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ENATIOMERIC ANALYSIS OF DULOXETINE HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS

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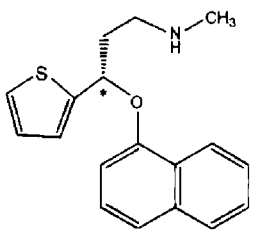
Introduction: Pharmaceutical companies have begun to appreciate that the safety and efficacy of many racemic drugs could be improved if they were marketed as the most active or least toxic enantiomer.[1] The enantiomers of chiral drugs often exhibit different pharmacological properties, and more and more chiral drugs are being developed as single isomers to avoid the use of larger doses or the risk of toxic effects.[2] Duloxetine hydrochloride is an active substance not described in any Pharmacopoeia and has the chemical name (+)-(S)-N-methyl-γ-(1-naphthalenyloxy)-2-thiophenepropanamine hydrochloride. The chemical structure of duloxetine hydrochloride is characterized as an optically active molecule, which presents one asymmetric carbon and therefore two enantiomers are possible. The S-enantiomer has been selected based on both in vitro and in vivo studies. According to the manufacturing process described, the S-enantiomer is routinely obtained and the R-enantiomer is considered as a specified impurity.[3]

Objective: The aim of the present work will be to develop and validate chiral chromatographic methods to determine S-Duloxetine in pharmaceutical formulations using liquid chromatography (LC) and capillary electrophoresis (CE). Also to perform stability studies and determine the possibility of chiral inversion of the S to R duloxetine form when exposed to factors as pH, temperature, ionic concentration, etc.

Materials and Methods: In the selection and optimization of LC conditions different chiral stationary phases and cyclodextrins will be tested in order to reach a satisfactory separation. Other factors including selection of mobile phase, flow, pH, choose of wavelength for detection, injection volume and analysis temperature will be studied. During the development of the technique for CE different experimental conditions are going to be tested and optimized considering the characteristics of the drug. Factors as size and extent of fused-silica capillary, mode and time of injection, composition, concentration and pH of the electrolyte, applied voltage and temperature of analysis will be tested. Compliance of the system as the resolution between the enantiomers, chromatographic capacity factor, peak asymmetry, theoretical plates and precision of injection will be investigated.

So far, the samples of pharmaceutical formulation Cymbalta® and standards of the S an R form of duloxetine were purchased. Thus, the objective is to establish procedures that can contribute to the scientific and technological field, improving the area of quality control, ensuring the safety and efficacy of pharmaceutical products.



Molecular structure of duloxetine

References:
1. I. Ali et al., CHIRALITY 19:453–463 (2007).
2. J. Yang et al., CHORMATOGRAPHY 66: 389-393 (2007).
3. European Medicines Agency (EMEA, 2005), www.emea.europa.eu/humandocs/PDFs/EPAR/cymbalta/19256704en6.pdf Acessed in 12.07.2010

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