A Study on the Chemical Compositions of the Yinqiaosan (Lonicerae and Forsythiae Powder) at Different Time of Later-decoction by Gas Chromatography Mass Spectrometry

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ABSTRACT

Background: Yinqiaosan (Lonicerae and Forsythiae Powder), as a famous prescription of Dr. Wu Jutong in Qing dynasty of China, has the effects of diaphoresis cooling, fire-purging, and detoxication. It is mainly used in the treatment of influenza, hand-foot-mouth disease, esophagitis, pneumonia, acute tonsillitis, mumps, and other viral infections. It is one of the widely used traditional Chinese medicine prescriptions with proven curative effects in clinical use. Objective: To research the material basis of Yinqiaosan decoction when decocting mint, herb schizonepetae in different length of later-decoction time, to find the influence on volatile components of Yinqiaosan decoction decocted later in different length of time, to lay the foundation to further clarify the after-decoction mechanism of Yinqiaosan, and the specification of Yinqiaosan decoction process. Materials and Methods: Gas chromatography mass spectrometry method is used to analyze the volatile components of Yinqiaosan decoction samples decocted for 0, 3, 5, 8, and 10 min. Results: Later-decocting mint and herb schizonepetae at different time when decocting Yinqiaosan had a significant influence on the volatile components of the solution. 54 different chemical components were identified: 25 were identified when later-decocting the sample for 3 min; 13 were identified when later-decocting the sample for 5 min; 11 were identified when later-decocting the sample for 8 min; 7 were identified when later-decocting the sample for 10 min; and 26 were identified when later-decocting the sample for 0 min. There were more volatile components in the sample after-decocted for 3 min. A total of 54 different chemical components were identified in different later-decoction solution samples. These components form the basis of the Yinqiaosan drug effect. Conclusions: The length of later-decoction time of mint and herb schizonepetae was confirmed to be 3 min when decocting Yinqiaosan.

Summary:

- Later-decocting mint and herb schizonepetae at different time had a significant influence on the volatile components of the solution
- Fifty-four different chemical components were identified in different later-decocting solution samples
- There were more volatile components in the sample after-decocted for 3 min
- The volatile components content was high. These components form the important basis of the Yinqiaosan drug effect.
- Total ion flow diagram of volatile oils in the Yinqiaosan sample with mint, herb schizonepetae after 3 min decoction.

INTRODUCTION

The Yinqiaosan (Lonicerae and Forsythiae Powder), as a famous prescription of Dr. Wu Jutong in Qing dynasty of China, is believed to have the effects of diaphoresis cooling, fire-purging, and detoxication. It is mainly used in the treatment of influenza,1,2 hand-foot-mouth disease,3 esophagitis, pneumonia, acute tonsillitis, mumps, and other viral infections. It is one of the widely used traditional Chinese medicine (TCM) prescriptions with proven curative effects in clinical use. Later-decoction is a special and common method for decocting herbs in TCM. Volatile materials, such as mint and amomum cardamomum, are added later during the decoction, usually 5–10 min before the end of the decoction since they are easy to volatilize or destroy when decocting due to their heavy volatile oil content. Later-decoction helps prevent losing the volatile components of the medicine and the effective constituent from being destroyed and decomposed, and thus plays an important role.
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in ensuring the decocting quality. Yinqiaosan is composed of 9 prepared Chinese crude drugs including Lonicerae Japonicae Flos, Forsythiae Fructus, Menthae Haplocalycis Herba, Schizonepetae Herba, Platycodonis Radix, Arctii Fructus, Sojae Semen Praeparatum, Glycyrrhizae Radix Et Rhizoma, and Lophatheri Herba, wherein Menthae Haplocalyx Herba and Schizonepetae Herba are rich in volatile materials and later-decoction becomes necessary. The experiment described in this study was to study the material basis of Yinqiaosan decoction when decocting mint, herba schizonepetae at different time length of later-decoction, and to find its effects on volatile components of the Yinqiaosan decoction by gas chromatography-mass spectrometry (GC-MS). And also to lay a foundation for further clarification of the later-decoction mechanism of Yinqiaosan, and the specifications of the decoction process.

MATERIALS AND METHODS

Reagents and materials

Agilent6890/5975B GC-MS made in American and G1701DAD.03.00.611 workstation; NIST05 standard mass spectrometry database.

The Yinqiaosan medicinal pills were purchased from Nanjing Haichang Chinese Medicine Group Corporation with source herbs identified as follows: L. japonicae Flos (the dried buds of L. japonica Thunb.), Forsythiae fructus (the dried fruits of Forsythia suspense (Thunb. Vahl), Menthae HaplocalycisHerba (the dried aerial parts of Mentha haplocalyx Briq.), Schizonepetae Herba (the dried aerial parts of Schizonepeta tenuisfolia Briq.), Arctii fructus (the dried ripe fruits of Arctium lappa L.), Platycodonis Radix (the dried roots of Platycodon grandiflorum (Jacq.) A. DC.), Sojae Semen Praeparatum (the fermentation products of mature seeds of Glycine max (L.) Merr.), Glycyrrhizae Radix Et Rhizoma (the dried roots and rhizomes of Glycyrrhiza uralensis Fisch.), and Lophatheri Herba (the dried stems and leaves of Lophatherum gracile Brongn.).

Gas chromatography and mass spectrometry conditions

Chromatographic column: HP-5MS quartz capillary column (30.0 mm × 0.25 mm × 0.25 μm); temperature of injection port: 250°C; temperature programming: Initial temperature at 60°C, rising to 150°C at 3°C/min, to 180°C at 10°C/min, and to 250°C at 3°C/min and then kept for 5 min; sample amount: 2 μL; carrier gas: Helium (purity >99.99%); flow velocity: 1.0 mL/min; splitless.

Elion source; ion source temperature: 230°C; temperature of the quadrupole: 150°C; temperature of the interface port: 220°C; electron
Sample preparation

Measuring with precision, the following samples were collected respectively: L. japonicae Flos (9 g), Forsythiae Fructus (9 g), Arctii Fructus (9 g), Platyodonis Radix (6 g), Sojae Semen Praeparatum (5 g), Glycyrrhizae Radix Et Rhizoma (5 g), Lophatheri Herba (4 g), Menthae Haplocalycis Herba (6 g), and Schizonepetae Herba (5 g). They were mixed in 464 mL of distilled water (8 times of prescription total dosage, V/W) and soaked for 30 min.

Later-decocting the sample for 0 min: Decocted to boiling with strong heating fire using traditional marmite, after that, decocted for 15 min with gentle heating fire. The decocted solution was then immediately filtered while it is hot, and its volume was measured, and then purified water was added to the decocted solution until a certain volume is reached.

Later-decocting the sample for 3 min: Decocted to boiling by traditional marmite with strong heating fire, after that, decocted for 15 min with gentle heating fire (later-decocting them for 12 min, add Menthae Haplocalycis Herba and Schizonepetae Herba in and decocting them for 3 min). The decocted solution then immediately filtered while it is hot, and its volume is measured, and then purified water was added to the decocted solution until a certain volume is reached.

Later-decocting the sample for 5 min: Decocted to boiling by traditional marmite with strong heating fire, after that, decocted for 15 min with gentle heating fire (later-decocting them for 10 min, add Menthae Haplocalycis Herba and Schizonepetae Herba in and decocting them for 5 min). The decocted solution then immediately filtered while it is hot, and its volume is measured, and then purified water was added to the decocted solution until a certain volume is reached.

Later-decocting the sample for 8 min: Decocted to boiling by traditional marmite with strong heating fire, after that, decocted for 15 min with gentle heating fire (later-decocting them for 7 min, add Menthae Haplocalycis Herba and Schizonepetae Herba in and decocting them for 8 min). The decocted solution then immediately filtered while it is hot, and its volume is measured, and then purified water was added to the decocted solution until a certain volume is reached.

Later-decocting the sample for 10 min: Decocted to boiling by traditional marmite with strong heating fire, after that, decocted for 15 min with gentle heating fire (later-decocting them for 5 min, add Menthae Haplocalycis Herba and Schizonepetae Herba in and decocting them for 10 min). The decocted solution then immediately filtered while it is hot, and its volume is measured, and then purified water was added to the decocted solution until a certain volume is reached.

Later-decocting the sample for 3 min also contained (R)-(+)‑3‑methylcyclohexanol (existed in herba schizonepetae), phenylethyl alcohol (existed in lophatherum gracile), (S)‑isomenthone (existed in mint), cyclohexanol, 5‑methyl‑2‑(1‑methyl‑1‑)‑trans‑, 4‑terpineol, 2‑methyl‑5‑(1‑methyl‑1‑)‑cyclohexanol, and other chemical compositions, such as vanillin, 2,5‑bis (1,1‑dimethyl‑1‑)‑phenol, and 3‑Homoadamantanol. Later-decocting the sample for 5 min was the highest. The sample later-decocted for 3 min also contained (R)‑(+)‑3‑methylcyclohexanol, menthone, pulegone, 2‑octyl diethyl acetal, 1,2‑cyclohexanediol, 2,5‑bis (1,1‑dimethyl‑1‑)‑phenol, n‑hexadecanoic acid, 2‑cyclohexen‑1‑one, etc., which were mostly found in mint and herba schizonepetae. The sample later-decocted for 8 min contained 3‑methylcyclohexanol, cyclohexanol, 5‑methyl‑2‑(1‑methyl‑1‑)‑trans‑, 25‑trans‑, and 5‑methyl‑2‑(1‑methyl‑1‑)‑cyclohexanol, which existed in mint, and 2‑methylene borane was detected in the sample later-decocted for 10 min; later-decocted for 0 min, the following compounds were detected apart from the original 26: Sulfurous acid, butyl nonylester, 1‑chlooroacetadecane, 2,4‑bis (1,1‑dimethyl‑1‑)‑phenol, hexadecane, 10‑methylnonadecane, tetratetracontane, octadecane, 1‑chlooroacetadecane, tetratetracontane, beta‑iso‑methyl ionone, bromoacetic acid, octadecyl ester, pregnane, sulfuric acid, octadecyl‑2‑propyl ester, 5‑butyl‑6‑hexylcyclohexal‑sulfurous acid, eicosane, and so on. There were only trace amounts of original volatile components of mint, herba schizonepetae, lophatherum gracile in the decoction left. Only a small amount of 2‑cyclohexen‑1‑one, 3‑methylcyclohexanol, 2,6,6‑trimethyl‑2,4‑cycloheptadien‑1‑one, etc., was left. It can be concluded that since mint and herba schizonepetae...
were not later-decocted with other 7 medicines, chemical compositions of these medicines interacted with each other under high heat decoction, triggering chemical changes, and yielding new compounds; and the longer decocting time is responsible for the heavy loss of volatile components in mint and herba schizonepetae.

**CONCLUSIONS**

The experiment found that different time patterns of later-decoction of mint and herba schizonepetae had a significant influence on their volatile components. The sample in which mint and herba schizonepetae were boiled for 10 minutes demonstrated the highest percentage of monoterpenoids, while the sample in which they were boiled for 5 minutes showed the highest percentage of sesquiterpenoids and furanocoumarinoids. Therefore, the decoction time of these two materials is an important factor that influences the chemical composition of the decoction, and further studies are needed to determine the optimal decoction time for each of these materials.
Schizonepetae were later-decocted for 3 min contained more volatile components with high concentration, which are also the important pharmaceutical basis of the Yinqiaosan. Therefore, when decocting Yinqiaosan, the best length of later-decoction time for mint and herba schizonepetae should be 3 min.

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Conflicts of interest
There are no conflicts of interest.

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