The Scientific Impact of Mexican Steroid Research 1935–1965: A Bibliometric and Historiographic Analysis

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We studied steroid research from 1935 to 1965 that led to the discovery of the contraceptive pill and cortisone. Bibliometric and patent file searches indicate that the Syntex industrial laboratory located in Mexico and the Universidad Nacional Autónoma de México (UNAM) produced about 54% of the relevant papers published in mainstream journals, which in turn generated over 80% of the citations and in the case of Syntex, all industrial patents in the field between 1950 and 1965. This course of events, which was unprecedented at that time in a developing country, was interrupted when Syntex moved its research division to the US, leaving Mexico with a small but productive research group in the chemistry of natural products.

Introduction

Background

Historiography studies have stressed the need for new ways of documenting the early stages of Mexican scientific activity by examining both endogenous and exogenous factors needed to complement the mainly descriptive and externalist approaches commonly employed (Kleiche-Dray, Zubieta Garcia, & Rodriguez-Sala, 2013; Luna-Morales, Collazo-Reyes, Russell, & Pérez-Angón, 2009). Luna-Morales and coauthors identified four different modes of Mexican scientific production in the first half of the 20th century: amateur, institutional, academic, and industrial. The last of these emerged only at the end of this period as a result of the industrial activity associated with steroid research (Luna-Morales et al., 2009).

In the mid-20th century it was inconceivable to imagine that cutting-edge research like with steroids could be done in a country such as Mexico (Djerassi, 1992; Redig, 2005), but specific circumstances led to the creation of the Mexican Hormone Steroid Industry that had a huge impact, both scientific and social worldwide. Evidence of this is that in 1999 the Marker degradation (the first practical synthesis of the pregnancy hormone, progesterone) and the Mexican steroid industry were designated jointly by the American Chemical Society and the Chemical Society of Mexico as an International Historic Chemical Landmark (Raber, 1999).

This special case has attracted the attention of historians, philosophers, sociologists, and other specialists, but has yet to be analyzed from a historical bibliometric perspective (Hérubel, 1999). Our goal is to illustrate the role played by Mexican institutions and researchers through a detailed analysis of the scientific literature published at the time. We identified a wide network of institutional and international links needed to create a Hormone Steroid Industry, whose

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scientific achievements proved to be more widespread than previous studies had suggested.

Our study period of 1935–1965 begins with the pioneer of steroid research, Russell Marker's first publications on his research into plant steroids, and ends with the final documents from Mexico, after which time the main research effort was moved to the US.[1] We focus our attention on the new ways developed to obtain progesterone and the steroid research carried out in Mexico. Although the first Mexican paper in the field of steroid research did not appear until 1946, we found it necessary to include previous work on the subject published from 1935–1945 in order to place the Mexican contribution in its rightful historiographical context, in particular because the natural plant source that led to the major discoveries was found in Veracruz, in the west of Mexico.

The research activity was driven by scientific groups from Mexican academic institutions and the local Syntex laboratory that saw the emergence of a new pattern of publication for Mexico. In a short period of about 10 years (1944–1955), these groups became world leaders and were highly influential in mainstream journals in the area of organic chemistry (Chamizo, Garritz, & Kleiche-Dray, 2008; Kleiche-Dray, 2008). More notable is that this research generated several industrial patents and a sizably strong industry in hormonal steroids (Gereffi, 1978; Slater, 2000). Even though this process ended abruptly with the purchase of the Syntex Laboratories by Merck Laboratories from California (Gereffi, 1983), Mexico kept a research group specialized in natural products at the Universidad Nacional Autónoma de México (UNAM) (Rosenkranz, 1992) which continues to the present day.

The beginnings of Syntex, the most successful academic/industrial institution on steroid research worldwide, lies with E. Somlo and F.A. Lehmann, both war exiles, the former a Hungarian businessman and the latter a chemist, when they founded the Hormona Laboratories in Mexico City at the end of the 1930s (Olivares, 2000). Their aim was to meet the demand for pharmaceutical products whose supply dwindled as a result of the outbreak of the Second World War. North of the border, Marker, a chemist from Pennsylvania State College with the financial backing of Parke Davis & Co., embarked on a search for a plant source to improve the efficiency of industrial progesterone production using animal products. Progesterone was expensive because it was extremely difficult to make in any quantity (Raber, 1999). Marker's search took him to Mexico and to a type of wild yam called "Cabeza de Negro," which was to become the basis of a new synthetic and much cheaper procedure for progesterone production. Parke-Davis could not be convinced to support the commercialization of Marker's synthesis and in 1944 Hormona Laboratories became Syntex Laboratories, derived from the commercial alliance of Marker, Somlo, and Lehmann with the main objective of exploiting this new raw material for the production of progesterone. Syntex was to become one of the world's most important pharmaceutical companies and led the Mexican steroid industry "to blaze a remarkable path in the global marketplace" (Free, 1999, p. 239). After severing his ties with Syntex in 1945, due to a disagreement with his partners, but not before starting a new steroid company Botanica-Mex (Lehmann, 1992), Marker in 1949 at the age of 47 retired from chemical research (Redig, 2005).

Following Marker's departure, Syntex developed as an important research center where many talented scientists contributed to the growth of the steroid field, starting with G. Rosenkranz, who became the research leader in 1946 (Rosenkranz, 1992). He was able to reproduce Marker's original process to synthesize progesterone from another Mexican vegetable known as "Barbasco" (*Discorea composita*). This natural product was found to have a higher concentration of diosgenin than the original yam, which in turn could be transformed into androstenolone, an excellent source of testosterone and other related androgens (Lehmann, Bolivar, & Quintero, 1970). Another important figure was C. Djerassi, who developed the chemical process that led to the synthesis of cortisone and the anticonceptive pill at Syntex Laboratories in Mexico in 1951 (Goldzieher & Rudel, 1974), following his arrival there in 1949 (Ruiz Parra, 2004).

Methodological Considerations

In the present paper we adopt a different approach towards the study of the scientific and industrial activity developed in Mexico in the area of steroid research in the period 1935–1965. The literature written on the history of steroid research has focused on the specific contributions of individuals, institutions, and companies, the participation of Mexican peasants, and the industrial impact, without consideration of either the academic environment or of the scientific communication channels employed. Analysis of our bibliometric data combined with the study of certain parts of the papers (notes, footnotes, acknowledgments) deepens our understanding of the disciplinary and organizational structures that emerged in this period. It began with the use of a new raw material in the florescent steroid field that had an impact not only on the scientific community but also at the social, gender, commercial, and religious levels (Coleman, 2010; Drill, 1977; Goldzieher, 1993; Hirschmann, 1992). We also searched and studied the patents generated in Mexico during this period as another means to reconstruct the historiography of steroid research that cannot be ascertained from a study of the traditional scientific literature (Hogg, 1992).

Bibliometric approaches have proved relevant in many different contexts: policy decision making, individual and institutional evaluation, history of disciplines, bibliographic library management as well as other areas. In particular, we

[1]The literature on steroids mentions different years for this event so we decided to cut off our search when Syntex attains stock value (Zaffaroni, 1992) signifying impact beyond the academic sphere.

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are interested in studying the interrelationship between different bibliographic elements without discriminating against any type of scientific document or parts thereof, in our case the footnotes and acknowledgments, in order to establish trends and anomalies not generally observed through traditional research (Hérubel, 1999). The three malor dimensions in bibliometric studies: production, citation, and collaboration can all be applied in historical studies.

The study of partial or full-text, combined with bibliometric data, has not been a common practice; examples, however, can be found in Cronin's work on collaboration patterns revealed the acknowledgments in 20th century chemistry (Cronin, Shaw, & La Barre, 2004), as well as in the study of authorship and attribution practices in science and art (Cronin, 2012). The perspective achieved from combining basic bibliometric indicators with notes, footnotes, and acknowledgments in the text was useful for two main reasons: first, we were able to deepen our understanding of the elements and connections in the scientific communication web derived from the bibliometric information; and second, we were also able to recognize related aspects not apparent in the bibliometric data, but present in the scientific documents. These are important when working with historical scientific documents, as bibliographic databases extract information only from those structural fields found in modern scientific papers. For example, some of the affiliation addresses are found in the notes of earlier papers and are therefore not included in the bibliographic data set recovered from our database search. In order to distinguish these two types of occurrences, institutions that can be found directly in the affiliation field of the bibliographic reference recovered from databases we call primary affiliation and signify explicit participation of Mexican institutions in steroid research. The institutional names recovered from the notes and footnotes in the full text we term secondary affiliation. These add to the number of Mexican participants in each paper and also allow a fuller characterization of the flow of information within the scientific communication channels used in steroid research developed in Mexico.

In the construction and characterization of bibliometric indicators, bibliographic information can be selected from secondary sources or from the primary document. Basic information is standard to all scientific documents (books, articles, patents, notes, reports, etc.): for example, an author, date of publication, language of publication, and so on. Each type of scientific document has its own particular structure and style in which it is written. In their everyday work researchers adhere to these conventions; students are trained to follow the practices that underlie the scientific communication process (Russell, 2001).

The importance of considering other parts of the scientific document in addition to those traditionally represented in bibliographical records was highlighted by Cronin when he stated that acknowledgment data together with that on coauthorship networks form a solid base for indicators of collaboration and interdependence trends among scientists (Cronin, 2001). Acknowledgments have since been added as a field in the Web of Science (WoS) and used as an analytical tool, especially for funding data (Costas & Leeuwen, 2012; Díaz-Faes & Bordons, 2014).

In contrast to scientific documents, a patent is foremost a legal agreement conferring certain rights or privileges on the holder (Edwards, 1978). At the beginning of the 20th century there was controversy about the pertinence of patenting the findings of academic research (Weiner, 1987); in contrast, recent papers are exploring the relevance of patents as a fundamental part of the curriculum of the scientists (Guasch, 2007).

The strength of the production and citation averages of the Mexican research groups working on steroids can be easily appreciated just by examining the transition that took place in the field in mainstream journals during the period 1946–1965 due mainly to the Syntex group. Researchers at the Syntex Laboratories published over 54% of mainstream papers during this period, which in turn generated over 80% of all citations between 1944 and 1965. This is a situation never seen before at the international level for research groups associated with a developing country. Their contribution to the number of industrial patents was also overwhelming: 100% of the patents in the US related to steroids.

Materials and Methods

Bibliographic data of mainstream journal publications from 1935–1965 on the subject area of hormonal steroids were retrieved from three sources: WoS, Chemical Abstracts (CAS), and a local database on Mexican mainstream production in the first half of the 20th century (Luna-Morales et al., 2009). From CAS we also retrieved data on industrial patents registered by Mexican institutions in the subject area under study. In addition we searched the institutional database, TESIUNAM, on theses granted at UNAM. After selecting the names of the most productive researchers associated with Syntex, we looked for records where they appear as thesis advisers.

Our starting point for the formulation of the search strategies was the botanical literature on steroidal sapogenins, bearing in mind the need to highlight the change from animal to vegetable sources for the extraction of progesterone. This resulted in the use of the terms "sapoge -nin, nina, nins, nan (suffices in Spanish and English for the plant's scientific names), saponan, and steroid." The word "sapogenin" or any of the variants has to do with the properties of this family of plants; by adding "steroid" we translate the specific goal of our research (especially important for the use of subclasses in CAS) into a word/phrase type of search. Each database yielded different results; CAS gave us six different search combinations with the use of classes and subclasses, while in WoS the combination searches yielded 10. Because of the absence of a controlled vocabulary with respect to the content of the references, the search for these was a standard WoS topic, title, and abstract advanced search. The local database was used more as a control

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instrument to complement the mainstream bibliographic reference set with the use of library resources; institutional and author main searches were done with this resource. Of the 2,393 records retrieved, 1,011 met our general search criteria for articles on steroid research primarily related to natural vegetable sources. In 548 of these we found evidence of what we considered to be Mexican involvement in steroid research; that is to say, 410 with clear affiliation to at least one Mexican institution, plus 138 authored by R. Marker, prior to his sojourn in Mexico, marking the beginning of the experimentation with plants and the first associations with Mexican institutions.

An important part of our approach was to analyze the whole period from 1935 to 1965, even though the first time a Mexican address appears in our data was in 1946. By starting with 1935, the year of R. Marker's first paper on his search for a vegetable source of progesterone, we were able to span all published work that led up to the involvement of the Mexican institutions in steroid research.

Once the normalization process was complete, the next step was to recover the full text of papers in order to analyze their footnotes and acknowledgments. This we did with two main purposes in mind: first, to complete our bibliometric database essentially with respect to the affiliation field; and second, to complement the bibliometric results. The general process included: recovery of the full text (digital or print); analysis of the parts of the document where supplementary information could be found and addition of the appropriate fields to the database. It was possible to identify the gender of some of the participants from footnotes or by the prefix "miss" or by their full name.

Citations were recovered from WoS for all 78 years (1935–2012); counts were accumulated data starting from the publication year. An important finding from the revision of the full text was the presence of citations to patents. These were not added to the citation counts but referred to in our results due to the important role they play in the scientific communication process of this specialized field of study. In spite of the fact that steroidal research has been studied from the economic impact aspect, patents were not used as an information source. We consider that the bibliographic description of the patent recovered from CAS provides sufficient data in combination with our other findings to be of significance for our study.

Results and Discussion

Production

A total of 2,393 documents spanning the years from 1935 to 1965 were recovered. After filtering and erasing duplicates, 1,011 corresponded to papers published in mainstream journals, 548 of them with a Mexican association and 664 patent files, of which 563 were signed by a Mexican company. In the former case, only 54.4% of the papers had affiliations to a Mexican institution, while

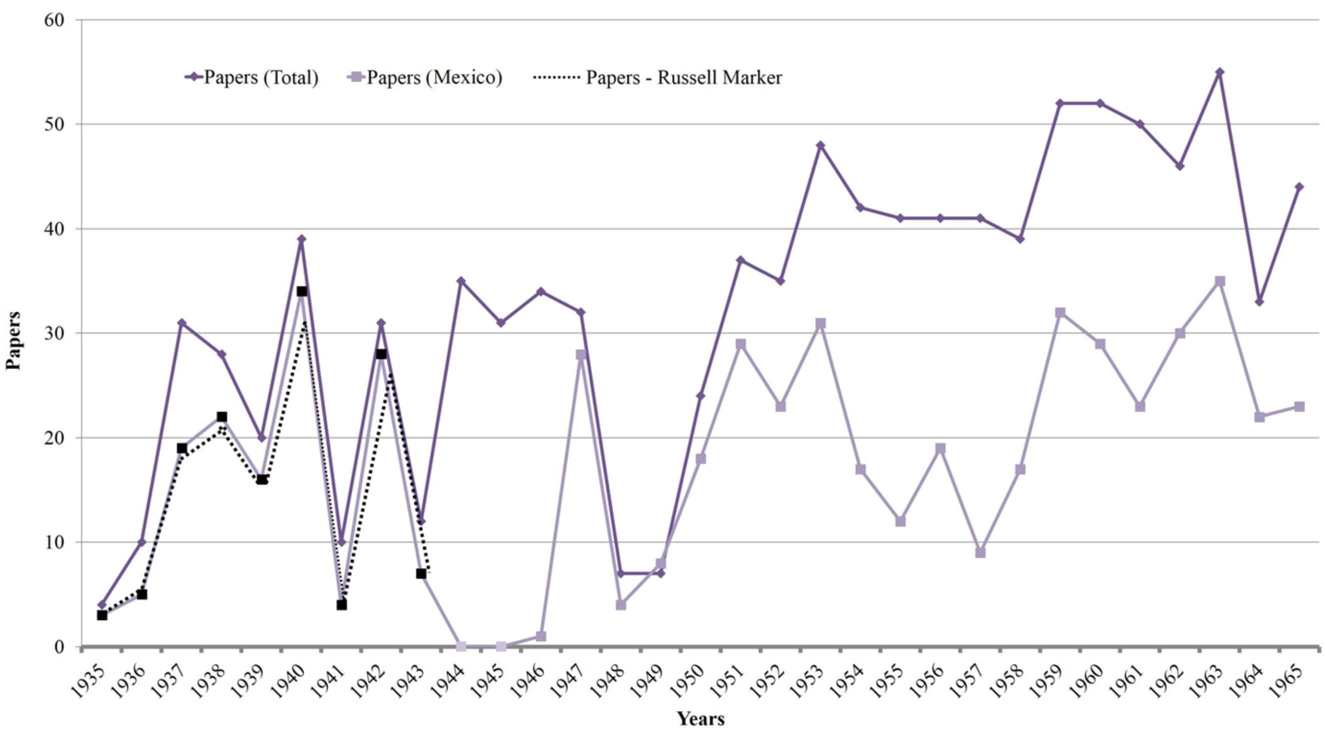

FIG. 1. Evolution of the number of papers on hormonal steroids registered in 1935–1965. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

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87.4% of the patents met our affiliation criteria. Figure 1 shows the distribution of documents published from 1935–1965. The dotted line shows R. Marker's production prior to his journey in Mexico, on the work that led to the discovery of Mexican yams and the synthesis of cortisone and progesterone.

Russell Marker's work clearly dominated production at this stage of our study period, accounting for 25.2% of all Mexican papers and 13.6% of the total production. Before 1946 Marker did not publish under a Mexican address; however, during this time we find evidence of his collaboration with Mexican institutions in the acknowledgments of his papers. In the period that follows he published with two different addresses: "Hotel Geneve, Mexico City, Mexico" and "Botanica-Mexico, S.A."; the first one was his home during his residence in Mexico, and the second the name of the second company he founded in the country (Lehmann, 1992). His last papers on steroid research were 24 published in 1947 and four in 1949. In the "Acknowledgment" section of the papers just mentioned, it is possible to appreciate the ensemble of participating institutions, as well as the details of the journey undertaken to collect and classify plants (Armería, 1972) that led to the discovery of "*Dioscorea mexicana*," colloquially named "Cabeza de Negro." One Mexican is mentioned among those involved:

> *"The extensive collections by the senior author were made possible only because of the kind and painstaking cooperation of the Botany Departments, Experimental stations and Range Ecology Departments of the following institutions: Texas A. and M. College, University of Arizona, University of California, New Mexico State College, North Carolina State College, Coker College, **University of Mexico**, Sol Russ College, University of Florida, Waco College, Purdy Botanical Gardens (Ukiah, Calif.), Laredo Cactus Gardens (Laredo, Texas), Missouri Botanicals Gardens, and Huntington Botanical Gardens (San Marino, Calif."* (Marker et al., 1943, p. 1199).

The quote was copied from the full text of the cited article. Even though such painstaking revision may seem like a lot of work, one of the advantages of historical bibliometrics is that the number of source documents is reasonably low and the benefits gained from a careful analysis of the full text is highly rewarding.

The period from 1935–1943, characterized by Marker's production prior to his settling in Mexico, is followed by 2 years of zero production in papers from Mexico and ultimately 21 years of intensive work authored mainly by researchers and students from Syntex that accounted for 35% (354) of the total production of papers (1,011) (Figure 1). Even though the difference between the total number of papers and those from Mexico in some years seems large, even more interesting is the fact that 29% (160) of the papers from Mexico were collaborations with authors from countries such as Belgium, Canada, Chile, Cuba, France, Guatemala, Israel, Switzerland, the UK, and the US; the communication among the majority of the participants in the race for the synthesis of cortisone and progesterone was intense.

According to Gereffi (1983) and Rasmussen (2002), the timing of the publication of new results in the steroid field was of strategic importance from economic and military standpoints. Consequently, we reviewed the supplementary information included in our database on the reception and publication dates for each article. We found that only 68.4% of the papers published from 1946 to 1965 included these dates, 51.5% of which were published within the same year of reception but the rest were delayed by at least some months. There was a general sense of urgency to publish in the race between pharmaceutical companies all over the world for the synthesis of steroids.

Articles published in meetings proceedings reinforced our data on the research done by Mexican institutions in the steroid field. We recovered 33 papers published in 19 proceedings of different meetings, most of which were held in the US.

Table 1 lists the primary and secondary affiliations of the Mexican institutions' participation in steroid research. Most of the literature on the history of steroid research acknowledges the Mexican contribution only via the Syntex Company. Although Syntex clearly dominates (64%) institutional production during the 20-year period shown in the table, we were able to identify the participation of a total of 15 other Mexican institutions in the period from 1946 to 1965. The "Papers" column refers to total papers (410) from 1946 to 1965 when Mexican institutions were actively involved and excludes the 138 papers published by Marker prior to 1946. The "Frequency" column refers to the number of times the institution appears as a secondary affiliation.

Table 1 includes only 410 documents of the total production of 548 (Figure 1) in order to illustrate two moments in the production dynamics: the first 9 years when Marker published 138 papers in the steroid research field and, although we found evidence of the first contacts made by the author with Mexican institutions, the affiliation field linkage was with North American institutions. The coverage in Table 1 includes all Mexican institutions publishing on steroids, including 28 papers authored by R. Marker with his two Mexican adscriptions: Hotel Geneve and Botanica-Mex.

In Table 1, a hyphen between the institutional names is used to connect the main collaborators among Mexican institutions with respect to steroid research; for example, the Syntex-UNAM collaboration is the strongest found between Syntex and any single Mexican university, with 29 papers. By taking into consideration secondary affiliations and not only coauthorships, we were able to show the full extent of the Mexican institutional participation and its connection to a wider collaboration network, especially when 5 of the 15 of the addresses recovered via secondary affiliations related to the thesis work of students.

From the data used to construct Table 1, we conclude that Syntex dominated production (82%) during the 21 years studied. But more than state the obvious, the relevant infor-

TABLE 1. Participation of Mexican institutions in steroid research (1946–1965).

Year	Primary affiliation	Papers	Secondary Affiliation	Frecuency
1946	Syntex	1	Syntex; Hotel Geneve	1
1947	Botanica-Mex (23); Syntex (2)	25	Hotel Geneve (6)	3
1948	Syntex (2); IPN; Syntex-IPN	4	IPN	1
1949	Syntex (4); Botanica-Mex (3); Hotel Geneve	8	Hotel Geneve (2); Hormosynth, S.A.	3
1950	Syntex (12); UNAM (3); Syntex-UNAM (2); IPN	16	Syntex	1
1951	Syntex (19); Syntex-UNAM (10)	29		0
1952	Syntex (20); Syntex-UNAM (2); Syntex-U Motolinia	23	U Motolinia	1
1953	Syntex (29); Syntex-UNAM (2);	31	Syntex (3)	3
1954	Syntex (14); Syntex-UNAM (2); UNAM	17		0
1955	Syntex (12)	12		0
1956	Syntex (15); UNAM (3); Syntex-UNAM	19	Syntex (2)	2
1957	Syntex (6); UNAM (2); Syntex-UNAM	9		0
1958	Syntex (16); UNAM-INIC	17	INIC	1
1959	Syntex (31); Syntex-UNAM; Syntex-U Motolinia	33	Syntex; UNAM; U Motolinia	3
1960	Syntex (26); Farquinal-Du Pont, Mexico; Syntex-UNAM; Syntex-IPN; UNAM	30	Du Pont, Mexico; UNAM; Syntex; IPN	4
1961	Syntex (20); Syntex-UNAM-IPN; UNAM; Laboratorios Hormona; Syntex-UNAM	24	UNAM (2); IPN; Syntex; Laboratorios Hormona	5
1962	Syntex (25); Syntex-UNAM (4); Syntex-IPN (2)	31	UNAM (2)	2
1963	Syntex (28); UNAM (2); Syntex-UNAM (3); Syntex-IPN; Syntex-UIA; Syntex-UNAM-U Guanajuato	36	Syntex (2); UIA; UNAM; U Guanajuato	5
1964	Syntex (22)	22	Syntex	1
1965	Syntex (18); UNAM (3); UNAM-UIA; Syntex-UNAM-UV	23	UIA; UV; UNAM	3
Total		**410**		

Note. IPN = Instituto Politécnico Nacional; UNAM = Universidad Nacional Autónoma de México; U Motolinia = Universdad Motolinia; INIC = Instituto Nacional de la Investigación Científica; Farquinal = Farmacéutica Química Nacional; UIA = Universidad Iberoamericana; U Guanajuato; UV = Universidad Veracruzana.

mation obtained from the affiliation field is that all institutions formed a collaboration web with only the exception of "Industria Nacional Químico-Farmaceutica, Laboratorios Farquinal, México," which appears only once in collaboration with DuPont. The UNAM is the second most productive Mexican institution, with 9% (84 papers) of which 41% (35) were published in scientific collaboration with Syntex, Wayne University, Universidad Católica de Santiago de Chile, Instituto Politécnico Nacional (IPN), Universidad de Guanajuato, or Universidad de Veracruz.

Table 2 shows the 51 sources where the papers of our interest[2] were published and the type of documents in each case.

The main tendencies in Table 2 are the predominance of the *Journal of the American Chemical Society* (JACS), accounting for more than 60% of papers, followed by a journal specialized in organic chemistry (12%), another chemistry, multidisciplinary[3] journal Journal of the Chemical Society, and in fourth position, the *Journal of Medicinal Chemistry*, each one with 2.3% of papers.

The specialized journal in the steroid field accumulated only seven papers and just four journals on the list are Mexican publications. These findings demonstrate the international character of the research and also the strategy used by the international research community in chemistry to make their work visible, preferring the more general, well-known titles to the more narrow specialized sources in the field.

The importance of listing all document types in Table 2 is because not all scientific discoveries are announced via articles. The most representative breakthrough in steroid research, the synthesis of progesterone and cortisone, was published in volume 73 of JACS, 1951, as a letter to editor.

Publication in proceedings points to the active participation of the Mexican researchers in academic events that gave them international exposure. This is reinforced by the fact that we found reference in the notes of 33 papers between 1950 and 1965 to participation in 19 different events, among them: Wisconsin Meeting of the American Chemical Society; Division of Medicinal Chemistry at the Chicago Meeting of the American Chemical Society; Atlantic City Meeting of the American Chemical Society; Los Angeles Meeting of the American Chemical Society; 6th National Medicinal Chemistry Symposium; Steroids and Natural Products Section of the Gordon Research Conference.

Articles (79%) were the main communication channels among chemists in the steroid field but the presence of other types of documents, like letters and notes,[4] each with 8%, is also significant. In spite of the relatively low percentages,

[2]548 when we include Marker's work.

[3]Journal categorization from *Journal Citation Reports*, attached to our bibliographic data extracted from Web of Science.

[4]In this case the type of document "Note" is different from the part of the document "notes"; in the first case we refer to the classification of documents used in the bibliographic databases, and the second refer to the complementary information found either at the end of each page or at the end of the document.

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TABLE 2. Source titles and document types in Mexican hormonal steroid research from 1935–1965.

	Source	Article	Letter	Note	Short communication	Others	Total
1	*Journal of the American Chemical Society*	276	37	20	0	1	**334**
2	*Journal of Organic Chemistry*	54	2	15	1	0	**72**
3	*Journal of the Chemical Society*	12	0	1	0	0	**13**
4	*Journal of Medicinal Chemistry*	10	2	0	0	1	**13**
5	*Tetrahedron*	10	2	0	0	0	**12**
6	*Ciencia (Mex.)*	7	0	0	0	0	**7**
7	*Steroids*	7	0	0	0	0	**7**
8	*Bulletin des Societes Chimiques Belges*	5	0	0	0	0	**5**
9	*Analytical Chemistry*	4	0	0	0	0	**4**
10	*Boletín del Instituto de Química de la Universidad Nacional Autóma de México*	4	0	0	0	0	**4**
11	*Chemistry & Industry*	4	2	9	0	0	**15**
12	*Acta Endocrinologica*	3	0	0	0	0	**3**
13	*Chemische Berichte*	3	0	0	0	0	**3**
14	*Journal of Biological Chemistry*	3	0	0	0	0	**3**
15	*Journal Of Pharmaceutical Sciences*	3	0	0	0	0	**3**
16	*Bulletin de la Societe Chimique de France*	2	0	0	0	0	**2**
17	*Endocrinology*	2	0	0	0	0	**2**
18	*Endokrinologie*	2	0	0	0	0	**2**
19	*Helvetica Chimica Acta*	2	0	0	0	0	**2**
20	*Journal of Chromatography*	2	0	0	0	0	**2**
21	*Revista de la Sociedad Química de México*	2	0	0	0	0	**2**
22	*Tetrahedron Letters*	2	0	0	0	0	**2**
23	*Applied Microbiology*	1	0	0	0	0	**1**
24	*Archives of Biochemistry and Biophysics*	1	0	0	0	0	**1**
25	*Beiträge zur Biochemie und Physiologie von Naturstoffen. Festschrift*	1	0	0	0	0	**1**
26	*Canadian Journal of Chemistry*	1	0	2	0	0	**3**
27	*Ciba Foundation Colloquia on Endocrinology*	1	0	0	0	0	**1**
28	*Chemical & Engineering News*	1	0	0	0	0	**1**
29	*Gazzetta Chimica Italiana*	1	0	0	0	0	**1**
30	*Journal of Bacteriology*	1	0	0	0	0	**1**
31	*Journal of Clinical Endocrinology and Metabolism*	1	0	0	0	0	**1**
32	*Journal Of The American Pharmaceutical Association*	1	0	0	0	0	**1**
33	*Memorias del Congreso Científico Mexicano. IV Centenario de la Universidad Nacional Autónoma de México*	1	0	0	0	0	**1**
34	*Mikrochemie Vereinigtmit Mikrochimica Acta*	1	0	0	0	0	**1**
35	*Proceedings North Central Weed Control Conference*	1	0	0	0	0	**1**
36	*Proceedings of the First International Congress on Hormonal Steroids*	1	0	0	0	0	**1**
37	*Proceedings of the Fourth International Congress of Biochemistry Vienna*	1	0	0	0	0	**1**
38	*Recent Progress in Hormone Research*	1	0	0	0	0	**1**
39	*Record of Chemical Progress*	1	0	0	0	0	**1**
40	*Revista Latinoamericana de Microbiologia*	1	0	0	0	0	**1**
41	*Tesis*	1	0	0	0	0	**1**
42	*Analyst*	0	0	0	0	1	**1**
43	*Angewandte Chemie-International Edition*	0	0	0	0	1	**1**
44	*Biochimica et Biophysica Acta*	0	0	0	1	0	**1**
45	*Experientia*	0	0	1	3	0	**4**
46	*Federation Proceedings*	0	0	0	0	2	**2**
47	*Fortschritte der Chemie Organischer Naturstoffe*	0	0	0	0	1	**1**
48	*Nature*	0	3	0	0	0	**3**
49	*Naturwissenschasten*	0	0	0	1	0	**1**
50	*Proceedings of the Chemical Society*	0	0	1	0	0	**1**
	Total	**438**	**48**	**49**	**6**	**7**	**548**

they played a vital role in the communication process of steroid research because of the need to be the first in publishing new results and to gain advantage over other research groups in the world (Herzog & Oliveto, 1992; Hogg, 1992; Rasmussen, 2002).

As well as the type of document used, the language of publication is an important element in the characterization of production. English was found to be the predominant language, with 89% of papers, most of them articles, notes, and letters. We also found documents in Spanish, French,

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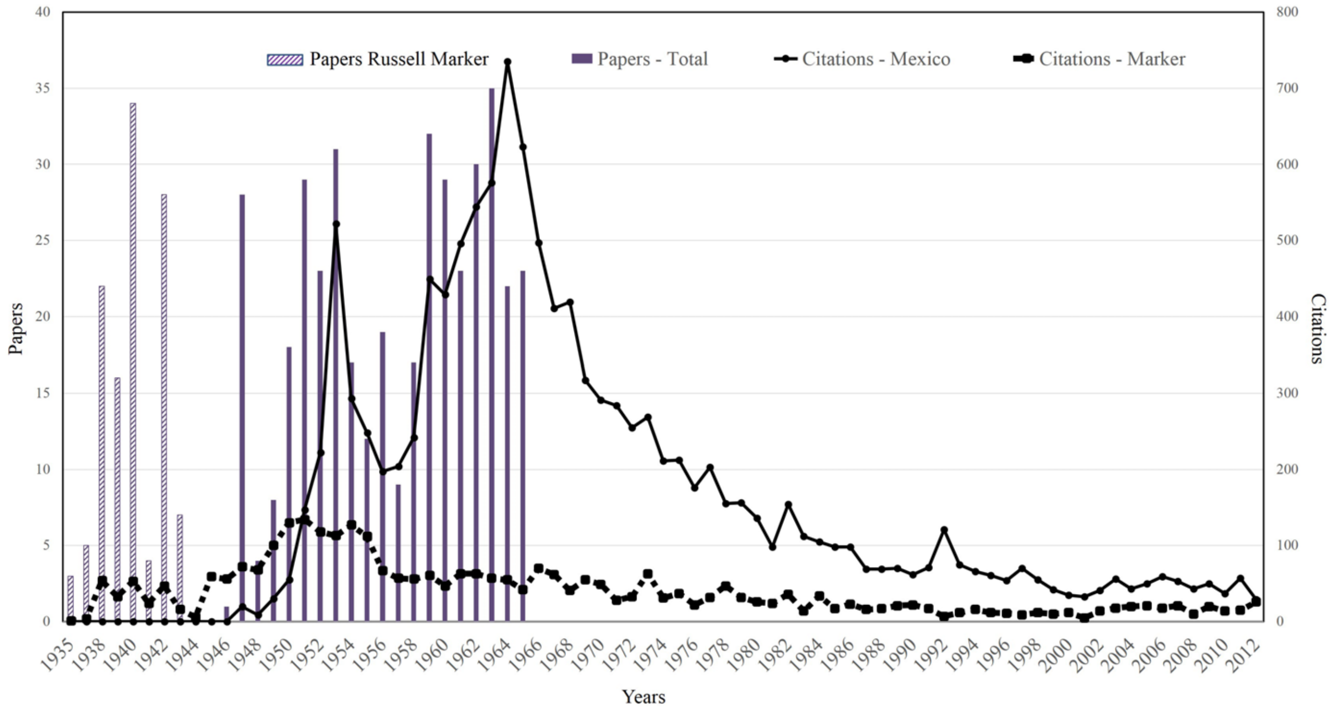

FIG. 2. Evolution of the number of papers on hormonal steroid research and their citations published in 1935–1965 in mainstream journals. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

and German, corresponding to the languages of the main collaborators of the leading authors, as well as to certain source publications.

In the 41st position we find the only incidence of a thesis indexed by CAS. From the review of the full text we found that 32 papers reported being part of the requirement for a bachelor or PhD degree, from eight different Mexican institutions: UNAM, IPN, Universidad Motolinia, Instituto Nacional de la Investigación Científica, Facultad de Química Berzelius, Universidad Iberoamericana, Universidad de Guanajuato, and Universidad de Veracruz.

Citations

The number of citations given to papers on steroid research published by Mexican institutions is presented in Figure 2. The high level of impact in this research field is evident from the noteworthy number of citations (14,588 citations) generated by the Mexican groups, as well as the historical importance of the research that continued to be cited over the 78 years (1935–2012) of our study period. The two peaks in Figure 2 represent the years of greatest impact of the production in steroid research as a whole; the first in 1953, accumulating 597 citations, and the highest point in 1964, with 810 citations.

Since the present study is one of the first to measure the impact of steroid research, it is not easy to set a comparative framework for our citations results. In the aforementioned bachelor's thesis with a citation/publication window from 1935–2007, similar to ours from 1935–2012, 14,852 citations were recovered from 839 papers in the period from 1935 to 2007 (López Orozoco, 2009). C. Djerassi citing Luis F. Fieser in a Gordon Conference on Natural Products mentions ~2,543 literature references found in the 1959 edition of Fieser's book *Steroids*, the acknowledged bible of the steroid field (Djerassi, 2006).

In Figure 2, the continuous line represents the citations given to papers with a Mexican institutional affiliation and the segmented line corresponds to the citations to Marker's work. Again, in this figure the papers published by Marker were separated by diagonal line bars from the papers with Mexican affiliations. His papers accumulated 21% of the total citations in three main stages from 1935 to 1943, with only 524 citations; the next 7 years when the papers captured more than 100 citations per year (834), and the rest during the following 57 years highlighting the historical importance of the contributions to the subject made by this author.

In the case of papers with a Mexican affiliation, the remaining citations (11,460) started 1 year after the first publication; in the first 3 years only 38 citations were given, followed by a 33-year period of high impact, accumulating more than 85% of total citations, followed by a period of progressively diminishing numbers of citations, and finally a period of stabilization in the impact of the research work.

Our baseline on steroid research for the period 1935–1965 starts with Marker's first paper published specifically in 1935. According to Laveaga (2005), R. Marker published a total of 147 articles on steroids and registered 75 patents during his stay at Parke, Davis & Company. However, the use of several bibliographic sources made it possible to

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TABLE 3. The 20 papers with the largest number of citations on hormonal steroid research.

	Author	Affiliation	Publication year	Source	Cites
1	Goldsmith, Dale PJ; Marker, Russell; Ruof, Clarence H; Ulshafer, Paul R; Wagner, RB; Wittbecker, Emerson.	CIBA Pharmaceutical,US; Hotel Geneve, Mexico; Du Pont Co., US; Merck and Co., US; Penn State Coll, US.	1947	JACS	464
2	*Mancera, Octavio*; Rosenkranz, George; Sondheimer, Franz	Syntex; Mexico	1953	*Journal of the Chemical Society*	210
3	Djerassi, Carl; *Miramontes, Luis*; Rosenkranz, George; Sondheimer, Franz.	Wayne University, US; Syntex, Mexico.	1954	JACS	181
4	Djerassi, Carl; ***Gatica, Josefina***; *Mancera, Octavio*; Rosenkranz, George.	Syntex; Mexico	1950	JACS	166
5	Djerassi, Carl; Kaufmann, Stephen; Pataki, J; *Romo, Jesus*; Rosenkranz, George.	Syntex; Mexico	1950	JACS	162
6	Cross, Alexander	Syntex; Mexico	1962	JACS	136
7	Bowers, Albert; Denot, E; Edwards, JA; Halpern, Otto; Villotti, R.	Syntex; Mexico	1962	JACS	111
8	Kaufmann, Stephen; *Martinez, H; Romo, Jesus*; Rosenkranz, George; Sondheimer, Franz.	Syntex; Mexico	1953	JACS	111
9	***Aguilera, Amanda***; Matthews, Joseph; ***Pereda, Ana Luisa***.	Syntex; Mexico	1962	*Journal of Chromatography*	109
10	*Batres, Enrique*; Bowers, Albert; Edwards, JA; Ringold, Howard; Zderic, John.	Syntex; Mexico	1959	JACS	106
11	***Amendolla, C***; Rosenkranz, George; Sondheimer, Franz.	Syntex; Mexico	1953	JACS	104
12	Marker, Russell; Tsukamoto, T; Turner, DL.	Kanazawa F, Japón; InstitutPahrmaMedClin, Alemania; Penn State Coll, US.	1940	JACS	104
13	Cross, Alexander; Harrison, IT.	Syntex; Mexico	1963	JACS	
14	*Batres, Enrique*; Halpern, Otto; Necoechea, E; Ringold, Howard.	Syntex; Mexico	1959	JACS	99
15	Djerassi, Carl; Ringold, Howard; Villotti, R.	Syntex, Mexico; Wayne University, US.	1960	JACS	99
16	Djerassi, Carl; *Mancera, Octavio*; Ringold, Howard; Rosenkranz, George; Sondheimer, Franz	Syntex; Mexico	1953	JACS	96
17	Marker, Russell; Rohrmann, E.	Penn State Coll; US	1940	JACS	95
18	Djerassi, Carl; *Mancera, Octavio*; Rosenkranz, George; Sondheimer, Franz.	Syntex, Mexico; Wiezmann Institute of Science, Israel; Wayne University, US.	1956	*Journal of Organic Chemistry*	94
19	Matthews, Joseph	Syntex; Mexico	1963	*Biochimica et Biophysica Acta*	93
20	*Becerra, R*; Bowers, Albert; *Cuellar, IL*; Denot, E.	Syntex; Mexico	1960	JACS	91

recover 138 (1935–1949) papers by R. Marker without the coauthorship of Mexican institutions in the subject area of steroid research for this period that received 3,098 citations. The citations before and after his arrival in Mexico represent 14% and 6% of total citations, respectively.

As the WoS does not consider citations to patents, these were retrieved from our full-text data. We found that 14 papers made reference to 19 patents: 10 from the US, three were German, and six Mexican during the years 1947 to 1963.

Table 3 lists in descending order the 20 most-cited articles, including the authors, institutional affiliation, year of publication, journal title, and the number of citations accumulated up to 2011. The papers authored by R. Marker are included. Several factors are evident from these data: the predominance of the JACS as the principal source of scientific communication in the field; the central role of Syntex; the participation of female researchers (highlighted); the importance of the scientific collaboration between Mexican and foreign institutions, the variety of scientists associated with Syntex, and the well-known participation of Mexican researchers (in italics).

Also noteworthy from Table 3 is the fact that 18 of the 20 papers were authored or coauthored by Syntex; only two were signed by a single author; the UNAM is the only other Mexican institution listed in the affiliation address; when we group the papers by decades, we find three from 1940 to 1949, 10 from 1950 to 1959, and seven from 1960 to 1969.

The scientific collaboration patterns suggest a highly concentrated institutional web with Syntex as the principal node at both the national and international level and a very diverse coauthor structure, mostly connected with Syntex (Hernández García, 2014).

Not all of the 20 references listed in Table 3 are articles: three are letters (positions 7, 8, and 9), one a note (position 2), and one a short communication (position 20). This emphasizes the importance of speed in the publication of results in

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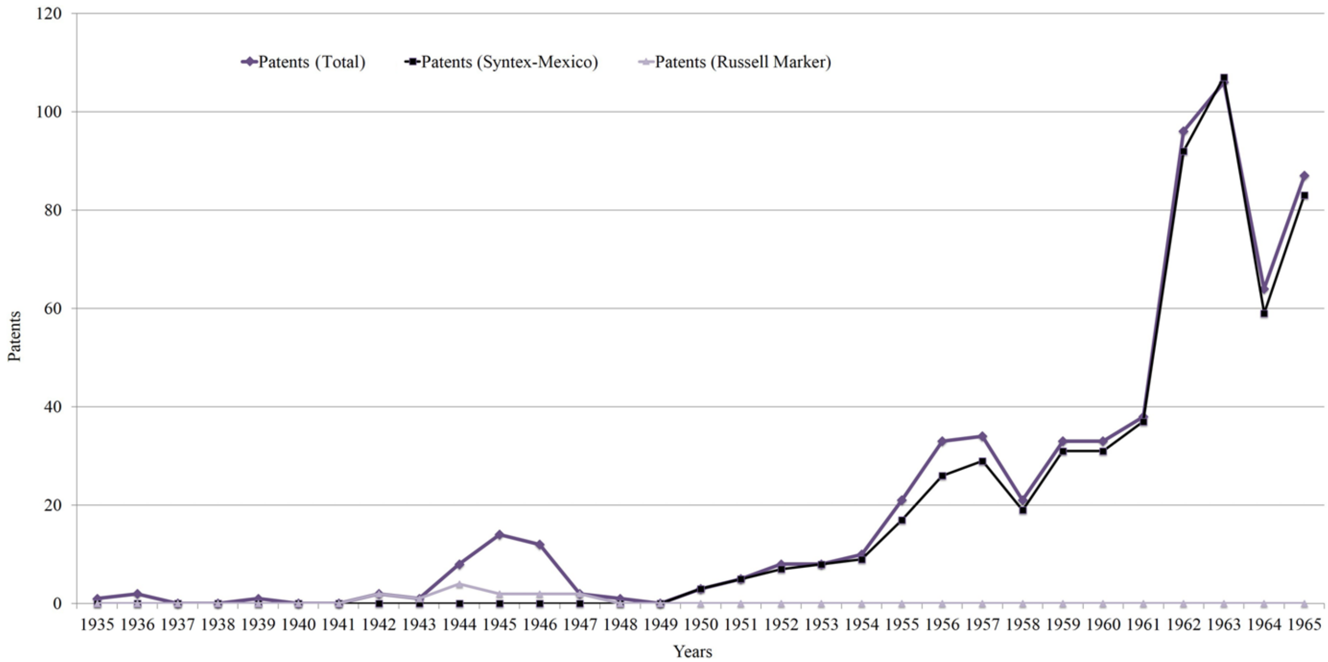

FIG. 3. Evolution of the number of patents in the hormonal steroid field, 1935 to 1965. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the steroid field at the time of our study period. Most of the papers listed were published in the 1950s, a historic decade in the synthesis of cortisone and oral contraceptives.

The names of the most active researchers in the field from both Mexican and international institutions are found among the authors listed in Table 3. Wherever possible we included full author names; women participated in 3 of the 20 most-cited papers; if we count the whole set of authors in our study period 18% were females (Hernández García, 2014). The affiliations correspond to those current at the time of publication; however, some authors associated with Syntex started as undergraduate or PhD students (J. Romo, O. Mancera, L. Miramontes), and some were supported by grants and fellowships from Wayne University, Eli Lilly, Squibb, or Pfizer.

Mexican researchers were involved in half of the 20 most-cited papers (in cursive); the Mexican researchers represent 30% of the total number of individual authors publishing during the total period of study. These were the ones who benefited most from the opportunity of working with their more experienced peers and participating in the "high-impact research" that constituted steroidal research in the mid-20th century.

Patents

Figure 3 compares the total number of patents in the steroid field for the period 1935 to 1965, with those authored by R. Marker or researchers from Syntex during the time the company was located in Mexico. In these 31 years, 642 patents were granted, 2% authored by Marker and 87% from Syntex, the rest correspond to companies like CIBA Co., Shionogi & Co., Merck & Co., Laboratories Jouveinal, Searle & Co., Monteclair Research Corp., Ellis-Foster Co., National Research Development Corp., and Laboratoires Français de Chimiotherapie, among others.

Unlike the production of papers, patenting was not a priority for R. Marker. Over a period of 6 years he was granted 13 patents, all connected with the corporation that sponsored most of his research, Parke Davis & Co. Syntex-Mexico dominates this scenario with a total of 107 patents granted from 1950 to 1963, although the total of patents granted to Syntex was 563.

In addition to the authors and the assignees, the patent references retrieved from CAS list the country of application[5] and the country of priority[6]; in the case of Marker's and the Syntex patents, the countries of application were the US, Germany, France, Netherlands, Great Britain, and Belgium; and Belgium, Mexico, France, and the Netherlands, the countries of priority of the applications.

Table 4 lists the names of the Mexican scientists associated with the Syntex patents granted during our study period. The majority were members of the Syntex research groups or students from the UNAM who also coauthored research papers as part of their graduate training at Syntex Laboratories. Table 4 was constructed by crossing information from our database with data collected from TESI-UNAM and from the full text and shows the importance of student participation in the patents on hormonal steroids research.

[5]Country where the patent was filed.

[6]Country with priority for exploitation of the patented artifact, knowledge, or process.

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TABLE 4. Mexican coauthors of the patents on steroids registered 1935–1965.

Patent year	Authors
1952	Luis Miramontes, Jesús Romo
1953	Jesús Romo
1954	Jesús Romo (2)
1955	Jesús Romo (3), Luis Miramontes (2), Octavio Mancera
1956	Luis Miramontes (3), Octavio Mancera
1957	Octavio Mancera (2), Felix Córdba, Jesús Romo
1958	Octavio Mancera (4), Enrique Batres (2), Jesús Romo
1959	Enrique Batres (2), Octavio Mancera (2), Jesús Romo (2)
1960	Octavio Mancera (5), Enrique Batres (2), Carlos Casas-Campillo, Jesús Romo (2), José Iriarte, Alberto Sandoval
1961	Octavio Mancera (3), Enrique Batres (2), Carlos Casas-Campillo (2), Jesús Romo, Jesús Romo Armería, Mercedes Velasco
1962	Octavio Mancera (6), Enrique Batres (5), José Iriarte, Jesús Romo
1963	José Iriarte (10), Octavio Mancera (4), Francisco Alvarez, Carlos Casas-Campillo, Mercedes Velasco
1964	Carlos Casas-Campillo (3), José Iriarte (3), Enrique Batres (2), Octavio Mancera, Mercedes Velasco
1965	Carlos Casas-Campillo (2), José Iriarte, Octavio Mancera, Mercedes Velasco

Note. Numbers in parentheses correspond to the number of times that Mexican students coauthored patents in each year.

In order to corroborate the original institution of the authors of the patent, information from the Bibliometric Database was crossed with that from the notes in the full text. All of them were connected in the first place to Syntex, and second to the Institute of Chemistry of the UNAM.

The participation of Mexican[7] students produced mutual benefits for Syntex and for the local universities:

> *". . . there was a formal agreement that the Institute* [of Chemistry, UNAM] *did the basic steroid research, communicated the results to Syntex and resulting papers were coauthored. . . . At that time transportation across the City was easy due to light traffic; when the Chemistry Institute was in Tacuba, students like Jesús Reynosa had a car, few people had cars in those days, so when he was told 'we need the dissolvent, go to Syntex,' he went and quickly returned. . . ."*[8]

A search in TESIUNAM[9] produced 27 undergraduate theses published between 1952 and 1965, with Syntex-related advisors: Enrique Batres, Albert Bowers, Howard J. Ringold, Ricardo Villoti, Joseph S. Matthews, Humberto Carpio, John Edwards, Alejandro Cross, Otto B. Halpern, Percy G. Holton, José Iriarte Guzman, Pierre Crabbe, Esteban Kauffmann, and Carl Djerassi. Luis Miramontes as well as a student or a Syntex collaborator, participated in six different patents.

Conclusions

The group of researchers in Mexico led by Syntex, created a scientific communication model characterized by multidisciplinary journals, with the article as the primary channel but with the inclusion of notes, short communications, and letters due to the importance of priority in the experimentation process and the announcement of new discoveries. Scientific collaboration was a significant social practice: both for the support and sharing of resources, as well as the training of young researchers and students from Mexican and foreign institutions.

The impact of the steroid research is reflected in the significant citations peaks, the numbers at certain moments, and the permanence in the accumulation of knowledge indicate a central role in the history of the field.

The patents derived from the academic research rank Mexico as an important reference for steroid research as does the recognition of the role played by Mexican students and researchers.

The alliance of Syntex Laboratories with the academic institutions and their involvement in patent production reinforce the concept of an industrial mode of scientific production that occurred when Mexican science: "*developed a new pattern of publication involving production and citation averages somewhat higher than those characteristic of the other three modes [amateur, institutional, and academic]*" (Luna-Morales et al., 2009, p. 1343).

Our study focused on key moments in steroidal research, such as the 1950s with the synthesis of progesterone and cortisone (Figure 1), or the impressive number of patents generated by Syntex (Figure 3). After the main research activity moved to Palo Alto, California, Syntex was left with a small but productive group, producing on average10 papers per year in the period 1965 to 2007 (López Orozoco, 2009).

Our study illustrates how information gathered from complementary sources and using complementary methods, in this case historical bibliometrics combined with the analysis of certain parts of the full-text documents, can lead to a more comprehensive view of events. In our case we were able to: (a) characterize an institutional network more complex than previous studies on steroid research had suggested, by extracting additional information on institutional adscriptions from footnotes and acknowledgments; (b) quantitatively illustrate the historic importance of steroid research; and (c) identify the participation of students (male and female) in scientific productivity as well as in the patent literature.

Acknowledgments

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[7]And foreign students too, but we are interested in the local participation.

[8]Personal communication, Dr. A. Romo de Vivar.

[9]Bibliographic database that registers the theses of all academic degrees granted by Universidad Nacional Autónoma de México. http://tesis.unam.mx/F

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