ISSN 0102-6593

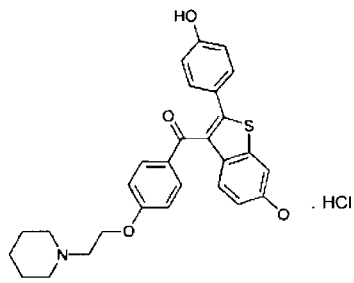
caderno de farmácia

Órgão Oficial da Faculdade de Farmácia da Universidade Federal do Rio Grande do Sul
volume 26, Suplemento, 2010

DEVELOPMENT AND VALIDATION OF ANALYTICAL METHODS FOR THE DETERMINATION OF RALOXIFENE HYDROCHLORIDE

Salazar, F. R.[1,*];; Bergold, A. M.[1];
[1]Laboratório de Química Farmacêutica, Faculdade de Farmácia, UFRGS
***Mestranda – Início: 2010/1**

Introduction: The decline in oestrogen levels is a major factor in postmenopausal osteoporosis, and there is evidence that giving hormone replacement therapy can ameliorate this condition. Newer non-hormonal agents have now been developed that exhibit agonist actions on some tissues and antagonist actions on others. These are termed *selective oestrogen receptor modulators* (*SERMS*) (RANG *et al*, 2006). Raloxifene is a SERM that has agonist activity on bone and the cardiovascular system, and antagonist activity on mammary tissue and the uterus. Although subject to a high first-pass effect, raloxifene has a very large volume of distribution and a long half-life (> 24 hours), so it can be taken once a day. Raloxifene has been approved in the USA for the prevention of postmenopausal osteoporosis. It is a non-steroidal benzotiophene derivative which prevents bone loss and also reduces serum cholesterol as a secondary activity (KATZUNG, 2006). It was developed by Eli Lilly Company and marketed as Evista® in the pharmaceutical form of tablets and in dosage of 60mg. Raloxifene hydrochloride molecular structure is presented above. Due to the relevance of this substance and the interesting of INCT-IF to synthesize this molecule, it becomes important to establish methodologies to assure the quality control of the pharmaceutical formulations and its therapeutical efficacy and security.
Objective: The aim of the present work will be to develop and validate methods for the determination of raloxifene hydrochloride, to be used in its quality control. The developed methods will be: non-aqueous titration, ultraviolet spectrophotometry (UV), liquid chromatography (LC) and capillary electrophoresis (EC).
Materials and Methods: In the selection of titration conditions the quantity of chemical substance that will be used, must be determined; for the titration 0,1M perchloric acid will be used. The best solvent and wavelength will be determined and also the ideal concentration range which obeys Lambert-Beer's law, will be selected for the UV method. Factors like selection of mobile phase, flow rate and pH, columns of different stationary phases, optimal wavelength for detection, injection volume and analysis temperature will be studied for the LC conditions. The influence of different parameters (nature and concentration of the running buffer, pH and applied voltage) on the migration time, peak symmetry and efficiency will be investigated to optimize the EC method. All proposed methodologies will be validated and comparative study will be performed (PAVITHRA & SIVASUBRAMANIAN, 2006 a,b; PEREZ-RUIZ *et al*, 2004).
Results and Discussion: Up till now, samples of pharmaceutical formulation of Evista® and the raloxifene hydrochloride raw material were purchased. A few tests, like melting point, solubility, dissection lost, humidity and infrared spectrophotometry were already performed.



Molecular structure of raloxifene hydrochloride

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Acknowldgements: Financial support from INCT_IF/Brazil and master scholarship from CNPQ/Brazil.