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Innovation Ecosystems against SARS-CoV Coronavirus: Pharmaceutical Industry

Ecosistemas de innovación contra el coronavirus SRAS-CoV: industria farmacéutica

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ABSTRACT

The article uses game theory to make a situational analysis of research and development (R&D) for treatments against the coronavirus SARS-CoV. The bioeconomic complexity causes a market failure with the virtual disappearance of the pharmaceutical industry. This requires government intervention for the implementation of a pharmaceutical industrial policy. The paper proposes the design and enactment of a National Pharmaceutical Policy (NPP) not based exclusively in the market. It proposed the creation of a National Academy of Mexican Traditional Medicine and the implementation of e-government solutions based on the Internet of Medical Things (IoMT)

Key words: bioeconomics; complexity; coronavirus; game theory; vaccines.

JEL CODE**:** C73; D20; F12; I11; L16; O31; O32; Q57

RESUMEN

El artículo utiliza teoría de juegos para realizar un análisis situacional de la investigación y desarrollo (I+D) de tratamientos contra el coronavirus SRAS-CoV. Se demuestra que los rendimientos crecientes en las TIC impulsan la demanda de otros bienes como las medicinas, pero no su producción. La complejidad bioeconómica ocasiona una falla de mercado con la virtual desaparición de la industria farmacéutica, lo que requiere de la intervención del gobierno en la creación de una política industrial en el sector farmacéutico. Se propone plantear una política farmacéutica nacional (PFN) que no se base, exclusivamente, en el mercado. Es necesaria la inversión pública para la creación de una Academia de Medicina Tradicional Mexicana y la búsqueda de soluciones de gobierno electrónico que implemente un sistema farmacéutico basado en el Internet de las Cosas Médicas (IoMT por sus siglas en inglés).

Palabras clave: bioeconomía; complejidad; coronavirus; teoría de juegos; vacunas.

Códigos JEL: C73; D20; F12; I11; L16; O31; O32; Q57.

ABSTRACT

The article uses game theory to make a situational analysis of research and development (R&D) for treatments against the coronavirus SARS-CoV. The bioeconomic complexity causes a market failure with the virtual disappearance of the pharmaceutical industry. This requires government intervention for the implementation of a pharmaceutical industrial policy. The paper proposes the design and enactment of a National Pharmaceutical Policy (NPP) not based exclusively in the market. It proposed the creation of a National Academy of Mexican Traditional Medicine and the implementation of e-government solutions based on the Internet of Medical Things (IoMT)

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INTRODUCTION

Severe acute respiratory syndrome (SARS) is a viral respiratory disease caused by a SARS-associated coronavirus (SARS-CoV). SARS was first identified in Asia in February 2003. Within a few months, the virus had spread to more than 24 countries in North America, South America, Europe, and Asia. According to the World Health Organization (WHO), 8,439 infected people had been identified as of July 2003, and 812 people had died from SARS (WHO, 2003). By June 2003, 20 suspected cases had been presented in Mexico in the states of Jalisco, Mexico, Morelos, Nuevo León, Querétaro and the Federal District, however, all cases were discarded after detection and referral to designated concentration hospitals. in each entity for this (Kuri & Santos, 2003). To date there is no vaccine against SARS-CoV.

In 2019, the virus that causes SARS had a mutation. The new virus has been called SARS-CoV-2, which causes the disease called COVID. First reported on December 31, 2019, SARS-CoV-2 spread from Wuhan, China. On March 11, 2020, the World Health Organization (WHO) declares the outbreak of the COVID19 disease caused by the new SARS-CoV-2 coronavirus a global pandemic (WHO, 2020). As of July 6, 2020, a total of 11, 520, 461 infected people and 535, 499 people had been confirmed dead, around 188 countries. At the same date in Mexico there were 256, 848 people infected and 30, 639 people dead (Hopkins, 2020).

Using game theory, a situational analysis of the research and development (R&D) of the SARS-CoV coronavirus treatment and vaccine at different levels is presented. First, a model of the viral dynamics of the coronavirus is presented. It is explained that, depending on the genetic adaptation strategy, the virus can mutate into a form with higher infectivity and lethality rates; or become less harmful to humans.

Second, a microeconomic analysis of the R&D investment decisions of pharmaceutical companies is presented. The types of incentives that are necessary in the face of changes in demand for a coronavirus vaccine are explained. Third, a macroeconomic analysis is presented using a Heckscher-Ohlin international trade model and a standard trade model with two goods and two inputs, medicines and information and communication technologies (ICT) and knowledge and information respectively.

It has recently been proven that such international trade models can present complex results (Wilkens, 2009). The case analyzed here considers that information and communication technologies (ICT), in particular through the IoMT (Internet of Medical Things), constitute a set of products technologically close to the set of products of the pharmaceutical industry. Under the assumption of diminishing returns to scale, there is an equilibrium that depends on the level of prices and technological requirements. However, it is an unrealistic assumption. On the one hand, information and knowledge as inputs tend to have increasing returns to scale; on the other, they are found in non-convex production possibilities spaces. In other words, different knowledge and information are not perfect substitutes in the production of different products. Which suggests the existence of economic complexity.

THEORY ANALYSIS: THE THEORY OF GAMES IN THE STUDY OF BIOECONOMIC COMPLEXITY

Game theory is a very useful mathematical tool to capture the interaction between genes, individuals, companies and countries, when the behavior of each one of the "players" has an effect on the others. Also, game theory is very useful in biology to capture genetic co-evolution. It is a way of modeling the strategic interaction between different “players” from the molecular level to the macroeconomic level (Kreps, 1990; Nowak, 2006).

One of the fundamental concepts in game theory is that of Nash equilibrium. John Nash developed this idea which can be described as follows: a Nash equilibrium is a strategy with the characteristic that no player can perform better by following an alternative strategy, assuming that the other players do not change their strategy. A Nash equilibrium requires that all actors follow their strategy simultaneously (Kreps, 1990).

In relation to the different types of games, be careful not to confuse concepts of economics and biology. Whereas in economics we call the actions that lead to a Nash equilibrium dominant strategies; In biology, we call the actions that lead to the Nash equilibrium evolutionarily stable strategies. Economic actors make rational decisions, while biological organisms adapt to the environment and mutate. In both types of games, however, it is about modeling the optimizing behavior of individuals, companies or genes and the results can be evaluated in terms of their efficiency in the use of resources. However, there will be situations, sometimes the most interesting ones, wherein simultaneous decisions of different players lead to sub-optimal results.

METHODOLOGICAL ANALYSIS

Viral dynamics and biosafety levels

The epidemiological transition theory (Omran, 1971) holds that people in developed countries have had a transition in their causes of death from infectious diseases to chronic degenerative diseases. The same theory predicted that, in the future, as levels of economic development increased, humanity as a whole would have the same transition, leaving infectious diseases behind and dying of diabetes, cancer, etc. Infectious diseases were then seen if not as a thing of the past, at the very least, as a problem of the poor. The expectations created by the theory of epidemiological transition led the health industry and public sector to concentrate their efforts on the care of diabetes, cancer, Alzheimer's disease, etc. In light of the current COVID-19 pandemic and following the epistemological logic proposed by Karl Popper (1962), it is possible to falsify the theory of the epidemiological transition, that is, it can be declared wrong. This makes research on the viral dynamics of infectious diseases a matter of life and death.

The SARS-CoV coronavirus has had at least two strains that have migrated from animals to humans, most likely through the consumption of bushmeat. Here we will call them SARS-CoV-1 and SARS-CoV-2. SARS-CoV-1 was the cause of the 2003 pandemic and no great pandemic power was attributed to it. By June of that year, the World Health Organization (WHO) declared that the virus had been eradicated from humans (WHO, 2003) and the search for any vaccine was abandoned due to lack of cases. Almost two decades later, in 2019, this coronavirus mutated into SARS-CoV-2. The latter would have a higher infectibility rate, although both viruses have biosafety level 2 (BSL-2) (CDC, 2003).

The level of biosecurity is related to its fatality rate. That is, how deadly it is to humans. Regarding the conditions that explain the level of mortality of a virus, we can mention at least two theories. On the one hand, Jared Diamond (1999) considers that the level of biosecurity is related to the co-evolution of the virus with humans. According to Diamond (1999), the longer a virus has spent living with humans, the better adapted it is and, therefore, the more lethal it is. It is a vision that we could call the predatory virus (Diamond, 1999). For his part, Peter Piotr (Edx, 2015), considers that a virus that kills its hosts is poorly adapted since it needs to keep its host alive in order to continue having a supply of newborn cells. This theory could be called the symbiotic virus (EdX, 2015). None of these theories have yet been falsified; that is, none have been declared false.

In terms of the evolutionary dynamics of SARS-CoV it could be expressed in its normal form as follows (Table 1):

Table 1. Standard form of the evolution of SARS-CoV

		Virus 2	
		Predator (Diamond)	**Symbiotic (Piotr)**
Virus 1	**Predator (Diamond)**	N/V, N/V	N, 0
	Symbiotic (Piotr)	0, N	N, N

Source: Own elaboration.

The Evolutionarily Stable Strategy (ESS) will allow a better adaptation of the virus. In the case of the model shown in Figure 1, there are two Nash equilibria (shaded) that would constitute ESS: predator-predator and symbiotic-symbiotic. For now, the biosafety levels of SARS-CoV-1 and SARS-CoV-2 are very similar, both viruses are BSL-2. Both have relatively low lethality levels. We could say that they are in the EES (symbiotic, symbiotic). This does not guarantee that the virus will not change its EES in the future, and will mutate, increasing its levels of infectivity and/or lethality.

The Microeconomic Model: The Complexity of Research and Development (R&D)

Suppose two pharmaceutical companies make investment decisions in research and development (R&D). They must decide between seeking treatment for a disease with a high market value such as Alzheimer's or one with a low value such as SARS. Table 2 shows the normal form of a game that represents these investment decisions.

Table 2. SARS-CoV Vaccine R&D Kit

		Company 2	
		Alzheimer	**SRAS**
Company 1	**Alzheimer**	$Q_A/2$, $Q_A/2$	Q_A, Q_{SRAS}
	SRAS	Q_{SRAS}, Q_A	$Q_{SRAS}/2$, $Q_{SRAS}/2$

Source: Own elaboration.

With an equivalent market value, wherein QA = QSRAS, the dominant strategy is for one company to produce Alzheimer's treatments and another company to produce SARS treatments (Nash equilibria are shown in shaded cells).

For their part, if the value of the demand for Alzheimer's treatment is greater than the market value of the SARS treatment, both companies will invest in Alzheimer's treatment. Before the COVID19 pandemic, Alzheimer's was the most common dementia among older adults, especially in developed countries. It is estimated that in 2010, 46.8 million people around the world had dementia at a total cost of $818 billion. By 2030, it was estimated that 74.4 million people would have dementia globally and the cost of caring for these people could reach $ 2 trillion. In the absence of effective therapies, it is estimated that the number of people with dementia could reach 131.5 million by 2050 (Regmi *et al*., 2014).

In our model, we assume that before the COVID19 pandemic, the value of the demand for Alzheimer's treatments was a certain number of times higher than the value of the demand for SARS treatments: QA = aQSRAS. Table 3 shows the normal form of the game with these values.

Table 3. SARS-CoV Vaccine R&D Kit

		Company 2	
		Alzheimer	**SRAS**
Company 1	**Alzheimer**	$aQ_{SRAS}/2$, $aQ_{SRAS}/2$	aQ_{SRAS}, Q_{SRAS}
	SRAS	Q_{SRAS}, aQ_{SRAS}	$Q_{SRAS}/2$, $Q_{SRAS}/2$

Source: Own elaboration.

When a> 2 the dominant strategy of both companies is to invest in R&D for Alzheimer's treatment (Nash equilibrium is shown in the shaded cell). The result is an incomplete market for R&D in SARS treatments.

In this sense, incentives for R&D are necessary to find a treatment against SARS. The literature documents at least two types of incentives: pushes (eg subsidies, tax forgiveness); and pulls (eg prizes, patent purchase, advance purchase commitment). Both types of incentives differ in the targeting of inputs or outputs, respectively. While push incentives subsidize R&D inputs, pull incentives reward R&D results (Anderson & Mueller, 2017).

Table 4 shows a subsidy (SSRAS) that drives R&D, where the search for a vaccine against SARS-CoV is subsidized. The amount of the subsidy to generate R&D in SARS must be:

$$(1)\ S_{SARS} > [(2a-1)/2]*Q_{SARS}$$

The subsidy is then a function of the size of the $QSRAS_{demand}$. With this result, the Nash equilibrium would be (SARS, SARS).

Table 4. Subsidized SARS-CoV Vaccine R&D Kit (Push Program)

		Company 2	
		Alzheimer	**SRAS**
Company 1	**Alzheimer**	$aQ_{SRAS}/2$, $aQ_{SRAS}/2$	aQ_{SRAS}, $Q_{SRAS}+S_{SRAS}$
	SRAS	$Q_{SRAS}+S_{SRAS}$, aQ_{SRAS}	$Q_{SRAS}/2+S_{SRAS}$, $Q_{SRAS}/2+S_{SRAS}$

Source: Own elaboration.

When analyzing a program that draws on R&D, it is necessary to take into account the uncertainty of the results. Acemoglu and Linn (2004) have built a model linking innovation rates to current and future market size and study the relationship between market size and innovation in the pharmaceutical industry. They use an innovation function characterized by:

$$(2)_{nj}(t) = djZj\ (t)$$

There is free entry into R&D and each company has access to technology that generates a flow of innovation$_{dj}$ for every dollar spent on treatment j at time t.$_{Zj}$ (t) is a firm's investment in treatment j at time t. Differences in$_{dj}$ account for the possibility that scientific progress may be more difficult in some diseases than others. In our model we assume that j can be A or SARS.

Based on Acemoglu and Linn (2004), the returns of the company with the best treatments for disease j at time t have the form:

$$(3)_{Yj}= (a-1)_{bQj}$$

Where abQj corresponds to the size of the demand for treatment j.

Again, based on Acemoglu and Linn (2004), the discounted value of returns for companies that win innovation awards can be expressed by the function:

$$(4)_{Rj}=_{Yj}+dj\ (Pj(t)\ -Zj(t))$$

Where Pj is the award obtained for the best innovation j. Table 5 shows the value of the returns of the companies that win innovation awards. To generate R&D in SARS as the dominant strategy, the premium must be a function of the size of demand and the rate of innovation. With this result, the Nash equilibrium would be (SARS, SARS).

$$(5)\ _{PSRAS\&gt}\ ;\ [(a-ab-b) * QSRAS + _{dSRAS} * _{ZSRAS}] / _{dSRAS}$$

Table 5. SARS-CoV Vaccine R&D Kit with Prize (Pull Program)

		Company 2	
		Alzheimer	**SRAS**
Company 1	**Alzheimer**	$aQ_{SRAS}/2$, $aQ_{SRAS}/2$	aQ_{SRAS}, R_{SRAS}
	SRAS	R_{SRAS}, aQ_{SRAS}	$R_{SRAS}/2$, R_{SRAS}

Source: Own elaboration.

In terms of fiscal cost, subsidies would be cheaper than awards:$_{SSRAS}<_{PSRAS}$. However, SSRAS subsidies guarantee investment in R&D for SARS, but not innovation. On the other hand, the$_{PSRAS}$ (dSRAS$_{)}$awards consider the innovation rate and somehow guarantee higher amounts of investment in R&D with some success in new treatments. In this sense, for the subsidies to be as successful as the awards they must be of the same amount$_{SSRAS}$ = PSRAS (dSRAS); that is, subsidies should also be a function of the innovation rate.

The Macroeconomic Model: The Complexity of International Trade

The model used here is a Heckscher-Ohlin model with two goods and two inputs. Medicines, information and communication technologies (ICT) and information and knowledge, respectively. First, it is necessary to define the production possibilities frontier under the following parameters.

aMc = knowledge used for the production of a unit of drugs (mg).
aMi = information used for the production of a drug unit (mg).
aTc = knowledge used for the production of an ICT unit (IoT devices).
aTi = information used for the production of an ICT unit (IoT devices).
C = supply of knowledge in the economy.
I = supply of information in the economy.

The production possibilities frontier (fpp) is defined by the following pair of equations:

(6)$_{QM} \bullet_{aMc} +_{QT} \bullet aTc \leq C$

(7)$_{QM} \bullet_{aMi} +_{QT} \bullet aTi \leq I$

For its part, the value of production is given by the isovalue equation:

(8) $V = P_M \bullet Q_M + P_T \bullet Q_T$

Where QM is the production of medicines,$_{QT}$ the production of ICT,$_{PM}$ is the price of medicines and$_{PT}$ is the price of ICT. The balance will depend on whether the relationship between knowledge and information used in the production of medicines is greater or less than the relationship between knowledge and information used in the production of ICT. For the moment suppose this relationship as defined by equation (9).

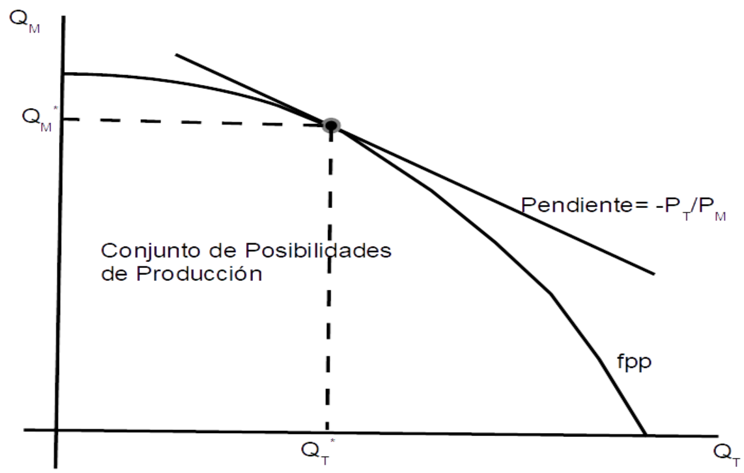
(9) aMc / $_{aMi}$&gt ; $_{aTc}$ / $_{aTi}$

which is equivalent to .

(9.1) aMc / $_{aTc}$&gt ; $_{aMi}$ / $_{aTi}$

Graph 1 shows the shape of the fpp with decreasing returns to scale and the point of tangency with the isovalue function that satisfies the first-order conditions. The convex form of the fpp says that information can be substituted for knowledge and vice versa; and that the opportunity cost in terms of ICT to produce one more unit of medicines increases as the economy produces more medicines and less ICT. However, the economy produces at the point where the value of output is maximized. That is, where the isovalue line furthest from the origin is reached and which still intersects with the set of production possibilities, in this case a closed and bounded set.

Graph 1. Production Possibilities Frontier and isovalue function in the Heckscher-Ohlin model



Source: Own elaboration (Spanish version).

Now let's expand the Heckscher-Ohlin model and include consumers (standard business model) with a Cobb-Douglass utility function as shown in equation 5.

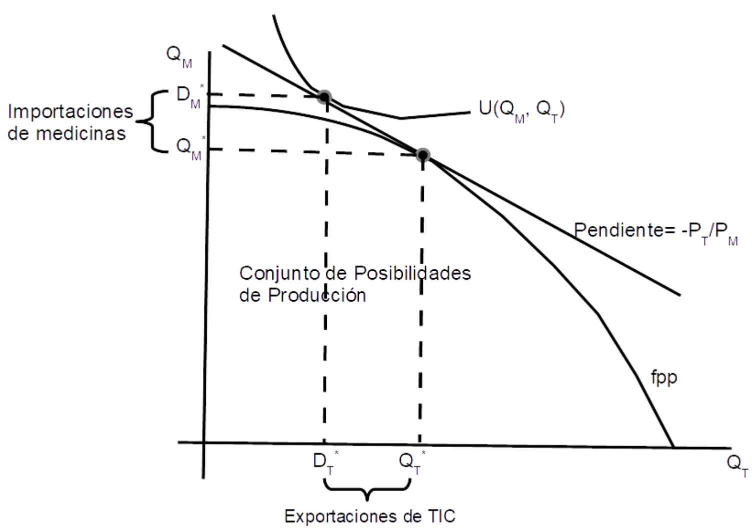
(10) $U (M, T) = M\alpha^{T\beta}$

where $1> \alpha> 0$, $1> \beta> 0$ and $\alpha + \beta = 1$.

Likewise, the value of consumption in an economy must be equal to the value of production. So the isovalue function is equivalent to the budget constraint. From equations (10) and (11) we can derive the demand for medicines and ICT. The equilibrium sample in graph 2.

(11) $P_M \bullet D_M + P_T \bullet D_T = P_M \bullet Q_M + P_T \bullet Q_T$

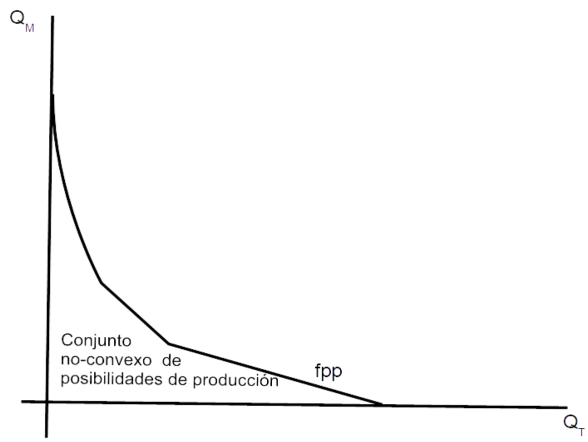
Graph 2. Production, consumption and trade in the standard model



Source: Own elaboration (Spanish version).

The model shows that ICT exports have allowed a greater demand for medicines and, therefore, the need to import them. With increasing returns to scale in both sectors, the set of production possibilities loses convexity. Graph 3 shows the set and the production possibility frontier with increasing returns.

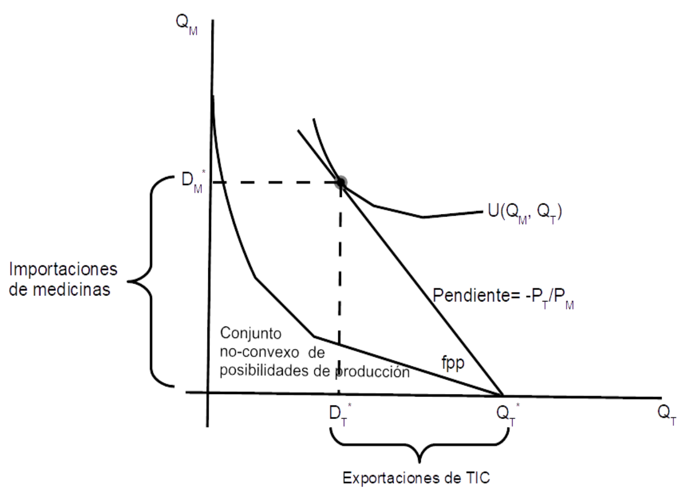
Graph 3. Set and production possibilities frontier with increasing returns to scale in both sectors



Source: Own elaboration (Spanish version).

With increasing returns to scale, market equilibrium is specialization in one of the sectors as shown in Figure 4. At a given price relationship, the optimal basket is a corner solution, using all the inputs in the production of ICT and zero in the production of medicines, which implies greater imports of medicines and a greater dependence on the outside in such a sector. strategic as the pharmacist.

Graphic 4. Production, consumption and trade with increasing returns to scale in both sectors.



Source: Own elaboration (Spanish version).

An algebraic way of looking at fpp with constant increasing returns to scale is with the following equation:

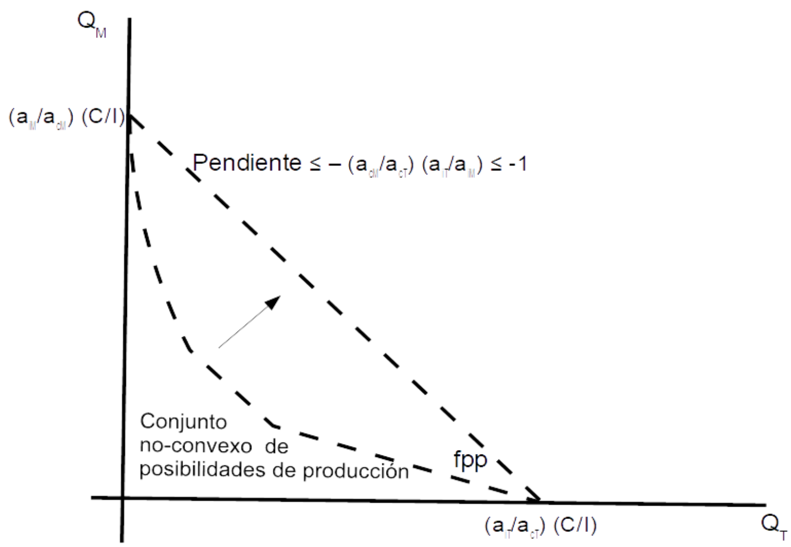
$$(12)\ ({}_{acM}/{}_{aiM}) \bullet_{QM} + ({}_{acT}/\ aiT_{)} \bullet\ QT \leq_{C} / I$$

where is it obtained from

$$(12.1)\ QT_{=}\ ({}_{aiT}/{}_{acT})\ (C / I)\ -_{(}acM_{/}acT)_{(}aiT\ /{}_{aiM})_{QM}$$

Graph 5 shows how the set of production possibilities only reaches convexity when there are constant returns to scale and the slope of the fpp is given by - (acM /acT) $({}_{aiT}/{}_{aiM})$ = -1. This is equivalent to $({}_{acM}/$ aiM$_{)}$= (acT$_{/}$aiT)$_{;}$that is, when both sectors are equally intensive in information and knowledge, at least in relative terms.

Graph 5. Set and production possibilities frontier of increasing returns to scale constants.



Source: Own elaboration (Spanish version).

DISCUSSION

To better understand the effect of "push" and "push" incentives on the dynamics of infectious disease treatment innovation, let's try to understand two successful cases that have won the Nobel Prize in Physiology and Medicine. In 2015 the Nobel Prize was awarded to the discovery of artemisinin and ivermectin, both drugs that improve the treatment against malaria, onchocerciasis and lymphatic filariasis respectively. The award was awarded jointly, one half to professors William C. Campbell (2015,2016) and Satoshi Ōmura (2015) for their discoveries concerning therapies against infections caused against multicellular parasites; and another half to Professor Youyou Tu (2015) for his discoveries related to antimalarial therapies.

In his reception *lecture, Invermectin: A Reflection on* Simplicity, Professor Campbell (2015) said:

> *"I am using the word 'simplicity' here in the context of science, but I do not mean to suggest that science is simple; nor do I mean that the development of the drug ivermectin was an exercise in simplicity. My intention is rather to highlight the element of simplicity in science and I hope to do so by pointing out the importance of simplicity in the birth of the drug ivermectin. It has been widely recognized that simplicity is of particular importance to scientists and indeed simplicity is celebrated in science as an element of beauty. However, here I want to talk about simplicity not as an aesthetic element, but as a utilitarian element ... " (Campbell, 2015, 2016).*

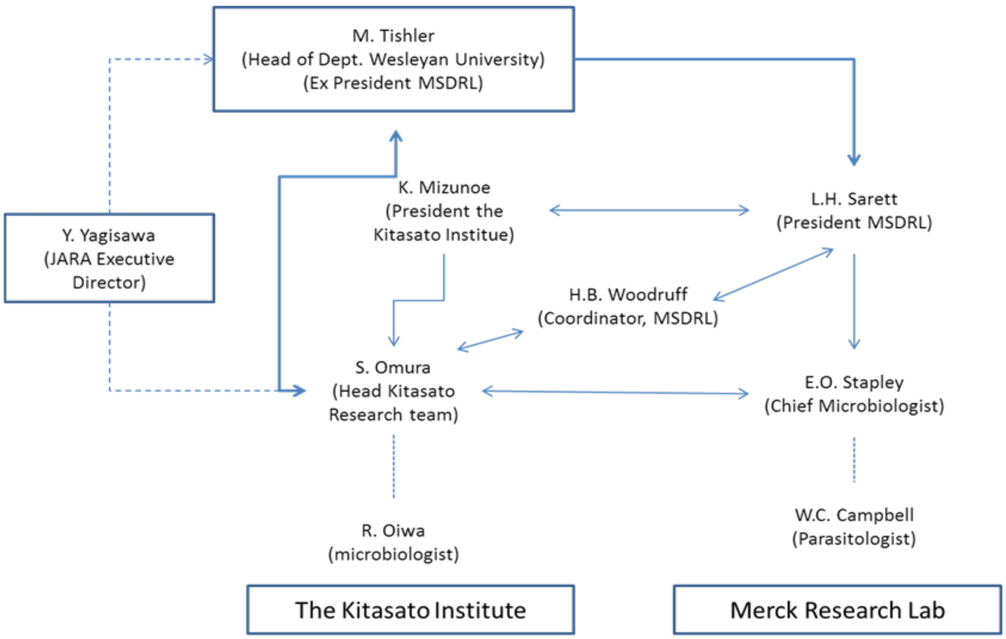
In this sense, thinking that the discovery of treatments such as ivermectin or artemisinin are the result of a single "push" or "pull" incentive is not enough. The models shown in the previous sections are still a simplification of reality. But even though scientists appreciate simplicity, the medical treatment development process remains complex. For example, among the many players involved in the development of Invermectin are *Merck & Co. Inc.*on the business side and the Kitasato Institute in Tokyo on the non-profit side. The R&D process involved microbiologists, chemical specialists in fermentation and analysis, parasitologists, biochemists, veterinarians, etc. There were at least 125 scientists and technicians involved who published more than 70 scientific articles over more than ten years (Campbell, 2015).

Since 1973, the number of scientists and organizations involved in the search for the hitherto unknown avermectins involved diverse teams of people with multiple sources of funding. Professor Satoshi Ōmura (2015), in his Nobel Prize reception conference recalls how:

> *"... the discovery of avermectins was the result of a large multidisciplinary research project that involved international cooperation between public institutions such as the Kitasato Institute in Japan and private pharmaceutical companies such as Merck, Sharp and Dohme in the United States. But the most successful story of this public-private partnership has been the commitment, skill and quality of scientific exchanges and cultivating them among the team of scientists who managed to overcome professional differences, nationality and sometimes even goals ... " (Ōmura, 2015)*

The R&D, distribution and health impact of these drugs depended on an unprecedented combination of drug donation programs, an international consortium of public and private organizations, multilateral agencies, donors, governments, non-governmental organizations (NGOs). , scientists, health workers, as well as from the community of people affected by the disease (Ōmura, 2015). Figure 1 shows the flow of collaborations between scientists and organizations in the search for avermictins.

Figure 1. Kitasao-MSDRL Collaboration, 1973 in English



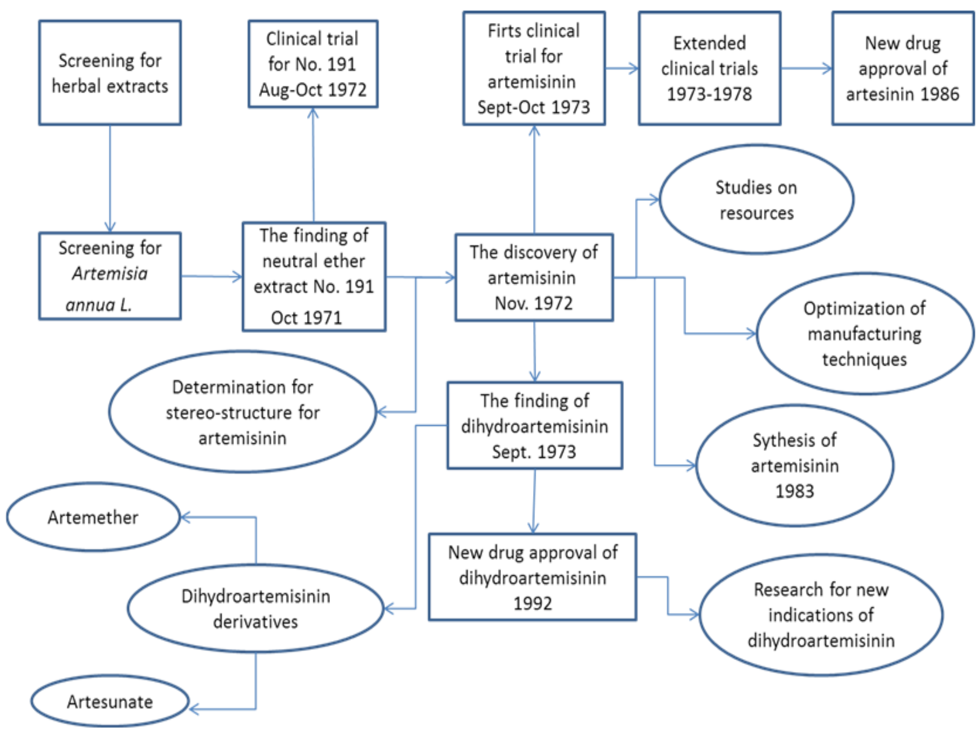
Source: Ōmura (2015).

An element frequently ignored but that we could consider a type of rise, is biodiversity and traditional knowledge. For example, the main source of ivermectins is literally the soil of Japan. Ivermectins are a multipurpose drug derived from a microorganism discovered in Japanese soil. Currently, Invermectin is taken completely free by more than 250 million people (Youyou, 2015).

Traditional knowledge of biodiversity was also very important in the discovery of artemisinin, the antimalarial treatment that earned Profr the Nobel Prize. You You You. The term "Qinghao" is a generic synonym used to refer in Chinese to the herbs of the Artemisia family. Qinghao has been one of the most common herbs in traditional Chinese medicine for the past two thousand years.

In traditional Chinese medical terms, the herbs of the Artemisia family offer the function of cleansing deficient heat, cooling and detoxifying the blood, eliminating fever and ostopyrexia, releasing from summer heat, relieving fevers of malaria, removing jaundice. , etc. In the classical Chinese herbal text, Sheng Nong of the Qin and Han dynasties from around 221 BC to AD 220, Qinghao is listed with clinical applications ranging from relief of rashes to lice treatment and improvement of eyesight. Different authors from ancient China documented the use of the Qinghao herb, however, few details were provided on the species or parts of the plant that are useful for clinical use. Figure 2 shows a flow chart of R&D work at the Academy of Traditional Chinese Medicine in the search for artemisinin (Youyou, 2015).

Figure 2. R&D Flow Chart at the Chinese Academy of Traditional Medicine in English



Source: Youyou Tu (2015).

The push for a malaria treatment became a military priority during the Cold War, when Southeast Asia was one of the areas of greatest endemism. During the Vietnam War in 1964, the United States Army's malaria casualties reached five times more than direct combat casualties. In 1965, about half of all US troops in Vietnam were infected with malaria. Without traditional Chinese knowledge at its disposal, the US military tested about 214,000 compounds between 1965 and 1972 without any success. Simultaneously, and in opposition to the US troops. In the US, the army of the People's Republic of China began a secret R&D program in the search for antimalarial treatments in 1964. In 1967 antimalarial research became a priority for the Chinese army, testing different compounds between 1967 and 1969, similarly, without any success. In 1969, the Chinese army asked the Academy of Traditional Chinese Medicine to participate in the search for antimalarial treatments. Professor Tu You You was appointed as head of the research team. In this sense, the financing of the army was fundamental in the discovery of artemisinin (Youyou, 2015).

Although the R&D of pharmaceutical products requires the combination of highly specialized knowledge in microbiology, biochemistry, use and knowledge of biodiversity, ICTs also play an important role. In international health, there is consensus on the usefulness of countries establishing a coordinated action plan among all actors in the pharmaceutical field to ensure the availability and quality of drugs and promote their rational use, fostering the development of the pharmaceutical industry. The World Health Organization (WHO) has recommended that countries develop a National Pharmaceutical Policy (NFP), which is defined as

> *"A commitment to an objective and an action guide that expresses and prioritizes the medium and long-term goals established by the government for the pharmaceutical sector, and identifies the main strategies to achieve them" (Wrtiz et al., 2013).*

An NFP involves the public and private sectors and must address matters related to the regulation, production, distribution, prescription, dispensing and consumption of medicines (Wrtiz *et al.,* 2013).

In Mexico, the hospital pharmacy model used by the Ministry of Health in public hospitals requires pharmaceutical professionals not only to manage the storage and distribution of drugs, but also their safe and efficient use. Which involves qualified human resources in the pharmaceutical sector that are often not available. In addition, there is a growing need to expand surveillance in the sale of prescription drugs beyond antibiotics (Wrtiz *et al.,* 2013).

On the other hand, in an evaluation carried out to units of medical specialties of chronic diseases (UNEMES-EC) of Mexico in 2012, in their supply of medicines it was found that of 17 basic medicines related to the care of diabetes mellitus, hypertension and overweight / obesity, only 13.3 percent of the units reported a complete supply of essential drugs and this supply was more frequent in those units with an outsourced pharmacy service. Of the total number of patients interviewed, 35 percent had ever had to buy drugs with their own resources (Contreras *et al.,* 2013).

Drug supply systems are one of the main determinants of the availability of drugs, as well as their total cost. In many developing countries the purchase of medicines represents the largest health expenditure after personal cost. Pharmaceuticals also constitute the largest health-related outlay in foreign currency (MSH, 2012).

In 2008 the Swiss-based International Pharmaceutical Federation developed a set of principles called the 2008 *Basel Statements.* This document contains 75 recommendations, grouped under six basic elements for the practice of hospital pharmacies. The statements contained in Table 6 are part of the supply of medicines, one of the six basic elements considered by the Basel Declarations 2008 (Shrestha *et al.,* 2018).

Electronic procurement systems emerge to manage the complex supply chains derived from globalization. In 2012 the World Trade Organization (WTO) revised its multilateral agreement on government procurement or procurement (Anderson & Müller, 2017). For its part, the European Union has legislated some guidelines on electronic procurement (*e-procurement*) in relation to the supply of the public sector and strategic sectors such as water, energy and transport, at least since 2004. In 2017 the European Council published a series of guidelines on government procurement that includes electronic procurement systems (EU, 2017).

The results of the model explain at least partially why there is a shortage of medicines in Mexico and in other countries. The existence of increasing returns raises opportunity costs and prevents private companies from developing in both sectors, especially in open economies where, at least theoretically, non-domestically produced products could be imported. This is a market failure that therefore requires government intervention. Two types of measurements are recommended:

1. In the short term, it is necessary to implement e-procurement or*e-procurement*systems that automate the supply chain of medicines in the public and private sectors.

2. In the medium term it is important to develop the national pharmaceutical industry. Promote professional study and research plans in pharmaceutical sciences and develop clusters for the production of medicines with public and private investment.

Table 6. Guidelines for the supply of medicines from the Basel Declarations 2008

Patient	Statement
17	The procurement process must be transparent, professional and ethical to promote equity and access and ensure accountability of the relevant governmental and legal entities.
18	Provisioning should be guided by the principle of provisioning for security.
19	Pharmaceutical sourcing is a complex process that requires the control of pharmaceutical personnel and a technically competent team.
20	The operational principles for a good procurement practice must be regularly reviewed and the different procurement models must be adapted to different situations and emerging needs in the most cost-effective way.
21	Procurement must be supported by strong quality control principles, to ensure that poor quality medicines are not distributed within the system. Proper storage to ensure quality maintenance throughout the value chain is necessary.
22	Procurement should not occur in isolation, but should be informed by the drug selection process.

23	Good provisioning must be supported by a reliable information system that provides accessible, accurate and timely information.
24	The existence of a formal mechanism for the request of funds is necessary, so that the pharmacy staff can make the purchases of medicines.
25	Each pharmacy should have contingency plans for drug shortages and for shopping during emergencies.

Source: Own elaboration.

A recently introduced technology to the pharmaceutical and biomedical markets is 3D printing (I3D). 3D printing technology can provide interesting propositions that link both recommendations. Over the last decade, the pharmaceutical paradigm has shifted towards patient-centered development. It focuses on *ad-hoc* doses to each patient and on prostheses and fabrics tailored to the patient, personalizing medical care. This technology allows from the manufacture of personalized medicines, to the bioengineering of tissues and organs, as well as the three-dimensional modeling of diseases. The first I3D method used in drug dose development was based on the 1993 *Three-dimensional printing techniques* (US Patent US 5,204,055 A). From there to the development of methods such as Stereolithography (SLA, STL), *Selective Laser Sintering* (SLS), *Selective Laser Melting* (SLM) or *Drop on Solid* (DoS) just to mention a few, almost 30 years. One of the latest advances has been the development of biorobotics. Biorobots are hybrid devices that attempt to imitate various biological processes, very useful in tissue regeneration, in the physiological supply of medicines and in frontier research in life and health sciences (Jamroz *et al*., 2018).

In Mexico, there have been important developments in e-procurement outside the pharmaceutical sector. In 2010, Arturo Delfin and Alberto Wario, two engineers in Guadalajara, Jalisco, the Mexican Silicon Valley, would obtain the patent for their invention, the *Replenishment Management System and Method* (US patent 7,711,612 B1). The patent, however, is in the name of the *International Business Machines Corporation* (IBM) based in Armonk, NY (USA). , and would be the key logistics piece of the plant that the transnational company has in Guadalajara. The solution increased the value of IBM's production in Guadalajara from $ 1,600 to $ 3,600 million, between 2009 and 2011 (Expansión, 2011).

The Guadalajara operation became an *e-business* epicenter and a global leader in *e-procurement* for IBM, exporting the concept to other IBM facilities around the world. *E-procurement* enables IBM manufacturing plants to avoid wasting material resources, reduce inventory costs and streamline processes. The IBM *e-procurement* platform is the fundamental piece to prevent waste from occurring: it monitors production system needs, requests replenishments, regulates manufacturing costs, and manages payments to suppliers (Expansión, 2011).

CONCLUSIONS

Searching for a SARS-CoV vaccine is a matter of national security. The private sector cannot meet the needs of the pandemic without funding and support from the public sector. Public-private partnerships are required to find the treatments and, if applicable, the SARS-CoV vaccine. This article presents a situational analysis of the R&D, supply, production and exchange of treatments against SARS-CoV. This represents an economic problem where industrial products are found within a product space whose coordinates are determined by information and knowledge (*know-how*). This space is a non-convex space similar to a Gruyère cheese full of holes. In other words, the *know-how* of a product can only be shared with those technologically closest products. In this sense, the idea of a non-convex product space in its input combinations goes against neoclassical economic theory and suggests the existence of non-linear behaviors. That is, it suggests the existence of economic complexity. (Hausmann & Klinger, 2007; Hidalgo & Hausmann, 2009).

The innovations needed in this ecosystem are the product of a complex process from an economic point of view. The creation of new inventions is characterized by dependence on the past, interdependence and interaction between heterogeneous agents capable of learning and reacting creatively. To understand the complexity, we resort to an emerging paradigm in different disciplines such as mathematics, physics, biology, computer science and economics that seeks to understand the endogenous change of systems (Antonelli, 2009).

The article presented a bioeconomic model that addresses:

1. The viral dynamics of SARS-CoV. It is difficult to determine which will be the evolutionarily stable strategies of the coronavirus, but it is thought that the mutation of SARS-CoV-2 to what we could call SARS-CoV-3 is not unlikely.

2. A game theory model that shows the microeconomic dynamics in the R&D decisions of the pharmaceutical industry. In this sense, fluctuations in demand are an important determinant in companies' decisions about which treatments to dedicate resources to. The pandemic generates an increase in the demand for treatments against SARS-CoV but it is a temporary increase that we hope will reduce in the near future. According to this model, the reduction in the demand for treatments against SARS-CoV would lead to abandonment in the search for treatments and, in this case, a vaccine by pharmaceutical companies.

3. A Heckscher-Ohlin macroeconomic model and a standard international trade model with two high-tech sectors (pharmaceutical and ICT) and two inputs (information and knowledge). Theoretically, the existence of increasing returns to

scale and the absence of convexity in the set of production possibilities lead to economic complexity and market failures. In other words, as a product of economic complexity, under certain conditions, medicine markets disappear.

The current emergency leads to the need to propose a national pharmaceutical policy (NFP) so that it is not based exclusively on the market. Public investment that involves ethical and national security criteria and not only market criteria is necessary. Based on the study of the development of antimalarial treatments in the People's Republic of China, it is necessary to create an Academy of Traditional Mexican Medicine with public funding as a national R&D center. Likewise, the economic complexity in the global medicine market and the current pandemic make it imperative to search for electronic government solutions for the supply of medicines. This requires a new paradigm of hospital care, where the development of digital systems and pharmaceutical and organic materials, as well as clinical patient care and pharmacology must go hand in hand in the implementation of *e-procurement proposals.* Solutions still under development, such as the electronic medical record, are also of great importance for the implementation of a pharmaceutical system based on the Internet of Medical Things (IoMT). The I3D represents an important technology in the future to provide patients with the necessary supplies for health care, as well as for scientific research.

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