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From Basic Research to Competitiveness: An Econometric Analysis of the Global Pharmaceutical Sector

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Abstract: The pharmaceutical sector is a flagship of the economy in most developed countries and is one of the most research-intensive sectors of modern economies. The aim of this paper was to determine the mutual relationships between the research and development (R&D) resources, various indicators of scientific performance and the competitiveness of the sector. We carried out a cointegration analysis of a time series of R+D resources, the number of academic papers published, as well as patents and the competitiveness of this sector in various developed states. The econometric analysis of time series is built on panel cointegration models. Based on the combination of different comprehensive and coherent international databases and applying the latest methods of modern time series analysis, the paper proves that, in most developed countries, a direct, significant, causal, lagged relationship between the monetary resources allocated to R&D and the number of academic papers, as well as the number of patents can be observed. In most cases, a causal relationship can be demonstrated between the number of academic papers and patents, but vice versa, this fact is not provable. This study highlights the complexity of innovation systems in the pharmaceutical sector. The results prove only a weak connection between the number of patents and the number of publications. When evaluating the efficiency of the utilisation of resources allocated to pharmaceutical R+D, the effect of the time lag should be considered.

Keywords: competitiveness; economic policy; international statistics; time series analysis; pharmaceutical sector

1. Introduction

The pharmaceutical industry is an elementary precondition in the realisation of sustainable development goals of the United Nations, [1,2]. The complex relation between UN Sustainable development goals [3] and innovative development of the pharmaceutical sector can be summarised as follows.

Development of new and cheaper drugs [4] is a necessary precondition for maintaining the health, motivation and capacities of the population, contributing to the reduction of poverty, which is a basic

development goal. The production of nutraceuticals and functional food [5] is important to achieve zero hunger as a development goal. Innovative products [6] contribute to gender equality. New technologies [7,8] are vital for water and energy conservation. Efforts to enhance the affordability of pharmaceuticals [9] contribute to the reduction of inequalities. The increasing significance of the "green chemistry" approach [10–12] in the pharmaceutical industry is a direct contribution to the decreasing carbon footprint [13], responsible production and consumption, and mitigation of climate change. The introduction of biodegradable materials [14] and other environmentally sustainable packages [15,16] help to preserve lifeforms that exist both below the water and on land. As a summary, it can be stated that the development of the pharmaceutical industry is a key factor to achieve the sustainable development goals of the UN [17].

The pharmaceutical industry can be characterised as a knowledge-intensive one. That is why it lends itself as an example for the analysis of the interrelations between financial resources allocated for research and development, intellectual outputs (patents and publications) and competitiveness. The goal of the current paper is an econometric analysis of these interrelations. There is an abundance of literature on the analysis of some aspects of the interrelations of the above factors, but to the best of our knowledge, the current study is the first attempt (1) to analyse all of these aspects simultaneously, (2) based on a relatively large number of countries, and a long range of time series, and (3) which applies the latest methods of econometric research.

2. Literature Review

Innovation is a key determinant of market success [4–8] and an important tool for increasing the competitiveness of companies as well as regions [9,10]. In addition, it has also been claimed that the emphasis on social components in the general mainstream of enterprise innovation activity is one of the strongest reasons for its successful functioning and development [11,12]. There is a considerable debate on measuring the efficiency of monetary resource allocation on research and development (RD) [13–15]. Table 1 offers an overview of the most important articles on this topic, showing the historic development of the analysis of this problem. During the last few decades, there has been an unprecedented investment in pharmaceutical research and development [16–18], partly as a consequence of the aging of the population [19]. Hence, understanding the economic effects of research is especially important for the pharmaceutical sector [20]. The application of traditional R&D models to the modern pharmaceutical industry is highly controversial [21], and there is an intense search for more efficient models and methods of R&D in the industry. The results of Achilladelis and Antonakis [22] have shown a statistically significant positive relationship between originality and commercial success in the pharmaceutical industry. Pharmaceutical product development is a very high-cost activity [23]. The seminal paper by [24] has proven that the pre-tax average cost of new drug development from out-of-pocket costs to the point of marketing approval was more than USD 230 million in 1987. According to the latest estimations by DiMasi et al. [24], the pre-tax direct ("out-of-pocket") cost for approval of a new drug is USD 1.395 billion, with the total R&D costs in the pre-and post-approval period being USD 2.87 billion. According to official data from the World Bank, the USD inflation was 214% between 1987 and 2015. That is why it can be stated that new drug development costs have increased by nearly 500% in real terms in the last three decades. At first sight, the efficiency of corporate innovation can be directly measured by the effects on stock-prices; however, this is somewhat indirect evidence [25,26].

The results of Chen and Chang [27] highlight a direct relationship between patent counts and a firm's market value in the pharmaceutical sector. Similar results have been obtained by Chang et al. [28], as well as Korsakienė et al. [23] and Kliestik et al. [29].

In the opinion of numerous specialists, there is an inherent conflict between profit-oriented and academic (publication-oriented) research [30,31]. This is manifested in the suppression or delay of the publication of results [32–36]. At the same time, Geuna and Nesta [37] highlight that publication and patent go hand in hand in the academic world. According to Agrawal and Henderson,

patenting may play a relatively small role in transferring academic knowledge. In an early publication, analysing the patenting and publication behaviour of scientists working at large American companies, Halperin and Chakrabarti [38] proved a positive correlation between publication and patenting activity. They highlight that capital-intensive sectors (e.g., pharmaceuticals) can be characterised by a high level of publications, patents, and elite scientists. According to analysis by Massachusetts Institute of Technology (MIT), there is a negative correlation between patenting and publishing activities. At the same time, results prove a positive correlation between the patenting and publication activity of German professors [39]. A similar result has been reported by Wong and Singh on the basis of statistical analysis of patents and the scientific papers of world-leading universities. Based on a wide-range literature survey, Bekelman et al. [40] have proven that biomedical research is heavily influenced by industry. This is why conflicts of interest arising from close industry–academia relations influence biomedical research. As a summary, it can be stated that the current literature is highly controversial on the evaluation of relationships between financial resources, academic publications, patents and competitiveness. The pharmaceutical sector is an important aspect of modern, developed economies and is of strategic importance [40–42], making its competitiveness a crucial factor.

Table 1. Some results of the application of econometric models to determine economic effects of R&D.

Source	Method	Results
Coe and Moghadam [43]	Aggregate production function for a 20-year period of the economic development of France.	Government infrastructure, business sector capital, residential capital and research and development capital have a significant influence on aggregate production function.
Coe and Helpman [44]	21 Organisation for Economic Co-operation and Development (OECD) countries and Israel, economic data from 1971-1990.	Foreign R&D has a positive effect on domestic factor productivity, but this depends on the openness of the economy. High rates of return of R&D in domestic output and international spillovers.
Thirtle et al. [45]	Ten EU countries and the USA, agriculture, cointegration.	Total Factor Productivity (TFP) calculations, returns to R&D are seriously biased if spillovers are ignored.
Funk [46]	Trade patterns and international spillovers of OECD countries and Kao et al. [47] panel cointegration model.	There is no significant relationship between import patterns and R&D spillovers, exporters receive significant R&D spillover from customers.
Edmond [48]	Pedroni's test for panel cointegration to determine the coefficients, estimated in Coe and Helpman [44] model.	Cointegration coefficients are less robust when more heterogeneity is allowed; the elasticity coefficient of productivity on foreign R&D is unstable.
del Barrio-Castro et al. [49]	OECD database.	Average years of schooling influence the effect of international R&D.
Gutierrez and Gutierrez [50]	Panel data on TPF productivity from 47 countries in a 32-year period.	TFP is influenced by domestic and international R&D, a significant role of geographical location.
Liu [51]	Cointegration analysis on R&D input intensity and independent innovation ability of Chinese enterprises on the basis of enterprise-level data from between 1991 and 2003.	Bi-directional mutual relationship and stable long-term equilibrium between R&D intensity and innovation.
Yoo [52]	Long- and short-run causality between public and private R&D expenditure in Korea.	Bi-directional causality between private and public R&D.
Bottazzi and Peri [53]	Employment in R&D and patent applications in OECD countries.	Knowledge spillovers are sufficiently strong to create long-run endogenous growth.
Coe and Helpman [44]	21 OECD countries and Israel, economic data from 1971–2004.	TFP, domestic and foreign R&D capital are cointegrated; human capital is cointegrated with Total Factor Productivity (TFP); considerable differences between countries.
Frantzen [54]	Panel cointegration test on the effect of domestic and foreign R&D on the productivity base of 22 manufacturing sectors of 14 OECD countries between 1972 and 1994.	Log of TFP and logs of domestic and foreign R&D are cointegrated. Dynamic Vector Autoregressive (VAR) model suggests that, in the majority of sectors, causation runs from the R&D are cointegrated. A dynamic VAR model suggests that, in the majority of sectors, causation runs from the R&D variables to TFP, a long-run causation in nature.

Table 1. *Cont.*

Source	Method	Results
Teixeira and Fortuna [55]	Portugal data from 1960 to 2001, cointegration.	Significant effect of human capital and R&D efforts on TFP.
Cho et al. [56]	Oil prices, energy consumption and R&D in EU countries, cointegration.	Significant role of R&D on renewable energy consumption.
Voutsinas and Tsamadias [57]	Greek economic data 1987–2007 to determine effect of public and private R&D on TFP.	A 1% increase in the total R&D capital increases TFP by 0.038%, whereas a 1% increase in the public R&D capital raises TFP by 0.075%.
Khan and Salim [58]	Australian country level data on R&D and TFP between 1953 and 2009.	Cointegration between R&D and productivity growth, unidirectional causality from R&D to TFP.
Sussex et al. [59]	Medical research costs in UK between 1982 and 2012.	A 1% increase in public sector expenditure is associated with a 0.81% increase in private sector expenditure.
Meyer and Meyer [60]	Brazil, Russia, India, China and South Africa (BRICS) data on relationships between economic growth, employment and established business ownership	Established business ownership is a significant predictor of employment

Source: Authors' own editing, 2019.

Consequently, it can be stated that all over the world there is an intense debate on mutual relationships among academic productivity (PUBL), intellectual property (PAT), R&D resources (RD) and competitiveness, measured by the Balassa index of revealed comparative advantages (RCA), trade specialisation index (TCP) and the Volrath index of competitive advantages (VRCA). The global pharmaceutical industry is a research-intensive, highly innovative sphere of the global economy, offering opportunities to study and understand the dynamics of these processes. The results of this analysis can be applied to the formation of R&D strategies in different countries.

3. Hypothesis Development

As a summary of the literature survey, it can be stated that there are considerable gaps in our knowledge of the relationships among finance, academic performance, patenting and competitiveness, as (1) the majority of previous research was based on panel time series, which necessarily contains a high level of data agglomeration.

This can be explained by a previous lack of time series which satisfied the minimal demands in terms of length for a reliable, country-level time series analysis (at least 20–23 years). (2) There are no sector-specific, internationally comparable results for pharmaceutical R&D and competitiveness analysis. Based on the results of previous research, four hypotheses have been developed.

These state that there is a positive, significant, time-lagged causative relationship between (H_1): financial resources allocated to R&D in the pharmaceutical industry and the academic performance (measured by number of publications) in pharmacy; (H_2): financial resources and the number of patents; (H_3): academic performance and the Balassa index of competitiveness; (H_4): the number of patents and the competitiveness of the sector; (H_5): academic performance (number of publications) and the number of patents; (H_6): the number of patents and academic performance; (H_7): material resources allocated to RD and the competitiveness of the sector. The system of the hypotheses of our paper is summarised in Figure 1.

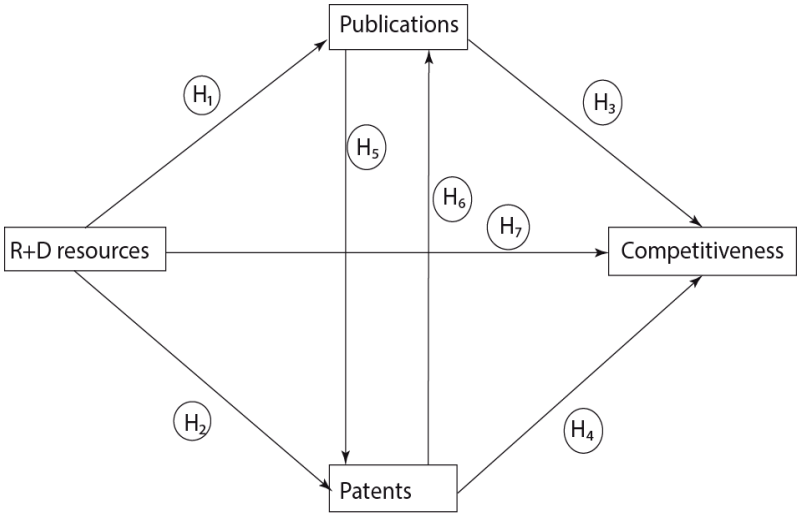

Figure 1. Conceptual model of research.Source: Authors' own research, 2019.

4. Methodology

4.1. Databases

The electronic database of the OECD served as the primary database of the research (OECD, 2016) for deriving R&D data and performance in the pharmaceutical industry in the states examined. The OECD consists of 34 countries, but there was a lack of data for detailed analysis in a considerable number of countries. This comprehensive website has a section dedicated to socio-economic data on OECD member states and numerous further important economic entities. The database has been built based on a wide range of national and international statistical data and contains comparable data in a transparent form [61,62]. Although most of the available time series embrace the period 1990–2013, in some cases, the time series are longer. Due to differences in national statistical systems, the time series are relatively sparse. The OECD database contains economic data on Current International Dollar, taking into consideration the differences in the purchasing power parity of national currencies [63]. To make the current prices comparable, we have recalculated the data to the 2011 USD value, based on the World Bank database [64]. Data on academic publications have been collected with the help of the Web of Science™ (hereinafter: WoS) system of the Institute for Scientific Information (ISI, now part of Thomson Reuters). There are some arguments for using its most important competitor, Scopus, of Reed Elsevier [15,65,66]; however, based on the number of papers and citations, largely independent of the field of science, an extremely high correlation between the "performance" of these two databases has been proven. The rigorous, systematic analysis of academic publications began only a few decades ago [67], but the publication and patent data can offer a longer time series.

We have applied the publication data starting from 1990, because (1) the other-economic-time series are shorter, and (2) as a consequence of the rapid proliferation of published papers, there has been a structural brake on the trend of statistics publications in the last few decades. The same is true for general publications. The structure of the data used for the analysis is presented in Table 2. Data were organised and manipulated on an Excel worksheet. Among the experts dealing with time series analysis, there is a considerable (but rather informal) debate on the necessary length of time series to apply for analysis. Granger, one of the "founding fathers" of modern time series analysis, remarks that the "most important macroeconomics series are rather short". That is why he would conduct a "post-sample" evaluation of time series and suggest the application of "cross-validation techniques"; however, he does not offer any sample size formula. We have applied the rule that time series must have at least 20 data registered to be selected as a basis for analysis.

Table 2. Structure of input data (countries with time series available for at least 20 years are indicated by black cells, however, time series that were too short have been excluded from the analysis indicated by white cells).

Countries	Pharm R&D	Pharm Export	Pharm Patents	Publications
Australia	X	X	X	X
Austria		X	X	X
Belgium	X	X	X	X
Canada		X	X	X
Chile			X	
Czech Republic	X	X	X	
Denmark		X	X	X
Estonia		X	X	
Finland		X	X	X
France	X	X	X	X
Germany	X	X	X	X
Greece	X	X	X	
Hungary	X	X	X	X
Iceland	X	X	X	
Ireland		X	X	
Israel	X	X	X	X
Italy	X	X	X	X
Japan		X	X	X
Korea	X	X	X	
Luxemburg		X	X	
Mexico	X	X	X	
Netherlands		X	X	X
New Zealand		X	X	
Norway	X	X	X	
Poland		X	X	
Portugal		X	X	
Slovak Republic			X	
Slovenia	X	X	X	
Spain	X	X	X	
Sweden	X	X	X	
Switzerland	X	X	X	
Turkey		X	X	
United Kingdom	X	X	X	
United States	X	X	X	

Source: Authors' own research, 2019.

4.2. Models Applied

This indicator is generally accepted and widely applied for analysis of the competitiveness of different sectors around the world (e.g., Freund and Pierola [68]). The original index of revealed comparative advantage:

$$RCA_{ij} = \frac{\frac{x_{ij}}{\Sigma x_j}}{\frac{x_j}{\Sigma x_j}},$$

where j is the exported product category, i is the economic entity (in most cases, a country) under investigation, Σx_i denotes the total export of country i, and Σx_j symbolises the total export of product j in the world. In the last few decades, various alternative measures have been proposed to modify the original index, although this form has remained the most popular [69]. To avoid any bias, we have determined the relative position of the pharmaceutical industry in states of investigation on the basis of the trade specialisation coefficient (TSC).

This coefficient is calculated as follows:

$$TSC = \frac{(x_{ij} - y_{ij})}{(x_{ij} + y_{ij})},$$

where x_{ij} is the export value of the product j in I country and y_{ij} is import of product j in country i. A higher TSC value indicates a higher level of export competitiveness of a given country, while a lower TSC value indicates a lower level of competitiveness [70]. This indicator has been applied for analysis of the Indian pharmaceutical sector by Mahajan et al. [71].

To obtain a clearer picture, we have determined the Vollrath index of relative trade advantage: this indicator is the difference between revealed competitive advantage in exports and imports [72]. It is well documented that a relatively short time span of data can decrease the power of individual unit root tests [73]; therefore, in the second part of this paper, the panel cointegration analysis method is applied to overcome this problem. The cointegration analysis of panel data consists of four steps: (1) test for a panel unit root; (2) test for cointegration data by employing the heterogeneous panel cointegration tests; (3) the long-run relationship is estimated for heterogeneous cointegrated panels; (4) once the panel cointegration is established, we establish a panel error correction model to examine short-run and long-run causalities between R&D resources, intellectual outputs and different indicators of competitiveness.

In this research, three types of panel unit root tests have been applied. The first one is the panel-based unit root test of Levin et al. [74], which allows for individual (in our case: country-specific) intercepts, and the degree of persistence in individual regression error and trend coefficients to vary across different entities. According to Ladu and Meleddu [75], this test is relevant for panels of moderate size, but in some cases, contemporaneous correlations cannot be removed by simple subtraction of cross-sectional averages. Another problem is that the assumption of the identity of entities with respect to the presence or absence of a unit root is restrictive. That is why we have cross-checked our results using the second test developed by Im et al. [76]. This approach is not as restrictive as the Levin–Lin–Chu test because it allows the heterogeneity of coefficients. The Fisher test is an application of augmented Dickey–Fuller and Phillips–Perron tests for panel data and "is widely recommended" according to literature survey of Maddala and Wu [77].

The panel cointegration has been analysed by Pedroni [78] and Kao et al. [47] using Fischer tests, as well as Fischer [79]. The Pedroni test allows for heterogeneity in the long-run cointegration vectors and in the dynamics associated with short-run deviation from long-range vectors among panel entities. This test system is based on asymptotic distributions of seven different statistics: four of them are based on pooling along the within-dimension (panel cointegration statistics) and three are built on pooling along the between-dimension (mean panel cointegration statistics). The results of Wagner and Hlouskova [80] show that the efficiency of the Pedroni test is relatively low in the case of small samples and short time series; therefore, we have cross-checked our results by Kao and Fischer tests.

The aim of the panel cointegration procedure is the identification of any long-run relationship between the investigated variables. If this relationship is proven, there is a possibility to determine long-range relations between different variables [81]. For this purpose, we have applied the Dumitrescu–Hurlin test of causality [82]. We have considered the model, including lagged dependent variables correlated with the error term. The Arellano and Bond [83] algorithm has been applied to determine the relations between different variables.

The short-run responses of variables on changes in the value of another variable has been tested by the Dumitrescu–Hurlin test of causality of [82], as well as an ordinal least square technique. The fixed-effect ordinary least squares (FE–OLS) model assumes that each entity (in this case, a country) is different, and individual heterogeneity can be characterized by an individual intercept. If the error terms are correlated, the random-effect model (RE–OLS) should be used Hoechle [84]. We have tested whether the fixed effect is preferred over the random effects based on the Hausman test [85]. The null hypothesis of this test is that the random effects model is appropriate (difference in coefficients is not systematic).

One of the basic concepts of our research is the causality between the investigated time series [86]. According to the classic definition of causality, "X is said to Granger-cause Y if Y can be better predicted using the histories of both X and Y than it can be by using the history of Y alone." The absence of

Granger causality has been tested by the following Vector Autoregression (VAR) model: (2) There are different methods of causality testing (e.g., Lütkepohl and Netšunajev [87]). In this analysis, we have applied the Toda–Yamamoto procedure [88], which allows us to derive robust conclusions. The level of integration of time series has been checked by an Augmented Dickey–Fuller test and Kwiatkowski–Phillips–Schmidt–Shin (KPSS) test algorithm using the Eviews 8.1 program package [89]. The lags have been determined on the basis of the Akaike Information Criterium. The competitive position of the pharmaceutical industries of various countries has been characterised on the basis of the revealed comparative advantage index, developed by Balassa [90].

The availability of data has been a limitation to our research from the aspects of the methods applied. In the case that more data is available for the four variables analysed, the panel cointegration approach could be applied, but under the current conditions, the simple method used offered more pieces of practically relevant information.

5. Results and Discussion

Panel unit root tests have been performed both on levels and first differences of the variables and both with constant and with constant and trend in Table 3.

Table 3. Results of Levin–Lin–Chu (LLC), Imm–Pesharan–Shinn (IPS), Individual Root Augmented Dickey–Fuller (ADF–Fisher) and Phillips–Person panel cointegration test (PP–Fisher) tests.

	Variables	LLC	IPS	ADF-Fischer Chi-Square	PP-Fischer Chi-Square
RD (level)	**Individual intercept**	−5.234 *** [0.000]	−1.544* [0.061]	49.333 [0.148]	84.399 *** [0.000]
	Individual intercept and trend	−2.695 *** [0.003]	−1.562 * [0.059]	66.904 *** [0.004]	149.502 *** [0.000]
	None	7.160 [1.000]		7.156 [1.000]	6.810 [1.000]
D(RD) (first difference)	**Individual intercept**	−18.925 *** [0.000]	−19.217 *** [0.000]	342.403 *** [0.000]	361.865 *** [0.000]
	Individual intercept and trend	−15.693 *** [0.000]	−18.439 *** [0.000]	333.197 *** [0.000]	638.538 *** [0.000]
	None	−18.571 *** [0.000]		374.320 *** [0.000]	448.052 *** [0.000]
PUBL (level)	**Individual intercept**	−3.061 [1.000]	0.112 [0.544]	54.506 * [0.062]	66.279 * [0.005]
	Individual intercept and trend	−2,870 *** [0.002]	−2.665 *** [0.004]	72.375 *** [0.001]	123.359 *** [0.000]
	None	−5.658 [1.000]		2.273 [1.000]	2.084 [1.000]
D(PUBL) (first difference)	**Individual intercept**	−2.695 *** [0.003]	22.810 *** [0.000]	405.735 *** [0.000]	615.071 *** [0.000]
	Individual intercept and trend	7.160 [1.000]	−20.744 *** [0.000]	390.392 *** [0.000]	480.876 *** [0.000]
	None	−18.925 *** [0.000]		505.227 *** [0.000]	615.071 *** [0.000]
PAT (level)	**Individual intercept**	−14.903 *** [0.000]	−11.680 *** [0.000]	209.145 *** [0.000]	260.677 *** [0.000]
	Individual intercept and trend	−3.065 *** [0.001]	−2.240 ** [0.012]	96.586 *** [0.000]	127.755 *** [0.000]
	None	3.602 [0.998]		19.257 [0.997]	33.986 [0.736]
D(PAT) (first difference)	**Individual intercept**	−10.599 *** [0.000]	−17.094 *** [0.000]	297.268 *** [0.000]	407.650 *** [0.000]
	Individual intercept and trend	−13.129 *** [0.000]	−23.971 *** [0.000]	524.793 *** [0.000]	2196.161 *** [0.000]
	None	−21.375 *** [0.000]		463.554 *** [0.000]	601.177 *** [0.000]
RCA (level)	**Individual intercept**	−9.789 *** [0.000]	−12.650 *** [0.000]	230.343 *** [0.000]	250.925 *** [0.000]
	Individual intercept and trend	−15.050 *** [0.000]	−13.905 *** [0.000]	237.923 *** [0.000]	288.850 *** [0.000]
	None	−2.232 ** [0.012]		233.120 *** [0.000]	262.656 *** [0.000]
D(RCA) (first difference)	**Individual intercept**	−37.299 *** [0.000]	−33.381 *** [0.000]	589.096 *** [0.000]	379.076 *** [0.000]
	Individual intercept and trend	−33.893 *** [0.000]	−31.705 *** [0.000]	598.819 *** [0.000]	4538.01 *** [0.000]
	None	−35.068 *** [0.000]		858.194 *** [0.000]	4366.23 *** [0.000]
TSC (level)	**Individual intercept**	−5.214 *** [0.000]	−4.060 *** [0.000]	95.287 *** [0.000]	132.095 *** [0.000]
	Individual intercept and trend	−0.446 [0.327]	-0.538 [0.295]	59.588 ** [0.023]	173.970 *** [0.000]
	None	3.969 *** [0.000]		109.026 **** [0.000]	115.136 *** [0.000]
D(TSC) (first difference)	**Individual intercept**	−18.533 *** [0.000]	−19.119 *** [0.000]	330.858 *** [0.000]	333.604 *** [0.000]
	Individual intercept and trend	−15.846 *** [0.000]	−19.541 *** [0.000]	390.267 *** [0.000]	904.160 *** [0.000]
	None	−23.366 *** [0.000]		507.458 *** [0.000]	759.408 *** [0.000]
VRCA	**Individual intercept**	−2.623 *** [0.004]	−2.536 *** [0.005]	66.398 *** [0.005]	83.500 *** [0.000]
	Individual intercept and trend	−5.116 *** [0.003]	−5.928 *** [0.000]	125.040 *** [0.000]	360.909 *** [0.000]
	None	1.198 [0.115]		51.183 [0.110]	61.339 ** [0.016]
D(VRCA)	**Individual intercept**	−25.151 *** [0.000]	−25.665 *** [0.000]	462.757 *** [0.000]	489.980 *** [0.000]
	Individual intercept and trend	−25.945 *** [0.000]	−29.320 *** [0.0000]	749.123 *** [0.0000]	2409.670 *** [0.000]
	None	−30.301 *** [0.000]		747.591 *** [0.000]	1137.38 *** [0.000]

Notes: denotes the P-value. *, **, and *** denote the significant level of 10%, 5%, and 1%, respectively. Source: Authors' own research, 2019.

As our results show, the variables are stationary time series of level data. Under these conditions, the traditional cointegration tests are not necessary, and we can skip the second step of the analysis.

The long-range relations between the investigated time series have been analysed by causality and regression analysis. The Dumitrescu–Hurlin test of panel data on causality indicates a strong, bidirectional relationship between the number of patents and publications in Table 4. The number of patents significantly influences the Balassa index and the Volrath index, but not the value of Trade Specialisation Coefficient (TSC). A possible explanation of this result is that rich countries have increased imports of medical products. Interestingly, there is a significant relationship between the trade specialization and the Volrath competitiveness index. The rising competitiveness index increases the R&D expenditures and the intellectual output. This can be explained by the fact that the increasing role of a given sector in the economy generates further propensity to invest into the research and development in the sector concerned.

Table 4. Results of the Dumitrescu–Hurlin panel causality test.

Hypothesis	W-Statistics	Z-bar Statistics	Probability
PAT→PUB	15.16	2.29	0.02
PAT→RCA	20.24	4.46	0.00
PAT→RD	10.86	0.45	0.65
PAT→TSC	11.56	0.75	0.45
PAT→VRCA	13.90	1.75	0.08
PUB→PAT	12.67	1.22	0.22
PUB→RCA	12.67	1.23	0.22
PUB→RD	8.90	−0.38	0.70
PUB→TSC	16.66	2.93	0.00
PUB→VRCA	16.29	2.77	0.01
RCA→PAT	20.83	4.71	0.00
RCA→PUB	15.53	2.44	0.01
RCA→RD	17.34	3.22	0.00
RCA→TSC	20.77	4.68	0.00
RCA→VRCA	11.19	0.60	0.55
RD→PAT	15.93	2.62	0.01
RD→PUB	20.85	4.72	0.00
RD→RCA	17.43	3.26	0.00
RD→TSC	14.54	2.02	0.04
RD→VRCA	12.92	1.33	0.18
TSC→PAT	13.20	1.45	0.15
TSC→PUB	9.95	0.07	0.95
TSC→RCA	16.71	2.95	0.00
TSC→RD	12.19	1.02	0.31
TSC→VRCA	11.38	0.67	0.50
VRCA→PAT	13.79	1.70	0.09
VRCA→PUB	10.46	0.28	0.78
VRCA→RCA	11.36	0.67	0.51
VRCA→RD	14.18	1.87	0.06
VRCA→TSC	20.18	4.43	0.00

Source: Authors' own research, 2019.

The Arellano–Bond method applied to determine the long-run relationships did not result in significantly different lag values; therefore, we have focused only on the coefficients of different independent variables in Table 5. The effect of the number of patents on TSC is rather obvious. In the case of publications and R&D resources, this relation is less evident.

Results of the calculations support hypotheses H_1 and H_2. Indeed, there is a strong relationship between resources and intellectual output. Hypotheses H_3 and H_4 have been supported, but it should be highlighted that competitiveness is a multidimensional concept, thus the correlation between different determinants of competitiveness varies. Hypothesis H_7 has been proven in the case of TSC

and Vollrath indices of competitiveness. Hypothesis H_6 has been supported, but H_5 could not be proven as the number of publications does not increase the patents.

Table 5. Results of the Arellano–Bond test.

Independent Variables	Dependent Variables		
	Balassa Index of Competitiveness	Trade Specialisation Coefficient	Vollrath Index of Competitiveness
	Variables in the Level		
Resources for research and development	0.236	−1.38	1.29
Number of publications	0.385	1.96 *	2.72 **
Number of patents	0.141	2.08 **	0.94
Constant	0.90	−3.66	−6.59

* and ** denote the significant level of 10% and 5%. Source: Authors' own research, 2019.

The results of the Hasuman test show that the random effects model is more appropriate in the case of level data (Table 6).

Table 6. Results of the Hasuman test.

	Coefficients of Fixed Effect Model	Coefficients of Random Effect Model	Difference	Standard Error
Dependent variable: RCA, level Chi square: 9.05**				
RD	0.25	0.22	0.03	0.03
PUB	−0.10	−0.24	0.14	0.05
PAT	0.11	0.14	−0.03	0.01
Dependent variable: TSC, level Chi square: 9.44**				
RD	−0.03	−0.01	−0.02	0.01
PUB	0.06	0.03	0.03	0.01
PAT	0.01	0.02	0.00	0.00
Dependent variable: VRCA, level Chi square: 19.94*				
RD	0.02	0.01	0.00	0.00
PUB	0.12	0.09	0.02	0.01
PAT	0.01	0.02	-0.01	0.00

Source: Authors' own research, 2019.

Results of the FE–OLS have not yielded a significant, positive relationship between the number of patents, the number of academic publications and the RCA index (Table 7). In the case of the TSC index, the number of patents has been significant to the value of the TSC index. The value of the Volrath index has been positively influenced by the number of patents and publications. This fact highlights the importance of intellectual output necessary to achieve long-range competitiveness, as shown in Table 7.

Table 7. Results of FE–OLS analysis.

	Balassa Index of Revealed Competitive Advantages			
	Coefficient	**Std.error**	**Z**	**P > |z|**
LGRD	0.222	0.078	2.860	0.004
LGPUBL	0.236	0.111	2.120	0.034
LGPAT	0.139	0.045	3.090	0.002
CONST	−0.114	0.264	−0.430	0.665
	Trade Specialization Coefficient			
	Coefficient	**Std.error**	**Z**	**P > |z|**
LGRD	−0.009	0.027	−0.340	0.734
LGPUBL	0.031	0.039	0.790	0.431
LGPAT	0.048	0.015	3.200	0.000
CONST	−0.451	0.098	−4.620	0.000
	Vollrath Index of Competitive Advantages			
	Coefficient	**Std.error**	**Z**	**P > |z|**
LGRD	0.014	0.023	0.630	−0.030
LGPUBL	0.094	0.032	2.880	0.030
LGPAT	0.018	0.013	1.420	−0.007
	−1.062	0.093	−11.460	−1.244

Source: Authors' own research, 2019.

Contrary to our previous expectations, there were no significant causal relationships between the financial resources allocated to R&D by business enterprises and the Balassa competitiveness index. In this way, hypothesis H_7 is not supported. On the contrary, the material resources allocated to RD are considerably influenced by the Balassa index in numerous countries in Table 8. This—at first surprising—fact can be explained by the high level of complexity of pharmaceutical development (the time window is relatively short to offer a possibility to apply longer—e.g., >7 years – lags), but the changes in the relative importance of the pharmaceutical sector involve a change in the amount of money allocated for research and development.

Table 8. Results of Granger causality analysis on the effect of the monetary resources allocated for R&D on the Balassa index of revealed comparative advantages and the trade specialisation coefficient.

Dependent Variable	**Monetary Resources, Allocated for R&D**					
Independent Variable	**Balassa Index of Competitiveness**			**Trade Specialisation Coefficient**		
	Chi-Square	**Degrees of Freedom (df)**	**Prob.**	**Chi-Square**	**df**	**Prob.**
Greece	4.8385	2	0.089 *	5.8715	2	0.091 *
Hungary	11.251	5	0.046 **	13.4157	5	0.008 **
Mexico	16.527	2	0.000 ***	17.0123	2	0.000 ***
Sweden	7.5469	2	0.023 **	8.1547	2	0.009 ***
Switzerland	13.618	4	0.008 ***	14.872	4	0.000 ***

* significant at 10% level, ** significant at 5% level, *** significant at 1% level. Source: Authors' own research, 2019.

There has been a significant causal relationship between the number of pharmaceutical patents and the Balassa index of revealed competitiveness, supporting hypothesis H_4 in Table 9. It is important to emphasise the relatively long lag periods (at least 4 years). Obviously, the TSC values show more significant differences than the RCA. This fact shows the importance of the time-factor, as well as the indirect effect between R&D resources and competitiveness. Our results have not provided a conclusive result regarding the effect of the number of patents on competitiveness.

Table 9. Results of Granger causality analysis on the effect of the number of patent applications on the Balassa index of revealed competitiveness.

Countries	Dependent Variable: Balassa Index of Competitiveness			Trade Specialisation Coefficient		
	Independent Variable: Number of Patents			Independent Variable: Number of Patents		
	Chi-Square	Chi-Square	df	Chi-Square	Chi-Square	df
Austria	19.461	8	0.012 **	22.214	8	0.000
Australia	16.159	8	0.056 *	17.221	8	0.022 **
Denmark	14.235	6	0.027 **	14.005	6	0.020
Finland	16.052	8	0.041 **	16.987	8	0.038 **
France	8.0202	8	0.431	9.222	8	0.412
Germany	12.726	6	0.047 **	12.213	6	0.057 *
Greece	36.338	8	0.000 ***	39.477	8	0.000 ***
Ireland	36.263	8	0.000 ***	38.997	8	0.000 ***
Italy	13.787	8	0.087 *	14.12	8	0.075 *
Netherlands	12.805	6	0.046 **	11.128	6	0.053 *
Norway	19.559	6	0.003 ***	21.125	6	0.001 ***
Spain	21.520	8	0.005 ***	22.547	8	0.002 **
Switzerland	15.667	6	0.015 **	18.142	6	0.000 ***
United Kingdom	21.056	8	0.007 ***	20.145	8	0.009 **
United States	17.171	8	0.028 **	16.125	8	0.0312 **

Source: Authors' own research, 2019. *significant at 10% level, ** significant at 5% level, *** significant at 1% level.

6. Conclusions

Based on the analysis performed, it is evident that the different indicators investigated always contain a relatively considerable lag. This highlights the crucial importance of strategic thinking in decision making concerning pharmaceutical-related research and development. It is clear that there is a direct, important relationship between the material resources allocated to R&D, and the number of patents, as well as competitiveness. This fact proves that without a long-range strategy and considerable material resources allocated to R&D, there is no possibility to improve a competitive position in the international pharmaceutical market. It is an extremely important lesson to learn, i.e., that the innovation system in general and in the pharmaceutical sector, in particular, has a considerable lag: it is an over-simplification to expect rapid results from an increase in financial resources, and vice versa: the current limitations on resources devoted to R&D will limit practical healing work after several decades and substantial institutional reforms are expected to be required in the future [91].

It is important to see that our data contained only the financial resources allocated by business entities for R&D. It can be concluded that, in some cases, central (governmental) resources are necessary to bolster competitiveness. Based on the results, the three recommendations for the future development of research policies are as follows:

1. The boosting effect of the state is a necessary development of R&D activity even in branches dominated by large-scale enterprises.
2. The optimal resource utilization for R&D requires international cooperation because the time between the achievement of academic results and economic advances is rather long and the risk is relatively high—there is no straightforward relationship between intellectual success and international competitiveness.
3. The efficiency of resources allocated to R&D activity can be evaluated and measured by economic indicators only in a long-range perspective.
4. Currently, increasingly complex regulation related to the introduction of new pharmaceutical products increases the time-gap between the conceptualisation of new innovation and its introduction to the market.

In the future, an important direction of research will be the application of panel-cointegration methods for obtaining a more accurate picture of the relationship between different factors influencing

the competitiveness of the pharmaceutical industry. It should be taken into consideration that, with passing time, the longer time series will offer a more favourable possibility to analyse the interplay of different causes. Last but not least, it should be mentioned that an enterprise-level investigation could shed light on important differences between the effect of innovation in the case of generic and brand pharmaceutical companies.

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