Propagation in Korean Herbal Medicine and Commercialization of African Medicinal Plants in Traditional Korean Medicine (TKM)

Antonio Edmilson Camelo Juniora†, Richard Komakech2,3,4†, Yong-goo Kim3, Gilbert Motlalepula Matsabisa5, and Youngmin Kang2,3*

2. University of Science & Technology (UST), Korean Medicine Life Science, Daejeon 34054, Republic of Korea
3. Korea Institute of Oriental Medicine (KIOM), Yuseongdae-ro, Yuseong-gu, Daejeon 34054, Republic of Korea
4. Natural Chemotherapeutics Research Institute (NCRI), Ministry of Health, P.O. Box 4864, Kampala, Uganda
5. University of the Free State, 205 Nelson Mandela Drive, Bloemfontein 9300, Republic of South Africa

Abstract

Traditional and complementary medicine (T&CM) plays an integral role in providing health care worldwide. This article provides a brief of the Korean herbal medicine propagation and some of the glocalized medicinal plants in the Korea herbal market. In fact, there is a heavy reliance on herbal medicinal plants in traditional medicine. However, due to the increasing demand in the glocal market and change in the climatic conditions, the use of improved propagation technology is inevitable to enhance mass production of these important medicinal plants. A number of studies are being undertaken to develop the in vitro propagation protocols for a number of the important medicinal

†Both authors contributed equally to this work.
*Correspondence: Prof. Youngmin Kang Ph.D.
University of Science & Technology (UST), Korean Medicine Life Science, Daejeon 34054, Republic of Korea
E-mail: ym kang@ust.ac.kr
Received 2018-09-21, revised 2018-11-14, accepted 2018-11-18, available online 2018-11-22
doi:10.22674/KHMI-6-2-10
plants. The steps undertaken during the in vitro propagation process of the medicinal plants at KIOM were outlined. Botany, ethnopharmacological uses, and chemical composition of medicinal plants under study in Korea Institute of Oriental Medicine (KIOM) have also been outlined. Based on the literature review, we obtained information on Panax ginseng and Harpagophytum procumbens; some of the major glocalized medicinal plants in Korea market. The robust in vitro propagation of plants in KIOM involves the process of sterilization, shooting, rooting and acclimatization with the maintenance of the environmental conditions. P. africana, P. multiflorum, R. glutinosa, A. kusnezoffii, T. kirilowii, and Pinellia ternate are some of the important medicinal plants under in vitro propagation study at KIOM. Increase in the glocal use of P. ginseng and H. procumbens has further strengthened the demand for them both for research purpose and therapeutic application. Through advanced in vitro propagation technology, not only can the increasing glocal demand for herbal medicinal plants be met but also the climatic effects on medicinal plants can be mitigated.

Keywords: glocal, herbs, Korean herbal medicine, in vitro propagation

Introduction

Globally, Traditional and complementary medicine (T&CM) plays an important role in health-care system\(^1\). Indeed, the use of plants for the treatment and management of the myriad of diseases has been in existence since time immemorial, and it is estimated that approximately 40% of the population in developed countries\(^2\)-\(^4\). In developing countries, 80% of the populace still rely on natural medicines for their primary healthcare needs\(^5\)-\(^9\). This high level of dependence on natural medicine is attributed to the cultural acceptability and ease of their accessibility\(^10\). The medicinal activities of these plants are attributed to the various secondary metabolites contained in them\(^11\). Harpagophytum procumbens: which is one of the highly commercialized plants is known for its potent anti-inflammatory activity\(^12\). Based on the classified collection of the medical formulas, the Euihang Yoochui in 1477, Traditional Korean Medicine (TKM) is considered to be very unique\(^13\). The uniqueness of TKM is due to the fact that it does not focus on the internal body systems which in most cases is enhanced by dissection but instead focuses on the careful observation of natural bodily functions as they manifest in order to diagnose a given disease condition\(^14\). The uniqueness of TKM is best understood by the Korean Medicine doctors who normally undertake a 4–7 years course at the University\(^8,\!^10\). In fact, the major component of TKM is the Sasang medicine in which the herbs used for the treatment and management of diseases are prepared into a formula which can take the form of decoction, capsules, syrups, pills, plaster, powder, and medicated wine\(^11,\!^12\). These herbs are characterized by four natures (Temperature)-hot, warm, cool and cold and five flavors (Tastes)-pungent, sweet, sour, bitter and salty\(^12\). Besides the flavors and natures of the herbs, one should critically know its combinations, and dosage is critically considered before applying it to patients\(^12\). The pungent, sour, bitter and salty herbs are mainly used to treat diseases in So–Eum (SE) and
Tae-Eum (TE) patients while the sweet herbs are usually used for So-Yang (SY) and Tae-Yang (TY) disease conditions. Due to globalization, TKM has been influenced over the years leading to the commercialization of medicinal plants with foreign origin in Korea including Harpagophytm procumbens from South Africa (Traditional African Medicine) which has been used over the years for treating a number of diseases including pharacopuncture treatment of arthritis in Korea. Indeed, the fact that herbal medicinal plants play an integral role in Korean Medicine; a lot of research has been conducted to produce quality medicinal plants to meet the ever-increasing demand and also limit the effect of climate change.

This article, therefore, gives a brief insight on the in vitro propagation process of the herbal medicinal plants at Korea Institute of Oriental Medicine (KIOM) and some of the glocalized medicinal plants in the Korea herbal market.

**Discussion**

1. **In vitro propagation and production of medicinal plants**

The growth of herbal markets have increased substantially in South Korea and the world at large. Consequently, a number of plants are being researched on for possible mass production at KIOM including but not limited to Polygonum multiflorum, Rehmannia glutinosa, Aconitum kusnezoffii, Prunus africana, Trichosanthes kirilowii, and Pinellia ternate to meet the market needs. The in vitro establishment is influenced by a number of factors including plant growth regulators, the culture environment, and suitable explants with the ability to adapt to the in vitro conditions and its totipotency potential. The use of nodal segments in a direct plant regeneration by inoculating it in the suitable plant culture medium supplemented with suitable plant growth hormones to give rise to shoots is one of the common plants in vitro propagation techniques. In fact, the induction of shoots in explants is accomplished by the application of exogenous cytokinins which promotes the initial growth of axillary buds by the breakdown of apical dominance. In vitro culture is a significant tool in the propagation of many plant species, and allows the propagation of species which are difficult to obtain in nature to enhance the multiplication of high-quality genetic material with superior genotypes. Furthermore, the in vitro plant propagation method has numerous advantages compared to conventional propagation methods. Indeed, plants propagated in vitro are genetically homogenous, they are healthy without infections, can be produced independently of a season or environmental conditions, propagation efficiency is extraordinarily high, and preservation of a large number of stock plants in vitro is possible in a small area.

Four basic stages are followed during the in vitro propagation process: sterilization of the explants, shoot proliferation, Rooting, and acclimatization.

1) Sterilization of the explants

In the process of sterilization, the common contaminants of the explants including fungi and bacteria are removed. The sterilization process is mainly done using double distilled water, 70%
ethanol, and 3% sodium hypochloride following a laid down procedure.

2) Shoot proliferation
Shoot proliferation from the explants is achieved by subculturing the explants in a suitable medium with 3% sucrose supplemented with suitable cytokinins which may be 6-Benzylaminopurine (BAP), Thidiazuron (TDZ), Kinetin (KN), isopentenyl adenine (2iP), or Zeatin at a given concentration maintained at 25°C ± 1°C, 16 hr-light/8 hr-dark to enhance the shooting.

3) Rooting
This is achieved by transferring the proliferated shoots to the suitable medium containing suitable auxin hormones which may be Indole-3-butyric acid (IBA), Naphthalene acetic acid (NAA), isopentenyl adenosine (IPA), or Indole-3-acetic acid (IAA) at a given concentration maintained at 25°C ± 1°C, 16 hr-light/8 hr-dark to enhance the rooting.

Figure 1. Acclimatization and plant transfer to the prepared garden. A. Plants in the growth chamber. B. Plants transferred to the greenhouse. C. Plants transferred to the prepared garden (field test).
4) Acclimatization of the medicinal plants in the greenhouse

During the acclimatization process, the medicinal plants produced by mass in vitro propagation are transferred to the growth chamber (Figure 1A) and maintained under a 16/8 hr. light and dark photoperiod at 22°C and 90% relative humidity and watered regularly for three weeks. The growing shoots are partially covered with a thin transparent polythene bag to reduce desiccation due to excessive water loss. Thereafter, the acclimatized plants are then transferred to the greenhouse (Figure 1B) with regulated parameters such as temperature, relative humidity, and CO₂ in addition to regular watering to enhance plant growth and development. After five weeks, the plants are then transplanted to the prepared garden (Figure 1C) with suitable soil conditions.

<table>
<thead>
<tr>
<th>Plant</th>
<th>Compound name</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prunus africana</td>
<td>Ursolic acid (C₃₀H₄₈O₃)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Ursolic acid" /></td>
</tr>
<tr>
<td></td>
<td>Oleanolic acid (C₃₀H₄₈O₃)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Oleanolic acid" /></td>
</tr>
<tr>
<td></td>
<td>Atraric acid (C₁₀H₁₂O₄)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Atraric acid" /></td>
</tr>
<tr>
<td></td>
<td>Ferulic acid (C₁₀H₁₀O₄)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Ferulic acid" /></td>
</tr>
</tbody>
</table>

Table 1. Some of the phytochemicals in Prunus africana. Chemical structures obtained from https://pubchem.ncbi.nlm.nih.gov/
2. Medicinal plants under in vitro propagation study at KIOM

A number of medicinal plants are under study to establish their in vitro propagation protocols at KIOM including:

1) Prunus africana (Korean name-아프리칸 뷔나무)

Prunus africana (Figure 2A) is one of the plants being researched on in KIOM. It is one of the most widely used plant species in traditional medicine. This plant is commonly known as Pygeum; a large tree which grows in tropical Africa between altitude 500 and 3000 m\(^2\)). \(P. \) africana is an endemic plant to Sub-Saharan Africa, and its stem bark is greatly used in traditional medicine for the treatment and management of a number of disease conditions such as benign prostatic hyperplasia, prostate cancer, diabetes, malaria, chest pain, gastrointestinal conditions, wound healing, and skin infections\(^{23,24}\). The high medicinal activities of this plant have been attributed to the synergistic actions of the numerous bioactive constituents in it including but not limited to ursolic acid, oleanolic acid, ataric acid, ferulic acid (Table 1), N-Butylbenzene-sulfonamide, beta-Sitosterol, and lauric acid\(^{24}\). This somewhat explains why this plant is greatly used in traditional medicine. Due to the over demand for this plant, the wild population has been depleted and hence the need for the in vitro propagation to restore its wild population.

2) Polygonum multiflorum (Korean name-하수오)

Polygonum is a plant genus belonging to family Polygonaceae (Figure 2B). It is a perennial herbaceous plant with a dark brown root tuber and stem length of about 3 m consisting of alternate leaves\(^{25}\). This plant is highly valued for its extensive medicinal activities\(^{26}\). The stem and root of this plant are used singly or in combination with other remedies in traditional medicine for treating various diseases and disorders including aging, low libido, dizziness, atherosclerosis, diabetes, liver injury, anemia, neurasthenia, hypercholesterolemia, cancer, and alopecia\(^{27}\). The plant is known to prevent baldness and premature graying of hair due to its ability to promote hair growth and melanin production\(^{28}\). In fact, the medicinal activities of this plant are mainly attributed to phytochemicals in it including flavonoids, anthraquinones, phenolics, stilbenes, and tannins\(^{29}\). To meet the demand for this plant, therefore, through in vitro propagation, studies are being conducted at KIOM to produce medicinal roots with increased biomass including that of \(P. \) multiflorum based on optimum growth conditions.
Figure 2. Different plants under study at KIOM. A. Potted Prunus africana plant growing in Chungnam National University greenhouse. B. Field test for in vitro propagated Polygonum multiflorum produced at KIOM. C. Trichosanthes kirilowi roots. D. Pinellia ternata plant.

3) *Rehmannia glutinosa* (Korean name-지황)

*Rehmannia glutinosa* (Family Scrophulariaceae) are herbs with an average height of about 20 cm. It has fleshy rhizomes; purple/red stems with basal leaves which are usually rosulate and decreases upwards in size; flowers are axillary or in terminal racemes. This herb is taken to nourish Yin and strengthens the kidney in TKM. Furthermore, the root is commonly used in traditional medicine to replenish lost blood, treat back pain, cough, hectic fever, diabetes, urinary incontinence, uterine bleeding among others. The plant has astringent properties that make it useful in stopping the bleeding. Indeed, this herb has a great nourishing effect of the body especially for the growth, development, and well-being of the body. The plant contains numerous compounds including saccharides, amino acid, iridoids, and inorganic ions.
4) *Aconitum kusnezoffii* (Korean name-이삭바잣)

*Aconitum kusnezoffii* (Family Ranunculales) is a perennial plant that can grow up to 5 feet; leaves are dark green, palmately lobed with five to seven segments which are spirally or alternately arranged with the lower leaves longer than the ones above them. Herbal soups and meals are prepared from *A. kusnezoffii* roots and administered to treat and manage a number of disease conditions. Despite the fact that this plant is known to contain highly toxic alkaloids, they have been used in traditional Korean herbal medicine to treat a number of disease conditions such as abdominal disorders, headache, and rheumatism due to the fact that it exhibits cardiotonic, anti-inflammatory and analgesic effects. This plant is known to contain a number of bioactive compounds including alkaloids, amide alkaloids, flavonoids, flavonol glycosides, diterpenoid and nor-diterpenoid compounds which greatly enhances its medicinal values.

5) *Trichosanthes kirilowii* (Korean name-하늘타리)

*Trichosanthes kirilowii* is a member of plant family Cucurbitaceae. It is a perennial climber growing to 6 m at a fast rate. It is a monoecious plant although both sexes can be found on the same plant. *Trichosanthes* root is traditionally used for the treatment of numerous diseases including diabetes in most of the Asian countries especially in China, Taiwan, and Eastern Asia. Indeed, *T. kirilowii*, called “Kwalu” in Korean, has traditionally been one of the most important herbal drugs used in TKM and other countries in North East Asia. Although other parts can also be used in traditional medicine, the root (Figure 2C) above is the most important part of this plant. Indeed, studies indicate that the high medicinal values of the roots of this plant are attributed to the numerous phytochemicals (Table 2) in it including allantoin, nicotinic acid, xanthine, adenine, uracil, thymine, guanosine, uridine, phenylalanine, tyrosine, furoic acid, p-hydroxybenzoic acid.

6) *Pinellia ternata* (Korean name-반하)

*Pinellia ternata* (Family Araceae) is a small perennial herb (Figure 2D) that spreads by rhizomes but also possesses small bulblets at the base of each leaf. Leaves are trifoliate, while the flowers are of the spathe or spadix form: orthotropous ovaries, and the oblong-ovoid berry-like green fruits. It has been traditionally used to treat a cough, vomiting, infection, and inflammation. The plant is also widely used to treat insomnia in traditional Chinese medicine. Some of the phytochemicals that have been isolated from the roots of *P. ternata* includes (E)-p-coumaryl alcohol, 3,4-dihydroxycinnamy alcohol, sachaslide 1, and coniferin (Table 3). The presence of these chemicals may explain the medicinal values of this plant and its subsequent use in traditional medicine.
<table>
<thead>
<tr>
<th>Plant</th>
<th>Compound name</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allantoin (C₄H₆N₄O₃)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical structure" /></td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid (C₆H₄NO₂)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical structure" /></td>
<td></td>
</tr>
<tr>
<td>Trichosanthes kirilowii</td>
<td>Uracil (C₄H₄N₂O₂)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical structure" /></td>
</tr>
<tr>
<td></td>
<td>Xanthine (C₃H₄N₂O₂)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical structure" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plant</th>
<th>Compound name</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pinellia ternata</em></td>
<td>P-Coumaryl alcohol (C₆H₁₀O₂)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical Structure" /></td>
</tr>
<tr>
<td></td>
<td>Sachaliside 1 (C₁₂H₂₀O₇)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical Structure" /></td>
</tr>
<tr>
<td></td>
<td>Coniferin (C₁₀H₂₂O₈)</td>
<td><img src="https://pubchem.ncbi.nlm.nih.gov/" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>

Table 3. Some of the phytochemicals in *Pinellia ternata*. Chemical structures obtained from https://pubchem.ncbi.nlm.nih.gov/

### 3. Commercialized Glocal Medicinal Plants in Korea market.

The term glocal has been used in a phenomenon that impacts on both local and global communities. In reference to this, therefore, it is important to note a number of glocal medicinal plants form the backbone of TKM including:

1) *Panax ginseng* (Ginseng) (Korean name-인삼)

As Korea’s most popular herbal dietary supplement, *P. ginseng* has been widely distributed across the country through a number of stores and globally. Indeed, ginseng is one of the primary products in the dietary herbal products in Korea and is contained in a number of products including red ginseng (*hongsam*), black ginseng (*heuksam*), wild ginseng (*sansam*), and
white ginseng (baeksam)⁴⁶. In fact, _P. ginseng_ is one of the most valuable of all traditional medicinal plants especially in Korea, China, and Japan and has been used to treat and manage a number of health conditions for more than 2000 years⁴⁷. Indeed, the name _panax_ is literally translated to mean “all healing”; probably stemming from a traditional school of thought that _ginseng_ can treat all kinds of human diseases and disorders⁴⁷. It’s this therapeutics strength of _P. ginseng_ that has made it very popular globally.

2) _Harpagophyllum procumbens_ (Devil’s claws) in Traditional African Medicine

(Korean name-악마의 발톱: 천수근)

This medicinal plant belongs to plant family Pedaliaceae; commonly referred to as devil’s claw is one of the few commercialized glocl medicinal plants⁴⁸. It is a weedy, perennial plant with the creeping stems spreading from the central thick tuberous tap root⁴⁹. Leaves are greyish-green and irregularly divided into several lobes; flowers tuberous, either yellow and violet, or uniformly dark violet; fruits characterized by numerous long “arms” with sharp grapple-like hooks⁵⁰,⁵¹. The thick, fleshy, tuberous secondary tap roots of _H. procumbens_ are usually dried and used in traditional medicine throughout its distribution range and beyond⁴⁹. This unique, rare and highly valuable medicinal plant is found widely spread in the Kalahari Desert of Southern Africa especially in South Africa, Namibia, Botswana, Zambia, Zimbabwe, and Mozambique⁵⁰,⁵¹. The thick, fleshy, tuberous secondary tap roots of _H. procumbens_ are usually dried and used in traditional medicine throughout its distribution range and beyond⁴⁹. In fact, the plant has been used in traditional medicine since time immemorial to treat myriad of diseases and disorders including edema, fever, allergies, and analgesia⁴⁹,⁵². Due to the numerous health benefits, the plant has been traded widely all over the world under the pharmaceutical name of Harpagophyti radix and is mostly registered as herbal medicine in France and Germany or as a food supplement in Netherlands, United Kingdom, United States, and South Korea⁴⁸. In South Korea, _H. procumbens_ plant species is important for the treatment and management of a number of disease conditions including pharamacopuncture treatment of arthritis¹³ and is known to have potential analgesic and anti-inflammatory activities⁵². In fact, the presence of a myriad of the principle bioactive phytochemicals (https://pubchem.ncbi.nlm.nih.gov/) including iridoid glycosides, harpagoside, harpagoside, isocytose, caffeic acid, procumbide, procumboside, and cinnamic acid in the tuberous roots of _H. procumbens_ may explain the anti-inflammatory and analgesic potential of this plant. Consequently, the high demand for this plant and its products has over the years put huge pressure on the wild population and as such, _H. procumbens_ species has been listed under CITES in Annex D.
Conclusion

Medicinal plants play an integral role in the provision of basic healthcare throughout the world. This study provides valuable insights into the propagation methods of some of the traditional herbal medicinal plants as one of the major ways to mitigate the future shortage of herbal medicines in the global markets. The study further showed that medicinal plants including *P. ginseng* and *H. procumbens* are not only highly valuable in the local market but rather they are equally very important in the global market. The potent and versatile medicinal activities of these herbal plants that enabled them to be used for treatment and management of several diseases and disorders may be attributed to the presence of the numerous biologically active compounds contained in them. However, further preclinical and clinical studies are required to validate these phytochemicals for possible use in drug development.

Acknowledgements

This work was supported under the framework of international cooperation program (Korea–South Africa Cooperative Research Project for Excavation of Candidate Resources of Complementary & Alternative Medicine) managed by National Research Foundation of Korea (Grant: 2017093655, KIOM: D17470). Additionally, this work was equally supported by Grants from Development of Foundational Techniques for the Domestic Production of Herbal Medicines (K18405) and Establishment of international cooperation research base for contribution of herbal resources in Africa (K18915) from the Korea Institute of Oriental Medicine (KIOM), through the Ministry of Science & ICT, Republic of Korea. Equally, financial support was provided by University of Science and Technology under the Global Internship Program (2018 summer).

References


38. Ryu SY, Lee SH, Choi SU, Lee CO, No Z, Ahn JW. Antitumor activity of Trichosanthes kirilowii