A review of medicinal plant species with elemene in China

Shuling Wang¹, Zhenkun Zhao¹,², SUN Yun-ting³, Zhaowu Zeng¹, Xiaori Zhan¹, Chenglu Li¹ and Tian Xie¹ *

¹Research Center for Biomedicine and Health, Hangzhou Normal University, Hangzhou, Zhejiang, 310012, People’s Republic of China.
²College of Life and Environmental Sciences, Hangzhou Normal University, Hangzhou 310012, People’s Republic of China.
³Hangzhou Hospital of Traditional Chinese Medicine, Hangzhou, 310007, People’s Republic of 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 β-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 β-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 leucopoenia, 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 *Rhizarra Curmuma* 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 β-elemene, γ-elemene and δ-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 β-elemene has marked the characteristics of wide spectrum of antineoplastic activity, alleviating the aches cancer-caused, and increasing leukocyte improving
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 Re(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 (Belliardo 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 CO\(_2\) as an extraction fluid also results in a low environmental impact. Using CO\(_2\) that is supercritical 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 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
rapid method. While each method has its own merits and
drawbacks, the field distillation units are extremely po-
pular 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 quantita-
tive recovery, better accuracy, lower detection limits, etc.

PLANT SPECIES WITH HIGH ELEMENE CONTENT

In the past years, many plant species have been iden-
tified 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 consi-
derable 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 CO₂
extraction. Among the plant species with β-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) extract-
ted 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 me-
thod (Huang et al., 1998). C. winterianus is an important
natural flavorant, and the essential oil from its leaves is
wildly 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.

β-elemene is as the main ingredient in elemene
injection that also contains a small amount of γ-Elemene,
δ-elemene and other terpenoids. A large number of
Table 1. Forty-four plant species.

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<td>2</td>
<td>Michelia figo (flower, leaf, rootstock)</td>
<td>Hydrodistillation</td>
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<td>(\beta)-Elemene (33.43, 32.71, 33.58), (\gamma)-elemene (11.24, 11.60, 10.23), (\delta)-elemene (3.09, 4.88, 3.12)</td>
<td>Dian et al. (2006)</td>
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<td>3</td>
<td>Michelia macclurei (leaves)</td>
<td>Hydrodistillation and the distillate dried over anhydrous sodium sulfate</td>
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<td>4</td>
<td>Alisma orientalis (rootstock)</td>
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<td>Solidago decurens (leaves)</td>
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<td>6</td>
<td>Inula racemosa (a cultivated variety, roots)</td>
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<td>Magnolia grandiflora (leaves)</td>
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<td>Kalimeris indica (plant)</td>
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<td>No.</td>
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<td><em>Angelica keiskei</em> (plant)</td>
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<td>GC-MS</td>
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<td>Na (2006)</td>
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<td>Myoporum bontiodes (plant)</td>
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<td>Steam distillation combined with dichloromethane extraction and the distillate dried over anhydrous sodium sulfate</td>
<td>GC-MS</td>
<td>γ-Elemene (5.80)</td>
<td>Tong et al. (2004)</td>
</tr>
</tbody>
</table>

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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