

# FEASIBILITY OF PATENT RETRIEVAL AS AN AUXILIARY FOR BIOTECHNOLOGICAL INNOVATION - THE CASE OF CORDYCEPS MILTARIS

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#### Abstract

This study demonstrates the availability and possibility of a patent retrieval and analysis model for biotechnological innovation to obtain patents in an empirical cordyceps militaris researching case. The conventional framework of R&D is possibly time-consuming and lack of efficiency. Moreover, the outcomes could easily fail to meet market demand and suffer loss ultimately. This study proposed a useful of patent retrieval and analysis model to facilitate R&D in biotech industry. The model includes innovations trimmed after evaluating current market situations, business capacity and priority to make their market values stand out. The practical evaluation concepts could include relative skills and current industrial developments in relative areas of technology, and barriers of patent applications. The purpose of the model application is to obtain patents in an efficient way. As completing field experiments by using this model, this innovational result had already successfully obtained patent from Intellectual Property Office of Taiwan in 2008. The results of this study are as following: First, this empirical case showed that the analysis of patent information retrieval is a potentially useful tool to build up practical development processes to achieve invention patents. Second, the patent retrieval and analysis can improve efficiency and feasibility for biotech industry in patent acquisition.

## Key Words: Cordyceps, Patent Retrieval, Patent Analysis, Innovation Technology, Empirical Research

#### Introduction

Currently, the economic developments in Taiwan, SME's (Small to Medium Enterprises) flexibility and their operation characteristics have a highly stable fluctuation in the economy. According to the research of White Paper on Small and Medium Enterprises in Taiwan 2015 had shown that, in 2014, 13,500,003,049 SME had recently hit at very high record, they had been occupied 97.61% among the entire entrepreneurs. In terms of sale, in 2014, SME's sales value worth 11 trillion and 8 hundred billion yuan, occupied 29.42 % among the entire entrepreneur's ratio, shown that Taiwan SME, they are playing pivotal role. However, the competitive in the Global Market has been a keen competition, the product life cycle had been slightly shorten; the key factor for entrepreneur to survive is from rapid response to market and continuous innovation. Many entrepreneurs couldn't be the same as they continuous

controlled the market, and had the ability and capability to have creative innovation in their mind, with the rapid re-leased to rapid market change and the new demand (Dollingers, 2003). At the same time, Robeson and O'Conner (2007) indicated [Patent] is the element to create the new innovation. For the enterprise's survival, many enterprise companies proposed their research ideas based on R&D personnel's development capabilities and experiences. Then, based on the company's industry pattern and marketing determined whether to put their focus on the product development. But, after we put so much efforts and R&D expenses, we found out there is an overlapped between our enterprise company and other enterprise companies. In Europe, they kept repeating their Research development each year, and because of this, they wasted 20 billion in total (Hsieh, Pao-Nuan, 1988). Therefore, to avoid this result happened, or committed copyrights these huge risks happened to us. At the same time, we create new innovation, we also need to add in patent retrieval as a secondary way to research and create innovation. Next step is to protect intellectual property right, is to achieve the elimination of the barriers and use the old materials to create the new opportunity for new innovation. Therefore, these case researches had done the actual biotechnology industry operation and promote successful experiences of the new creative innovation, help enterprise based on the patent information, execute the product development and ensure all the R&D results has possessed the legal protection of the reference model.

## Literature Review

#### Cordyceps

Cordyceps (cordyceps militaris) is also known as "Cordyceps militaris" and "Cordyceps." Currently, cordyceps is utilizing biotechnology artificial nurture, analyzing contained ingredients of the parasites, in order to formulate an alternative medium grain worm, implanting ophiocordyceps. Monitoring wild worms growth environments, appropriate luminosity, temperature and humidity. Developing cordyceps fruiting body, when the fruiting bodies became mature, it can be harvested immediately. Amongst all the species, Cordyceps militaris is considered as the oldest source of some useful chemical constituents (Das SK et al., 2010). It is a potential harborer of biometabolites for herbal drugs (Cui JD. 2015), and a multifunctional herbal drug Cordyceps militaris as an anti-tumor agent (Wada T et al., 2017).

Cordyceps militaris produces cordycepin (3'-deoxyadenosine), which has various activities, including anti-oxidant, anti-tumoral, anti-viral, and anti-inflammatory (Kato T et al., 2017). The caterpillar fungus Ophiocordyceps sinensis is a medicinal mushroom increasingly was using as a dietary supplement for various health conditions, including fatigue, chronic inflammation, and male impotence (Martel J et al., 2017; Li Nan et al., 2001). Cordyceps militaris effectively recovered cyclophosphamide-induced decreases in IL-2, interferon- $\gamma$ , tumor necrosis factor-a, and IL-10 level (Shin JS et al., 2018). It may be applied as an agent for immune boosting therapy in immune suppressed patients (Kwon HK et al., 2018). Modern research shown that, for anti-cancer, cordyceps can boost the immune system, bacteriostat, resisting ageing, resisting antiprotozoal diseases, resisting anti- virus, and to provide trace elements. Vitamin effects are also being affirmed (Wenyuan Xiang and Mudian Ping, 1998; Ji sand, Shi Xiaobing and Chun Yi, 1999; Tang Ke-Xuan, 2005). Based on past research and found that Cordyceps militaris has strong activity on the immuregulation, tumor, virus, infection (Fan HT et al., 2013). Technically, in clinical, it can be used to treat tuberculosis, coughing, neurasthenia, chronic nephritis, cancer and other diseases.

Meanwhile, it can regulate immune function; enhance the body's resistance of diseases (Liu Yin-hua, 1999). Medicine effects of Grass cordyceps species expressed that cordyceps mycelium have an ability to enhance "male hormones". Studies indicated: cordyceps in humans can induce ovarian granulose cells (GLC) to generate steroids produced enzyme estradiol (E2). As well as native rats, "leydig cells" (Leydig Cells) and MA-10 mouse's leydig tumor cells can also be induced by testosterone (testosterone) being produced (Huang, 2004; Hsu, 2003). Experimental studies shown that cordyceps significantly shown the affect to enhance the rat's plasma testosterone level. (Huang, 2004; Yu, 2006)

Therefore, according to our abovementioned, we can understand cordyceps have many potential effects, through excluding can be public or being part of patent application. And, this study intends to be directly against possible projects to be processed to marketing estimation. In the future, we need to find out which products that we sent to the market sales have the most innovative research and development to complete the patent process.

## Innovation and Technology

The first person to propose the concept of academic was the economist

Schumpeter (Schumpter, 1934), based on the viewpoint of economics, he defined innovation as "the use of invention and discovery, prompting the concept of economic development". He claims: "invention first, then innovation". In other words, the truly innovative behaviors impact in a very wild range; involving new ideas, generate new inventions, new product design, new producing process, new marketing strategies and developing new market, so on. Continuously, scholars said that if Drucker thinks the innovation is "the ability to give the resource to create the power of wealth". Garcia and Calantone (2002) think that innovation process is repeatedly. Marquish (1982) proposed that innovation can be divided into three types: 1. "incremental innovation": the product, services or the process make little change innovation; 2. "System innovation": must spent more time, and expense to do the improvement, therefore, we get the specific results. 3. "Breakthrough innovation" (Radical innovation): it may affect the entire industry or even create the new innovation of the entire industry, whether incremental or breakthrough type of innovation is the driven to the entire industry. But breakthrough innovation will be a dramatic change to the entire industry. Betz (2003) considered that innovation was a new product, process or service guide to the market.

And the innovation divided into product innovation, process innovation and service innovation. Tidd et al. (2001) thinks that the innovation refers to enterprise provided the products, services, and methods in order to redesigned or modified to enable enterprise to survive or core process. Knight (1967) will be divided into four types of innovation: product or service innovation, production process innovation, organizational structure innovation and employee innovation. Betz (1987) use the innovation base on different techniques separate them into: product innovation, program innovation, and service innovation. Gobeli and Brown (1987) think different types of innovations can be based on producer's concepts and depending on the skills. From the increase in consumer's interest will be divided into technical innovation, incremental innovation, breakthrough innovation and use of innovation.

However, innovation with unpredictable characteristic, is occurring in the confusion (Druker, 1998). On the other words, whether the incremental or breakthrough innovation, are the subject of the innovation, and the innovation elements alternation in a complex phenomenon emerge, is technological improvement. Hsu (2007) proposed balanced refining innovation and exploring new innovation generate new ideas, thinks that essential innovation is at lower risk, there are rules to follow in a professional way. Exploring new innovation is at very high risk, no rules to follow, is a different value innovation. Therefore, the contradiction between exploration and essential process is more focus on how important to achieve the balance between them. Chiesa et al. (2008) indicates, the numbers of patents can be used as a performance indicator; Deeds, D.L., (2001) indicates the number of patents can be part of company's developing techniques. Hirschey and Richardson (2001) claims that in a investor's point of view, the products affirmed by patents are the useful indicator. Hereof et al., (2003) shown patent's value and citation amounts is related. Hirschey and Richardson (2004) indicates patent is a beneficial effect to stock price. Von Wartburg et al. (2005) research and development activities have been positively recommend the documents that were provided. Choy et al. (2007) indicates that integrating all kinds of technological interventions for patent analysis can help the industry to predict the future trends, and develop better research and development strategies. Silverberg and Verspagenb (2007) indicated that the distribution analysis of the key innovation's level, through the use of patents, can be an indicator to the significance of innovation. Reitzig

(2004) examine the patent owner's patent indicator and other markets value. The action to sue the patent's infringement can be a positive affect patent owner's market value. Hereof and Hoisl (2007) a product inventor, created a huge legal monetary value.

## Patent Retrieval and Analysis

The importance of intangible assets is much higher than that of tangible assets in nowadays knowledge based economy, especially in the raising era of technology industries. Patent rights has now become the most influential. concrete types of intellectual assets, needless to say that intelligence itself is one type of commercial goods. The more intellectual assets were built, the stronger competitive advantages. In another word, continuous invention is an important operative strategy for a business to cultivate international competitiveness. How a business protects its invention by patents is an essential issue to units such as R&D. marketing, human resources, and others. Claiming a patent right not only protects developers' rights and interests, it also helps developers to familiar developmental trends in their professional fields which would be required for future product innovation. With thorough patent retrieving and analysis during product development and marketing, one can get hold of the trends of relative products, potential developmental difficulties, and competitive patent claims in prevention of infringement. Since patent claims can cover from technology, private rights, laws, public interests, to commercial trades, patent itself is a comprehensive subject that should receive additional attention on its practical applications and designs.

According to the second regulation of "Patent Act," there are three types of patents: Invention, Utility Model, and Design Patents. To elaborate parts that closely relate to this study in Invention Patent, the invention first has to utilize technical thoughts regulated under natural laws. The technical character of an invention patent could be a new invention or a new method invention, which includes new application, new utilization, or new purpose. To be more specific, this character could be an (1) invention of a new matter, which covers a new substance (for example, compound X) or a new article like *cordyceps militaris*; (2) invention of a new method, which covers a manufacture method, such as the methods with visible products to produce compound X or to culture cordyceps militaris, or the methods with invisible products to identify polysaccharides in mushroom samples or to suppress bacteria with compound X; (3) invention of a new purpose, for example taking compound X for bacteriostatic as never before (i.e. new utilization or application). As for utility model patent, it protects by definition an innovation of the shape, structure, or installation of an article produced under technical thought regulated under natural law. This patent does not apply to new methods, new applications, new biomaterials, or shapeless matters.

As known, there are enormous entries in patent database. Searching and analyzing prior arts allow one to understand whether there is the same or similar technique, study the development strategies of competitors and defeat them. The purposes of patent searching and analysis are thus to: (1) avoid repetitive R&D; (2) minimize developmental schedule; (3) reduce risk of infringement; (4) raise validity to suppress closely related patents in competitors' hands; and (5) study technical development strategies of competitors.

Patent retrieving is a procedure of using keywords to fish entries in a specific patent database. The flowchart or framework of patent searching includes: 1) define the purpose of the search, 2) limit ranges, 3) use appropriate searching tools and 4) objectively perform and present the search. The purpose of patent literature related to data mining could be dynamic and complex, as it could be classified for personal, business, industrial, or national uses. Setting the search purpose at the national level allows one to evaluate technical competitiveness of countries. Setting the search purpose at personal level allows one to understand his or her R&D strength. There are also other purposes of a patent retrieval: patent analysis of a new technique, commodification of a patented technique, industrial analysis of a patented technique, patent ownership of competitors and suppliers. There are many aspects toward the range of a search that can help to acquire entries more precisely and rapidly, such as by countries, patent types, time frames, and many more. All tricks lay in how one manipulates the language, and what to fill in different search entry columns. As talking about search tools, it is an art of choosing appropriate software provided by either commercial software developers or national IPO, and personal data-mining skill.

Under an objective patent retrieval, results could be more valuable with the aid of theoretically objective search engine and professionally subjective analysis. Search results are most often presented as figures or tables to enhance overall observation and assessment. How to present search results is the tactic that has to work along with planned patent layout and application strategies in order to signify its value. In addition, the value of a patent retrieval also lays within the background information which provides operative information and is often used at business or national level. Almost all developed countries provide online patent document information within their engine systems of patent retrieval, such as World Intellectual Property Organization (WIPO), United States Patent and Trademark Office (USPTO), European Patent Office (EPO), Japan Patent Office (JPO), and Taiwan Intellectual Property Office (TIPO). Patent titles, patent numbers, IPC, ownership, name of inventors or examiners can be used as patent retrieval keywords in patent retrieval systems mentioned above.

## **Empirical Analysis**

## Patent Information Retrieval And Analysis

This study included information from database of TIPO, State Intellectual Property Office of the P.R.C. (SIPO), USPTO, and EPO (Table 1). Invention patents were first filtered with technical terms related to *cordyceps*, published and patented before October 2005 (Table 2 - 6). Most *cordyceps* invention patents were recipes of compound medicines, culture methods, identification methods, or as potential candidates within other Chinese medicine recipes. These results were further filtered to include only those use *cordyceps* as a key ingredient within recipes or products.

Grouping results by their application fields, three categories came out: medical, animal, and daily supplies. As learned from medical categories, cordyceps had been used to treat diseases of lung, kidney & liver, tumors, and osteoporosis. These patents suggested hindrances of related commercial product development to some extent, but also the possibility to develop a male fertility improvement product. (See Table 6.)

 Table 1. Summary of Inventive Patent Retrieval of Cordyceps Militaris

 Unit: Piece

Country / Region	Before October 2005	Results of applications
Taiwan	41	5
P.R.C	287	8
U.S	26	4
EU	24	2

Data Source: This study

Table 2. Results of Patent Retrieval related to	o Cordyceps Militaris in Taiwan
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Patent No.	Patent Titles	Application date	In Approval Public
200513258	(Hepatitis C adjuvant therapy)	2003.10.07	•
200509953	(Osteoporosis therapeutics and osteoclast formation inhibitors)	2004.04.14	•
278037	(A method for the isolation of active ingredients of Cordyceps sinensis which can improve renal function)	1993.12.28	•
1229084	(A substance having a steroid structure, a method for producing the same, and an antitumor agent containing the same)	1999.02.26	·
582999	(A method of isolating the active part of lung function was isolated from Cordyceps sinensis)	1999.11.18	•

Data Source: This study

Patent No.	Patent Titles	Application date	In Pub- lic	Approval
CN1127633	(A Cordyceps Militaris bath solution and its preparation method)	1995.11.16	•	
CN1337221	(Superfine Cordyceps cosmetics and its pro- duction methods)	1996.10.21	•	
CN1245073	(Placenta Cordyceps capsule for the treat- ment of viral hepatitis)	1999.08.03	•	
CN1348703	(Cordyceps powder green feed additive)	2001.10.15	•	
CN1349758	(Cordyceps-containing tourism health food and its preparation method)	2001.11.20	•	
CN1686515	(A kind of Cordyceps Dripping Pill for re- plenishing lung and kidney and its preparation method)	2005.03.21		•
CN1709220	(Cordyceps Militaris Polypeptide nano-series skin care cosmetics and its preparation method)	2005.06.21		•
CN1213506	(Cordyceps feed additive and its production method)	1997.10.07		•

## Table 3. Results of Patent Retrieval related to Cordyceps Militaris in P.R.C

Data Source: This study

Table 4. Results of Patent Retrieval related to	<i>Cordyceps Militaris</i> in U.S
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Patent No.	Patent Titles	Application date	In Pub- lic	Approval
US20030095982A1	Fraction of <i>Cordyceps sinensis</i> and method of isolation thereof	2002.08.13	٠	
US20050074428A1	Adjuvant agent for hepatitis C	2004.01.13	•	
US20050013830A1	Agents for treating osteoporosis and inhibiting osteoclast formation	2004.04.16	•	
US20040208891A1	Active compound from fraction of <i>cordyceps sinensis</i> and use thereof	2004.05.10	•	

Data Source: This study

Table 5. Results of Patent Retrieval related to	<i>Cordyceps Militaris</i> in EU
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Patent No.	Patent Titles	Application date	In Pub- lic	Approval
EP67000B1	Production of a nitrogen-containing poly- saccharide having antitumor activity	1982.05.24		•
EP200458B1	Hair tonic composition	1986.04.22		•

Data Source: This study

## Define R&D Goal

Male infertility is often evaluated through sperm count and motility. According to WHO definition set at 1999, bad sperm quality included any one of the following: less than 2 C.C. semen in each ejaculation, less than twenty million sperm per C.C., less than 50% sperm with good activity, less than 50% sperm with forward motility, or less than 14% sperm with good morphology. Thus, we quantified these features to justify the experiment.

## Invention Of New Study Design

After patent retrieving and analysis in various patent databases, there was no patent filed for "improvement of male infertility" by using *cordyceps*. Hence, it was qualified to patent internationally.

The core technique of this patent application was a new application of *cordyceps* on improvement on male infertility, which integrated Chinese traditional medicine and nowadays biotechnology. The goal of the study was to enhance sperm count and activity, and reduce number of immature and abnormal sperms. Although *cordyceps* is a well-known and widely used herbal medicine, there was lack of scientific proven efficacy on improvement of male infertility. Therefore, we artificially cultivated *cordyceps* in balanced grain media instead of insects, and studied efficacy in feed-animals in order to answer whether dietary therapy was capable to replace complementary therapy in infertility treatment.

To design appropriate claim range for *cordyceps* based male infertility improvement product, claims had to "design around" existed literatures and prior arts in order to achieve best claim range and feasibility. Since the goal of the study was to increase sperm count and quality in animals and ultimately improve male fertility, the experimental directions included: (1) a new cordyceps application on improving male fertility, as justified in sperm count and quality; (2) a new cordyceps-containing recipe that were capable of treating or preventing male infertility, which could be in medical acceptable carriers, excipients, or attenuant.

## Results

In the present study confirm the feasibility of a patent, in order to carry out Cordycepts boars feeding experiments "to increase the number of male pig sperm and vitality values" and "to reduce the breeding male immature and abnormal sperm count." In response to these two levels were implemented.

Medical area		Animal Area		Necessities	
Applications	Patent No.	Application	Patent No.	Applications	Patent No.
Lungs 1		Feed Addi-		Body lotion	
8-		tives 1		:	
	TW582999		CN1348703		CN1127633
	CN1686515 US20040208891A1		CN1213506		
	US20040208891A1 US20030095982A1				
Kidney :				Shampoo 1	
Trianey .	TW278037			Shampoo	EP200458B1
	CN1686515				
Liver :				Cosmetics :	
	TW200513258				CN1337221
	CN1245073				CN1709220
	US20050074428A1			U aalthu arr	
Cancer 1				Healthy sup-	
				plement 1	
	TWI229084 EP67000B1				CN1349758
Osteoporosis	EI 07000D1				
	TW200509953				
	US20050013830A1				

#### Table 6. Applications of Cordyceps Militaris's Patent items in the world

Data Source: This Study

And by analyzing the composition presented in Table 7.

Items	Mycelium	
Cordycepin	1,892	mg/100g
Cordycepic acid	2,162	mg/100g
Cordycepic polysaccharide	4.2	g/100g
Superoxide Dismutase	3,120	U./g
Zn (zinc)	23	mg/100g
Ca (calcium)	251	mg/100g
Mg (magnesium)	162	mg/100g
Se (selenium)	0.23	mg/100g

Table 7. Main Ingredients of Cordyceps Militaris (Lin, 2007)

First, the 10 Duroc male pigs, Landrace (Landrace) male pig 4 randomized (n = 7), divided them into two groups and fed experimental control group was not added. Dosage: 10 g / day / each male pigs. There synchronous feeding pigs experimental group and the control group or without added continuously feeding 50 days, once a week collecting semen, semen volume was measured in each group of animals, semen samples in total sperm count, sperm motility and sperm count normal value. From the results show, Duroc, Landrace boar fed through add Cordycepts (composition shown in Table 7), 10 grams per day, and after 50 consecutive day trial, and was not added to feed Cordycepts control group, add feeding mycelia of Cordyceps sinensis male pigs in the test group, the average total sperm count increased by 26%; average total sperm motility value increases by 54%; and the average total normal sperm count increased by 50%. Cordyceps mycelium showing Add fed in the feed, indeed increase sperm count and vitality of the experimental male pigs only, in order to enhance their reproductive capacity.

Secondly, in accordance with the above embodiment of the feeding experiment, continuous feeding 50 days, once a week collecting semen, semen sample was measured in each group of pigs neck protoplasm immature sperm, the piece protoplasm of immature sperm, and other abnormal sperm and other content. From the results show, Duroc, Landrace male feeding pigs after adding 10 grams per day, and 50 consecutive days after the feeding test, compared with the control group fed without adding to add the test group fed male pigs, the average total sperm neck protoplasm immature sperm count reduction of 41%; average total sperm piece protoplasm of immature sperm count by 5%; and an average total sperm other abnormal sperm count decreased by 9%. Cordyceps mycelium showing Add fed in the feed, can really reduce boar semen test public immature and / or abnormal sperm count, in order to enhance their reproductive capacity. Summarizes the experimental results are presented in Table 8.

## **Conclusion and Suggestions**

In this study, innovative R&D procedures, to develop new applications *Cordyceps* products through patent information retrieval and analysis, finding even the current development in the field has the value of future patent applications in the patent technology, but by the market analysis and evaluation, was put into experimental animals the study. After this patent, technology, market analysis, selected with

		Control Group	Range %
Categories	Test Group%	%	U
Semen volume / ml	10	5	5
Sperm motility ( % )	16	0	16
Normal sperm ( % )	51	2	49
Proximal plasma droplet sperm ( % )	-41	4	45
Distal plasma droplet sperm ( % )	-1	-12	11
Abnormal sperm ( % )	-14	8	22
Number of sperm / c.c ( $\times 10^6$ )	29	5	24
Number of total sperm ( $\times 10^6$ )	36	10	26
Number of sperm motility / c.c ( $\times 10^6$ )	59	5	54
Number of normal sperm /c.c ( $\times 10^6$ )	57	7	50
Number of distal plasma droplet sperm /c.c ( ×10 <sup>6</sup>	5		41
)	-32	9	
Number of distal plasma droplet sperm /c.c ( ×10 <sup>6</sup>	5		5
)	-3	-8	
Number of abnormal sperm /c.c ( $\times 10^6$ )	3	12	9

#### Table 8. Summary of Experimental Results

\*Negative Value means diminishment

"Cordyceps enhance male fertility effect" as the product development of the spindle, and then the medicinal efficacy assessment and market assessment, analysis and further patent retrieval, and then through the experimental study has clearly demonstrated that Cordyceps overcome sperm obstacles to development, to enhance the effectiveness of male fertility, and has made Taiwan invention patent (famous for the invention first I No. 298 258), the official name for the invention "Cor*dycepts* enhance the fertility of male animals use" in 2008, patents for the period July 1, 2008 to March 22, 2026. Thus, the invention patent for the

achievement successfully demonstrated patent retrieval methods to enhance the effectiveness of the feasibility of having a corporate R&D. The following conclusions: (i) through patent information retrieval analysis, development of innovative products in line mode, you can achieve the object of the invention patents obtained by the present case-studies; (ii) to provide enterprise product development to create new models for the beginning of the development idea, to save human and material resources to achieve synergy with the patent; (iii) the scientific data in support of force, confirms the combined benefits of innovation and R&D model patent obtained.

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