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The role of Western herbal medicine in the treatment of gout

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ABSTRACT

Gout has been recognised as a clinically distinct disease for over four millennia. It is one of the most prevalent inflammatory arthropathies and a true crystal deposition disease. Current consensus holds that its management in primary orthodox healthcare is sub-optimal. This study aimed to identify whether herbal medicine offers an effective alternative or complementary approach for managing patients with acute and chronic gout.

Three approaches were taken: a survey of medical herbalists to gauge contemporary approaches; historical and contemporary texts were scrutinised to identify any herbs indicated for gout; and an evidence review to establish the current evidence base for the herbal treatment of gout.

While gout was not a frequent presentation in practice, the majority of medical herbalists surveyed had treated it at some point in time. Moreover, most reported herbal medicine had a definite benefit for patients with gout, usually taking effect within one or two months. In general, the herbs used in clinical practice were mainly chosen for their ability to eliminate uric acid (*Apium graveolens*, *Urtica* spp, *Taraxacum officinale*) or as anti-inflammatories (*Harpagophytum procumbens*, *Filipendula ulmaria*, *Salix* spp, *Betula* spp, *Curcuma longa* and *Guaiacum* spp.). There was some agreement in the more popular herbs cited for gout in herbal texts and prescribed by practitioners, and given the lack of scientific evidence identified, suggests herb choice was largely influenced by traditional use.

A paucity of evidence was highlighted regarding the effectiveness of Western herbal medicine for gout, a single clinical trial was identified; however, it was of poor quality with unclear or high risks of bias.

Given the effectiveness of herbal medicine in treating patients with gout reported by practitioners, together with the lack of a strong evidence-base identified in this study, further research is warranted. Practice-based evidence, such as the systematic collection of clinical treatment outcomes in practice, together with large, well-designed pragmatic clinical trials are required to establish the effectiveness of herbal medicine in the treatment of gout.

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1. Introduction

Gout has long been recognised as a clinically distinct disease: identified by the Egyptians over 4650 years ago and later documented by Hippocarates and Plato (Nuki and Simkin, 2006; Porter and Rousseau, 1998). It is one of the most prevalent inflammatory arthropathies and a true crystal deposition disease, directly attributable to the presence of monosodium urate (MSU) crystals in joints and other tissues (Doherty, 2009; Roddy, 2011a). Recent studies in UK primary care estimate a 5-year prevalence of 1.4% overall (Annemans et al., 2008) and similarly, a 10-year prevalence of 2.24% for men and 0.60% for women (Parsons et al., 2011). In both studies, women represented 18% of the study population with gout.

Multiple risk factors contribute to the development and progression of gout and can be classified as either non-modifiable risk factors, namely genetics, age and gender, or modifiable risk factors including hyperuricaemia, diet, alcohol, medications, comorbidities, body mass index and physical fitness (Crittenden and Pillinger, 2011; Doherty, 2009; Dubchak & Falasca, 2010; Neogi, 2011; Smith et al., 2010; Teng et al., 2006; Underwood, 2006). These latter risk factors are often the focus of multifaceted interventions in the management of gout.

Gout is predominantly managed in primary care (Roddy, 2011b), with recommendations that optimal treatment involves both pharmacological and non-pharmacological approaches, individually tailored according to the clinical phase of gout, risk factors and patient preference (Underwood, 2006; Zhang et al., 2006).

In acute gout, the mainstay of treatment is anti-inflammatory medication. Oral non-steroidal anti-inflammatory drugs (NSAIDs) and/or colchicine are first-line agents (Zhang et al., 2006), with systemic corticosteroids used when NSAIDs and colchicine are contraindicated or ineffective (Gonzalez, 2012). In acute monoarticular gout, joint aspiration followed by intra-articular corticosteroid injection is considered most effective (Roddy, 2011b). Adjuvant non-pharmacological treatments such as ice packs, rest and elevation of the affected joint may also be employed (Map of Medicine, 2012; Underwood, 2006).

The therapeutic aim in chronic gout is to prevent further acute flare-ups and joint damage through long-term management of serum urate levels: keeping these sufficiently low, to promote the dissolution of existing MSU crystals and prevent new crystal formation (Roddy, 2011b). Initially, non-pharmacological approaches are usually suggested including weight loss, dietary modification, low alcohol consumption, and ensuring sufficient fluid intake and exercise (Jordan et al., 2007; Underwood, 2006; Zhang et al., 2006). The decision to pharmacologically treat hyperuricaemia often follows the failure of these non-pharmacological approaches, resulting in frequent and difficult to control gout attacks, or chronic low-grade inflammation. Urate-lowering agents, such as allopurinol and febuxostat, are usually taken for life, and on initiation are given in combination with flare prophylaxis as they tend to cause 'rebound' flares (Shipley, 2011).

Gout management by orthodox healthcare is currently sub-optimal with physicians failing to follow treatment guidelines, frequent prescription of gout medications in individuals with (multiple) contraindications and patient preference and compliance issues (Chandratre et al., 2012; Doherty et al., 2012; Keenan et al., 2011; Lipworth et al., 2011). Thus, does herbal medicine offer an effective alternative or complementary approach to ensure the successful management of gout?

As a consequence of gout's early recognition as a clinical disease, long pre-dating modern medicine, there is an extensive tradition of herbal treatment exemplified by its mention in historical, and contemporary, pharmacopoeia and *Materia medica* (*e.g.* Culpeper, 1995; Fisher, 2009; Watkins et al., 2011). Current treatment by medical herbalists represents the culmination of millennia of clinical experience, which may be expected to have led to the evolution of some of the most effective herbal approaches to gout.

The aim of this study was to identify herbs that may benefit the treatment of patients with acute or chronic gout, through: examining historical and contemporary texts to identify herbal treatments; reviewing the current evidence base; and surveying herbalists to gauge contemporary herbal approaches.

2. Methodology

2.1. *Herbal texts*

To identify herbs traditionally, or more recently, used for the treatment of gout in Western herbal medicine, a selection of easily accessible historical and contemporary texts from Europe, North America and Australia, addressing the medicinal use of herbs was searched and all references to gout recorded. The texts spanned approximately 860 years, from around 1150 to 2011: 12th (Hildegard von Bingen, 1998), 17th (Culpeper, 1995), 19th (Cook, 1869; Fernie, 1897 [transcribed 2006]), 20th (Bartram, 1998; Grieve and Leyel, 1992; Priest and Priest, 1983; Vickery, 1995) and 21st centuries (Allen and Hatfield, 2004; Barker, 2007; Barnes et al., 2007; Bone, 2003; Felter, 1922; Fisher, 2009; Hoffmann, 2003; Kress, 2011; Menzies-Trull, 2009; Mills and Bone, 2000; Thomsen, 2005; Tobyn et al., 2011; Weiss, 2001; Wood, 2004, 2008a, 2008b)

2.2. *Literature review*

To identify clinical studies including observational, cohort and (randomised)-controlled trials, pertaining to the use of herbal medicine in gout, an electronic search was conducted of six online databases: MEDLINE (1946 to 2013 February 08); EMBASE (1974 to 2013 February 08); AMED (1985 to February 2013); CINAHL (1981 to February 2013); Web of Science (1970 to February 2013) and The Cochrane Library (1898 to Issue 1, January 2013). A systematic search protocol was designed and adapted to each database with the basic search strategy [gout OR synonyms] AND [herbal medicine OR synonyms] and utilised database-specific controlled vocabulary (*e.g.* for MEDLINE protocol see Appendix A). The quality of randomised

controlled trials was assessed using the Cochrane Collaboration risk of bias assessment tool (Higgins et al., 2011).

2.3. Survey of medical herbalists

To explore the contemporary approach of medical herbalists to patients with gout a cross-sectional survey was conducted. This utilised a short questionnaire specifically designed for this study and comprising of 13 questions: 10 closed, 1 open and 2 mixed (with both closed and open elements) covering the patient presentation of gout, herbal prescriptions, conventional treatment, effectiveness of herbal treatment plus overall experience of the herbalist.

Two forms of the questionnaire were designed: an online version hosted by SurveyGizmo® (www.surveygizmo.com) and a postal version (see Appendix B).

Multiple approaches were used to contact all current, practising members of The National Institute of Medical Herbalists (NIMH), as identified in the *Register of Qualified Members 2011/2012*, its addendum (current 21st May 2012), and *Find a Herbalist* (http://www.nimh.org.uk/?page_id=1627, [accessed 2nd June 2012]). An email invitation containing a link to the online survey was sent to all members with a listed email address or listed website providing a contact email address or option to message directly ($n=470$). All other UK-based NIMH members were sent a postal questionnaire and stamped return-address envelope ($n=61$). In total, 531 herbalists were contacted, excluding two non-UK eligible herbalists not contactable electronically. Initial email or website-mediated invitations were sent 6th June 2012 and reminders sent 18th June 2012. The online survey was available for completion for 4 weeks (6th June–3rd July 2012). All postal surveys were sent *via* Royal Mail (2nd Class) on 8th June 2012.

All statistical analyses were performed using IBM SPSS Statistics v20.

3. Results

3.1. Herbal texts

Table 1 shows the herbs identified by 21 authors in 24 historic and contemporary Western herbal texts. Thirty-one herb species or genera, representing at least 51 species, were indicated for treating gout by a minimum of *three* different authors. A further 131 herb species or genera were indicated by one or two authors only. In terms of the number of herbal texts, it is accepted as a possible limitation that these may cite from each other; however this was considered acceptable on the basis that all the texts quoted were those regularly referred to by herbalists.

Six herbs were cited by a third or more authors: *Apium graveolens* ($n=10$, 48%); *Urtica* spp. ($n=9$, 43%); *Aegopodium podagraria* ($n=8$, 38%); *Arctium lappa* ($n=8$, 38%); *Eupatorium* spp. ($n=8$, 38%); and *Colchicum autumnale* ($n=7$, 33%). Interestingly, *Urtica* spp. is cited relatively consistently in herbals post-Culpeper, but 800-years elapsed between von Bingens' mention of *A. graveolens* and its subsequent reference.

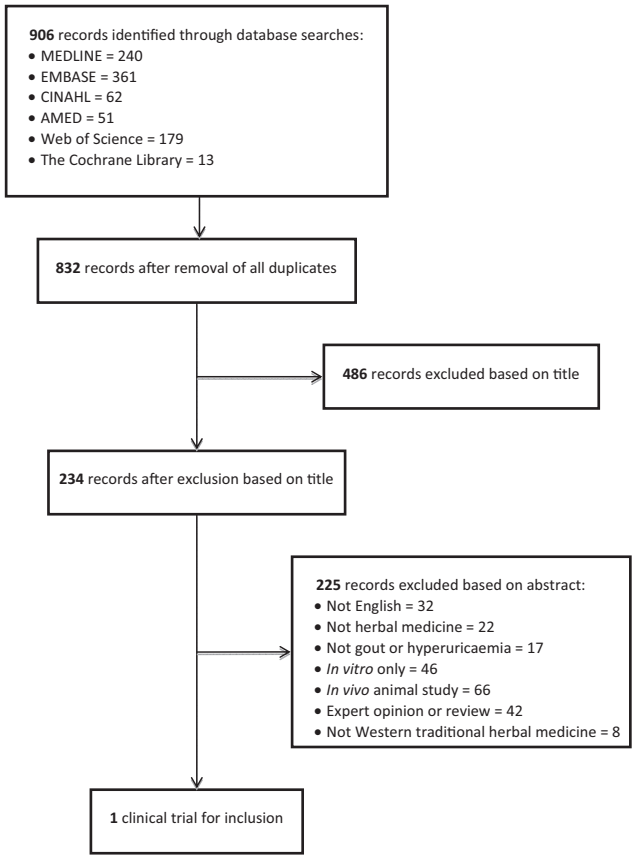

Fig. 1 – Selection of studies for inclusion in the review

3.2. Literature review

Electronic database searches generated 832 potentially relevant studies; subsequent screening led to the identification of one clinical trial for inclusion in the review (Fig. 1).

This single randomised controlled trial aimed to establish the treatment effect of Gouticin [a herbal formulation comprising *A. graveolens* (100 mg), *C. autumnale* (50 mg), *Withania somnifera* (75 mg), *Smilax chinensis* (75 mg), *Tribulus terrestris* (100 mg) and *Zingiber officinale* (100 mg)], dosage: Tab 500 mg (3× per day), compared to Allopurinol (300 mg 1× per day) in patients with hyperuricaemia (Akram et al., 2010). One hundred out-patients with hyperuricaemia were randomised to receive Gouticin ($n=50$) or Allopurinol ($n=50$), in addition, all patients were given the same dietary and lifestyle advice. Serum uric acid, urea, creatinine, creatinine clearance and uric acid clearance were assessed at baseline, 6, 12 and 18 weeks. The results showed a significant hypouricaemic effect for both Gouticin (mean serum uric acid: before 10.03 mg dl^{-1}, after 4.74 mg dl^{-1}) and Allopurinol (mean serum uric acid: before 10.18 mg dl^{-1}, after 5.27 mg dl^{-1}): however, Gouticin was superior to Allopurinol ($p<0.03$). Furthermore, side effects were noted for Allopurinol but not Gouticin. The study concluded Gouticin was superior to Allopurinol for treating hyperuricaemia. However, unclear risks of bias associated with the randomisation, allocation and blinding processes and statistical analyses, together with a high risk of bias of incomplete outcome data indicated that overall

Table 1 – Herb species identified for the treatment of gout by at least 3 different authors (books by the same author have been combined): columns: texts in ascending order of original publication date; rows: herbs in descending order of the total number of texts each was identified in for the treatment of gout. Species from the same genus are combined. Asterisks (*) indicate a herb's mention in a specific herbal text.

Herb species	1150s	Herbal text								2003
	Hildegard von Bingen, 1998	Culpeper, 1995	Cook, 1869	Fernie, 1897	Felter, 1922	Grieve and Leyel, 1992	Priest and Priest, 1983	Vickery, 1995	Bartram, 1998	Weiss, 2001	Hoffmann, 2003
Apium graveolens	*								*		*
Urtica dioica; U. urens		*		*		*				*	*
Aegopodium podagraria	*	*		*		*		*			
Arctium lappa				*			*		*		
Eupatorium spp. incl. *E. purpureum; E. fistulosum; E. maculatum*						*	*		*		*
Colchicum autumnale				*	*				*	*	*
Salix alba; S. fragilis; S. pentandra; S. purpurea; S. nigra									*		*
Artemisia vulgaris; A. absinthium; A. ponticam; A. abrotanum	*			*		*					
Betula pendula; B. alba											*
Daucus carota				*							*
Guaiacum officinale						*			*		*
Smilax spp. incl. *S. ornata; S. china; S. officinalis*						*			*		
Armoracia rusticana				*		*		*			
Cichorium intybus				*		*					
Filipendula ulmaria									*		
Harpagophytum procumbens									*		
Sambucus nigra; S. canadensis; S. humilis		*	*			*					
Tanacetum balsamita; T. vulgare				*		*		*			
Bellis spp. incl. *B. perennis*		*		*		*					
Elymus repens											*
Fragaria vesca				*		*					
Fraxinus excelsior						*					
Helleborus niger	*	*		*							
Juniperus communis		*					*				
Mentha pulegium		*				*					
Populus nigra; P. x gileadensis		*									
Rubus nigrum				*							
Trigonella foenum-graecum						*					
Vaccinium myrtillus; V. macrocarpon											
Verbena officinalis		*									
Veronica spp. incl. *V. officinalis; V. chamaedrys, V. beccabunga*	*			*							
Total for table	5	9	1	14	1	15	3	3	9	2	9
Other herbs identified by 1 or 2 authors only	13	41	5	24	4	36	1	1	5	0	0
Grand total	18	50	6	38	5	51	4	4	14	2	9

Table 1 – (*Continued*)

Herb species	2003		Herbal text							2011	Count
	Mills and Bone, 2000 and Bone, 2003	Allen and Hatfield, 2004	Thomsen, 2005	Barker, 2007	Barnes et al., 2007	Wood, 2004, 2008a, 2008b	Fisher, 2009	Menzies-Trull, 2009	Kress, 2011	Tobyn et al., 2011	
Apium graveolens	*		*	*	*	*	*	*			10
Urtica dioica; U. urens	*		*			*	*				9
Aegopodium podagraria						*		*			8
Arctium lappa			*	*	*	*	*				8
Eupatorium spp. incl. *E. purpureum; E. fistulosum; E. maculatum*			*		*	*	*				8
Colchicum autumnale				*						*	7
Salix alba; S. fragilis; S. pentandra; S. purpurea; S. nigra			*	*	*	*					6
Artemisia vulgaris; A. absinthium; A. ponticam; A. abrotanum							*			*	5
Betula pendula; B. alba	*		*	*			*				5
Daucus carota				*	*					*	5
Guaiacum officinale			*		*						5
Smilax spp. incl. *S. ornata; S. china; S. officinalis*			*			*	*				5
Armoracia rusticana				*							4
Cichorium intybus				*			*				4
Filipendula ulmaria	*		*	*							4
Harpagophytum procumbens			*		*		*				4
Sambucus nigra; S. canadensis; S. humilis		*									4
Tanacetum balsamita; T. vulgare		*									4
Bellis spp. incl. *B. perennis*											3
Elymus repens	*						*				3
Fragaria vesca				*							3
Fraxinus excelsior		*		*							3
Helleborus niger											3
Juniperus communis							*				3
Mentha pulegium					*						3
Populus nigra; P. x gileadensis				*			*				3
Rubus nigrum				*					*		3
Trigonella foenum-graecum					*		*				3
Vaccinium myrtillus; V. macrocarpon					*	*	*				3
Verbena officinalis		*								*	3
Veronica spp. incl. *V. officinalis; V. chamaedrys, V. beccabunga*		*									3
Total for table	5	5	10	13	10	8	14	2	1	4	143
Other herbs identified by 1 or 2 authors only	2	6	4	8	2	5	4	1	1	3	166
Grand total	7	11	14	21	12	13	18	3	2	7	309

Table 2 – Symptoms and consequences of gout for which patients sought treatment, ranked in descending order of overall frequency. Data are also presented separately for herbalists with experience of acute gout only, chronic gout only or both acute and chronic gout.

	Acute gout only ($n=10$)	Chronic gout only ($n=20$)	Both acute and chronic gout ($n=59$)	Overall ($n=89$)	Ranked 1st–3rd ($n=81$[a])
Joint pain	9	17	56	82	73
Swollen joint(s)	10	13	50	73	46
Joint tenderness	7	13	48	68	28
Hot joint(s)	9	12	45	66	16
Joint stiffness	5	15	35	55	18
Mobility problems	4	11	36	51	29
Erythema/redness	6	8	37	51	4
Low mood	4	8	11	23	4
Tophus/tophi	1	2	15	18	4
Pruritic/itchy skin	1	3	12	16	4
Malaise	1	1	11	13	4
Dry skin	0	3	5	8	1
Fever	0	0	3	3	0
Skin ulceration	0	0	2	2	0
Other	1	4	5	10	3

[a] Eighty-four respondents ranked at least one feature in order of frequency of presentation; however, three postal surveys were excluded as multiple features were equally ranked, thus, $n=81$.

the study was not of high quality (after Higgins et al., 2011).

3.3. *Survey of medical herbalists*

3.3.1. *Herbalists' characteristics and experience of patients with gout*

Of the 531 invitations to participate in the survey, 142 surveys were completed: a 26.7% response rate. Respondents reported practising for between 0.2 and 36 years ($n=142$, median = 8 years). A majority of the 142 respondents had treated gout ($n=90$, 63%); further, herbalists who had treated patients with gout had been practicing significantly longer than those who had not (Mann–Whitney $U=3518.5$, $p<0.0001$; treated gout: median = 10 years, $q1=6$, $q3=17.75$, $n=90$; not treated gout: median = 4 years, $q1=1$, $q3=8.5$, $n=52$).

Eighty-nine respondents reported the number and type of gout patients treated over the last 5 years. The median was two gout patients ($q1=1$, $q3=4$), however inter-individual variation was large: ranging from 0 to 40 patients over the period. In addition, 23% of all patients with gout treated by respondents were female (87 of 380 patients). Most of these 89 respondents had treated both chronic and acute gout ($n=59$, 66%), whilst, twice as many respondents had treated chronic gout only ($n=20$, 23%) compared to acute gout only ($n=10$, 11%).

3.3.2. *Patient presentation of gout*

Eighty-nine respondents provided information on patients' presentation. Overall, the majority identified features associated with joint inflammation: joint-pain ($n=82$, 92%), swelling ($n=73$, 82%), tenderness ($n=68$, 76%), heat ($n=66$, 74%), stiffness ($n=55$, 62%), erythema ($n=51$, 57%) and mobility issues ($n=51$, 57%). Other features were identified by approximately a quarter of respondents or less (Table 2). Compared to herbalists with experience of chronic gout only, respondents who had encountered acute gout only reported a greater proportion of patients presenting with swollen joints, hot joints and erythema and a lesser occurrence of stiffness, dry skin and mobility problems (Table 2).

Joint pain ranked in the top three most common presentations substantially more than any other feature ($n=73$), followed by swollen joints ($n=46$), mobility problems ($n=29$) and joint tenderness ($n=28$), all other features ranked in the top three under 20 times (Table 2).

3.3.3. *Herbal prescriptions for gout*

Seventy-nine respondents identified and ranked at least three preferred herbs for treating gout: sixty-three herbs were named in total. However, only 11 herbs were identified by more than 10% of respondents (Table 3). Eighty six percent ($n=68$) of these 79 respondents mentioned *A. graveolens*, most ranked it in their top three ($n=66$, 83.5%) and 53.2% ($n=42$) indicated it their first choice treatment. The second most popular herb *Urtica* spp. including *U. dioica*, was reported by 50.6% ($n=40$) of respondents, 44% ($n=35$) ranked it in their top three and 13.9% ($n=11$) named it as their first choice treatment. Other herbs identified by over 20% ($n\geq16$) of respondents were: *Harpagophytum procumbens*, *Filipendula ulmaria*, *Salix* spp. and *Taraxacum officinale* (radix, folia and unspecified combined[2]).

Of the 321 separate herb choices given by respondents, a single form (*e.g.* given as a tincture, tea or capsule) of the herb was indicated in 257 cases and more than one form in 60 cases, no corresponding form was provided in 4 cases: a total of 381 herb choice × form were indicated. Overall, tinctures were utilised in two-thirds of cases (66%, $n=252$), teas represented a fifth of prescriptions (19%, $n=73$), and capsules, topical and other forms were each cited in approximately 5% ($n=15$–23) of cases.

[2] Not all respondents specified whether they were referring to *T. officinale* radix or folia therefore for the purpose of this study no differentiation was made even though it is acknowledged that therapeutically these parts have different properties and uses.

Table 3 – Herbs of choice indicated by at least 10% of respondents for treating patients with gout. Ranked in descending order of overall preference (1 indicating 1st choice).

Herb	Rank					Total	%
	1	2	3	4	5		
Apium graveolens	42	12	12	2	0	68	86.0
Urtica spp.	11	15	9	2	3	40	50.6
Harpagophytum procumbens	2	9	5	5	3	24	30.4
Filipendula ulmaria	0	10	9	2	1	22	27.8
Salix spp.	3	3	4	4	2	16	20.3
Taraxacum officinale	0	5	6	4	1	16	20.3
Betula spp.	4	2	2	2	0	10	12.6
Guaiacum spp.	1	3	1	2	3	10	12.6
Curcuma longa	1	2	3	1	2	9	11.4
Arctium lappa	0	3	2	2	1	8	10.1
Galium aperine	2	2	1	2	1	8	10.1
Grand Total	79	79	79	52	32	321	

Table 4 – Reasons identified by respondents for the use of specific herbs.

Reason	*n*	Reason	*n*
Anti-inflammatory	82	Kidney support	5
Eliminate uric acid	60	Lymphatic	5
Diuretic	51	Anti-hypertensive	4
Pain relief	37	Demulcent	4
Detoxifying	21	Eliminative	4
Depurative	18	Traditional	3
Anti-rheumatic	13	Anti-allergy	2
Circulation	12	Anti-oxidant	2
Hepatic	11	Anti-spasmodic	2
Cooling	10	Anti-uric acid	2
Gout specific	9	Kidney/liver function	2
Alkalising	5	Other	29
Antacid	5		
		Grand total	398

Sixty-two respondents provided reasons for the selection of 252 of the 321 herb choices. Justifications were scrutinised and coded: 398 separate reasons were itemised, falling into 25 categories (Table 4). Two distinct sets of reasons emerged: firstly, those addressing inflammation, most significantly herbs attributed with anti-inflammatory ($n=82$), pain-relieving ($n=37$) and cooling ($n=10$) properties; and secondly herbs associated with excess build-up of metabolites particularly uric acid, primarily those attributed with the elimination of uric acid specifically ($n=60$), diuresis ($n=51$), detoxification[3] ($n=21$) and depuratives *i.e.* herbs which promote channels of elimination ($n=18$).

3.3.4. *Orthodox and over-the-counter medication*

Seventy-nine respondents provided information on the orthodox medications gout patients were taking. Most reported treating patients on painkillers (58.2%, $n=44$) and NSAIDs (54.4%, $n=43$). Furthermore, 43% ($n=34$) had seen patients who had been prescribed xanthine oxidase inhibitors and 5% ($n=4$) uricosuric agents *i.e.* gout-specific drugs. Approximately a quarter of respondents had treated patients taking no orthodox medications (26.6%, $n=21$). Twelve herbalists (15%) had treated patients on other medications, which included diuretics, beta-blockers, hypotensives, 'heart medication', simvastatin, glucosamine sulphate, chondroitin, *H. procumbens* and nettle tea.

3.3.5. *Effectiveness of herbal medicine*

Seventy-seven respondents rated the effectiveness of herbal medicine in treating patients with gout (Fig. 2). Irrespective of which form(s) of gout respondents had experience of, the most frequent rating was 4 (overall: 46.8%, $n=36$). In total, a large majority (79.2%, $n=61$) rated herbal medicine as definitely or very effective (rating ≥ 4).

Seventy-six respondents provided information on the time it took for herbal medicine to succeed in treating patients with gout (Table 5). Three herbalists indicated separate times for acute ($n=3$) and chronic ($n=2$) cases, thus $n=78$.

Overall, two-thirds of the 78 responses indicated herbal medicine succeeded in treating gout in under a month (39.7%, $n=31$) or within 1–2 months (37.2%, $n=29$) of starting

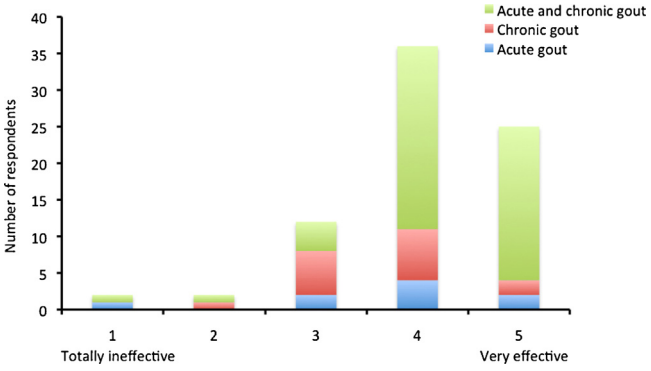

Fig. 2 – Cumulative bar chart showing frequency distribution of perceived effectiveness of herbal medicine in treating patients with gout, rated on a 5-point Likert scale according to respondents' personal experience: shading indicates form(s) of gout respondents had experience of treating.

[3] This refers to the reduction of harmful substances produced by the body's own metabolic processes through oxidation, conjugation and excretion of molecules from cells and tissues. Also known as xenobiotic metabolism, this includes enzymes such as cytochrome P450 oxidases and glutathione S-transferases.

Table 5 – Time taken for herbal medicine to work when treating patients with gout. Median is given along with upper (*q*3) and lower (*q*1) quartiles, and minimum and maximum values. Data are provided separately for respondents with experience of treating acute gout only, chronic gout only, or both acute and chronic gout.

	Acute only ($n=11$)	Chronic only ($n=18$)	Acute and chronic ($n=49$)
Time taken			
<1 month	9	3	19
1–2 months	2	7	20
3–4 months		7	7
5–6 months		1	2
>6 months			1
Average			
Median (months)	<1	1–2	1–2
*q*1 (months)	<1	1–2	<1
*q*3 (months)	<1	3–4	1–2
Minimum (months)	<1	<1	<1
Maximum (months)	1–2	5–6	>6

treatment. However, the response varied significantly depending on the form(s) of gout treated (Kruskal–Wallis $H=11.64$, d.f. = 2, $p=0.003$). Pair-wise comparisons revealed significant differences between all groups: acute *vs* chronic gout only (Mann–Whitney $U=26.5$, $p=0.001$); acute *vs*. acute and chronic gout (Mann–Whitney $U=143.5$, $p=0.009$); and chronic *vs*. acute and chronic gout (Mann–Whitney $U=306$, $p=0.043$). Respondents experienced in acute gout only reported quickest success, whilst those experienced in chronic gout indicated slowest success; herbalists who had treated both acute and chronic gout reported intermediate times.

3.3.6. *Lifestyle and dietary recommendations*

Seventy-four of 78 (95%) respondents provided dietary and/or lifestyle recommendations for gout patients: of these 72 gave details. These were scrutinised and coded, resulting in forty-three recommendations including 'other' (suggestions noted only once). Seven dietary changes were cited by a quarter of respondents or more: reduction/avoidance of purines (47.2%, $n=34$), meat (38.8%, $n=28$), alcohol (33.3%, $n=24$) and caffeine (25%, $n=18$) consumption; and increased fluid (45.8%, $n=33$), vegetables (33.3%, $n=24$) and fruit (27.8%, $n=20$) intake, cherries in particular were indicated by 16.7% ($n=12$) of herbalists.

Generally, respondents advised increased fruit and vegetable consumption, however, specific items were considered best avoided including oxalate-rich fruit and vegetable, solanaceous foods, spinach, sorrel, rhubarb, strawberries, citrus/oranges and acidic fruits. Lifestyle advice included increasing exercise (19.4%, $n=14$) and external treatments for the affected area (23.6%, $n=17$). One-off dietary and lifestyle recommendations were cited by 29.2% ($n=21$) and 9.7% ($n=7$) of herbalists, respectively.

4. Discussion

4.1. *Patients with gout*

In general, although gout was not frequently seen in practice, the majority of those surveyed had treated patients with gout (63%; $n=90$). Interestingly, the likelihood of herbalists treating a patient with gout appeared to be related to the number of years they have been practising.

Female patients accounted for 23% of all patients with gout in this study. Whilst not large, this is greater than found in recent UK epidemiology studies of 18% in primary care (Annemans et al., 2008; Parsons et al., 2011) and is consistent with women's greater tendency to use complementary and alternative therapies than men (Bishop and Lewith, 2010).

4.2. *Form and presentation of gout*

Herbalists were more likely to have treated chronic (89%; $n=79$) than acute (77%; $n=69$) gout, although the majority (66%; $n=59$) had treated both. One limitation of the study was not distinguishing those herbalists with experience of acute and chronic gout in the same and different patients, which may have influenced herb choice.

Overall, the most common presentations were of joint-pain, swelling, tenderness and heat, all consistent with the underlying inflammatory pathology associated with gout, and also reflected in the reasons for herb choice which frequently cited anti-inflammatory and pain-relief actions. In addition, mobility issues, joint stiffness and erythema were also common. Furthermore, the apparent differences in presentation of acute and chronic gout, although not tested statistically *i.e.* greater frequency of symptoms associated with acute inflammation (swollen joints, hot joints and erythema) and lesser occurrence of symptoms and consequences associated with chronic joint inflammation (stiffness, dry skin and mobility problems) in acute compared to chronic gout, are totally consistent with the recognised clinical pictures (McCarty, 2008; Roddy, 2011a).

Interestingly, whilst mobility issues ranked sixth most frequent presentation, it ranked third most important. This suggests that whilst not always a presenting feature of gout, when it is, it has greater influence than some other symptoms and consequences of gout.

4.3. *Orthodox medication*

The number of herbalists reporting patients with gout on specific orthodox medications followed a similar pattern to orthodox treatment recommendations with regard to

anti-inflammatory drugs, in descending frequency NSAIDS, colchicine, oral corticosteroids and corticosteroid injections (Gonzalez, 2012; Zhang et al., 2006). However, the most frequent orthodox medication was for pain relief. In addition, a large minority had treated patients on urate lowering drugs indicative of chronic gout. Other drugs were also specified, signifying patients with comorbidities.

The survey did not ascertain whether patients continued on orthodox drugs or not whilst receiving herbal treatment: whilst this complicates the study outcomes, it does reflect true clinical practice. Moreover, many of the herbs prescribed had similar actions to prescription drugs. This is an area that would benefit from further research, namely to explore the concurrent use of herbal and orthodox medicines on patient outcomes.

A quarter of herbalists also reported treating patients taking no orthodox medication. It can only be speculated, that these patients may: prefer herbal medicine; have found orthodox medication of little, or no, benefit or experienced side-effects or adverse reactions; or be reluctant to commence or continue lifelong urate-lowering therapy (Chandratre et al., 2012; Doherty et al., 2012).

4.4. *Herbs for gout*

Generally, herbalists' reasons for including the main herbs identified in the survey were to address the inflammatory nature of gout and the associated excess of metabolites, specifically uric acid. Some herbs mentioned less frequently addressed patient-specific issues *e.g.* anti-hypertensives and thymoleptics.

Overwhelmingly, the most popular herb prescribed by herbalists was *A. graveolens* followed by *Urtica* spp and this mirrored the herbs most frequently identified in the herbal texts for the treatment of gout. In both cases, herbalists stated the primary reasons for choice were their diuretic and/or uric acid eliminative effects (actions also attributed to *T. officinale* another popular choice). In addition, *A. graveolens* was also identified as anti-inflammatory (or cooling), analgesic and anti-rheumatic or gout specific, and *Urtica* spp. on the basis of depurative and detoxifying actions. The main actions attributed to these herbs are consistent with the underlying pathology of gout and herb indications outlined in contemporary texts: which also identify a lack of research (*e.g.* Bone, 2003; Fisher, 2009; Hoffmann, 2003; Mills and Bone, 2000; Wood, 2008b). In a recent *in vitro* study of *A. graveolens* the ethanolic extract was found to inhibit xanthine oxidase activity (Iswantini et al., 2012), supporting its role in gout. While only two herbalists indicated an anti-inflammatory and none analgesic action of *Urtica* spp, *in vivo* rodent studies show ethanol extracts of *U. diocia* and *U. urens* possess significant analgesic and anti-inflammatory activities (Chrubasik et al., 2007a; Marrassini et al., 2010).

A further six of the most popular herbs were included, primarily, for their anti-inflammatory/cooling action: *H. procumbens*, *F. ulmaria*, *Salix* spp, *Betula* spp, *Curcuma longa* and *Guaiacum* spp. All were additionally chosen for their analgesic, anti-rheumatic or gout-specific action, or based on traditional use. In general, studies have primarily been *in vitro* explorations of individual constituents or less frequently *in vivo* animal studies: but generally support anti-inflammatory activities (Bonaterra et al., 2010; Bone, 2003; Duwiejua et al., 1994; Fisher, 2009; Trouillas et al., 2003). *C. longa* and *H. procumbens* have received greater attention especially regarding musculoskeletal conditions, including some clinical trials which support their role in inflammatory and painful conditions (Chrubasik et al., 2007b; Denner, 2007; Mobasheri et al., 2012; Ramadan et al., 2011).

There was some consistency in the herbs cited for gout in herbal texts and prescribed by practitioners: of the top 11 identified (indicated by >10% herbalists and >20% of herbal texts), 6 were common to both *A. graveolens*, *U. dioica*, *A. lappa*, *Salix* spp, *Betula* spp, *Guaiacum* spp. Such agreement may indicate herb choice was largely influenced by traditional use, further supported given the lack of an evidence-base. Interestingly, *C. longa* was not specifically mentioned for gout in any herbal texts, although its anti-inflammatory action in other rheumatological conditions is noted (*e.g.* Bone, 2003). However, conspicuous by its absence in the practitioner survey is *A. podagraria*, its Latin- and common-name 'goutweed' underlining its close historical association with gout. There appears to be little research on this herb, although there is *in vitro* evidence that it inhibits COX-1 activity (Prior et al., 2007). The reasons for its absence can only be speculated, but may suggest it is relatively less effective compared with other herbs and thus become redundant, alternatively, it may simply have fallen out of use/fashion.

4.5. *Form of herb prescribed*

Whilst the majority of herbs were prescribed as tinctures (66%; $n = 252$), almost a fifth were (also) prescribed as teas. The reasons for practitioner choice were not elucidated and thus a limitation of the study. However, tinctures may be preferred for patient convenience, while the use of teas is particularly pertinent in gout to aid increased elimination of uric acid through the kidneys.

4.6. *Dietary and lifestyle recommendations*

An overwhelming majority of herbalists provided dietary and/or lifestyle advice including the reduction of purines, meat, alcohol and caffeine, and increases of fluids, vegetables and fruit in the diet, along with increasing exercise levels. All are consistent with current orthodox recommendations (Jordan et al., 2007; Zhang et al., 2006).

Approximately a quarter of herbalists recommended or prescribed eating cherries or drinking cherry juice. Evidence from small-scale studies supports their inclusion in the diet of patients with gout: these found eating cherries lowered serum urate in women (Jacob et al., 2003) whilst drinking juice long-term was anti-inflammatory and reduced acute gout flares (Schlesinger and Schlesinger, 2012).

4.7. *Effectiveness of herbal treatment*

Based on their own experience, almost four-fifths of respondents considered herbal medicine as markedly successful in treating gout: rating it at least 4 out of 5. It is important to acknowledge the subjective nature of this measure, which is open to various biases *e.g.* recall bias, and herbalists and/or

patients perceiving or reporter greater/lesser effects than might be assessed objectively (Podsakoff et al., 2003; van de Mortel, 2008).

A majority of herbalists reported the success of herbal treatment within the first month (39%; $n=31$) or two (37%; $n=29$): with acute gout responding significantly quicker than chronic gout. However, acute gout attacks usually resolve spontaneously over a few weeks (Roddy, 2011a), so it is hard to discern from this study, any effect(s) due to herbal treatment. Conversely, the reported success of herbal medicine in chronic gout may be considered more reliable: most report response within 1–2 or 3–4 months. This suggests that when no effect is found after 4 months it may be prudent for herbalists to reassess treatment.

4.8. *Evidence-base for the herbal treatment of gout*

The current evidence-base is weak. A single study was identified which suggested the herbal medicine tested was effective, however, there were issues regarding quality resulting in unclear or high risks of bias. Thus, further high-quality studies are required to elucidate the effectiveness of herbal medicine in treating patients with gout.

4.9. *Limitations of the study*

Along with the limitations already mentioned in the discussion, there are several additional considerations:

- Herbal texts: most texts included in this study were recent publications (≤10 years old), as access to older texts was difficult and further compounded by time constraints. Reference to a greater body of historical works would have provided more balance and may have identified additional herbs previously used for gout.
- Sample bias: the survey was distributed to NIMH members only, while the largest professional body in the UK it must be recognised that it only represents a fraction of the practitioners of Western herbal medicine. Consequently, the applicability of the results to the wider herbal community is unclear.
- Form of gout: while herbalists indicated whether they had treated chronic and/or acute gout, the survey did not allow those who had treated both to answer the subsequent questions separately for the two forms, which may have elucidated the results further.
- Orthodox medication: the use of orthodox medication by some patients confounds the results of this survey. Many herbalists reported treating patients with gout already on orthodox medicine, but the survey did not clarify if these patients continued with orthodox drugs or not whilst receiving herbal treatment. Furthermore, the survey did not allow herbalist who had treated both patients taking orthodox medicines and patients who did not, to separately report on the effectiveness (and time to success) of herbal treatment in these cases, which may have ascertained with more certainty the effects of the herbal treatment.
- Comorbidities: the orthodox drugs and herbal actions reported indicated some patients had comorbidities. A question requesting comorbidities to be documented may have helped to elucidate some of the treatment choices and recommendations further.

5. Conclusion

This study provides insight into the contemporary treatment of gout with herbal medicine. A survey of herbal practitioners indicated that whilst a majority had treated gout, it was not regularly seen in practice. Nonetheless, when it did present, most practitioners reported a definite benefit to patients from herbal treatment, usually within one or two months of the commencement of treatment.

The main herbs used in clinical practice were chosen on the basis of their ability to address the inflammatory nature of gout and associated uric acid excess. Two herbs, *A. graveolens* and *Urtica* spp, were strongly linked with gout; they were the favourite practitioner choices and also cited most in herbal texts. Their popularity for treating gout was largely due to their use as diuretics and to eliminate uric acid: reasons also given for *T. officinale*'s frequent inclusion in prescriptions too. Additionally, *H. procumbens*, *F. ulmaria*, *Salix* spp, *Betula* spp, *C. longa* and *Guaiacum* spp. were popular practitioner choices attributed primarily with anti-inflammatory but also analgesic and/or anti-rheumatic or gout-specific activities. Furthermore, it is important to emphasis that herbal practitioners usually dispense a mixture of herbs, covering a range of actions, it is therefore difficult to attribute the effectiveness of any herbal treatment to a single herb.

The current evidence base for the herbal treatment of gout was found lacking: with only *in vitro* studies of individual constituents and less frequently *in vivo* animal studies for the majority of herbs. Clinical trials to date, with the exception of the one trial included in the evidence review, have been exclusively of TCM-formulae which include many herbs not in the Western herbal medicine *materia medica*. Furthermore, the one clinical trial identified was of questionable quality with unclear or high risks of bias.

In light of the benefit of herbal medicine to patients with gout reported by practitioners and the paucity of a clinical evidence-base, both identified in this study, further research is justified. This includes the systematic collection of clinical treatment outcomes in practice, together with well-designed pragmatic clinical trials to establish the effectiveness of herbal medicine in treating patients with gout.

Acknowledgements

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Appendix A.

MEDLINE search protocol

1 EXP gout/
2 gout$.ti,ab.
3 podagra.ti,ab.
4 arthragra.ti,ab.
5 chiragra.ti,ab.
6 toph$.ti,ab.
7 hyperuricemia/

8 hyperuric?emia.ti,ab.
9 hypouric?emic.ti,ab.
10 or/1-9
11 EXP pharmacognosy/
12 EXP Phytotherapy/
13 Plants, Medicinal/
14 EXP medicine, traditional/
15 EXP Plant Extracts/
16 EXP Plant Oils/
17 Ethnopharmacology/
18 Ethnobotany/
19 herb$.ti,ab.
20 (plant or plants).ti,ab.
21 phytotherap$.ti,ab.
22 phytomedicin$.ti,ab
23 botanical$.ti,ab
24 pharmacognosy.ti,ab.
25 ethnopharmacolog$.ti,ab.
26 ethnomedicin$.ti,ab.
27 ethnobotan$.ti,ab.
28 or/11-27
29 10 and 28

Appendix B.

The postal survey was formatted so that it consisted of a cover letter and a 2-sided single sheet of A4 on which the questionnaire was printed. Below is a slightly reformatted version of the survey, so that it falls within the margins requirement of this current document: horizon grey lines delimit pages.

Western Medical Herbalist's treatment of Gout

1. How long have you been practising as a Medical Herbalist? _____ years

2. Have you ever treated a patient with Gout? (please circle) Yes / No (If No, please go to **Q12**)

3. In the last ***five*** years how many patients with gout have you treated? _____ patients

a. How many of these patients with gout were female? _____

4. Please indicate whether your experience of treating patients with gout includes (tick one only):
☐ Acute gout only ☐ Chronic gout only ☐ Both, Acute and Chronic gout

5. What specific symptoms and consequences associated with gout did patients seek treatment for? (tick all that apply)

a. Please rank the 3 most common in descending order of frequency (1-most to 3– least common).

	Rank			Rank	
☐	____	Joint pain	☐	____	Joint stiffness
☐	____	Swollen joint(s)	☐	____	Joint tenderness
☐	____	'Hot' joint(s)	☐	____	Erythema/rednes
☐	____	Dry skin	☐	____	Pruritic/itchy skin
☐	____	Skin ulceration	☐	____	Tophus/tophi
☐	____	Fever	☐	____	Malaise
☐	____	Low mood	☐	____	Mobility problem
☐	____	Other, please specify			

_____

6. Which herbs have you prescribed for gout? Please identify at least 3 and place in descending order of preference.

Space is also provided should you wish to provide the justification for use of each e.g. action, energetic principle, *etc*

Herb	**Reason for use**
1. _____	_____
2. _____	_____

3. _____ _____

4. _____ _____

5. _____ _____

7. In what form were the herbs identified in Question 6 prescribed? (please tick all that apply)

Herb	Tea	Tincture	Capsule	Topical	Other, please specify
1.	☐	☐	☐	☐	☐ _____
2.	☐	☐	☐	☐	☐ _____
3.	☐	☐	☐	☐	☐ _____
4.	☐	☐	☐	☐	☐ _____
5.	☐	☐	☐	☐	☐ _____

8. What, if any, orthodox medications were patients taking (please tick all that apply)

- ☐ None
- ☐ Painkillers *e.g.* Paracetamol, codeine
- ☐ Non-steroidal anti-inflammatory drugs *e.g.* ibrufen, aspirin
- ☐ Gastroprotective agents *i.e.* H2-receptor antagonists, misoprostol, proton-pump inhibitors
- ☐ Colchicine
- ☐ Oral corticosteroids *e.g.* prednisolone
- ☐ Corticosteroid injection(s)
- ☐ Urate-lowering drugs (please be as specific as possible, indicating type below):
  - ☐ Xanthine oxidase inhibitors *e.g.* Allopurinol, Febuxostat
  - ☐ Uricosuric agent *e.g.* Sulfinpyrazon, Probenecid, Benzbromarone
  - ☐ Pegloticase
  - ☐ Anakinra
- ☐ Other, please specify

_____ _____

9. In your experience of treating gout, how effective, on a 1 to 5 scale, would you rate herbal medicine? (Please circle)

Totally ineffective **-1-** **-2-** **-3-** **-4-** **-5-** Very effective

10. If successful how long did it take for herbal treatment to work?

☐ <1 month ☐ 1-2 months ☐ 3-4 months ☐ 5-6 months ☐ >6 months ☐ N/A

11. Did you recommend any lifestyle or dietary modifications? (please circle) Yes / No

a. If yes, please provide further details of the recommendations given in the box below.

12. In the last ***five*** years how many patients have you treated? _____ patients (in total)

13. Please add any further comments you feel are relevant here:

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