Methodology for Identifying Pharmaceutical Key Molecules Using Technology Foresight of Patent Documents

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Pharmaceutical companies use patents to protect the majority of their potential innovations. The content of patent documents is reverted into highly significant information, since the technical knowledge protected may be used for the research and development of new inventions or improvements. The pharmaceutical sector is one of the sectors that most protects its inventions because of the high costs incurred in the research and development of new products.

The different forms of patent protection in the pharmaceutical sector include the processes for producing a given active pharmaceutical ingredient (API). The first process patent applications are normally filed in the early stages of research, and in some cases are filed together with the actual patent for the molecule. When a product is successful on the market there is a technology race and other companies/researchers start to investigate potential routes for producing the molecule to find new ways of synthesizing it or improve aspects of its manufacture, such as using simpler reagents or reducing the number of stages in the synthesis process. These new routes are also protected by patents, as they may replace the route in the original patent.

Using technology foresight based on patent documents for production processes is a way of identifying key molecules for the production of a given API, since they contain descriptions of the reagents and intermediates involved in the process, and the physicochemical reaction conditions. Identifying the molecules is strategic, because it is through them that the number of synthesis stages can be reduced, and new production routes and/or analogous drugs can be developed.

This study sets forth a methodology for identifying the key molecules for an API, which can be summarized into the following six steps:

1) search for and select the process patents that explain the synthesis route, with an exact description of the inputs and intermediates involved;
2) identify all the inputs and intermediates present in the routes patented;
3) select the inputs and intermediates most frequently used in the routes;
4) compare the chemical structures of the most frequently cited inputs and intermediates with the target API;
5) seek producers/suppliers of the inputs and intermediates that are most structurally similar to the API;
6) select the key molecules for the API considering their structural similarity and the existence of a producer/supplier.

We also present the findings of a case study that used this methodology to search for key molecules (structurally similar reagents or intermediates) for the production of zidovudine, an API for antiretrovirals widely used in HIV/AIDS treatment around the world.

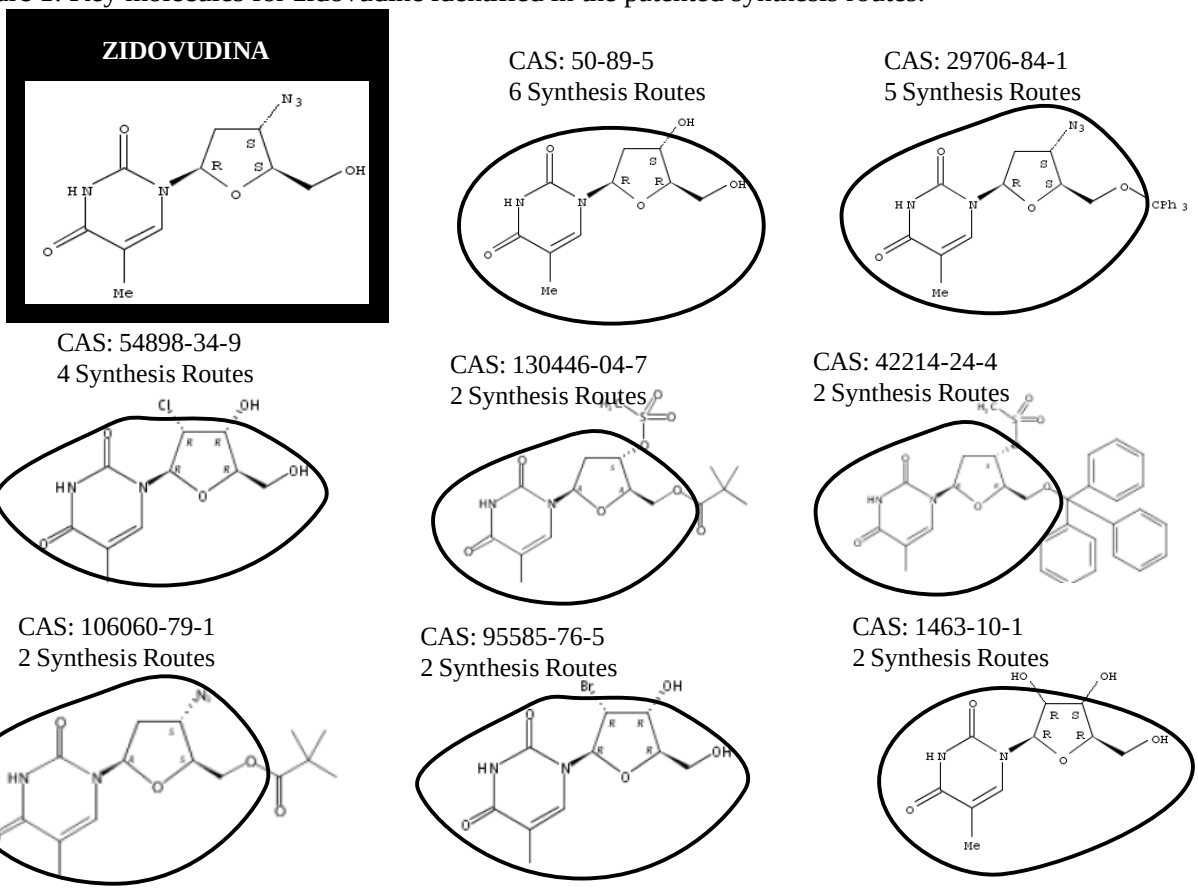
Patents for the synthesis of zidovudine were searched for and selected from the SciFinder Scholar® database, since it has filters that enable only documents for the synthesis of the target product whose

production route is detailed to be selected. The search covered patent applications filed since 1985, the year when the priority patent application for zidovidine was filed.

The search of the SciFinder Scholar® database yielded 21 patent documents for the zidovidine production process. After a qualitative analysis, 25 different synthesis routes for zidovudine were identified. All the reagents and intermediates from these routes were retrieved, and VantagePoint® software was used to select the ones that appeared most frequently. Of the 111 different molecules identified, it was found that 28 were present in more than one route. These 28 molecules' structural formulas were retrieved from the database and compared with that of zidovudine. Also, in line with the proposed methodology, a survey of producers/suppliers of the molecules was conducted.

Having selected the inputs that were most structurally similar to zidovudine and which had producers/suppliers, eight molecules were considered key for the production of zidovudine. These are demonstrated in Figure 1 below.

Figure 1: Key molecules for zidovudine identified in the patented synthesis routes.



Source: Based on the structural formulas extracted from the SciFinder Scholar® database

It is concluded that by processing data from patent documents, which in this study involved the synthesis reactions for an active pharmaceutical ingredient, it is possible to identify key molecules and even alternative molecules for the production of a drug. The proposal also envisages selecting advanced intermediates produced in other countries that could be acquired for the final synthesis of the drug by means of simple reactions. This could reduce costs and facilitate the production of drugs used in medicines with wide market acceptance.