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# Simultaneous Estimation of A Three Component Mixture of Aspirin, Caffeine and Orphenadrine Citrate by Uv Spectrophotometric Method of Absorbance Correction for Interference

KEYWORDS: Aspirin, Caffeine, Orphenadrine citrate

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**ABSTRACT** *A simple, rapid, sensitive, accurate and economical UV spectrophotometric method was developed and validated for the simultaneous estimation of aspirin, caffeine, and orphenadrine citrate by absorbance corrected for interference method using 0.1 N NaOH as solvent. The method employs measurement of aspirin at 308 nm, measurement of corrected interference at 278 nm for estimation of caffeine and at 224 nm for estimation of orphenadrine citrate. Beer's law was obeyed in the concentration range of 3-24 µg/mL for aspirin, 1-12 µg/mL for both caffeine and orphenadrine citrate with r2 value of 0.999, 0.999, and 0.994 respectively. Accuracy was determined by recovery studies and showed percent recovery ranging from 95.76-100.33% for aspirin, 100.7-102% for caffeine and 100.66-105% for orphenadrine citrate. The mean RSD was found to be less than 2%. The developed method can be used in QC laboratory for routine analysis to ensure the identity, purity, and performance of the drug product.*

**Introduction**

Aspirin, 2-(acetyloxy) benzoic acid is an analgesic, antipyretic and anti-inflammatory agent. It directly and irreversibly inhibits the activity of COX-1 and COX-2 to decrease the formation of prostaglandins and thromboxanes from arachidonic acid. It also has platelet aggregation inhibitory effect (Drug Profile, 2013). Caffeine (1,3,7-trimethyl-2,3,6,7tetrahydro-1H-purine-2,6-dione) is a CNS stimulant and is used together with NSAIDs for simple headaches (Drug Profile, 2013). Orphenadrine citrate, [dimethyl({2-[(2-methylphenyl)(phenyl)methoxy]ethyl})amine is an anticholinergic drug of ethanolamine antihistamine class used to treat painful muscle spasms (Drug Profile, 2013).

The method is based on the principle that if the identity, concentration and absorptivity of the absorbing interferents are known, it is possible to calculate their contribution to the total absorbance of the mixture. The concentration of the absorbing component of interest is then calculated from corrected absorbance.

Review of literature revealed two derivative spectroscopic methods (Abdel-hay, Galal, and Ragab, 2007) and one HPLC method (Darwish,, Salama and Mostafa, 2012) for the simultaneous estimation of aspirin, caffeine, and orphenadrine citrate. However no UV spectroscopic absorbance corrected for interference method was found available for estimation of aspirin, caffeine and orphenadrine citrate. Therefore it was desirable to develop a simple and sensitive UV spectroscopic absorbance corrected for interference method for the estimation of aspirin, caffeine, and orphenadrine citrate in combined dosage form. The method employs measurement of aspirin at 308 nm, measurement of corrected interference at 278 nm for estimation of caffeine and at 224 nm for estimation of orphenadrine citrate.

**Materials and methods**

UV visible double beam spectrophotometer, LABINDIA ANALYTICAL UV 3000+ was used for the study.

**Materials:**

Chemicals of analytical grade and solvents of spectroscopic grade were used. Gift sample of orphenadrine citrate was provided by RL Fine Chemicals, Bangalore; aspirin and caffeine from West Coast Laboratories, Mumbai.

**Methods:**

**Selection of solvent:**

After assessing the solubility of the three drugs and spectra in different solvents, 0.1 N NaOH was selected as the solvent for the present study.

**Preparation of working standard solution:**

Standard stock solutions of aspirin, caffeine, and orphenadrine citrate were prepared by dissolving 10 mg each in 10 ml 0.1 N NaOH. From the stock solution, working standard solution was prepared by appropriate dilution to 10 ml with the same solvent.

**Selection of analytical wavelengths**

Working standard solutions of aspirin, caffeine, and orphenadrine citrate prepared individually from the standard stock solution were scanned in the wavelength range from 200-400 nm to finalize the analytical wavelength for the present study.

**Construction of calibration graphs**

From the working standard solutions, solutions of different concentrations were prepared for all the three drugs and their absorbance was measured for aspirin at 308 nm, measurement of corrected interference at 278 nm for estimation of caffeine and at 224 nm for estimation of orphenadrine citrate. Linearity range was determined by graphical plot with co-ordinates of absorbance vs. concentration.

**Determination of absorptivity coefficients**

Absorptivity coefficients were calculated for all the 3 drugs in their linearity range at 308 nm, 278 nm, and 224 nm using the formula:

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a=A/c l

where a = absorptivity coefficient
A = absorbance
c = concentration in g/ ml
l = pathlength ( 1cm)

The absorptivity values for aspirin (x), caffeine (y), and orphenadrine citrate (z) were determined at 308 nm, 278 nm, and 224 nm respectively and substituted to generate the following equations:

At 308 nm, $C_x = A_1/144$ .....(1)
At 278 nm, $C_y = A_2 - 108.21c_x/522.86$ .....(2)
At 224 nm, $Cz = A_3 - (432.14c_x + 339.81c_y)/154.83$ .....(3)

Application of the method to the analysis of aspirin, caffeine and orphenadrine citrate in the three component mixture:

Tablets, twenty in number each containing 385 mg aspirin, 30 mg caffeine and 25 mg orphenadrine citrate were obtained. The average weight of each tablet was determined. The tablets were crushed to fine powder and an accurately weighed quantity of powder equivalent to 10 mg of aspirin was transferred to 100 ml volumetric flask and extracted with 0.1 N NaOH by shaking it for 20 min. The volume was made up with the same solvent and filtered to obtain sample stock solution. From this 0.96 ml was transferred to 10 ml volumetric flask and volume made up to obtain working sample solution of the three drugs and its absorbance was measured at all the three selected wavelengths. The content of aspirin, caffeine and orphenadrine citrate in sample solution of tablet was calculated using proposed method.

**Results and Discussion**

A UV spectrophotometric method for the simultaneous estimation of aspirin, caffeine and orphenadrine citrate using absorbance corrected for interference was developed. The solvent selected for the study was 0.1 N NaOH as the absorptivity for aspirin was 144, caffeine was 522.86, and orphenadrine citrate was 154.83 respectively and found to be satisfactory by measuring the absorbance of aspirin, caffeine, and orphenadrine citrate respectively. From the overlain spectra (Fig 1), 308 nm, 278 nm and 224 nm were selected as the wavelengths for the study as at 308 nm only aspirin showed absorbance, at 278 nm aspirin and caffeine showed absorbance and hence absorbance corrected for caffeine was calculated by deducting the contribution of aspirin towards the total absorbance of mixture. At 224 nm all the drugs showed absorbance and hence for estimation of orphenadrine citrate, the absorbance of aspirin and caffeine were corrected for interference.

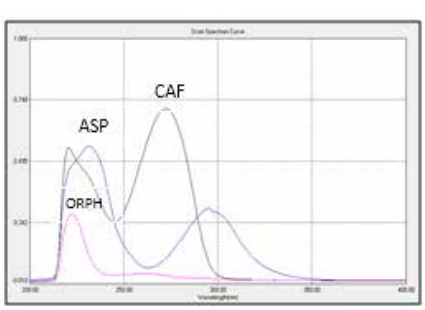


**Fig 1: Overlain spectrum of aspirin, caffeine and orphenadrine citrate**

**Table 1: Results of tablet analysis by proposed method using absorbance corrected for interference**

| Drug | Labelled amount (mg) | Amount found (mg) | % Label claim | % R.S.D |
|---|---|---|---|---|
| Aspirin | 385 | 386.26 | 100.32 | 0.375 |
| Caffeine | 30 | 29.81 | 99.38 | 2.25 |
| Orphenadrine citrate | 25 | 26.08 | 104.33 | 1.91 |

**Method Validation**

The method was successfully applied for the simultaneous determination of aspirin, caffeine, and orphenadrine citrate and was validated for the following parameters:

**Linearity and Range**

The linearity range was found to be 3-24 µg/ml for aspirin and 1-12 µg/ml for both caffeine and orphenadrine citrate. The trend line equations obtained were y=0.013x+0.012, y=0.049x+0.011 and y=0.018x-0.010 with the regression coefficients 0.999, 0.999 and 0.994 for aspirin, caffeine and orphenadrine citrate respectively.

**Accuracy**

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different concentration levels of 80%, 100%, and 120%. The method showed mean absolute recovery ranging from 95.76-100.33% for aspirin, 100.7-102% for caffeine and 100.66-105% for orphenadrine citrate which was found to be within the acceptance criteria of 95% to 105% indicating minimum interaction of tablet excipients with the drug component.

**Precision**

R. S. D. was found to be less than 2% indicating high degree of precision and reproducibility of the test results on replicate analysis of the three component mixture by the proposed method.

The validated method was applied for the analysis of aspirin, caffeine and orphenadrine citrate in the tablet formulation. From analysis, amount of aspirin was determined to be 386.26 mg, caffeine 29.81 mg and orphenadrine citrate 26.08 mg, which confirmed with the label claim of the tablet.

**Conclusion**

The study describes a novel UV spectrophotometric method for the estimation of aspirin, caffeine and orphenadrine citrate in the tablet formulation by absorption correction for interference. The validated method is simple, sensitive, accurate, precise and can be used for routine analysis of the three component mixture of aspirin, caffeine and orphenadrine citrate.

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