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RESEARCH ARTICLE

Quinolone Antibacterials: Commentary and Considerations Regarding UV Spectra and Chemical Structure

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Objective: Antibacterial quinolones represent an important class of pharmaceutical compounds that are widely used in therapy. Analytical methods that rely on their property to absorb light in the UV range are commonly used for their analysis. In the current study we present an interpretation of the relationship between chemical structure – UV spectra based on the comparative examination of UV spectral behavior of the eighteen quinolone derivatives and four model compounds.
Methods: Eighteen quinolone derivatives and four model compounds were selected and their UV spectra were recorded in different solvents (methanol, 0.1M HCl, 0.1M NaOH).
Results: The studied compounds show three absorption maximum values located around 210-230 nm, 270-300 nm and 315-330 nm values. A general characteristic was observed as the absorption bands exhibited both hypsochrome and bathochrome shifts, by comparison in different solvents. Most commonly we observed a slight hypsochrome shift at acidic pH (protonated form prevails) and basic pH (anionic form prevails). The structural differences are reflected in changes of UV spectra only when there are auxochrom substituents or different basic substituents are present in the quinolones structure.
Conclusions: The correlations between the chemical structure of quinolone derivatives and their UV spectra using model compounds were established. This study provides useful information that can be used successfully in various UV spectrophotometric analysis methods or in more complex analytical methods using UV detection, and also in pharmacodynamic and kinetic studies.

Keywords: antibacterial quinolones, fluoroquinolones, UV spectrophotometry

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Introduction

Antibacterial quinolones are a class of synthetic antibacterial compounds, with broad antibacterial spectrum and with a particular mechanism of action interfering with DNA replication, preventing bacterial DNA from unwinding and duplicating. The evolution of quinolones began with the introduction in therapy of the nalidixic acid (NAL) in 1962 for the treatment of urinary tract infections. After the discovery of NAL a series of quinolones having a 1-substituted-1,4-dihydro-4-oxopyridine-3-carboxyilic structure have been developed (Figure 1), but the real breakthrough began with the introduction of fluoroquinolones, which have a fluorine atom attached to the central ring system, typically at the C-6-position [1].

The increasing therapeutic importance of this pharmaceutical class is closely linked with their chemical and analytical properties. Therefore in this study we selected a number of eighteen quinolone derivatives of different generations commonly used in human or veterinary therapy and also four model compounds used for comparative analysis [2]. Antibacterial quinolones have the property of absorbing light in UV, as the quinolone ring presents a characteristic UV spectrum. The absorption maximum

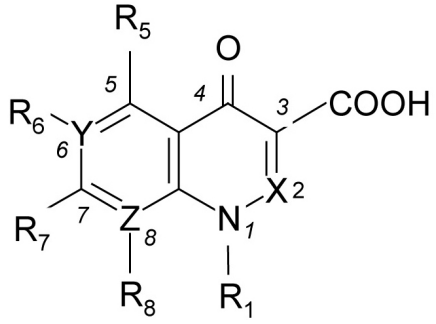

Fig. 1. General structure of the studied antibacterial quinolone derivatives

values for the quinolone ring are situated at 227, 270 and 314 nm, which correspond to the substituted polynuclear aromatic compounds (a three-band absorption spectrum). The starting point for the interpretation of these spectra is the fact that benzene and aromatic compounds present complex spectra which can be explained by $\pi \rightarrow \pi^*$ transitions and the presence of low excitations states [3]. The use of UV spectrophotometry in the analysis of quinolones has several compelling advantages related to the: high selectivity, low interference, easy method development and also economic aspects. UV spectrophotometric methods can be used successfully in the pharmaceutical analysis of quinolones, in particular for qualitative control and quantitative determinations but also in pharmacodynamic

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and pharmacokinetic studies. Also UV detection is usually used for the determination of quinolones when using more complex methods of analysis like high performance liquid chromatography (HPLC) or capillary electrophoresis (CE), in the studies of metal complexes of quinolone derivatives etc. [4, 5, 6, 7, 8, 9].

The present paper presents a comparative study of the spectral behavior in UV of eighteen quinolone derivatives: amifloxacin (AMI), ciprofloxacin hydrochloride (CIP), difloxacin (DIF), 3'-methyl-difloxacin (3M-DIF), enoxacin (ENO), enrofloxacin (ENR), levofloxacin (LEV), lomefloxacin (LOM), moxifloxacin hydrochloride (MOX), nalidixic acid (NAL), norfloxacin (NOR), 8-fluoro-norfloxacin (8F-NOR), ofloxacin (OFL), pefloxacin mesylate (PEF), 8-fluoro-pefloxacin (8F-PEF), pipemidic acid (PIP), sarafloxacin (SAR), and sparfloxacin (SPA). The structural characteristics of the studied compounds are summarized in Table I.

For a better understanding of the UV spectrum of the quinolone derivatives four model compounds were studied, their structural characteristics being presented in Table II.

Our objectives focused on a comparative study of the spectral behavior in UV of the eighteen quinolone derivatives and also on the establishment and interpretation of chemical structure – UV spectrum relationship. This comprehensive study brings valuable information in analysis field of quinolones derivatives which has not been published in this manner yet as we know so far.

Methods

The antibacterial quinolone derivatives were purchased as follows: enrofloxacin (ENR), levofloxacin (LEV), nalidixic acid (NAL), pipemidic acid (PIP), and sparfloxacin (SPA) from Sigma-Aldrich (Germany), ciprofloxacin hydrochloride (CIP) and ofloxacin (OFL) from Ranbaxy Laboratories Limited (India), difloxacin (DIF), sarafloxacin (SAR) and 3'-methyl-difloxacin (3M-DIF) from Orichem International LTD (China), amifloxacin (AMI), lomefloxacin (LOM), 8-fluor-norfloxacin (8F-NOR), 8-fluor-pefloxacin (8F-PEF) from Chinoin Pharmaceutical & Chemical Works (Hungary), enoxacin (ENO) from Fluka (Germany), moxifloxacin hydrochloride (MOX) from Bayer Schering Pharma AG (Germany), norfloxacin (NOR) from Smruthi Organics Limited (India), and pefloxacin mesylate (PEF) from Laropharm (Romania). The model compounds were purchased as follows: 1-(2-fluorophenyl)-

Table II. Chemical structures of model compounds

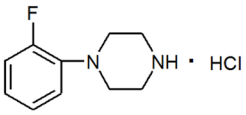
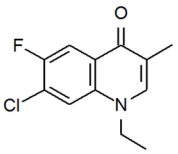
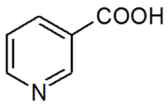
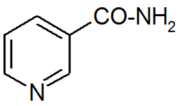
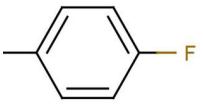
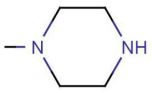
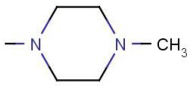
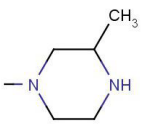
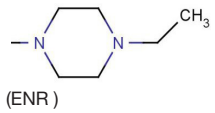
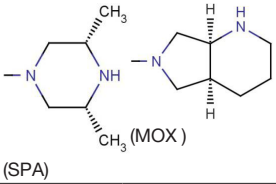
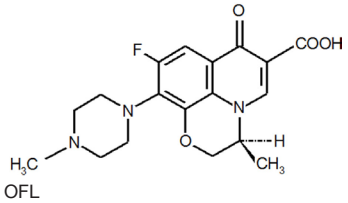
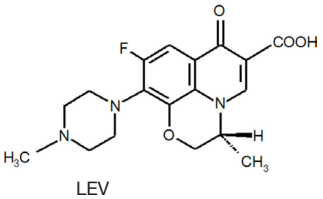
No.	Model compounds	Chemical structure
1	1-(2-Fluorophenyl)-piperazine hydrochloride	
2	7-Chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid	
3	Nicotinic acid	
4	Nicotinamide	

Table I. Structural characteristics and differences in the group of the studied QNs

Position	R, Y, Z	Substituents and atoms for the Y, Z positions (examples of compounds)				
1	R1	$-C_2H_5$ (ENO, LOM, PEF, PIP, NAL, NOR)	-NH-CH_3 (AMI)	 (CIP, ENR, MOX, SPA)	 (DIF, SAR)	
5	R5	$-NH_2$ (SPA)				
6	R6	-F (All the compounds excepting NAL and PIP)				
	Y	N (PIP)	C (All the compounds excepting NAL and PIP)			
7	R7	$-CH_3$ (NAL)	 (CIP, ENO, NOR, PIP, SAR)	 (AMI, DIF, PEF)	 (LOM, 3M-DIF)	 (ENR)
						 (MOX) (SPA)
	Z	N (ENO, PIP)	C (All the compounds excepting PIP and ENO)			
8	R8	$-O-CH_3$ (MOX)	-F (LOM, SPA)			
Tricyclic derivatives						
		 OFL		 LEV		

piperazine hydrochloride and nicotinic acid from Sigma-Aldrich (Germany), nicotinamide from Merck (Germany) and 7-chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid synthesized in Department of Pharmaceutical Chemistry, Semmelweis University from Budapest [10]. All the reagents used throughout the study were of analytical grade. Purified water was obtained from a Milli-Q Plus water-purification system (Millipore, USA).

The spectrum were recorded in the region 190 nm - 500 nm with an Analytik Jena UV-VIS Specord 210 spectrophotometer (Germany) provided with matched 1 cm path length quartz cells and processed with the software WinASPECT (Analytik Jena, Germany). The samples were prepared by dissolving the substances in methanol, 0.1M HCl and 0.1M NaOH. Stock solutions of 10 μg/mL were prepared in each solvent (methanol, 0.1M HCl and 0.1M NaOH), and then working standard solutions were prepared by suitable dilutions of stock solution with same solvent.

Results

Absorption maxima of the studied quinolone derivatives in different solvents are presented in Table III. The absorption maxima of each compound were compared with the ones from the literature, including European Pharmacopoeia [11].

The absorption of UV light is influenced by the nature of the solvent (solvatochromism phenomenon). The changes are due to analyte-solvent interactions that modifies the energy difference between the ground state and excitation. For some substances the effect appears to be hypsochromic, but for others a bathochromic effect can be observed. Solvents used in this study, absorb UV light at different wavelengths, ultrapure water at 200 nm, methanol at 210 nm (in 1 cm cells against ultrapure water as the reference). This issue was studied by verifying the absorption of the three solvents selected against ultrapure water, as their absorbances were insignificant [12].

UV spectra of NAL. We recorded the UV spectra of NAL in methanol and 0.1M NaOH (Figure 2); NAL being an acidic compound (protonation macroconstant log$K$ = 6.13) cannot be dissolved in 0.1 M HCl [13]. The UV absorption spectrum does not present significant shifts of the wavelength in the two solvents.

UV spectra of AMI. The UV spectra of AMI recorded in both acidic and alkaline medium exhibited a hypsochromic displacement of the absorption maximum in comparison with the spectrum recorded in methanol. In a basic medium the intensity of the absorption band increases with a maximum at 328 nm and 337 nm, with a bathochromic shift compared with the spectrum recorded in methanol.

UV spectra of CIP. The UV spectrum of CIP in 0.1M NaOH showed a slight increase in the second (λ_2) and third (λ_3) absorption maximum (bathochromic shift) in comparison with the spectrum recorded in methanol (Figure 3). An explanation for this bathochromic shift is the intensification of the conjugation phenomenon in a basic medium (sodium salt formation). For these two peaks also appears a clear increase in the intensity of the absorption band.

UV spectra of DIF and 3'M-DIF. In both acidic and alkaline mediums DIF exhibit a hypsochromic shift of the absorption maximum in comparison with the spectrum

Table III. UV absorption maxima (nm) of the studied quinolone derivatives

No.	Compound	Solvent	λ1 (nm)	λ2 (nm)	λ3 (nm)	λ4 max (nm)	λ5 (nm)	λ6 (nm)
		0.1M HCl	-	-	-	281	319	331
1	AMI	Methanol	-	-	-	286	320	333
		0.1M NaOH	-	-	-	274	328	337
		0.1M HCl	-	-	-	279	317	330
2	CIP	Methanol	-	-	-	279	318	332
		0.1M NaOH	-	-	-	273	323	335
		0.1M HCl	-	-	-	280	317, 318	330
3	DIF	Methanol	-	-	-	285	319	321
		0.1M NaOH	-	-	236	275	324	335
		0.1M HCl	-	-	-	282	318	-
4	3'M-DIF	Methanol	-	-	-	284	319	-
		0.1M NaOH	-	-	238	275	325	335
		0.1M HCl	-	-	-	270	340	-
5	ENO	Methanol	-	-	221	273	345	-
		0.1M NaOH	-	-	231	267	347	-
		0.1M HCl	-	-	-	278	317	330
6	ENR	Methanol	-	-	-	282	319	-
		0.1M NaOH	-	-	-	272	323	335
		0.1M HCl	-	-	226	288	321	
7	LOM	Methanol	-	-	-	291	320	-
		0.1M NaOH	-	-	230	285	329	-
		0.1M HCl	-	-	219	296	327	362
8	MOX	Methanol	-	-	214	294	333	-
		0.1M NaOH	-	-	244	292	339	-
		0.1M HCl	-	-	-	-	-	-
9	NAL	Methanol	-	-	209	259	320	328
		0.1M NaOH	-	-	227	259	336	
		0.1M HCl	-	-	225	278	317	-
10	NOR	Methanol	-	-	227	283	318	332
		0.1M NaOH	-	-	240	273	324	336
		0.1M HCl	-	-	225	288	320	-
11	8F-NOR	Methanol	-	-	-	292	320	-
		0.1M NaOH	-	-	235	288	320	-
		0.1M HCl	-	-	227	295	327	-
12	OFL	Methanol	-	-	227	298	327	-
		0.1M NaOH	234	249	257	289	334	-
		0.1M HCl	-	-	228	295	327	
13	LEV	Methanol	-	-	228	300	327	-
		0.1M NaOH	231	249	257	289	334	-
		0.1M HCl	-	-	225	278	317	-
14	PEF	Methanol	-	-	227	281	318	332
		0.1M NaOH	-	-	-	273	324	336
		0.1M HCl				288	320	
15	8F-PEF	Methanol				285	327	
		0.1M NaOH			225	284	329	
		0.1M HCl	-		218	276	323	-
16	PIP	Methanol	-		217	275	325	-
		0.1M NaOH	-	-	231	273	333	-
		0.1M HCl	-	-	-	281	318	329
17	SAR	Methanol	-	-	-	284	319	-
		0.1M NaOH	-	-	236	275	324	335
		0.1M HCl	-	-	225	296	365	-
18	SPA	Methanol	-	-	225	307	377	-
		0.1M NaOH	-	-	227	292	363	-

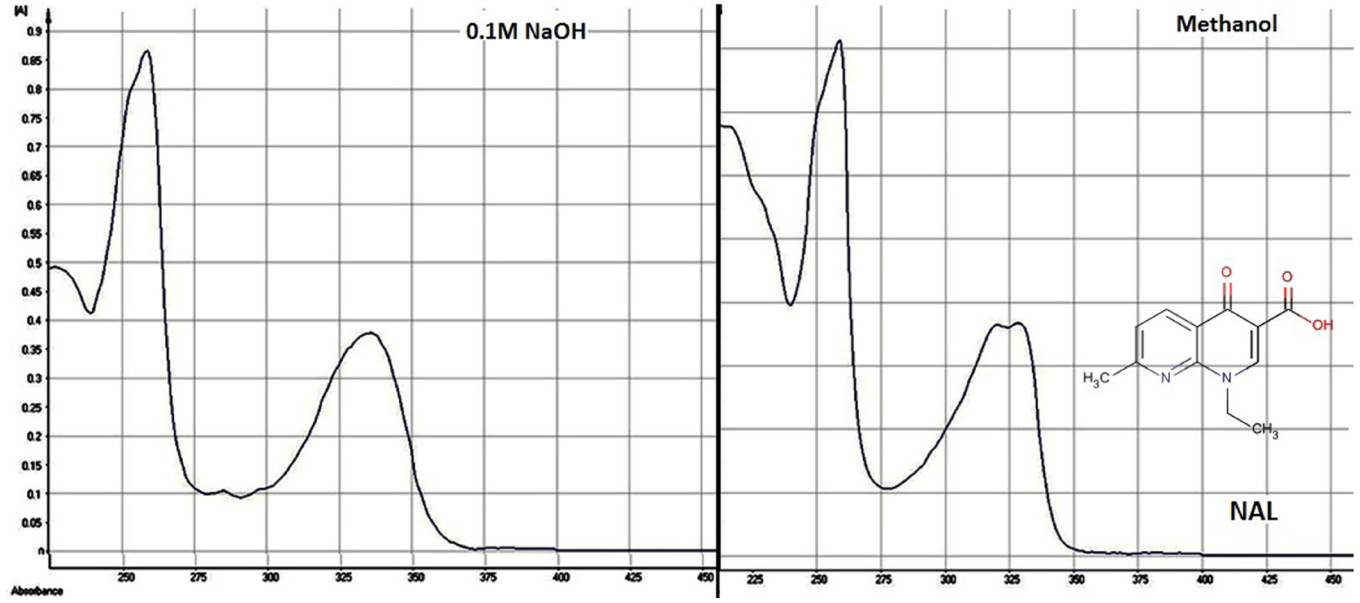


Fig. 2. The recorded UV spectra of NAL

recorded in methanol. In 0.1M NaOH showed a slight increase of the third (λ_3) and fourth (λ_4) absorption maximum in comparison with the spectra in methanol, with an increase in the intensity of the absorption band. This bathochromic shift can be also explained, due to the conjugation phenomenon in a basic medium. In the case of UV spectra recorded for 3'M-DIF in 0.1M HCl and 0.1M NaOH, a slight hypsochromic shift was observed in comparison with the spectrum recorded in methanol. The methyl in position 3 of the piperazine substituent, doesn't modify the spectral properties of the quinolone derivative, which is very similar to those of DIF and SAR (des-methyl-difloxacin).

UV spectra of ENO. ENO presents characteristic UV spectrum, with an absorption band higher in the case of the third (λ_3) absorption maximum compared to the other quinolone derivatives, in all three used solvents. UV spectra recorded in both 0.1M NaOH and 0.1M HCl present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. In this case, the absorption band in basic environment of the third maximum (347 nm) increases greatly in comparison with the spectrum in acidic environment (Figure 4). This bathochromic shift can be explained, due to the conjugation phenomenon in a basic medium. ENO is a naphtyridine derivative, which has an extra nitrogen atom in its structure, compared with the classic quinoline structure of most of the compounds under study. From this point of view, similar to NAL, we can observe a similar spectral behavior in the case of the last absorption maximum (λ_5).

UV spectra of ENR. UV spectra recorded in both 0.1M NaOH and 0.1M HCl present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. Notable is the fact that the absorption maxima values for ENR are very close to those obtained for CIP (Table III). This resemblance comes from the structural similarity, ENR differing only by 4'-ethyl substituent on the piperazine moiety. UV spectra recorded for ENR has a wavelength shift of the absorption maximum to smaller values respectively in 278 nm (acidic medium) and 272 nm (basic medium), almost identical to those of the CIP. As in the case of CIP, the spectrum recorded in 0.1N NaOH exhibited a slight increase in the second (λ_2) and third (λ_3) absorption maximum (bathochromic shift)

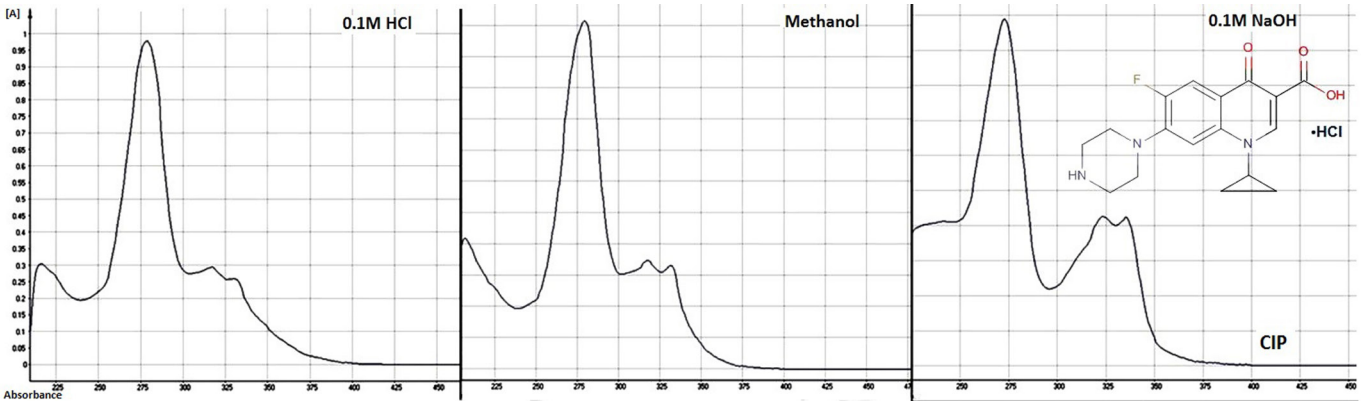


Fig. 3. The recorded UV spectra of CIP

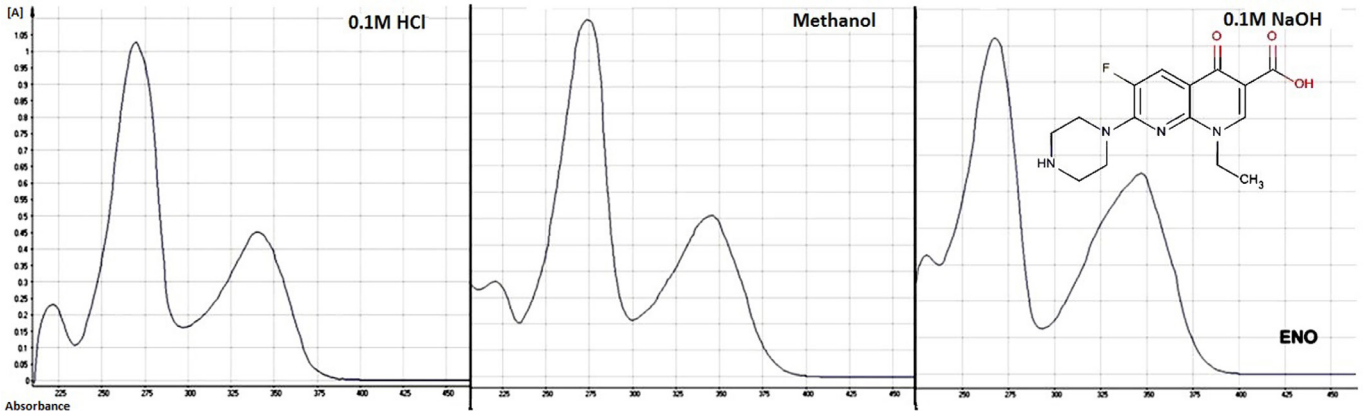


Fig. 4. The recorded UV spectra of ENO

in comparison with the spectrum recorded in methanol. For these two peaks also appears a noticeable increase of the absorption band.

UV spectra of LOM. In the case of LOM, the UV spectra recorded in both 0.1M NaOH and 0.1M HCl present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. The UV spectrum in 0.1M NaOH is characterized by a slight increase of the third (λ_3) absorption maximum (bathochromic shift) in comparison with spectrum registered in methanol, accompanied by an increase in the absorption band. The fluorine atom in the 8 position of the quinoline nucleus, has a minimal influence as UV spectrum, even if it is more electronegative heteroatom than carbon, with unshared electrons ($\pi \rightarrow \pi$ or $p \rightarrow \pi$ link); the unshared electrons are strongly retained by the fluorine atom (unlike other heteroatoms, such as Br or I, which are less electronegative). Compared with the NOR UV spectra, to which LOM it differs structurally by the fluorine atom in the position 8 on the quinoline nucleus and a 3'methyl substituent on the piperazine moiety, all three absorption maximum appears an increase in increment of 8 - 12 nm.

UV spectra of MOX. MOX have a particular UV spectra characterized by a high absorption band, regardless of the medium in which it is recorded. MOX contains a methoxy substituent in the position 8 of the quinoline nucleus and a bicyclic pyrrolidino – piperidine ring in the 7-position, leading to the characteristic UV spectrum. The bathochromic (acidic medium) and hypsochromic (alkaline medium) shifts of the absorption maximum in comparison with the spectrum recorded in methanol are negligible (Figure 5).

UV spectra of NOR and 8F-NOR. In the case of NOR, the UV spectra recorded in both 0.1M NaOH and 0.1M HCl present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. The UV spectrum recorded in 0.1N NaOH is characterized by a significant bathochromic shift for the first (λ_1), third (λ_3) and fourth (λ_4) absorption maximum (240 nm) in comparison with the spectra recorded in 0.1M HCl and methanol. NOR presents a UV spectrum very similar to that of CIP, due to very similar structural characteristics. NOR spectrum shows an additional maximum absorption, at 225 nm (in 0.1M HCl), 227 nm (in methanol) and 240 nm (in 0.1M NaOH). In the case of the NOR UV spectrum recorded in methanol absorption maximum is situated at a different wavelength (283 nm) and is more intense compared to CIP (279 nm). The recorded spectra for 8F-NOR, are very similar to those of NOR, the fluorine atom in position 8 having a minimal influence on the absorption of UV light. The UV spectrum of the difluoro derivative, 8-F-NOR, increases the absorption band of the third peak.

UV spectra of OFL and LEV. Also the UV spectra for OFL recorded in acidic and alkaline medium present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. In a basic

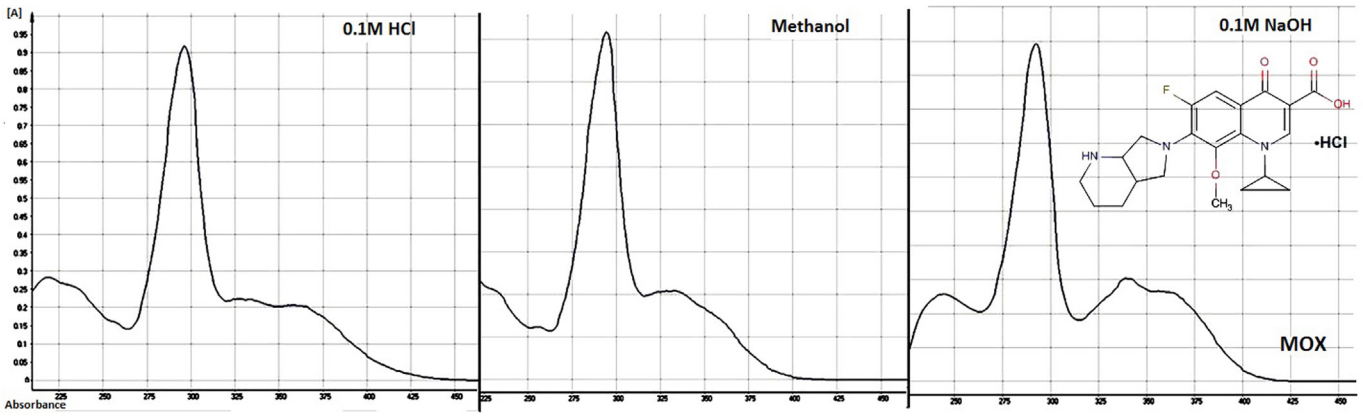


Fig. 5. The recorded UV spectra of MOX

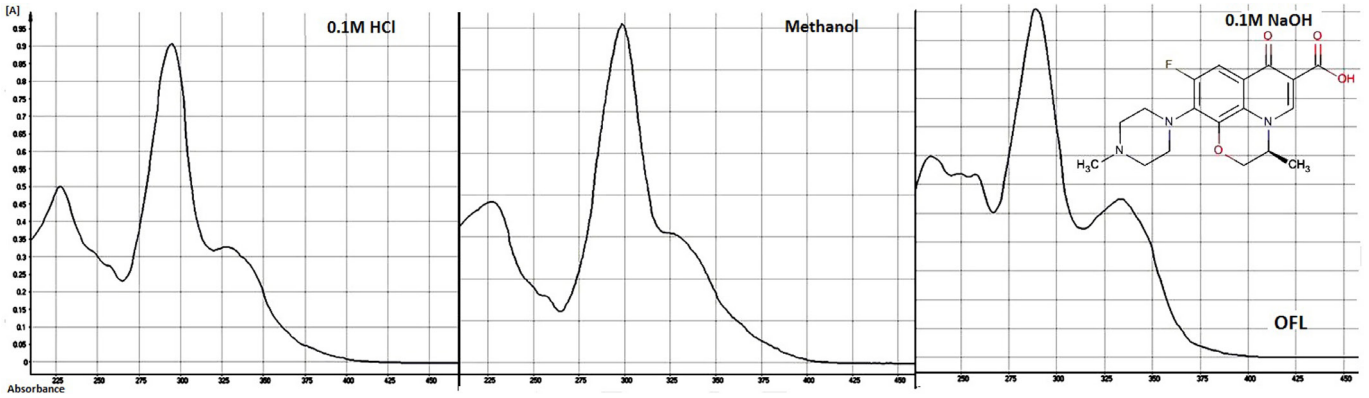


Fig. 6. The recorded UV spectra of OFL

medium an increase in the absorption band of the third absorption maximum is noticeable (Figure 6). The tricyclic chemical structure of OFL brings the possibility of $\pi \rightarrow \pi^*$ transitions. The solution in 0.1M HCl is colored in yellow, because in an acidic environment the protonated form is prevalent and the chromophore absorbs radiation in visible light, probably because oxonium salt is formed due to the oxygenated cycle. In a basic medium, the yellow color disappears, as OFL is predominantly in an anionic form. OFL is a racemic substance due to an asymmetric carbon atom in position 2, which has a methyl substituent; thus is a mixture of two enantiomers R-(+) and S-(-). Levofloxacin is the active pure enantiomer S-(-), the UV spectrum of the LEV is similar to that of OFL.

UV spectra of PEF and 8F-PEF. The registered spectra for PEF are similar to those of NOR, even though we used pefloxacin mesylate salt, from the structural point of view NOR and PEF differ only in a methyl group in the 4'-position of the piperazine substituent. Both PEF and 8F-PEF present a slight bathochromic shift of the absorption maximum in acidic medium (288 nm) in comparison with the UV spectrum recorded in methanol. The 8F-PEF spectra are similar to those of 8F-NOR.

UV spectra of PIP. PIP pyrimido-pyridine derivative can be dissolved in methanol, due to the piperazine substituent in the 7 position, as opposed to the NAL. UV absorption spectrum does not show significant shifts, as the wavelengths at which the absorption maximum occurs are around 275 nm in all the three solvents. A bathochromic shift with an increase in band intensity is observed in 0.1M NaOH, while the first maximum (231 nm) shows a bathochromic shift with decreased intensity of the absorption band (the conjugation phenomenon appears in a basic medium).

UV spectra of SAR. Structurally SAR is des-methyl-difloxacin, consequently similarities the UV spectra of DIF are evident. The UV spectra for SAR recorded in both acidic and alkaline medium present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol. Like in the case of DIF, the recorded spectrum in 0.1M NaOH shows a slight increase of the third λ_3 and fourth λ_4 (bathochromic shift) in comparison with the spectrum recorded in methanol, with a clear increase in the intensity of the absorption band.

UV spectra of SPA. The UV spectra for SPA recorded in both 0.1M NaOH and 0.1M HCl present a hypsochromic shift of the absorption maximum in comparison with the spectrum recorded in methanol (Figure 7). A characteristic of the SPA spectrum is that the first absorption maximum (λ_1) does not present significant shifts regardless of the used solvent. In the case of all three UV spectra recorded of the SPA appears an absorption band around 225 nm, most likely due to the unshared electrons of the amino group in position 5.

UV spectra of model compounds. For a better understanding and interpretation of the UV spectra of the quinolone derivatives under study the UV spectra of some model compounds (Table II) was registered using as solvent metha-

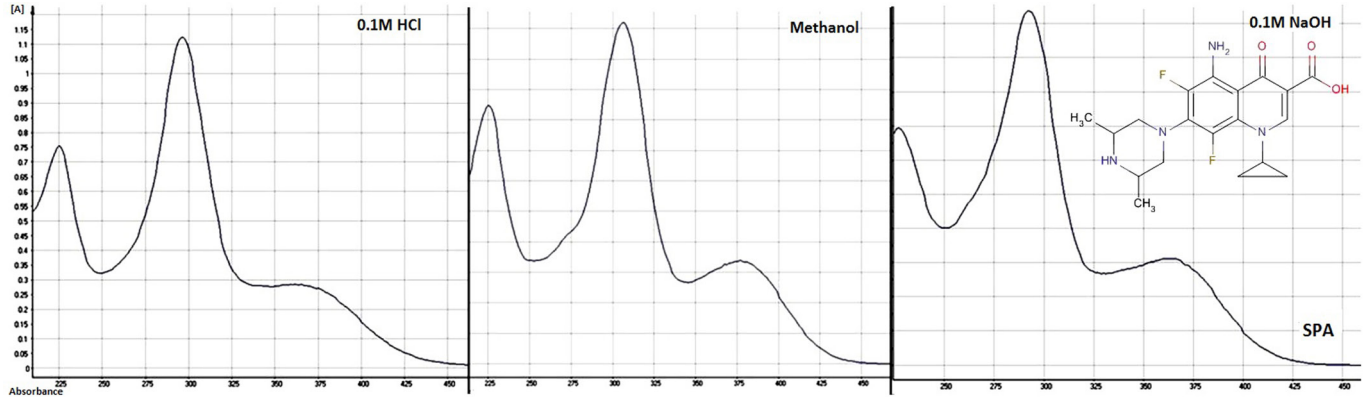


Fig. 7. The recorded UV spectra of SPA

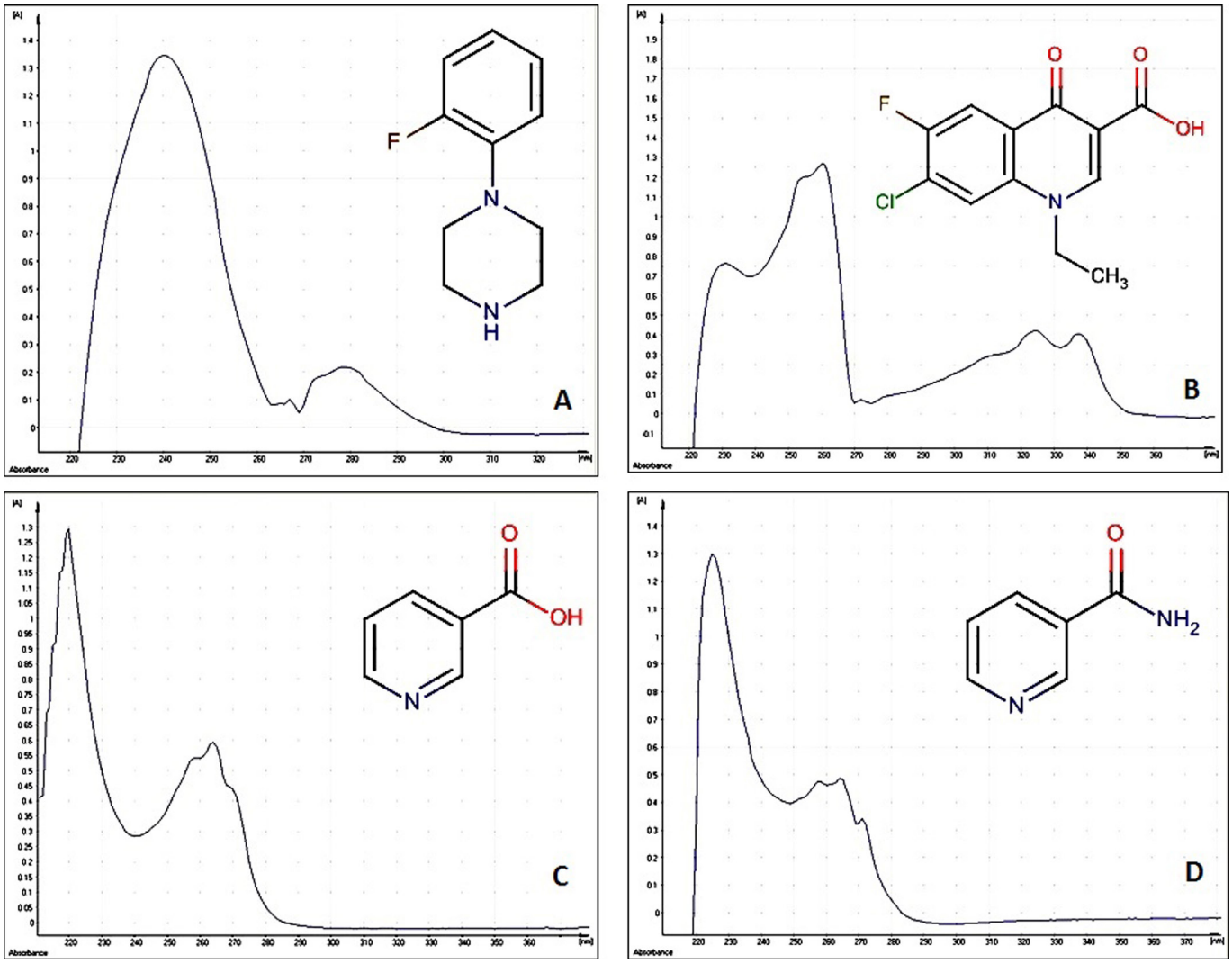


Fig. 8. The recorded UV spectra of the model compounds in methanol (A) 1-(2-fluorophenyl)-piperazine hydrochloride, B) 7-chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, C) nicotinic acid, and D) nicotinamide

nol. The considerations for model compounds which were selected are the following: 1-(2-fluoro-phenyl)-piperazine (hydrochloride) contains a piperazine moiety grafted onto a fluorinated benzene ring; the 7-chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid is a quinoline derivative without piperazine substituent while nicotinic acid and nicotinamide contain a carbonyl group on a pyridine ring. The four compounds selected present in their structure one important pharmacophore, characteristic to the general structure of quinolone derivatives (Figure 8 and Table IV).

Table IV. Absorbance maximum values (in methanol) of the model compounds

Model compound	Absorbance maximum values (nm)					
1-(2-Fluorophenyl)-piperazine hydrochloride		240	267	279		
7-Chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid	230		260		324	337
Nicotinic acid	220	259	264			
Nicotinamide	225	258	264	271		

Discussion

The UV spectra recorded for the studied quinolone derivatives show three absorption maxima characteristic of substituted polynuclear aromatic systems (210 - 230 nm, 270 - 300 nm, 315 - 330 nm).

The UV spectra and assignment of 4-oxo group. Knowing that the benzene has a maximum UV absorption at 260 nm, and naphthalene shows three UV absorption maximum at 221 nm, 286 nm and 312 nm (registered in methanol), in the case of quinolone derivatives the high intensity band is situated in the range of 270 nm - 290 nm corresponding to the carbonyl group in position 4 and is due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transitions. An analogy can be made with UV spectrum of acetone, which has two absorption maxima at 187 nm (less relevant in the case of UV spectra) and 270 nm [3, 14, 15, 16].

The UV spectra and assignment of quinolone nucleus. The 7-chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, from the structural point of view can be considered as a bicyclic compounds trough a condensation of a benzene ring with a substituted pyridine ring. The compound showed three absorption maximum in UV,

similar to the data characteristic to naphthalene structure, which absorbs UV light at 221 nm, 285 nm and 311 nm. The first peak appears at 230 nm and seems to be similar to the absorption peaks at 220 nm and 225 nm in the case of UV spectra of nicotinic acid and nicotinamide. The second absorption maximum at 260 nm is due to both the benzene ring and carbonyl group. In addition, the UV spectrum of 7-chloro-6-fluoro-1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid also presents two very similar absorption maxima at 324 and 337 nm, which corresponds to the third absorption maximum given by the naphthalene condensate nucleus. Moreover, as we have shown above, all the compounds under study (quinolone and naphthyridine structures) has an absorption band in the range 315-330 nm.

The UV spectra and assignment of carboxylic group. The carboxyl group in position 3 of the quinoline nucleus, most likely, causes the appearance of a absorption band around 275 nm, supported by the values of benzoic acid maximum (273 nm) as compared to benzene (255 nm), but also by the bicyclic structure of naphthalene. In the case of UV spectra of nicotinic acid (contains a carboxylic group) and nicotinamide (contains a amide group) a slight bathochromic shift (259 nm) for the first absorption maximum and a hypsochromic shift (264 nm) in the case of the second absorption maximum was observed in comparison with pyridine, which absorbs UV light at 251 and 270 nm [16, 17, 18]. In the case of NAL, these considerations are in contradiction with finding of Park H-R and contributors [19].

The 6-fluoro substituent influence of the UV spectra. In the interpretation of the UV spectrum of 1-(2-fluoro-phenyl)-piperazine we observed that piperazine does not absorb UV light, so the piperazine substituent does not affect the absorption bands in the UV range of the studied quinolone derivatives. Absorption band which may be attributed to the phenyl-benzene component is located at 267 nm, as benzene absorbs UV light around 255 nm; the bathochromic shift of the peak of benzene absorption is probably due to the electronegativity of fluorine atom, similar to the introduction of atoms of Cl or Br substituents on the benzene ring [17, 20].

The 5-amino substituent influence of the UV spectra. The introduction of the 5-position of an amino group in the structure of the SPA, is most likely responsible for the bathochromic shift of the absorption maximum: 307 nm in the UV spectrum of SPA to 291 nm in the UV spectrum of LOM or 377 nm in the UV spectrum of SPA to 320 nm in the UV spectrum of LOM. Similarly, the amino group is a strong auxochrom for benzene in the aniline structure, having an intense absorption band at 230 nm and a low intensity at 280 nm [16].

The methoxi group influence of the UV spectra. Compared to the CIP (absorption maximum at 318 nm), without the 8-methoxy moiety, MOX absorption maximum (294 nm) presents a hypsochromic a shift of the absorption maximum; probably due to a $p \rightarrow \pi$ conjugation with the heteroatom ring is sterically hindered by other adjacent substituents. The methoxy substituent of MOX influences the absorption spectra, but the influence of the $\sigma \rightarrow \sigma^*$ transitions from the bicyclic substituent are poor. This observation is substantiated by the UV spectra of benzene methoxy-benzene (absorption maxima 255 nm/275 nm), where a clear bathocromic shift is observed [17, 21]. UV absorption maxima of the compounds under study differ depending on the solvent in which they were recorded. Thus, in 0.1M HCl are predominant the protonated forms of the compounds while in 0.1M NaOH the anionic sodium salts are formed [10].

The naphtiridine and pyrimido-pyridine structure influence of the UV spectra. UV spectra of NAL and ENO naphthyridine derivatives, are similar, although the NAL structure does not contain a piperazine substituent present in ENO (piperazine substituent does not affect the absorption bands in UV). The 6-fluoro auxochrom present in ENO seems to be responsible for the bathochromic shift of ENO in methanol with a λ_{max} (273 nm) compared with NAL (259 nm). However, no significant differences were observed between the UV spectra of the ENO, a fluorinated 6-naphthyridine derivative with a piperazine substituent just like other quinoline derivatives. The UV spectrum of PIP falls within the pattern of quinolone derivatives with three absorption maximum values. Notably, the absorption bands are low in the zone of the first and third absorption maximum compared to the λ_{max}. The basic pyrimido-pyridine structure does not modify the characteristic aspect of the quinolone UV spectrum.

Conclusions

The recorded UV spectra of the quinolone derivatives present three absorption maximum (210-230 nm, 270-300 nm, 315-330 nm), characteristic to the quinolone structure obtained through a condensation of a benzene with dihydro-4-pyridone heterocycle. The most frequent shift of the absorption band was a slight hypsochromic shift in 0.1N HCl (predominant protonated form) and 0.1 NaOH (predominant anionic form) in comparison with the spectrum recorded in methanol. Structurally analogous compounds show similar spectra in the UV (e.g. ENR and CIP, NOR and PEF). Structural differences are reflected in the minimal change in UV spectra, only when there are substituents which are auxochroms (fluor, amino, methoxy substituents on the quinoline, naphthyridine, pyrimido-pyridine structures). Differences between UV spectra of compounds with pyrimido-pyrimidine or naphthyridine nucleus in comparison with the ones with quinolone structure exist but there are not notable. The property to absorb UV light characteristic quinolone derivatives is of particular importance in developing UV spectrophotometric analysis methods or those using a UV spectrophotometric detector (HPLC, CE). Relationships between chemical structure and UV spectra are not yet fully decoded, but the

present study provides useful information that can be used successfully in various research works.

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