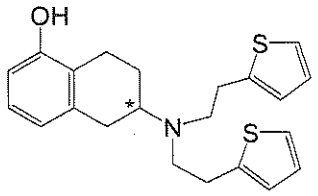
Therefore, normative research on the impurity is directly related to the quality and safety of marketed drugs.

By understanding the chemical structure and synthetic pathway of the impurities and by identifying the parameters which affect the content of impurities in the end product, management of impurities in medicinal active substance may be greatly enhanced. To monitor the impurities in the medicinal active substance, it is required to establish a quality standard to determine suitable separation and detection conditions, so as to control the impurities well. In the quality standard, the currently widely used impurity detection methods mainly comprise high performance liquid chromatography (HPLC) and like.

SUMMARY

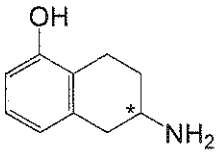
In one embodiment, the present disclosure provides a new, isolated compound as a reference compound for determining an impurity in rotigotine or a preparation thereof. The reference compound has a chemical name of 5,6,7,8-tetrahydro-6-[N,N-bis[(2-thienyl)ethyl]] amino-1-naphthol. In one aspect, there is provided a compound of~~and is represented by~~ formula (I):



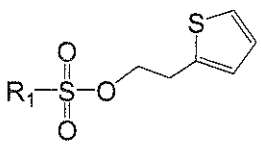
compound of formula (I)

in which (*) represents a chiral center, and the compound of formula (I) is a R or S configuration or a racemic mixture.

In another aspect, there is provided a method for preparing a~~The~~ compound of formula (I) as disclosed herein~~may be prepared by the following method~~, which comprises: reacting a compound of formula (II) with a compound of formula (III), and purifying the resulting compound of formula (I),



compound of formula (II)



compound of formula (III)

in which the compound of formula (II) is a R or S configuration or a racemic mixture, and R_1 is methyl, trifluoromethyl, methylphenyl or nitrophenyl, preferably 4-methylphenyl or 4-nitrophenyl, more preferably 4-methylphenyl.

In a further aspect, there is provided a use of a~~The~~ compound of formula (I) as disclosed herein~~may be used~~ as a reference compound for qualitatively or quantitatively determining an impurity in rotigotine or a preparation thereof, particularly, by high pressure liquid chromatography analysis. In yet another aspect, there is provided a method for determining the content of an impurity in rotigotine or a preparation thereof by high pressure liquid chromatography analysis, wherein the compound as defined above is used as a reference compound. The compound of formula (I) is dissolved in a solution to prepare a reference solution. Rotigotine or the preparation thereof is dissolved in a solution to prepare a test solution. HPLC chromatograms of the reference solution and the test solution are obtained by high pressure liquid chromatography analysis respectively. The retention time in the HPLC chromatograms of the reference solution and the test solution are compared to determine the test solution contains the compound of formula (I). More specifically, the peak areas of the compound of formula (I) in the HPLC chromatograms of the reference solution and the test solution are compared, and the content of the compound of formula (I) in rotigotine or the preparation thereof in weight percent is determined by an external standard method.

In various embodiments, the isolated compound of formula (I) has a purity of at least 95%, preferably, the isolated compound of formula (I) has a purity of at least 98%; and more preferably, the isolated compound of formula (I) is free of any other compounds or impurities.

In a further embodiment, the present disclosure also provides a high-purity rotigotine, containing the compound of formula (I) in an amount less than 0.5 weight percent.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig.1 is a high resolution mass spectrum of 5,6,7,8-tetrahydro-6-[N,N-bis[(2-thienyl)ethyl]]amino-1-naphthol.

Fig. 2-1 is an HPLC chromatogram of 5,6,7,8-tetrahydro-6-[N,N-bis[(2-thienyl)ethyl]]amino-1-naphthol.

Fig. 2-2 is an HPLC chromatogram of rotigotine.

DETAILED DESCRIPTION

One embodiment of the present disclosure provides a compound of formula (I):