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Development strategies of advanced bio-prototype based on particle design technology

Woo Sik Choi[1,2]*, Shigeki Toyama[2] and Won Hoon Park[2]

[1]College of Pharmacy, Pusan National University, Busan 46288, Republic of Korea.
[2]The Korea Association of Powder Process Industry and Engineering (KAPPIE), Yangsan 50616, Republic of Korea.

*Corresponding author. E-mail: wschoi@pusan.ac.kr. Tel: +82-10-5529-7283. Fax: +82-55-372-0604.

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ABSTRACT

This study deals with the establishment of the "Institute of Bio-High-Tech Prototype Development (IBHPD)" based on the application of particle design technology (PDT) to promote the activity of bio-industry. Advanced bio-prototypes for various fields related to biotechnology are included, such as final or mid-products and raw material powder as healthy (functional) foods, including bio-cosmetics and raw materials of pharmaceuticals. The Institute accepts creative proposals suggested by the creative proposal of anyone for the achievements of researchers from various fields. The validity and feasibility of the proposal are evaluated using a pre-determined feasibility test. The Institute decides to support the proposal if it is judged to be useful not only for the Korean market but also for the world market. Once authenticated, the particle design technology (PDT) is repeatedly applied to the proposal. Also, other fundamental technologies and government regulations are thoroughly examined in advance. Here, as one example of the Seeds of Bio-Prototype, we have examined the Sibjeondaebo-tang of Oriental Medicine, which has been preserved and developed as a traditional medicine in many Asian countries such as China, Japan, India, Vietnam, and Korea. In every region or country, there are health-oriented, unique and delicious traditional dishes. They are considered as good examples of bio-prototypes.

Key words: Loess, bio-products, particle design technology, chinese herbal medicine, bio-prototype.

Abbreviations: BT, Biotechnology; **IBHPD,** institute of bio-high-tech prototype development; **KAPPIE,** the Korea association of powder process industry and engineering; **KIOM,** Korea institute of oriental medicine; **KRIBB,** Korea research institute of bioscience and biotechnology; **KRICT,** Korea research institute of chemical technology; **MBRI,** Mogam biotechnology research institute; **NCC,** national cancer center; **PDT,** particle design technology; **WP-KBM,** World Premium Korean Bio-Medicals

INTRODUCTION

Everyone wishes to be healthy. In other words, everyone has a modest desire to live a happy life to be healthy and aging with a sound mind. Bio-high-technology researchers have achieved significant breakthroughs through their dedication to basic and applied research. Their achievements have not always resulted in effective biological products, but they are indispensable fruits development of science and technology in the future.

As a solution to this problem, we propose the establishment and operation of the Institute of Bio-High-Technology Prototype Development (IBHPD) under the University or KAPPIE. The IBHPD uses various ingenious and creative ideas for bio-fields to obtain their practical results (data or discovery). The IBHPD committee assessesthe validity or commercialization feasibility of the proposal. If the review result of the bio-prototype is

recognized as the valuable bio-prototype, the IBHPD committee selects the proposal for a prototype development project and then starts its development. After confirming the efficacy and safety of the subsided prototype, the bio-prototype will be finally and officially recognized as the successful bio-products. To create novel bio-products, the Institute utilizes the fully elemental technologies for each step to minimize the side effects and maximize the efficacy of bio-products, namely healthy functional food, cosmetics, the raw material of medicine, and so on. The prescription may be derived by experts of Western medicine and Oriental medicine as well as experts on particle design technology.

As a result of the activity of various bio Institute in Korea, Korea commands a 5% share in the global bio-industry market. In 2010, the global market was $1560 billion and the domestic market was $9.0 billion. Korea creates world-class bio-products through the 10 WP-KBM (World Premium Korean Bio-Medicals) and by developing related products in cooperation with University and KAPPIE. It is estimated that Korea can extend its share of the world market to 16% within 10 years based on the fundamental research on ultra-fine grinding. Herein, the 10 WP-KBM has been named according to the WPM, World Premium Materials, 2010 Materials Development Program of the Ministry of Knowledge Economy, Korea (http://www.motie.go.kr/motie/ne/rt/press/bbs/bbs; Choi, 1998).

A series of appeals have been made to the government regarding the establishment of the Institute, IBHPD through presentations at conferences of home and abroad (Choi, 2007; Choi et al., 2009). Also, the establishment of the Institute would give the members of KAPPIE a sense of pride that they can contribute to the technology development of the bio-industry through bio-products and industrial materials under the cooperation between members who actively participate in the installation of test laboratory for bio-prototypes.

THE BRIEF PRESENT STATE OF THE KOREAN BIOTECHNOLOGY INDUSTRY

The hybrid of Western medicine and Eastern medicine will take advantage of ancient traditional oriental medicine, which is to be treated as an important axis for the development of advanced bio-prototypes. By 2015, the Ministry of Health and Welfare in the Korean Government had invested a total of 1 trillion Won and announced 10 trillion Won Korean medicine industrial markets. Although the Government has supported the herbal medicine sector, the level of support was insufficient in 2011. In 2015, a five-year investment of about 1.0099 trillion Won was announced and promoted. This policy of the government is considered to be well-matched with the partial objectives of the Institute.

Jung (2016) in reports of Hyundai Economic Research Institute refers to Table 1 based on the source of UBS: “Extreme Automation and Connectivity: The global, regional, and investment implications of the Fourth Industrial Revolution,” January 2016. Table 1 shows the ranking of six countries with five elements to prepare the Fourth Industrial Revolution and the status of Korea. A flexible labor market, technology level, education system, technology infrastructure, and legal system are considered as the most important aspects of the Fourth Industrial Revolution. The largest bank in Switzerland, UBS, as a member of the World Economic Forum (WEF), evaluated the five elements that could best adapt to the Fourth Industrial Revolution. As a result of this evaluation, developed countries are ranked highly in terms of the labor market, education, infrastructure, legal system, and so on. Emerging countries are ranked very low due to a poor skilled worker-oriented job structure and lack of technology infrastructure. Switzerland, the United States, Japan, and Germany are at the top, while Korea and China are at the 25th and 28th positions, respectively. To maximize the benefits of the Fourth Industrial Revolution, the labor market flexibility in developed countries and the law-and-regulation issues in developing counties should be improved (Jung, 2016).

As a vision for the development of biotechnology in Korea, the basic plan for the promotion of biotechnology, that is, the government-wide master plan for the national support for biotechnology development has been prepared to provide policy direction and guidance of Government. The Korean vision is to achieve a “Health life” and “Prosperous Bio-economy,” and “Joining the Group of Global Top 7 Biotechnology Nations” to 2016. At present, some are already made and remaining is ongoing forward (http://www.hw.go.kr/). Table 2 shows the brief introduction of major biotechnology research institutes already established in Korea.

Theses slogans are to be the goal and expectation of leaders working in the biotechnology field. The biotechnology and the bio-industry have been recognized as one of the future engines for growth. They are required to drive the world economy in the wake of the success of information and communication technology of Korea. The Korean government has selected the biotechnology industry as one of the areas that need national support and intensive fostering. Along with research and development in the biotechnology sector, the government is also encouraging the research and discussion of the ethical, legal, social impact, and implications to establish a balance between technological advances and ethical issues.

OVERVIEW OF THE INSTITUTE OF BIO-HIGH-TECH PROTOTYPE DEVELOPMENT (IBHPD)

Major developments

The integration manual of PDT and element technology for

Table 1: Ranking of six countries evaluated by five elements to prepare the Fourth Industrial Revolution and the status of Korea.

Rank	Country	Labor market flexibility	Tech. level	Education System	SOC	Legal level	Overall protection
1	Switzerland	1	4	1	4.0	6.75	3.4
5	United States	4	6	4	14.0	23.00	10.2
12	Japan	21	21	5	12.0	18.00	15.4
13	Germany	28	17	6	9.5	18.75	15.9
25	Korea	83	23	19	20.0	62.25	41.5
28	China	37	68	31	56.5	64.25	55.6

Table 2: Brief introduction of major Biotechnology Research Institutes in Korea.

- Korea Research Institute of Bioscience and Biotechnology (KRIBB) (www.kribb.re.kr)
  - Founded in 1985
  - Fundamental research for the origins of living phenomena and cutting-edge BT.
- Korea Research Institute of Chemical Technology (KRICT) (www.krict.re.kr)
  - Founded in 1976
  - Key research areas: Green growth chemical tech.; Cutting-edge chemical substances
- Korea Institute of Oriental Medicine (KIOM) (www.kiom.re.kr)
  - Founded in 1994
  - Key projects: Acupuncture, Four-phase constitution, Brain vasculature, Diabetes Complex diseases
- National Cancer Center (NCC) (www.ncc.re.kr)
  - Founded in 2000 as a government center dedicated to overcoming cancer
- Mogam Biotechnology/Research Institute (MBRI) (www.mogam.re.kr)
  - The first non-profit research foundation approved by the Korean Government.
  - Green Cross Corporation donated funds to found MBRI in 1984.
  - A leading pharmaceutical company in Korea and manufacturer of the world's best-selling hepatitis B vaccine, Hepavax.

bio-prototype development are made by following categories: 1) Particle design methods for the development of novel functional materials created through the sophisticated combination of various materials (inorganic, organic, metallic), 2) the control of particle size distribution; the morphology of materials (large particles, medium particles, small particles, and the size of ultrafine particles), 3) optimized operation processes such as milling, granulation, and compaction are utilized in combination with the manual set of integrated technologies.

Professor Masumi Koishi contributed an article entitled "Polyhedron-like Particle Design Technology for the Advanced Functional Fabricating of Fine Particles" in the special issue about the composition and function of the particles and provided the following description (Koishi, 2013). For example, the technology road maps of APPIE's Technical Division activities, especially granulation technical division, fine Nano-technology technical division, battery manufacturing technology technical division, static electricity utilization technology technical division, wet process technical division, mixing and molding technical division, and grinding technical division are greatly utilized for this Institute. Future technologies are described in the technology road map of each technical division in APPIE. It is considered to be essential to perfect the understanding and integrated usage of particle design technology (APPIE, 2014). A practical guide book for PDT had been published and "the compass – like hint and easiness to apply ideas" makes the best powder material for creating the final form, where the morphology of the best powder material for

Table 3: The basic outline and management strategy of IBHPD.

Step	Main activities	Important activities	Authority
1st	Receipt of bio-prototypes	- Seed providers (Universities, Institutions, and the general public),	Proposer
	Proposal review	- Needs consumers (Industry, Public authorities),	KAPPIE
		- Consultation on proposals: efficiency, reliability, timeliness, economics, technology	BPDC
2nd	Prototype production	- Application of bio-prototype test lab. in company concerned	Member
	Allocating of preparing TL	- Particle Processing Technology	BPDC
	Complement need	- Joint research with the University related	Ind. & Univ. Coop.
	Meet challenges	- Particle design of the main ingredient and raw materials	Test lab.
		- Manufacturing bio-prototype by a combination of unit operations	Test lab.
3rd	Evaluation of prototype	- Primary efficacy and safety assessment	ISC
4th	Recheck of properties	- Repeat the above steps until the final goal is reached	KAPPIE
	Completed prototype	- Cooperation with related institutions for the final check	
	Final technology transfer	- Establishment of PDT confirmed for bio-products	
		- All contracts signed for know-how to the proposer	

the Institute advances to the next step, which is the construction of a joint technology Industry-Academy-Government support system and the practical training center. Then by the specialized step of element technology and biotechnology processes, finally the novel bio-prototype of the last step is created with the proper and desired function.

A series of the contents is to make the particle shape of the nano-scale level, to create an integrated powder form, to create the non-familiar form of learning from nature and to challenge the basic and new industrial changes (Koishi, 2013). It is considered that a key point of many-particle factors on particle size design is the particle size and surface, packing of particles, and formulation of components, in which this idea on particle size design can be expanded from a particulate scale to a molecular scale.

Establishment strategy

The basic outline and management strategy of the Institute of Bio-High-Tech Prototype Development are briefly summarized in Table 3.

BPDC refers to the configuration of the bio-prototype development committee in IBHPD. Particle processing technology refers to the use of advisory and technical road maps of APPIE technical divisions in Japan, and ISC refers to the installation and operation of the SMEs' Integrated Support Center in University working incorporation with the Institute (Buglistello, 1968).

Organization

The Institute is organized, established, and managed as a think tank under University or KAPPIE. Under the construction spirit of the Institute, each member of KAPPIE installs and operates in voluntary participation a special prototype test laboratory using its know-how voluntarily, while the University or KAPPIE establishes and manages a bio-prototype development expert committee for consultation between the relevant Authorities.

The bio-prototype test laboratory (Test Lab.), which is voluntarily installed and operated by each member company, is determined simultaneously with the establishment of the Institute from Government. The decision to establish the test laboratory is made by the public offering or recommendation of the expert committee. Suggested items of the Institute are shown in Table 4. The companies that participate in the establishment of a specific test laboratory should receive special incentives from the Government to compensate for the risk of failure.

The bio-prototype development special committee will be composed of seven to nine experts from the relevant institutions, including a chairman. KAPPIE convenes expert meetings of the bio-prototype development special committee on request. The committee deliberates important issues and makes cooperative decisions to establish the best methods to facilitate the completion of the bio-prototype. Table 4 shows the major components of the Institute and the outline of the operating method. The key function is to ensure the validity of the bio-prototype

Table 4: Major components of the Institute and the outline of the operating method.

1	Bio-tech prototype professional development committee of 7 to 9 persons.
2	Special test laboratories installed in member's companies: Basic powder technology: Unit operations such as grinding, granulation, and so on. Purpose-oriented technology: Medicine, food, cosmetics, high value-added products, and so on. Next generation-oriented: Energy, Traditional technology, 3D printing technology, AI, and so on.
3	Integrated Support Center of bio-prototype development in the University for small-medium businesses

Table 5: Sources of seeds for the development of healthy functional foods bio-prototypes, raw materials for medicine, and cosmetic bio-prototypes.

1	Basic-and-applied research papers and practical or dormant patents from related institutes
2	Traditional recipes and tasting methods
3	Prescriptions of many traditional oriental herbal medicines, for example, Sibjeondae-tang
4	Feedback on bio-products in traditional markets and supermarkets
5	Lectures on healthy living by experts via public TV or radio broadcasts.

based on particle design technology. According to validation data, members are to be assigned to the test laboratory bio-prototype for each manufacturing process. The integrated support centers for small-medium companies installed in the university will serve to evaluate the efficacy and safety of the bio-prototype. As previously mentioned, better bio-prototype will be created out through a series of processes.

The main roles of ISC are as follows: 1) Measurement and analysis support for basic and applied physicochemical properties of bio-prototypes; 2) Efficacy validation support for bio-prototypes; 3) Safety assessment support for bio-prototypes.

Establishment site of the Institute and its networks

The Institute is installed and operated as a think tank of the University or KAPPIE. To promote smooth and mutual cooperation with other research institutions, it is recommended that the Institute is configured with the relevant universities. The bio-prototype development special committee and the network of similar institutions are connected via the relevant websites and useful information is also disclosed in principle.

SOURCES OF SEEDS AND CONSIDERATION OF THEIR UTILIZATION

Table 5 shows the information sources of prototype health (functional) foodstuffs including raw materials for medicines and cosmetics prototypes. The reason for selecting Sibjeondaebo-tang as a typical example of a seed that is used in many Chinese herbal prescriptions is as follows: the cooperation of Western and Eastern experts; the treatment is widely used in Korea, Japan, and China; the comprehensive reviews available over a long-time period and it is a multiple purpose prescription well-known for enhancing well-being and patient recovery. The possibility to challenge for various usages of bio-prototypes and the intermediary of chemical engineering thinking for unlocking issues are shown. Here, 'tang' means the herb extract in hot water.

Table 6 shows a summary of 10 Chinese herbal medicines that use Sibjeondaebo-tang and related data. As a typical example of particle design, the reason why Sibjeondaebo-tang is selected is that it comprised two Chinese herbal prescriptions and composed of 4 kinds of Chinese herbal medicines including two Chinese herbals. Sibjeondae-tang is commonly used to increase vitality or energy or if the body feels cold. It is widely prescribed to protect the body when it is weak due to a decrease in physical strength after illness, fatigue, or anorexia (Standard Chinese Herbal Prescription Drug Information, 2013; Lee et al., 2010; Lee et al., 2010; Jeon et al., 1999; Kim et al., 1999; Park and Choi, 1998; http://www.jah.ne.jp/~kakp; http://www.tsumura.co.jp/english/kampo/2016). Table 4 highlights the following: 1) The main chemical components and major actions in each herbal medicine, 2) an examination of the pharmacological chemical composition of the active drugs used in the present medical formulation,

Table 6: Summary of 10 Chinese herbal medicines used in Sibjeondaebo-tang.

Prescription	Latin name	Main ingredient	Ratio(g)*	Part	Pharmacological action
Sagunja-tang	PANAX GINSENG C.A. Meyer	Ginsenoides Rg1, Rb1	3.75	Root	Warm body & metabolism
	ATRACTYLODIS RHIZOMA ALBA	Atractylon, Acetoxyatractylon	3.75	Roots	Water's uneven distribution
	PORIA SCLEROTIUM	Pachymic acid, Triterpenoid comp.	3.75	Sclero.	Diuretic inhibiting
	GLYCYRRHIZAE RADIX	Liquiritin, Glycyrrhizin	3.75	Root	Relieves tension
Samul-tang	REHMANNIAE RADIX	5-hydroxymethyl-2-furaldehyde	3.75	Root	Control of the blood
	PAEONIAE RADIX	Albiflorin, Paeonniflorin	3.75	Root	Relax of muscles
	CNIDII RHIZOMA	Ferulic acid	3.75	Roots	Stimulating blood flow.
	ANGELICAE GIGANTIS RADIX	Nodakenin	3.75	Roots	Improves Gynecological
Other 1	ASTRAGALIRADIX	Isoflavone,l-canavanine	3.75	Root	Water disorder of the body
Other 2	CINNAMOMICORTEX	Cinnamicaldehyde cinnamic acid	3.75	Bark	Moving of stagnating

*Dose is referred to prescription of 'Doguibogam' as the reference from the book: Korea Institute of Oriental Medicine, (2013), "Standard Chinese Herbal Prescription Drug information 2013", pp. 223-257.

3) a preclinical examination of efficacy when some herbs are added or removed from the prescription, and 4) basic research regarding the existing and unidentified active ingredients in medicinal plants as well as the useful treatment processing technology. From the perspective of bio-product creation as well as the establishment of particle design technology, it is very important to examine the formulation of currently available medicines, their ingredients, contents, and dose, including the main pharmacological action of each Chinese herbal medicine using classical and experimental data.

It is also suggested that the use of recently developed AI robotics will help engineer breakthroughs in this field shortly. The close collaboration between various interdisciplinary research studies, such as basic research on standardization of traditional Chinese medicines, the compositional structure of medicinal herbal plants, and their pharmacological actions, is highly recommended (Wu et al., 2013; Sung-Hoon and In-Rak, 1997).

Herein, the mixing ratio refers to the prescription of "Doguibogam", an encyclopedia of Clinical Medicine on Oriental Medicine edited by Hur (2005) in the "Standard Chinese herbal Prescription Drug information 2013," Korea Institute of Oriental Medicine in 2013.

Sibjeondaebo-tang has some important pharmacological functions and effects including the suppression of bacteria proliferation, tumor formation and transition suppression, reduced immune response, hematopoietic function recovery, and early reaction inhibition. It also causes neuroglia of oxidative damage defense effects and Alzheimer's dementia prevention and protection, blood clotting inhibition, creation of blood clots and prevent, no liver damage, reduction of ammonia in blood, and liver metabolic deficiency recovery, healing and regeneration of skin wounds, radiation protective effect, increase in iron bioavailability, no change of heavy metal of its concentration in blood and antioxidant properties (Standard Chinese Herbal Prescription Drug Information, 2013; Lee et al., 2010; Lee et al., 2010; Jeon et al., 1999; Kim et al., 1999; Park and Choi, 1998; http://www.jah.ne.jp/~kakp).

Sibjeondaebo-tang is composed of Sagunja-tang and Samul-tang, Pamul-tang, and includes other two herbals of the astragali radix and cinnamomic cortex. Sagunja-tang is composed of four types of Chinese herbal medicine, Panax ginseng C.A. Meyer, atractylodisrhizoma alba, poriasclerotium, and glycyrrhiza radix. The prescription is used to improve gastrointestinal function, water retention and exhaustion. Samul-tang is composed of 4 types of Chinese herbal medicine, Rehmanniae radix, radix, Cnidii, rhizome, and Angelicaegigantis radix. The prescription improves the circulation and warms the body. It is a good prescription for women because it helps smooth the skin and balance hormones (http://www.tsumura.co.jp/english/kampo/2016). As previously discussed, it can be seen that the herbal medicines used in Sibjeondaebo-tang have been widely used as a single prescription, as well as a combination prescription for various medicines. It implies that they can be used as an important medicinal bio-based raw material for the bio-prototype.

Here, as an example of the Seeds of bio prototype, we are examined the Sibjeondaebo-tang of Oriental medicine, which is very useful in daily life, has been preserved and developed as a traditional medicine in many countries such as China, Japan, Vietnam, and India. On the other hand,

religious groups that have long lived in a particular living environment are known to have preserved and developed unique health prescriptions and food prescriptions, which are different from the general civil society (Oh et al., 2008). Also, generations of family generations have developed and preserved inherited food recipes that convey their unique flavors of their own. Therefore, they are deemed worthy enough to challenge for the creation of advanced bio-prototypes in earnest.

Several important achievements are anticipated with the establishment of this Institute. The particle design techniques, which have been repeatedly identified during the development of new bio-prototypes in laboratories, can contribute to the development of other biotechnology products, industrial products, and high-tech products. It is expected to create synergy effects in the creation of new branded technology products, such as the development of new products, improving the quality of existing products, and developinghigh value-added products that meet global standards. The commercialization of basic research through the meeting of Seeds and Needs is expected to extend biotechnology to other areas of the industrial materials industry (Koishi, 2013; APPIE, 2014).

It is also believed that there is a strong need to explore international research relationships to expand the philosophy of traditional Chinese and Indian medicine, such as Ayurveda and traditional Chinese medicine (Kim, 2005). In any region or country, there are unique and delicious dishes of a healthy tradition. It is a very meaningful way for bio experts and entrepreneurs to gather their wisdom and develop bio prototypes for those who suffer from unaided body care. Anyone interested in this project will believe that this project will succeed if you participate actively.

CONCLUSION

The institute should promote research and development through focused investments to create advanced bio prototypes through the use of powder material manufacturing technology and the application of composite and functional particles. To fully achieve this project, planning joint research projects between the central and local governments, their related research and supporting institutions, and related research institutes are very important not only to ensure efficient use of the national budget but also to achieve good results.

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