more to 746 more)	⨁⨁◯◯ Low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Pain - intermediate term or long term – no studies were identified that reported on this outcome												
Back-specific functional status – short term												
1	randomized trials	serious[a]	not serious[b]	not serious	serious	none	Percentage decline in modified Aarhus score in the placebo group median 0% (IQR -13; 5); low dose group 44% (IQR 18; 60); high dose group 54% (IQR 19; 90) (p< 0.001) (n=210).				⨁⨁◯◯ Low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Back-specific functional status - intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

Web Annex D.D4: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Salix spp.	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adverse events												
1	randomized trials	serious[a]	not serious[b]	serious[f]	serious	none	3/140 (2.1%)	6/70 (8.6%)	RR 0.25 (0.06 to 0.97)	**64 fewer per 1000** (from 81 fewer to 3 fewer)	⨁◯◯◯ Very low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Serious adverse events: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation - short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Change in medication - short term												
1	randomized trials	serious[a]	not serious[b]	serious[e]	serious[c]	none	13/140 (9.3%)	33/70 (47.1%)	RR 0.20 (0.11 to 0.35)	**377 fewer per 1000** (from 420 fewer to 306 fewer)	⨁◯◯◯ Very low	
Population subgroup 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Change in medication - intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; RR: risk ratio

Explanations

a. Risk of bias downgraded 1 level due to high or unclear risk of bias in allocation concealment, selective reporting, similar groups at baseline, co-interventions, and compliance.
b. Inconsistency not assessed, only one study included in this analysis.
c. Imprecision downgraded 1 level due to few events.

d. Imprecision downgraded 1 level due to small sample size.
e. Indirectness downgraded 1 level because baseline consumption of medication not reported. Tramadol provided by trial investigators as a rescue medication.
f. Indirectness downgraded 1 level because some events may be attributed to a co-intervention (Tramadol).
g. Imprecision downgraded 1 level due to wide confidence intervals that encompass a potential benefit and no effect.

GRADE Table 8. ***What are the benefits and harms of White willow [Salix spp.] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with no intervention***?

No trials

GRADE Table 9. ***What are the benefits and harms of White willow [Salix spp.] in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with usual care***?

No trials