Master Thesis Abstract

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" Analytical Study on Some Drugs used for Treatment of the Gastrointestinal Tract "

The thesis comprises four parts:

Part I: General Introduction

This part comprises a brief idea about gastrointestinal disorders and GIT drugs' classification and mechanism of action.

Part II: Simultaneous Determination of Nifuroxazide and Drotaverine hydrochloride in Pure Forms and in Pharmaceutical Preparation

This part includes a general introduction about the chemistry and mode of action of nifuroxazide and drotaverine hydrochloride, followed by a presentation of the reported methods used for their quantitative determination. Experimental, results and discussion are also given.

This part comprises three sections:

Section (A): Simultaneous Determination of Nifuroxazide and Drotaverine hydrochloride by the Spectrophotometric Method

In this section, nifuroxazide could be determined in presence of drotaverine hydrochloride using a zero order spectrum with an analytically useful maximum at 364.5 nm. The absorbance obeyed Beer's law over a concentration range 2 – 10 $\mu g.ml^{-1}$ with mean percentage recovery 100.08 ± 0.606 %. Determination of drotaverine hydrochloride in presence of nifuroxazide was obtained by second derivative D_2 spectrophotometry at 243.6 nm. The peak height response obeyed Beer's law over a concentration range of 2 – 10 $\mu g.ml^{-1}$ with mean percentage recovery 99.82 ± 1.461 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the

pharmaceutical formulation containing the above drugs with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated ones indicating no significant difference with respect to accuracy and precision.

Section (B): Simultaneous Determination of Nifuroxazide and Drotaverine hydrochloride by the Spectrodensitometric Method

In this section, both drugs are separated on a silica gel plate using chloroform: acetone: methanol: glacial acetic acid (6: 3: 0.9: 0.1 v/v/v/v) as a mobile phase and UV detection of both bands at 365 nm over a concentration range of 0.2 – 1 μg.band^{-1} for both drugs, with mean percentage recoveries 99.99 ± 0.148 % and 100.00 ± 0.335 % for nifuroxazide and drotaverine hydrochloride respectively.

The selectivity of the proposed method was checked using laboratory prepared mixtures. It was successfully applied to the analysis of the pharmaceutical formulation containing the above drugs with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Section (C): Simultaneous Determination of Nifuroxazide and Drotaverine hydrochloride by the RP-HPLC Method

In this section, a RP-HPLC method was applied which utilizes acetonitrile: water (40/60 v/v, adjusted to pH 2.55 by orthophosphoric acid) as a mobile phase and pentoxifylline as internal standard. The flow rate is 1 ml.min^{-1} and the effluent is detected at 285 nm at ambient temperature over a

concentration range 2 – 10 µg.ml^{-1} for both drugs with mean percentage recoveries 100.24 ± 1.511 % and 100.08 ± 0.778 % for nifuroxazide and drotaverine hydrochloride respectively.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the pharmaceutical formulation containing the above drugs with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Part III: Determination of Bisacodyl in Pure Form and Pharmaceutical Preparations by Three Stability Indicating Methods

This part includes a general introduction about the chemistry and mode of action of bisacodyl, followed by a presentation of the reported methods used for its quantitative determination. Experimental, results and discussion were also given.

This part comprises three sections:

Section (A): Spectrodensitometric Determination of Bisacodyl in Presence of its Degradation Products

In this section, bisacodyl was determined via separation from its degradation products on silica gel plates using chloroform: acetone (9: 1 v/v) as a mobile phase with UV detection of the separated bands at 223 nm over a concentration range of 0.2 – 1.4 µg.band^{-1} with mean percentage recovery 100.35 ± 1.923 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the

pharmaceutical formulations containing bisacodyl with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the HPLC reference method. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Section (B): Spectrophotometric Determination of Bisacodyl in Presence of its Degradation Products

In this section, a fourth derivative D_4 spectrophotometric method was applied, which allows determination of bisacodyl in presence of its degradation products in raw material at 223 nm using acetonitrile as solvent with obedience to Beer's law over a concentration range 2 – 18 $\mu g.ml^{-1}$ with mean percentage recovery 99.77 ± 1.056 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures.

The results obtained for the analysis of pure samples of bisacodyl were statistically compared with those obtained by applying the HPLC reference method and no significant difference between the results was obtained.

Section (C): Determination of Bisacodyl in presence of its Degradation Products by Three Spectrophotometric Multivariate Methods

In this section, the spectrophotometric data of bisacodyl and its degradation products using absolute ethanol as solvent were processed by three chemometric techniques namely classical least squares (CLS), principal component regression (PCR) and partial least squares (PLS). A training set consisting of 15 mixtures containing different ratios of Bisacodyl and its degradation products was used for construction of the three models. A validation set consisting of 6 mixtures was used to validate the prediction ability of the suggested models. The three mentioned chemometric methods were applicable over a concentration range between 2 - 14 $\mu g.ml^{-1}$ with mean

percentage recovery 99.97 ± 0.865, 100.01 ± 0.749 and 99.97 ± 0.616 for the three mentioned models respectively.

The selectivity of the proposed method was checked using laboratory prepared mixtures (validation set) and it was successfully applied to the analysis of the pharmaceutical formulation containing bisacodyl with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the HPLC reference method. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Part IV: Stability Indicating Methods for Determination of Metopimazine in Presence of its Oxidative Degradation Product

This part includes a general introduction about the chemistry and mode of action of metopimazine, followed by a presentation of the reported methods used for its quantitative determination. Experimental, results and discussion were also given.

This part comprises three sections:

Section (A): Spectrofluorimetric Determination of Metopimazine in Presence of its Oxidative Degradation Product.

In this section, metopimazine was determined by measuring its native fluorescence in presence of its oxidative degradate at λ_{em} 505 nm upon excitation with λ_{ex} 336 nm after applying in a finally processed equation over a concentration range 0.1 - 2 $\mu g.ml^{-1}$ with mean percentage recovery 100.64 ± 1.349 %.

The method was further applied to the in vitro determination of metopimazine in spiked human serum. The mean % recovery (n = 4) was 98.09 ± 0.390 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the pharmaceutical formulation containing metopimazine with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Section (B): Spectrophotometric Determination of Metopimazine in Presence of its Oxidative Degradation Product.

In this section, a second derivative D_2 spectrophotometric method was applied. It allows determination of metopimazine without interference of its oxidative degradate at 270.5 nm using methanol as a solvent, with obedience to Beer's law over a concentration range 1 - 16 $\mu g.ml^{-1}$ with mean percentage recovery 100.13 ± 1.660 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the pharmaceutical formulation containing metopimazine with recovered interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

Section (C): Spectrodensitometric Determination of Metopimazine in Presence of its Oxidative Degradation Product.

In this section, metopimazine was determined via separation from its oxidative degradate on silica gel plates using chloroform: methanol (6: 4 v/v) as a mobile phase and UV detection of the separated bands at 265 nm over a

concentration range of 0.4 – 1.4 µg.band^{-1} with mean percentage recovery 100.18 ± 1.562 %.

The selectivity of the proposed method was checked using laboratory prepared mixtures and it was successfully applied to the analysis of the pharmaceutical formulation containing metopimazine with no interference from other dosage form additives.

The validity of the suggested procedure was further assessed by applying the standard addition technique.

The results of the proposed method were statistically compared with the reference method adopted by the manufacturer company. The t and F values were found to be less than the tabulated figures indicating no significant difference with respect to accuracy and precision.

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