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Application of normalized spectra in resolving a challenging Orphenadrine and Paracetamol binary mixture

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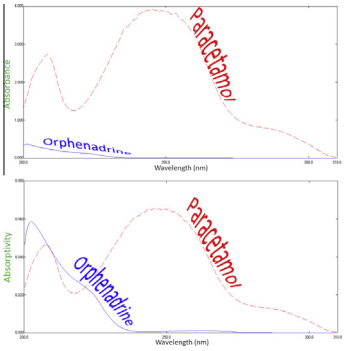
HIGHLIGHTS

- Normalized spectra and how to be used in resolving challenging mixture.
- Smart techniques utilizing the division spectra for simultaneous determination of binary mixture.
- Advantages of the proposed methods over the conventional spectrophotometric techniques.

GRAPHICAL ABSTRACT

Normalized spectra have a great power in resolving spectral overlap of challenging Orphenadrine and Paracetamol binary mixture, four smart techniques utilizing the normalized spectrum were used in this work, namely, amplitude modulation, simultaneous area ratio subtraction, simultaneous derivative spectrophotometry and ratio H-point standard addition method.



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ABSTRACT

Normalized spectra have a great power in resolving spectral overlap of challenging Orphenadrine (ORP) and Paracetamol (PAR) binary mixture, four smart techniques utilizing the normalized spectra were used in this work, namely, amplitude modulation (AM), simultaneous area ratio subtraction (SARS), simultaneous derivative spectrophotometry (S^1DD) and ratio H-point standard addition method (RHPSAM). In AM, peak amplitude at 221.6 nm of the division spectra was measured for both ORP and PAR determination, while in SARS, concentration of ORP was determined using the area under the curve from 215 nm to 222 nm of the regenerated ORP zero order absorption spectra, in S^1DD, concentration of ORP was determined using the peak amplitude at 224 nm of the first derivative ratio spectra. PAR concentration was determined directly at 288 nm in the division spectra obtained during the manipulation steps in the previous three methods. The last RHPSAM is a dual wavelength method in which two calibrations were plotted at 216 nm and 226 nm. RH point is the intersection of the two calibration lines, where ORP and PAR concentrations were directly determined from coordinates of RH point. The proposed methods were applied successfully for the determination of ORP and PAR in their dosage form.

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Introduction

The combination of a skeletal muscle relaxant (SMR) and a non-steroidal anti-inflammatory drugs (NSAID) is superior to single agents alone [1]. Orphenadrine citrate; (±)-N,N-Dimethyl-2-[(o-methyl-α-phenylbenzyl)oxy]ethylamine citrate [2] is a centrally acting muscle relaxants drug, acting by depressing the appropriate neurons within the nervous system so that somatic nerve impulses fail to be generated [3]. Paracetamol; N-(4-Hydroxyphenyl)acetamide [2] is a centrally and peripherally acting analgesic and antipyretic agent. It is effective for treatment of minor, non-inflammatory conditions in patients who are prone to gastric symptoms [4]. Pharmaceutical formulations containing both Orphenadrine citrate (ORP) and Paracetamol (PAR) show combined skeletal muscle relaxation with analgesic and antipyretic efficacy. This combination is used worldwide for better therapeutic activity of both drugs as ORP is known to increase and prolong the antinociceptive effects of PAR [4]. The chemical structures of ORP and PAR are shown in Fig. 1.

Several methods have been reported in the literature for the determination of ORP in single dosage form or in biological fluids and others for PAR in single or combined dosage form. The techniques used include spectrophotometry [5–8], electrochemistry [8,9], and chromatography [10–14]. However, very limited analytical techniques have been reported in the literature for the simultaneous determination of ORP and PAR in their combined formulations, in spite of the longstanding commercial distribution of their tablets. These techniques are RP-HPLC [15], capillary electrophoresis [16], and two reported spectrophotometric methods for analysis of this mixture. The first method depends on spiking all samples with the minor analyte (ORP) plus using 77 samples as a calibration set in order to simultaneously estimate both constituents using artificial neural network "ANN" modeling [17], while the other method [18] is a colorimetric determination of ORP after reaction with 1-amino naphthalene and sodium nitrite then heating for 6 min at 50 °C to give an orange color having a maximum absorbance at 462 nm.

Obviously, ORP and PAR binary mixture is considered to be an analytically challenging mixture, from the spectrophotometric point of view. This is attributed not only to the large difference in proportions between ORP and PAR, which exceeds 1:12, respectively, but also to their respective absorptivities, which justifies the paucity of spectrophotometric applications on this mixture. The motivation to develop new spectrophotometric techniques is not only the achievement of better performance parameters but also to solve problems in actual applications on such a challenging mixture. In other word, the present work, is focusing on the spectral overlap of two components' normalized spectra in order to resolve this mixture of large difference between its components' proportions, the study reveals the applicability of several spectrophotometric techniques all utilizing the ratio spectra using normalized spectrum as a divisor.

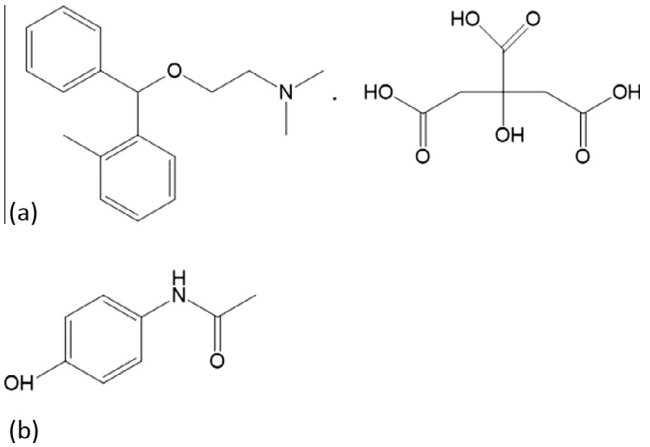

Fig. 1. Chemical structures of Orphenadrine citrate (a) and Paracetamol (b).

Experiment

Apparatus and software

A dual beam Shimadzu (Kyoto/Japan) UV–Vis. spectrophotometer, model 1650 UV-PC. The bundle software, UV PC personal spectroscopy software version 3.7 (SHIMADZU) was used to process absorption and derivative spectra, scans were carried out in the range from 200 nm to 400 nm at 0.1 nm intervals using 1.00 cm quartz cells.

Materials and reagents

Orphenadrine citrate (ORP) and Paracetamol (PAR) standard materials were kindly supplied by National Organization for Drug Control and Research (NODCAR), Giza, Egypt. The purity was found to be 99.73 ± 0.993% and 100.59 ± 1.026% for ORP and PAR, respectively, according to the reported PR-HPLC method [15].

Norgesic® Tablets, manufactured by iNova Pharmaceuticals (Aust) Pty Ltd. B.N. NG07A, claimed to contain Orphenadrine citrate BP 35 mg Paracetamol 450 mg per tablet.

Norgesic™ Tablets, manufactured by E.I.P.I.C.O. Egyptian Int. Pharmaceutical Industries CO. A.R.E. under the license of 3 M Health Care, England B.N.1308736, claimed to contain Orphenadrine citrate BP 35 mg Paracetamol BP 450 mg per tablet.

The solvent used in this work was methanol (E. Merck, Darmstadt, Germany).

Solutions

Stock standard solutions (1.0 mg mL^{-1})

Stock standard solutions of ORP and PAR were prepared by weighing accurately 50.0 mg of ORP and PAR bulk powder into two separate 50-mL volumetric flasks; 25.0 mL methanol was added in each, shaken for few min, and diluted to the volume with methanol.

Working standard solutions (100.0 μg mL^{-1})

Working standard solutions were prepared by transferring 5.0 mL of the drugs stock standard solution (1.0 mg mL^{-1}), separately, into two 50-mL measuring flasks and the volume was completed to the mark with methanol.

Laboratory prepared mixture solutions

ORP and PAR synthetic mixtures were prepared by transferring different aliquots from their respective stock standard solutions (1.0 mg mL^{-1}) equivalent to 0.5, 1.5 and 2.0 mg of ORP and 5.0, 6.0 and 7.0 mg of PAR into nine separate 10-mL volumetric flasks. The prepared nine mixtures contain three different concentration levels of the two drugs, for ORP (50.0, 150.0 and 200.0 μg mL^{-1}) and for PAR (500.0, 600.0 and 700.0 μg mL^{-1}), surrounding the dosage form ratio.

Pharmaceutical formulation solutions

Ten tablets of Norgesic® and Norgesic™ were separately weighted and finely powdered. Amounts of powdered tablets equivalent to 12.5 mg of ORP (160.7 mg of PAR) were accurately weighted and transferred into separate 250-mL beakers, sonicated