

# Extraction of Pharmaceutical Composition from Chinese Eaglewood and Its Therapeutic Efficacy

Zhihong Pan,<sup>a,b</sup> Jian Qiu,<sup>c,\*</sup> Haishan He,<sup>c</sup> Qingde Li,<sup>d</sup> and Huajie Shen<sup>c</sup>

There are few reports on the effect of Chinese eaglewood extractions on the relationship between a stroke-induced nerve and the motor dysfunction caused by the nerve dysfunction. In this study, lipids were successfully induced from white Eaglewood, and the cause of extraction were analyzed. Controlled clinical experiments were conducted to study the effects of Chinese eaglewood extracts as a drug therapy on the recovery of nerve and motor function of stroke patients. Such effects were further analyzed using the electroencephalograms (EEGs) test, the Fugl-Meyer upper extremity scale, and the Fugl-Meyer lower extremity scale. The results of the study showed that the nerve function recovery of stroke patients through compensatory effects was promoted by using Chinese eaglewood extracts, and the motor function recovery of patients was further improved. Thus, from the results of the Fugl-Meyer upper extremity and lower extremity scales, the motor functions of the stroke patients were gradually recovered during the clinical experiments, which indicated nerve function recovery. The RNA extraction results showed high RNA purity without the presence of proteins and that interfering substances can be obtained by using the mixed inducer agent. This study demonstrated the feasibility for the application of Chinese eaglewood extracts and its therapeutic efficacy.

**Keywords:** *Chinese eaglewood; Chemical induction; Pharmaceutical composition; Nerve function; Motor function*

**Contact information:** *a: College of Material Science and Engineering, Northeast Forestry University, Harbin 150040, China; b: Zhongshan Polytechnic, Zhongshan 528400, China; c: College of Material Engineering, Southwest Forestry University, Kunming 6500224, China; d: Foshan University, Foshan 528000, China; \*Corresponding author: qiujiangswfu@foxmail.com*

## INTRODUCTION

Stroke is a medical condition in which the stenosis and occlusion of blood vessels cause their rupture, ultimately resulting in the partial or total loss of brain nerves and limb functions (Kim *et al.* 2017). According to medical statistics, stroke is common in middle-aged and elderly people; the vast majority of these patients are over 50 years old. It can be said that stroke has become one of the major diseases that endangers the health and safety of middle-aged and elderly people (Bartolo *et al.* 2014). At present, the treatment of stroke patients is mainly divided into two stages. The first stage is surgical treatment, and the second stage is postoperative rehabilitation. The main purpose of postoperative rehabilitation treatment is to restore normal body functions (Zhou and Turndorf 1998). Stroke fatality rates are declining during postoperative rehabilitation. Nerve and motor dysfunctions are the main postoperative sequelae. After surgery, many patients have trouble taking care of themselves, which causes great difficulties for themselves, as well as their families (Ferreri and Rossini 2013).

Modern medical research shows that there is a causal relationship between nerve dysfunctions and motor dysfunctions of stroke patients. Specifically, the motor dysfunctions can be largely attributed to impaired nerve functions (Purvin 1996; Eldar 2000). Hence, treating the motor dysfunctions of stroke patients should begin with the recovery of their nerve functions. The extract from Chinese eaglewood is a potent Chinese herbal medicine that has a variety of therapeutic effects. In recent years, some studies on Chinese eaglewood extracts have shown that it has a certain stimulatory effect on the recovery of damaged nerve functions. In this context, this investigation examines Chinese eaglewood extracts as a drug rehabilitation treatment for stroke patients, and examines whether such extracts can promote the recovery of nerve function of stroke patients during the rehabilitation stage. The findings of this study can provide some references for subsequent investigations.

## CHINESE EAGLEWOOD AND ITS MEDICINAL VALUE

Chinese eaglewood actually refers to the wood-containing resins in the Chinese eaglewood tree, which is a tree from the Thymelaeaceae family. It is a commonly used Chinese herbal medicine (He *et al.* 2012) that is mainly produced in Taiwan, Hainan, Guangdong, and Guangxi (China). Chinese eaglewood is difficult to cultivate naturally. It is generated only after being stimulated by physical, chemical, or biological attack (*i.e.*, fungal); and for this reason, this herbal medicine is very expensive (Großmann 2017). The main chemical components of Chinese eaglewood extracts are sesquiterpenoids and 2-(2-phenylethyl) chromones, which were isolated from the ethyl ether dissolved part of the ethanol extract of eaglewood detected from spectral analysis and chemical synthesis.

It has been confirmed that these extractives can be used to treat chest distress, shortness of breath, kidney deficiency, vomiting, arrhythmia, kidney stones, *etc.* Such extractives have good efficacy in treating digestive, respiratory, urinary, and cardiovascular diseases (Tamuli *et al.* 2005). In recent years, Chinese eaglewood has transitioned from a traditional Chinese herbal medicine to a modern-day medical treatment for specific issues. For example, some researchers have discovered that certain chemical extracts from Chinese eaglewood can act as an analgesic and a calming agent; hence, the extractives can be used as an anesthetic (Bhuiyan *et al.* 2009). Some investigators (Lin *et al.* 2016; Martin *et al.* 2017) have also studied the effects of Chinese eaglewood extracts on the nervous system of mice as test subjects. These investigators found that Chinese eaglewood not only can sedate the central nervous system, but also to some extent it can restore its functions. Experimenters injected Chinese eaglewood extracts into mice's central nervous systems and their limb mobility improved. Later, investigators conducted further research and found that Chinese eaglewood extracts can regenerate impaired nerve cells, which exert compensatory effects. (Ding *et al.* 2018).

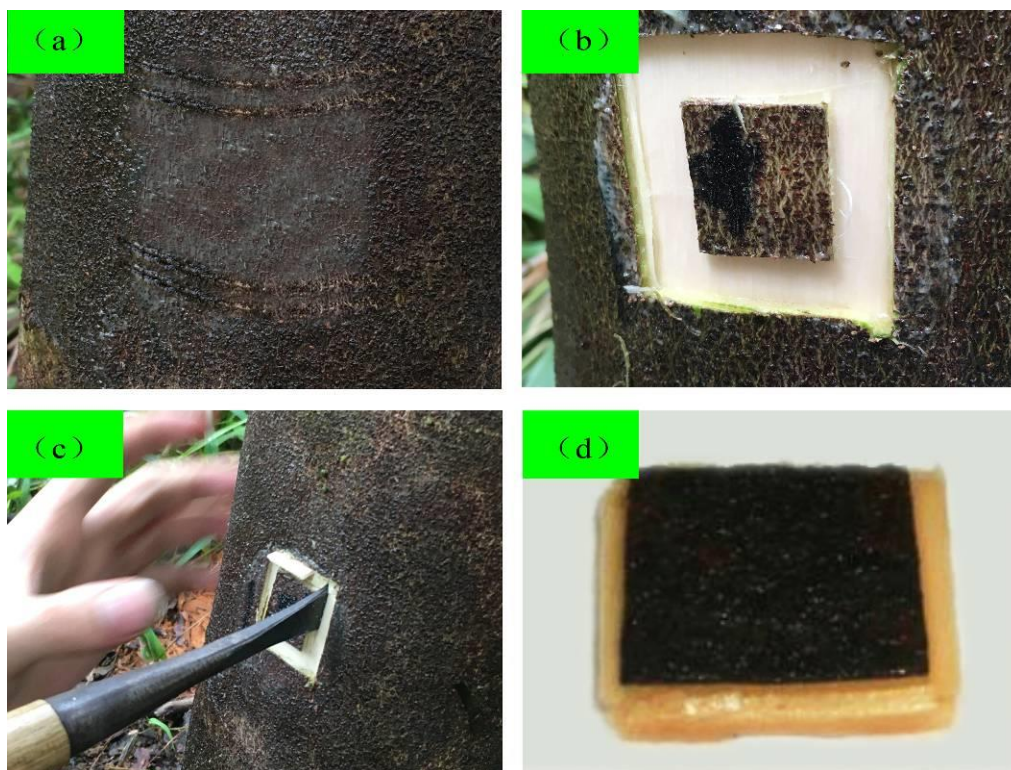
The above literature review illustrates the medicinal value of Chinese eaglewood extracts, which can affect the recovery of impaired nerve system functions. Therefore, this investigation presents the results from clinical experiments to study the efficacy of Chinese eaglewood extracts as drug therapy for the recovery of nerve and motor functions with stroke patients.

## EXPERIMENTAL

### Materials

#### *Sample collection methods*

The double-line sampling method (Fig. 1) was used to reduce the effects of sampling error and to minimize the damage to the plants. First, the lanolin coating on the surface of the treated areas was gently scraped to prevent bark damage. Next, two 2 cm × 3 cm rectangles that reached the xylem were cut into the tree using a box cutter. Tweezers were used to remove the bark and xylem between the rectangles. The wood block remaining in the center (containing the bark and xylem) was removed using a hammer and a chisel; the removed rectangular sample was then rapidly placed in formalin-aceto-alcohol (FAA) stationary liquid (5% formalin, 5% acetic acid, and 90% ethanol) with a concentration of 50% (Shanghai Sangkang Biotechnology Co., Ltd., Shanghai, China).



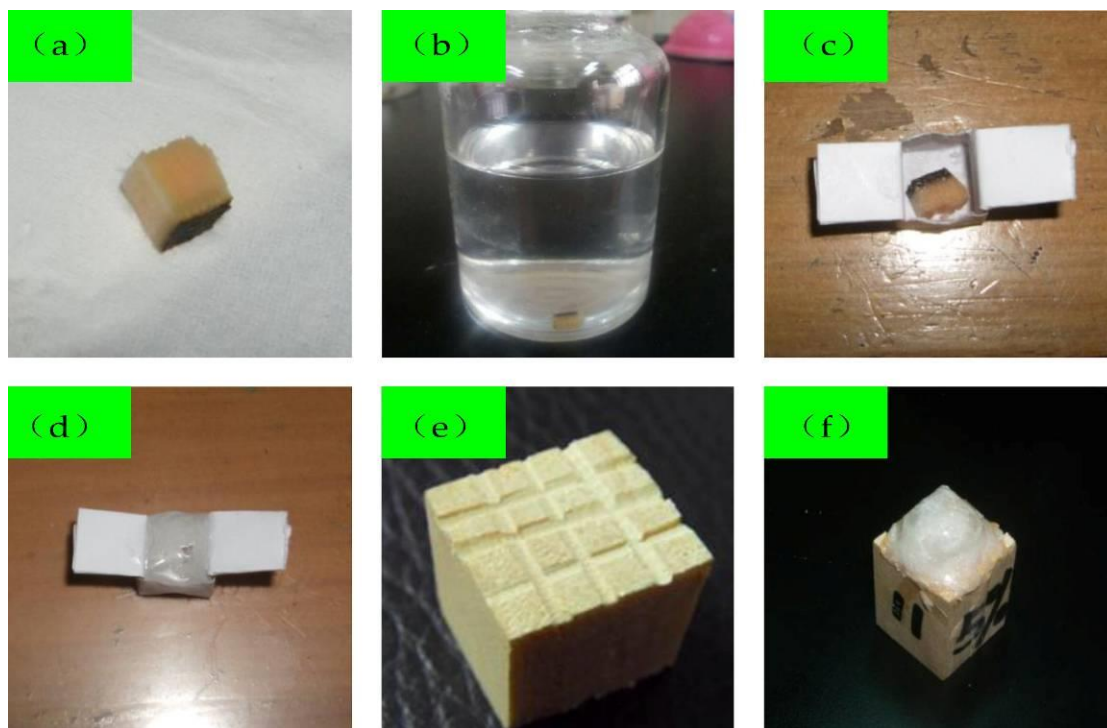
**Fig. 1.** The sampling of living woods using the double-line method: (a) double lines were cut out in the center location that was treated with agents; (b) surrounding bark and xylem were removed; (c) sample remaining in the middle was removed using a hammer and a chisel; and (d) sample was fixed with FAA for further study.

#### *Sample collection time*

Samples were collected on day 180 after the initial agent treatment. Samples initially treated on May 1, 2017 were collected on Oct. 27, 2017; these were denoted as the first induction period. Samples initially treated on June 25, 2017 and collected on Dec. 22, 2017 were denoted as the second induction period. Samples initially treated on August 20, 2017 and collected on Feb. 16, 2018 were denoted as the third induction period.

### Sample embedding

The samples fixed in FAA were cut into 5 mm × 5 mm × 5 mm cubes and adhered to a patterned 1-cm wood block cushion using polyethylene glycol 4000 (PEG 4000, Sangon Biotech Co., Ltd., Shanghai, China) using the following protocol (Fig. 2). First, the samples in FAA were placed into distilled water and submerged under a vacuum. The samples were kept in distilled water for one day to dilute the FAA stationary liquid. Subsequently, the samples were dehydrated using a gradient of PEG 4000 (20%, 40%, 60%, 80%, and 100%) at 70 °C for 12 h retention time per gradient. The samples were then placed into small paper cartons to solidify in the 100% PEG 4000 at a low-temperature. The cartons were then dismantled after solidification. The solidified samples were adhered to the patterned cushion block (patterning increased the cementation surface area) using 100% PEG 4000 and were kept in a low-temperature environment until solidification was completed.



**Fig. 2.** The embedding process using PEG 4000: (a) small sample after distilled water soaking and washing to remove FAA; (b) sample dehydration using a series of gradient polyethylene glycol concentrations; (c) sample placed into small carton for PEG embedding; (d) sample embedded in solidified PEG; (e) cushion block with sawed lines; and (f) sample adhered to the cushion block.

### Sample slicing

The solidified samples were sliced using a microtome (Yamato TU-213 large-scale microtome; Pan Sun Enterprise Co., Ltd., Taiwan, China) equipped with a microtome knife blade (Feather A35; Nobleryder Technology Co., Ltd., Beijing, China) that was suitable for cutting hard materials. The knife moved vertical to the cambium at an angle of 10° between the blade side and wood block surface. This caused the blade to slice through the phloem and then the xylem, which resulted in a slice thickness of 20 μm ± 5 μm. The microtome sample was glued onto a glass slide using 2 to 3 drops of water-



soluble glue. Tweezers were used to place the cover glass over the sample that was on the glass slide. Pressure was slowly applied to the cover. Excess glue and bubbles were removed. The sample was then placed horizontally and allowed to dry (Fig. 3).



**Fig. 3.** Sliced samples: (a) phloem and (b) xylem

## Methods

### *Ethical review of research*

Before extract from eaglewood was used for clinical trials, the experimental protocol was reviewed by the Clinical Research and Experimental Animal Ethics Committee of Northeast Forestry University, which is a medical ethics review professional institution in China. After review, the ethics committee approval specified that extract from Chinese eaglewood meets “Guidelines for the Quality Management of Drug Clinical Trials” of the State Food and Drug Administration of China, “Ethical Review of Biomedical Research Concerns” of the National Health and Family Planning Commission, the International Code of Ethics for Human Biomedical Research promulgated by the International Committee of Medical Scientific Organizations, and the Helsinki Declaration. The ethics committee agreed to the plans to conduct clinical pre-tests.

### *Extraction method and integrity detection of ribonucleic acid (RNA)*

The RNA was extracted using the RNeasy Plant Mini Kit (Qiagen, Dusseldorf, Germany) following the manufacturer’s instructions. A sample (1.0 g) was frozen using liquid nitrogen and then ground into a fine powder. The total RNA was extracted and preserved at -80 °C. Electrophoresis was performed using a 1% agarose gel (DYCP-31CN agarose horizontal electrophoretic apparatus, Beijing Liu Yi Instrument Factory, Beijing, China) to detect the integrity of RNA. A NanoDrop DN-10000 ultraviolet-visible (UV-Vis) spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA) was used to determine the RNA purity. The average of five test samples from each group was presented.

### *RNA extraction method and integrity detection*

A total of 0.5 g of the sample powder that passed through a 60-mesh screen was added to a conical flask. Then, 10 mL trichloromethane (Sangon Biotech Co., Ltd., Shanghai, China) was added to the sample. The conical flask was sealed, shaken, soaked (overnight in chilled conditions), shaken again, and filtered. The filtrate liquor was collected and then evaporated using a water bath at 70 °C. The resulting residue was dissolved in trichloromethane, and the liquid was transferred into a 1-mL measuring

flask. Finally, trichloromethane was added to the conical flask and mixed well. The liquid was filtered through a 0.5- $\mu\text{m}$  Millipore filter, and the filtrate was collected. The filtrate and the N-alkane solution were injected into gas chromatograph mass spectroscopy (GC-MS; model: QP2010E, Shimadzu Corp., Tokyo, Japan) under the same test conditions.

The chromatographic conditions adopted a Rtx-5 MS capillary column (30 m  $\times$  0.25 mm, 0.25- $\mu\text{m}$ -thick) with the inlet temperature of 260  $^{\circ}\text{C}$  under high purity helium carrier gas. The flow rate was 1.0 mL $\cdot\text{min}^{-1}$ , and the split ratio was 1/30. Its temperature program stayed at 90  $^{\circ}\text{C}$  for 4 min at first, then the temperature was raised to 160  $^{\circ}\text{C}$  for 5 min at a speed of 2.5  $^{\circ}\text{C}\cdot\text{min}^{-1}$ , the temperature was increased again to 180  $^{\circ}\text{C}$  for 5 min at 0.3  $^{\circ}\text{C}\cdot\text{min}^{-1}$ , and finally it was raised to 230  $^{\circ}\text{C}$  for 120 min at a speed of 1  $^{\circ}\text{C}\cdot\text{min}^{-1}$ .

The mass spectrometry conditions adopted electron impact ion source with 70 eV electron energy. The ionization voltage was 1 kV, the interface temperature was 250  $^{\circ}\text{C}$ , the ion source temperature was 230  $^{\circ}\text{C}$ , the solvent delay was 5 min, and the mass scan range was 50 to 500 m/z.

The spectrum matching library was the NIST 05 MS database. The AMDIS software (National Institute of Standards and Technology, v. 2.65, Washington DC, USA) was applied to process the spectrogram and determine the extracted mass spectrometry information. Then, the area normalization method was used to calculate the relative percentage of sesquiterpenoids content.

#### *Clinical analysis of drug extraction*

The test subjects analyzed in this investigation were 55 moderate stroke patients from a medical rehabilitation center (Tianjin TEDA Hospital Rehabilitation Center, Tianjin, China). Moderate stroke patients were chosen as test candidates because their nervous systems were damaged, but not irreversibly damaged as those found in severe stroke patients; additionally, severe stroke patients cannot even participate in the clinical experiment due to cognition impairment or to complete paralysis. The clinical experiments lasted for 3 months (12 weeks). Before the experiments, the patients were randomly divided into an experimental group and a control group, of which the former had 23 patients and the latter had 22 patients. During the experiments, the subjects in the experimental group were treated with the Chinese eaglewood extracts, whereas the control group was not treated with the extract. Both groups used general rehabilitation therapy.

**Table 1.** Comparison of the Two Groups

	<b>Experimental Group</b>	<b>Control Group</b>	<b>p-value</b>
Age	55.8 $\pm$ 4.57	56.1 $\pm$ 3.80	0.095
Height (cm)	167 $\pm$ 5.77	167 $\pm$ 3.79	0.211
Mass (kg)	70.18 $\pm$ 4.20	71.28 $\pm$ 3.77	0.231

According to the statistical analysis (Table 1), there were no significant differences between the two patient groups in terms of their average age, height, and mass, which met the requirements for a clinical experiment design.

#### **Evaluation Indices**

It was noted earlier that the main symptoms of stroke patients are nerve and motor dysfunctions, and nerve dysfunctions are the main cause of motor dysfunctions. Hence, when observing whether the patients' motor functions have been recovered, the

researchers also need to observe how the patients' nerve systems are recovered. To this end, the following three indices were used in the evaluations.

#### *Nerve excitability*

Experiments were conducted to examine nerve excitability by monitoring the brainwaves of the experimental and control groups. Studies have shown that the mean and variance of electroencephalograms (EEGs) are effective indicators of nerve excitability. A higher excitability results in a greater mean and variance of EEGs and *vice versa* (Hlustík and Mayer 2006; Zorowitz 2010).

#### *Upper extremity motor function*

A Fugl-Meyer upper extremity scale was used to evaluate the upper extremity motor function recovery of the patients. The Fugl-Meyer upper extremity scale is commonly used to evaluate medical rehabilitation. The scale focuses on the flexibility of the patients' palms, knuckles, elbows, and shoulders (Takeuchi *et al.* 2005). The scale ranges from 0 to 100 points. A score of less than 50 points indicates that the patient has a serious functional impairment, whereas a score of 50 to 75 points indicates that there is a moderate dysfunction. A score of 75 to 90 points indicates that there is a mild dysfunction.

#### *Lower extremity motor function*

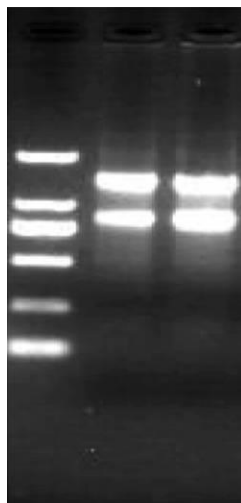
A Fugl-Meyer lower extremity scale, similar to the upper extremity motor scale, was used to evaluate the recovery of lower extremity motor function. The Fugl-Meyer lower extremity scale focuses on the flexibility of the ankle, knee, and hip joints (Hummelsheim *et al.* 1996). The scale is the same as the corresponding upper extremity scale. A higher score results in better recovery.

## RESULTS AND DISCUSSION

### **Determination of Agarwood Formation Effects in *A. sinensis***

#### *Determination of RNA extraction purity*

The higher the extraction purity of RNA, the more it can be analyzed to explore the healing mechanism. Therefore, RNA was taken as one of the experimental indicators in this study. The RNA extraction is rich in polysaccharides and polyphenols, which have similar activation and recovery effects on the human brain. However, the RNA activity was high and the extraction of RNA was difficult. *A. sinensis* has a highly activated endogenous RNA, which makes it difficult to extract high-quality RNA from its tissue samples, especially from the trunk. Furthermore, RNA is an important material for molecular biology researchers. To avoid the effects of individual differences with artificially induced agarwood formation, six parallel *A. sinensis* samples were used at each sampling time (Fig. 4). Two parallel samples were randomly selected, and the determination results of RNA extraction purity indicated that the RNA bands extracted were clear and the typical three banding patterns of 28S, 18S, and 5S were visible. In addition, the brightness of 28S was approximately twice that of the 18S band without significant degradation, as well as residues or pollution of impurities, indicating that the RNA integrity extracted through this method was suitable.



**Fig. 4.** The electrophoretic diagram of RNA at the agarwood formation position in induced *A. sinensis* extracted using a Qiagen kit

#### RNA integrity

An ultraviolet visible spectrometer (Spectrophotometer/G27-200035; Agilent Technologies, Inc., Santa Clara, CA, USA) was used to determine the  $OD_{260}/OD_{280}$  and  $OD_{260}/OD_{230}$  ratios of the RNA samples. The  $OD_{260}/OD_{280}$  ratios of the RNA obtained by using the mixed agent were all between 1.8 and 2.0, which indicated that the RNA purity was relatively high with few proteins or other interfering substances (Table 2). Using methyl jasmonate inducer to induce *A. sinensis* for agarwood formation, the  $OD_{260}/OD_{280}$  ratio of extracted RNA was 2.13 and 1.67. In this case, the RNA purities were lowered by 37.34% and 52.87%, respectively, when using the mixed agent.

**Table 2.** Determination Results of Total RNA Quality Through Different Methods

Agent	$OD_{260}/OD_{280}$	$OD_{260}/OD_{230}$	Concentration (ng· $\mu$ L <sup>-1</sup> )
Me-JA	2.13	1.97	87.38
ET	1.67	1.49	65.73
Me-JA and ET	1.96	2.37	139.46

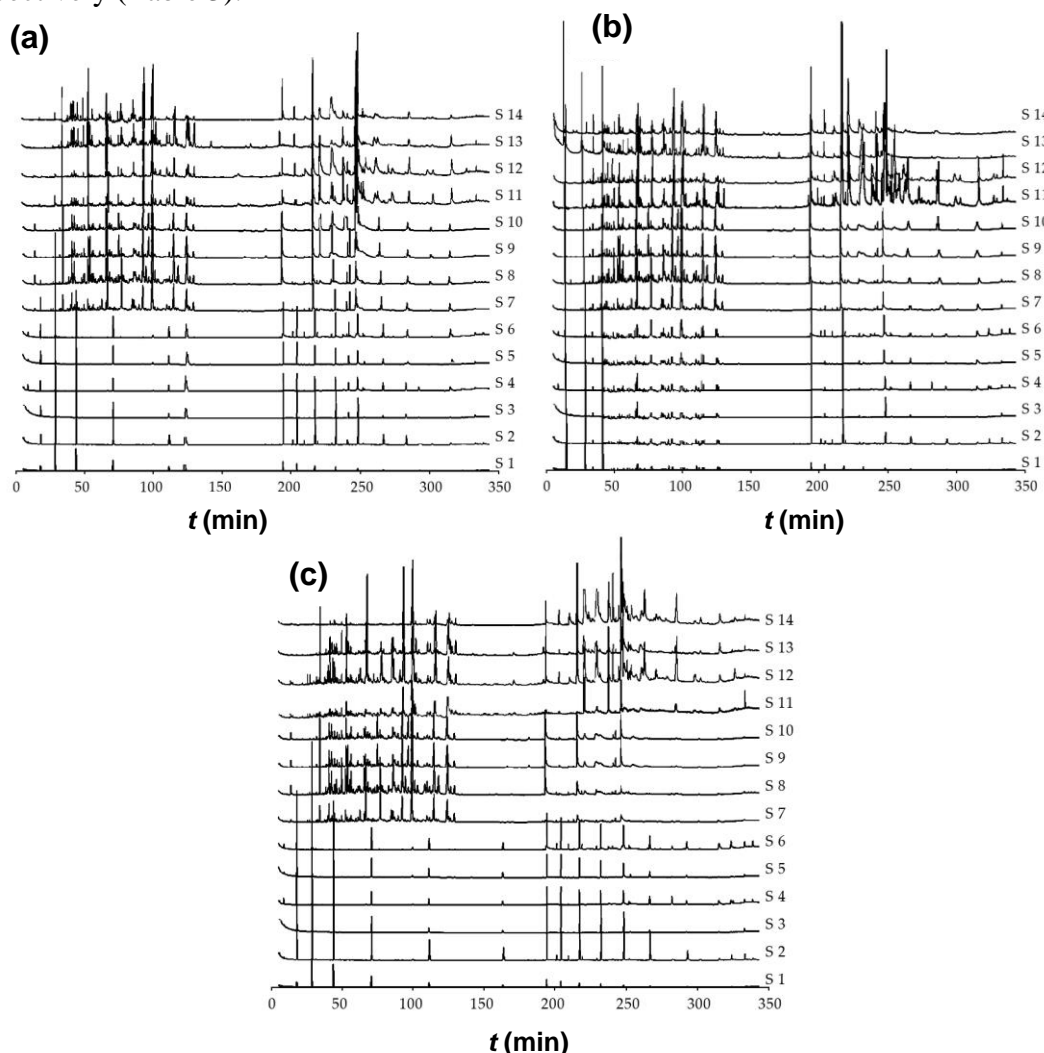
#### Analysis of the accumulation of sesquiterpenoids at different times before and after the induction of *A. sinensis* to form agarwood

The GC-MS technique analyzed the compositional change and accumulation situation of sesquiterpenoid secondary metabolites at different times before and after induction (Fig. 5). The automated mass spectral deconvolution and identification system (AMDIS) was combined with the correction of the GC retention index (RI); this system was used to determine the sesquiterpenoids from the wood extracts (Table 3). No sesquiterpenoid secondary metabolites were detected until two months into the artificial treatment; 13 sesquiterpenoids were detected in the samples between four and six months, which included isoaromadendrene epoxide, aromadendrene oxide-(1), agarospirol, guaial, 2-(4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl)-prop-2-en-1-ol, longipinocarvone, germacrone, viridifloro, baimuxianal, longifolenaldehyde, eudesma-5,11(13)-dien-8,12-olide, velleral, and 6-(1-hydroxymethylvinyl)-4,8a-dimethyl-3,5,6,7,8,8a-hexahydro-1H-naphthalen-2-one. When using Me-JA, mixed agent, and Et to induce *A. sinensis* for six months, there were 9, 11, and 12



sesquiterpenoids identified in the generated lipid substances, respectively. Finally, the detection frequency of baimuxianal was highest (at 80%) for the samples.

The peak area normalization of the GC elution graphs for the first 100 min was performed. During the first two months, there was no sesquiterpenoid secondary metabolite detected. However, in all of the data of agarwood formation between the following four to six months, sesquiterpenoids were detected with increasing frequency. The relative percentages of total sesquiterpenoids in the generated lipid substances through the use of the above three hormones were 32.4%, 36.4%, and 25.5%, respectively (Table 3).



**Fig. 5.** GC elution peaks before and after the addition of hormones to induce *A. sinensis* for agarwood formation: (a) methyl jasmonate; (b) ethephon; and (c) mixed agent of methyl jasmonate and ethephon (agarwood formation: S1 and S2 denote 0 months; S3 to S6 denote 2 months; S7 to S10 denote 4 months; and S11 to S14 denote 6 months)

## Determination of Agarwood Formation Effects in Nerve

### Nerve excitability

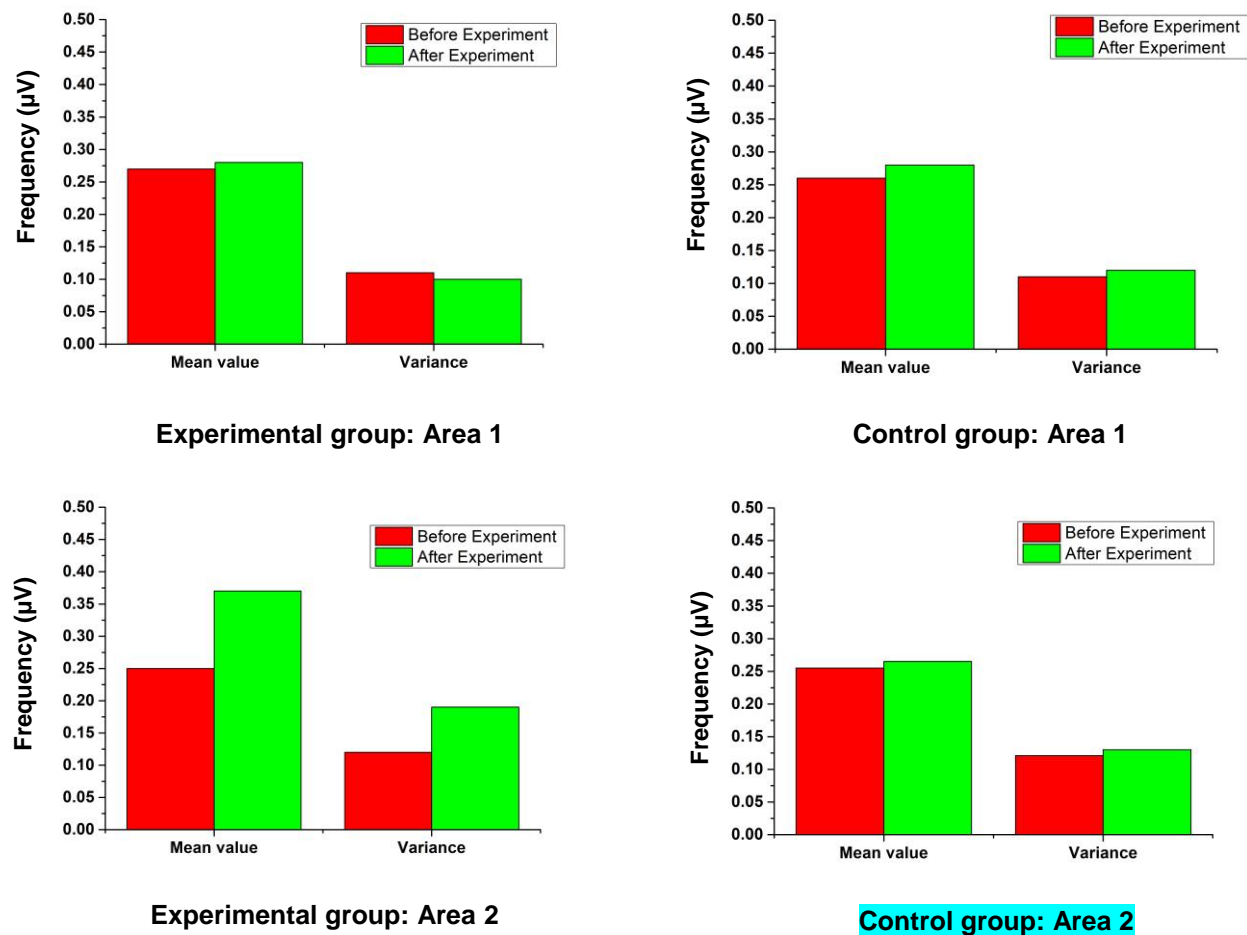
Some studies have shown that stroke damage to nerve cells can be irreversible (*i.e.*, cannot be restored to their normal functions). To explore whether Chinese eaglewood extracts can recover damaged nerve functions in stroke patients as well as find

out its specific mechanism, this paper intends to monitor the EEG signals in the damaged nerve structure and its surroundings simultaneously. For the sake of differentiation, the damaged nerve region is referred to as region 1 and its surrounding area is referred to as region 2.

**Table 3.** Dynamic Variation of Sesquiterpenoids Before and After Using Hormones to Induce *A. sinensis* for Agarwood Formation

No.	Chemical Name	Formula	RT	RI	Relative Percentage Content (%) (Sample Were Treatment After Six Months)		
					Me-JA	ET	Me-JA and ET
1	Isoaromadendrene epoxide	C <sub>15</sub> H <sub>24</sub> O	30.41	1575.4	1.333/(3)	1.965/(2)	1.750/(2)
2	Aromadendrene oxide-(1)	C <sub>15</sub> H <sub>24</sub> O	33.98	1620.6	0.180 0/(1)	0.215 0/(2)	-
3	Agarospirol	C <sub>15</sub> H <sub>26</sub> O	34.74	1628.4	-	0.510 0/(1)	-
4	Guaiol	C <sub>15</sub> H <sub>26</sub> O	36.23	1644	3.620/(1)	2.600/(1)	-
5	2-(4a,8-dimethyl-1,2,3,4,4a,5,6,7-ctahydronaphthalen-2-yl)-prop-2-en-1-ol	C <sub>15</sub> H <sub>24</sub> O	43.74	1715.3	1.247/(3)	2.670/(1)	0.660 0/(1)
6	Longipinocarvone	C <sub>15</sub> H <sub>22</sub> O	46.38	1734.4	3.170/(2)	3.775/(1)	1.350/(1)
7	Germacrone	C <sub>15</sub> H <sub>22</sub> O	46.72	1737	1.500/(2)	2.860/(1)	2.360/(2)
8	Viridifloro	C <sub>15</sub> H <sub>26</sub> O	47.54	1742.8	0.910/(1)	2.130/(1)	0.400 0/(1)
9	Baimuxianal	C <sub>15</sub> H <sub>24</sub> O <sub>2</sub>	59.14	1819.5	3.423/(1)	6.327/(3)	2.715/(2)
10	Longifolenaldehyde	C <sub>15</sub> H <sub>24</sub> O	67.81	1865.4	4.000/(3)	2.340/(1)	1.860/(1)
11	Eudesma-5,11(13)-dien-8,12-olide	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub>	81.63	1927.4	15.51/(3)	-	20.50/(1)
12	Velleral	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub>	81.94	1928.6	-	31.13/(1)	23.63/(2)
13	6-(1-hydroxymethyl-vinyl)-4,8a-dimethyl-3,5,6,7,8,8a-hexahydro-1H-naphthalen-2-one	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub>	100.9	2000.1	6.63/(1)	0.450 0/(1)	-
Relative percentage content of total sesquiter-penetration (%) before 100 min (n = 3)					32.40 ± 5.9	25.52 ± 10	36.44 ± 18
Ratio of baimuxianal in total sesquiterpenetration (%)					10.60	24.80	7.45

Clinical experiment lasted for 12 weeks; data of the three indices were collected every two weeks



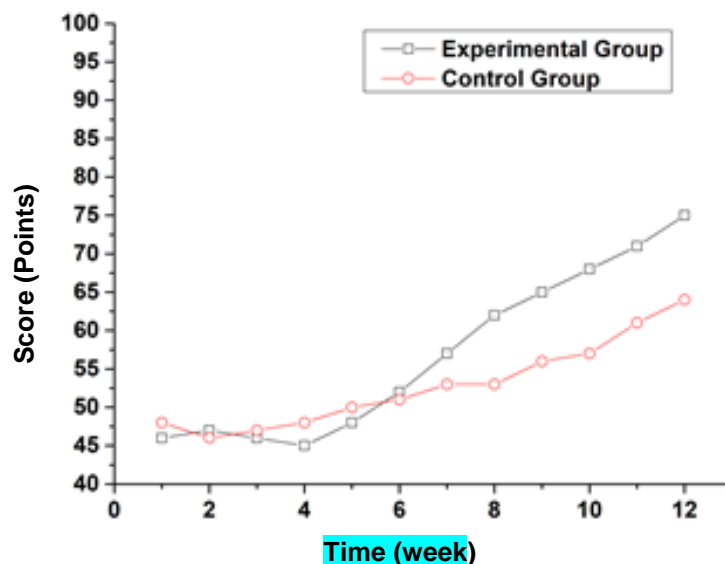
**Fig. 6.** EEG test results

Figure 6 plots the data from the patients' brain wave activities from EEG measurements. The data from the above experiments showed that when Chinese eaglewood extracts were used as drug therapy, it significantly improved the nerve excitability of region 2. Judging from the experimental data, this effect began to appear from the third week. Region 2 is not the part of the stroke patient where his/her nerve function was damaged, but rather the surrounding part of the damaged region. This result showed that Chinese eaglewood extracts did not help recover the impaired nerve function, but rather it could enhance the function of the surrounding region of the damaged nerve cells. Therefore, there was a significant compensatory effect between the nerve cells, where the functions of the damaged nerve cells were replaced by functions of the surrounding ones.

#### *Upper extremity motor function*

Figure 7 shows the results from the Fugl-Meyer upper extremity scale in the experiment. It was observed that during the 12-week clinical experiments, the scores of the experimental group and the control group during the first six weeks were nearly identical. However, after week six, the scores of the experimental group began to increase more rapidly than the control group, which indicated that the efficacy of the combined therapy on the experiment group was appreciably better than that of the control group.

When the experiments began, the average Fugl-Meyer upper extremity scores of the experimental group and the control group were 46 and 48 points, respectively, which indicated no significant difference ( $p > 0.05$ ). The scores at the sixth week for the two groups were recorded again, which were 52 and 51 points, respectively; these results indicated that there was no significant difference ( $p > 0.05$ ) between the two groups. From the seventh week, the score of the experimental group became significantly higher than that of the control group. At the end of the experiments, the average score of the patients in the experimental group was 75 points, whereas that of the control group was 64 points. These results indicated that Chinese eaglewood extracts began to exert their drug effect starting at week 7. Compared to those only under general rehabilitation therapy (control group), the patients treated with the combined therapy using Chinese eaglewood extracts (experimental group) showed better recovery.



**Fig. 7.** Results of the Fugl-Meyer upper extremity scale

#### *Lower extremity motor function*

Figure 8 shows the results of the Fugl-Meyer lower extremity scale in the experiments. During the 12-week clinical experiment, the scores of the experimental group and the control group in the first three weeks were nearly identical. However, after week six, the scores of the experimental group began to rise more rapidly than the control group, which indicated that the addition of Chinese eaglewood extracts combined with general rehabilitation therapy (experimental group) greatly improved the recovery of stroke patients *versus* general rehabilitation alone (control group).

The data presented in Fig. 8 were examined in greater detail in a similar fashion as the earlier data with the upper extremity case. When the experiments began, the average scores of the experimental group and the control group against the Fugl-Meyer lower extremity scale were 41 and 43 points, respectively; this result indicated that neither group was statistically significant ( $p > 0.05$ ) from one another. In the third week, the average scores of the two groups were 42 and 43 points, respectively, which still showed that there was no significant difference with the two groups. This observation indicated that the effects of Chinese eaglewood extracts as a drug therapy had not

manifested their benefits. After the fourth week, the average score of the experimental group became significantly higher than that of the control group. At the end of the experiments, the average score of the patients in the experimental group was 78 points, whereas that of the control group was 56 points. This observation indicated that Chinese eaglewood extracts as drug therapy began to show their effect starting at week 4.

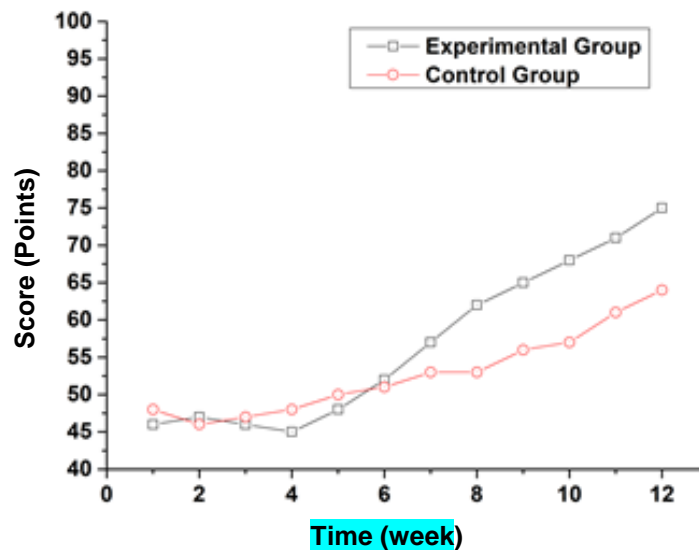


Fig. 8. Results of the Fugl-Meyer lower extremity scale

## CONCLUSIONS

This investigation studied the effects of Chinese eaglewood extracts, a traditional Chinese herbal medicine, on the rehabilitation of stroke patients that have nerve and motor dysfunctions. The research results showed that Chinese eaglewood extracts as a drug therapy can promote the recovery of the nerve and motor functions of stroke patients. The investigation further analyzed the results from the clinical experiments and reached the following conclusions.

1. The use of Me-JA, mixed agent, and Et to induce *A. sinensis* to generate lipid substances was like that stimulated by physical traumas and fungal infections to the Chinese eaglewood tree.
2. Chinese eaglewood extracts as a drug therapy had positive effects on diminishing nerve and motor dysfunctions of stroke patients.
3. From the EEG test results, it was observed that the EEG means and variances in the impaired nerve region did not show significant differences between the results of drug therapy and the results of treatment with extracts. Moreover, it was the surrounding region of the impaired nerves that showed the greatest improvements in terms of EEG means and variances. This observation indicated that the Chinese eaglewood extracts could not help recover the impaired nerve region, but it could make its surrounding region around the impairment more active to replace the impaired functions (*i.e.*, the compensatory effect).

4. In relation to the Fugl-Meyer upper extremity and lower extremity scales, the motor functions of the stroke patients were gradually recovered during the experiments, indicating nerve function recovery in stroke patients.

## ACKNOWLEDGMENTS

This paper relating to the effect of medicine on the human body only represents personal views. The medical data provided in the paper is only for reference and cannot replace the advice of doctors and other medical personnel.

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