INTRODUCTION

In Korea, continuous improvements in the standard of living and the development of health and medical technologies have led to longer average life spans and substantial growth of the elderly population. Elderly patients suffering from chronic diseases take many medications, and adverse reactions to these medications occur at a higher rate than in younger patients.\(^1\)\(^-\)\(^2\) In particular, elderly patients often take dietary supplements, and sales revenue from dietary supplements in Korea has been increasing rapidly.\(^3\) According to a study published in 2010 by Ock et al., 62% of adult respondents aged 30 to 69 reported taking dietary supplements. Ginseng was the most commonly used dietary supplement, followed by multivitamins, glucosamine, probiotics, and vitamin C.\(^4\)

In other countries, reports on the use of dietary supplements and research on possible interactions with prescription drugs in elderly patients have been actively conducted for many years. According to a study published in 2000, 42.1% of adults in the United States were taking dietary supplements and 22.5% were taking medications.\(^5\)
at least one type of dietary supplements in 1997, and approximately 10% of individuals who reported taking dietary supplements were over 65 years old.\textsuperscript{5-6}) Most elderly patients take several medications, and a considerable number of them take these medications in combination with dietary supplements.\textsuperscript{7}) However, information on the safety of dietary supplements and their diverse medicinal effects is scarce. For these reasons, elderly patients who take dietary supplements are often exposed to risks arising from interactions between prescription drugs and dietary supplements. These risks can be exacerbated because patients often do not report dietary supplement use to medical experts, such as doctors and pharmacists.\textsuperscript{8}) Therefore, pharmacists should be made aware of whether elderly patients take dietary supplements and provide patients with information on possible interactions that may occur.

The purpose of this study was to investigate the use of dietary supplements in the elderly patients with chronic diseases who visit a community pharmacy and determine potential dietary supplement-prescription drug interactions by comparing the supplement list with the list of prescription drugs for each individual patient.

\textbf{METHODS}

\textbf{Study Subjects and Period}

The subjects of this study were patients who visited a large community pharmacy located near the Boramae Medical Center in Seoul, Korea, between March 2, 2011, and April 27, 2011. We limited the subjects to elderly patients over 65 years of age who had chronic diseases, including hypertension, diabetes, hyperlipidemia, dementia, chronic kidney disease, chronic liver disease, chronic gastrointestinal disease, and chronic pulmonary disease. All elderly patients with chronic diseases who visited the pharmacy were invited to participate. After the purpose and methods of the study were explained, patients who agreed to participate were finally included. We also got verbal informed consents from patients for searching their prescription drug histories using computerized database at the pharmacy.

\textbf{Data collection regarding dietary supplement usage was conducted using a face-to-face interview in which the pharmacist directly explained each question to the patient and filled in the response at the time of prescription drug dispensing. Then the list of drugs prescribed for each elderly patient was reviewed only for those who responded to the interview using the computerized database at the pharmacy, and we consulted the existing literature to determine potential risks caused by interactions between dietary supplements and the listed prescription drugs.}

The interview questions were composed as follows:

First, questions about sex and age were included to determine the demographic attributes of the survey respondents. The respondents were asked to provide their self-evaluated health conditions and whether they take dietary supplements. In cases where the interview respondent reported taking dietary supplements, follow-up questions were asked regarding the use of these supplements.

Questions about the use of dietary supplements were formulated as follows:

First, the respondents were provided with a list of common dietary supplements and were asked to select those that they had consistently taken (more than three times a week) for the last six months. The list of common dietary supplements consisted of seven items (red ginseng, ginseng, omega-3, glucosamine, aloe, vitamin C, and vitamin E) that have known interactions with prescription drugs and are among the top ten supplements in terms of sales revenue based on the 2009 Dietary Supplements Production Performance statistics data provided by the Korea Food and Drug Administration.\textsuperscript{3}) Four additional supplements were included in the interview (saw palmetto, coenzyme Q10, garlic, and ginko leaves) because interactions with prescription drugs have been reported for these supplements.\textsuperscript{9-15})

Second, respondents were asked how they started to take dietary supplements and how they obtained information on dietary supplements when they started taking them. Respondents were also asked whether they felt that their health improved as a result of the dietary sup-
Supplements, and they were asked to assess the degree of improvement and report any adverse reactions. In addition, we inquired as to the type of adverse reaction that was experienced to investigate whether adverse reactions differ depending on dietary supplements.

Next, respondents were asked whether they reported their use of dietary supplements to a health professional and which health professional they consulted. For those who did not respond to the question, they were asked the reason for not reporting their dietary supplement use and whether a health professional had asked about their supplement intake.

Interactions between dietary supplements with prescription drugs in the elderly respondents with chronic diseases were analyzed as follows:

First, after the interview was completed, the list of prescription drugs for each patient was obtained through the computer system at the pharmacy. Based on an individual patient’s reported use of dietary supplements, known interactions between prescription drugs and dietary supplements were examined. Potential interactions between dietary supplements and prescription drugs were identified using literature search that was conducted using PubMed to identify relevant studies published prior to April 2011. We searched for nine different dietary supplement product names, all of which at least one of the respondents reported taking, in combination with the following search terms: “prescription drug”, “interaction”, and “adverse effect.” We also used the search terms “herbal”, “dietary supplements”, “prescription drug”, “herbal medicine,” and “interaction” to search for additional information on general dietary supplement-prescription drug interactions.

Risks were classified to assess dietary supplement-prescription drug interactions. Cases where at least one occurrence of a specific interaction was reported were classified as “potential interactions,” and cases where the literature indicated that an interaction is theoretically possible, yet no cases have been reported, were classified as “possible interactions.”

We performed a frequency analysis of the data to express responses regarding demographic attributes, such as age and sex, as well as experimental responses, such as the use of dietary supplements, in terms of the percentage of respondents. To investigate whether the distribution of the responses to the questions related to the use of dietary supplements were significantly correlated with sex, age and self-evaluated health conditions, we used the chi-squared and Fisher’s exact tests. Data collection and statistical processing were conducted using SPSS version 18.0, and the level of statistical significance was set at p < 0.05.

RESULTS

General Attributes of the Respondents

Out of 167 patients who were asked to participate, a total of 143 patients (85.6%) responded to the interview during the study period, and 65 (45.5%) of the respondents reported taking dietary supplements consistently for six months.

The largest number of respondents, 58 subjects (40.6%), were in the 65 to 69 age group, and 29.4% were in the 70 to 74 age group. There were more females than males at 85 (59.4%) and 58 (40.6%) individuals, respectively. With regards to the patients’ self-evaluated health condition, the largest number, 57 patients (39.9%), reported that their condition was “poor” (Table 1).

<table>
<thead>
<tr>
<th>Demographic Attributes</th>
<th>Number of individuals</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>58</td>
<td>40.6</td>
</tr>
<tr>
<td>70-74</td>
<td>42</td>
<td>29.4</td>
</tr>
<tr>
<td>75-79</td>
<td>21</td>
<td>14.7</td>
</tr>
<tr>
<td>80+</td>
<td>22</td>
<td>15.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>58</td>
<td>40.6</td>
</tr>
<tr>
<td>female</td>
<td>85</td>
<td>59.4</td>
</tr>
<tr>
<td>Self-evaluated Health Condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>good</td>
<td>42</td>
<td>29.4</td>
</tr>
<tr>
<td>fair</td>
<td>44</td>
<td>30.8</td>
</tr>
<tr>
<td>poor</td>
<td>57</td>
<td>39.9</td>
</tr>
<tr>
<td>Total</td>
<td>143</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Use of Dietary Supplements

Thirty-eight elderly patients (58.5%) were taking one type of dietary supplement, 18 patients (27.7%) took 2 types, and 9 patients (13.8%) took 3 or more types of supplements. Patients were able to select multiple dietary supplements from the list provided, and 107 dietary supplements were taken by the 65 dietary supplement users. Among these, red ginseng was the most commonly used supplement (used by 34 respondents, 31.7%), followed by omega-3 (23 respondents, 21.5%) and glucosamine (13 respondents, 12.1%) (Table 2).

In response to the question about how they started to take dietary supplements, the largest number (36 respondents, 55.4%) reported that they decided to take supplements based on recommendations by their friends or relatives. The second leading reason (12 respondents, 18.5%) was the advice from the patient’s pharmacist. With respect to the preferred source of information regarding dietary supplements, friends or relatives were the most common source (41 respondents, 64.1%) followed by broadcasts or advertisements (12 patients, 18.8%) and pharmacists (9 patients, 14.1%).

Twenty respondents (30.8%) reported feeling that their health improved while taking dietary supplements. Four respondents (6.2%) reported feeling that their health deteriorated, and 41 respondents (63.1%) were not sure. Thus, the majority of respondents reported no effects of dietary supplements. Of the 65 respondents who took dietary supplements, 10 (15.4%) detected adverse reactions while taking them. The adverse reactions experienced included indigestion (3 patients, 30.3%), nausea (2 patients, 20.0%), dizziness (3 patients, 30.0%), as well as edema and flushing (1 patient each). None of the patients were informed or aware of the possibility of adverse reactions to dietary supplements prior to taking them.

Of the respondents who took dietary supplements, 22 (33.8%) notified their doctors or pharmacists of their current dietary supplement use before they were prescribed prescription drugs. Twelve of these respondents (54.5%) notified only their doctors, and 1 respondent (4.5%) notified only their pharmacist. Nine respondents (40.9%) notified both their pharmacists and doctors. Of the 43 respondents (66.2%) who did not notify a health professional of their use of dietary supplements, 31 respondents (72.1%) reported that they thought they did not need to inform their care providers because it was simply a dietary supplement. More than half of the respondents (38 participants, 59.4%) reported that they had been asked by their doctors or pharmacists regarding whether they had been taking dietary supplements. Twenty-nine respondents (76.3%) reported that they were asked by their doctors only, 4 respondents (10.5%) were asked by their pharmacists only, and the remaining 5 respondents (13.2%) were asked by both their doctors and pharmacists.

Factors Affecting the Use of Dietary Supplements

The investigation of the relationship between the demographic attributes of the elderly patients with a chronic disease who responded to the interview revealed that the age or sex of the respondent did not affect whether dietary supplements were taken (p > 0.05). However, the rate of dietary supplement use was lowest when patients reported the condition of their health to be “poor” (p < 0.05) (Table 3).

Interactions between Dietary Supplements and Prescription Drugs

Analysis of the cases where dietary supplements and prescription drugs were taken concurrently reveals that 13
patients (20.0%) were concurrently taking prescription drugs that can interact with the dietary supplements reportedly taken. A total of 21 incidences of potential or possible interactions were discovered; there were 3 potential and 18 possible interactions.

All three reported incidences of potential interactions were related to the use of ginkgo leaves with one incident each related to the concurrent use of cilostazol, an antiepileptic medication, and ibuprofen. There were 18 incidences of possible interactions, 6 of which were related to garlic and aspirin or other anticoagulant or antiplatelet agents. Two possible interactions stemmed from the concurrent use of ginkgo leaves and aspirin, and 3 incidences of potential interaction were observed between ginseng and aspirin and other anticoagulant or antiplatelet agents. In addition, there were 5 incidences of potential interactions between ginseng and an antihypertensive drug, and 2 incidences of potential interactions between vitamin E and aspirin (Table 4).

Of the 13 patients who were exposed to potential or possible interactions, 9 patients (69.2%) were exposed to 1 incidence, 1 patient (7.7%) was exposed to 2 incidences, 2 patients (15.4%) were exposed to 3 incidences, and 1 patient (7.7%) was exposed to 4 incidences.

### Table 3. Demographic Attributes and Use of Dietary Supplements

<table>
<thead>
<tr>
<th>Demographic Factors</th>
<th>Use of Dietary Supplements</th>
<th>Overall</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (%)</td>
<td>No (%)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>27</td>
<td>31</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>46.6%</td>
<td>53.4%</td>
<td>100.0%</td>
</tr>
<tr>
<td>70-74</td>
<td>20</td>
<td>22</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>47.6%</td>
<td>52.4%</td>
<td>100.0% 0.97</td>
</tr>
<tr>
<td>75-79</td>
<td>9</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>42.9%</td>
<td>57.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>80+</td>
<td>9</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>40.9%</td>
<td>59.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>21</td>
<td>37</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>36.2%</td>
<td>63.8%</td>
<td>100.0% 0.08</td>
</tr>
<tr>
<td>female</td>
<td>43</td>
<td>42</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>50.6%</td>
<td>49.4%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Self-evaluated Health Condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>good</td>
<td>30</td>
<td>12</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>71.4%</td>
<td>28.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>fair</td>
<td>23</td>
<td>21</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>52.3%</td>
<td>47.7%</td>
<td>100.0% 0.00</td>
</tr>
<tr>
<td>poor</td>
<td>11</td>
<td>46</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>19.3%</td>
<td>80.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>78</td>
<td>143</td>
</tr>
<tr>
<td></td>
<td>45.5%</td>
<td>54.5%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

### Table 4. Potential and Possible Interactions Between Prescription Drugs and Dietary Supplements (n = 65)

<table>
<thead>
<tr>
<th>Dietary Supplements</th>
<th>Prescription Drugs</th>
<th>Interactions</th>
<th>Type</th>
<th>Number of Incidences</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic</td>
<td>Aspirin and other anticoagulant or antiplatelet agents</td>
<td>Increased risk of bleeding</td>
<td>Possible</td>
<td>6</td>
<td>20-23</td>
</tr>
<tr>
<td>Ginko Leaves</td>
<td>Cilostazol</td>
<td>The bleeding time is increased by prolonging the effects of cilostazol</td>
<td>Potential</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Antiepileptics (valproic acid and phenytoin)</td>
<td>The level of antiepileptic in the blood drops below the required amount, possibly leading to a fatal seizure</td>
<td>Potential</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Aspirin</td>
<td>Increased risk of bleeding</td>
<td>Possible</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Ibuprofen</td>
<td>Increased risk of bleeding</td>
<td>Potential</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Aspirin and other anticoagulant or antiplatelet agents</td>
<td>Increased risk of bleeding</td>
<td>Possible</td>
<td>3</td>
<td>24-28</td>
</tr>
<tr>
<td></td>
<td>Antihypertensive drugs</td>
<td>Hypotension induced by nitric oxide production or calcium channel blockade</td>
<td>Possible</td>
<td>5</td>
<td>29-30</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Aspirin</td>
<td>Potentiates the antiplatelet activity of aspirin</td>
<td>Possible</td>
<td>2</td>
<td>31</td>
</tr>
</tbody>
</table>
DISCUSSION

This study observed the proportion, type, and regimen of dietary supplement use in elderly patients with chronic diseases and analyzed potential and possible interactions with prescription drugs taken concurrently in those patients who reported taking dietary supplements. In a study of the use of dietary supplements by healthy individuals conducted in Korea on 6,201 adults between the ages of 30 and 69 over the period of approximately one month, 62% of the 3,000 respondents reported taking dietary supplements. We observed a lower rate for individuals that were 65 years of age and older (45.1%), which might be because we included smaller number of dietary supplement items than the previous study.

Ginkgo leaves, which are mainly used to treat memory loss, diseases related to peripheral blood vessels, and tinnitus, can easily be obtained without a prescription. However, when ginkgo leaves and cilostazol are administered together, ginkgo leaves strengthen the effects of cilostazol and lead to prolonged bleeding times. When taken with an antiepileptic drug, ginko leaves can lower the antiepileptic drug concentration in blood below the required level due to their effects on cytochrome P450(CYP)2C19, which can result in a fatal seizure. One published report has described a 55-year-old male who incurred a potential interaction when taking ginkgo leaves concurrently with prescribed valproic acid and phenytoin. Ginkgo leaves also exhibit antiplatelet activity. One report has described a patient who took ginkgo leaves together with aspirin and experienced serious bleeding, including a brain hemorrhage. A similar case has been reported regarding the concurrent use of ginkgo leaves and ibuprofen: a coma patient died from a fatal brain hemorrhage due to the involvement of ginkgo leaves in the coagulation mechanism within the body. In the study presented here, respondents reported 5 (4.7%) potential or possible interactions related to ginkgo leaves out of 107 potential incidents.

Garlic is a dietary supplement that alleviates cardiovascular diseases by lowering blood pressure and reducing blood lipids. Garlic also reduces the function of platelets by suppressing the production and secretion of molecules such as platelet activating factor, adenosine, prostaglandins, and thromboxanes. These effects due to interactions with garlic require attention, especially when an elderly patient with cardiovascular disease takes garlic and aspirin or an antiplatelet agent at the same time. In this study, 6 (5.6%) out of 107 incidences involved possible interactions related to garlic.

Ginseng, which resulted in 8 (7.5%) possible interactions out of 107 incidences of taking dietary supplements in this study, is currently widely used for diverse purposes including the treatment of erectile dysfunction, cancer prevention, and stamina reinforcement. Although the mechanism of action is not yet fully identified, ginseng is known to affect the cardiovascular, endocrine, and central nervous systems. An *in vitro* test has revealed that ginseng hinders platelet aggregation by suppressing the production of thromboxane A2. In addition, a case has been reported in which a 72-year-old female who had taken a medication containing ginseng exhibited vaginal bleeding. Therefore, although no clinical studies or case reports have been described, interactions between ginseng and antiplatelet agents, such as aspirin, taken concurrently are thought to be likely. Furthermore, ginseng can cause hypotension due to the production of nitric oxide and calcium channel blockade, necessitating care when taken together with antihypertensive drugs.

Vitamin E is a dietary supplement widely used for the prevention of cardiovascular complications and as an antioxidant. Vitamin E strengthens the antithrombotic effects of aspirin by blocking the initial stage of the platelet activation process induced by collagen. In this study, 2 out of 107 incidences (1.9%) of taking dietary supplements involved possible interactions between prescription medications and vitamin E.

In our study of elderly patients with chronic diseases, only 22 respondents (33.8%) notified their doctors or pharmacists of their use of dietary supplements. Furthermore, 12 (54.5%) respondents notified their doctors only, making it difficult for pharmacists to know whether patients were taking dietary supplements. This lack of disclosure created
an obstacle for pharmacists to provide information on interactions between dietary supplements and prescription drugs. Thirty-one respondents (72.1%) who did not notify health professionals of their use of dietary supplements reported that they did not feel the need to report it because they were simply dietary supplements; this finding suggests that there is a need for education on the effects of dietary supplements on prescription drugs. The other three patients (7.0%) who did not report their use of dietary supplements explained this lack of disclosure by saying that they were not asked about it, indicating that pharmacists should be more proactive in pursuing this topic with elderly patients with chronic diseases. This can also be seen in the response to the question of whether a doctor or pharmacist inquired about the respondent’s use of dietary supplements. Of the 65 respondents who reported taking dietary supplements, 38 (59.4%) reported that they were asked about their use of supplements, but 29 of these 38 respondents (76.3%) reported that they were asked only by their doctor.

Elderly patients with chronic diseases receive information on dietary supplements mostly from friends or relatives and in many cases also start taking them based on the recommendations of friends or relatives; thus, elderly individuals often lack sufficient information on interactions with prescription drugs. In addition, because patients generally do not talk about the fact that they take dietary supplements and are not asked about supplement use nearly half of the time, pharmacists should take proactive steps to rectify this dangerous situation.

Our study suggests that use of dietary supplements by elderly patients with chronic diseases was not related to age or sex, and elderly patients use more supplements when they perceive their health to be good. Therefore, proactive monitoring of interactions is needed even in elderly patients who are in a younger age group and feel that they are in relatively good health. Because the number of different dietary supplements taken by the elderly respondents and the self-evaluated condition of health did not affect whether respondents reported their use of dietary supplements, pharmacists should ask elderly patients whether they take dietary supplements regardless of these factors and examine the possibility of interactions.

The limitations of this study included the relatively small number of interview respondents (143 persons) and the fact that the subjects were limited to elderly patients who visit one large pharmacy adjacent to the Boramae Medical Center in Seoul. The number of respondents was smaller than we expected because few elderly patients with chronic diseases visit a pharmacy themselves, and often their guardian or agent will go to the pharmacy on their behalf. Furthermore, even when elderly patients visited the pharmacy in person, it was difficult to conduct the interview because communication between the interviewer and respondent was not smooth. In addition, the list of dietary supplements that were actually taken relied on self-reporting, and thus, the results could have been affected by the patients’ knowledge level and ability to remember their list of supplements. Another limitation was that we did not investigate the number of patients with each chronic disease. We also did not analyze the type and regimen of dietary supplements according to types of patients’ chronic diseases. There was possibility that we might miss prescription drugs that could interact with dietary supplements patients were taking since some patients could visit other pharmacies to get their prescription filled.

Of the elderly patients with chronic diseases in Korea who took part in the interview, 65 respondents (45.5%) were taking dietary supplements, and 13 (20.0%) were exposed to potential or possible interactions between dietary supplements and prescription drugs. Proactive instruction by pharmacists and further assessments of interactions between dietary supplements and prescription drugs could facilitate safer and more effective use of medications through the prevention of interactions that can occur in elderly patients with chronic diseases.

REFERENCES

3. Korea Food and Drug Administration. The 2009 dietary
www.khsa.or.kr/board/view.asp?bbsid=2&fromDate=&is
Admin=&page=2&searchType=&searchValue=&seq=588&to
Date (accessed on November 2, 2012).
4. Ock SM, Hwang SS, Lee JS, et al., Dietary supplement use
by South Korean adults: Data from the national
complementary and alternative medicine use survey
5. Eisenberg DM, Davis RB, Ettner SL, et al., Trends in
alternative medicine use in the United States, 1990-1997:
results of a follow-up national survey. JAMA. 1998; 280:
1569-75.
6. Astin JA, Pelletier KR, Marie A, et al., Complementary and
alternative medicine use among elderly persons: one-year
analysis of a Blue Shield Medicare supplement. J Gerontol
7. Stewart RB, Cooper JW. Polypharmacy in the aged.
8. Elder NC, Gillcrist A, Minz R. Use of alternative health
care by family practice patients. Arch Fam Med. 1997; 6:
181-4.
9. Izzo AA, Ernst E. Interactions between herbal medicines
and prescribed drugs: an updated systematic review. Drugs.
2009; 69: 1777-98.
10. Aruna D, Naidu MU. Pharmacodynamic interaction studies
of Ginkgo biloba with cilostazol and clopidogrel in healthy
and herb-drug interactions: experience with Ginkgo biloba
12. Robertson SM, Davey RT, Voell J, et al., Effect of Ginkgo
biloba extract on lopinavir, midazolam and fexofenadine
13. Vaes LP, Chyka PA. Interactions of warfarin with garlic,
ginger, ginkgo, or ginseng: nature of the evidence. Ann
14. Engelsen J, Nielsen JD, Winther K. Effect of coenzyme Q10
and Ginkgo biloba on warfarin dosage in stable, long-term
warfarin treated outpatients. A randomised, double blind,
of botanical supplementation on human cytochrome
P450 phenotypes: Citrus aurantium, Echinacea purpurea, milk
thistle, and saw palmetto. Clin Pharmacol Ther. 2004; 76:
428-40.
16. Ly J, Percy L, Dhanani S. Use of dietary supplements and
their interactions with prescription drugs in the elderly. Am J
17. Kupiec T, Raj V. Fatal seizures due to potential herb-drug
interactions with Ginkgo biloba. J Anal Toxicol. 2005; 29:
755-8.
and ginger on the pharmacokinetics and pharmacodynamics
59: 425-32.
biloba: evaluation of CYP2C9 drug interactions in vitro and
20. Hoffman T. Ginkgo, Vioxx and excessive bleeding--possible
drug-herb interactions: case report. Hawaii Med J. [Case
Reports], 2001; 60: 290.
21. Meisel C, Johna A, Roots I. Fatal intracerebral mass
bleeding associated with Ginkgo biloba and ibuprofen.
Atherosclerosis. [Case Reports Letter], 2003; 167: 367.
22. Wojcikowski K, Myers S, Brooks L. Effects of garlic oil on
platelet aggregation: a double-blind placebo-controlled cross-
over study. Platelets. 2007; 18: 29-34.
(Allium sativum) on blood lipids, blood sugar, fibrinogen
and fibrinolytic activity in patients with coronary artery
disease. Prostaglandins Leukot Essent Fatty Acids. 1998; 58:
257-63.
25. Burnham BE. Garlic as a possible risk for postoperative
26. German K, Kumar U, Blackford HN. Garlic and the risk of
27. Rose KD, Croissant PD, Parliament CF, et al., Spontaneous
spinal epidural hematoma with associated platelet
dysfunction from excessive garlic ingestion: a case report.
28. Park HJ, Lee JH, Song YB, et al., Effects of dietary
supplementation of lipophilic fraction from Panax ginseng on
cGMP and cAMP in rat platelets and on blood coagulation.
29. Abebe W. Herbal medication: potential for adverse
30. Hopkins MP, Androff L, Benninghoff AS. Ginseng face
cream and unexplained vaginal bleeding. Am J Obstet
in Panax ginseng. Planta Med. [Research Support, Non-U.S.
32. Greenspan EM. Ginseng and vaginal bleeding. JAMA.
33. Baek EB, Yoo HY, Park SJ, et al., Inhibition of Arterial
Myogenic Responses by a Mixed Aqueous Extract of Salvia
Milliorrhiza and Panax Notoginseng (PASEL) Showing
34. Cai BX, Li XY, Chen JH, et al., Ginsenoside-Rd, a new
voltage-independent Ca2+ entry blocker, reverses basilar
hypertrophic remodeling in stroke-prone renovascular

## Appendix: Survey of Status of Taking Dietary Supplements

1. Age
   ① 65-70 ② 71-75 ③ 76-80 ④ >80

2. Sex
   ① Male ② Female

3. What do you feel is your current health condition?
   ① Good ② Normal ③ Bad

4. What is the highest level of education that you have completed?
   ① Middle school ② High school ③ College

5. Have you taken dietary supplements consistently (more than three times a week) within the last 6 months?
   ① Yes ② No

   - Please continue answering only if you are taking dietary supplements.

6. What dietary supplements are you currently taking? (check all that apply)
   □ Red ginseng □ Garlic □ Ginkgo leaves □ Ginseng □ Omega-3 □ Glucosamine □ Saw Palmetto □ Coenzyme Q10 □ Aloe Vitamin C □ Vitamin E

7. How did you decide to take the dietary supplement?
   ① Recommendation from a doctor ② Recommendation from a pharmacist ③ Recommendation from a friend or relative ④ Broadcasting or commercials ⑤ Other ( )

8. Do you feel that your health condition has improved while taking the dietary supplement?
   ① Yes ② No ③ Not sure

9. Did you experience adverse reactions while taking the dietary supplement?
   ① Yes ② No

9-1. If you experienced an adverse reaction, what was it?
   ① Indigestion ② Nausea ③ Dizziness ④ Bleeding or delayed stop of bleeding ⑤ A skin reaction, such as a rash ⑥ Other ( )

10. What is your main source of information regarding dietary supplements?
    ① Doctor ② Pharmacist ③ Friend/relative ④ Broadcasting and commercials ⑤ Other ( )

10-1. Were you able to learn a lot about the efficacy of your supplements through your source of information?
   ① Yes ② No

10-2. Were you able to learn a lot about adverse reactions that can occur through your source of information?
   ① Yes ② No

11. Have you ever notified a health professional of your usage of dietary supplements before receiving prescription drugs?
   ① Yes ② No

11-1. If yes, whom did you notify?
   ① Doctor only ② Pharmacist only ③ Both

11-2. If no, what was the reason?
   ① There was no need to report because it was simply a dietary supplement.
   ② I thought I should but I forgot.
   ③ Other ( )

12. Have you ever been asked whether you were taking dietary supplements before receiving prescription drugs?
   ① Yes ② No

12-1. If yes, by whom were you asked?
   ① Doctor only ② Pharmacist only ③ Both