Table S1. Key data from included systematic reviews.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Agbabiaka (2009)[12]	AEs	Saw palmetto (*Serenoa repens*)	BPH Lower UTI	>100 (~773)	CRs CS NRCTs RCTs UCT	No	5	Mild to moderate AEs	Abdominal pain Cerebral haemorrhage Death Decreased libido Diarrhoea Fatigue Headache Nausea Rhinitis	NM	39 GI upset	Mild to severe	PhD	None declared	Fellowship from Dr Willmar Schwabe Pharmaceuticals
Basch (2003)[49] USA	AEs Drug interactions Toxicity	Alfalfa (*Medicago sativa*)	Diabetes Hyperlipi-daemia	<10 (~26)	CR CS	No	2	Mild to moderate AEs	Bacterial infections Dermatitis Diarrhoea GI upset Lupus-like syndrome Pancytopenia	NM	15 GI upset	Mild to severe	MD	NM	Privately funded
Basch (2004)[13] USA	AEs Drug interactions Toxicity	Thyme (*Thymus vulgaris*)	Alopecia areata Bronchitis Cough	<10 (~10)	RCT SRS	No	–5	Only mild AEs	Allergic response Dizziness Headache Hypotension	NM	4 ASR	Mild	MD	NM	NM
Basch (2004)[14] USA	AEs Drug interactions Toxicity	Lavender (*Lavandula angustifolia Miller*)	Anxiety Cancer	<10 (~7)	CS NRCT RCTs	No	–5	Only mild AEs	Anorexia Nausea Reversible neutropenia Vomiting	NM	4 ASR 2 GI upset	Mild	MD	NM	NM
Basch (2004)[15] USA	AEs Drug interactions Toxicity	Boswellia (*Boswellia serrata*)	Asthma Crohn's disease OA RA Ulcerative colitis	<100 (~24)	Comparison study NRCTs RCTs Review	No	–5	Only mild AEs	Abdominal fullness Diarrhoea Epigastric pain GI upset Nausea and acid reflux	NM	20 GI upset 4 ASR	Mild	MD	NM	NM
Basch (2006)[16] USA	AEs Drug interactions Toxicity	Calendula (*Calendula officinalis*)	Otitis media Radiation dermatitis Wound healing	<10 (~10)	Comparison study CS RCTs	No	0	Only mild AEs	Difficulties experienced but no further information	NM	9 allergy	Mild	MD	NM	NM
Borelli (2008)[48] Italy	AEs Safety	Black cohosh (*Cimicifuga racemosa*)	Menopausal symptoms	<100 (~851)	CS NRCTs RCTs SRS	No	5	Mild to moderate AEs	Acute hepatitis GI upset Multiorgan failure Rash	2 weeks –3 months	~28 GI upset ~18 ASR	Mild to severe	Pharmacology	NM	NM
Brendler (2006)[17] Germany	AEs Drug interactions Toxicity	Devil's claw (*Harpagophytum procumbens DC*)	Rheumatic conditions	>10 (~78)	CS RCTs	No	0	Only mild AEs	Allergy Diarrhoea	NM	5 GI upset	Mild	Ethnobotany	NM	NM
Coon (2002)[18] UK	AEs Drug interactions	Ginseng (*Panax ginseng*)	Healthy individuals Various clinical conditions	>100 (~674)	CRs Epidemiology studies RCTs SRS	No	2	Only mild AEs	Anxiety Burning sensation Cold/flu GI disorder Headache Insomnia Pain Skin problem Sleep problem	10 days of headache	135 GI upset 130 burning sensation 36 cold 10 headache	Mild	PhD	NM	Fellowship from Pharmaton SA, Lugano, Switzerland
Daniele (2005)[19] Italy	AEs	Verbenaceae (*Vitex agnus-castus*)	Various clinical conditions	<100 (~517)	CRs CS RCTs SRS Surveys	No	5	Only mild AEs	Acne Erythematous rash GI disturbance Headache Menstrual disorder Nausea Pruritus	NM	129 GI upsets 120 ASR 60 gynaecological problem	Mild	Pharmacology	None declared	None declared

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Daniele (2006)[20] Italy	AEs	Hawthorn (*Crataegus spp.*)	CHF	<100 (~204)	Cohort study OS RCTs UCT	No	5	Only mild AEs	Circulation failure Dizziness/vertigo Erythematous rash Fall GI complaint GI haemorrhage Headache Migraine and palpitation Nausea	104 weeks	33 GI upset 21 dizziness/ vertigo 17 headache/ migraine	Mild to moderate	Pharmacology/ physiology	None declared	None declared
Dugoua (2007)[21] Canada	AEs Drug interaction Toxicity	Cinnamon bark (*Cinnamomum spp.*)	Chronic salmonellosis *Helicobacter pylori* infection Oral candidiasis in HIV Type 2 diabetes	<10 (~55)	CR CS OS RCT	No	3	Only mild AEs	Allergic reaction Diarrhoea Dizziness Loss of consciousness Mouth burning syndrome Skin irritation Stomach upset Urticaria Vomiting	NM	41 ASR	Mild	Pharmaceutical sciences/ naturopathy	None reported	Grant from New Chapter (manufacturer of cinnamon natural health product) and Sick Kids Foundation
Dugoua (2008)[22] Canada	AEs	Blue cohosh (*Caulophyllum thalictroides*)	Pregnancy and lactation (not a clinical condition *per se*)	<100 (~10)	CRs In-vitro studies	No	2	Mild to moderate AEs	Acute MI Perinatal stroke Profound CHF Severe multiorgan hypoxic injury Abortifacient properties	Several weeks	10 endangered fetus	Severe	Pharmaceutical sciences/ naturopathy	NM	NM
Giles (2005)[25] USA	AEs Drug interactions Toxicity	Butterbur (*Petasites hybridus*)	Allergic rhinitis Asthma Migraine (prevention) Skin diseases	<100 (~10)	Open study RCT Review	No	0	Only mild AEs	Constipation Diarrhoea Difficulty breathing Discoloration of stool Dysphagia GI upset Pruritis Severe nausea Vomiting	NM	NM	Mild	PharmD	NM	NM
Hackman (2006)[50] USA	AEs Drug interactions Toxicity	Agave (*Agave americana*)	NM	<10 (~20)	CRs	No	2	Only mild AEs	Contact dermatitis Leukocytoclastic vasculitis	7–10 days	15 contact dermatitis	Mild	BS	NM	NM
Hammerness (2003)[45] USA	AEs Drug interactions Toxicity	St John's wort (*Hypericum perforatum*)	Mild to moderate depression	>100 (~8 mlnimum)	Case series CCTs CRs CS MAs RCTs Review SRS	No	4	Only mild AEs for safety and serious concerns for drug interactions	Anxiety Dizziness Dry mouth in 1–3% of patients Fatigue GI symptoms Headache Sedation Skin reaction	4–6 weeks	27 ASR	Mild	MD	NM	Privately funded

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Huntley (2005)[24] UK	AEs	*Echinacea spp.*	Healthy volunteers Various clinical and non-clinical conditions	<100 (~1090)	From clinical trials to CRs and SRSs	No	4	Only mild AEs	GI upset and rash (most frequent) to allergic reaction (rarely)	24–48 hours	182 GI upset 143 ASR	Mild	PhD	None reported	Boots the Chemists
Jacobs (2002)[25] USA	AEs	Milk thistle (*Silybum marianum*)	Liver disease	<100 (~18)	Cohort studies CRs RCTs	Yes (for effectiv-eness)	5	Only mild AEs	Dermatological symptom Gastroenteritis (multipreparation of milk thistle) GI symptom Headache	NM	25 GI upset	Mild	MD MPH	NM	Contract 290-97-0012 to Agency for Healthcare Research and Quality, Rockville, Maryland
Johnson (2007)[44] USA	AEs Safety	*Capsicum spp.*	Atopic eczema Cancer Diabetes Pain	<100 (~215)	In-vivo studies RCTs	No	–5	Only mild AEs	ASR Burning sensation Cough/sneezing	30 minutes–24 hours	157 burning sensation 16 coughing/ sneezing	Mild to moderate	Cosmetics	NM	NM
Keifer (2007)[51] USA	AEs Drug interactions Toxicity	Peppermint (*Mentha piperita*)	Various clinical conditions	<100 (IE)	CCT CRs CS In-vivo studies MA RCTs	No	2	Mild to moderate AEs	Acute lung injury Acute renal failure Bradycardia Contact dermatitis Heartburn Hypersensitivity Muscle tremor Perianal burning Tachycardia	NM	44 tachycardia 4 hyper-sensitivity 2 skin rash	Mild to severe	MD	NM	NM
Kienle (2011)[46] Germany	AEs Safety	Mistletoe (*Viscum album*)	Cancer	<100 (~13)	Phase I trials RCTs	No	5	Mild to moderate AEs	Anxiety Cutaneous rash Dry eyes Fatigue Fever GI upset Headache Hypokalaemia Lassitude Liver toxicity Mild infection Pain Rise in temperature	NM	5 liver toxicity 2 angioedema/ urticaria	Mild to severe	Medical methodology	Declared	Weleda, Wala, Helixor and Novipharm
Liu (2001)[26] Denmark	AEs Safety	*Genus phyllanthus*	HBV	<100 (~46)	RCTs	Yes	4	Only mild AEs	Light nausea Decreased appetite Stomach ache (n=4)	20–40 days	46 GI upset	Mild	MD	NM	Danish Medical Research Council Grant on Getting Research into Practice (GRIP), Denmark
Nelsen (2002)[27] USA	AEs Drug interaction Toxicity	Red clover (*Trifolium pratense*)	Asthma Cancer Gout Menopausal symptoms Pertussis	<100 (IE)	CS RCTs	No	1	Mild to moderate AEs	NM	NM	NM	Mild to moderate	PharmD	NM	NM
Sarma (2008)[28] USA	Safety Toxicity	Green tea (*Camellia sinensis*)	Cancer prevention	>100 (~162)	CS SRS	No	3	Mild to moderate AEs	Liver damage Pain	9 days–5 months	34 liver damage	Mild, moderate and severe	PhD	None declared	US Pharmacopeia

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Savovic (2005)[29] UK	Blood coagulation	*Ginkgo biloba*	Patients taking concomitant anticoagulant medication Healthy volunteers Various clinical conditions	<10 (~56)	Mostly RCTs	No	5	Only mild AEs	Platelet aggregation Other coagulation abnormalities	NM	10 platelet aggregation disorder 10 GI upset	Mild	PhD	Potential declared	Dr Willmar Schwabe Pharmaceuticals
Sweeney (2005)[30] USA	AEs Contamination Drug interactions Toxicity	Dandelion (*Taraxacum officinale*)	Hepatitis BPain	<10 (~7)	CS	No	0	Mild to moderate AEs	Fever Intestinal blockage Liver damage Loss of appetite Platelet aggregation Stomach upset Vomiting	NM	5 ASR	Mild to moderate	PharmD	NM	NM
Taibi (2007)[31] USA	AEs	Valerian (*Valeriana officinalis*)	Insomnia	<100 (~67)	RCTs	No	5	Only mild AEs	Diarrhoea Dizziness Drowsiness Headache Nausea	NM	8 GI upset 8 hangover 3 headache	Mild	Nursing	NM	NIH grants: R21-AT-002108, P30-NR04001, and T32-NR07039
Tiffany (2002)[32] USA	AEs Drug interaction Toxicity	Horse chestnut seed extract (*Hippocastanaceae*)	Chronic venous insufficiency	<100 (IE)	OS RCTs SR	No	1	Only mild AEs	Dizziness GI upset Headache Muscle spasm Nausea Nephrotoxicity Pruritis	NM	2 headache/ dizziness	Mild	MD	NM	Privately funded
Ulbricht (2003)[33] USA	AEs Drug interaction Toxicity	Chaparral (*Larrea tridentate*)	Cancer	<100 (~69)	CR	No	2	Moderate to severe AEs	Cirrhosis Hepatitis Liver failure Renal cyst Renal cell carcinoma	1–17 weeks	59 ASR 8 liver damage 2 kidney failure 2 fever	Severe	PharmD	NM	Privately funded
Ulbricht (2004)[34] USA	AEs Drug interaction Toxicity	Belladonna (*Herbae pulvis standardisatus*)	Headache IBS Menopausal symptoms Otitis media PMS	<100 (~20)	NRCT OS RCTs	No	–5	Moderate to severe AEs	Acute psychosis Agitation Blurred vision Coma Confusion Constipation Convulsions Dizziness Drowsiness Dry mouth Excitement Flushing Hallucinations Headache Hyperreflexia Lightheadedness Mydriasis Photophobia Pupillary dilation Respiratory arrest Sedation Skin problem Slurred speech Tachycardia Unsteadiness Urinary retention Vertigo	NM	8 neurological AE 7 psychiatric AE 6 cardiovascular AE	Moderate to severe	PharmD	NM	NM

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Ulbricht (2005)[35] USA	AEs Drug interactions Toxicity	Lemon balm (*Melissa officinalis*)	Anxiety Cognitive performance Dyspepsia Herpes simplex Insomnia	<100 (~17)	CS RCT	No	0	Only mild AEs	Diarrhoea EEG changes Headache Nausea Reduced alertness Sleep disturbances Tiredness	NM	28 tiredness/ sleep disturbance	Mild	PharmD	NM	NM
Ulbricht (2005)[36] USA	AEs Drug interactions Toxicity	Guggul (*Commifora mukul*)	Hyperlipidaemia	<100 (~36)	CS RCTs	No	1	Mild to moderate AEs	Allergy GI upset Headache Hypersensitive skin Inhibition of platelet aggregation and increased fibrinolysis Renal failure Rhabdomyolysis	48 hours–2 weeks	22 headache 15 GI upset 6 ASR	Mild to moderate	PharmD	NM	NM
Ulbricht (2005)[37] USA	AEs Drug interactions Toxicity	Kava (*Piper methysticum*)	Anxiety disorders	<100 (~303)	CRs RCTs	No	3	Moderate to severe AEs	Allergy Apathy Death GI upset Liver failure Shortness of breath Tachycardia	NM	69 GI upset 31 liver damage	Moderate to severe	PharmD	NM	NM
Ulbrcht (2007)[47] USA	AEs Drug interactions Toxicity	Fenugreek (*Trigonella foenum-graecum*)	Diabetes	<10 (~15)	Case studies CS RCTs SRs	No	2	Only mild AEs	Allergic reaction Bronchospasm Diarrhoea and flatulence Dizziness Numbness of head	NM	8 acute and chronic hypoglycaemia 4 GI upset	Mild	PharmD	NM	NM
Ulbricht (2007)[38] USA	AEs Drug interactions Toxicity	Banaba (*Lagerstroemia speciosa*)	Diabetes	<10 (IE)	RCT	No	1	Only mild AEs	None reported	NM	NM	Mild	PharmD	NM	NM
Ulbricht (2007)[52] USA	AEs Drug interactions Toxicity	*Aloe vera*	Various clinical conditions	<100 (IE)	CRs RCTs SRs	No	2	Mild to moderate AEs	Acute hepatitis Abdominal cramping and diarrhoea Death Delayed wound healing Erythema Excess bleeding Photodermatitis Potassium depletion Skin dryness Soreness Stinging	NM	22 skin dryness	Mild to moderate	PharmD	NM	NM
Ulbricht (2008)[53] USA	AEs Drug interactions Toxicity	Blessed thistle (*Cnicus benedictus*)	Dyspepsia Viral infection	<10 (0)	Anecdotal data Animal studies Post-market surveillance	No	2	Only mild AEs	Allergy/ hypersensitivity Stomach irritation Vomiting	NM	NM	Mild	PharmD	NM	NM

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Ulbricht (2009)[39] USA	AEs Drug interactions Toxicity	Chia (*Salvia hispanica*)	CVD	<10 (0)	RCTs	No	0	Only mild AEs	GI upset	NM	NM	Mild	PharmD	NM	NM
Ulbricht (2009)[54] USA	AEs Drug interactions Toxicity	Green-lipped mussel (*Perna canaliculus*)	Asthma OA RA	<100 (IE)	CRs Post-market surveillance RCT	No	2	Mild to moderate AEs	Fluid retention GI upset Gout Heart failure Hepatitis Liver failure Lung dysfunction Skin rash	NM	3 toxic hepatitis 2 abnormal liver function	Mild to severe	PharmD	NM	NM
Ulbricht (2009)[55] USA	AEs Drug interactions Toxicity	Bilberry (Vaccinium myrtillus)	Various clinical conditions	<10 (IE)	Comparative study Post-market surveillance	No	2	Only mild AEs	GI discomfort Heartburn Nausea	NM	22 GI discomfort	Mild	PharmD	NM	NM
Ulbricht (2010)[56] USA	AEs Drug interactions Toxicity	Umckaloabo (*Pelargonium sidoides*)	Acne Bronchitis Common cold	<10 (~60)	CRs Post-market surveillance RCTs	No	2	Mild to moderate AEs	Angioedema Bronchospasm Circulatory failure Conjunctivitis Diarrhoea Dyspnoea GI irritation Hepatotoxicity Increased risk of bleeding Skin rash Tachycardia	NM	34 skin rash with itching 17 angioedema or systemic involvement	Mild to severe	PharmD	NM	NM
Ulbricht (2010)[40] USA	AEs Drug interactions Toxicity	Stevia (*Stevia rebaudiana*)	Hyperglycaemia Hypertension	<10 (~8)	CCTs RCTs	No	0	Mild to moderate AEs	Asthenia Abdominal fullness Dizziness Myalgia and muscle weakness Nausea	1 week	4 GI upset	Mild to moderate	PharmD	NM	NM
Ulbricht (2010)[57] USA	AEs Drug interactions Toxicity	Spearmint (*Mentha spicata, Mentha viridis*)	Various clinical conditions	<100 (IE)	NRCTs RCTs	No	2	Only mild AEs	Contact cheilitis Contact dermatitis Erythema and blistering Heartburn Pain	NM	6 cheilitis 3 dermatitis	Mild	PharmD	NM	NM
Ulbricht (2010)[58] USA	AEs Drug interactions Toxicity	Rosemary (*Rosmarinus officinalis*)	Various clinical conditions	<100 (IE)	CRs Post-market surveillance RCTs	No	2	Only mild AEs	Allergic reactions Contact dermatitis Perforation of gastric antrum Seizures or epilepsy	NM	4 contact dermatitis	Mild	PharmD	NM	NM
Ulbricht (2011)[59] USA	AEs Drug interactions Toxicity	Saffron (*Crocus sativus*)	Various clinical conditions	<10 (IE)	Equivalence trials Market surveillance RCTs SR	No	2	Only mild AEs	Allergic reaction Anaphylactic reaction Contact dermatitis	NM	4 allergic reaction	Mild	PharmD	NM	NM

Continues

Table S1. Continued

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: Range (N* (n†))	Primary data: Type	Meta-analysis?‡	Quality of SR	Overall judgment	AEs: Type	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Ulbricht (2011)[60] USA	AEs Drug interactions Toxicity	Gymnema (*Gymnema sylvestre R. Br.*)	Constipation Diabetes Hyperlipidaemia Weight loss	<10 (IE)	CS NRCT RCT	No	2	Only mild AEs	Hypoglycaemic episode	NM	1 hypoglycaemia	Mild	PharmD	NM	NM
Ulbricht (2011)[61] USA	AEs Drug interactions Toxicity	Senna (*Cassia senna*)		<100 (IE)	Case–control studies CCTs CRs Post-market surveillance RCTs SRs	No	2	Mild to severe AEs	Abdominal pain Bleeding Bloating Cachexia Cancer Chronic liver damage Colon perforation Cramping Diarrhoea Finger clubbing Flatulence Hepatitis Hypertrophic osteoarthropathy Incontinence Nausea Nephrocalcinosis Portal vein thrombosis Skin rash Tetany Vomiting	NM	7 severe GI upset 6 chronic liver damage	Mild to severe	PharmD	NM	NM
Vermaak (2011)[41] Republic of South Africa	AEs	Masson (*Hoodia gordonii*)	Obesity	<10 (~2)	Case studies In-vivo studies	No	–5	Mild to moderate AEs	Acute hepatitis (unlike causality)	NM	2 liver damage	Severe	Pharmaceutical Sciences	NM	NM
West (2006)[42] USA	AEs Safety Toxicity		Advanced cancer Healthy individuals	<100 (~6)	Case studies CR RCTs	No	–5	Only mild AEs	Acute hepatitis (causality questioned) Hyperkalaemia Hepatotoxicity	1–11 months	4 liver damage	Mild to severe			Manufacturer of Noni Juice- *Tahitian Noni Intl*
Wu (2003)[43] USA	AEs Safety Toxicity	Tumeric (*Curcuma longa*)	AIDS Chronic uveitis Post-surgery RA	<10 (~3)	CCT CS In-vivo studies RCTs	No	–1	Only mild AEs	Gastric irritation Mild transient giddiness	NM	2 GI upset	Mild	Stomatology	NM	NIH grants K-16 DE00386 and T32 DE07204

AE, adverse effect; AIDS, acquired immune deficiency syndrome; ASR, adverse skin reaction; BPH, benign prostatic hyperplasia; CAM, complementary and alternative medicine; CCT, controlled clinical trial; CHF, congestive heart failure; CR, case report; CS, case series; COI, conflict of interest; CVD, cardiovascular disease; EEG, electroencephalogram; GI, gastrointestinal; HBV, hepatitis B virus; HFS, herbal food supplements; HIV, human immunodeficiency virus; HM, herbal medicine; IBS, irritable bowel syndrome; IE, inestimable; MA, meta-analysis; MD, Doctor of Medicine; MI, myocardial infarction; MPH, Master of Public Health; NIH, National Institutes of Health; NM, not mentioned; NRCT, non-randomised controlled trial; NS, not specified; OA, osteoarthritis; OS, observational study; PharmD, Doctor of Pharmacy; PhD, Doctor of Philosophy; PMS, premenstrual syndrome; QRCT, quasi randomised controlled trial; RA, rheumatoid arthritis; RCT, randomised controlled trial; RRC, retrospective review of cases; RTI, respiratory tract infection; SR, systematic review; SRS, spontaneous reporting scheme; TGV, thunder god vine; UCT, uncontrolled trial.

*Range of primary data.

†Total number of patients experiencing AEs, if estimable.

‡Scoring: each question is scored as 1, 0 or –1; a score of ⩽0 means the review has major flaws, 1–2 means minor flaws and 3–5 means minimal or no flaws; 1 means that: (a) the review states the databases used, the date of the most recent searches and includes some mention of search terms; (b) the review searches at least two databases and looks at other sources; (c) the review states in the overview the criteria used for deciding which studies to include; (d) the review reports how many studies were identified by searches, the numbers of studies excluded and the appropriate reasons for excluding them; (e) the conclusions made by the author(s) are supported by the data and/or analysis reported in the review; 0 means that the above-mentioned criteria were partially fulfilled; and –1 means that none of the above criteria were fulfilled. This is an operationalisation of the Oxman criteria,[11] adapted from Ernst et al (2011).[10]

Table S2. Aims and conclusions from systematic reviews.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Agbabiaka (2009)[12] *Serenoa repens*	To assess 'all available human safety data of *Serenoa repens* monopreparations'	'Currently available data suggest that *S. repens* is well tolerated by most users and is not associated with serious adverse events. The majority of adverse events are mild, infrequent and reversible, and include abdominal pain, diarrhoea, nausea and fatigue, headache, decreased libido and rhinitis. We found no evidence for drug interactions with *S. repens*. However, higher quality reporting of adverse events is essential if safety assessments are to be improved in future'	(–/+)
Basch (2003)[49] *Medicago sativa*	To undertake a clinical decision support tool for the safety of alfalfa	'…there is currently insufficient information from clinical trials to adequately evaluate the safety or efficacy of alfalfa for any indication'	(–/+)
Basch (2004)[13] *Thymus vulgaris*	'An evidence-based systematic review including scientific evidence, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing [of thyme]'	' …caution is warranted with the use of thyme oil, which should not be taken orally and should be diluted for topical administration due to potential toxic effects'	(+)
Basch (2004)[14] *Lavandula angustifolia Miller*	'An evidence-based systematic review including scientific evidence, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing [of lavender]'	'In recommended doses, lavender is generally considered to be well-tolerated, with minimal adverse effects'	(+)
Basch (2004)[15] *Boswellia serrata*	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing [of *Boswellia*]'	'General: Boswellia is generally believed to be safe when used as directed, although safety and toxicity have not been systematically studied in humans'	(+)
Basch (2006)[16] *Calendula officinalis*	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology and dosing [of marigold]'	'…there is insufficient evidence to support the safety of these ingredients in cosmetic formulations'	(+)
Borelli (2008)[48] *Cimicifuga racemosa*	'The aim of this systematic review was to evaluate the clinical evidence for or against the safety of black cohosh'	'In conclusion, black cohosh has been associated with serious safety concerns that urgently require further investigation'	(–/+)
Brendler (2006)[17] *Harpagophytum procumbens* DC	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interaction, adverse effects, toxicology, and dosing [of devil's claw]'	'There is a growing body of scientific evidence suggesting that devil's claw is safe and beneficial in the short-term management of pain related to degenerative joint disease or osteoarthritis...'	(+)
Coon (2002)[18] *Panax ginseng*	' ...to document and evaluate all the available safety data on *P. ginseng* root extracts'	'Collectively, these data suggest that *P. ginsengmonopreparations* are rarely associated with adverse events or drug interactions. The ones that are documented are usually mild and transient. Combined preparations are more often associated with such events but causal attribution is usually not possible'	(+)
Daniele (2005)[19] *Vitex agnus-castus*	'...to evaluate all the available human safety data of VAC monopreparations'	'Although further rigorous studies are needed to assess the safety of VAC, the data available seem to indicate that VAC is a safe herbal medicine'	(+)

Continues

Table S2. Continued.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Daniele (2006)[20] *Crataegus* spp.	'The aim of this article is to assess the safety data of all available human studies on hawthorn monopreparations'	' In conclusion, all data reviewed in this article seem to indicate that hawthorn is well tolerated even if some severe adverse events were reported; this suggests that further studies are needed to better assess the safety of hawthorn-containing preparations. Moreover, the unsupervised use of this drug can be associated with problems, especially if given with concomitant medications'	(+)
Dugoua (2007)[21] *Cinnamomum verum*, *C. zeylanicum* and *C. aromaticum*	' ...to systematically review the scientific literature for preclinical and clinical evidence of safety, efficacy, and pharmacological activity of common and cassia cinnamon'	'...common and cassia cinnamon appear to be generally well tolerated'	(+)
Dugoua (2008)[22] *Caulophyllum thalictroides*	'To systematically review the literature for evidence on the use, safety and pharmacology of blue cohosh, focusing on issues pertaining to pregnancy and lactation'	'There is an urgent need to conduct a retrospective or prospective cohort study of midwifes using blue cohosh to determine its safety at the time of delivery, as any scientific evidence of safety or harm is more likely to be in the files of the midwifery practices than in governmental databases or hospitals'	(–/+)
Giles (2005)[23] *Petasites hybridus*	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of butterbur]'	'The plant's pyrrolizidine alkaloids are thought to be hepatotoxic, carcinogenic, mutagenic, and nephrotoxic. However, commercially available extracts have the pyrrolizidine alkaloids removed'	(+)
Hackman (2006)[50] *Agave Americana*	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of agave]'	'Avoid in patients with known allergies to plants in the *Agavaceae* family. Use cautiously in patients trying to conceive due to possible contraceptive effects'	(+)
Hammerness (2003)[45] *Hypericum perforatum*	'This evidence-based presentation of the literature includes a brief description of pharmacodynamics and clinical applications, followed by a systematic review of adverse effects, toxicity, and drug interactions'	'While it is generally well tolerated, there is accumulating evidence of clinically significant interactions of St. John's wort and drugs, particularly when used with medications metabolized by the cytochrome P-450 system'	(+)
Huntley (2005)[24] *Echinacea* spp.	' ...to systematically review the information on the safety of echinacea from clinical studies, case reports, surveillance schemes and other investigations'	'Short-term use of echinacea is associated with a relatively good safety profile, with a slight risk of transient, reversible, adverse events. The association of echinacea with allergic reactions is supported by the present evaluation. While these reactions are likely to be rare, patients with allergy or asthma should carefully consider their use of echinacea. The use of echinacea products during pregnancy and lactation would appear to be ill-advised in light of the paucity of data in this area'	(+)
Jacobs (2002)[25] *Silybum marianum*	' ...to determine the efficacy and safety of this herb [milk thistle] for the treatment of liver disease'	'Treatment with milk thistle appears to be safe and well tolerated'	(+)
Johnson (2007)[44] *Capsicum* spp.	To assess safety of *Capsicum annuum* extract, *Capsicum annuum* fruit extract, *Capsicum annuum* resin, *Capsicum annuum* fruit powder, *Capsicum frutescens* fruit, *Capsicum frutescens* fruit extract, *Capsicum frutescens* resin, and capsaicin.	It is concluded that *Capsaicin* spp' are safe as cosmetics in the practices of use and concentration as described in the safety assessment, when formulated not to be irritating'	(+)

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Table S2. Continued.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Keifer (2007)[51] *Mentha piperita*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology and dosing [of peppermint]'	'Reports of adverse reactions are rare but may include hypersensitivity reactions, contact dermatitis, heartburn, perianal burning, bradycardia, and muscle tremor when taken orally'	(–/+)
Kienle (2011)[46] *Viscum album*	To systematically review all experiments and clinical studies investigating higher dosages of *Viscum album* in animals and humans and assessing immune parameters or infections or adverse drug reactions	'Application of higher dosages of VAE or ML is not accompanied by immunosuppression; altogether VAE seems to exhibit low risk but should be monitored by clinicians when applied in high dosages'	(–/+)
Liu (2001)[26] Genus *Phyllanthus*	'To evaluate the efficacy and safety of genus *Phyllanthus* for chronic hepatitis B virus (HBV) infection...'	'No serious adverse event was reported. Based on this review *Phyllanthus* species may have positive effect on antiviral activity and liver biochemistry in chronic HBV infection'	(+)
Nelsen (2002)[27] *Trifolium pratense*	'The authors systematically review this herb [red clover] in terms of pharmacology, efficacy, safety, side effects, standardization, dosing, toxicology as well as other parameters'	'Caution should be taken with patients on hormone replacement therapy (HRT) or oral contraceptives (OCPs), as red clover binds to intracellular estrogen receptors and may enhance estrogenic effects. Red clover may alter platelet aggregation/contains coumarin, and therefore may theoretically be unsafe in persons with bleeding disorders/coagulopathies or taking anticoagulants'	(–/+)
Sarma (2008)[28] *Camellia sinensis*	To systematically review 'the safety information for green tea products in order to re-evaluate the current safety class to which these products are assigned'	' ...the safety information for green tea arising form diverse sources provides a signal for the possibility of liver damage caused by products that contain concentrated green tea extracts'	(–/+)
Savovic (2005)[29] *Ginkgo biloba*	' ...to investigate the effects of *Ginkgo biloba* preparations on blood coagulation parameters'	'Available evidence does not demonstrate that extract of *G. biloba* causes significant changes in blood coagulation parameters. A limited number of studies on concomitant use of *G. biloba* with ASA or warfarin also do not suggest that *G. biloba* has an additive effect to the clinical effects of these two drugs'	(+)
Sweeney (2005)[30] *Taraxacum officinale*	To undertake an evidence-based systematic review of dandelion by the Natural Standard Research Collaboration	'Dandelion is generally regarded as safe with rare side effects including contact dermatitis, diarrhea, and gastrointestinal upset'	(–/+)
Taibi (2007)[31] *Valeriana officinalis*	' ...to examine the evidence on the efficacy of valerian as a sleep aid with specific attention to the type of preparations tested and the characteristics of the subjects studied'	'Overall, the evidence, while supporting that valerian is a safe herb associated with only rare adverse events, does not support the clinical efficacy of valerian as a sleep aid for insomnia'	(+)
Tiffany (2002)[32] *Hippocastanaceae*	To undertake a multidisciplinary clinical review of horse chestnut	'In the future, a longer and adequately powered randomized trial is warranted to compare HCSE [horse chestnut seed extract] to standard of care, and to further assess safety and long-term efficacy'	(+)
Ulbricht (2003)[33] *Larrea tridentate* (DC) Coville, *Larrea divaricata* Cav	'An evidence-based systematic review including scientific evidence, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing [of Chapparal]'	'Chaparral and NDGA are generally considered unsafe and are not often recommended for use'	(–)
Ulbricht (2005)[34] *Herbae pulvis standardisatus*	To undertake an evidence-based systematic review of belladonna by the Natural Standard Research Collaboration	'There is extensive literature on the adverse effects and toxicity of belladonna, related principally to its known anticholinergic actions'	(–)

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Table S2. Continued.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Ulbricht (2005)[35] *Melissa officinalis* L.	'An evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of lemon balm]'	'Lemon balm has been assigned to the FDA Generally Recognized As Safe (GRAS) list in the United States. No serious side effects have been reported, although there is limited research of long-term effects'	(+)
Ulbricht (2005)[36] *Commifora mukul*	'To evaluate the scientific evidence on guggul for hyperlipidemia including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing [of guggul]'	'Guggul may cause stomach discomfort or allergic rash as well as other serious side effects and interactions. It should be avoided in pregnant or breast-feeding women and in children. Safety of use beyond 4 months has not been well studied'	(–/+)
Ulbricht (2005)[37] *Piper methysticum*	'This systematic review discusses the proposed uses, dosing parameters, adverse effects, toxicology, interactions and mechanism of action of kava'	'Because kava is not available in many areas of the world, individuals can instead turn to alternative therapies for anxiety treatment'	(–)
Ulbricht (2007)[47] *Trigonella foenum-graecum*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology and dosing [of fenugreek]'.	'Literature review reveals no reports of clinically significant harmful adverse effects. Fenugreek has traditionally been considered safe and well tolerated'	(+)
Ulbricht (2007)[38] *Lagerstroemia speciosa*	'This study is an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of banaba]'	'Banaba is generally considered to be safe when taken orally for 15 days for the treatment of Type II diabetes'	(+)
Ulbricht (2007)[52] *Aloe vera*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology and dosing [of aloe vera]	'Oral aloe products should be used cautiously in patients with diabetes or glucose intolerance, and in patients using glucose-lowering agents. ...Avoid oral aloe latex in patients with renal insufficiency, cardiac disease, electrolyte abnormalities, ileus, acute surgical abdomen, bowel obstruction, fecal impaction, or appendicitis'	(–/+)
Ulbricht (2008)[53] *Cnicus benedictus*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology and dosing [of blessed thistle]	'Blessed thistle is generally considered to be safe when used in recommended doses for short periods of time, with few reported adverse effects. Allergic cross-sensitivity may occur with other members of the Compositae family'	(+)
Ulbricht (2009)[39] *Salvia hispanica*	'To evaluate the scientific evidence on chia (*Salvia hispanica*) including history, folkloric precedent, expert opinion, pharmacology, dosing, interactions, adverse effects, and toxicology. This review serves as a clinical support tool'	'The preliminary clinical evidence supporting the efficacy of Salvia hispanica in CVD prevention warrants further investigation into its safety and efficacy as a dietary supplement and a functional food'	(+)
Ulbricht (2009)[54] *Perna canaliculus*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of green-lipped mussel]'	'Green-lipped mussel products have been generally well tolerated in clinical trials. However, possible side effects of Seatone use have been noted by the Australian Rheumatism Association'	(–/+)

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Table S2. Continued.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Ulbricht (2009)[55] *Vaccinium myrtillus*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of bilberry]'	The long-term safety and side effects of bilberry have not been extensively studied. Safety is often presumed based on bilberry's history as a food source.	(+)
Ulbricht (2010)[56] *Pelargonium sidoides*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of umckaloabo]	Use cautiously in patients with liver disease or who are using hepatotoxic agents, anticoagulants or antiplatelets, or in patients with heart conditions, asthma or other respiratory conditions.	(–/+)
Ulbricht (2010)[57] *Mentha spicata*, *Mentha viridis*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of spearmint]	'Avoid with known allergy/hypersensitivity to spearmint or other members of Lamiaceae (Labiatae) family, such as basil, mint, rosemary, sage, savory, marjoram, oregano, thyme, lavender, and perilla'	(+)
Ulbricht (2010)[58] *Rosmarinus officinalis*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of rosemary]	'Based on historical use and available research, it appears that rosemary is well tolerated with few documented cases of adverse events. Avoid with known allergy/hypersensitivity to rosemary, its constituents, or members of the Labiatae or Lamiaceae families'	(+)
Ulbricht (2011)[59] *Crocus sativus*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of saffron]'	'Reports of adverse effects are lacking in the available clinical study data. Saffron is likely safe for most individuals when used at levels commonly found in the diet'	(+)
Ulbricht (2011)[60] *Gymnema sylvestre* R. Br.	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of gymnema]	Aside from hypoglycemia and potentiation of the effects of hypoglycemic drugs following chronic use of gymnema, no clinically significant adverse effects have been associated with oral gymnema in the available literature, in studies up to 20 months in duration	(+)
Ulbricht (2011)[61] *Cassia senna*	To undertake 'an evidence-based systematic review including written and statistical analysis of scientific literature, expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing [of senna]	'Avoid long term use of senna, due to the potential for side effects, some serious'	(–)
Ulbricht (2010)[40] *Stevia rebaudiana*	' ...to evaluate the scientific evidence on stevia, including expert opinion, folkloric precedent, history, pharmacology, kinetics/ dynamics, interactions, adverse effects, toxicology, and dosing'	'Evaluation of two long-term studies (1 and 2 years in length, respectively) indicates that stevia may be effective in lowering blood pressure in hypertensive patients, although data from shorter studies (1-3 months) did not support these findings'	(–/+)
Vermaak (2011)[41] *Hoodia gordonii*	'This review offers an up-to-date overview of all the current available knowledge pertaining to *H. gordonii* achieved by systematic analysis of the available literature'	' ...the biological activity of all chemical constituents, clinical efficacy, and especially safety are insufficient or completely absent causing great concern as *H. gordonii* is one of the most widely consumed anti-obesity products of natural origin'	(–/+)
West (2006)[42] *Morinda citrifolia*	'To describe the safety of this fruit, a literature review and data from new studies are presented'	'Data from clinical studies, toxicity tests, and chemical test have substantiated the use of this juice as a safe food'	(+)

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Table S2. Continued.

Author (year) herb	Aim/quote (where appropriate)	Conclusion/quote	Direction of conclusion
Wu (2003)[43] *Curcuma longa*	' ...to summarize the literature on the safety and anti-inflammatory activity of curcumin'	'Curcumin has been demonstrated to be safe in six human trials and has demonstrated anti-inflammatory activity'	(+)

FDA, food and drug administration; ML, mistletoe lectins; NDGA, nordihydroguaiaretic acid; NS, not specified; VAC, *Vitex agnus-castus* L.; VAE, *Viscum album* extract.
(–/+), moderate safety concerns; (–), major safety concerns; (+), minor or no safety concerns.

Table S3. Examples of excluded systematic reviews.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Boon (2006)[63] Canada	AEs	Essiac Evening primrose oil Garlic Ginger Green tea Lycopene Mistletoe *Panax ginseng* Reishi Shiitake Soy Tumeric	Cancer	131	Cohort studies NRCTs RCTs UCTs	No	2	Only mild AEs	Allergic reactions Anorexia Bleeding Body odour Confusion Cough Dizziness Dyspepsia Dysuria and polyuria Emesis Fatigue Fever GI upset Heartburn Insomnia Manic episodes Mastalgia Nausea Night sweats Pain Palpitations	NM	NM	NM	Pharmacy	NM	NM
Borrelli (2005)[86] Italy	AEs	Ginger (*Zingiber officinale*)	Pregnancy (not a clinical condition *per se*)	7	Cohort study RCTs	No	4	Mild to moderate AEs	Abdominal discomfort Diarrhoea Drowsiness Headache Heartburn Low birth weight Reflux ($p<0.05$)	NM	NM	NM	PhD	NM	NM
Cameron (2011)[64] Australia	AEs Safety	Ash bark Aspen bark Aspen leaf Blackcurrant seed oil Borage seed oil *Boswellia serrata* Capsaicin Cat's claw Evening primrose oil Feverfew Golden rod herb TCR TIR TKR *Tripterygium wilfordii* Willow bark	RA	22	RCTs	No	5	Only mild AEs Moderate to severe AEs for TGV	For TGV: aplastic anaemia death (causality unclear) diarrhoea fever hair loss headache For capsaicin: burning sensation For other HM: no significant differences between treatment and control groups	NM	NM	Mild to severe for TGV Mild to moderate for other HMs	Exercise science	None declared	None declared (external)

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Canter (2006)[87] UK	AEs	TGV (*Tripterygium wilfordii*)	RA	2	RCT	No	5	Moderate to severe AEs	Abdominal pain Anorexia Blisters Constipation Death Diarrhoea Facial rash Flatulence Hair loss Headache Heartburn Indigestion Nausea Tinnitus Vaginal spotting	Death after 1 month	n NM.m.	Mild to severe	PhD	NM	NM
Chen (2007)[65] People's Republic of China	AEs Safety	TCR	Influenza	2	RCTs	No	5	Mild to moderate AEs	GI upset	NM	NM	NM	Epidemiology	None declared	Chinese Medical Board of New York (CMB), USA
Cheng (2009)[66] People's Republic of China	AEs Safety	TCR	Functional constipation	35	RCTs	Yes	5	Only mild AEs	Abdominal pain Diarrhoea	NM	NM	NM	TCM	NM	Health and Health Services Research Fund of Hong Kong Health, Welfare and Food Bureau, No. 05060161
Chung (2006)[67] People's Republic of China	AEs	Cannabis TCR TIR	Parkinson's disease	9	RCTs	No	5	Mild to moderate AEs	Altered taste Confusion Constipation Cystitis Detachment Diarrhoea/loose stool Dizziness Dry mouth Forgetfulness Lethargy Mild dizziness Nausea Musculoskeletal Pain Paranoia Poor concentration Urinary tract infection Vivid dreams Vomiting	NM	NM	Mild	BSc	NM	Research grants of Hong Kong Baptist University and Eu Yan Sang Ltd

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Coon (2004)[88] UK	AEs	*Andrographis paniculata*	Upper respiratory tract infections	11	CS Phase I trial RCTs	No	4	Only mild AEs	Allergic reactions Bad taste in mouth Chest pain Decreased libido Diarrhoea Dizziness Drowsiness Fatigue Headache Heartburn Nausea Rash Vomiting	NM	NM	Mild	PhD	NM	Fellowship from Pharmaton SA, Lugano, Switzerland
Cui (2010)[68] People's Republic of China	AEs Safety	TCR	Degenerative disc disease with chronic neck pain	4	RCTs	No	5	Mild to moderate AEs	Watery stool Abdominal pain Stomach ache Pruritus Reddish skin Small blisters on Skin	30 minute	NM	NM	TCM	State Administration of Traditional Chinese Medicine of the People's Republic of China (06-07JQ05)	State Administration of Traditional Chinese Medicine of the People's Republic of China(06-07JQ05), China
Ernst (2002)[69] UK	AEs	*Agnus castus* Alcoholic herbal tincture Blue cohosh Castor oil Dong quai Echinacea German herbal mixture Ginseng *Montanoa tomentosa* *Polygonum multiflorum*, Pyrrolizidine alkaloids Raspberry leaf St John's wort TCR *Tripterygium wilfordii*	NS	22	CRs CS Retrospective surveys Epidemiology surveys	No	3	Mild to moderate AEs	Abortifacient Birth defects Emmanagogue Low birth weight (fetus) Mutagenic Oxytocic action Premature birth	Several weeks (after blue cohosh)	NM	NM	MD PhD FRCP	NM	NM
Flower (2009)[70] UK	AEs Safety	TCR	Endometriosis	2	RCTs	Yes	5	Only mild AEs	Acne Dry mouth Rectal tenesmus Weight gain	NM	NM	Mild	CAM	None declared	Complementary Medicine Research Unit, UK

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Frazier (2009)[84]	Toxicity	*Atractylis gummifera* Black cohosh Boh-Gol-Zhee Camphor *Centella asiatica* Chaparral leaf Chaso Comfrey Fu Fang Qing Germander Golden germander Greater celandine Jin Bu Huan Kava Linghzi Ma huang Senna Sho-saiko-to Skullcap *Teucrium capitatum* Valerian	Anxiety Bone disorders Insomnia (intended use) Leprosy Menopausal symptoms Rheumatism Weight loss to chronic viral hepatitis	NM	NM	No	1	Mild to moderate AEs	Acute and chronic hepatitis Acute hepatocellular injury Acute liver failure Cholestatic hepatitis Cirrhosis Encephalopathy Hepatic fibrosis Hepatic granulomas Hepatic necrosis Isolated γ-glutamyl transpeptidase increase Microvesicular steatosis Renal failure Reye's syndrome Veno-occlusive disease and subsequent fatal liver failure	NM	NM	Severe lactic acidosis (kombucha tea)	MD	None declared	NM
Guo (2006)[71] UK	AEs Safety	Panax ginseng TCR	COPD	14	RCTs	No	5	Mild to moderate AEs	Constipation Dry mouth	NM	NM	Mild to moderate	PhD	NM	Bionorica AG, Neumarkt, Germany
Liu (2009)[72] Peoples Republic of China	AEs Safety	TCR	Drug dependence (heroin detoxification)	21	RCTs	Yes	4	Only mild AEs	Blurred vision Dizziness Dry mouth Dysuria Fatigue Headache Inappetency Instability of gait Nausea Sagging Somnolence	NM	NM	Mild to moderate	MD	NM	National Basic Research Program of China (973 Program, 2003CB515400), the National High Technology Research and Development Program of China (863 Program, 2006AA02Z4D1)
Martin (2004)[73] UK	AEs Safety	Bitter orange oil *Solanum chrysotrichum Schldl* Solanum nigrescens Tea tree oil	Fungal infections	7	NRCT RCTs	No	4	Only mild AEs	6 AEs in total	NM	NM	NM	PhD	NM	Fellowship from Boots Company, Nottingham, UK

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
May (2009)[74] Australia	AEs Safety	*Melissa officinalis* *Salvia officinalis* TCR	Dementia	13	RCTs	Yes	5	Only mild AEs	Abdominal distension Abdominal pain Agitation Appetite loss Belching Decrease of appetite Diarrhoea Dizziness Liver dysfunction (unspecified in which group) Nausea Oral bitterness Urticaria Vomiting Wheezing	NM	NM	Mild	TCM	NM	Australian Postgraduate Award
Mehri (2011)[89] IRA	AEs Safety	Stinging nettle *(Urtica dioica)*	Diabetes	1	Clinical analysis	No	5	Only mild AEs	NM	NM	NM	NM	Pharmacy	NM	None declared
Naser (2011)[83] Germany	Toxicity	Black cohosh	Menopausal symptoms	5	RCTs	Yes	0	Only mild AEs	NM	NM	NM	NM	MD	Yes, potential	First author is an employee of Schaper & Brummer GmbH & Co. KG, manufacturer of isopropanolic black cohosh extract
Pittler (2003)[1] UK	Toxicity	Aristolochia Bajiaoloan Cascara sagrada Celandine Chaparral Germander Jin bu Huan Kava Ma huang Pennyroyal Senna Skullcap TCR	Various (from asthma to weight loss)	52	Various (clinical and laboratory data)	No	5	Mild to moderate AEs	From transient elevations of liver enzyme levels to fulminant liver failure and death	Once only-several years	NM	Yes (severe acute liver failure)	MD PhD	NM	NM
Pittler (2004)[90] UK [90]	AEs	Feverfew *(Tanacetum parthenium* L.)	Migraine	5	RCTs	No	5	Only mild AEs	GI symptoms Mouth ulceration	NM	NM	Mild and reversible	MD PhD	None declared	None declared
Pittler (2005)[75] UK	AEs	*Ephedra sinica* *Garcinia cambogia* Guar gum *Ilex* *Paullinia cupana* *Pausinystalia yohimbe* *Plantago psyllium* *paraguariensis*	NS	80	Largely anecdotal	No	5	Mild to moderate AEs	Death Hepatic injury Heart palpitation Risk of psychiatric, autonomic or GI AE	NM	NM	Severe diarrhoea (after *Plantago psyllium)*	MD PhD	NM	NM

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Qin (2011) Peoples Republic of China[81]	AEs	TCR (Free and Easy Wanderer Plus)	Depression	14	RCTs	Yes	5	Only mild AEs	Constipation Dizziness Dry mouth Headache Tachycardia	NM	NM	NM	Regenerative medicine	None declared	None declared
Rathbone (2007)[76] UK	AEs, safety	TCR	Schizophrenia	7	RCTs	Yes	5	Only mild AEs	Constipation	NM	NM	NM	Psychiatry	None declared	NM
Setty (2005)[82]	AEs and toxicity	American, common or holy basil Cat's claw Crack Devil's claw Evening primrose Feverfew Ginger Purple, white or violet willow Stinging nettle Thunder god vine *Tripterygium wilfordii*	Rheumatic diseases	70	Mostly very good	No	–1	Mild to moderate AEs	Alopecia Altered bleeding time (feverfew) Amenorrhoea Angular stomatitis Diarrhoea Diastolic hypertension Dry mouth Dyspepsia Emmenagogue Flatulence Gastritis GI upset (devil's claw) Headache Nausea (gingerols) Nephrotoxicity (cat's claw) Oral ulcers Osteoporosis (thunder god vine) Rash Skin pigmentation Upset stomach Urticarial rash Vaginal spotting Vomiting Weight gain/loss	NM	NM	NM	MD	NM	NM
Shi (2008)[77]	AEs	TCR TTR	IBS	22	Good	Yes	5	Mild to moderate AEs	Abdominal pain Chest pain Constipation Diarrhoea Distension Dizziness GI discomfort Headaches Hoarseness Loss of hair Nausea Paraesthaesia disturbance Pruritus Shortness of breath Sleepiness Upper GI discomfort	NM	NM	NM	Chinese medicine	NM	NM
Tu (2009)[78] Peoples Republic of China	AEs Safety	TCR	Dysfunctional uterine bleeding	4	QRCT RCTs	Yes		Only mild AEs	None serious reported	NM	NM	NM	TCM	NM	NM

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Table S3. Continued.

Author (year) Country	Type of safety concerns	Herbal medicine evaluated	Clinical conditions	Primary data: No of reports*	Primary data: Type	Meta-analysis?	Quality of SR†	Overall judgment	AEs: Type/clinical outcome	AEs: Duration	AEs: Frequency	AEs: Severity	First authors' degree/ background	Conflict of interest	Source of funding
Ulbricht (2009)[80] USA	AEs	Essiac	NM	19	Anecdotal reports CR CS Unpublished investigations	No	1	Moderate to severe AEs	Allergies Anaphylaxis Arrhythmias Atonic colon Bradycardia Cardiac toxicity Colic Dermatitis Diarrhoea Extensive hepatic necrosis Haematuria Hypokalaemia Nausea Neuromuscular dysfunction Pain Seizure Severe metabolic acidosis with subsequent hepatic failure and neonatal jaundice Vomiting	NM	NM	NM	PharmD	NM	None declared
Vogler (1999)[91] UK	AEs	*Aloe vera*	Diabetes and hyperlipidaemia	10	CCT RCTs	No	4	Mild to moderate AEs	Burning (topical application) Contact dermatitis Mild itching	NM	NM	Mild	PhD	NM	NM
Zhu (2008)[79] Australia	AEs	TCR	Women with primary dysmenorrhoea	39	RCTs	Yes	5	Only mild AEs	'No significant adverse effects were identified'	NM	NM	NM	CAM	Yes	University of Western Sydney and Cochrane Menstrual Disorders and Subfertility Group

AE, adverse effect; AIDS, acquired immune deficiency syndrome; BSc; Bachelor of Science; CAM, complementary and alternative medicine; CCT, controlled clinical trial; COPD, chronic obstructive pulmonary disease; CYP3A, cytochrome P450 3A; CR, case report; CS, case series; CVD, cardiovascular disease; HBV, hepatitis B virus; HFS, herbal food supplements; HM, herbal medicines; GI, gastrointestinal; IBS, irritable bowel syndrome; MD, Doctor of Medicine; NM, not mentioned; NRCT, non-randomized controlled trial; NS, not specified; OA, osteoarthritis; PharmD, Doctor of Pharmacy; PhD, Doctor of Philosophy; PMS, premenstrual syndrome; QRCT, quasi-randomized controlled trial; RA, rheumatoid arthritis; RCT, randomized controlled trial; RRC, retrospective review of cases; SR, systematic review; SRS, spontaneous reporting scheme; TAR, traditional Arab remedies; TCM, traditional Chinese medicine; TCR, traditional Chinese remedies; TGV, thunder god vine; TIR, traditional Indian remedies; TKR, traditional Korean remedies; TTR, traditional Tibetan remedies; UCT, uncontrolled trial.

*Range of primary data.

†Total number of patients experiencing AEs, if estimable.

‡Scoring: each question is scored as 1, 0 or –1; a score of ⩽0 means the review has major flaws, 1–2 means minor flaws and 3–5 means minimal or no flaws; 1 means that: (a) the review states the databases used, the date of the most recent searches and includes some mention of search terms; (b) the review searches at least two databases and looks at other sources; (c) the review states in the overview the criteria used for deciding which studies to include; (d) the review reports how many studies were identified by searches, the numbers of studies excluded and the appropriate reasons for excluding them; (e) the conclusions made by the author(s) are supported by the data and/or analysis reported in the review; 0 means that the above-mentioned criteria were partially fulfilled; and –1 means that none of the above criteria were fulfilled. This is an operationalisation of the Oxman criteria,[11] adapted from Ernst et al (2011).[10]