PROCEDURE FOR THE ENANTIOSELECTIVE PREPARATION OF PROFENS AND PHENIDATES

DESCRIPTION OF THE TECHNOLOGY

Researchers from the Universitat Jaume I have developed and patented a new procedure for the efficient production of enantiopure forms of certain drugs of great commercial interest. The invention consists of an industrial method for the enantioselective synthesis of anti-inflammatory drugs, analgesics and medication for the treatment of attention deficit hyperactivity disorder, specifically, profens and phenidates. This method provides a simple direct means to obtain enantiopure forms of the abovementioned chiral drugs, thereby improving performance and limiting the generation of sub-products or residues.

Enantiomers are two isomeric forms of a chiral molecule that are mirror images of each other but are non-superposable. Both forms may be present together in the same drug, and can have different properties.

Profens, such as ibuprofen, are widely commercialised products. Nevertheless, although only one of the enantiomeric forms is active, some profens, such as ibuprofen, are marketed as a mixture of the two enantiomers; in other cases only the active enantiomer is commercialised. In those cases in which the mixture is commercialised, the underlying reason is that the enantiomer that is not active is not toxic and because no effective means of industrial enantioselective synthesis exists. There is a need for a method of preparing phenidates and profens in an enantioselective manner.

Different situations can be observed depending on the effects produced by a chiral drug in the organism. There are chiral drugs in which each of their enantiomeric forms can trigger opposing effects in the organism. In other cases the effect is similar but one enantiomer is more active than the other. In still other cases one enantiomer is active and the other remains inactive; and it is also possible that one enantiomer has a beneficial effect whereas the other is toxic.

In view of the drawbacks that may sometimes result from administering both chiral forms of the same drug, the pharmaceutical industry finds itself obliged to search for new stages of synthesis that enable them to obtain the desired chiral version, but without the other inactive, toxic or inefficient portion. One common method employed in industry to achieve this is to prepare the drug as a racemate (mixture of both enantiomers) and then carry out a resolution that allows the two chiral forms to be separated. Dexmethylphenidate (focalin), for example, is prepared by resolution. The problem with resolution, however, is that half the product is wasted.

The most efficient solution would be a directly enantioselective form of synthesis, without the need for an additional process involving its subsequent separation. And this is exactly what this invention offers: a procedure which can be applied at the industrial level that allows the synthesis of only one of the enantiopure forms of certain chiral drugs, such as profens and phenidates.

This procedure is simpler (since it dispenses with the intermediate resolution stage and therefore reduces the number of synthesis steps), allows for a more efficient use of the initial raw materials and reduces the generation of residues or sub-products. Furthermore, unlike other methods of enantioselective synthesis of profens, the procedure developed by the UJI does not use sophisticated reagents, which makes it much easier to implement at the industrial level.

SECTORS FOR COMMERCIAL APPLICATION

The technology is aimed at the pharmaceutical industry. More specifically, the invention can be applied by firms dedicated to the production of active ingredients and of anti-inflammatory drugs, analgesics and medicines indicated for the treatment of attention deficit hyperactivity disorder (ADHD).

TECHNICAL ADVANTAGES AND COMMERCIAL BENEFITS

The use of this technology can be beneficial for firms in the pharmaceutical sector and those working with active ingredients as it provides a procedure for preparing profens and phenidates in an enantioselective manner on an industrial scale. The main advantages of the invention are the following:

- It enables enantiopure forms of the drug to be obtained without the need to prepare it as racemate (a mixture of both enantiomers) and later carry out a resolution, which results in the loss of half the

product, and the process of synthesis is simplified.

- They are methods of synthesis that do not utilise sophisticated reagents, which makes it much easier to apply on an industrial scale.
- By using small amounts of phase-transfer catalysts (PTC), no toxic residues are generated and the final product obtained is free of any traces of toxic pollutant metals.

STAGE OF DEVELOPMENT OF THE TECHNOLOGY

Validated at the experimental level within a laboratory setting.

INDUSTRIAL AND INTELLECTUAL PROPERTY RIGHTS

This invention is protected by means of a Spanish patent with reference number P201830342 and filed on 04-05-2018.

COLLABORATION SOUGHT

- Licence agreement for use, manufacture or commercialisation.
- Development of applications.

RELATED IMAGES

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