ejpmr, 2023, 10(6), 68-73

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

A CASE STUDY OF RELIEF EFFECT OF HERB MIXTURE ON DRY COUGH

Man Kyu Huh*

Food Science and Technology Major, Dong-eui University, Busan 47340, Republic of Korea.

***Corresponding Author: Dr. Man Kyu Huh**

Food Science and Technology Major, Dong-eui University, Busan 47340, Republic of Korea.

Article Received on 03/04/2023 **Article Revised on 24/04/2023** **Article Accepted on 14/05/2023**

ABSTRACT

A persistent dry cough can be caused from a upper respiratory infection or bronchitis. This study investigated the degree of cough relief with various plants that help relieve cough in Korea. The medicines used are *Liriope platyphylla*, *Luffa aegyptiaca*, *Zingiber officinale*, *Angelica decursiva*, *Pseudocydonia sinensis*, and *Pyrus ussuriensis*. The average number of coughs the day before taking herbal medicine was 96.4 times over day (both of day and night). The number of coughs on the 12th day after taking herbal medicine decreased to 27.6 times. The number of coughing times while sleeping was shown 17.1 times before taking herbal medicine and the 12th day of taking the herbal medicine averaged 6.0 times. The average time spent sleeping deeply was 3.8 hours before taking the herbal medicine and it was 4.5 hours after 12 days after taking the herbal medicine. The inhibitory effects of herbal medicines for nitric oxide (NO) radical scavenging activities were investigated. It was observed that scavenging activities go on increasing with enhancements in concentration of herbal medicines in the assay mixture. NO radical scavenging activities was evaluated 6.7% on 50 mg/L and 39.9% on 1200 mg/L.

KEYWORDS: Dry cough, *Liriope platyphylla*, *Luffa aegyptiaca*, nitric oxide (NO) radical scavenging.

INTRODUCTION

Coughing is a sudden, involuntary, and explosive exhalation movement in the airway. It acts to remove foreign substances or excessively produced secretions.[1] Cough is an airway protective mechanism resulting from a coordinated series of respiratory, laryngeal, and pharyngeal muscle activity and serves both preventative and corrective roles in pulmonary health.[2] Coughing is a normal defense mechanism that defends the respiratory tract, and it immediately reacts when abnormal situations occur in the lung parenchyma and airways, so it is also called a "lung guard dog" as it informs the pathological condition of the respiratory tract. Although coughing may be entirely voluntary, it is usually a physiologic reflex. As such, it is mediated through a reflex arc made of sensory receptors, afferent nerve fibers, a center, efferent nerve fibers, and effector muscles.[3]

Liriope Tuber is the roots of *Liriope platyphylla* Wang et Tang or *Ophiopogon japonicus* Ker-Gawler. These plants are species of flowering plant from East Asia. This small herbaceous perennial has grass-like evergreen foliage and lilac-purple flowers which produce single-seeded berries on a spike in the fall. *L. platyphylla* is one of the well-known herb used in oriental fork medicine for treatment asthma and bronchial and lung inflammation since ancient times.[4] The monocotyle flowering plant *L. platyphylla* is known to have antioxidant and anti-inflammatory effects[5,6] and immunomodulatory abilities[7] and has been widely used for lung and respiratory diseases. In particular, it is effective for treating bronchitis, pharyngitis, and asthma accompanied by dry cough.[8,9] Ramalingam and Kim[10] reviewed discusses extensively the phytochemical and pharmacological activities in vitro and in vivo on *Liriopes radix*.

Luffa is the genus name of a group of gourds also known as vegetable sponges, dishcloth gourds, running okra, strainer vine, Chinese okra, California okra, and loofah. *Luffa cylindrica* is a sub-tropical plant, which requires warm summer temperatures and long frost-free growing season when grown in temperate regions. The main commercial production countries are China, Korea, India, Japan and Central America.[11] *Luffa aegyptiaca*, one of genus *Luffa*, is an annual species of vine cultivated for its fruit is called Egyptian cucumber. The species is native to South and Southeast Asia. Young green fruits can be boiled and eaten as a vegetable. Angled luffa is *L. acutangula*, while the smooth-fruited version is *L. cylindrica*, or the same as *L. aegyptica*. According to Muthumani et al.[12], the plant seeds possess hepatoprotective, anesthetic ctivity, anti-inflammatory, anti-helminthic, antimicrobial, anticancer, and enzyme inhibitor effects. The dry fruit of *L. aegyptiaca* and *L. cylindrica* can be used as a sponge. Several bioactive compounds have been isolated from various parts of the *L. cylindrica*. Apigenin, rho-coumaric acid, luteolin, kaempferol, quercetin, and apigenin-7-O-beta-D-glucuronopyranoside were isolated

from the leaves.[13,14]

Ginger (*Zingiberis rhizoma*) consists of the whole or cut rhizome of *Zingiber officinale* Roscoe (Zingiberaceae) and it is a miraculous drug having a lot of medicinal benefits. Ginger plants have been extremely popular as spice and to treat a host of ailments throughout Asia, especially in India and China, for over 5000 years. *Z. officinale* is also a strong historical medicinal background and used by different systems of medicine for various ailments. Main constituents are sesquiterpenoids, with (-)-zingiberene. Sesquiterpene Lactones (SLs) are natural products responsible for its anti-inflammatory activity.[15]

Angelica decursiva (Miq.) Franch. et Sav. is an important traditional medicinal plant form the genus Angelica, family Umbelliferae.[16] The root of *A. decursiva* has been frequently used in traditional medicine as anti-inflammatory, antitussive, and analgesic agents and expectorant, especially for treating cough, asthma, bronchitis, and upper respiratory tract infections.[17-19] *A. decursiva* has antioxidant.[20]

Pseudocydonia sinensis (Thouin) C.K.Schneid. or Chinese quince is a deciduous or semi-evergreen tree in the family Rosaceae, native to southern and eastern China. It is the sole species in the genus Pseudocydonia. Its hard, astringent fruit is used in traditional Chinese medicine[21] and as a food in East Asia. The fruits of the *P. sinensis* were widely used in traditional Chinese medicine. For example, It is used in Korea to treat asthma, the common cold, sore throats, mastitis and tuberculosis.[22-24] It contains several medically active constituents including organic acids plus the flavonoids rutin and quercetin. It contains total polyphenol, flavonoid and phenolic acid content of fruit which showed antioxidant activity[25] and anti-inflammatory.[26]

The genus Pyrus (Rosaceae) is widely distributed in Asia, Europe and North Africa.[27] Rehder[28] described 15 principal species, 6 varieties, and 5 related species in *Pyrus*. However, this inconsistency concerning the number of identified species reflects a difficulty in the classification of Pyrus species.

Traditional medicinal plants are often cheaper, locally available and easily consumable, raw or as simple medicinal preparations. They contain a number of pharmaceutical compounds. The objective of the current study was to evaluate inhibitory effects on dry cough using several medicinal plants.

MATERIALS AND METHODS

Sample extract

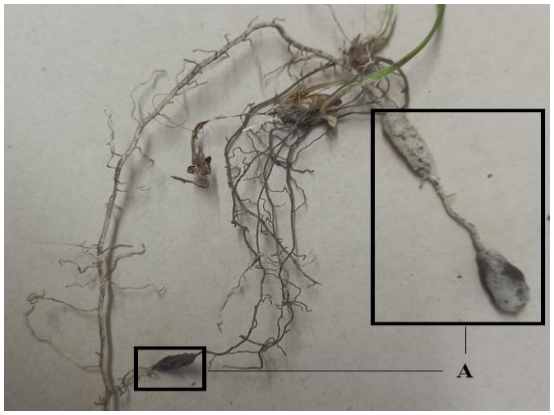
Roots of *Liriope platyphylla* were collected directly from the native habitat of a mountain. The root of *L. platyphylla* has a bulging part in the shape of a peanut. It was used as a material (Fig. 1). Many researchers overlooked this part because they used only the roots. The roots were immersed in water for 2 days and washed several times to remove soil and foreign substances.

The sample was treated with hot distilled water. The mixture of boiling group was further stirred with a magnetic bar at 100℃ for one day. The sample was treated with ultrasound at 60℃ for two hours. The ultrasound extraction was carried out using an ultrasonic bath (5510, Branson, USA) and a grinding mixer. Extracted sample was filtered. The sample was evaporated to remove solvent under reduced pressure and controlled temperature by using rotary vacuum evaporator (N-1001S-W, Eyela, Tokyo, Japan). To get dry powder, samples placed in a low temperature vacuum chamber.

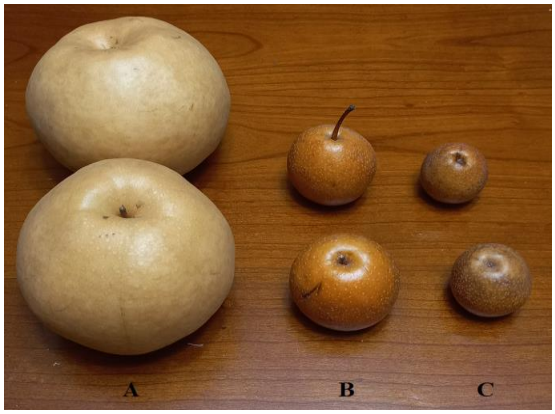
When *Luffa aegyptiaca* was sufficiently grown, the stem was cut to collect the outflow liquid. Many researchers cut blue scrub fruits and use them for medicinal purposes, which also contains very little pharmacological effect.

Zingiber officinale and *Pyrus ussuriensis* (Fig. 1) purchased on the market. Each 500 g of *Z. officinale* and *P. ussuriensis* was added to 1,500 ml of water and boiled in a stainless steel. The mixture of boiling group was further stirred with a magnetic bar at 100℃ 100℃ for one day. The sample was treated with ultrasound at 60℃ for two hours. The samples were ground with distilled water and a grinding mixer. They were squeezed out with the muslin cloth. The samples were evaporated as *L. platyphylla* and *Pyrus ussuriensis.*

The fruit of *Pseudocydonia sinensis* is hard and astringent, though it softens and becomes less astringent after a period of frost. The 400 g dry fruits treated as *Zingiber officinale* for the experiment.



A is the swollen part of the root and is used as a medicine



A: *Pyrus pyripolia* var. *culta,* B: *Pyrus pyrifolia,* C: *Pyrus ussuriensis.*

Figure 1: The swollen roots of *Liriope platyphylla* (left) and *Pyrus ussuriensis* (right) used in this study.

Composition (g/kg) of the experimental herbs

The composition of the sample is shown in Table 1. Since the juice of *Luffa aegyptiaca* is a liquid, the undiluted solution was taken and used in an experiment.

Table 1: The composition of herbs.

Species	Amount (g or ml)
Liriope platyphylla	2 g
Luffa aegyptiaca	100 ml
Zingiber officinale	2 g
Angelica decursiva	2 g
Pseudocydonia sinensis	2 g
Pyrus ussuriensis	2 g

Antitussive effective assay

The number of coughs generated was measured at intervals of 5 seconds for 15 minutes.

Nitric oxide

NO concentration was measured by using Griess reagent system. Sodium nitroprusside in aqueous solution at physiological pH spontaneously generates nitric oxide[29] which interacts with oxygen to produce nitric ions that can be estimated by using Greiss reagent. Sodium nitroprusside (5 mM) in phosphate buffer saline (PBS) was mixed with 3.0 ml of different concentrations (0.1–5 mg/ml) of the Suaeda maritime extract and incubated at 25ºC for 150 min. The samples were added to Greiss reagent (1% sulphanilamide, 2% H_3PO_4 and 0.1% napthylethylene diamine dihydrochloride). The absorbance of the chromaphore formed during the diazotization of nitrite with sulphanilamide and subsequent coupling with napthylethylenediamme was read at 546 nm using the Microplate Reader (VersaMax, Califonia, USA) and referred to the absorbance of standard solutions of catechin treated in the same way with Griess reagent as a positive control. The range of extract concentrations and measurement frequencies were established experimentally.

RESULTS

Table 2 shows the number of coughs per day. On December 1, the average number of coughs the day before taking herbal medicine was 96.4 times over day (both of day and night). On December 4, the number of coughs on the third day after taking herbal medicine was 68.8 times. On December 7, the number of coughs on the sixth day after taking herbal medicine was 41.0 times. The number of coughs on the 12th day after taking herbal medicine on December 13 decreased to 27.6 times.

The average number of times woke up from sleep was 6.3 times before taking herbal medicine. On the 12th day of taking herbal medicine, the number of waking up from sleep decreased to 2.8 on average. Compared to the first day, times woke up from sleep decreased by 55.6% on the 13th day.

On December 1, the degree of pain in the neck while coughing was very severe, but on the 12th day after taking herbal medicine, it turned into a slight pain.

The amount of sputum discharged through coughing on December 1 was very high, so it was slightly discharged on the 12th day after taking herbal medicine.

Table 2: Clinical symptoms progress by date after taking herbal medicines.

Date	No. of cough/day	No. of times woke up during sleeping	A sore throat	Sputum
1 December	96.4±16.9	6.3±0.4	+++	A lot
4 December	68.8±11.4	4.6±0.5	+++	A lot
7 December	41.0±8.6	3.8±0.7	++	Moderate or more
10 December	32.2±6.1	3.4±0.5	++	Not a lot
13 December	27.6±5.1	2.8±0.4	+	Moderate

The number of coughing times while sleeping was shown in Figure 2. On December 1, it averaged 17.1 times. The 12th day of taking the herbal medicine averaged 6.0 times.

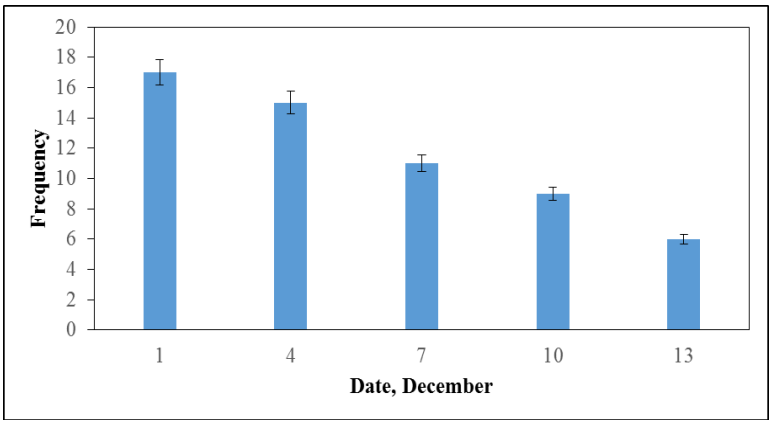


Figure 2: The frequency of coughing for 1 day at night after taking medication.

The average time spent sleeping deeply was 3.8 hours before taking the herbal medicine (Fig. 3). The average time of deep sleep during sleep was 4.5 hours after 12 days after taking the herbal medicine. Compared to the first day, time spent sleeping deeply increased by 18.4% on the 13th day.

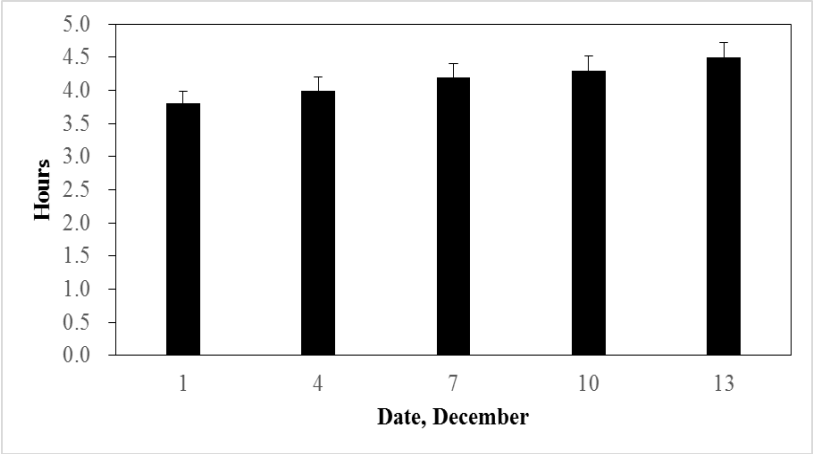


Figure 3: The change of good night's sleeping hours for one day after taking the medication.

In this study, the inhibitory effects of herbal medicines for nitric oxide (NO) radical scavenging activities were investigated (Table 3). It was observed that scavenging activities go on increasing with enhancements in concentration of herbal medicines in the assay mixture. NO radical scavenging activities was evaluated 6.7% on 50 mg/L and 39.9% on 1200 mg/L. There was significant difference among four concentrations (50, 100, 200, 400, 800, and 1200 mg/L) ($p < 0.05$).

Table 3: The percentages of NO inhibition activity at various concentrations of the medication.

Concentration (mg/L)	Data (%)			
	First	Second	Third	Mean±SD
50	4.3	8.0	7.8	6.7±2.0
100	10.2	14.6	15.9	13.6±3.0
200	18.2	22.0	23.8	21.4±2.8
400	30.2	35.7	29.3	31.7±3.5
800	35.2	41.0	34.2	36.8±3.7
1200	39.8	42.6	37.3	39.9±2.7

DISCUSSION

Physians have used antitussives, expectorants, and mucolytic agents as the cough prescriptions.[30] Antitussive drugs can be divided into drugs used in central organs and drugs that act on peripheral organs according to the mechanism of action. Drugs used in central organs are divided into narcotic opioids, non-narcotic opioids, and nonopioid. Typical drugs as narcotic opioids are codein, hydrocodone, and morphine, which have proven to have limited cough suppression effects, but the results are not constant,[31] and there is a risk of drowsiness, constipation, digestive disorders, abuse or dependence at appropriate doses.[30] Dextromethorphan is non-narcotic opioids and is a commonly contained drug in cough and cold medicines. The effects of this drug are also inconsistent.[32] Peripheral acting antipyretic, which is widely used in Korea, is levodropizine.[33] This drug has side effects of the central nervous system (dizziness, headache) and gastrointestinal relations (misery, vomiting, and diarrhea), and should not be administered to infants,

patients with chronic renal failure, and consciousness disorders.[32]

In some cases, cough suppression treatment is needed to reduce cough discomfort, and the mechanism of action of each drug should be well understood and prepared for side effects. Herbal medicine is also toxic, and *Pinellia rhizoma* is typically a cough suppressant, but it is toxic when used as a living plant. It is not easy to remove toxic substances from this plant. Ginseng, which has a high saponin content, is also used as a medicine because it helps relieve coughs, and people with high fever can have side effects.

Yang[6] examined total soluble solid, reducing sugar, antioxidant and sensory properties regarding LTD (Liriope Tuber Dried), LTSD (Liriope Tuber Steamed and Dried), LTASD (Liriope Tuber Alcohol-Steamed and Dried), LTDR (LTD Roasted), LTSDR (LTSD Roasted) and LTASDR (LTASD Roasted). The anti-oxidative activity of the roasted LT samples were higher than that of all dried LT samples. In particular, the LTASDR sample showed significantly high figures in DPPH scavenging activity, ABTs scavenging activity, nitrite scavenging activity and xanthine oxidase inhibitory activity.

NO, an anti-inflammatory indicator, mediates important physiological functions such as vascular homeostasis and apoptosis-induced action in normal physiological conditions, but a large amount of NO kills normal cells and induces inflammation, acting as a substance that causes acute or chronic inflammatory diseases.[33] In this study, a nitric oxide (NO) radical scavenging activities of herbal mediciens would be useful for the prevention of anti-inflammatory.

CONCLUSIONS

Herbal medicies in clouding *Liriope platyphylla, Luffa aegyptiaca, Zingiber officinale, Angelica decursiva, Pseudocydonia sinensis,* and *Pyrus ussuriensis* may be useful compounds for studies connected with dry cough.

REFERENCES

1. Sohn JW. Antitussive and mucoactive drugs. J Korean Med Assoc, 2013; 56: 1025-30.
2. Malvè M, del Palomar AP, López-Villalobos JL, Ginel A, Doblaréet M. FSI analysis of the coughing mechanism in a human trachea. Ann Biomed Eng, 2010; 38(4): 1556-65.
3. Farzan S. Chapter 38 Cough and Sputum Production. In: Walker HK, Hall WD, Hurst JW (eds.). Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition, Boston; Butterworths, 1990.
4. Lee YC, Lee JC, Seo YB, Kook YB. *Liriopis* tuber inhibit OVA-induced airway inflammation and bronchial hyperresponsiveness in murine model of asthma. J Ethnopharmacol, 2005; 101: 144-52.
5. Jang AS. Particulate matter and bronchial asthma. Korean J Med., 2015; 88: 150–5.
6. Yang MO. Antioxidant and sensory properties of hot water extract of liriope tubers treated at various preprocess. J East Asian Soc Dietary Life, 2013; 23: 645-53.
7. Kim HW, Yang SY, Kim MH, Uk NU, Park YC. Protective effects of Maekmundong-tang on elastase-induced lung injury. J Korean Oridental Med., 2011; 32: 63-78.
8. Hsu CH, Lu CM, Chang TT. Efficacy and safety of modified Mai-Men-Dong-Tang for treatment of allergic asthma. Pediatr Allergy Immunol, 2005; 16: 76-81.
9. Colletti A, Cicero AFG. Nutraceutical approach to chronic osteoarthritis: from molecular research to clinical evidence. Int J Mol Sci., 2021; 22: 12920, https://doi.org/10.3390/ijms222312920.
10. Ramalingam M, Kim SJ. Phytochemical and pharmacological overview on *Liriopes radix*. Trop J Pharm Res., 2016; 15(11): 2517-26.
11. Oboh IO, Aluyor EO. Luffa cylindrica-an emerging cash crop. Afr J Agri Res., 2009; 4(8): 684-8.
12. Muthumani P, Meera R, Mary S, Mathew J, Devi P, Kameswari B, et al. Phytochemical screening, anti-inflammatory, bronchodilator and antimicro‑bial activities of the seeds of Luffa cylindrica. Res J Pharm Biol Chem Sci., 2010; 1(4): 11-22.
13. Liang L, Liu CY, Li GY, Lu LE, Cai YC. Studies on the chemical components from leaves of *Luffa cylindrica* Roem. Yaoxue Xuebao, 1996; 31: 122-5.
14. Si C, Wu L, Zhu Z. Chemical constituents and antioxidant activity of *Luffa cylindrica* leaves. ICNPTM-047. Proceedings of International Conference of Natural Products and Traditional Medicine (ICNPTM' 09) Xi'an, Shaanxi Province, People's Republic of China., 2009; 196.
15. Rehman M, Akram M, Naveed A, Jabeen Q. et al. Zingiber officinale Roscoe (pharmacological activity). J Med Plant Res., 2011; 5(3): 344-8.
16. He Y, Zhong Y, Bao Z. et al. Evaluation of *Angelica decursiva* reference genes under various stimuli for RT-qPCR data normalization. Sci Rep., 2021; 11: 18993. https://doi.org/10.1038/s41598-021-98434-6.
17. Ali MY, Seong SH, Jannat S, Jung HA, Choi JS. Ethnobotany, phytochemistry, and pharmacology of *Angelica decursiva* Fr. et Sav. natural product sciences. The Kor Soc Pharm (KAMJE), 2019; 25(3): 181. https://doi.org/10.20307/nps.
18. Islam MN, Choi RJ, Jin Se, Kim YS, Ahn BR, Zhao D, Jung HA, Choi JS. Mechanism of anti-inflammatory activity of umbelliferone 6-carboxylic acid isolated from *Angelica decursiva*. J Ethnopharmacol, 2012; 144: 175-81.
19. Lim HJ Lee JH, Choi JS, Lee SK, Kim YS, Kim HP. Inhibition of airway inflammation by the roots of *Angelica decursiva* and its constituent, columbianadin. J Ethnopharmacol, 2014; 155: 1353-61.
20. Zhao DIslam N, Ahn BR, Jung HA, Kim BW, Choi JS. In vitro antioxidant and anti-inflammatory

activities of *Angelica decursiva*. Arch Pharm Res., 2012; 35: 179-92.
21. Lim TK. *Pseudocydonia sinensis*. Edible Medicinal And Non-Medicinal Plants. Springer Netherlands, 2012; 4: 515-22.
22. Mihara S, Tateba H, Nishimura O, Machii Y, Kishino K. Volatile components of Chinese quince (*Pseudocydonia sinensis* Schneid). J Agric Food Chem, 1987; 35: 532-7.
23. Chung TY, Cho DS, Song JC. Volatile flavor components in Chinese quince fruits, *Chaenomeles sinensis* Koehne. Korean J Food Sci Technol, 1988; 20: 176-87.
24. Hamauzu Y, Yasui H, Inno T, Kume C, Omanyuda M. Phenolic profile, antioxidant property, and antiinfluenza viral activity of Chinese quince (*Pseudocydonia sinensis* Schneid.), quince (*Cydonia oblonga* Mill.), and apple (*Malus domestica* Mill.) fruits. J Agric Food Chem., 2005; 53: 928-34.
25. Grygorieva O, Klymenko S, Vergun OM, Mnahoncakova E, Brindza J, Margarita T, Ivanisova E. Evaluation of the antioxidant activity and phenolic content of chinese quince (*Pseudocydonia sinensis* Schneid.) fruit. Acta Sci Pol Technol Aliment, 2020; 19(1): 25-36.
26. Osawa K, Miyazaki K, Imai H, Arakawa T, Yasuda H, Takeya K. Inhibitory effects of Chinese quince (*Chaenomeles sinensis*) on hyaluronidase and histamine release from rat mast cells. Natural Medicines, 1999; 53: 188-93.
27. Katayama H, Uematsu C. Pear (*Pyrus* species) genetic resources in Iwate, Japan. Genet Resour Crop Evol, 2006; 53: 483-98.
28. Rehder A. Manual of Cultivated Trees and Shrubs. 2nd ed. Macmillan, New York: 1940.
29. Marcocci L, Maguire JJ, Droy MT. The nitric oxide scavenging properties of *Gingo biloba* extract EGb 761. Biochem Biophys Res Commun, 1994; 15: 748-55.
30. Kim SH. Antitussives, mucolytic agents and expectorants in clinical practice. The Kor J Med., 2010; 78(6): 682-6.
31. Dicpinigaitis PV. Currently available antitussives. Pulm Pharmacol Ther., 2009; 22: 148-51.
32. Sohn JW. Antitussive and mucoactive drugs. J Kor Med Assoc, 2013; 56(11): 1025-30.
33. Chang BY, Lim DE, Han JH, Lee JS, Cho HK. Relief effect of medicinal herb mixture HAE series on respiratory symptoms. Kor J Pharmacogn, 2015; 46: 334-41.