Work outsourced to Indian biotech and pharma companies is not yet significantly innovative

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Many Indian biotech and pharma companies undertake contract research for companies based abroad. In order to quantify the inventorship associated with this outsourcing, we have studied the US patents assigned to non-Indian companies, with inventors based in India. Of the 4094 patents in all disciplines, only 20 were relevant, an insignificant number. If creative skills in the drug discovery process are not being honed, the prospects of original drug discovery in India are poor. This should be a matter of concern to the Indian government and others concerned with the price of future drugs.

Keywords: Biotech and pharma industries, innovation, outsourcing, patents.

INDIA'S pharma industry is large and well known. Its strength has been the production of low-cost generics, which are used around the world, in both developing and developed countries, and this has led to its being called 'the pharmacy of the developing world'[1]. Although the industry has begun to do novel drug discovery work, so far it has not brought out any new drug. In contrast to the pharma industry, the country's biotech industry is much smaller, and less well known. Nevertheless, it has a number of companies doing work that is quite different from the pharma companies and some of this relates to drug discovery[2,3]. Many of these companies carry out work that is outsourced from the US or Europe. As a way of quantifying the innovativeness associated with executing this outsourced work – and thereby obtaining a window into the innovative R&D work going on in the Indian companies – we have undertaken a study of the US patents that have been assigned to non-Indian companies, but that have inventors based in India.

Methods

In order to identify each pertinent patent, we accessed the United States Patent and Trademark Office's Quick Search option at http://patft.uspto.gov/netahtml/PTO/search-bool.html. The following search was done, where 'IN' stands for India: ('IN' as 'Inventor Country') ANDNOT ('IN' as 'Assignee Country'). This was done using the most recent time-period option, that is '1976 to present', and data were collected up to 31 December 2009. We went on to classify the patents based on the assignees, whose work ranged from cereals to aerospace. In addition to companies, the assignees included universities, research institutions, other non-profit organizations and government agencies. There were also patents that listed individuals as assignees, and those that listed inventors but no assignee. Finally, and in error, the search also pulled up some patents assigned to Indian entities. For further analysis we selected a patent only if it (i) was assigned to a (non-Indian) pharma or pharma–biotech company, and (ii) was concerned with these areas of work. For the relevant patents, the inventor, a co-inventor or another knowledgeable colleague was then contacted in order to determine whether the inventor had done the work in India or elsewhere (see Supplementary File 1 for further details of methodology).

Results

The search for patents assigned to non-Indian organizations that had at least one inventor based in India yielded 4094 patents. The patents were then sorted into those that were relevant or non-relevant (Figure 1). Some were not considered further, for the following reasons: 371 listed no assignees, four were assigned to individuals, 38 were assigned to Indian organizations and 37 were assigned to foreign subsidiaries of Indian companies (details in Supplementary File 2). This left 3644 patents that were studied further. Of these, only 207 (6%) (details

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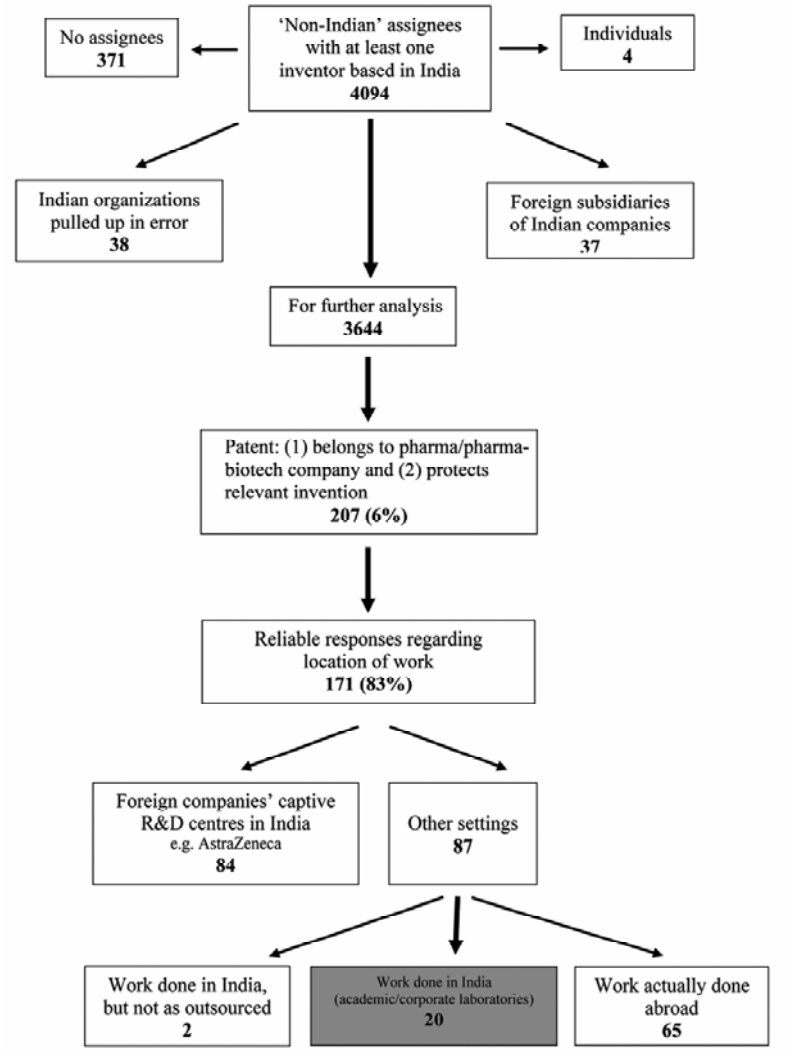

Figure 1. Flow chart of how patents were classified in order to identify those that represented work outsourced by foreign pharma and pharma–biotech companies to home-grown Indian companies.

in Supplementary File 3) were of interest since each patent fulfils three conditions: (i) it is assigned to a non-Indian pharma or pharma–biotech company, (ii) it embodies inventions related to these areas, and (iii) it lists one or more inventors based in India.

For the 207 patents, we went on to contact each India-based inventor (as listed on the patent), or his/her then colleagues, to determine whether or not the work had been done in India. We obtained an unequivocal answer for 171 (83%) of these patents. We also determined the type of organization in which the work on these 171 patents was done. The location of work fell into two broad categories: (a) Foreign companies' captive R&D centres in India. (b) Other academic or corporate settings. Of the 171 patents, 84 were in category (a), where work was carried out at the Indian research centres of companies such as AstraZeneca and Hoechst Aktiengesellschaft. The remaining 87 patents were in category (b). Within the latter category, there were four sub-categories: (i) work was truly outsourced to India (20 cases), (ii) the work was a continuation of a project initiated abroad (one case), (iii) compounds were sourced by a foreign company from an Indian academic institution (one case), and (iv) work that was actually carried out abroad (65 cases). For work done abroad, the inventors had returned to India when the patents were filed, and hence their apparent location in India during the course of the work. Thus there were only 20 cases of outsourcing to Indian academia or companies (Table 1). A total of five foreign companies outsourced the work that resulted in these 20 patents.

We further examined the timelines for applying for, and the issuance of, these 20 patents (Figure 2). The patents were mostly applied for between 1998 and 2006, and were largely issued between 2001 and 2009 (all dates inclusive).

Discussion

Of the large number of patents that are assigned to foreign companies that have one or more inventors based in India, about 6% is assigned to pharma or pharma–biotech

Table 1. The 20 US patents representing work carried out during outsourcing to Indian firms

Company	US patent number	Patent title
Abbott Laboratories (Abbott Park, IL)	5424444	Method of preparing enantiomerically-pure 3-methyl-5-(1-alkyl-2(S)-pyrrolidinyl) isoxazoles
Basilea Pharmaceutica AG (Basel, CH)	7423157	Substituted benzimidazoles and their use for inducing apoptosis
Basilea Pharmaceutica AG (Basel, CH)	7385061	Furazanobenzimidazoles
Genzyme Corporation (Cambridge, MA)	7576234	Synthesis of 2-alkyl amino acids
Genzyme Corporation (Cambridge, MA)	7294718	Synthesis of a 4-methylthiazole-4(S)-carboxylic acid compound
Genzyme Corporation (Cambridge, MA)	7285676	Synthesis of chiral 2-alkyl amino acids
Genzyme Corporation (Cambridge, MA)	7038073	Synthesis of 2-alkyl amino acids
Genzyme Corporation (Cambridge, MA)	7002036	Synthesis of 2-alkyl amino acids
Genzyme Corporation (Cambridge, MA)	6903220	Synthesis of chiral 2-alkyl amino acids
Genzyme Corporation (Cambridge, MA)	6875883	Synthesis of benzonitriles from substituted benzaldehyde
Genzyme Corporation (Cambridge, MA)	6875882	Synthesis of benzonitriles from substituted benzoic acid
Genzyme Corporation (Cambridge, MA)	6861532	Synthesis of 2-alkylcysteine
Genzyme Corporation (Cambridge, MA)	6846958	Synthesis of benzimidate from benzoic acid
Les Laboratoires Servier (Courbevoie Cedex, FR)	7521566	Process for preparation of perindopril and salts thereof
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6566538	Substituted oxygen alicyclic compounds, including methods for synthesis thereof
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6541647	Methods of synthesis of substituted tetrahydrofuran compound
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6433197	Substituted oxygen alicyclic compounds, including methods for synthesis thereof
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6403814	Method for synthesizing diaryl-substituted heterocyclic compounds, including tetrahydrofurans
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6310221	Methods for synthesis of substituted tetrahydrofuran compound
Millennium Pharmaceuticals, Inc. (Cambridge, MA)	6255498	Method for synthesizing diaryl-substituted heterocyclic compounds, including tetrahydrofurans

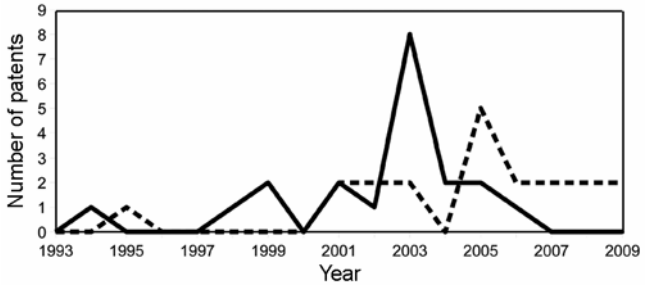

Figure 2. The timelines of (a) the application for and (b) the grant of 20 US patents connected to outsourcing to Indian firms. The solid line is for patent applications and dotted line for granted patents.

companies. This itself is a surprising finding, since globally, the pharma industry is one of the few where patents are important to commercial launches[4]. Thus, this number itself is indicative of the small size and low innovativeness of this industry in India.

Within the small number of pharma or pharma–biotech patents, about half are assigned to companies that have captive research centres located in India, and only 20 patents have directly resulted from outsourcing to Indian organizations so far. We first consider the conditions under which patents would arise during the outsourcing process. Discussion with scientists in companies in India revealed that the contract between the foreign client and the Indian contract research organization (CRO) would determine whether or not the latter's scientists may be listed as inventors on any resultant patents (Saberwal, unpublished). There are various situations in which this may happen such as: (i) if the CRO proposed a project based on its technology or capabilities to a client, in which case the client would fund the project and own the results, but the CRO scientists would be the inventors on the patent; (ii) the CRO and client company were both involved in conceptualizing the project, or (iii) if, during the course of carrying out the commissioned work, the CRO scientists created intellectual property. Even in these cases, the contract may preclude listing CRO scientists as inventors on a patent, and their contribution may instead be reflected in the higher financial returns to the CRO. Alternatively, as has sometimes happened in India, the client company did not expect the CRO to be innovative, and therefore this issue was not covered in the outsourcing agreement. Thus, the inventorship on a patent related to outsourced work may not be a perfect measure of innovative activity in the Indian company, but it provides one lens through which to understand the R&D activities of such companies. We have separately analysed US patents assigned to all home-grown pharma and pharma–biotech companies in India[5], and the current study supplements the earlier one.

Even as imperfect measures, these studies should serve as baselines for quantifying such innovative activity in the future. We would like to briefly discuss the issue of patent counts being an imperfect measure of inventive or innovative activities. Aside from patent counts, in Western nations, the R&D budgets, the number of products on the market or in development, and the number of products from each firm that are amongst the top selling, are some

of the other parameters used to quantify the innovation in this sector[6]. Nevertheless, in the Indian context, the lack of success in bringing out a new drug to date means that some of these parameters cannot be used. Indian companies do have products in development, but these efforts have not yet been quantified. Due to the inability to verify company statements, any self-declarations of molecules in development are also imperfect measures of R&D. Furthermore, the companies doing such product development are generally different from those doing outsourced work, although in the last few years some CROs have begun co-development programmes with Western companies [http://findarticles.com/p/articles/mi_hb5255/is_19/ai_n30977545/].

Just a few years ago it was reported that 36% of interviewed multinational companies had an interest in outsourcing discovery science[7]. Outsourcing is certainly happening, and many Indian companies are surviving or growing due to such contracts. To be noted is that all of the 20 inventions relate to chemistry and not to biology. This is not surprising since over 95% of the US patents assigned to Indian biotech or pharma companies are chemistry inventions[5]. What is somewhat surprising is that the patents have all been rather recent, over the last decade or so, and also that the number of applications has fallen to zero in the last three years of this study. Although the number is small, and it may be risky to draw conclusions from such a time-series, it is clear that there has been no large upsurge of patenting in recent years. Thus, there is probably a long way to go for Indian companies to undertake highly innovative work, at least in the context of outsourcing. Subsequent discussions with company scientists have confirmed that much of outsourced work is very basic and routine (Saberwal, unpublished), although the situation is slowly changing.

We wish to emphasize that this study does not attempt to quantify the inventorship associated with collaborative or co-development projects, where the assignees would be both a foreign company and an Indian company. Nor does it quantify the in-house R&D of Indian companies. It is focused on outsourcing projects alone, where the Indian company is not an assignee. It would be interesting to do another study to understand why more innovative projects are not outsourced and what the patterns of IP management in outsourcing contracts are. Ideally one should also compare the figures for outsourcing to India with those for China in order to compare the R&D activity of two large countries with growing pharma and pharma–biotech industries. However, a study such as that reported here requires a feel for local institutions and knowing at least some of the local company scientists in order to elicit their responses, and their assistance in contacting colleagues in other companies, on the question of where the work was performed. A comparative study with China would therefore have to be carried out separately, perhaps by researchers based there.

Conclusion

Using a quantitative, patent-based method we have found that an insignificant amount of patentable, innovative work has been carried out so far as part of the outsourcing process to Indian pharma and pharma–biotech companies. This finding should be a matter of concern to the Indian government that the domestic Indian industry is not big or sophisticated enough to attract more outsourced R&D work that involves inventorship by the Indian company. R&D is cheaper in India, and one assumes that any new drug that is ultimately developed here would be cheaper than a broadly similar one developed in the US or Europe. However, if creative skills in the drug discovery process are not being honed, the prospects of original drug discovery in India are poor and this will hinder affordable medicine in future. As the Government's newer initiatives to promote R&D in companies take effect[8], it will be interesting to re-examine the situation in a few years.

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Note: The supplementary files are available at http://www.ibab.ac.in/research_supply_mat.html

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