Identification and Characterization of Potent CYP2B6 Inhibitors in Woohwangcheongsimwon Suspension, an Herbal Preparation Used in the Treatment and Prevention of Apoplexy in Korea and China


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ABSTRACT:

Woohwangcheongsimwon is a traditional medicine for treating hypertension, arteriosclerosis, coma, and stroke in China and Korea. To assess potential interactions of herb and drug metabolism, commercially available Woohwangcheongsimwon suspensions were examined for their potential to inhibit the activity of nine human cytochrome P450 enzymes. The Woohwangcheongsimwon suspensions showed strong inhibition of CYP2B6 activity. To identify individual constituents with inhibitory activity, the suspension was partitioned using hexane, ethyl acetate, and dichloromethane, and each fraction was tested for its inhibitory effect on CYP2B6-catalyzed bupropion hydroxylation. The hexane fraction possessed inhibitory activity, and gas chromatography/mass spectrometry analysis identified borneol and isoborneol as major constituents of the hexane fraction. These two terpenoids moderately inhibited CYP2B6-catalyzed bupropion hydroxylase activity in a competitive manner, with $K_i$ values of 9.5 and 5.9 $\mu$M, respectively, as well as efavirenz 8-hydroxylase activity, with $K_i$ values of 22 and 26 $\mu$M, respectively. Additionally, reconstituted mixtures of borneol and isoborneol, at the same concentrations as in the Woohwangcheongsimwon suspension, had comparable potency in inhibiting bupropion hydroxylation. These in vitro data indicate that Woohwangcheongsimwon preparations contain constituents that can potently inhibit the activity of CYP2B6 and suggest that these preparations should be examined for potential pharmacokinetic drug interactions in vivo.

Herbal medicines have received much attention as alternatives to conventional clinical therapy, and consumption of herbal medicines in Asian, North American, and European countries has increased dramatically in recent years (Eisenberg et al., 1998; De Smet and Debeer, 2002). A recent report indicates that as many as 16% of prescription drug users consume herbal dietary supplements (Kaufman et al., 2002). With the widespread use of herbal medicines, the risk of herb-drug interactions is a growing medical issue, and physicians and pharmacists are concerned about adverse effects such as hepatotoxicity and drug interactions (Kaplowitz, 1997; Suchard et al., 2004). Several medicinal herbs, including St. John’s wort (Henderson et al., 2002; Mills et al., 2004), ginkgo biloba (Yin et al., 2004), and kava (Anke and Ramzan, 2004), have been reported to cause herb-drug interactions. Interactions among therapeutic drugs as well as interactions of drugs with food and herbal medicines have attracted attention.

The modulation of drug-metabolizing enzymes is one of the main mechanisms of drug interactions (Guengerich, 1997). Cytochrome P450 (P450) monooxygenases are probably the most important enzymes in the detoxification and bioactivation of a number of therapeutic drugs. The P450 family comprises a group of enzymes with broad substrate specificity, which leads to herb-induced drug interactions with some P450 substrates (Ueng et al., 2002). In recent years, in vitro systems using human liver microsomes or recombinant P450 enzymes with tandem mass spectrometry have been established as tools for evaluating potential inhibitory effects of drugs on P450 enzyme activity (Dierks et al., 2001; Kim et al., 2005). Accordingly, in vitro evaluation systems are now widely used in screening procedures to exclude candidate drugs with potent P450-inhibiting effects (Baranczewski et al., 2006).
In a previous study, we screened the P450-inhibiting effects of 20 herbal medications commonly used in Korea. This screening revealed that Woohwangcheongsimwon suspension showed a potent inhibitory effect on CYP2B6-mediated bupropion hydroxylase activity (Kim and Liu, 2007). Furthermore, Woohwangcheongsimwon suspension was one of the most widely used traditional Chinese medicines for the emergency and acute treatment of stroke, numbness, hypertension, epilepsy, and arteriosclerosis. It contains 29 herbs; the main components are *Calcium bivis*, *Moschus*, *Borneol syntheiticum*, *Radix gingseng*, and *Rhizoma dioscoreae* (Lee et al., 2005). Woohwangcheongsimwon suspension has been commercially available and has been commonly used in China, Taiwan, and Korea. Simply because of its widespread use, Woohwangcheongsimwon suspension is highly likely to be used in combination with various drugs.

In this study, we investigated the effects of Woohwangcheongsimwon suspension on human P450 activity, using human liver microsomes, to assess the probability of herb-drug interactions. Through this study, we have identified components having a CYP2B6-inhibiting effect comparable with that of thioTEPA and have shown that these components inhibit CYP2B6 activity in a competitive manner.

### Materials and Methods

#### Chemicals and Reagents.

Borneol, bupropion, chloropropamide, chloroxazone, coumarin, dextromethorphan, isoborneol, phenacetin, thioTEPA, tolbutamide, β-NADP, glucose 6-phosphate, and glucose 6-phosphate dehydrogenase were purchased from Sigma-Aldrich (St. Louis, MO). Hydroxybupropion and pooled human liver microsomes (H161) were obtained from BD Gentest (Woburn, MA). S-Mephytonyi and midazolam were purchased from Ultrafine Chemical Co. (Manchester, UK). Efavirenz and 8-hydroxyefavirenz were purchased from Toronto Research Chemicals, Inc. (Toronto, ON, Canada). All other chemicals and solvents were of the highest grade available.

#### Samples of Woohwangcheongsimwon Suspension.

Woohwangcheongsimwon suspensions manufactured by various pharmaceutical companies including the product of Kwang-Dong Pharmaceutical Co., Ltd (lot 06004) were obtained from a local pharmacy (Table 1). Samples were stored at 4°C until use. All samples were tested soon after the package was opened. Kwang-Dong Woohwangcheongsimwon (aqueous solutions) was used for each experiment as a representative.

#### Inhibitory Effects of Woohwangcheongsimwon on P450 Activity.

The inhibitory potency of Woohwangcheongsimwon suspension was determined with cytochrome P450 assays in the presence and absence of Woohwangcheongsimwon suspension, using pooled human liver microsomes. Phenacetin O-deethylase, coumarin 7-hydroxylase, bupropion hydroxylase, paclitaxel 6β-hydroxylase, tolbutamide 4-hydroxylase, S-mephytonyi 4-hydroxylase, dextromethorphan O-demethylase, chloroxazone 6-hydroxylase, and midazolam 1’-hydroxylase activities were determined as probe activities for CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A, respectively, using cocktail incubation and tandem mass spectrometry, as described previously (Kim et al., 2005). Briefly, the incubation mixtures containing pooled human liver microsomes (0.25 mg/ml), P450-selective substrates, and Woohwangcheongsimwon suspension (0–1.7%, v/v; 0–1,000 μg/ml, dry weight basis) were preincubated for 10 min at 37°C. The reaction was initiated by adding a NADPH-generating system (1.3 mM NADP, 3.3 mM glucose 6-phosphate, 3.3 mM MgCl2, and 1.0 unit/ml glucose-6-phosphate dehydrogenase) and was incubated for 15 min at 37°C in a shaking water bath. After incubation, the reaction was stopped by placing the tubes on ice and adding 100 μl of ice-cold acetonitrile. The incubation mixtures were then centrifuged (10,000 g for 5 min at 4°C). Aliquots of the supernatants were injected into an LC/MS/MS system. All incubations were performed in triplicate, and mean values were used for analysis. To evaluate the effect of preincubation on inhibitory potency, Woohwangcheongsimwon suspension was preincubated for 20 min with the NADPH-generating system, buffer, and microsomes. The reaction was started by adding the P450-selective substrates. The substrates were used at the following concentrations: 50 μM phenacetin, 5 μM coumarin, 50 μM bupropion, 10 μM paclitaxel, 100 μM tolbutamide, 100 μM S-mephytonyi, 5 μM dextromethorphan, 50 μM chloroxazone, and 5 μM midazolam.

#### Fractionation of Woohwangcheongsimwon Suspension and Identification of the CYP2B6-Inhibitory Components.

The Woohwangcheongsimwon suspension (100% 5 ml, v/v) was sequentially extracted with n-hexane, ethyl ether, ethyl acetate, and dichloromethane. The hexane-soluble fraction of Woohwangcheongsimwon suspension was subjected to GC/MS. The GC/MS analysis was carried out on a Shimadzu GC-2010 GC instrument, connected to a QP-5000 mass spectrometer (Shimadzu, Tokyo, Japan) with electron impact ionization (EI mode, 70 eV). The column was a DB-WAX capillary column (60 m × 0.32 mm i.d., 0.25-μm film thickness; Agilent Technologies, Wilmington, DE), and the oven temperature was raised from 80 to 250°C at a rate of 10°C/min with a 4-min hold at 80°C and a 2-min hold at 250°C. Helium was used as the carrier gas, at a flow rate of 1.5 ml/min. The temperatures of the injection port, ion source, and interface were 170, 200, and 270°C, respectively.

#### Assay of Bupropion Hydroxylase and Efavirenz 8-Hydroxylation Activity of Human CYP2B6.

Assays for bupropion hydroxylase and efavirenz 8-hydroxylation activity of human CYP2B6 were performed according to the methods of Kim et al. (2005) and Ward et al. (2003), with minor modifications. Briefly, each incubation was performed with 0.25 mg/ml pooled human liver microsomes (H161) in 100 mM phosphate buffer (pH 7.4) at a final volume of 1.5 ml. The incubation mixtures, containing one of the CYP2B6 isoform-specific substrates, an inhibitor (Woohwangcheongsimwon suspension, 0–1.7% v/v; 0–1,000 μg/ml, dry weight basis; borneol or isoborneol dissolved in methanol, 0–50 μM), and human liver microsomes were preincubated for 5 min at 37°C. The final concentration of methanol for the incubation condition was 1.0%. The substrates were used at concentrations approximately equal to their respective K<sub>i</sub> values (50 μM bupropion and 10 μM efavirenz) for the determination of IC<sub>50</sub> values. For the determination of K<sub>i</sub> values, various concentrations of substrates (20–100 μM bupropion and 2–10 μM efavirenz) were also used. After preincubation, the reactions were initiated by

<table>
<thead>
<tr>
<th>Code</th>
<th>Pharmaceutical Company</th>
<th>Content&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Dosage&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Kwang-Dong Pharmaceutical Co., Ltd.</td>
<td>586.3 ppm</td>
<td>30 ml</td>
</tr>
<tr>
<td>B</td>
<td>Dae-Han New Pharm Co., Ltd.</td>
<td>246.3 ppm</td>
<td>50 ml</td>
</tr>
<tr>
<td>C</td>
<td>Ik-Su Pharmaceutical Co., Ltd.</td>
<td>559.8 ppm</td>
<td>50 ml</td>
</tr>
<tr>
<td>D</td>
<td>SamSung Pharmaceutical Industry Co., Ltd.&lt;sup&gt;c&lt;/sup&gt;</td>
<td>969.3 ppm</td>
<td>20 ml</td>
</tr>
<tr>
<td>E</td>
<td>Cho-Sean Pharmaceutical &amp; Trading Co., Ltd.</td>
<td>440.3 ppm</td>
<td>50 ml</td>
</tr>
<tr>
<td>F</td>
<td>SamSung Pharmaceutical Industry Co., Ltd.&lt;sup&gt;c&lt;/sup&gt;</td>
<td>848.3 ppm</td>
<td>20 ml</td>
</tr>
</tbody>
</table>

<sup>a</sup>Content in Woohwangcheongsimwon suspension measured using GC/MS.

<sup>b</sup>Dosage filled in one bottle of each product, and one or two bottles are available per day for an adult.

<sup>c</sup>Contains l-muscone.

<sup>d</sup>Acori graminei rhizoma is substituted for A. kwang-dong pharmaceutical company.

<table>
<thead>
<tr>
<th>Code</th>
<th>Pharmaceutical Company</th>
<th>Content&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Dosage&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>Code Pharmaceutical Company</td>
<td>848.3 ppm</td>
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</tr>
<tr>
<td>L</td>
<td>Bade-han New Pharm Co., Ltd.</td>
<td>649.9 ppm</td>
<td>50 ml</td>
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<td>M</td>
<td>Dae-Han New Pharm Co., Ltd.</td>
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<td>N</td>
<td>Dae-Han New Pharm Co., Ltd.</td>
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<td>50 ml</td>
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<td>Dae-Han New Pharm Co., Ltd.</td>
<td>1433.2 ppm</td>
<td>20 ml</td>
</tr>
<tr>
<td>P</td>
<td>Dae-Han New Pharm Co., Ltd.</td>
<td>1003.2 ppm</td>
<td>30 ml</td>
</tr>
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</table>

<sup>a</sup>Contains l-muscone.

<sup>b</sup>Acori graminei rhizoma is substituted for A. kwang-dong pharmaceutical company.

<sup>c</sup>Dae-han new pharm co., ltd.
addition of a NADPH-generating system (3.3 mM glucose 6-phosphate, 1.3 mM β-NADPH, 3.3 mM MgCl₂, and 1.0 unit/ml glucose-6-phosphate dehydrogenase) and stopped after 15 min by placing the incubation tubes on ice and adding 100 µl of ice-cold acetonitrile, containing an internal standard (2 µM chlorpropamide for bupropion or 0.5 µM ritalin for efavirenz). The incubation mixtures were centrifuged (10,000g for 5 min at 4°C), and aliquots of the supernatants were analyzed by LC/MS/MS. The reaction rates were linear with incubation time and microsomal protein content under these conditions.

**LC/MS/MS Analysis.** All metabolites of the P450 isoform-specific substrates, excluding 8-hydroxyefavirenz, were measured by tandem mass spectrometry as described previously (Kim et al., 2005). The concentration of 8-hydroxyefavirenz was measured by LC/MS/MS as described elsewhere (Fan et al., 1999).

**Results**

**Effects of Woolhawangcheongsimwon Suspension on P450 Activity.** The effects of Woolhawangcheongsimwon suspension (500 µg/ml) on nine P450 activities are shown in Fig. 1. Of the P450 isoform activities tested, CYP2B6-catalyzed bupropion hydroxylation was most strongly inhibited by Woolhawangcheongsimwon suspension (IC₅₀ 110 µg/ml) (Table 2); the hydroxybupropion formation rate was decreased to 14% of control activity at the highest concentration tested (1000 µg/ml). To determine whether the inhibition by Woolhawangcheongsimwon suspension was substrate-specific, we examined the inhibitory effect of Woolhawangcheongsimwon suspension on CYP2B6-catalyzed efavirenz hydroxylation and found that Woolhawangcheongsimwon inhibited it too, with an apparent IC₅₀ of 190 µg/ml (Table 2; Fig. 2). Woolhawangcheongsimwon suspension showed weak inhibition of CYP2C9 and CYP2E1, with IC₅₀ values of 620 and 700 µg/ml, respectively (Table 2) and minimal or negligible inhibition of the other P450s tested (Fig. 1). The inhibitory potency of Woolhawangcheongsimwon suspension was not reduced significantly after preincubation with microsomes in the presence of a NADPH-generating system (Fig. 1). The reproducibility of the inhibitory effects of different Woolhawangcheongsimwon suspensions on CYP2B6 activity was examined. Regardless of manufacturer, the Woolhawangcheongsimwon suspensions inhibited CYP2B6 activity to the same extent (Fig. 3).

**Identification of the CYP2B6-Inhibiting Components in Woolhawangcheongsimwon Suspension.** To identify the major components responsible for the inhibitory effect on CYP2B6 activity, Woolhawangcheongsimwon suspension was sequentially partitioned with various organic solvents. Of the fractions partitioned, the n-hexane fraction exhibited a strong inhibitory effect on CYP2B6 activity (Fig. 4). The n-hexane fraction was subjected to GC/MS analysis, and two major peaks were detected (Fig. 5). These two peaks (P1 and P2) were identified as the major components responsible for the inhibitory effect.

**TABLE 2**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>CYP1A2</th>
<th>CYP2A6</th>
<th>CYP2B6</th>
<th>CYP2B6</th>
<th>CYP2C8</th>
</tr>
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<tbody>
<tr>
<td>Phenacetin</td>
<td>&gt;1.5</td>
<td>&gt;1.5</td>
<td>0.18 ± 0.0018</td>
<td>0.32 ± 0.034</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td>Bupropion</td>
<td>&gt;1000</td>
<td>&gt;1000</td>
<td>110 ± 1.1</td>
<td>190 ± 20</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>Efavirenz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td></td>
<td></td>
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</table>

**TABLE 2**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>CYP2C9</th>
<th>CYP2C19</th>
<th>CYP2D6</th>
<th>CYP2E1</th>
<th>CYP3A4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolbutamide</td>
<td>1.0 ± 0.18</td>
<td>&gt;1.5</td>
<td>&gt;1.5</td>
<td>&gt;1.5</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td>S-Mephenytoin</td>
<td>&gt;1000</td>
<td>&gt;1000</td>
<td>700 ± 53</td>
<td>700 ± 53</td>
<td>&gt;1000</td>
</tr>
</tbody>
</table>

*IC₅₀ values are based on dry weight of Woolhawangcheongsimwon suspension.
FIG. 3. Reproducibility of CYP2B6 inhibition by several Woohwangcheongsimwon suspensions (■) and their corresponding reconstituted mixtures of borneol and isoborneol (□). Pooled human liver microsomes (0.25 mg/ml, H161) were incubated with bupropion (50 μM) in the absence or presence of several manufacturers’ Woohwangcheongsimwon suspensions (500 μg/ml) or the corresponding reconstituted solutions of borneol and isoborneol. The reconstituted mixtures contained the same borneol and isoborneol concentrations as in the Woohwangcheongsimwon suspensions, which were determined by GC/MS. Data represent the mean ± S.D. of triplicate experiments. A, Kwang-Dong Pharmaceutical Co., Ltd; B, Dae-Han New Pharm Co., Ltd; C, Ik-Su Pharmaceutical Co., Ltd; D, SamSung Pharmaceutical Industry Corp., Ltd; E, Cho-Seon Pharmaceutical & Trading Co., Ltd; F, SamSung Pharmaceutical Industry Corp., Ltd. Table 1 lists the Woohwangcheongsimwon suspensions tested. The representative control activity of bupropion hydroxylation was 2.3 pmol/min/mg of protein.

identified as isoborneol and borneol, respectively, by cochromatography and GC/MS spectral data of authentic compounds (Fig. 6). Electron impact spectra of P1 and P2 revealed a molecular ion (M+) at m/z 154 and a base peak at m/z 95.1. Applying this to the mass spectra of borneol and isoborneol, we can identify fragment peaks resulting from the loss of H2O at m/z = 136 and the loss of ethane at m/z = 110, which corresponds to a reverse Diels-Alder reaction. The fragment peak at m/z = 95 is due to the loss of a methyl group (Donald et al., 2001).

Inhibitory Effects of Borneol and Isoborneol on P450 Activity. The inhibitory effects of borneol and isoborneol from Woohwangcheongsimwon suspension toward nine major human P450 isoforms were investigated to clarify the selectivity of inhibition. Borneol and isoborneol strongly inhibited microsomal CYP2B6 activity but showed little or no inhibition of the other eight P450s tested (Fig. 7).

The Lineweaver-Burk plots, Dixon plots, and secondary reciprocal plots indicated that borneol and isoborneol competitively inhibited CYP2B6-catalyzed bupropion hydroxylase activity, with apparent K_i values of 9.5 and 5.9 μM, respectively (Fig. 8; Table 3). The K_i value of thioTEPA, a typical CYP2B6 inhibitor, was simultaneously determined (1.8 μM) (Fig. 8; Table 3). To determine whether the inhibition by these monoterpenes was substrate-specific, we examined their inhibitory effects on CYP2B6-catalyzed efavirenz 8-hydroxylation and found that borneol and isoborneol competitively inhibited the activity, with K_i values of 22 and 26 μM, respectively (Table 3).

Discussion

Some difficulties have occurred in patients taking prescription medicines and herbal preparations, owing at least in part to a lack of information on herb-drug interactions arising from drug metabolism or absorption (Kim and Liu, 2007). Herbal preparations are taken as over-the-counter products in many Asian countries, including China, Japan, and Korea. To reduce the number of adverse interactions, it is necessary to study drug-herbal preparation interactions.

In the present study, we evaluated the P450-inhibitory effect of Woohwangcheongsimwon suspensions, a traditional Chinese medicine widely used for emergency and acute treatment of stroke and numbness. In human liver microsomes with a NADPH-generating system, Woohwangcheongsimwon suspension moderately inhibited metabolic CYP2B6-catalyzed bupropion hydroxylation activity. Woohwangcheongsimwon suspension (100% 5 ml, v/v) was sequentially partitioned with the same volume of n-hexane, ethyl ether, ethyl acetate, and dichloromethane, and the inhibitory effect of each fraction on CYP2B6-catalyzed bupropion hydroxylase activity was determined in pooled human liver microsomes (H161). Data represent the mean ± S.D. of triplicate experiments. W, Woohwangcheongsimwon suspension; A, hexane extracts; B, ethyl ether extracts; C, ethyl acetate extracts; D, dichloromethane extracts; E, residuals. The representative control activity of bupropion hydroxylation was 2.3 pmol/min/mg of protein.

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CYP2B6 substrate (Ward et al., 2003). Borneol and isoborneol showed negligible inhibitory effects on the other P450s tested (Fig. 7).

Borneol and isoborneol are major components of borneolum (Dryobalanops aromatica), one of the major herbal extracts in Woohwangcheongsimwon suspension (Park et al., 2003). To reconfirm that the inhibition of CYP2B6 activity by Woohwangcheongsimwon suspension resulted from borneol and isoborneol, we quantified the borneol and isoborneol concentrations in Woohwangcheongsimwon suspensions from several manufacturers, prepared standard solutions with the same borneol and isoborneol concentrations, and showed that all of the reconstituted mixtures of borneol and isoborneol had similar inhibitory effects and that the extent of inhibition was comparable among the mixtures and their respective Woohwangcheongsimwon suspensions (Fig. 3). Thus, these newly identified monoterpenes probably contribute to the CYP2B6 inhibition caused by Woohwangcheongsimwon suspension. These results also suggest that Woohwangcheongsimwon suspensions from several manufacturers have similar inhibitory potencies although the concentration of the Woohwangcheongsimwon suspension tested is slightly high (500 μg/ml) in detecting differences between various formulations.

Borneol and isoborneol are monoterpenes; monoterpenes are found in the volatile essences of flowers and oils of various plants and in herbal medicines (Li Lin et al., 2006). Some are commonly used as food additives and as fragrance components in cosmetics, soaps, and cleaning products (Guitton et al., 1998). Borneol is often a major constituent of the essential oils of medicinal herbs such as the genus Micromeria (Sneyd et al., 1994) and rosemary (Tabanca et al., 2001). Thus, monoterpenes contained in those medicinal herbs may also affect CYP2B6 activity.

Woohwangcheongsimwon suspension is one of the most popular herbal medicines in Korea. It is commonly used in the treatment and prevention of apoplexy, hypertension, palpitations, convulsions, and unconsciousness and is composed of approximately 30 types of traditional drugs from herbs, animals, and even metals such as gold (Lee et al., 2005). In China, it is called Niuhuang Qinxin Wan and was recorded in the Prescriptions of Taiping Benevolent Dispensary during the Song dynasty. It is still produced at the Tong Ren Tang Pharmaceutical factory. Thus, because of its widespread use, Woohwangcheongsimwon presents a significant possibility for herb-drug interactions.
between Woohwangcheongsimwon and drugs that are cleared primarily by CYP2B6-mediated pathways should be examined in vivo, especially given the interaction potential of St. John’s wort in humans (Henderson et al., 2002).

In conclusion, by screening the inhibitory effects of Woowangcheongsimwon suspensions on the activities of nine P450 isoforms, we identified two components in Woowangcheongsimwon suspension, borneol and isoborneol, as potent inhibitors of CYP2B6. The inhibitory potencies of borneol and isoborneol were comparable with that of thioTEPA. These results suggest that the use of high amounts of this herbal preparation may cause an interaction with drugs metabolized by CYP2B6 in some individuals. It is important to note, however, that the inhibition of CYP2B6 activity in vitro does not necessarily translate into drug interactions in clinical situations. In vivo studies on the interactions between Woowangcheongsimwon suspension and CYP2B6 substrates are required to determine the clinical relevance of CYP2B6 inhibition by Woowangcheongsimwon.

References


Address correspondence to: Dr. Kwang-Hyeon Liu, Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan 614-735, South Korea. E-mail: dstlkh@inje.ac.kr
CORRECTION TO “IDENTIFICATION AND CHARACTERIZATION OF POTENT CYP2B6 INHIBITORS IN WOOHWANGCHEONGSIMWON SUSPENSION, AN HERBAL PREPARATION USED IN THE TREATMENT AND PREVENTION OF APOPLEXY IN KOREA AND CHINA”

In the article referenced above [Kim H, Kim KB, Ku HY, Park SJ, Choi H, Moon JK, Park BS, Kim JH, Yea SS, Lee CH, Lee HS, Shin JG, and Liu KH (2008) Drug Metab Dispos 36:1010–1015], one of the authors’ names was incorrect. The correct name is Soo-Jin Park. The hyphen was omitted.

The online version of this article has been corrected in departure from the print version.

The authors regret this error and apologize for any confusion or inconvenience it may have caused.