SIMULTANEOUS THIN-LAYER CHROMATOGRAPHY – DENSITOMETRIC ANALYSIS OF SIBUTRAMINE AND CITALOPRAM

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ABSTRACT
Due to the presence of sibutramine and citalopram in a number of drugs, neurotransmitter reuptake inhibitors. Sibutramine reduces the reuptake of serotonin, norepinephrine, and dopamine; citalopram is an antidepressant drug of the selective serotonin reuptake inhibitor. The thin-layer chromatography-densitometric behavior of some centrally acting serotonin reuptake inhibitors has been studied. The proposed analytical method is suitable for qualitative and quantitative analysis of sibutramine and citalopram.

Key words: sibutramine, citalopram, thin-layer chromatography-densitometric analysis

INTRODUCTION
Sibutramine (racemic mixture of R(+) and S(−) enantiomers of dimethyl-1-[1-(4-chlorophenyl)cyclobutyl]-N,N,3-trimethylbutan-1-amine) is usually available as sibutramine hydrochloride monohydrate and citalopram ((RS)-1-[3-(dimethylamino) propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile) – as citalopram hydrobromide. Sibutramine exerts its pharmacological actions predominantly via its secondary and primary amine metabolites. The parent compound, sibutramine is a potent inhibitor of serotonin (5-hydroxytryptamine) and norepinephrine reuptake in vivo, but not in vitro.1-3 As a central serotonergic and noradrenergic reuptake inhibitor, sibutramine activates a combination of serotonin and noradrenaline-mediated mechanisms to increase satiety and energy expenditure and decrease body weight.1,3,4 Sibutramine and its metabolites were identified by liquid chromatography/tandem mass spectrometry (LC/MS/MS) system.

The European Medicines Agency (EMEA) announced results of its safety review of drugs containing sibutramine and citalopram, citing the SCOUT date.4-6. Spectrophotometric7-9 and HPLC10-14 methods have been reported for analysis of sibutramine and citalopram. In the present article, we study sibutramine and citalopram using thin-layer chromatography (TLC)-densitometric method.

MATERIAL AND METHODS
Sibutramine and citalopram used as standard substances are of LC grade quality. All solvents and reagents used were of analytical grade quality from Merck (Darmstadt, Germany). 0.01M Phosphate buffer was prepared according to the chemical almanac (pH 7). A quantity of a ground capsules mass, equal to the average weight of one tablet was sonicated in ethyl acetate, filtered and evaporated and reconstitution of an aliquot of the extract was spotted on a silica gel thin-layer plate. The TLC plate was developed in an unsaturated chromatographic chamber containing 100 ml 0.01 M Phosphate buffer – acetonitril (35:65). Temperature, the mobile phase was allowed to travel 12 cm. The percentage of the active ingredient content of each capsule obtained by procedure was in the range of the amount except for one brand of sibutramine capsules and citalopram tablets. The products, applied as samples in the following study, are Reductil 10 mg, Abbot batch 550428 (containing sibutramine) and citalopram hydrobromide. We used Densitometer-E-BOX Vilber Lourmat apparatus (Fig. 1) with the following characteristics:
- it needed no additional PC
- Analysis and publication quality images
- Highly sensitive CCD camera, 12 bit image
- Compact Flash management background
- IP-address
- Print Option
- Optical Zoom
- Opportunity for optimum distribution of pixel.

STANDARD SOLUTION PREPARATION
The reference solution was prepared with concentration of 1 mg/ml sibutramine and 1 mg/ml citalopram, diluted in volumetric flask with ethyl acetate. The sample solution preparation of the samples containing 1 mg/ml analyzed substances were pre-

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pared by direct weighting of the accurate amount of 0.0010 ± 0.0001 g commercially available products and their dissolution in 100.0 ml volumetric flask with ethyl acetate.

RESULTS AND DISCUSSION

The Rf of sibutramine and citalopram were 0.50 and 0.20, respectively. The reliability of the method was assessed by evaluation of linearity 14000-24000 ng per band for sibutramine and 400-2400 ng per band for citalopram, accuracy 98.85 ± 0.29% for sibutramine and 98.95 ± 0.30% for citalopram and specificity in accordance with ICH guidance.

TLC-densitometry is preferred because of its simplicity, ease and low cost. All analytical parameters are verified for the different pharmaceutical dosage forms, which allows the validation of the proposed TLC-densitometric method and its application in pharmaceutical practice.

ACCURACY

Model mixtures containing placebo and mix sibutramine and citalopram as analyzed substances were prepared with concentration of sibutramine and citalopram equivalent to 50%, 100% and 150%, for determination of the methods accuracy. These samples were analyzed three times each.

LINEARITY

Six standard solutions with decreasing concentration were prepared and analyzed for determination of linearity. The standard deviation and the correlation coefficients were calculated.

SPECIFICITY

Samples containing sibutramine capsules and samples containing citalopram tablets dosage forms, reference substances and placebo were analyzed for determination of the analytical parameter specificity. There were not spots of the placebo solutions. This shows that there is no influence of the ingredients on the behavior of the analyzed sibutramine and citalopram in the desired TLC analytical zone.

CONCLUSIONS

All analytical parameters are verified for the different pharmaceutical dosage forms, which, allows the validation of the proposed TLC—densitometric method and its application in pharmaceutical practice. TLC—densitometry is preferred due to its simplicity, ease and low cost. The proposed analytical method is suitable for qualitative and quantitative analysis of Sibutramine and Citalopram.

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