REVIEW

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A review of phytotherapy of gout: perspective of new pharmacological treatments

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The purpose of this review article is to outline plants currently used and those with high promise for the development of anti-gout products. All relevant literature databases were searched up to 25 March 2013. The search terms were 'gout', 'gouty arthritis', 'hyperuricemia', 'uric acid', 'xanthine oxidase (XO) inhibitor', 'uricosuric', 'urate transporter 1(URAT1)' and 'glucose transporter 9 (GLUT9)'. Herbal keywords included 'herbal medicine', 'medicinal plant', 'natural products', 'phytomedicine' and 'phytotherapy'. 'anti-inflammatory effect' combined with the words 'interleukin-6 (IL-6)', 'interleukin-8 (IL-8)', 'interleukin-1β (IL-1β)', and 'tumor necrosis factor α (TNF-α)'. XO inhibitory effect, uricosuric action, and anti-inflammatory effects were the key outcomes. Numerous agents derived from plants have anti-gout potential. In *in vitro* studies, flavonoids, alkaloids, essential oils, phenolic compounds, tannins, iridoid glucosides, and coumarins show the potential of anti-gout effects by their XO inhibitory action, while lignans, triterpenoids and xanthophyll are acting through their anti-inflammatory effects. In animal studies, essential oils, lignans, and tannins show dual effects including reduction of uric acid generation and uricosuric action. Alkaloids reveal inhibit uric acid generation, show anti-inflammatory effects, or a combination of the two. Phenolic compounds and flavonoids inhibit uric acid production, show uricosuric anti-inflammatory effects. In the rare human studies, colchicine from *Colchicum autumnale* showed anti-inflammatory effects while for other plant extracts, although revealing anti-gout potential, further phytochemical investigations are needed to identify their active constituents. Besides, the plants which give antioxidant activities are much potent in the management of gout and need to be further investigated. The current review is a detailed discussion of the potential of medicinal plants for treatment of gout.

1. Introduction

Gout is a common medical problem whose prevalence is increased with increasing age and reaches 9% in men and 6% in women older than 80 years of age. The Rochester Epidemiology Project has indicated that primary gout (that is, patients without diuretic exposure) incidence doubled over the past years (Arromdee et al. 2002). Gout is mediated by the supersaturation and crystallization of uric acid within the joints.

Hyperuricemia is viewed as a necessary but not sufficient precondition for the development of urate crystal deposition disease. The amount of urate in the body depends on the balance among dietary purine intake, endogenous purine synthesis, and renal excretion. Hyperuricemia results from the overproduction of urate (10%), from underexcretion of urate (90%), or often a combination of the two. Approximately one third of urate elimination inside the body occurs in the gastrointestinal tract, with the remainder excretes in the urine (Choi et al. 2005). Microcrystals of monosodium urate monohydrate (MSU) that precipitate in joint tissues from supersaturated body fluids or are shed from preexisting articular deposits result in inflammatory response, namely acute gouty arthritis (Schumacher 1996; Terkeltaub 2006). Thus, gout can be divided into two types: chronic gout which is always accompanied by hyperuricemia, and acute gout.

There are three stages in the management of gout: (i) treating the acute attack; (ii) lowering excess stores of uric acid to prevent flares of gouty arthritis and to prevent tissue deposition of urate; and (iii) providing prophylaxis to prevent acute flares (Schlesinger 2004). Thus, approaches to treat gout have inspired mechanism-based therapies that decrease uric acid production, promote renal uric acid excretion or depress urate reabsorption, and resist inflammation.

Urate-lowering therapy is generally believed to be the most effective way to treat chronic gout with hyperuricemia (Schlesinger 2004). The goal of anti-hyperuricaemic therapy is to reduce serum uric acid levels below the threshold required for supersaturation of extracellular fluid, thus decreasing the incidence of recurrent attracts of gout arthritis (Borges et al. 2002). XO is an enzyme that catalyzes the final two steps in purine catabolism, ultimately generating uric acid, therefore, XO inhibitors are employed as a significantly effective meditator by the suppression of uric acid generation in the treatment of gout (Borges et al. 2002). The use of uricosuric agents is another powerful uric-lowering therapy in the management of gout, instead of inhibiting uric acid production, as this method

exerts its effect by promoting uric acid excretion. In detail, uricosuric agents can modulate human URAT1, GLUT9 and organic anion transporter 1(OAT1) (Shi et al. 2012). Advances in the understanding of crystal-induced inflammation indicate that gout shares many pathogenetic features with other inflammatory disorders. Cytokines and chemokines that play a role in gouty inflammation include IL-1β, TNFα, IL-6, IL-8, granulocyte colony-stimulating factor, CXCL1 (KC, Groα), chemokine (C-C motif) ligand 2 (CCL2, monocyte chemoattractant protein-1), chemokine (C-C motif) ligand 3 (macrophage inflammatory protein-1), Leucocytes, neutrophils, macrophages, and so on are the cells most studied in gouty inflammation (Busso and So 2010). Therefore, some potent anti-inflammatory medications may have therapeutic potential in selected subsets of patients with gout. It is noteworthy that the natural remedies, particularly medicinal plants with anti-inflammatory effect for gout are typically used to treat acute gout or to reduce the risk for rebound gout attacks during the initiation of urate-lowering therapy but do not lower serum levels of uric acid (Choi et al. 2005).

For thousands of years, natural products especially the plant medicines have played a highly significant role all over the world in the treatment and prevention of human diseases (Chin et al. 2006). Natural products discovered from medicinal plants have provided numerous clinical useful medicines and can be predicted to remain an essential component in the search for new medicines (Balunas and Kinghorn 2005). Because current treatments for gout result in undesirable side effects and tend to be expensive, natural products devoid of such disadvantages offer a great opportunity. Thus, we focus on the medicinal plants and their active chemical constituents currently used and those with the potential to be developed as anti-gout medications in the future. The anti-gout effects of these medicinal plants include three mechanisms i.e. the decrease of uric acid production, uricosuric effects and anti-inflammatory activities (as shown in Tables 1 , 2 and 3).

2. Methods

We used the following key words: 'gout', 'gouty arthritis', 'hyperuricemia', 'uric acid', 'XO inhibitor', 'uricosuric', 'URAT1' and 'GLUT9'. Herbal keywords included, 'herbal medicine', 'medicinal plant', 'natural products', 'phytomedicine' and 'phytotherapy'. 'Anti-inflammatory effect' combines with the words 'IL-6', 'IL-8', 'IL-1β' and 'TNF-α'. Additionally, the reference lists of articles were reviewed for extra relevant studies.

3. Results

3.1. Reduction of uric acid generation — XO inhibitory effect

3.1.1. In vitro studies

To identify the compounds with anti-XO properties of *Amyena scandens* Danser (Loranthaceae), Electrospray Tandem Mass Spectrometry (ESI-MS-MS) coupled with UV and Diode Array LC techniques were employed, results indicated that Galloyl-containing oligomeric proanthocyanidins might be the main contributor of the XO inhibitory effect (Gariboldi et al. 1998). Some Indian medicinal plants used for the treatment of gout and related symptoms were tested for their XO inhibitory activity, among all the medicinal plants, the hydroalcoholic extract of *Coccinia drandis* and *Vitex negundo* leaves, the methanolic extract of *Datura metel* and *Strychnos nux-vomica* leaves, showed excellent inhibitory effects against XO (Umamaheswari et al. 2007). In addition, *Erythrina stricta*, another Indian medicinal plant, the chloroform fraction of its hydromethanolic extract of the leaves exhibited significant XO inhibitory potency, followed by the pet-ether, ethyl acetate. The presence of phenolic and flavonoid content in the extract would have contributed towards XO inhibition (Umamaheswari et al. 2009). Screening of potential XO inhibitors from 122 Chinese medicinal plants demonstrated that many of those medicinal plants, for example, *Glechoma longituba*, *Lycopus eruopaeus* and *Scutellaria barbata* exhibited strong effects while the methanol extract of the twig of *Cinnamomum cassia* was the most active (Kong et al. 2000). Besides, according to some relative phytochemical researches of those medicinal plants (Chang et al. 1996; Chang and Chiang 1995; Cos et al. 1998; Jayatilake et al. 1993; Reddy and Lokesh 1994; Zhou et al. 1999), it can be predicted that most of the natural XO inhibitors presented in the active extracts might be polyphenols. *Chrysanthemum sinense* was determined to be the most potent XO inhibitor among all of the plants, furthermore, its active compounds caffeic acid, luteolin, eriodictyol and 1,5-di-*O*-caffeoylquinic acid have also demonstrated significant XO inhibition (Nguyen et al. 2004). Extracts prepared from hydrodistillation of *Cinnamomum osmophloeum* leaves presented strong XO inhibition activity. The essential oil presented in the plant might be the main contributor to the inhibitory effect among which cinnamaldehyde exhibited the most potent XO inhibition (Wang et al. 2008). Both of the extracts and the main polyphenolic compounds of *Geranium sibirium* showed relatively good antioxidant capacity and XO inhibitory effects, moreover, of the polyphenolic compounds separated from the ethyl acetate fraction, geraniin, corilagin and gallic acid showed XO inhibitory capacity (Wu et al. 2010). *Hyoscyamus reticulatus*, *Achillea fragrantissima*, *Pimpinella anisum, Origanum syriacum* and *Origanum vulgare* inhibited XO, and results indicated that *Hyoscyamus reticulatus* had the most potent XO inhibitory potential (Bustanji et al. 2011).

Aapigenin-4'-*O*-(2″-*O*-*p*-coumaroyl)-β-D-gluco-pyranoside, from *Palhinhaea cernua*, showed good XO inhibitory activity, this result highlighted the fact that acylated flavones glycosides in plants are deserving multidisciplinary attention (Jiao et al. 2006). *Populus nigra* and *Betula pendula* were identified to have significant XO inhibition among 27 plant species from the Czech Republic (Havlik et al. 2010). *Phyllanthus niruri* gave strong *in vitro* XO inhibition by its methanolic extract of leaves. However, *in vivo* studies indicated that the antihyperuricemic effect of *Phyllanthus niruri* methanol extract may be mainly due to its uricosuric action and partly through XO inhibition (Murugaiyah and Chan 2009). Although the phytochemical screening in this study revealed that phyllanthin, hypophyllanthin, phyltetralin and niranthin the researchers isolated from the active fraction did show relatively poor XO inhibition effect, it can be speculated by the previous studies that the other compounds like flavanoids, polyphenols and tannins that *Phyllanthus niruri* contains may be responsible for the observed XO inhibitory activity. Screening of Piperaceous plants for XO inhibitors revealed that the extract of the leaves of *Piper betle* possessed potent activity. Activity-guided purification obtained hydroxychavicol as an active principle. It is noteworthy that hydroxychavicol is a more potent XO inhibitor than allopurinol in this test system (Murata et al. 2009). Extracts of *Pistacia integerrima* showed both *in vitro* and *in vivo* XO inhibition, it was believed that the presence of flavonoids including quercetin-3-*O*-β-D-glucopyranoside, rutin, kaempferol-3-*O*-β-D-glucopyranoside, quercetin-3-*O*-(6″-*O*-syringyl)-β-D–glucopyranoside, and kaempferol-3-*O*-(4″-*O*-galloyl)-α-L-arabinopyranoside, acquired from *Pistacia integerrima* were responsible for inhibitory effect (Ahmad et al. 2008). Some flavonol glycosides and more specifically kaempferol and quercetin glycosides isolated from two legume plant extracts, *Vicia faba* and *Lotus edulis*,

Table 1: *In vitro* studies considering anti-gout effect of plants

Plant	Family	Part of use	IC_{50}/EC_{50}	Active compound	Effect	References
Acacia confusa Merr	Leguminosae	Ethanol extract of heartwood	IC_{50} is 0.076 μM for okanin and 0.274 μM for melanoxetin	Okanin and melanoxetin	Reduction of uric acid generation activity	(Tung and Chang 2010)
Amyena scandens	Loranthaceae	Acetone-water extract of leaves	IC_{50} is 58.9 μg/ml	Galloyl-containing oligomeric proanthocyanidins	Reduction of uric acid generation activity	(Gariboldi et al. 1998)
Angelica sinensis	Umbelliferae	Methanol extract of rhizome	IC_{50} is 40 μg/ml		Reduction of uric acid generation activity	(Kong et al. 2000)
Arctium lappa L.	Compositae	80% ethanol extract of seeds		Arctigenin	Anti-inflammatory activity (inhibition of TNF-α, IL-6)	(Zhao et al. 2009)
Artemisia anomala	Asteraceae	Methanol extract of whole plant	IC_{50} is 36 μg/ml for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)
Artemisia vulgaris L.	Asteraceae	Methanol extract of leaves	IC_{50} is below 20 μg/ml for crude extract		Reduction of uric acid generation activity	(Nguyen et al. 2004)
Betula pendula Roth	Betulaceae	Methylene chloride–methanol extracts of leaves	IC_{50} is 8.3 μg/ml for crude extract	Total phenol content.	Reduction of uric acid generation activity	(Havlik et al. 2010)
Blumea balsamifera L.	Asteraceae	Methanol extract of aerial parts	IC_{50} is below 20 μg/ml for crude extract		Reduction of uric acid generation activity	(Nguyen et al. 2004)
Bridelia ferruginea	Euphorbiaceae	Acetone extract of stem bark	IC_{50} is 27.3 ± 3.8 μg/mL; 2.41 ± 0.21 μg/mL; 20.3 ± 1.7 μg/mL; 2.60 ± 0.05 μg/mL; for active compounds respectively	3-O-Methylquercetin, myricetin, quercetin 3-O-glucoside, quercetin	Reduction of uric acid generation activity	(Cimanga et al. 2010)
Caesalpinia sappan L.	Caesalpiniaceae	Methanol extract of wood	IC_{50} is below 20 μg/mL for crude extract		Reduction of uric acid generation activity	(Nguyen et al. 2004)
Chrysanthemum indicum	Asteraceae	Methanol extract of flowers	IC_{50} is 22 μg/mL	Luteolin and apigenin	Reduction of uric acid generation activity	(Kong et al. 2000)
Chrysanthemum sinense SABINE	Asteraceae	Methanol extract of flowers	IC_{50} is 5.1 μg/mL for crude extract and 1.3 μM for luteolin	Caffeic acid, luteolin, eriodictyol and 1,5-di-*O*-caffeoylquinic acid	Reduction of uric acid generation activity	(Nguyen et al. 2004)
Cinnamomum osmophloeum	Lauraceae	Extract prepared from hydrodistillation of leaves	IC_{50} is 16.3 ± 0.2 μg/mL	Cinnamaldehyde	Reduction of uric acid generation activity	(Wang et al. 2008)
Cooccinia drandis Voigt	Curcubitaceae	Hydroalcoholic extract of leaves	IC_{50} is 21.25 μg/mL for crude extract		Reduction of uric acid generation activity	(Umamaheswari et al. 2007)
Datura metel	Solanacecae	Methanol extract of leaves	IC_{50} is 76.75 μg/mL for crude extract		Reduction of uric acid generation activity	(Umamaheswari et al. 2007)
Erythrina stricta	Papilionacecae	Hydromethanolic extract of leaves	IC_{50} is 21.2 ± 1.6 μg/mL; 30.2 ± 2.2 μg/mL; 44.9 ± 1.4 μg/mL, respectively	Phenolic and flavonoid	Reduction of uric acid generation activity	(Umamaheswari et al. 2009)

Table 1: (Continued)

Plant	Family	Part of use	IC_{50}/EC_{50}	Active compound	Effect	References
Eucommia ulmoides Oliv	Eucommiaceae	Methanol extract of whole plant			Anti-inflammatory activity (by reducing TNF-α, IL-8, IL-1β)	(Tsai et al. 2010)
Fraxinus rhynchophylla	Oleaceae	Methanol extract of bark	IC_{50} is 28 μg/mL for extracts	Fraxetin and esculetin	Reduction of uric acid generation activity	(Kong et al. 2000)
Geranium sibiricum	Geraniaceae	Aqueous extract of leaves	IC_{50} is 129.88 μg/mL, 222.89 μg/mL and 105.41 μg/mL respectively for active compounds	Geraniin, corilagin and gallic acid.	Reduction of uric acid generation activity	(Wu et al. 2010)
Glechoma longltuba	Lamiatae	Methanol extract of whole plant	IC_{50} is 48 μg/mL		Reduction of uric acid generation activity	(Kong et al. 2000)
Hyoscyamus reticulatus	Solanaceae	Aqueous extract of leaves	IC_{50} is 12.8 μg/mL for crude extract		Reduction of uric acid generation activity	(Bustanji et al. 2011)
Ilex paraguariensis	Aquifoliaceae	Methanol extract of whole plant			Anti-inflammatory activity (by reducing TNF-α, IL-8, IL-1β)	(Tsai et al. 2010)
Inga verna	Fabaceae	Ethanol extract of branches and leaves	IC_{50} is 27.3 μg/mL (XO-inhibitory effect), 12.7 μg/mL (superoxide scavenging capacity) and 11.6 μg/mL (free radicals scavenging effects) for ethanolic extract, respectively	Ellagic and gallic acids	Reduction of uric acid generation, superoxide scavenging and free radicals scavenging activities	(Vivot et al. 2001)
Larix laricina	Pinaceae	Methanol extract of inner bark	86.3% XO inhibition at 100 μg/mL for crude extract	Phenols and tannin	Reduction of uric acid generation activity	(Owen and Johns 1999)
Ligusticum brachylobum	Umbelliferae	Methanol extract of rhizome	IC_{50} is 34 μg/mL for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)
Lotus edulis	Leguminosae	Methanol extract of aerial parts	IC_{50} is 410 μg/mL for crude extract	Luteolin-7-glucoside		(Spanou et al. 2012)
Lycopus europaeus	Lamiatae	Water extract of whole plant	IC_{50} is 26 μg/mL for crude extract	Luteolin-7-glucoside	Reduction of uric acid generation activity	(Kong et al. 2000)
Morinda morindoides	Rubiaceae	Extract of leaves	IC_{50} is 0.55 ± 0.09 μM and 0.75 ± 0.32 μM, for active compouds, respectively	Luteolin and apigenin	Reduction of uric acid generation activity	(Cimanga et al. 1999)
Morus alba	Moracecae	Methanol extract of twig	IC_{50} is 57 μg/mL for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)

Table 1: (Continued)

Plant	Family	Part of use	IC_{50}/EC_{50}	Active compound	Effect	References
Palhinhaea cernua		Ethanol extract of whole plant	IC_{50} is 23.59 ± 0.43 μg/mL for apigenin-4'-O-(2″-O-*p*-coumaroyl)-β-D-glucopyranoside	Apigenin-4'-O-(2″-O-*p*-coumaroyl)-β-D-glucopyranoside	Reduction of uric acid generation activity	(Jiao et al. 2006)
Phyllathus niruri	Euphorbiaceae	Methanol extract of leaves	IC_{50} is 39.39 μg/mL	Phyllanthin, hypophyllanthin and phyltetralin	Reduction of uric acid generation activity	(Murugaiyah and Chan 2009)
Myagropsis myagroides	Phaeophyta	80% methanol extract of whole plants		Fucoxanthin	Anti-inflammatory activity (inhibition of TNF-a, IL-1β, and IL-6)	(Heo et al. 2010)
Piper betle	Piperaceous	50% ethanol extract of leaves	IC_{50} is 16.7 μg/mL for 4-allyl-1,3-hydroxychavicol	4-allyl-1,3-hydroxychavicol	Reduction of uric acid generation activity	(Murata et al. 2009)
Piper kadsura	Pinaceae	Methanol extract of stems	IC_{50} is 28 μg/mL for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)
Pistacia integerrima	Anacardiaceae	Hydroalcoholic extract of leaves	IC_{50} is 19 μg/mL for n-BuOH and 20 μg/mL for ethyl acetate extracts, respectively.	Rutin, quercetin-3-O-β-D-glucopyranoside, kaempferol-3-O-β-D-glucopyranoside, quercetin-3-O-(6" -O-syringyl)-β-D –glucopyranoside, kaempferol-3-O-(4"-O-galloyl)-α-L-arabinopyranoside	Reduction of uric acid generation activity	(Ahmad et al. 2008)
Polygonum cuspidatum	Polygonaceae	Water extract of rhizome	IC_{50} is 38 μg/mL for crude extract	Resveratrol	Reduction of uric acid generation activity	(Kong et al. 2000)
Populus nigra L.	Salicaceae	Methylene chloride–methanol extracts of bark	IC_{50} is 25.9 μg/mL for crude extract	Total phenol content	Reduction of uric acid generation activity	(Havlik et al. 2010)
Salvia miltiorrhiza	Lamiaceae	Extract of roots	IC_{50} is 5.2 μg/mL and 1.08 μg/mL respectively, for active compounds,	Lithospermic acid	Reduction of uric acid generation and anti-inflammatory activities	(Liu et al. 2008; Soung et al. 2003)
Scutellaria barbata	Lamiatae	Methanol extract of leaves	IC_{50} is 46 μg/mL for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)
Sinofranchetia chinensis	Lardizabalaceae	Methanol extract of stem	IC_{50} is 49.3 μM for liquiritigenin and 55.8 μM for isoliquiritigenin	Liquiritigenin and isoliquiritigenin	Reduction of uric acid generation activity	(Kong et al. 2000)
Smilax china L.	Liliaceae	Ethyl acetate fraction from 80% ethanol extract of rhizome	IC_{50} is 250 μg/mL for ethyl acetate fraction, 42.60 μM for caffeic acid, 37.53 μM for resveratrol, 42.20 μM for rutin and 40.69 μM for oxyresveratrol, respectively.	Caffeic acid, resveratrol, rutin and oxyresveratrol	Reduction of uric acid generation activity	(Chen et al. 2011)

Table 1: (Continued)

Plant	Family	Part of use	IC_{50}/EC_{50}	Active compound	Effect	References
Smilax glabra	Liliaceae	Methanol extract of rhizome	IC_{50} is 33 μg/mL for crude extract		Reduction of uric acid generation activity	(Kong et al. 2000)
Stereospermum personatun	Bignoniaceae	Extracts of both stem and stem bark	IC_{50} is 54.2 μg/mL for acetone extract and 79.88 μM for specioside; SC_{50} is 6.78 μg/mL for acetone extract and 7.88 μM for verminocide	Specioside and verminocide	Reduction of uric acid generation and antioxidant (DPPH) activities	(Kumar et al. 2005)
Strychnos nux-vomica	Loganiaceae	Methanol extract of leaves	IC_{50} is 6.80 μg/mL		Reduction of uric acid generation activity	(Umamaheswari et al. 2007)
Tamus communis	Dioscoreaceae	85% aqueous methanol of whole plant	IC_{50} is 40 μg/mL for ethyl acetate extract	Polyphenol and flavonoid	Reduction of uric acid generation and antioxidant activities	(Boumerfeg et al. 2009)
Tetracera scandens L.	Dilleniaceae	Aqueous methanol of root and stem	IC_{50} is below 20 μg/mL for crude extract		Reduction of uric acid generation activity	(Nguyen et al. 2004)
Veratrum grandiflorum Loes,	*Liliaceae*	Extract of roots		Resveratrol (trans-3,5,40-trihydroxystibene)	Anti-inflammatory activity (downregulates inflammatory gene products such as IL-1b, and IL-6)	(Aggarwal et al. 2004; Shishodia and Aggarwal 2006)
Vicia faba	Leguminosae	Methanol extract of aerial parts	IC_{50} is 540 μg/mL for extract		Reduction of uric acid generation activity	(Spanou et al. 2012)
Vitex negundo	Lamiaceae	Hydroalcoholic extract of leaves	IC_{50} is 76.75 μg/mL		Reduction of uric acid generation activity	(Umamaheswari et al. 2007)

were demonstrated to be potent XO inhibitors (Spanou et al. 2012). Four phenolic compounds, isolated from the traditional African medicine *Bridelia ferruginea*, in addition to their superoxide scavenging activities, strong XO inhibition was also seen by the enzyme test system. Moreover, study of the structure–activity relationship demonstrated that for flavonoids, the XO inhibitory activity was reduced by methylation of the hydroxyl functionality at C-3 and in rings A and B (Cimanga et al. 2010). Lithospermic acid, derived from the roots of *Salvia miltiorrhiza*, showed both XO inhibition and antioxidant effects (Liu et al. 2008). The extracts of *Tamus communis L.* were efficient inhibitors of XO, and had significant antioxidant and free radical scavenging properties which could be attributed to phenolic compounds. The ethyl acetate extract reached the highest inhibitory effect level for sheep XO (Boumerfeg et al. 2009). Among the 14 constituent flavonoids of *Morinda morindoides*, luteolin and apigenin turned out to be the most potent inhibitors of XO activity, whereas chrysoeriol 7-neohesperidoside and aglycones chrysoeriol were devoid of any effect against XO activity and superoxide scavenging activity (Cimanga et al. 1999). Okanin and melanoxetin isolated from the ethyl acetate fraction of *Acacia confusa* Merr. (Leguminosae) were first demonstrated for their XO-inhibitory performance in Tung's study, and it is noteworthy that both of the two compounds performed better than allopurinol in this study (Tung and Chang 2010). The antioxidant and XO inhibitory potentials of *Stereospermum personatum* were reported, both the extract and the active compounds showed strong potential (Kumar et al. 2005). The methanol extract of the stem of *Sinofranchetia chinensis* inhibited the activity of XO *in vitro*. Bioassay-guided purification led to the isolation of liquiritigenin and isoliquiritigenin as the main XO inhibitors, in addition, the inhibition of enzyme activity was found to be dose dependent for both of the compounds (Kong et al. 2000). The ethanolic extract of *Inga verna* branches and leaves gave inhibitory properties of XO with an additional superoxide scavenging capacity, moreover, the antioxidant potential was also confirmed. The two main constituents ellagic and gallic acid may be responsible for its multifarious active properties (Vivot et al. 2001). Among 288 extracts, prepared from 96 medicinal plants used in Vietnamese traditional medicine to treat gout and related symptoms, the methanol extracts of *Artemisia vulgaris*, *Caesalpinia sappan*, *Blumea balsamifera*, *Chrysanthemum sinense* and methanol–water extract of *Tetracera scandens* exhibited strong XO inhibitory activity. *Larix laricina* exhibited the highest XO inhibitory activity among 26 species plants traditionally used for the treatment of gout and related symptoms by indigenous people of northeastern North America. The effect was indicated to be positively correlated with its phenolic content, and tannin content (Owen and Johns 1999). *Smilax china* L. and four of its ingredients, caffeic acid, resveratrol, rutin and oxyresveratrol showed *in vitro*

Table 2: Animal studies considering anti-gout effect of plants

Plant	Family	Part of use	Active compound	Dose	Animal	Effect	Reference
Acanthopanax senticosus	Araliaceae	70% ethanol extract of herbal roots mixtures		100 mg/kg body weight oral per day for mixed extracts (for 6 days)	Neutrophilic inflammation rats	Anti-inflammatory activity	(Jung et al. 2007)
Angelica sinensis	Umbelliferae						
Scutellaria baicalensis	Labiatae						
Achyranthes bidentata BL *Atractylodes lancea* DC *Phellodendron chinense* Schneid	Amaranthaceae Asterceae Rutaceae	Extract of powdered mixture materials (phellodendron cortex, atractylodes rhizome and achyranthes root)		978 mg/kg body weight oral per day	Hyperuricemic mice	Reduction of uric acid generation, decrease of urate reabsorption and enhance urate excretion activities	(Wang et al. 2010)
Biota orientalis	Cupressaceae	Ethanol extract of whole plant	Quercetin and rutin	100 mg/kg body weight oral per day (for 3 days)	Hyperuricemic mice	Reduction of uric acid generation activity	(Zhu et al. 2004)
Cinnamomum cassia	Lauraceae	Methanol extract of stem bark	Cassia oil (Cinnamaldehyde)	600 mg/kg body weight oral per day for cassia oil	Hyperuricemic mice	Reduction of uric acid generation and uricosuric activities (by blocking UAT activation)	(Zhao et al. 2006)
Cinnamomum osmophloeum	Lauraceae	Extract prepared from hydrodistillation of leaves	Cinnamaldehyde	(Cinnamaldehyde) 150 mg/kg body weight oral per day	Hyperuricemic mice	Reduction of uric acid generation activity	(Wang et al. 2008)
Cooccinia drandis	Curcubitaceae	Hydroalcoholic extract of leaves	-	200 mg/kg body weight oral per day	Hyperuricemic mice	Reduction of uric acid generation activity	(Umamaheswari et al. 2007)
Dinocarpus longan Lour	Sapindaceae	Water extract of seed	Gallic acid, corilagin, ellagic acid	80 mg/kg body weight intraperitoneally per day for crude extract	Hyperuricemic rats	Reduction of uric acid generation and uricosuric activities	(Hou et al. 2012)
Dioscorea nipponica Makino	Dioscoreaceae			0.8 mg/kg body weight oral per day (for five days)	Gouty arthritis rats	Anti-inflammatory activity	(Yao et al. 2012)
Emblica officinalis G.	Euphobiaceae	Triphala powder, an Indian ayurvedic herbal formulation) (mixture of dried and powdered fruits of the three plants in equal proportions)		1 g/kg body weight oral per day	Gouty arthritis mice	Anti-inflammatory activity	(Sabina and Rasool 2008)
Terminalia belerica L.	Combretaceae						
Terminalia chebula R.	Combretaceae						

Table 2: (Continued)

Plant	Family	Part of use	Active compound	Dose	Animal	Effect	Reference
Jatropha isabellei	Euphorbiaceae	70% ethanol extract of the rhizome	Alkaloids	300 mg/kg body weight oral per day for crude extract	Gouty arthritis rats	Anti-inflammatory and pain relief activities	(Silva et al. 2012)
Lodendron chinense	Rutaceae	Water extract of cortex	Berberine	480 mg/kg body weight oral per day	Hyperuricemic mice and normal mice	Reduction of uric acid generation activity	(Kong et al. 2004)
Lychnophora trichocarpha	Asteraceae	Ethanol extract of aerial parts	Apigenin (XO inhibition), luteolin, apigenin, lupeol, lychnopholide and eremantholide	250 mg/kg body weight oral per per day for crude ethanolic extract	gouty arthritis mice	Anti-inflammatory and urate-lowering activities	(de Souza et al. 2012)
Mangifera indica L.	Anacardiaceae	Ethanol extract of leaves		100, 200 mg/kg body weight by oral per day for crude extract	Gouty arthritis rats	Anti-inflammatory activity	(Jiang et al. 2012)
Morus alba L.	Moraceae	Extract of twigs	Morin (3,5,7,2',4'-Pentahydroxy-flavone)	5, 10, 20 mg/kg body weight by oral per day	Hyperuricemic rats	Reduction of uric acid generation and uricosuric activities	(Yu et al. 2006)
Morus alba L.	Moraceae	60% ethanol extract of twigs	Mulberroside A		Hyperuricemic mice	Uricosuric activity	(Wang et al. 2011)
Morus alba L.	Moraceae	95% ethanol extract of branches	Mulberroside A, resveratrol, rutin, quercetin and morin	10, 20 and 40 mg/kg body weight for crude extract by oral per day	Hyperuricemic and normal mice	Uricosuric activity	(Shi et al. 2012)
Paederia scandens LOUR.	Rubiaceae	70% ethanol extract of aerial parts		2.25, 4.5 g/kg body weight oral per day (for 9 days)	Gouty arthritis rats	Anti-inflammatory activity	(Ma et al. 2009)
Phyllanthus niruri	Euphorbiaceae	Methanol extract of leaves	Phyllanthin, hypophyllanthin and phyltetralin	50 mg/kg body weight oral per day for methanol extract and 10 mg/kg for phyllanthin, hypophyllanthin and phyltetralin	Hyperuricaemic rats	Reduction of uric acid generation and uricosuric activities	(Murugaiyah and Chan 2009)
Piper nigrum L.	Piperaceae		Piperine	30 mg/kg body weight oral per day	Gouty arthritis mice	Anti-inflammatory activity	(Sabina et al. 2011)
Pistacia integerrima	Anacardiaceae	Ethyl acetate fraction of hydroalcoholic extract of leaves	Rutin, quercetin-3-O-β-D-glucopyranoside, kaempferol-3-O-β-D-glucopyranoside, quercetin-3-O-(6''-O-syringyl)-β-D–glucopyranoside, kaempferol-3-O-(4''-O-galloyl)-α-L-arabinopyranoside	80 mg/kg body weight oral per day	Hyperuricemic mice	Reduction of uric acid generation activity	(Ahmad et al. 2008)

Table 2: (Continued)

Plant	Family	Part of use	Active compound	Dose	Animal	Effect	Reference
Salvia mitiorrhiza	Lamiaceae	Extract of roots	Lithospermic acid	10, 20 and 30 mg/kg body weight by oral per day respectively	Gouty arthritis model rats	Reduction of uric acid generation and antioxidant activities	(Liu et al. 2008; Soung et al. 2003)
Smilax china L.	Liliaceae	Ethyl acetate fraction from 80% ethanol extract of rhizome	Caffeic acid, resveratrol, rutin and oxyresveratrol	125–500 mg/kg body weight by oral per day for ethyl acetate fraction	Hyperuricemic rats	Reduction of uric acid generation and fractional excretion of urate activities	(Chen et al. 2011)
Vitex negundo	Lamiaceae	Hydroalcoholic extract of leaves		200 mg/kg body weight by oral per day	Hyperuricaemic mice	Reduction of uric acid generation activity	(Umamaheswari et al. 2007)
Vitis vinifera	Chardinnay and Shiraz	Aqueous acetone of seeds	Procyanidins	200 mg/kg body weight by oral per day (for 3 days) for aqueous acetone faction	Hyperuricaemic mice	Reduction of uric acid generation activity	(Wang et al. 2004)

suppression of XO action, as well as *in vivo* anti-hyperuricemic effect when orally administrated in hyperuricemic rats, and the anti-hyperuricemic effect may due to both XO inhibitory effect and fractional excretion of urate activity (Chen et al. 2011).

3.1.2. Animal studies

The extract of *Biota orientalis* and its flavonoid constituents, quercetin and rutin elicited dose-dependent hypouricemic effects, as well as significant inhibitory actions on the XDH and XO activities when orally administered to hyperuricemic mice liver at doses of 100 mg/kg body weight, while intraperitoneal administration at the same scheme did not produce any observable hypouricemic effect. So the conclusion can be drawn that the hypouricemic effects are partly due to the inhibition of XDH/XO activities in mouse liver (Zhu et al. 2004). The extract of *Cinnamomum osmophloeum* prepared from hydrodistillation displayed a significant XO inhibitory activity in mice. The essential oil, especially cinnamaldehyde was determined as the most effective content of the extract (Wang et al. 2008). Cassia oil, isolated from *Cinnamomum cassia*, when orally administrated in hyperuricemic mice at 600 mg/kg was found to be as potent as allopurinol. The hypouricemic effects of cassia oil could be explained, at least partly, by inhibiting liver *in vivo* activities of xanthine dehydrogenase (XDH)/XO. Additionally, the urate transporter (UAT), which is responsible for the regulation of blood urate levels and displaying some similarities to the enzyme uricase, can be blocked by oxonate thus inducing hyperuricemic action. In this study, it was speculated that another mechanism of the hypouricemic action of cassia oil might be explained by activating the blocked UAT activity induced by oxonate in the hyperuricemia model of mice (Zhao et al. 2006). Oral administration of methanolic extracts of *Coccinia grandis* and *Vitex negundo* produced a significant decrease in the serum urate level which was similar to that of allopurinol (Umamaheswari et al. 2007). *Lodendron chinense* is one herb of *Ermiao wan*, a Chinese medicinal formula, the water extract possessed *in vivo* potent hypouricemic effects in both hyperuricemic mice and normal mice. Additionally, liver XDH and XO inhibitory effect were also found (Kong et al. 2004). From the previous study, the major component, berberine, seemed to be responsible for its XO inhibition (Chang et al. 1994). However, further studies should be undertaken to identify the compounds that are responsible for the inhibitory effect. *Phyllanthus niruri* methanol extract showed a moderate *in vivo* XO inhibitory activity, while treating with it intraperitoneally exhibited increase in urinary uric acid excretion, moreover, the active constituents, three lignans, phyllanthin, hypophyllanthin and phyltetralin of this plant showed better activity in increasing urinary uric acid excretion (Murugaiyah and Chan 2009). Lithospermic acid which was isolated from the roots of *Salvia miltiorrhiza* extract had marked *in vivo* hypouricemic and anti-inflammatory effects of rats through XO inhibitory effect and antioxidation (Liu et al. 2008). Procyanidins from grape (*Vitis vinifera*) seeds, when orally administrated to the oxonate-pretreated hyperuricaemic mice, apart from its dose-dependent hypouricaemic effect, significantly decreased the hepatic activities of XDH and XO. However, it seemed that except for the XO inhibitory activity, other mechanisms might be responsible for the hypouricaemic effect (Wang et al. 2004).

3.1.3. Human studies

No reports about human studies under this mechanism were found.

3.2. Uricosuric effect — increase of urate excretion and reduced urate reabsorption

3.2.1. Animal studies

Intraperitoneal injection of Longan seed (*Dimocarpus longan* Lour) extract in hyperuricemic rats resulted in the reduction of urate by modulating both XO and urate transporters (Hou et al. 2012).When being orally administrated to crystal-induced gouty arthritis rats, the ethanol extract from *Mangifera indica* L. (Anacardiaceae) was able to decrease ankle swelling significantly, the beneficial anti-gouty arthritis effect may be mediated by inhibiting TNF-α and IL-1β expression in the synovial tissues (Jiang et al. 2012). Both the extracts and constituents of *Morus alba* L. showed strong antyhyperuricemic effect by their uricosuric action. The ethanol extract of *Morus alba* L. significantly reduced serum urate levels and increased 24 h-urine

Table 3: Human studies considering anti-gout effects of plants

Plant	Family	Part of use	Active compound	Study design	NO. of subjects	Comparator	Duration of treatment	Effect	Reference
Achyranthes bidentata BL	Amaranthaceae	Extract of powdered mixture materials (phellodendron cortex, atractylodis rhizome, achyranthes root and coix seed)		A randomized, double-blind controlled parallel group clinical trial	60	Allopurinol	1week	Decrease of uric acid level activity	(Renbin et al. 2008)
Atractylodes lancea DC *Coix lacryma-jobi* L. *Phellodendron chinense* Schneid	Asteraceae Poaceae Rutaceae								
Colchicum autumnale	Lily	Extract of corm	Colchicine	A randomized, double-blind placebo-controlled parallel group clinical trial	45	Placebos (oral)	2days	Anti-inflammatory activity	(Ahern et al. 1987)
Krachiap daeng	Malvaceae	Prepared tea bag			9		15 days	Uricosuric and uric acid clearance activities	(Prasongwatana et al. 2008)
Hibiscus sabdariffa L.	Malvaceae	Water extract of whole plant		A randomized, double-blind parallel group clinical trial	36		different concentrations for various periods of time	Decreases in the urinary concentrations of creatinine, uric acid, citrate, tartrate, calcium, sodium, potassium and phosphate	(Kirdpon et al. 1994)

urate excretion, and fractional excretion of uric acid by regulating renal organic ion transporters in hyperucemic mice (Shi et al. 2012). Although the precise mechanisms and active compounds which are responsible for the urate-lowering effects are not completely understood, it can be speculated that stilbenes (mulberroside A and resveratrol), and flavonoids (rutin, quercetin and morin) may contribute by the regulation of renal organic ion transporters in hyperuricemia with kidney dysfunction. Of note, Morin (3,5,7,2',4'-pentahydroxyflavone), which occurs in the twigs of *Morus alba* L. has been previously demonstrated *in viv*o uricosuric action in hyperuricemic rats by acting on the kidney to inhibit urate reabsorption. Additionally, *in vitro* XO inhibitory action was also found in this study (Yu et al. 2006). In a further publication, uricosuric effects of morin in hyperuricemic mice have also been demonstrated, the active effects were exerted by suppressing urate reabsorption and promoting urate secretion in the kidney (Wang et al. 2010). Mulberroside A is a major stilbene glycoside of *Morus alba* L., which strongly decreased serum acid levels and increased urinary urate excretion in hyperucemic mice (10–40 mg/kg). Mulberroside A may elicit its uricosuric effect by inhibiting urate reabsorption via renal mGLUT9 and mURAT1, and promoting renal urate secretion via mOAT1in hyperuricemic mice (Wang et al. 2011). Quercetin, a flavonoid present in various plants, demonstrated increased urate excretion and reduced serum urate levels, as well as down-regulation of the renal expression levels of GLUT9 and URAT1 in hyperuricemic animals. The results indicated that quercetin might have the potential for the prevention of hyperuricemia with kidney dysfunction (Kong et al. 2012). *Sanmiao* wan is a traditional Chinese recipe composed of Phellodendri cortex, Atractylodes

rhizome and Achyranthes root. It produced dual hypouricemic actions by suppressing hepatic XO to reduce uric acid production and down-regulating renal mURAT1 to decrease urate reabsorption and enhance urate excretion in hyperuricemic mice (Wang et al. 2010).

3.2.2. Human studies

Tea made from dry *Hibiscus sabdariffa* was significantly effective in increasing uric acid excretion and clearance human models with and without a history of renal stones. Although many chemical constituents of this extract have already been identified, the one (or ones) that contributes to the uricosuric effect is required to be further established (Prasongwatana et al. 2008). Workers studied, in thirty-six normal Thai subjects, the changes in urine composition that follow the consumption of *Hibiscus sabdariffa* extract at different concentrations and for various periods of time (Kirdpon et al. 1994). It was demonstrated that consumption of *H. sabdariffa* extract resulted in significant decreases in the urinary concentrations of creatinine, uric acid, citrate, tartrate, calcium, sodium, potassium and phosphate. The traditional Chinese formula *Simiao Tang* was evaluated for its clinical effects in 60 subjects, results indicated that this recipe significantly improved the symptoms and signs of gouty arthritis by increasing excretion of uric acid. Besides, no significant side effect or reaction was found after taking *Simiao Tang* (Renbin et al. 2008).

3.3. Anti-inflammatory effects

3.3.1. In vitro studies

Arctigenin is a bioactive constituent from dried seeds of *Arctium lappa* L. (Compositae), it suppresses pro-inflammatory cytokines secretion, including TNF-α, IL-6 in a dose-dependent manner (Zhao et al. 2009). Duzhong (*Eucommia ulmoides* Oliv.), and Yerba mate (*Ilex paraguariensis*), in spite of their antimicrobial effect against *Propionibacterium acnes*, also showed anti-inflammatory activities by reducing the secretion of proinflammatory cytokines such as TNF-α, IL-8, IL-1β by human monocytic THP-1 cells (Tsai et al. 2010). It was suggested that the two medicinal plants have high potential to be used in the management of gouty arthritis. However, the phytochemicals which are responsible for both of those activities are still unknown, and further studies are needed. Lipopolysaccharide-stimulated RAW 264.7 macrophages were employed to assess anti-inflammatory effect of fucoxanthin, which was isolated from brown algae (*Myagropsis myagroides*, family: Phaeophyta). Results indicated that the release of TNF-a, IL-1β, and IL-6, and the mRNA expression levels of those cytokines were reduced by the addition of fucoxanthin in a dose-dependent manner (Heo et al. 2010). Resveratrol existed in various plants including hellebore (*Veratrum grandiflorum* Loes, family: Liliaceae), grapes, berries and peanuts (Shishodia and Aggarwal 2006), it has been identified *in vitro* anti-inflammatory agent because it can down-regulate inflammatory gene products such as IL-1b, and IL-6 (Aggarwal et al. 2004), all of which play a crucial role in gouty arthritis.

3.3.2. Animal studies

A mixture of root extracts from *Acanthopanax senticosus, Angelica sinensis and Scutellaria baicalensis* was demonstrated to diminish MSU crystal-induced inflammation by reducing neutrophil recruitment and expression of pro-inflammatory factors and increasing the level of the potentially anti-inflammatory PGD_2 (Jung et al. 2007). Protein-Chip technique has been employed in the investigation of anti-inflammatory mechanisms of Rhizoma *Dioscoreae Nipponicae* (Dioscoreaceae), it was demonstrated that this herbal medicine exerted its effect via up-regulating seven and down-regulating seven proteins, besides, both the tumor necrosis factor-related apoptosis-inducing ligand and neuropilin-2 could be identified as key contributors to the pathomechanism of acute gouty arthritis (Yao et al. 2012). Triphala is the most commonly used Indian ayurveda herbal formulation, comprising the fruits of three trees, *Emblica officinalis* Gaertn (Euphobiaceae), *Terminalia belerica* Linn (Combretaceae), and *Terminalia chebula* Retzr (Combretaceae). Evaluation of the effects of this formulation in MSU-induced gouty arthritis mice suggested that Triphala treatment at the dose of 1 g/kg body weight per day possessed anti-inflammatory effects as evidenced by a significant reduction of paw oedema, a remarkable inhibition of lysosomal enzyme release, a drastic reduction of lipid peroxidation levels, a significant increase in the anti-oxidant status, and a significant decrease of inflammatory mediator TNF -α (Sabina and Rasool 2008). The crude extract of *Jatropha isabellei* presented not only antinociceptive but also anti-inflammatory effects in a rat model of gouty arthritis, and it was acting in a way that was similar to the alkaloid colchicine, which might be due to the alkaloid constituents presented in this plant. However, a hypouricemic effect was not seen in a hyperuricaemic model (Silva et al. 2012). The ethanolic extract of *Lychnophora trichocarpa*, and its ethyl acetate fraction were demonstrated to elicit both anti-inflammatory and anti-hyperuricemic properties at the same time. Its active constituent, apigenin showed XO inhibitory activity *in vivo*, while other constituents, luteolin, lupeol, lychnopholide and eremantholide C exerted urate-lowering effects via other mechanisms rather than XO inhibition. Results also suggested that both the extract and fraction can limit monosodium urate (MSU)-induced acute inflammatory response which might be due to the combined effects of lupeol, β-sitosterol, lychnopholide, eremantholide C, luteolin and apigenin (de Souza et al. 2012). Piperine is an alkaloid from the family of Piperaceae, and it significantly decreased the levels of lysosomal enzymes, lipid peroxidation, TNF-α, and paw volume, and at the same time increased the activities of antioxidant status when orally administrated in MSU-induced mice. It is clear that piperine inhibits the MSU-induced inflammation and can be regarded as therapeutic drug for the treatment of acute gouty arthritis (Sabina et al. 2011). *Paederia scandens* (Lour.) Merrill (Rubiaceae) is a Chinese traditional herbal medicine. When given orally (2.25, 4.5 g extract/kg body weight) to gouty arthritis rats, inhibition of inflammatory response was observed. Results indicated that it possessed anti-inflammatory effects by down-regulating crystals-induced TNF-α and IL-1β production in synovial tissue and inactivating NF-κB pathway transmembrane signal transduction, which plays a crucial role in the pathogenesis of this disease (Ma et al. 2009). Lithospermic acid from *S. miltiorrhiza* showed suppressive effects on gouty arthritis. Its anti-inflammatory effect is mainly mediated through inhibiting the production of superoxide and direct superoxide scavenging (Liu et al. 2008).

3.3.3. Human studies

Colchicine, an alkaloid derived from autumn crocus *Colchicum autumnale* has been used to treat inflammatory diseases for more than 2000 years. The evidence basis for the effectiveness of the drug as an anti-inflammatory remains primarily limited to neutrophil-mediated and some (but not all) disorders characterized by periodic inflammation (Terkeltaub 2009). The effect of its anti-acute gouty action by reducing pain and inflammation has been established for many years. In the first and only con-

trolled double blind study of colchicine in acute gout to date, when given colchicine orally to 22 of the 45 subjects, 73% of the colchicine-treated group achieved a greater than 50% reduction in pain within 48 hours, however, gastrointestinal toxicity limited the potential for a full clinical response (Ahern et al. 1987).

4. Discussion

Gout is a metabolic disorder associated with abnormal amounts of uric acid in the body, resulting in the deposition of urate crystals in the joints and kidneys, causing inflammation as well as gouty arthritis. Uric acid level is the key factor for the prevention of gout and related disorders (Lin et al. 2000). Despite the protective role that the XO inhibitor allopurinol exerts on urate levels of hyperuricemia and gout, the side effects such as hypersensitivity syndrome (Singer and Wallace 2005), Stevens-Johnson syndrome (Fritsch and Sidoroff 2000) and renal toxicity (Horiuchi et al. 2000), is limiting its value. Uricosuric drugs such as benzbromarone, probenecid, sulfinpyrazone, or losartan are beneficial for uric acid excretion via inhibiting URAT1 and GLUT9 to various degrees (So and Thorens 2010). However, the risk of severe hepatoxicity has been a major concern with benzbromarone (Lee et al. 2008). Over the years, natural plant products comprise one of the most popular complementary and alternative medicines for inflammatory disorders for the superiority that medicinal plant therapies always comprise more than one active ingredient thus can treat inflammation through multiple targets (Yao et al. 2012). Accordingly, recent research interest is focused on searching for more effective and safer agents for gout from medicinal plants.

Under the three main mechanisms of pathogenesis, medicinal plants that can be potent in the treatment of gout are collected and described, together with their active phytochemicals. Ten classes of compounds derived from plants with anti-gout potential are extracted. Flavonoid compounds are very potent anti-gout mediators due to their multiple effects correlated with different mechanisms, including genistein, astilbin, apigenin, quercetin, myricetin, liquiritigenin, isoliquiritigenin, rutin, procyanidin, luteolin, apigenin-4'-O-(2″-O-p-coumaroyl)-β-D-glucopyranoside, and so on, exhibit *in vitro*, *in vivo*, or both of the two XO inhibitory effect even with different inhibition modes (Chen et al. 2011; Cimanga et al. 1999; Cimanga et al. 2010; Gariboldi et al. 1998; Huang et al. 2011; Jiao et al. 2006; Kong et al. 2000; Kong et al. 2012). Morin, rutin and quercetin reveal both XO inhibitory activity and uricosuric action (Shi et al. 2012; Yu et al. 2006). Luteolin and apigenin give anti-inflammtory effect (de Souza et al. 2012). Among phenolic compounds, eriodictyol, okanin, caffeic acid, oxyresveratrol, phenols, total phenol content from *Populus nigra* L. polyphenol show XO inhibitory activity (Boumerfeg et al. 2009; Chen et al. 2011; Havlik et al. 2010; Nguyen et al. 2004; Owen and Johns 1999; Tung and Chang 2010). Both resveratrol and lithospermic acid give not only XO inhibitory activity but also anti-inflammatory effects (Aggarwal et al. 2004; Liu et al. 2008; Shishodia and Aggarwal 2006; Soung et al. 2003). Tannin compounds like geraniin, corilagin and gallic acid elicit uricosuric action while ellagic acid is a XO inhibitor (Hou et al. 2012; Vivot et al. 2001; Wu et al. 2010). Berberine is a potent XO inhibitor (Kong et al. 2004), while other alkaloids, colchicine and piperine give very good anti-inflammatory activity (Ahern et al. 1987; Sabina et al. 2011). Of note, colchicine is a classical anti-gout drug with effects of both pain relief and inflammation resistance. Additionally, the crude extract of *Jatropha isabellei* that is rich of alkaloids also presents antinociceptive and anti-inflammatory effects (Silva et al. 2012). An essential oil component, cinnamaldehyde, shows dual urate-lowering effects, XO inhibitory and uricosuric action (Wang et al. 2008). The later effect is exerted via blocking UAT activation (Zhao et al. 2006). An iridoid glucoside, specioside and two coumarins, fraxetin and esculetin reveal XO inhibitory(Kong et al. 2000; Kumar et al. 2005). Lupeol, a triterpenoid, exerst anti-inflammatory effects (de Souza et al. 2012). The lignans, arctigenin exert anti-inflammatory activities through inhibition of the iNOS pathway (Zhao et al. 2009), other three lignans, phyllanthin, hypophyllanthin and phyltetralin exhibit both XO inhibitory and uricosuric action (Murugaiyah and Chan 2009). The only phytochemical compound isolated from phycophyta in this review is fucoxanthin, a kind of xanthophyll, possesses potential anti-inflammatory activity (Heo et al. 2010). Besides, according to some of the results (Boumerfeg et al. 2009; Kumar et al. 2005; Vivot et al. 2001; Wu et al. 2010), we suggest that plants which give antioxidant activities should be highly potent in the management of gout because they often share XO inhibitory effects. Furthermore, it is generally believed that plants with higher phenolic content show good antioxidant activity. In other words, there is a direct correlation between total phenol contents and antioxidant activity (Biglari et al. 2008; Brighente et al. 2007; Salazar et al. 2008). Thus it can be stated that the phenolic content of the plant may be a good indicator of its antioxidant capacity (Chanda and Dave 2009), and even of its potential to be used in anti-gout treatment. However, the mechanisms of anti-gout effect by the antioxidants are needed to be established in future studies.

Lifestyle factors, including adiposity and dietary habits, appear to contribute to serum uric acid levels and the risk for gout (Choi et al. 2005). Thus, we suggest that management of gout in patients should combine potent mediators with healthy lifestyle.

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