

## Review

# A review of medicinal plant species with elemene in China

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Some researchers suggest that many plant species or extracts have medicinal value; in particular, some have great antitumor potential. *Rhizoma curcuma* is the dried roots of *Curcuma phaeocaulis*, *C. kwangsinensis* and *C. wenyujing* in Chinese herbal medicine and the essential oil from it has been shown to inhibit tumor cell growth mainly due to its elemene component. Elemene has marked the characteristic of wide spectrum of antineoplastic activity and low adverse toxicity, especially  $\beta$ -elemene. Commercialized elemene injection is produced by *R. curcuma*, and applied as a national second-class new drug of antitumor in China. Literature reveals that many other plant species contain  $\beta$ -elemene or isomers in their essential oils from plant or parts of plant, and may represent a potential alternative to *R. curcuma* in the elemene processing industry and for use in antineoplastic medicine. This review summarizes the list of plants studied for their constituents of essential oils, and forty-four plant species are given much attention.

**Key words:** Elemene, plant species, medicine, *Rhizoma curcuma*.

## INTRODUCTION

Cancer has taken the leading cause of mortality all over the world and many drugs have been developed and are developing to treat it (Jemal et al., 2009). In China, various Chinese herbal medicines have also been developed and employed in cancer treatment. Many studies have demonstrated beneficial effects of Chinese herbal medicine or its extracts on the survival rates/time, quality of life and immune function of cancer patients when used alone or in conjunction with conventional therapies like chemotherapy (Zhou et al., 2005). Some Chinese herbal medicines have also been shown to increase the responsiveness of cancer to conventional therapies and to alleviate radiation-induced xerostomia, chemotherapy-

induced leucopenia, nausea and vomiting. Other studies have proved that some Chinese herbal medicines or extracts are beneficial for relieving symptoms related to cancer such as pain, and may offer an alternative approach to standard care for advanced cancer (Zhang, 2000; Wang et al., 2007), such as camptothecin, paclitaxel, and ginsenoside (Shen et al., 2010). Elemene is also one of the essential components extracted from *Rhizoma Curcuma* used in Chinese herbal medicine.

Since the groundbreaking works on elemene were conducted by Shi (1981) and Guo et al. (1983), interest in elemene has increased dramatically. Fu et al. (1994) isolated  $\beta$ -elemene,  $\gamma$ -elemene and  $\delta$ -elemene from *R. curcuma* which in Chinese herbal medicine is the dried roots of *Curcuma phaeocaulis*, *C. kwangsinensis* and *C. wenyujing*. Since then, many studies have been conducted and  $\beta$ -elemene has marked the characteristics of wide spectrum of antineoplastic activity, alleviating the aches cancer-caused, and increasing leukocyte improving

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immune function, synergetic effect with chemotherapy or radiotherapy, etc. Most importantly, it has been shown to have low adverse toxicity by contrast with most anti-cancer drugs used clinically (Tang et al., 2010; Rui et al., 2007). Elemene injection commercialized with the main ingredient  $\beta$ -elemene and a small amount of  $\gamma$ -elemene and  $\delta$ -elemene and other terpenoids, is produced by *R. curcuma* and has already been an application as a national second-class new drug of anti-tumor in China (Li et al., 2005). For the purpose of hunting for better water solubility and anti-tumor activity derivatives, structural modifications of  $\beta$ -elemene have been designed, such as glycoside derivatives containing heteroatom S or Se (Yang et al., 2008),  $\beta$ -elemene mono-substituted amino acid (Cheng et al., 2008), radioactive derivative of  $\text{Re}(\text{CO})_3$  (Cheng et al., 2007),  $\beta$ -elemene-13-yl alkyl selenides (Hong-Xing et al., 2008) etc. But none of these derivatives' anti-tumor activity has been examined. Another isomer,  $\gamma$ -elemene has also been determined from many plants and its anti-tumor activity has not been examined too (Figure 1).

Herbs have been the basis of traditional Chinese medicines and continue to provide new remedies to human kind; therefore, a great deal of effort has been devoted to identifying useful chemicals from plants. Actually, recent reports indicate that there are many plant species with elemene in their essential oils. In some of them, the relative contents of elemene are very high. However, only *R. curcuma* is used in the elemene processing industry up till now. This review covers medicinal species with high content of elemene, mostly native to China, and the purpose is to survey the total elemene content of medicinal plants and to evaluate potential sources for elemene injection for medicinal purposes. Of all the reviewed species, forty-four species listed subsequently were given much attention

## AN OVERVIEW OF THE METHODS USED TO ASSAY ELEMENE CONTENT

Elemene is one of the volatile natural compounds. Volatile compounds are usually referred to essential oils, which are liquid, volatile, limpid, insoluble in water and soluble in organic solvents with a generally lower density than that of water (Bakkali et al., 2008). Essential oil can be isolated from the plant's tissue by using distillation, solvent extraction, solid phase micro-extraction and supercritical fluid extraction. It has been found that gas chromatography-mass spectrometry (GC-MS) is the most common and reliable method to identify the component of essential oils.

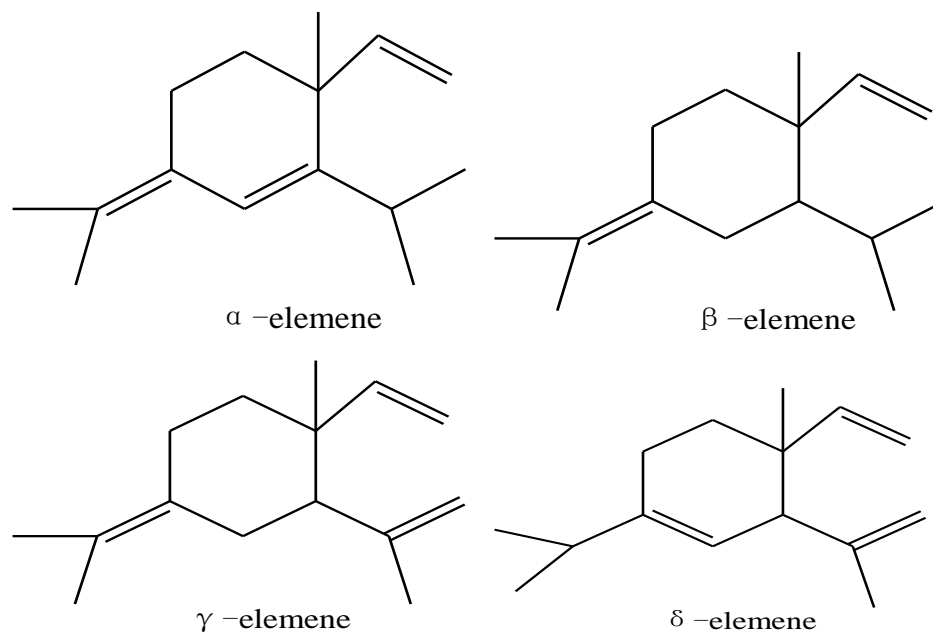
Distillation accounts for the major share of essential oils being produced today. Hydrodistillation is one of the oldest and easiest methods being used for the extraction of essential oils. In this method, the raw plant material is fully dipped in water. When heated, volatile compounds

along with steam are condensed and separated in another vessel connected to the heater by a pipe. The only difference for steam distillation from hydrodistillation is that the raw plant material should be separated from boiling water. The distillate generated by distillation will be purified by solvent extraction (Eiri Board, 2011). Organic solvents are preferred, such as methanol, ethanol, ether, petroleum ether and acetic ether. Distillation requires a relatively large amount of sample and some volatile components will be lost at the high extraction temperature. Compared to distillation, solvent extraction works at lower temperatures, which reduces the energy consumption and some heat-sensitive compounds can be conserved and extracted. It also extracts non-volatile resinous components with the volatile compounds (Huang et al., 2009). Only solvent extraction is not good when estimating elemene content. Solid phase micro-extraction is a relative new sampling and concentration method. Originally developed for the analysis of pollutants, this method is suitable for detecting volatile compounds emitted by plants (Tholl et al., 2006; Mayre et al., 2008). It is a simple, sensitive and solvent-free technique for analysis of volatile compounds from an herb sample (Belliaro et al., 2006).

Headspace solid phase micro-extraction in combination with gas chromatography-mass spectrometry (GS-MS) has been used for analysis of volatile compounds (Zhang et al., 2007), and it is pretty good to determine elemene content in herbs. Supercritical fluid extraction is environmentally benign, avoiding the use of organic solvents. Supercritical fluid extraction has shown some advantages as compared to the former traditional extraction methods using organic solvents or distillation. For example, the potential to process stuffs at mild temperatures under chemically inert conditions and using  $\text{CO}_2$  as an extraction fluid also results in a low environmental impact. Using  $\text{CO}_2$ , that is supercritical  $\text{CO}_2$  extraction, supercritical fluid extraction meets most of the requirements of the Montreal Protocol for solvents that do not contribute to ozone depletion. In addition, when using  $\text{CO}_2$  as an extracting solvent, the extraction selectivity can be varied through adjustment of the pressure and/or temperature (Javier et al., 2003; Abbas et al., 2008). However, supercritical fluid extraction has its limitations. The required consumes energy, and large investment is needed for the equipment.

GS-MS is a widely used assay like identifying and quantifying volatile and semi-volatile organic compounds in mixtures, determining molecular weights and elemental compositions of unknown organics in mixtures, structurally determining unknown organics in complex mixtures both by matching their spectra with reference spectra and by a priori spectral interpretation (Settle, 1997), and for these functions it is employed to estimate the elemene content in many studies.

Although, many methods are available to extract essential oils, it is important to employ a consistent and



**Figure 1.** Four isomeric compounds of elemene.

rapid method. While each method has its own merits and drawbacks, the field distillation units are extremely popular due to their very simple construction, cost-effective sample preparation and easy operation. All the methods mentioned have been modified and improved in recent years to exhibit higher analyte enrichment, more quantitative recovery, better accuracy, lower detection limits, etc.

### PLANT SPECIES WITH HIGH ELEMENE CONTENT

In the past years, many plant species have been identified with elemene in their essential oils, apart from *C. phaeocaulis*, *C. kwangsinensis* and *C. wenyujing*. In this work, available literatures have been reviewed and much attention has been given to these herbs with high content of elemene in their essential oils. Essential oils from forty-four plant species have been found to contain considerable elemene. They can probably be plant sources in the elemene processing industry as shown in Table 1.

### CONCLUSION

This study focused on plants to understand their potential uses in the elemene processing industry belonging to several different families. Unfortunately, none of these plants' antineoplastic activity has been studied *in vitro* or *in vivo* other than *R. curcuma*.

The essential oil from *R. curcuma* contains 27.83% elemene in the industrial processing by supercritical CO<sub>2</sub> extraction. Among the plant species with  $\beta$ -elemene or its

isomers in their essential oils, four species contain elemene more than 27.83% that is, *Nigella damascena*, *Michelia figo*, *Alisma orientalis*, and *Solidago decurens*. That means they have a brilliant future to be used for raw material in the elemene processing industry.

Essential oil contains many constituents and these constituents have different biological activities, such as *Artemisia annua*, *Sarcandra glabra*, *Cymbopogon winterianus*, etc. Artemisinin (QingHaoSu, QHS) extracted from *A. annua*, has shown the effect to treat severe malaria, efficiently, quickly and with low toxicity (Qian, 2007). Elemene has also been identified in the essential oil from *A. annua*, but neglected. Phenylpropanoid-substituted catechin glycoside isolated from *S. glabra* was shown to have remarkable potent hepatoprotective activity (Zhu, 2008). Meanwhile, the essential oil contains 15.92% elemene from *S. glabra* analyzed by GC-MS method (Huang et al., 1998). *C. winterianus* is an important natural flavorant, and the essential oil from its leaves is widely used. The relative content of elemene is 5.12% in the remains of leaves of *C. winterianus* after flavor oil has been extracted (Zhou et al., 2005). Dou et al. (2005) successfully got non-dominant components of citronella oil by vacuum distillation which yielded terpenoid compounds in which the content of elemene is 70%. The mixture has been showed to have antineoplastic activity. Today, we care more about resource conservation. These valuable plant resources should be made full use of, which make much sense.

$\beta$ -elemene is as the main ingredient in elemene injection that also contains a small amount of  $\gamma$ -Elemene,  $\delta$ -elemene and other terpenoids. A large number of

Table 1. Forty-four plant species.

S/N	Species	Methods to prepare essential oils	Assay methods	Isomers and their contents (%)	References
1	<i>Nigella damascene</i> (seed)	Hydrodistillation combined with ether extraction and the extract dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (73.24)	Filippo et al. (2002)
2	<i>Michelia figo</i> (flower, leaf, rootstock)	Hydrodistillation	GC-MS	$\beta$ -Elemene (33.43, 32.71, 33.58), $\gamma$ -elemene (11.24, 11.60, 10.23), $\delta$ -elemene (3.09, 4.88, 3.12), respectively	Dian et al. (2006)
3	<i>Michelia macclurei</i> (leaves)	Hydrodistillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (14.56), $\gamma$ -elemene (9.18), $\delta$ -elemene (1.3)	Huang et al. (2009)
4	<i>Alisma orientalis</i> (rootstock)	Headspace solid-phase micro-extraction	GC-MS	$\beta$ -Elemene (3.31), $\delta$ -elemene (30.41)	Li et al. (2009)
5	<i>Solidago decurens</i> (leaves)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (6.92), $\delta$ -elemene (21.73)	Zhu et al. (2009)
6	<i>Inula racemosa</i> (a cultivated variety, roots)	Steam distillation combined with ether extraction	GC-MS	Elemene (26.77)	Yang et al. (2008)
7	<i>Magnolia grandiflora</i> (leaves)	Supercritical CO <sub>2</sub> extraction	GC-MS	$\beta$ -Elemene (18.81), $\gamma$ -elemene (0.91), $\delta$ -elemene (1.02)	Liu et al. (2008)
8	<i>Atractylodes carlinoides</i> (roots)	Hydrodistillation	GC-MS	$\gamma$ -Elemene (18.932)	Zuo et al. (2009)
9	<i>Chrysanthemum morifolium</i> var. <i>jinhua</i> (flowers), <i>C. morifolium</i> var. <i>hangbaiju</i> (flowers), <i>C. morifolium</i> (flowers), <i>C. morifolium</i> var. <i>dayangju</i> (flowers), <i>C. morifolium</i> var. <i>gongju</i> (flowers)	Steam distillation combined with ether extraction	GC-MS	$\beta$ -Elemene (17.6, 14.7, 11.6, 5.84, 5.73, respectively)	Jiang et al. (2005)
10	<i>Kalimeris indica</i> (plant)	Steam distillation	GC-MS	$\gamma$ -Elemene (17.452)	Ma et al. (2002)
11	<i>Podocarpus nagi</i> (leaves)	Steam distillation	GC-MS	$\alpha$ -Elemene (7.102), $\beta$ -elemene (9.577)	Yang et al. (2008)
12	<i>Sarcandra glabra</i> (plant)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	Elemene (15.92)	Huang et al. (1998)

Table 1. Contd

13	<i>Cinnamomum glanduliferum</i> (leaves)	Purchased in Yibin area, Sichuan province	GC-MS	$\beta$ -Elemene (0.15), $\delta$ -elemene (13.69)	Lin et al. (1987)
14	<i>Evodia ruatecarpa</i> var. <i>bodinieri</i> (green fruit)	Headspace solid-phase micro-extraction, steam distillation extraction and the distillate dried over anhydrous sodium sulfate and petrol ether extraction , respectively	GC-MS	$\alpha$ -Elemene (0.66), $\beta$ -elemene (11.79), $\gamma$ -elemene (1.0)	Yang et al. (2009)
15	<i>Fortunella crassifolia</i> (peel)	Steam distillation	GC-MS	$\alpha$ -Elemene (1.33), $\beta$ -elemene (1.86), $\gamma$ -elemene (3.77), $\delta$ -elemene (4.52)	Huang et al. (2007)
16	<i>Mangifera indica</i> (fragrances from commercial ripe fruit and full ripe fruit)	Thermal-desorption cold trap	GC-MS	$\beta$ -Elemene (9.21), $\gamma$ -elemene (2.61)	Zheng et al. (2008)
17	<i>Gynura divaricata</i> (roots, stem, leaves)	Steam distillation combined with acetic ether extraction	GC-MS	Elemene (4.00, 6.26, 10. 63, respectively)	Xian et al. (2008)
18	<i>Dipterocarpus tubinatus</i> (stem)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene(0.9), $\alpha$ -elemene(9.50)	Ren et al. (2007)
19	<i>Ainsliaea pertyoides</i> var. <i>albotomentosa</i> (plant)	Steam distillation	GC-MS	$\beta$ -Elemene(6.38), $\gamma$ -elemene(3.23)	Li Xiang et al. (2006)
20	<i>Aglaia odorata</i> (flowers)	Purchased in Fuzhou, Zhangzhou and Chongqing	GC	$\beta$ -Elemene(9.30)	Lin et al. (1981)
21	<i>Zingiber mioga</i> (flowers)	Steam distillation combined with ether extraction and the extract dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (7.31), $\gamma$ -elemene (0.86)	Lv et al. (2004)
22	<i>Polygonatum cyrtoneuma</i> (roots)	Steam distillation combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (8.611)	Yu et al. (2008)
23	<i>Hyssopus cuspidatus</i> (plant)	Steam distillation combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\gamma$ -Elemene (8.35)	Fu et al. (2008)
24	<i>Alpinia oxyphylla</i> (fruit)	Soxhlet extraction by petroleum ether	GC-MS	$\beta$ -Elemene (4.50), $\gamma$ -elemene (3.38)	Chen et al. (2010)

Table 1. Contd

25	<i>Kadsura coccinea</i> (roots)	Steam distillation	GC-MS	$\beta$ -Elemene (7.03), $\gamma$ -elemene (0.80)	Peng et al. (2006)
26	<i>Lantana camara</i> (leaves, flowers)	Steam distillation combined with ether extraction and the distillate dried over anhydrous magnesium sulfate	GC-MS	$\beta$ -Elemene (5.735, 3.149), $\gamma$ -elemene (0.946, 1.059), $\gamma$ -elemene (1.148, 0.952), respectively	Zhou (2009)
27	<i>Angelica keiskei</i> (plant)	Steam distillation combined with normal hexane extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\gamma$ -Elemene (7.42)	Zhang et al. (2010)
28	<i>Notopterygium incisum</i> (roots)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (6.78), $\gamma$ -elemene (0.15), $\delta$ -elemene (0.54)	Yang et al. (2006)
29	<i>Leonurus sibiricus</i> (plant)	Steam distillation	GC-MS	$\beta$ -Elemene (trace), $\gamma$ -elemene (6.50)	Wang et al. (1991)
30	<i>Scutellaria baicalensis</i> (plant)	Steam distillation combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\gamma$ -Elemene (6.23)	Gong et al. (2009)
31	<i>Dictamnus dasycarpus</i> (root bark)	Steam distillation	GC-MS	$\beta$ -Elemene (4.41), $\delta$ -elemene (1.61)	Li et al. (2006b)
32	<i>Angelica sinensis</i> (roots)	Solid phase micro-extraction	GC-MS	$\gamma$ -Elemene (5.92)	Liu et al. (2007)
33	<i>Aristolochia debilis</i> (roots)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\alpha$ -Elemene (5.60)	Qiu et al. (2005)
34	<i>Schefflera kwangsiensis</i> (stem)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (5.146)	Xu et al. (2005)
35	<i>Elsholtzia rugulosa</i> (plant)	Supercritical CO <sub>2</sub> extraction combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\delta$ -Elemene (4.98)	Hu et al. (2006)
36	<i>Clausena excavate</i> (leaves)	Steam distillation combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (4.09), $\delta$ -elemene (0.71)	Na (2006)

Table 1. Contd

37	<i>Hydrocotyle sibthorpooides</i> (plant)	Steam distillation	GC-MS	$\beta$ -Elemene (5.80), $\gamma$ -elemene (0.41)	Mu et al. (2004)
38	<i>Nardostachys chinensis</i> (roots)	Steam distillation	GC-MS	Elemene (5.93)	Li (2009)
39	<i>Parakmeria nitida</i> (leaves)	Steam distillation combined with ether extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (3.23), $\gamma$ -elemene (2.383)	Yang et al. (2009)
40	<i>Piper puberulum</i> (plant)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\beta$ -Elemene (5.22), $\delta$ -elemene (0.22)	Teng et al. (2009)
41	<i>Daucus carota</i> (fruit)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	$\gamma$ -Elemene (5.27)	Wang et al. (2003)
42	<i>Hypericum patulum</i> (plant)	Steam distillation and the distillate dried over anhydrous sodium sulfate	GC-MS	Elemene (4.98)	Zhang et al. (2009)
43	<i>Myoporum bontiodes</i> (plant)	Steam distillation combined with ether extraction and the distillate dried over anhydrous magnesium sulfate	GC-MS	$\gamma$ -Elemene (4.93)	Xu et al. (2006)
44	<i>Ligustrum robustum</i> (leaves)	Steam distillation combined with dichloromethane extraction and the distillate dried over anhydrous sodium sulfate	GC-MS	$\gamma$ -Elemene (5.80)	Tong et al. (2004)

experiments proved elemene injection were applications as a national second-class new drug of anti-tumor in China in 1994. Over the years, further basic researches were related to elemene injection, which had a significant inhibitory effect on a variety of tumor cells, as well as tumor cell apoptosis and differentiation, reversal of multidrug resistance of tumor cells and anti-metastases. Combined with radiotherapy and immunity, and

mild toxicities.

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