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R&D Innovation Patterns and Patent Application Strategy of Top-Selling Drugs: Insights from Patentometric

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Abstract

This article discusses the closed or open innovation patterns adopted by top-selling drugs and their patent application strategy throughout the drug lifecycle. The research samples are 151 top-selling drugs that have ever annual revenue of US $1 billion between 2015 to 2021 identified from the PharmaCompass database and their 1,167 patents listed in the FDA Orange Book. 151 top-selling drugs approved in US FDA from 1988 to 2020. When companies apply a new drug application in the USA, the company needs to submit relevant patents that can reasonably defend against generic drug infringement and list the patent application numbers in the US FDA Orange Book. Besides, we also collected detailed drug lifecycle information from the Orange Book and patentometric information from the USPTO database according to the patent application number listed in the Orange Book. This study uses each new drug's patents listed in the Orange Book, and through the patent holder's information, explores the participant composition in each new drug's R&D process to define the innovation patterns of each new drug. We also compare the innovation patterns' proportions across different drug types. Finally, by utilizing information like the drug's approval date and patent application date, we analyze the differences in patent application scale and patent activity periods across different innovation patterns throughout the drug lifecycle. The results show four innovation patterns. 21.85% of drugs are closed innovation, and the others are open innovation (OI) patterns—30.46% contract, 32.45% coopetition, and 15.23% network open innovation (OI). The top-selling drugs in the general anti-infective disease category have significantly tended to adopt network OI compared to the proportion of antineoplastic and immunomodulating agents and nervous system disease. Besides, from the comparison of patent strategies among the four innovation patterns, the results show that the contract OI drugs have smaller patent scale and shorter patent active period, while on the contrary, network OI drugs have larger patent scale and longer patent active periods. The results provide the pharmaceutical industry with insights into how to use internal and external innovation to find a more efficient and effective R&D management process, diversify a product portfolio to reduce R&D costs, and improve productivity in drug development. Additionally, the study examines the types of patent strategies used to protect drugs under each innovation model.

Introduction

In response to the growing volume and diversity of innovation research in the pharmaceutical industry, Romasanta, van der Sijde, and van Muijlwijk-Koezen (2020) conducted a comprehensive analysis of research topics within innovation

management in the pharmaceutical sector. By employing textual and citation-based clustering analysis on publications from leading innovation management journals, they identified key thematic areas shaping the field. Their findings indicate that strategic alliances have emerged as the most rapidly expanding research focus over the past decade, both in terms of scholarly output and its impact, as measured by citation frequency. Keywords associated with this theme, such as "alliance," "partner," "experience," and "collaborate," underscore the sector's increasing emphasis on cooperative research and development (R&D) initiatives.

The drug discovery and development process is inherently complex, resource-intensive, and time-consuming, requiring a delicate balance between efficacy, safety, regulatory compliance, and commercial viability. Given the substantial financial and operational risks involved, the traditional closed innovation model—where a single firm independently drives pharmaceutical R&D—has increasingly been supplanted by open innovation strategies. This paradigm shift has led to the proliferation of external collaboration mechanisms, including the establishment of dedicated R&D centers, technology licensing agreements, mergers and acquisitions (M&A), and strategic partnerships with competitors and academic institutions (Wellenreuther, Keppler, Mumberg, Ziegelbauer, & Lessl, 2012; Dong & McCarthy, 2019). These collaborative approaches enable firms to leverage complementary expertise, mitigate research risks, and enhance their pharmaceutical product pipelines.

Therefore, many articles within the strategic alliance literature analyze each stage of the alliance, from initiation to management and performance evaluation, while also exploring the factors contributing to its success (Romasanta et al., 2020). However, in the pharmaceutical industry, the product lifecycle of each drug, from R&D exploration, clinical trials, to market launch, can span more than ten years. The information about collaborators or collaboration models through the drug lifecycle may not always be publicly available information. As a result, the research method on pharmaceutical R&D collaboration alliances primarily consists of literature reviews discussing the types of collaborative alliances, case studies examining the management of the collaboration process, or constructing R&D cooperation networks based on publicly available web news. There has been little practical data to verify the innovation performance in the collaboration alliances.

Given that patents offer strong appropriability, we use top-selling drugs with annual revenue of US $1 billion in the U.S. pharmaceutical industry to study the types of R&D innovation patterns of successful drugs based on patentometrics. In the U.S., the Waxman-Hatch Act requires the listing of patents related to each approved New Drug Application in the "Orange Book," including the NDA number, product number, active ingredient(s), trade name, and expiration dates and codes associated with each patent. We can collect patent protection timelines throughout the drug lifecycle of each drug. From a patentometric perspective, we integrate three sources of pharmaceutical data: annual revenue of top-selling drugs (PharmaCompass database), the drug lifecycle information for each drug (FDA Orange Book), and detailed patent information (USPTO). We construct the lifecycles of 151 blockbuster drugs and their patent application timelines and patent applicants. Through a systematic and structural investigation of how pharmaceutical R&D collaboration

works between universities and companies, this research aims to help fill this knowledge gap and provide insights that could enable practitioners to improve the effectiveness of pharmaceutical R&D.

In addition, in the pharmaceutical industry's drug innovation process, different participants possess varying expertise, such as universities engaged in basic research, small companies involved in early drug discovery, and large pharmaceutical companies responsible for late-stage drug development and marketing (Bianchi, Cavaliere, Chiaroni, Frattini, & Chiesa, 2011; Stuart, Ozdemir, & Ding, 2007). Some scholars have explored the driving factors like partner selection from small biotechnology startups or large pharmaceutical companies (Diestre & Rajagopalan, 2012; Mason & Drakeman, 2014). Therefore, this study not only distinguishes the R&D types of new drug development but also explores open innovation R&D models. It examines whether high-profit drug holders get involved in drug R&D process during the research discovery, clinical trial, or market launch phases or if they remain uninvolved in the R&D process and act purely as marketers of the drug. Finally, we also want to study how successful drugs file patents to protect market exclusivity. Different types of R&D innovation patterns exist in the pharmaceutical industry, providing the opportunity to examine how patent protection behavior and time to market differ between closed innovation and open innovation. When drug developers use external knowledge through technology licensing, M&A, and cooperation with competitors or universities, what is the difference in the patent protection strategies among them?

Reference review: R&D innovation patterns in the pharmaceutical industry

Table 1. Comparison of R&D innovation Pattern from reference review.

Author(s)	*Pattern & Definitions*
Felina, E., & Zenger, T.R. (2014)	**Closed Innovation**: Internal innovation processes relying on own resources (e.g. Authority-based, Hierarchy, Consensus-based hierarchy). **Open Innovation**: External innovation processes collaborating with outside parties. (e.g. Markets/Contracts, Partnerships/alliances, Contests/tournaments, Users/communities)
Jackie Hunter and Susie Stephens (2010)	**Closed Innovation:** a model in which firms generate, develop, and commercialize ideas using solely internal resources, maintaining a vertically integrated structure that ensures full control over intellectual property (IP). **Open Innovation:** a paradigm that integrating both internal and external knowledge sources to enhance new product development, foster collaborations with external entities, and enable the commercialization of internal ideas beyond the originating firm.
David Cavalla (2003)	**Contracts:** formalized agreements established to secure external resources necessary for completing specific developmental tasks that cannot be sufficiently addressed internally. These contracts

	emphasize efficient resource allocation and risk mitigation, with compensation typically tied to the completion of designated work, while maintaining minimal dependence on external technology. **Collaborations:** strategic alliances designed to integrate external technologies into an organization's internal discovery processes, thereby enhancing research productivity. **Licensing:** comprehensive agreements that provide access to external products or, in some cases, technologies, to bolster an organization's development pipeline.
Liangsu Wang et al. (2015)	**Traditional Pharma-Academic Partnership:** firms provide financial support to academic researchers in exchange for research outcomes, fostering a structured collaboration aimed at advancing scientific knowledge and achieving specific research objectives. **Open Crowdsourcing:** firms utilize crowdsourcing platforms to seek innovative ideas and solutions from external scientific communities. **Academic Centers of Excellence:** collaborations between pharmaceutical firms and academic institutions, often facilitated by co-located scientists, aim to bridge the gap between academic research and industrial application. **Biotech Co-Creation:** pharmaceutical companies engage with biotech start-ups, pooling resources and expertise to co-develop innovative biotechnological solutions. **Pharmaceutical Peer Risk Sharing:** collaborative ventures between pharmaceutical companies to jointly develop clinical candidates, sharing financial and operational risks in drug development. **Innovation Centers:** pharmaceutical companies establish innovation hubs in key biomedical regions to foster collaborative research, development, and commercialization.
Yeolan Lee et al. (2019)	**Crowdsourcing Open Innovation (OI):** organizations engage in outsourcing problem-solving tasks to leverage collective intelligence to gather novel ideas, solutions, or knowledge, which are then integrated into New Product Development (NPD) processes. **Coopetition Open Innovation (OI):** by sharing resources, expertise, and capabilities across various stages of the NPD or value chain functions, organizations can address complex challenges, overcome limitations, and enhance innovation outcomes. **Science-Based Open Innovation (OI):** companies partner with research institutions such as universities and government laboratories to gain access to cutting-edge scientific knowledge.

	Network Open Innovation (OI): organizations collaborate within networks or consortia to tackle highly complex and interdependent problems. By combining diverse expertise and coordinating efforts across multiple entities.
Alexander Schuhmacher et al. (2022)	**Traditional R&D:** firms primarily rely on internal R&D while selectively incorporating external knowledge through M&A, in-licensing, corporate venture (CV) funds, and collaborations with academia or industry partners. External innovation is limited to portfolio complementation. **Network-Based R&D:** firms expand on traditional R&D by regularly engaging in long-term OI collaborations with multiple partners. **Ecosystem-Enabled R&D:** firms go beyond network-based R&D by leveraging diverse OI processes to acquire technologies and knowledge from multiple sources. They strategically build an open R&D ecosystem, integrating a large number of external contributors.

US FDA orange book and patent linkage system

The Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Act, was enacted in 1984 with the objective of increasing the availability of cost-effective generic drugs to consumers, thereby reducing overall expenditures for U.S. consumers and the healthcare system. Simultaneously, the patent term extension provision within the Act incentivizes brand-name pharmaceutical manufacturers to continue investing in new drug research and development (R&D) by compensating for the regulatory approval timeframe. The Hatch-Waxman Act comprises several key provisions, including the exemption allowing generic drug testing, market exclusivity protections, extensions of patent terms, a streamlined approval process for new drugs, and patent linkage, with the latter being the most intricate and debated aspect. Under the patent linkage framework, the U.S. Food and Drug Administration (FDA) is responsible for compiling and publicly disclosing patent data associated with approved pharmaceutical products, which is recorded in the Approved Drug Products with Therapeutic Equivalence Evaluations, widely recognized as the "Orange Book." When submitting a New Drug Application (NDA) for approval, the applicant must provide not only comprehensive scientific evidence and clinical trial results demonstrating the drug's safety and efficacy but also patent documentation that may serve as a legal basis for preventing generic market entry. This ensures that the FDA includes the listed patents in the Orange Book, allowing for a structured approach to patent enforcement.

Additionally, the Hatch-Waxman Act stipulates that when a generic drug manufacturer submits an Abbreviated New Drug Application (ANDA), it must include one of four specified certifications: (1) Paragraph I, asserting that no relevant patents are recorded in the Orange Book; (2) Paragraph II, indicating that while relevant patents are listed, they have already expired; (3) Paragraph III,

acknowledging the existence of relevant patents but committing to launch the generic drug only after patent expiration; and (4) Paragraph IV, challenging the validity of a listed patent or asserting that the generic drug will not infringe upon it.

The most robust form of patent protection is granted to patents covering the composition of matter, which primarily safeguard the active pharmaceutical ingredient (API) in the drug, followed by patents on novel formulations and drug delivery mechanisms. However, because composition of matter inventions and patent filings for API and original formulations typically occur at the early stages of the drug development cycle, the remaining patent term once the drug reaches the market is often limited, given the extensive time and financial resources required for clinical development and regulatory approval.

The effectiveness of composition of matter patents in protecting repositioned drugs largely depends on whether generic alternatives can be utilized through off-label use to achieve the same therapeutic outcome. In contrast, method of use patents, which cover specific indications or dosing regimens, are often regarded as incremental protections that do not provide the same level of market exclusivity as composition of matter patents. To prolong exclusivity and mitigate the impact of generic competition, pharmaceutical companies continuously invest in R&D throughout the drug lifecycle, securing additional product and method of use patents for the active molecule, thereby reinforcing a comprehensive patent protection strategy.

This study utilizes two primary indicators to evaluate the patent strategies of high-revenue pharmaceuticals: (1) patent scale, denoting the total number of patents registered in the Orange Book, and (2) patent active period, representing the temporal span between the earliest and most recent patent filings within a drug's patent portfolio. However, this analysis does not delve into the specific classifications of patents within each drug's portfolio, such as drug substance patents, product patents, or use patents.

Research Process: identify R&D innovation patterns and their patent protection behavior

This study 151 top-selling drugs with sales of more than one billion US dollars from 2015 to 2021. To search on Drugs@FDA to obtain data such as NDA number, Trade name, Active ingredient, NDA Applicant, IND filing date, NDA approval date, and patent-related information. Then use the Patent number to the USPTO Patent Public Search to search for the Patent applicant and Patent priority date, and integrate the search results into the variables of this study.

Step 1. Collecting patent data

Although the Orange Book offers patent information on each blockbuster drug, it does not contain detailed information on the patents, specifically whether those patents were internally developed by focal organizations or externally sourced. Detailed information on patents is collected from the United States Patent and Trademark Office (USPTO).

Step 2. Identifying R&D innovation patterns

The time and cost risks associated with drugs are very high. Considering the cost risk, in the new drug development process of drugs, in addition to independent research and development, open innovation will also be adopted, such as the establishment of R&D centers, technology licensing, mergers and acquisitions, and cooperation. Innovation and open innovation (OI) to increase the company's pharmaceutical product portfolio. In this study, the research models include closed innovation, contract open innovation, coopetition open innovation, and network open innovation. Open vs. closed innovation choice based on the use of internal or external knowledge in pharmaceutical drug development projects. If drug patents originated from the drug developer they were an internal knowledge source. If drug patents originated from external entities, they were an external knowledge source.

We identified three types of open innovation- contract, coopetition, and network. Biopharmaceutical companies are under immense pressure to improve their R&D productivity. In response, they have increased their portion of outsourced R&D spending on contract research services such as drug discovery, preclinical and clinical activities, or throughout an M&A deal to achieve lower costs, improve speed and flexibility, and minimize risks of new drug development. We called them the Contract OI meaning that the drug developer adopts external knowledge sources completely. Coopetition OI is defined as OI created between firms in the same industry. Coopetition OI can occur between competing firms over different value chain functions or different phases of new product development. Network OI is defined as collaborations between firms and external research organizations including universities, government labs, and other research institutes. External research organizations aim at developing pharma-related knowledge, meanwhile, companies invest in discovering potential scientific collaborators, gaining fundamental scientific knowledge, and turning this into an economic and societal benefit by developing and marketing new drugs (Bekkers & Freitas, 2008; Huang & Chen, 2017). For example, Gleevec was developed between 1987 and 1990 by a team of scientists at Ciba-Geigy in partnership with two researchers at the Dana-Farber Cancer Institute. It is used to treat chronic myelogenous leukemia and was promoted for use by oncologist Brian Druker of Oregon Health & Science University (Druker, 2008; Buchdunger & Zimmerman, 2013). After that, Ciba-Geigy also merged with Sandoz in 1996 to become Novartis, So Gleevec was owned by Novartis and has been registered for a total of 5 patents in the Orange Book. Patent applicants include companies and academic research institutions, such as Novartis, Ciba-Geigy, Dana-Farber Cancer Institute, and Oregon Health & Science University.

Table 2. Definition the closed and open innovation patterns.

		Whether the patent applicant (Drug Patent Holder) is the same as the drug applicant (NDA Applicant)	
		Same (Closed Innovation)	*Different (Open Innovation)*
Patent knowledge Source (patent applicant)	*Internal (I_R&D)*	Closed Innovation	-
	External (E_R&D)	-	Contract Open Innovation Coopetition Open Innovation Network Open Innovation

Step 3. Comparison of therapeutic market classes and patent protection behavior among the different R&D innovation patterns

The patent protection behavior contains four indicators and their definition are as follows. Patent scales are the total number of patents throughout the drug lifecycle; No. of patents before /after NDA is the total number of patents the application date before or after the new drug approved marketing date; the Patent active period is the years between the latest filing date and earliest filing date for patent application. Therapeutic market classes include ten therapeutic market areas-alimentary tract and metabolism (A), blood and blood-forming organs (B), cardiovascular system (C), genito-urinary system and sex hormones (G), systemic hormonal preparations, excluding sex hormones and insulins (H), general anti-infectives for systemic use (J), antineoplastic and immunomodulating agents (L), nervous system (N), respiratory system (R) and others.

The trends of top-selling drugs adopted innovation patterns

Our analysis of the 151 top-selling drugs in the sample revealed that 118 drugs (78.14%) were developed through open innovation (OI) projects, while 33 drugs (21.86%) were developed using closed innovation approaches. Within the OI projects, 30.46% of the drugs were associated with contract open innovation, 32.45% with coopetition, and 15.23% with network open innovation. The data indicates that collaborations between pharmaceutical companies or between pharmaceutical and biotechnology companies are the most prevalent forms of OI models in this sector, with coopetition OI being the dominant model.

OI may take the shape of networks, ecosystems, or consortia, where multiple entities contribute to new product development (Vanhaverbeke & Cloodt, 2006). According to Nambisan & Sawhney (2011), network OI is distinguished by the coordination processes required among multiple organizations within the network, which are necessary to manage the increasing complexity of technological advancements (Vanhaverbeke & Cloodt, 2006). Furthermore, Ritter & Gemunden (2003) assert that network OI is particularly effective in addressing challenges associated with the

intricacies of interconnected technologies. Consequently, network OI represents a relatively smaller proportion of the OI models within the pharmaceutical industry.

Table 3. Definition and example of four R&D innovation patterns.

Research Models (RMs)	*%*	*Drug name*	*NDA Applicant*	*Total patents*	*Innovation Source*	*Drug Patent Holder(s)*[*]
Closed Innovation (1)	21.85	Imbruvica	Pharmacyclics	40	I_R&D	Pharmacyclics
		Jakafi	Incyte	9	I_R&D	Incyte
		Kalydeco	Vertex	11	I_R&D	Vertex
Contract Open Innovation (2)	30.46	Linzess	Allergan	12	E_R&D	Ironwood; Microbia; Ironwood, Forest Laboratories
		Myrbetriq	Apgdi	10	E_R&D	Astellas; Yamanouchi
		Vyvanse	Takeda	18	E_R&D	New River; Shire
Coopetition Open Innovation (3)	32.45	Farxiga	AstraZeneca	37	I_R&D	AstraZeneca
					E_R&D	Alkermes; Amylin; Alkermes, Amylin; Amylin, AstraZeneca; Bristol Myers Squibb; Mitsubishi Electric; TecPharma Licensing
Network Open Innovation (4)	15.23	Genvoya	Gilead	16	I_R&D	Gilead
					E_R&D	Emory University; Japan Tobacco; Brother Kogyo Kabushiki Kaisha
		Gleevec	Novartis	5	I_R&D	Novartis
					E_R&D	Ciba-Geigy; Novartis, Dana-Farber Cancer Institute, Oregon Health & Science University

[*] Comma indicates that there are multiple applicants for the same patent; Semicolon indicates that the patent is from different applicants.

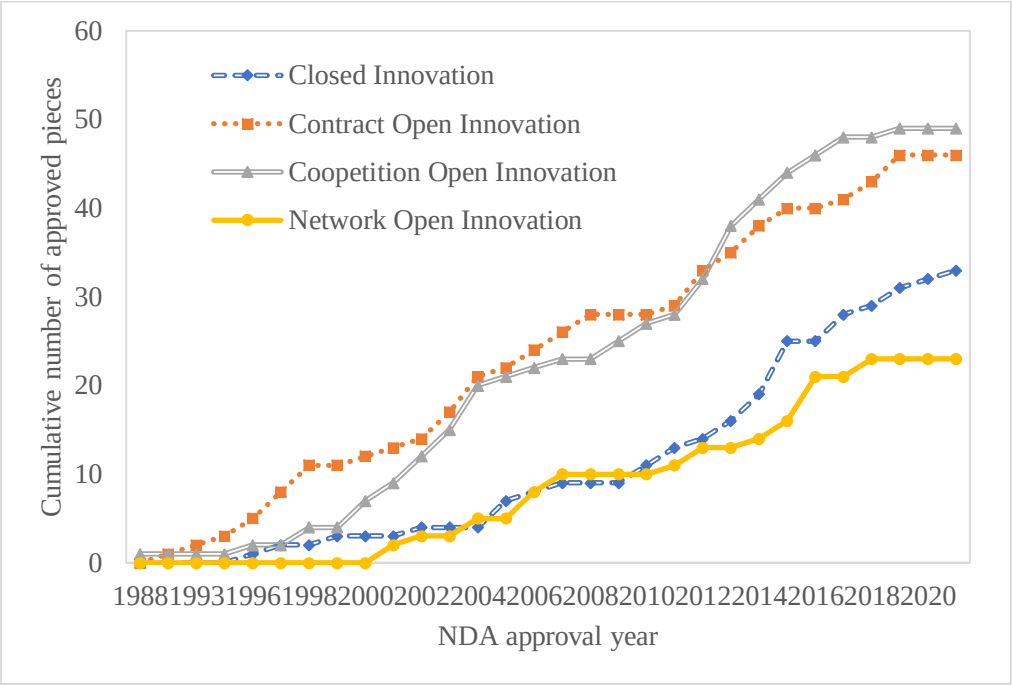

Figure 1. NDA approval cumulative trends of four innovation patterns.

In Table 4 the examination of research and development (R&D) innovation patterns across various Anatomical Therapeutic Chemical (ATC) classifications reveals that the first three categories—Closed Innovation, Contract Open Innovation, and Coopetition Open Innovation—demonstrate relatively consistent adoption rates across different ATC classifications. This uniformity is corroborated by statistical analysis, which shows no significant differences, suggesting that the disease types associated with new drug development within these three categories do not exhibit notable variation in their adoption of R&D innovation patterns.

Specifically, the association between the percentage distribution of Anatomical Therapeutic Chemical (ATC) codes and the network open-innovation model was found to be statistically significant, $\chi^2(27, N = 151) = 56.342$, $p = .001$. Subsequent comparisons of the proportions of ATC codes at the network open-innovation stage, utilizing z-tests, revealed that the proportion of General anti-infectives for systemic use (ATC code J) was significantly higher than that of Antineoplastic and immunomodulating agents (ATC code L) (46.7% vs. 9.8%, respectively) and Nervous system (ATC code N) (46.7% vs. 0.0%, respectively) at the $p < .05$ level.

Table 4. Comparison of drug R&D innovation patterns among therapeutic classes (TC).

TC codes / *R&D models*		*A*	*B*	*C*	*G*	*H*	*J*	*L*	*N*	*R*	*others*	*Total*	*Post-hoc*
(1)	Count	5_a	4_a	1_a	0_a	1_a	1_a	12_a	4_a	4_a	1_a	33	-
	% of RMs	15.2	12.1	3.0	0.0	3.0	3.0	36.4	12.1	12.1	3.0	100	
	% of TC	38.5	44.4	9.1	0.0	25.0	3.3	29.3	21.1	36.4	16.7	21.9	
	% of total	3.3	2.6	0.7	0.0	0.7	0.7	7.9	2.6	2.6	0.7	21.9	
(2)	Count	1_a	3_a	5_a	5_a	1_a	6_a	13_a	8_a	2_a	2_a	46	-
	% of RMs	2.2	6.5	10.9	10.9	2.2	13.0	28.3	17.4	4.3	4.3	100	
	% of TCs	7.7	33.3	45.5	71.4	25.0	20.0	31.7	42.1	18.2	33.3	30.5	
	% of total	0.7	2.0	3.3	3.3	0.7	4.0	8.6	5.3	1.3	1.3	30.5	
(3)	Count	4_a	2_a	5_a	2_a	2_a	9_a	12_a	7_a	5_a	1_a	49	-
	% of RMs	8.2	4.1	10.2	4.1	4.1	18.4	24.5	14.3	10.2	2.0	100	
	% of TCs	30.8	22.2	45.5	28.6	50.0	30.0	29.3	36.8	45.5	16.7	32.5	
	% of total	2.6	1.3	3.3	1.3	1.3	6.0	7.9	4.6	3.3	0.7	32.5	
(4)	Count	$3_{a, b}$	$0_{a, b}$	$0_{a, b}$	$0_{a, b}$	$0_{a, b}$	**14_b**	**4_a**	**0_a**	$0_{a, b}$	$2_{a, b}$	23	J>L,N
	% of RMs	13.0	0.0	0.0	0.0	0.0	**60.9**	**17.4**	**0.0**	0.0	8.7	100	
	% of TCs	23.1	0.0	0.0	0.0	0.0	**46.7**	**9.8**	**0.0**	0.0	33.3	15.2	
	% of total	2.0	0.0	0.0	0.0	0.0	9.3	2.6	0.0	0.0	1.3	15.2	
Total	Count	13	9	11	7	4	30	41	19	11	6	151	
	% of RMs	8.6	6.0	7.3	4.6	2.6	19.9	27.2	12.6	7.3	4.0	100	
	% of TCs	100	100	100	100	100	100	100	100	100	100	100	
	% of total	8.6	6.0	7.3	4.6	2.6	19.9	27.2	12.6	7.3	4.0	100	

Note: A: Alimentary tract and metabolism; B: Blood and blood forming organs; C: Cardiovascular system; G: Genito-urinary system and sex hormones; H: Systemic hormonal preparations, excluding sex hormones and insulins; J: General anti-infectives for systemic use; L: Antineoplastic and immunomodulating agents; N: Nervous system; R: Respiratory system.

Comparison of patent application strategy among the different innovation patterns

In Table 5 and 6, the coopetition and network open innovation (OI) models demonstrate the highest number of patents and the longest patent active periods throughout the drug development lifecycle, surpassing the contract open innovation (OI) model. While the contract OI model exhibits the fewest patents, it is characterized by the shortest R&D time required to bring a drug to market. This study reveals that the four R&D innovation patterns possess distinct characteristics, providing pharmaceutical companies with a range of strategic options to develop their product portfolios. Patents serve a critical role in governing the interactions between various stakeholders in open innovation, particularly by defining and safeguarding technological innovations, such as when large firms acquire startups. In the pharmaceutical industry, where R&D investments are substantial and development timelines are extended, patents are crucial for recouping R&D expenditures, leading to a high propensity for patenting (Arundel, 2001). Small, technology-based firms, often constrained by limited financial resources (Storey & Tether, 1998), tend to prioritize patent filings at later stages, if at all, to minimize costs, which contributes to the smaller patent scale and shorter patent active period observed in the contract OI model.

Table 5. Profile of patent application strategy among four innovation patterns based on ANOVA analysis.

RMs	*No. of patents (N=151)*							
	N	*Mean*	*SD*	*F-value*	*Significance or difference (Dunnett T3-test, p-values)*			*Post-hoc*
					(2)	*(3)*	*(4)*	
(1)	33	11.00	9.57	9.370/5.417 [a]	0.018	1.000	1.000	1,3,4>2
(2)	46	5.61	4.48	(0.000/0.002)		0.007	0.001	
(3)	49	10.41	8.81				0.998	
(4)	23	11.13	5.19					

[a] Welch/Brown-Forsythe, asymptotically F distributed. ** $p<0.05$; *** $p<0.001$.

Table 6. Profile of patent application strategy among four innovation patterns based on ANOVA analysis.

RMs	*Patent active period (N=151)*							
	N	*Mean*	*SD*	*F-value*	*Significance or difference (Scheffé-test, p-values)*			*Post-hoc*
					(2)	*(3)*	*(4)*	
(1)	33	13.35	5.10	12.147	0.108	0.228	0.074	3,4>2
(2)	46	9.70	6.37	(0.000)		0.000	0.000	
(3)	49	16.38	7.24				0.805	
(4)	23	17.99	6.42					

** $p<0.05$; *** $p<0.001$.

Conclusion

The rising pharmaceutical costs and sharply declining R&D productivity have prompted the pharmaceutical industry to seek external innovation models in the hope of producing breakthroughs in the R&D process to reduce R&D costs and improve productivity in drug development. The results in this study provide a reference for pharmaceutical companies to adopt these R&D innovation models, a comparison of patent scale at different life cycle stages, and patent active period among them to get more efficient and effective R&D management process and diversify a product portfolio in drug development.

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