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PAPER

Determination of photostability and photodegradation products of moxifloxacin in the presence of metal ions in solutions and solid phase. Kinetics and identification of photoproducts†

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Photostability of moxifloxacin (MOXI) after UVA irradiation in solutions and solid phase, with and without participation of Cu(II), Zn(II), Al(III), and Fe(III) was tested. The studies were carried out by the TLC-densitometric method and LC-MS/MS method. Elaborated and validated chromatography-densitometric method was used for assaying. It was shown that the number and type of photoproducts depend on the environment and type of the metal ion. The studied ions enhanced the degradation of MOXI in solutions, and the influence of Cu(II) and Fe(III) ions was higher than that of Zn(II) and Al(III) ions. In solid phase, in contrast to solutions, all metal ions decreased the photodegradation, however the influence of ions, Al(III) and Zn(II), was weaker than that of Cu(II) and Fe(III) ions. Identification of the degradation products performed with LC-MS/MS and ^{1}H NMR identified them as: 1-cyclopropyl-6-fluoro-7-amino-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-7-(2-oxo-octahydro-6*H*-pyrrolo[3,4-b]pyridine-6-yl)-1,4-dihydroquinoline-3-carboxylic acid, 7-[3-hydroxyamino-4-(2-carboxyethyl)pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

1. Introduction

Moxifloxacin (MOXI), 1-cyclopropylo-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*S*,7a*S*)-octa-hydro-6*H*-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinoline carboxylic acid monohydrochloride, is an antibacterial synthetic drug, belonging to the fourth generation of fluoroquinolones. The drug takes effect on aerobic, Gram-positive cocci (*Streptococcus pneumoniae* and *Staphylococcus aureus*) and Gram-negative bacilli of *Enterobacteriaceae* family, and *Pseudomonas aeruginosa*. Its activity against atypical bacteria of *Chlamydia* spp., *Mycoplasma* spp., and *Legionella* spp. genera, bacilli of genus *Mycobacterium* and anaerobe of *Bacteroides* and *Clostridium*[1–3] genera is of high value.

The mechanism of action of MOXI, similar to other fluoroquinolones, lies in inhibiting the activity of two bacterial enzymes – DNA gyrase (topoisomerase II) and topoisomerase IV – which regulate spatial arrangement of DNA in bacterial cells. These proteins can cut both strands of the nucleic acid and rejoin them. Inhibiting the activity of those enzymes by formation of irreversible complex drug/enzyme/DNA, disables DNA synthesis and leads to the bacterial cell death.[3,4]

Based on the literature it can be stated that the most used technique for determination of MOXI in pharmaceutical preparations and biological material analysis is HPLC.[5–10] The technique was also employed to assay MOXI and its derivatives.[11–13] Ligand-exchange liquid chromatography with chiral modifier in mobile phase was used to separate MOXI from its (*R*,*R*)-isomer.[14] LC-MS/MS with electrospray ionization can be used for analysis of MOXI in blood plasma.[15] Capillary electrophoresis with laser induced fluorescent detection used for the analysis of MOXI in body fluids, and capillary electrophoresis with spectrophotometric detection in UV range for testing its enantiomeric purity[16,17] can be worth mentioning among other separating methods. Beside the above mentioned methods, differential pulse polarography[18] and spectrophotometry[19–21] were used to assay MOXI.

Moxifloxacin assaying with TLC was described in two papers. Salem *et al.* proposed TLC for analysis of three fluoroquinolones, lomefloxacin, moxifloxacin, and sparfloxacin, in presence of their decarboxylated degradation products after acidic hydrolysis. For MOXI, TLC plates covered with silica gel were used as the solid phase, and a mixture of 0.3 M ammonium acetate solution : conc. ammonia : *n*-propanol (1 : 1 : 8 v/v/v) as the mobile phase.

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Measurement of the chromatographic spots was performed densitometrically at 290 nm wavelength.[19]

For stress studies of MOXI, Motwani *et al.* used HPTLC plates covered with silica gel and a mixture containing propanol : ethanol : 6 M ammonia (4 : 1 : 2 v/v/v) as the mobile phase. The chromatographic spots were registered densitometrically at 298 nm wavelength.[21]

Fluoroquinolones are a group of compounds which undergo photodegradation under UV light relatively easy. The degradation is diverse and depends on the conditions and structure of studied compounds.[22–27]

Photophysical properties of MOXI were investigated in aqueous media using stationary and time-resolved fluorimetry, and by laser flash photolysis and pulse radiolysis.[28,29] The effect of pH and irradiation conditions on the photolytic and TiO_2 mediated photocatalytic degradation of MOXI in aqueous solutions have been studied.[30]

Photodegradation of MOXI was conducted to assess the specificity of HPLC during 11 days in conditions consistent with the option 2 of ICH Q1B[31] directive and during 10 days with use of UV radiation at 254 nm. Authors of those studies did not state the presence of MOXI degradation products or observed its slight degradation.[13,14] Motwani *et al.* conducted MOXI stress studies. After irradiation of drug methanol solution for 8 h with UV light at 254 nm, they showed the presence of 2 products of degradation with 95.32% active substance recovery. In case of solar light irradiation for 24 h, they detected 5 products of degradation with MOXI recovery at 86.76%.[21]

In this study an attempt was made to test the photostability of MOXI exposed to UVA radiation in solutions and solid phase, with presence or absence of Cu(II), Fe(III), Zn(II), and Al(III) ions. In addition, LC-MS/MS and ^{1}H NMR were used to determine the structure of photodegradation products, as well as a new chromatography-densitometric assay was developed for MOXI determination in the presence of degradation products.

2. Experimental

2.1. Reagents

Standards substances. Moxifloxacin hydrochloride series Strasbourg Cedex; Code:Y0000703; Id:002IC0; Council of Europe – EDQM CS; Cat No. T30026 F-6081.

Metal salts solutions. To prepare the solutions of metal ions at 0.1 M concentration the following salts were used: (1.2488 g) $CuSO_4 \cdot 5H_2O$, (1.4337 g) $ZnSO_4 \cdot 7H_2O$, (0.9988 g) $Fe_2(SO_4)_3 \cdot H_2O$, (1.6753 g) $Al_2(SO_4)_3 \cdot 18H_2O$. Above given weighed portions of salts were transferred to 50 mL flasks and filled with water to required volume. Directly for testing, the obtained solutions were diluted with the same solvent to a final concentration of 0.025 M.

Standard solution. Weighed portions of the standard substance (6.6 mg moxifloxacin hydrochloride) were transferred to 100 ml flasks. 50 mL of water was added to the solutions for photodegradation studies in solutions or 50 mL of methanol to those for photodegradation studies in solid phase. The flasks were shaken until the substance dissolved, and the same solvent was supplemented to the required volume. Solutions at 60 μg mL^{-1} concentration relative to MOXI were prepared.

2.2 Preparation of samples for tests in solutions

Two millilitres of 60 μg mL^{-1} aqueous solution of MOXI were measured off on quartz dishes of 4 cm diameter, and 0.2 mL of water or of appropriate salt solution with 0.025 M metal ion concentration was added. The dishes were sealed with a quartz lid. The solutions were exposed to UVA radiation for a maximum of 168 h, and 20 μL were probed every 24 h for study.

2.3 Preparation of samples for tests in solid phase

Samples were prepared by measuring off 1.0 mL of 60 μg mL^{-1} methanol MOXI solution and 0.1 mL of water or appropriate salt aqueous solution on Petri dishes of 5 cm diameter. Samples were mixed and evaporated in water bath at 60 °C until dry matter was obtained. For each metal ion 5 identical samples were prepared. They were exposed to UVA radiation for 15 h. Every 3 h, contents of individual dish were dissolved in 1.0 mL of methanol and 20 μL was spotted onto TLC plate.

For each sample a dark control sample was prepared, which was protected with aluminum foil before irradiation.

2.4 Irradiation conditions

Irradiation was conducted in a climatic chamber KBF-ICH 240 APT.line™; (Binder GmbH, Tuttlingen, Germany) at 20 °C and 60% humidity using UVA radiation (320–400 nm) with maximum emission at 365 nm. The distance of the samples to radiation source was 13 cm. The UVA dose was determined by means of radiometer type VLX-3W, Vilber Lourmat, with a sensor CX-365, to be each time of 5.09×10^{-3} Jcm^{-2}min^{-1}.

2.5 TLC conditions

TLC was performed on a precoated TLC sheets of silica gel 60 with fluorescent indicator on aluminium (13 × 12 cm, cut from 20 × 20 cm, Art. 1.0554, Merck, Germany). Twenty microlitres of obtained solutions were applied using a Linomat V (Camag, Switzerland) sample applicator as 8 mm width bands with distance of 10.0 mm from the plate bottom, 16 mm from the edge of the plate, and 8 mm between the edges of the spots. 20 μL of non-irradiated MOXI solution was applied on the plates at the same time. Chromatograms were developed to a distance of 115 mm with methylene chloride : ethanol : toluene : *n*-butanol : ammonia 25% : water (6 : 6 : 2 : 3 : 1.8 : 0.3 v/v/v/v/v) as mobile phase in a glass chromatographic chamber (18 × 9 × 18 cm in size, Sigma–Aldrich, USA). The plate was dried at room temperature for 30 min. Identification of spots on chromatograms was achieved by means of a Camag TLC Scanner 3 with winCats 1.3.4 software at 294 nm. For identification, absorption spectra within the range 200–400 nm were recorded. Identification of constituents was done by comparison of position of peaks on chromatograms on the basis of retardation factors (R_F) and absorption spectra. Percentage ratio of constituent (%i) was calculated from quotient of peak area (Ai) to the sum of all peak areas (ΣA) on chromatograms according to formulation%i = (Ai/ΣA)100.

2.6 LC-MS/MS analysis

High performance liquid chromatography conditions. Liquid chromatography was performed using an Agilent 1100 (Agilent

Technologies, Waldbronn, Germany) LC system. Chromatographic separation was carried out with an XBridge C18 analytical column (30 mm × 2.1 mm, 3.5 μm, Waters, Ireland) set at 30 °C.

Two solvent mixtures were used: solvent A: acetonitrile – formic acid (0.01%) and solvent B: H_2O – formic acid (0.01%). The following gradient was used: 0–5 min, 0–100% A; 5–7 min, 100% A; 7–8 min, 100–0% A; 8–20 min, 100% B. The flow rate was set at 600 μL min^{-1}. A sample volume of 20 μL was injected into the analytical column for compound analysis.

Mass spectrometric conditions. Mass spectrometric analyses were accomplished on an Applied Biosystems MDS Sciex (Concord, Ontario, Canada) API 2000 triple quadrupole mass spectrometer equipped with an electrospray ionization (ESI) interface. ESI ionization was performed in the positive ionization mode. A standard polypropylene glycols solution (PPG standard) was used for instrument tuning and mass calibration at unit mass resolution according to the Applied Biosystems manual. The mass spectrometer was operated with a dwell time of 200 ms, and a 5 ms delay between scans for each transition on the first quadrupole (Q1) in range of 50 to 1000 amu.

To find the optimal parameters of ion path and ion source of the studied compound the quantitative optimization was done by direct infusion of MOXI at concentration of 1 μg mL^{-1} at a flow rate of 10 μL min^{-1} using a Hamilton syringe pump (Hamilton, Reno, Nevada).

The ion source parameters were as follows: ion spray voltage (IS): 5500 V; nebulizer gas (gas 1): 45 psi; turbo gas (gas 2): 45 psi; temperature of the heated nebulizer (TEM): 300 °C; curtain gas (CUR): 10 psi. Nitrogen (99.9%) from Peak NM20ZA was used as the curtain and collision gas. The ion path parameters for moxifloxacin were as follows: declustering potential (DP): 10 V; focusing potential (FP): 350 V; entrance potential (EP): 10 V; electron multiplier (CEM): 2500 V; collision cell entrance potential (CEP): 44 V; collision cell exit potential (CXP): 25 V, respectively. Data acquisition and processing were accomplished using the Applied Biosystems Analyst version 1.4.2 software.

2.7 ^{1}H NMR analysis

To identify the photodegradation products by ^{1}H NMR it was necessary to isolate individual constituents from the chromatograms. For this purpose, having developed the chromatograms and located the bands from photodegradation products, appropriate layers of gel were scraped off. The silica gel was shaken mechanically with 5.0 mL methanol for 1 h, and then filtered through a C_8 SPE column (Bakerbond spe™, J.T. Baker, Denver, Holland). The solvent was removed by distillation until a dry mass was obtained.

NMR spectra were measured in CD_3OD on a Varian Mercury-VX 300 spectrometer operating at 300.08 MHz (^{1}H) chemical shifts (δ in ppm) were referenced to solvent lock signal. All spectra were acquired at ambient temperature. Due to low sample concentration, for each ^{1}H NMR spectra 256 scans were accumulated with spectral width of 4.2 kHz and 16 k data points.

3. Results and discussion

3.1 TLC analysis

The chromatography–densitometric method turned out to be useful for assaying MOXI in the presence of photodegradation products. Good separation of MOXI from the degradation products was obtained using TLC plates with fluorescent indicator as the stationary phase and dichloromethane : ethanol : toluene : *n*-butanol : 25% ammonia : water (6 : 6 : 2 : 3 : 1.8 : 0.3 v/v/v/v/v) as the mobile phase. The obtained values of retardation factors were: for MOXI $R_F \approx 0.27$, and for the degradation products, both from the solid phase and solutions 0.15, 0.19, and 0.24. The mobile phase composition was different than the compositions in available literature, concerning MOXI assaying using TLC.[19,21]

In the established assaying conditions, no mutual peaks interference or influence of other components present in samples, were observed. Therefore, it was considered that the method meets the specificity criteria. The method is characterized by a wide linear range, from 0.03 μg/band to 1.5 μg/band, high sensitivity LOD = 12 ng/band. Good precision and intermediate precision RSD does not exceed 1.1% and the recovery from 100.34% to 101.50% (Table S1, ESI†).

Studies on the influence of changes in MOXI concentration in the range 20–120 μg mL^{-1} on photodegradation process demonstrated that the increase in MOXI concentration is accompanied by a linear growth in percentage content of degradation products at constant concentration of ions of metals (Fig. 1). An exception was constituted by the samples containing Fe(III) ions in the solid phase, in which MOXI degradation was not observed. Based on the obtained results solutions of MOXI at concentration of 60 μg mL^{-1} were used for further photodegradation studies.

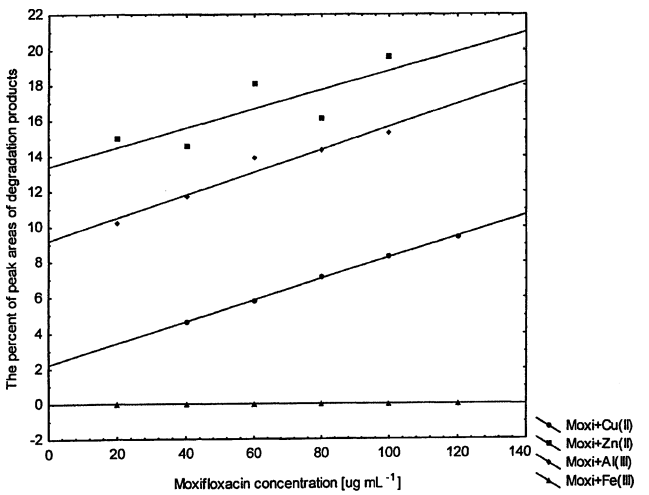


Fig. 1 Changes in percentage content of degradation products of MOXI, after exposure to UVA in solid phase in the presence of metal ions, in dependence on its concentration.

3.2 Photodegradation of moxifloxacin in solutions

Exposure of MOXI ($R_F \approx 0.27$) to UVA radiation in the absence of metal ions in solutions always resulted in one additional peak ($R_F \approx 0.24$) originating from the degradation product.

Moxifloxacin solutions exposed to UVA radiation for 24 h, 48 h, 72 h, 96 h, and 168 h were clear and did not show any visual changes. First changes giving evidence of MOXI degradation were recorded after 24 h (2.48%). Further irradiation caused degradation at 4.21% after 48 h. Degradation increased together with the time of irradiation, reaching 8.06% after 168 h.

Table 1 Kinetic parameters of moxifloxacin photodegradation in solutions, with and without the presence of metal ions

Sample composition	Rate constant k (h^{-1})	$t_{0.1}$ (h)	$t_{0.5}$ (h)	Correlation coefficient r
Fe(III)	2.94×10^{-3}	35.82	235.71	0.9693
Cu(II)	1.32×10^{-3}	79.77	525.00	0.9892
Zn(II)	7.65×10^{-4}	137.65	905.88	0.9799
Al(III)	6.68×10^{-4}	157.63	1037.42	0.9800
Without metal ions	5.41×10^{-4}	194.64	1280.96	0.9750

Table 2 Kinetic parameters of moxifloxacin photodegradation in solid phase, with and without the presence of metal ions

Sample composition	Rate constant k (h^{-1})	$t_{0.1}$ (h)	$t_{0.5}$ (h)	Correlation coefficient r
Without metal ions	48.10×10^{-3}	2.19	14.41	0.9974
Al(III)	19.10×10^{-3}	5.51	36.28	0.9990
Zn(II)	12.40×10^{-3}	8.49	55.88	0.9808
Cu(II)	3.45×10^{-3}	30.48	200.61	0.9522

Much larger degradation was observed in the samples with Cu(II), Fe(III), Zn(II) and Al(III) ions. Three products of photodegradation with $R_F \approx 0.15$ (P-I), $R_F \approx 0.19$ (P-II), and $R_F \approx 0.24$ (P-III), were observed in the presence of Fe(III) ions. In the presence of Al(III), two degradation products P-II and P-III were detected. In the samples containing Cu(II) or Zn(II) ions only one photoproduct P-III was observed in the chromatograms.

Comparing photodegradation results for the solutions containing metal ions, it can be stated that greater degradation occurs in them in comparison to analogous solutions, which did not contain metal ions, and it is dependent on the type of metal ion (Fig. S1, ESI†).

The highest concentration of photodegradation products after 168 h of irradiation was in the presence of Fe(III) 48.62% and Cu(II) 15.87%, while the lowest with Zn(II) 10.64% and Al(III) 8.67%. Parallel dark control tests showed no degradation of the studied compound.

Based on the chart of MOXI concentration changes (log c) in time-dependant manner (t), it was confirmed that photodegradation in solutions occurs according to the kinetics of first-order reaction (Fig. S2, ESI†).

The calculated kinetic parameters (Table 1) confirm higher MOXI degradation in the presence of metal ions.

Rate constants k describing photodegradation process in solutions containing ions have decreasing values from Fe(III), through Cu(II) and Zn(II), to Al(III). They are higher in comparison to the rate constant of MOXI photodegradation solutions, which do not contain the ions.

Calculated values $t_{0.1}$ and $t_{0.5}$ confirm higher MOXI degradation in the presence of metal ions, which indicates decreased drug stability. Zn(II) and Al(III) ions, have definitely weaker influence on the photodegradation process of MOXI in comparison to Fe(III) and Cu(II).

3.3 Photodegradation of moxifloxacin in solid phase

UVA irradiation of MOXI without metal ions in solid phase resulted to three additional peaks originating from the products of degradation: P-I, P-II and P-III.

Moxifloxacin degradation was stronger in comparison to the studies on solutions, and after 3 h of irradiation was 29%, and after 15 h 60.66%. In dark control samples presence of one additional peak, with $R_F \approx 0.24$, which percentage amount was 2.24%, was observed.

Similar to solutions, also in solid phase the metal ions influenced MOXI degradation. The influence depended on the type of ion and increased together with time of irradiation. The highest degradation, around 30%, was observed after 15 h exposition to UV radiation in presence of Al(III). It was lower in case of Zn(II) (~23%) and Cu(II) (~5%). Moxifloxacin did not decompose in case of Fe(III). Parallel control studies revealed no degradation of the studied compound in the samples containing Zn(II), and ~3% degradation in presence of Al(III) and Cu(II) ions.

Fig. S3, ESI† presents the results of MOXI degradation in solid phase with and without metal ions. Values of the retardation factor of peaks occurring on the densitograms obtained for solid phase are comparable with the values obtained for solutions. Changes in MOXI concentration (log c) in solid phase in time-dependent manner (t) with and without the presence of ions follow first-order reaction kinetics (Fig. S4, ESI†).

Rate constants k of MOXI photodegradation decrease in the presence of ions, whereas the $t_{0.1}$ and $t_{0.5}$ values increase in comparison to MOXI without metal ions (Table 2).

Based on the calculated kinetic parameters, it can be stated that Fe(III) ions do not result to MOXI degradation, as it is in case of solutions. Slight degradation occurs in the presence of Cu(II), and increases in case of Zn(II) and Al(III) ions.

3.4 Identification of photodegradation products

By comparing the results of densitometric studies on MOXI degradation in solutions and in solid phase, it can be assumed that independently of the type of studied phase and sample composition, similar degradation products are formed. Absorption spectra registered directly from the chromatograms can constitute a confirmation. They have similar shape as MOXI spectrum ($\lambda \approx$ 94 nm and $\lambda \approx 340$ nm) with maximum absorption shifted towards shorter wavelengths ($\lambda \approx 280$ nm and $\lambda \approx 330$ nm) (Fig. 2).

To confirm the identity of photodegradation products LC-MS/MS assays were performed for photodegradation of MOXI in solid phase samples, under conditions described in point 2.6. HPLC chromatogram for MOXI and photodegradation products in Fig. 3 is consistent regarding the number of peaks with the densitogram obtained in TLC.

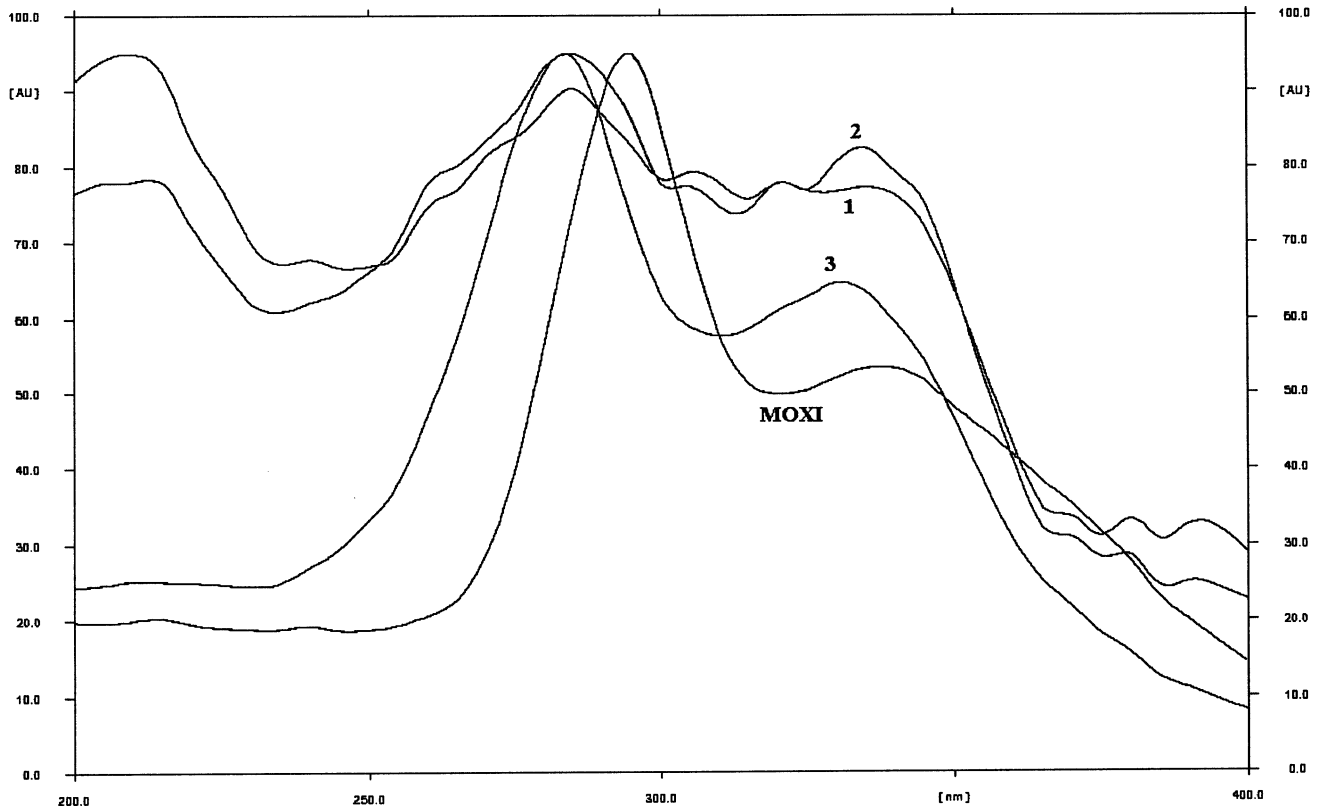


Fig. 2 Absorption spectra of MOXI and degradation products P-I (1), P-II (2), and P-III (3) after UVA exposure in solid phase.

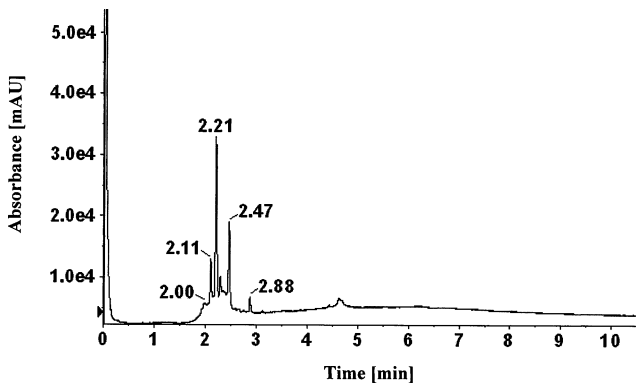
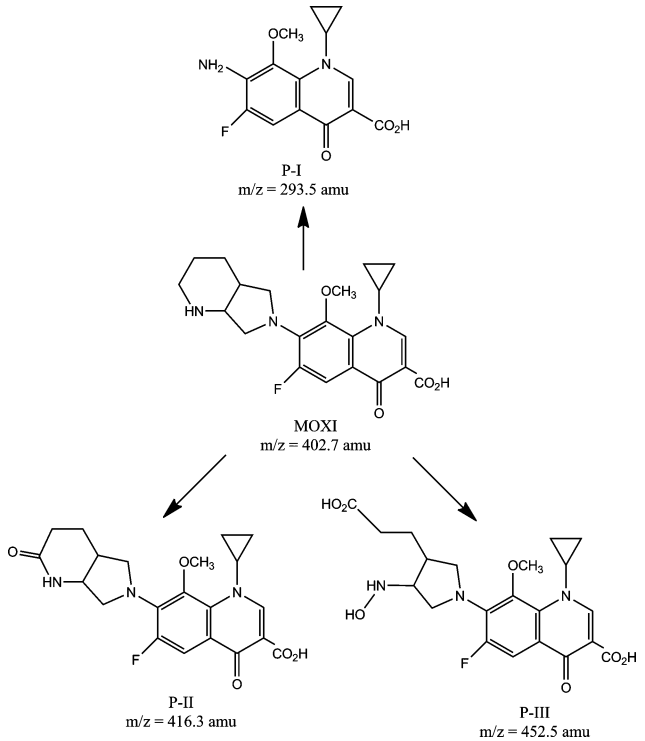


Fig. 3 Representative HPLC chromatogram obtained from MOXI exposed to UV radiation in solid phase for 15 h.

Protonated molecular ions of the main peak and peaks of degradation products in mass spectra (Fig. S5–S8, ESI†) can be attributed to the following compounds: MOXI (t_R = 2.21 min) m/z = 402.7 amu; P-II (t_R = 2.11 min) m/z = 416.3 amu 1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-7-(2-oxo-octahydro-6*H*-pyrrolo[3,4-b]pyridine-6-yl)-1,4-dihydroquinoline-3-carboxylic acid; P-III (t_R = 2.88 min) m/z = 452.5 amu 7-[3-hydroxyamino-4-(2-carboxyethyl)pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic, and P-I (t_R = 2.47 min) m/z = 293.5 amu 1-cyclopropyl-6-fluoro-7-amino-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid. Above described products are formed as a result of oxidation of (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-b]pyridine-6-yl group present in position 7 of 1,4-dihydroquinoline moiety of MOXI.

Analysis of ^{1}H NMR spectra of MOXI photodegradation products, despite the very small amount of the samples, supports the reaction scheme derived from the MS spectra. Aromatic region of the spectra is the same for all of them indicating no changes in this moiety – only one signal at δ 7.35 ppm is visible, which can be assigned to two protons of quinoline moiety, possessing the same chemical shift. Similarly all spectra exhibit a strong singlet at δ 3.68 ppm indicating the presence of unchanged methoxyl group in the same chemical neighbourhood. Analysis of aliphatic fragment of spectra is possible only through comparison between them due to strong signal overlapping and low sample concentration. Photoproduct P-I has no remarkable signals in range δ 4–5 ppm apart of solvent signal, indicating that it is very probable, that the diazabicyclic fragment of starting MOXI has been completely degraded (Fig. S9, ESI†).

Photoproducts P-II and P-III possess clearly visible signals in mentioned region, which can be assigned to protons of diazabicyclic moiety, closely to electron accepting substituents. This assumption supports the findings from the MS spectra, that during photolysis oxidation occurs yielding the 3-oxodiazabicyclic derivative. Further changes in signals pattern are observed in spectrum of sample 3. There are signals appearing at δ 3.5–3.8 ppm indicating downfield shift of aliphatic protons' signals which can be attributed to changes in substituents into more electrophilic groups. Taking into account the MS spectra of product P-III, it can be assumed that its structure originates from compound P-II after hydrolysis of amide bound and further oxidation of free



Scheme 1 The plausible degradation photoproducts of MOXI.

amine group yielding carboxyl and *N*-hydroxyamino substituents in aliphatic fragment (Fig. S10–S11, ESI†). Scheme 1 reports the plausible degradation patterns of MOXI under the conditions mentioned.

Moxifloxacin photodegradation process in solutions and solid phase, with and without metal ions, and identification of degradation products, described in this work, were not a subject of studies of any other authors. Papers cited earlier, which concerned MOXI photodegradation in solutions were limited only to determination whether the degradation occurred or not, and did not contain data regarding identification of obtained photoproducts.[13,14,21] In our previous publication, photostability of ciprofloxacin in solid phase with presence of metal ions, but in different conditions (wavelength, irradiation time), was studied.[22] After analysis of the result, it can be stated that MOXI in solid phase behaves in a different way, which can be attributed to a different chemical structure or mentioned differences in conditions under which the photodegradation studies were performed. The probable contribution of metal ions in the photodegradation process occurs due to their ability to form complexes with MOXI of different stabilities,[32] and may be due to charge transfer in the complex formed between the central atom and ligand.[33]

4. Conclusions

Moxifloxacin undergoes degradation in solutions and in solid phase with and without the presence of metal ions. Cu(II) and Fe(III) ions increase the MOXI degradation in solutions much more than Zn(II) and Al(III). In solid phase the influence of Zn(II) and Al(III) is stronger than that of Cu(II) and Fe(III).

Rate constants k and the times $t_{0.1}$ and $t_{0.5}$ confirm higher stability of MOXI in solutions without metal ions than with their presence. In solid phase the studied metal ions increase the stability of MOXI. Potential products of photodegradation of MOXI are: 1-cyclopropyl-6-fluoro-7-amino-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-7-(2-oxo-octahydro-6*H*-pyrrolo[3,4-b]-pyridine-6-yl)-1,4-dihydroquinoline-3-carboxylic acid, 7-[3-hydroxyamino-4-(2-carboxyethyl)pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

The chemical structure of degradation products was elucidated for the first time in this investigation. The established chromatography-densitometric method can be useful for MOXI assaying in the presence of its photodegradation products.

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