

# DENSITOMETRIC DETERMINATION OF RELATED SUBSTANCES AND IMPURITIES IN PROCESS CONTROL OF THE SYNTHESIS OF DOXAZOSIN MESYLATE

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Simple, fast and reliable quantitative TLC method for determination of impurities and related substances employed in process control of doxazosin mesylate synthesis is described.

Doxazosin mesylate is a quinazoline compound that is selective inhibitor of the  $\alpha_1$  subtype of alpha adrenergic receptors.

Its chemical name is 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(1,4-benzodioxan-2-yl-carbonyl) piperazine methanesulfonate. The empirical formula of doxazosin mesylate is  $C_{23}H_{25}N_5O_5 \cdot CH_4O_3S$  and molecular weight is 547.58.

Taking into account the route of synthesis of doxazosin mesylate and potential degradation pathways, four known impurities have been considered; two intermediate compounds, one synthetic impurity, and one degradation product.

The method separating all four impurities was developed and optimized in order to extend its applicability for determination of other potential impurities, which were encountered in process control during development stage.

As fast, low operating costs and simple sample preparation method, TLC was the method of choice for controlling production process. Due to more stringent requirements HPLC methods were developed and employed for assay and impurities determination in the final product.

Presented TLC method, developed for process control, has been validated in terms of important analytical parameters, thus ensuring not only fast, but also accurate and reliable results. This is especially important in dynamic environment where the whole process of production has to be done in accordance with GMP requirements.

Beside description of the developed method and validation of the same, paper is showing comparison of both, TLC and HPLC methods.

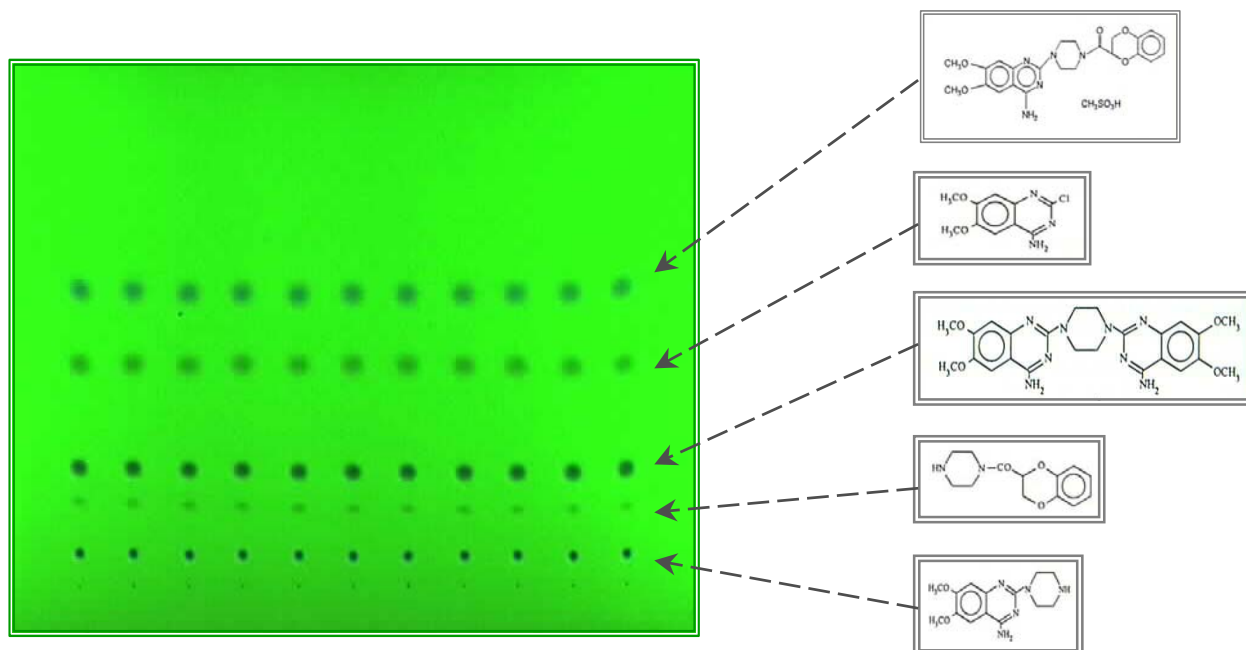


Figure1. TLC separation of impurities in process control of the synthesis of doxazosin mesylate