UV SPECTRA OF AQUEOUS OR ETHANOLIC SOLUTIONS OF TWENTY-SEVEN ACTIVE PHARMACEUTICAL INGREDIENTS

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ABSTRACT

INTRODUCTION: UV spectrophotometry is the simplest method of quantitative analysis of active pharmaceutical ingredients. It is widely used in developing active pharmaceutical ingredients, quantifying impurities, dissolution testing, and quantifying nucleic acids and proteins in pharmaceutical development. However, there is no convenient library of UV spectra of pharmaceutical ingredients in pure distilled water, and it is sometimes hard to find the necessary information in the literature.

AIM: This study aims to create a dataset of UV spectra of 27 common pharmaceutical ingredients in aqueous or (for those insoluble in water) ethanolic solutions and to review the analytical methods of determination of these ingredients based on these spectral data that were already developed.

MATERIALS AND METHODS: The aqueous (or ethanolic for those insoluble in water) solutions of 27 active pharmaceutical ingredients were prepared, and their UV spectra were recorded.

RESULTS AND CONCLUSION: UV spectra of aqueous solutions of amlodipine besylate, articaine hydrochloride, bendazole hydrochloride, betaxolol hydrochloride, carbamazepine, citicoline sodium, chloropyramine, clopidogrel bisulfate, dexketoprofen trometamol, drotaverine hydrochloride, 2-ethyl-6-methyl-3-hydroxypyridine succinate, ketorolac trometamol, loperamide hydrochloride, menadione sodium bisulfite, metamizole sodium, metoclopramide hydrochloride, metoprolol tartrate, moxifloxacin hydrochloride, nicotinic acid (niacin), norepinephrine hydrochloride (noradrenaline hydrochloride), paracetamol (acetaminophen), and valacyclovir, and ethanolic solutions of carvedilol, haloperidol, indapamide, ketoprofen, and spironolactone are presented. The wavelengths of absorbance maxima for each compound are given. The methods of UV-spectrophotometric determination of these active pharmaceutical ingredients available in literature are reviewed.

Keywords: *UV spectra, aqueous or ethanolic solutions, active pharmaceutical ingredients*

INTRODUCTION

Cleaning of pharmaceutical equipment is an important step in the production of pharmaceutical formulations. In order to reduce the risk of contamination of the product by other pharmaceutical ingredients and detergents, the residual quantities of contaminants in the cleaning rinse waters should be determined. To make this determination possible directly in the production area the method should be rapid and selective with respect to excipients, and its sensitivity and precision are less important (1). For this reason, the direct UV-spectrophotometric determination directly in the cleaning rinse waters with-

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out prior sample preparation is the excellent and obvious choice for the pharmaceutical ingredients that exhibit maxima in their UV spectra. However, in order to prevent equipment contamination, only distilled water and ethanol can be used as solvents when extracting the product residues from the equipment surface. Both European (2) and US (3) pharmacopoeias contain several UV-spectroscopic methods for quantitative determination of pharmaceutical ingredients in bulk samples and formulations. However, most often methanol is used as the solvent. In the dissolution kinetic tests, both hydrochloric acid and phosphate buffer solutions are used as dissolution media. In contrast, there is no convenient library of UV spectra of pharmaceutical ingredients in pure distilled water, and it is sometimes hard to find the necessary information in the literature.

AIM

This study aims to create a dataset of UV spectra of 27 common pharmaceutical ingredients in aqueous or (for those ones insoluble in water) ethanolic solutions and to review the analytical methods of determination of these ingredients based on these spectral data that were already developed. It is believed that these spectral data might help industrial analysts to create and validate the UV-spectroscopic methods of determination of common pharmaceutical ingredients in cleaning rinse waters of the industrial equipment.

MATERIALS AND METHODS

The active pharmaceutical ingredients were purchased from Aarti Drugs Ltd and identified using the IR spectroscopy according to the procedures described in European (2) and US (3) pharmacopoeias. A total of 96% ethanol, sodium hydroxide and hydrochloric acid (Ph. Eur. grade) were purchased from Sigma Aldrich. Laboratory glassware of 2nd grade was used. The water for solution preparation was first bidistilled and then additionally purified using Sartorius Arium Pro UV purification system. The analytical balance Sartorius Cubis II was used for weighting. The UV spectra were recorded using the spectrometers Agilent Cary 60 or Mettler Toledo UV7 in glass cuvettes with optical pathlength of 1 cm against the respective solvents. The spectra were recorded in the wavelength range from 200 to 400 nm with a step of 0.5 nm and scan rate of 200 nm/min. The wavelengths of the absorbance maxima were determined using the dedicated softwares supplied by spectrometer manufacturers.

For each pharmaceutical ingredient stock solutions with concentrations of 200 mg/L were prepared. Up to three working solutions with different concentrations were prepared from these stock solutions by dilution, and the UV spectra of these working solutions were recorded. The preparation of different stock and working solutions and the recording of spectra were repeated three times, the obtained spectra were compared with each other, and a maximum difference of ±1 nm for the absorbance maxima wavelengths was found.

RESULTS AND DISCUSSION

The obtained UV spectra are presented in Fig. 1 through 28.

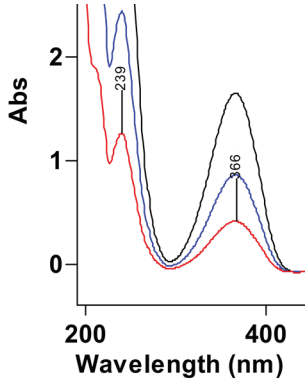


Fig. 1. The UV spectra of the aqueous solutions of amlodipine besylate with concentrations 25, 50, and 100 mg/L.

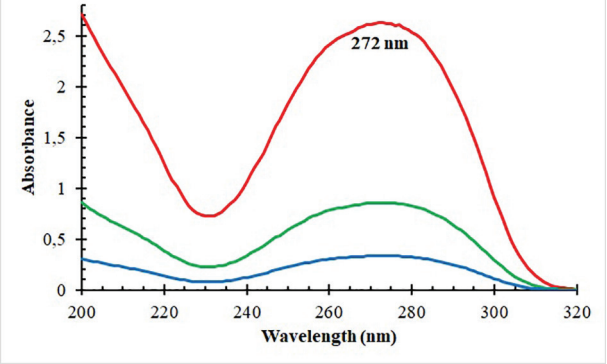


Fig. 2. The UV spectra of the aqueous solutions of articaine hydrochloride with concentrations 12.8, 32, and 80 mg/L.

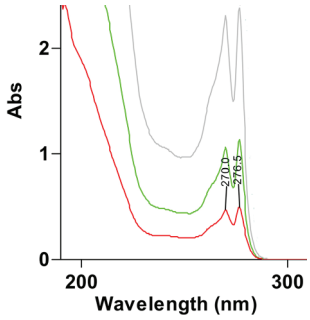


Fig. 3. The UV spectra of the aqueous solutions of bendazole hydrochloride with concentrations 12.5, 25, and 50 mg/L.

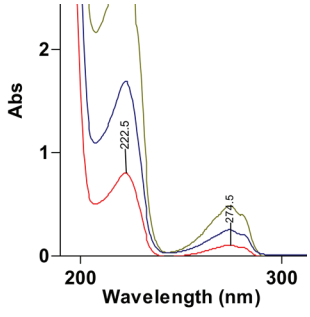


Fig. 4. The UV spectra of the aqueous solutions of betaxolol hydrochloride with concentrations 25, 50, and 100 mg/L.

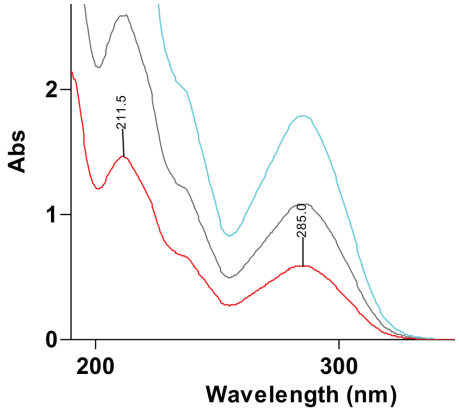


Fig. 5. The UV spectra of the aqueous solutions of carbamazepine with concentrations 25, 50, and 100 mg/L.

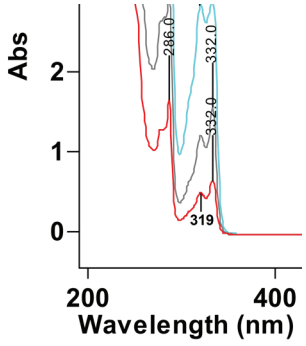


Fig. 6. The UV spectra of the ethanolic solutions of carvedilol with concentrations 50, 100, and 200 mg/L.

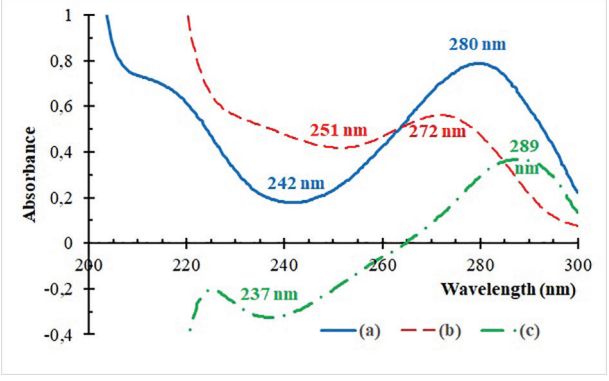


Fig. 7. The UV spectra of the solutions of citicoline sodium with concentration 35 mg/L in a) 1M NaOH, b) 1M HCl, and c) the difference spectrum.

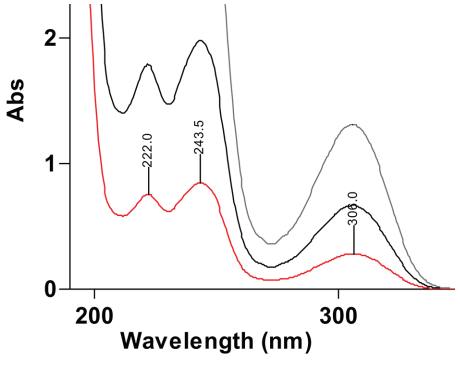


Fig. 8. The UV spectra of the aqueous solutions of chloropyramine with concentrations 17.5, 35, and 70 mg/L.

The UV spectrum of the aqueous solution of amlodipine besylate (Fig. 1) has a sharp maximum at 239 nm and a much broader and less sensitive peak at 366 nm. The spectrum is very similar to that of the solutions in methanol (2,3–5) and acetonitrile (3), where the maximum is at 237 nm. The UV-spectrophotometric methods of determination of amlodipine besylate in aqueous solution at 239 nm (6) and 366 nm (7) were already developed.

The UV spectrum of the aqueous solution of articaine hydrochloride (Fig. 2) has a single maximum at 272 nm. The same maximum exists in the solutions of the drug in 1 g/L HCl (2) and in phosphate buffered saline (8). A UV-spectrophotometric

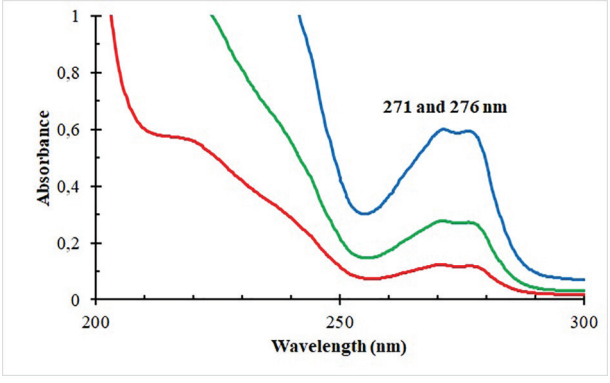


Fig. 9. The UV spectra of the aqueous solutions of clopidogrel bisulfate with concentrations 20, 40, and 80 mg/L.

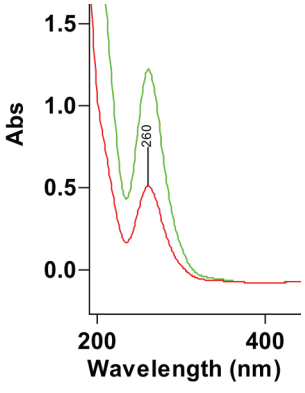


Fig. 10. The UV spectra of the aqueous solutions of dexketoprofen trometamol with concentrations 35 and 70 mg/L.

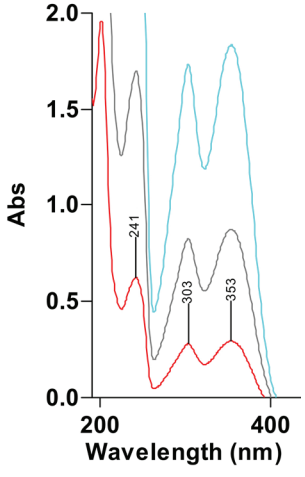


Fig. 11. The UV spectra of the aqueous solutions of drotaverine hydrochloride with concentrations 17.5, 35, and 70 mg/L.

method of determination of the drug in phosphate buffered saline was developed (8).

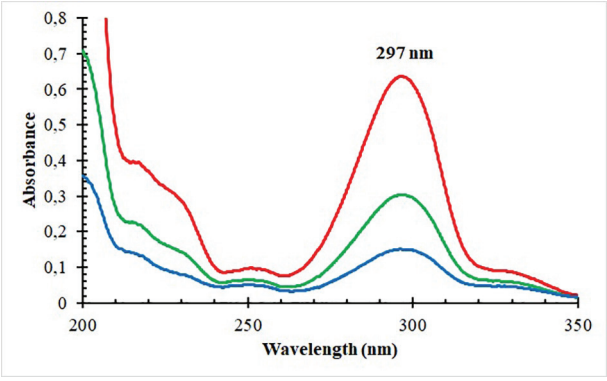


Fig. 12. The UV spectra of the aqueous solutions of 2-ethyl-6-methyl-3-hydroxypyridine succinate with concentrations 5, 10, and 20 mg/L.

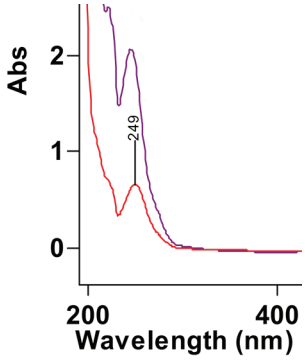


Fig. 13. The UV spectra of the ethanolic solutions of haloperidol with concentrations 25 and 50 mg/L.

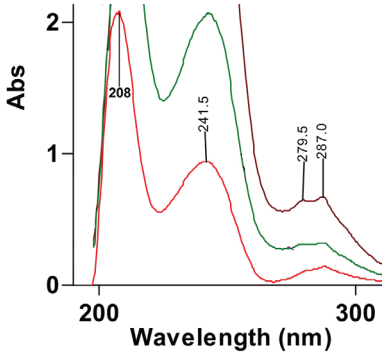


Fig. 14. The UV spectra of the ethanolic solutions of indapamide with concentrations 17.5, 35, and 70 mg/L.

The UV spectrum of the aqueous solution of bendazole hydrochloride (Fig. 3) has two partially overlapped peaks at 270 and 276.5 nm. The same maxima exist in the solution of the drug in 0.1 M HCl (9). A UV-spectrophotometric method of determination of the drug in acidic aqueous solution was developed (9).

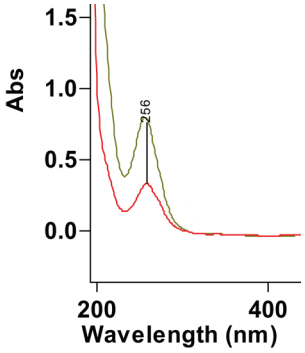


Fig. 15. The UV spectra of the ethanolic solutions of ketoprofen with concentrations 10 and 20 mg/L.

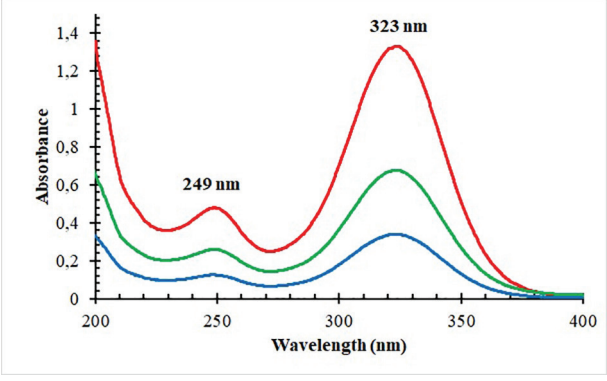


Fig. 16. The UV spectra of the aqueous solution of ketorolac trometamol with concentrations 5, 10, and 20 mg/L.

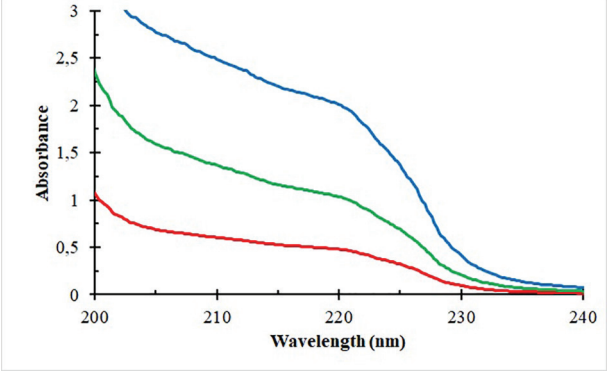


Fig. 17. The UV spectra of the aqueous solution of loperamide hydrochloride with concentrations 20, 40, and 80 mg/L.

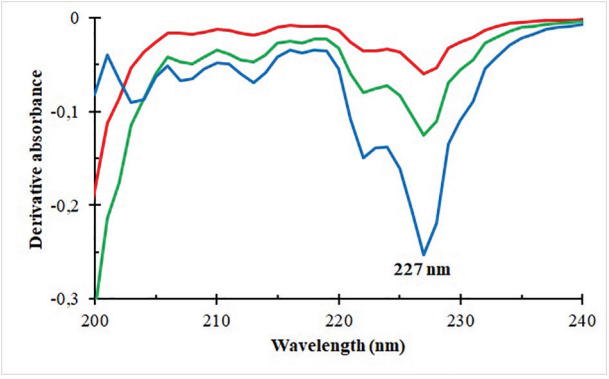


Fig. 18. The first derivative UV spectra of the aqueous solution of loperamide hydrochloride with concentrations 20, 40, and 80 mg/L.

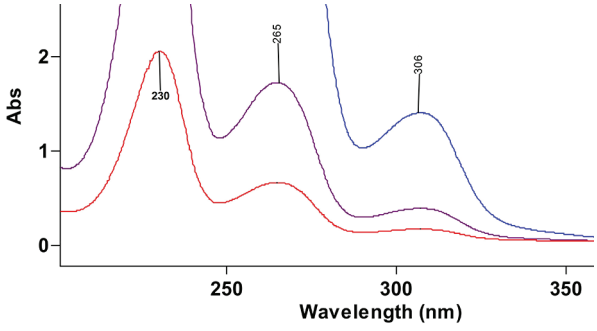


Fig. 19. The UV spectra of the aqueous solution of menadione sodium bisulfite with concentrations 25, 50, and 200 mg/L.

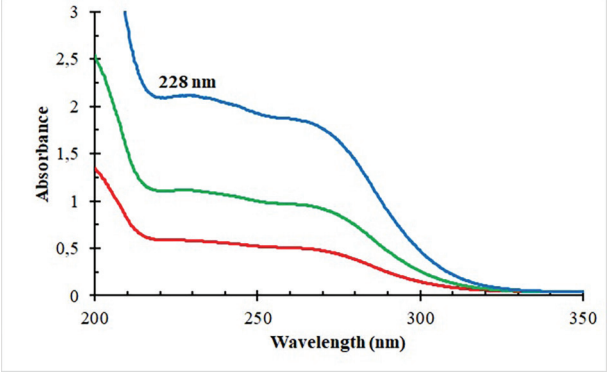


Fig. 20. The UV spectra of the aqueous solution of metamizole sodium with concentrations 20, 40, and 80 mg/L.

The UV spectrum of the aqueous solution of betaxolol hydrochloride (Fig. 4) has a sharp maximum at 222.5 nm and a much broader and less sensitive peak at 274.5 nm. The spectrum is very similar to that of the solution in the mixture of water, methanol, and acetonitrile (2,3), where the maximum is at 273 nm. A UV-spectrophotometric method of determination of betaxolol hydrochloride in aqueous solution at 224 nm (10) was already developed.

The UV spectrum of the aqueous solution of carbamazepine (Fig. 5) has a sharp maximum at 211.5 nm and a much broader and less sensitive peak at 285 nm. The spectrum is very similar to that of the

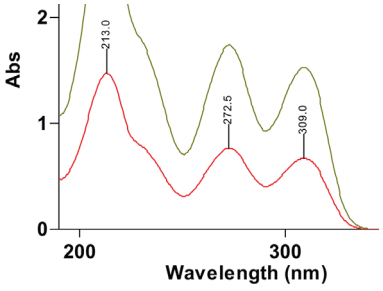


Fig. 21. The UV spectra of the aqueous solution of metoclopramide hydrochloride with concentrations 25 and 50 mg/L.

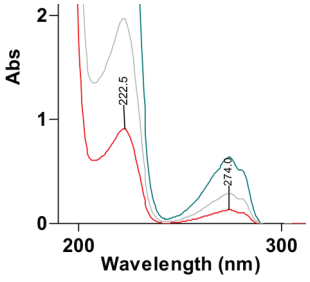


Fig. 22. The UV spectra of the aqueous solution of metoprolol tartrate with concentrations 17.5, 35, and 70 mg/L.

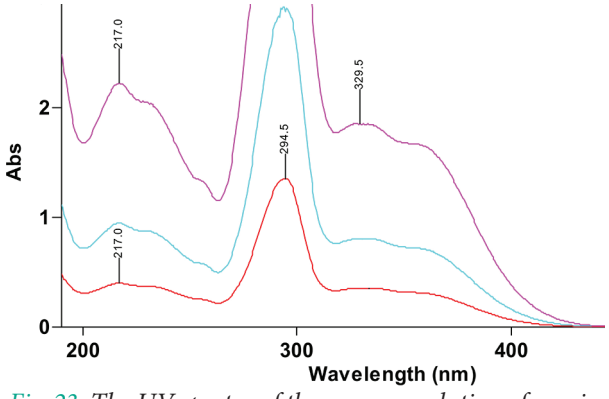


Fig. 23. The UV spectra of the aqueous solution of moxifloxacin hydrochloride with concentrations 17.5, 35, and 70 mg/L.

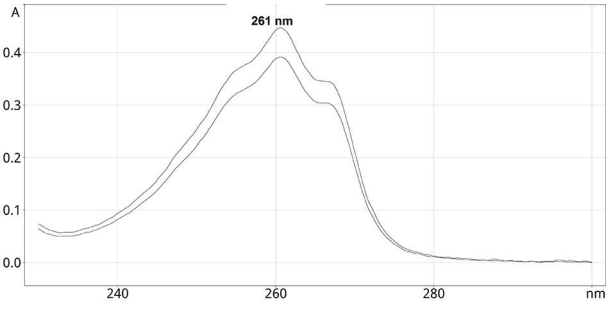


Fig. 24. The UV spectra of the aqueous solution of nicotinic acid (niacin) with concentrations 8 and 10 mg/L.

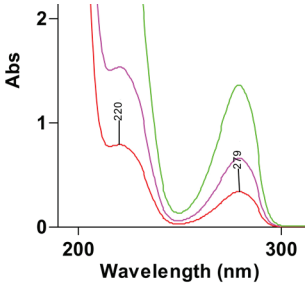


Fig. 25. The UV spectra of the aqueous solution of norepinephrine hydrochloride (noradrenaline hydrochloride) with concentrations 30, 60, and 120 mg/L.

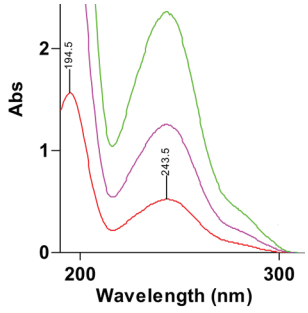


Fig. 26. The UV spectra of the aqueous solution of paracetamol (acetaminophen) with concentrations 6.25, 12.5, and 25 mg/L.

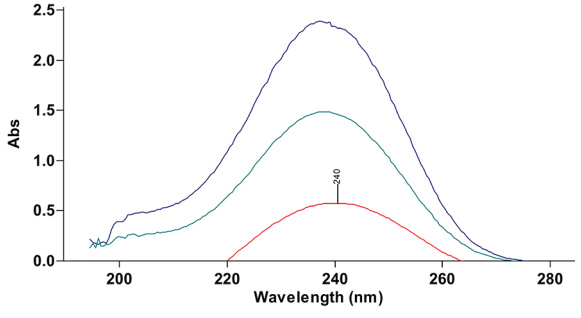


Fig. 27. The UV spectra of the ethanolic solution of spironolactone with concentrations 12.5, 25, and 37.5 mg/L.

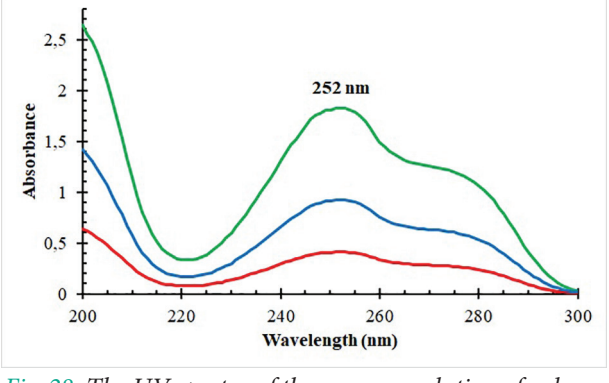


Fig. 28. The UV spectra of the aqueous solution of valacyclovir with concentrations 20, 40, and 80 mg/L.

solution in methanol (11–13), where the maximum is at 284 nm.

The UV spectrum of the ethanolic solution of carvedilol (Fig. 6) has a very sharp maximum at 286 nm and two partially overlapped and much less sensitive peaks at 319 and 332 nm. The UV spectrum of the solution of carvedilol in 0.1 M HCl also has a maximum at 286 nm, and the method for the dissolution studies of carvedilol tablets was developed (14). The spectrum of the solution of carvedilol in the mixture of ethanol and acetonitrile has an even more sensitive peak at 244 nm (15), and a method for determination of the drug at this wavelength was developed. There is also a method of determination of carvedilol in the solution in acetonitrile at the wavelength of 332 nm (16). A UV-spectrophotometric method of determination of carvedilol in aqueous suspension at 289 nm (17) was also developed.

The UV spectrum of the aqueous solution of citicoline sodium (Fig. 7) exhibits an acid-base behaviour, and its UV spectrum is pH-dependent. In strongly alkaline conditions, it has a maximum at 280 nm and a minimum at 242 nm, in strongly acidic conditions, it has a maximum at 272 nm and a minimum at 251 nm. The difference spectrum of the solution in 1M NaOH against the solution in 1M HCl has a maximum at 289 nm and a minimum at 237 nm. The methods of UV-spectrophotometric determination of citicoline sodium in the solutions of NaOH (18, 19), HCl (20), and those utilising difference spectroscopy (21, 22) were already developed.

The UV spectrum of the aqueous solution of chloropyramine (Fig. 8) has two partially overlapped maxima at 222 and 243.5 nm and a much broader and less sensitive peak at 306 nm. The UV spectra of the solutions of chloropyramine in 0.2 M NaOH and in ethanol exhibit a similar behaviour (23). The UV-spectrophotometric method of determination of chloropyramine in aqueous solution at 244 nm (24) was already developed.

The UV spectrum of the aqueous solution of clopidogrel bisulfate (Fig. 9) has a shoulder at 271 and 276 nm. The spectrum also exhibits a clear S-shape behaviour with two inflection points at 225 and 245 nm, which makes it possible to implement derivative spectroscopy for its determination. The UV-spectrophotometric method of determination of clopidogrel bisulfate in the acidified aqueous solution at 270 nm (25) was already developed. There are also methods of determination of the drug in acidified aqueous solution at 222 nm (26) and at 220 nm (27), and in methanolic solution at 203 nm (28).

The UV spectrum of the aqueous solution of dexketoprofen trometamol (Fig. 10) has a single maximum at 260 nm. The UV-spectrophotometric method of determination of dexketoprofen trometamol in aqueous solution at 260 nm (29) was already developed.

The UV spectrum of the aqueous solution of drotaverine hydrochloride (Fig. 11) has a sharp maximum at 241 nm and two much less sensitive peaks at 303 and 353 nm. The same maximum at 241 nm is also present in the UV spectrum of methanolic solution of the drug (30). The UV-spectrophotometric methods of determination of drotaverine hydrochloride in methanolic solution at 241 nm (30), in acidified aqueous solution at 303 nm (31), and at 353 nm (32) were already developed. There is also a method that utilises the wavelength of 230 nm for a methanolic solution of drotaverine (33), a method that utilises the derivative spectroscopy (34), and a method that uses the difference spectra between the acidic and alkaline aqueous solutions of drotaverine hydrochloride (35).

The UV spectrum of the aqueous solution of 2-ethyl-6-methyl-3-hydroxypyridine succinate (Fig. 12) has a single maximum at 297 nm. The UV-spectrophotometric method of determination of 2-ethyl-6-methyl-3-hydroxypyridine succinate in aqueous solution at 297 nm (36) was already developed.

The UV spectrum of the ethanolic solution of haloperidol (Fig. 13) has a single maximum at 249 nm. The spectrum is very similar to those of the solutions in methanol (37, 38) and of the aqueous suspension in phosphate buffer (39, 40), where the maxima are at 248 nm. The methods of determination of haloperidol in respective solvents were developed (37–40).

The UV spectrum of the ethanolic solution of indapamide (Fig. 14) has a very sharp maximum at 208 nm, a broad maximum at 241.5 nm and a shoulder at 279.5 and 287 nm (2). The spectrum is very similar to that of the aqueous suspension in phosphate buffer (41), where the maximum is at 240 nm.

The methods of determination of indapamide by derivative spectroscopy were also proposed (41, 42).

The UV spectrum of the ethanolic solution of ketoprofen (Fig. 15) has a single maximum at 256 nm (2). The spectrum is very similar to that of the solution in methanol (3, 43), where the maximum is at 258 nm. The UV spectra of ketoprofen dissolved in aqueous solutions containing sodium citrate, polyethylene glycol and polyvinyl pyrolidine (with the maximum at 256 nm) (44,45), urea, sodium acetate and sodium citrate (with the maximum at 260 nm) (46), and sodium hydrocarbonate (with the maximum at 260 nm) (47) were also recorded, and the corresponding methods of determination of ketoprofen were developed.

The UV spectrum of the aqueous solution of ketorolac trometamol (Fig. 16) has a broad maximum at 249 nm and a much sensitive peak at 323 nm. The UV-spectrophotometric methods of determination of ketorolac trometamol in water (48), methanol (49) and in acetate buffered solution (50) at 322 nm were proposed. A method of determination of the drug in phosphate or carbonate buffered solutions at 316 nm also exists (51). In addition, a method for determination of ketorolac trometamol in aqueous solutions utilising derivative spectroscopy was proposed (52).

The UV spectrum of the aqueous solution of loperamide hydrochloride (Fig. 17) has no maxima. The spectrum however exhibits a clear S-shape behaviour with an inflection point at 227 nm, and the first derivative spectrum (Fig. 18) has a minimum at this wavelength, which makes it possible to implement the derivative spectroscopy for its determination. The derivative spectrophotometric method of determination of loperamide hydrochloride in aqueous solution was already developed (53). There are also derivative spectrophotometric methods of determination of loperamide hydrochloride in ethanolic (54) and acidified methanolic (55, 56) solutions.

The UV spectrum of the aqueous solution of menadione sodium bisulfite (Fig. 19) has a sharp maximum at 230 nm, a broad maximum at 265 nm and a much broader and less sensitive peak at 306 nm. Only a derivative spectroscopy method of determination of this drug is available in the literature (57).

The UV spectrum of the aqueous solution of metamizole sodium (Fig. 20) has s wide plateau with an almost imperceptible maximum at 228 nm. The spectrum also exhibits a clear S-shape behaviour with an inflection point at 285 nm, which makes it possible to implement derivative spectroscopy for its determination. A method of determination of metamizole sodium in acidified aqueous solution at 258 nm (58), and a fourth-derivative spectrophotometric method in aqueous solution (59) were already developed.

The UV spectrum of the aqueous solution of metoclopramide hydrochloride (Fig. 21) has a sharp maximum at 213 nm and two much less sensitive peaks at 272.5 and 309 nm. The spectrum is very similar to that of the solution in methanol (60,61). The UV-spectrophotometric methods of determination of metoclopramide hydrochloride in methanolic solution at 272 nm (60,61), in acidified aqueous solution at 272 nm (62,63), in the solution in phosphate buffer at 272 nm (64,65), and in aqueous solution at 310 nm (66) were already developed.

The UV spectrum of the aqueous solution of metoprolol tartrate (Fig. 22) has a sharp maximum at 222.5 nm and a much broader and less sensitive peak at 274 nm. The UV spectrum of the methanolic (67) and aqueous (68–71) solutions of the related compound metaprolol succinate are very similar and exhibit the maxima at 223±1 nm (67–71). The UV-spectrophotometric methods of determination of both metoprolol succinate and metoprolol tartrate in methanolic and aqueous solutions were already developed (67–72). A derivative spectrophotometric method also exists (69).

The UV spectrum of the aqueous solution of moxifloxacin hydrochloride (Fig. 23) has a sharp maximum at 294.5 nm and two much broader and less sensitive peaks at 217 and 329.5 nm. The UV spectrum of the solution of moxifloxacin hydrochloride in a phosphate buffer has a maximum at 289 nm (73). The UV-spectrophotometric methods of determination of moxifloxacine hydrochloride in acidified (73–78) and neutral (79) aqueous solutions and in solution of phosphate buffer (73) were already developed.

The UV spectrum of the aqueous solution of nicotinic acid (niacin) (Fig. 24) has a single maxi-

mum at 261 nm. The spectrum is very similar to that of the solutions in the phosphate buffer (2,3) and in ethanol (80), where the maximum is at 262 nm. The UV-spectrophotometric methods of determination of nicotinic acid in ethanolic (80) and aqueous solutions (81,82) were already developed.

The UV spectrum of the aqueous solution of norepinephrine hydrochloride (noradrenaline hydrochloride) (Fig. 25) has a plateau with an almost imperceptible maximum at 220 nm and a much less sensitive peak at 279 nm.

The UV spectrum of the aqueous solution of paracetamol (acetaminophen) (Fig. 26) has a sharp maximum at 194.5 nm and a much broader and less sensitive peak at 243.5 nm. The spectrum is very similar to that of the acidified solution in methanol (2,83–85), where the maximum is at 244 nm. The UV-spectrophotometric methods of determination of paracetamol in methanolic (83–85) and aqueous solutions (86–88) were already developed. The method that utilises the difference spectra between the acidic and alkaline aqueous solutions of paracetamol also exists (89).

The UV spectrum of the ethanolic solution of spironolactone (Fig. 27) has a single maximum at 240 nm. The spectrum is very similar to that of the solution in methanol (3, 90, 91), where the maximum is at 238 nm. The UV-spectrophotometric methods of determination of spironolactone only in methanolic (90, 91) solutions were already developed. The method that utilises the derivative spectroscopy in methanolic solutions also exists (92).

The UV spectrum of the aqueous solution of valacyclovir (Fig. 28) has a single maximum at 252 nm. The same maximum exists in the solutions of the drug in Britton-Robinson buffer solution (93). In the solution of 0.1 M HCl (94) and 0.1 M H_2SO_4 (95) the spectrum of valacyclovir has a maximum at 255 nm. The UV-spectrophotometric methods of determination of valacyclovir in aqueous acidified (94, 95) and neutral (93,96–98) solutions were already developed.

CONCLUSION

This paper reviews the existing UV-spectrophotometric methods of determination of 27 active pharmaceutical ingredients in various solvents and presents the UV spectra of these ingredients in aqueous or ethanolic solutions. These data might be useful for the development of simple and rapid methods of determination of traces of pharmaceutical ingredients in industrial equipment cleaning rinse waters.

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