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RESEARCH ARTICLE

Stability of Aqueous and Oily Ophthalmic Solutions of Moxifloxacin

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ABSTRACT:
Objective. The purpose of this study was to investigate the stability of aqueous and oily ophthalmic solution of moxifloxacin fourth generation of fluoroquinolone. *Method.* The stability studies on the aqueous and oily ophthalmic formulations of moxifloxacin were carried out by exposing the formulations to accelerated (40^0 C and 75% RH) and room temperature storage conditions. During storage period, the formulations were periodically examined for pH and the remaining drug concentrations. *Results.* The accelerated and long term stability studies conducted on aqueous isotonic ophthalmic solutions of moxifloxacin indicate that moxifloxacin (0.5%, w/v) formulation of pH 7.2; containing, BAK (0.01%) and EDTA (0.01%) could provide a shelf life (t_{90}) of 2 years, and the formulation appears promising from corneal permeation point of view. Among all the oily formulations, moxifloxacin (0.05%, w/v) ophthalmic solution in castor oil, with adequate overage, containing benzyl alcohol (0.5%, v/v) appears ideal from stability point of view. *Conclusions.* Presence of benzyl alcohol, however, appears necessary to maintain sterility of the formulation during use, as eye drops are normally dispensed in multi dose containers. The degradation of moxifloxacin was found to follow first order kinetics.

KEY WORDS: Moxifloxacin, ophthalmic solutions, first order kinetics, benzyl alcohol.

1. INTRODUCTION:
Moxifloxacin {1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aS, 7aS)-octa-hydro-6H-pyrrolol (3, 4*b*) pyridin-6-yl]-4-oxo-3-quinoline carboxylic acid} is available as hydrochloride salt which is soluble in water. Moxifloxacin is a fourth generation fluoroquinolone with methoxy group in C-8 position and a bulky C-7 side chain [1]. Like other fluoroquinolones, moxifloxacin (0.5%w/v) eye drops require 1-2 drops administered 6 times daily or more in severe conditions. This fourth-generation fluoroquinolone has in vitro activity similar to that of ciprofloxacin and ofloxacin against Gram-negative bacteria like *Pseudomonas aeruginosa*, but enhanced activity against Gram-positive bacteria including *S. aureus.*

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The bactericidal activity of moxifloxacin is mediated by the inhibition of DNA gyrase (topoisomerase II) and topoisomerase IV, essential enzymes involved in bacterial DNA replication, transcription, repair, and recombination [2]. Moxifloxacin is an amphoteric molecule having pI at 7.77 (pKa_1 =6.25 and pKa_2 = 9.29). This fourth-generation fluoroquinolone has in vitro activity similar to that of ciprofloxacin and ofloxacin against gram-negative bacteria but enhanced activity against gram-positive bacteria including *S. aureus* [3-5].

Sitafloxacin (STFX) hydrate, a quinolone antimicrobial agent, has been reported to be photo-labile in aqueous solutions. The photodegradation rates (*k*) in neutral solutions were higher than those observed in acidic and alkaline solutions and maximum at the maximum absorption wavelength of STFX. Dechlorination was the key step in the photodegradation. The effect of halide

ions on the photodegradation of STFX was estimated**.** In the presence of bromide ions, instead of increased photostability of the STFX rate, a new photodegradation product was observed. The structure of this new photodegradation product was an 8-bromo form of STFX, which was substituted for chlorine at the 8-position, so the dissociation of C–Cl bond at the 8-position of STFX was the rate-limiting step in the initial process of the photodegradation. STFX generated ·C (carbon centered radical) and ·OH (hydroxyl radical) in the process of photodegradation in a pH 4.0 buffer. On the contrary, STFX did not generate C in the presence of chloride ion in a pH 4.0 buffer. The C was generated and then degraded into the above degradation products by photo-irradiation in the absence of chloride ion, but the·C immediately reacted with chloride when it was present. As a result, the C–Cl bond was recovered leading to a possible increase in the apparent photostability [6].

Moxifloxacin hydrochloride possesses two chiral centers and is the *S,S*-isomer. Its potential chiral impurities are the *R,R*-enantiomer, the *R,S*-diastereomer and the *S,R*-diastereomer. The FDA's Draft Guidance for Industry on the development of stereoisomeric drugs states that applications for an enantiomeric drug substance or applications for drug products containing an enantiomeric drug substance should include a stereochemically specific identity test and/or a stereochemically selective assay method. However, if it can be demonstrated that stereochemical conversion does not occur during stability testing of the drug substance and drug product, then stereoselective tests may not be needed In studies on degradation pathways, no isomeric impurities ≥0.05% were observed in stressed solid state moxifloxacin hydrochloride samples following storage at 40°C/75% RH, 60°C, or in a stability light chamber after 12 weeks. No isomeric impurities ≥0.05% were observed in stressed solutions of moxifloxacin following storage at 50°C under acidic, neutral, basic, or oxidizing conditions for 12 weeks or in a stability light chamber after 12 weeks. Considering the structure of moxifloxacin, racemization seems an unlikely pathway for degradation since inversion of the chiral centers would require cleavage of non activated C-C single bonds. Therefore, these studies provide confirmatory evidence that racemization is not a degradation pathway for moxifloxacin hydrochloride, either in the solid state or in solution [7] .

In a recent study, HPTLC method was used to investigate the kinetics of acidic (in 1M HCl) and alkaline (in 1M NaOH) degradation of moxifloxacin at different temperatures. A regular decrease in the concentration of moxifloxacin with increasing time intervals was observed at higher temperatures. At the selected temperatures (40, 50, 60, 70, 80 and 90 °C for acidic and alkaline degradation) the degradation process followed pseudo-first-order kinetics. The pH-rate profile of degradation of moxifloxacin in constant ionic strength buffer solutions was studied at 40°C using the HPTLC method. The degradation kinetics data, suggest that the drug is highly susceptible to acidic and alkaline degradation. The pH-rate profile study shows that moxifloxacin is most stable between pH 6.8 and 8.0 [8]. According to the International Conference on Harmonization (ICH) guidelines Q1A (R2) entitled 'stability testing of new drug substances and products', stress testing of the drug substance should be carried out to elucidate the inherent stability characteristics of the active substance[9]. The suspensions containing moxifloxacin (20 mg/mL) in a 1:1 mixture of Ora-Plus and Ora-Sweet or Ora-Sweet SF were stable for at least 90 days when stored in 2-oz amber plastic bottles at room temperature [10].

The *in vitro* corneal permeation characteristics of moxifloxacin from formulated aqueous and oily ophthalmic formulations have been reported [11, 12].
The purpose of the present investigation was to conduct stability studies on the aqueous and oily ophthalmic formulations of moxifloxacin.

2. MATERIALS AND METHODS:

2.1. Materials:

2.1.1. Moxifloxacin aqueous ophthalmic solution. Moxifloxacin hydrochloride (purity 99.97 % on anhydrous basis) was obtained from Ranbaxy Laboratories (India) as gift. Preservatives were received from central Drug House (India). All other chemicals used were of analytical reagent grade. USP type 1, glass ampoules of 2 mL capacity were obtained from Kejariwal Industries (New Delhi, India).

2.1.2. Moxifloxacin oily ophthalmic solutions. Moxifloxacin hydrochloride was obtained from Ranbaxy Laboratories Limited (Gurgaon, India) as a gift sample. Benzyl alcohol, a preservative was received from Central Drug House (New Delhi, India). Refined food grade vegetable oils used in the experiment were arachis (Adani Wilmar Limited, Ahmedabad, India), castor (Arora and Company, New Delhi, India), cottonseed (Argo Tech Limited, Secunderabad, India), olive (Figaro), (S O S Cueturo S. A., Madrid, Spain), sunflower, (Sundrop), (Agro Tech Foods Ltd, Secunderabad, India), soybean (Adani Wilmar Limited, Kutch, Gujrat, India) and sesame oils (Tilsona),(Recon oil Industries Pvt Limited, New Delhi , India).

All other chemicals purchased were of analytical grade and were used as received. USP type 1, glass ampoules

of 2 mL capacity were obtained from Kejariwal Industries (New Delhi, India).

2.2. Preparation of Test Solutions:

2.2.1. Moxifloxacin aqueous ophthalmic solutions:

Moxifloxacin aqueous ophthalmic solutions were prepared by dissolving various ingredients in 100 mL distilled water according to the formula given in Table 1.

2.2.2. Moxifloxacin oily ophthalmic solutions:

Oily ophthalmic solutions of moxifloxacin with or without benzyl alcohol (0.5% v/v) were formulated by dissolving moxifloxacin base in 100 mL oil according to the formula given in Table 2.

2.2.3. Stability testing for aqueous ophthalmic solutions of moxifloxacin:

The amber colored, USP type-I, 2 mL glass ampoules were washed with tap water and distilled water, followed by drying in an oven. The aqueous ophthalmic solutions of moxifloxacin were filled into dried glass ampoules and heat-sealed. The accelerated stability testing on ophthalmic formulations was conducted by storage at 40 ± 2 ^{o}C, and 75 ± 5% RH. The long-term stability studies were conducted by storage at room temperature. The samples of ophthalmic formulations kept under accelerated storage conditions were withdrawn at 0 day, 6 weeks, 3 months, 6 months and analyzed for moxifloxacin content by measuring absorbance at 291 nm in a UV spectrophotometer (1601 Shimadzu, Kyoto, Japan). The samples stored at room temperature were withdrawn at 0 day, 3 months, 6 months, and 12 months and analyzed for moxifloxacin contents. The samples of aqueous formulations were also tested for pH and appearance.

2.2.4. Stability testing for oily ophthalmic solutions of moxifloxacin:

The amber colored, USP type-I, 2 mL glass ampoules were washed with tap water and distilled water, followed by drying in an oven. The oily ophthalmic solutions of moxifloxacin were filled into dried glass ampoules and heat-sealed. The accelerated stability testing on ophthalmic formulations was conducted by storage at 40 ± 2 ^{o}C, and 75 ± 5% RH. The long-term stability studies were conducted by storage at room temperature. The samples of oily ophthalmic formulations kept under accelerated storage conditions were withdrawn at 0 day, 6 weeks, 3 months, 6 months and analyzed for moxifloxacin content. The samples of oily ophthalmic formulations kept under room temperature were withdrawn at 0 days, 6 weeks, 3 months and 6 months, and analyzed for moxifloxacin content. The samples of oily formulations were tested for appearance.

2.2.5. Method of analysis of moxifloxacin in oily ophthalmic solutions:

Each sample of oily ophthalmic solutions of moxifloxacin (5 mL) was subjected to five successive extractions with 10 mL of 0.1 N HCL. The aqueous phases were pooled, filtered, and volume was made up to 100 mL using 0.1 N HCL. The extract was analyzed for moxifloxacin content by measuring absorbance at 291 nm in a spectrophotometer (1601 Shimadzu, Kyoto, Japan) using 0.1 N HCl as blank.

Table 1: Composition of Aqueous Ophthalmic formulations of Moxifloxacin

Formulation code	Moxifloxacin (%,wt/vol)	pH	Tonicity modifier	Preservative (%,wt/vol)
MAF1	0.1	7.2	Sodium chloride	-
MAF2	0.2	7.2	Sodium chloride	-
MAF3	0.3	7.2	Sodium chloride	-
MAF4	0.4	7.2	Sodium chloride	-
MAF5	0.5	7.2	Sodium chloride	-
MAF6	0.5	5.5	Sodium chloride	-
MAF7	0.5	6.0	Sodium chloride	-
MAF8	0.5	6.5	Sodium chloride	-
MAF9	0.5	5.9B	Sodium chloride	-
MAF10	0.5	6.5B	Sodium chloride	-
MAF11	0.5	7.2B	Sodium chloride	-
MAF12	0.5	7.2	Sodium chloride	EDTA(0.01)
MAF13	0.5	7.2	Sodium chloride	BAK(0.01)
MAF14	0.5	7.2	Sodium chloride	BAK(0.01)+EDTA(0.01)
MAF15	0.5	7.2	Sodium chloride	BA(0.05)
MAF16	0.5	7.2	Sodium chloride	THM(0.005)
MAF17	0.5	7.2	Sodium chloride	PMA(0.002)
MAF18	0.5	7.2	Sodium chloride	PMN(0.002)

EDTA: disodium edetate, BAK: benzalkonium chloride, BA: benzyl alcohol, THM: thiomersal, PMA:phenyl mercuric acetate, PMN: phenyl mercuric nitrate.

*B: buffered formulation containing 0.0667M phosphate buffer

Table 2: Composition of Oily Ophthalmic formulations of Moxifloxacin

Formulation code	Moxifloxacin (%,wt/vol)	Oil	Benzyl alcohol (%,vol/vol)
MOF1	0.047	Cottonseed	-
MOF2	0.047	Cottonseed	0.5
MOF3	0.049	Castor	-
MOF4	0.049	Castor	0.5
MOF5	0.044	Olive	-
MOF6	0.044	Olive	0.5
MOF7	0.044	Arachis	-
MOF8	0.044	Arachis	0.5
MOF9	0.046	Soybean	-
MOF10	0.046	Soybean	0.5
MOF11	0.044	Sunflower	-
MOF12	0.044	Sunflower	0.5
MOF13	0.047	Sesame	-
MOF14	0.047	Sesame	0.5

3. RESULTS AND DISCUSSION:

Moxifloxacin ophthalmic solution is commercially available as 0.5 % w/v having pH between 7.2 and 7.3. The results of accelerated and long-term stability studies conducted on aqueous ophthalmic formulations of moxifloxacin are shown in Table 3 and 4. All the formulations except MAF1 and MAF 2 showed >90 % moxifloxacin content under accelerated storage condition for 6 month and room temperature storage condition for 1 year. There had been no change in the physical appearance of the formulations.

Table 3: Stability of Moxifloxacin in aqueous Ophthalmic Solutions under Accelerated Storage Conditions.

Formulations	Moxifloxacin content				pH			
	0 D	6W	3 M	6M	0 D	6W	3 M	6M
MAF1	100±0.55	91.34±0.57	89.50±0.57	88.00±0.37	7.2	7.1	7.1	7.1
MAF2	100±0.11	93.88±0.47	92.38±1.14	89.00±0.57	7.2	7.1	7.1	7.1
MAF3	100±0.10	94.34±0.16	93.12±0.33	90.05±0.67	7.2	7.1	7.1	7.1
MAF4	100±0.03	93.14±0.58	92.44±0.60	90.35±0.92	7.2	7.1	7.1	7.1
MAF5	100±0.33	93.83±0.60	92.12±1.14	90.77±0.60	7.2	7.2	7.1	7.1
MAF6	100±0.33	96.85±0.06	94.64±0.83	90.60±0.29	5.5	5.4	5.4	5.3
MAF7	100±0.18	95.17±0.56	93.36±0.70	90.05±0.55	6.0	5.9	5.7	5.6
MAF8	100±0.99	95.44±0.58	93.84±0.48	91.49±0.67	6.5	6.5	6.3	6.2
MAF9	100±0.57	97.18±0.35	96.59±0.11	93.01±1.14	7.2	7.1	7.1	7.1
MAF10	100±0.35	96.73±1.34	94.95±0.74	92.35±0.67	5.9	5.8	5.8	5.8
MAF11	100±0.34	97.06±0.10	95.83±0.37	92.87±1.50	6.5	6.4	6.3	6.3
MAF12	100±0.88	98.05±0.25	96.52±0.69	94.23±0.62	7.2	7.2	7.1	7.1
MAF13	100±0.10	98.55±0.57	97.12±0.12	94.56±0.86	7.2	7.1	7.1	7.0
MAF14	100±0.42	98.91±0.57	97.69±0.61	95.93±0.58	7.2	7.1	7.1	7.1
MAF15	100±0.33	97.84±0.09	96.09±0.63	94.12±0.69	7.2	7.2	7.1	7.1
MAF16	100±0.33	96.35±0.57	95.22±0.58	93.26±0.51	7.2	7.2	7.1	7.1
MAF17	100±0.33	96.71±0.62	95.54±0.60	93.12±0.77	7.2	7.2	7.0	6.9
MAF18	100±0.33	97.66±0.51	95.92±0.60	94.45±0.77	7.2	7.2	7.1	6.8

*Values are mean ± SE (*n*=3), D: days, W: weeks, M: months

Table 4: Stability of Moxifloxacin in aqueous Ophthalmic Solutions under Room Temperature Storage.

Formulations	Moxifloxacin content				pH				k_{cal} ($day^{-1} \times 10^{-4}$)	t_{90} days	Int_{calc} 2 years
	0 D	3 M	6M	12M	0 D	3 M	6M	12M			
MAF1	100±0.55	95.00±0.13	91.67±0.16	89.61±0.52	7.2	7.2	7.2	7.1	3.01	346	112.1
MAF2	100±0.11	95.89±0.16	93.31±0.05	90.00±0.60	7.2	7.2	7.2	7.1	2.89	360	111.1
MAF3	100±0.10	96.60±0.48	95.06±0.57	91.37±0.58	7.2	7.2	7.2	7.1	2.47	421	107.8
MAF4	100±0.03	95.92±0.23	93.75±0.21	90.51±0.07	7.2	7.2	7.2	7.1	2.73	381	109.8
MAF5	100±0.33	97.39±0.16	95.16±1.16	92.68±0.63	7.2	7.2	7.2	7.1	2.08	499	104.8
MAF6	100±0.33	96.75±0.59	94.19±0.49	90.48±0.60	5.5	5.5	5.4	5.3	2.74	379	109.9
MAF7	100±0.18	97.58±0.24	95.55±0.55	91.87±0.96	6.0	6.0	5.9	5.7	2.32	448	106.6
MAF8	100±0.99	97.01±0.07	95.70±0.05	92.59±0.57	6.5	6.5	6.4	6.4	2.11	493	105.0
MAF9	100±0.57	97.24±0.54	95.02±0.52	93.21±0.77	7.2	7.2	7.1	7.1	1.93	540	103.6
MAF10	100±0.35	97.63±0.73	95.71±0.64	93.89±0.58	5.9	5.9	5.9	5.8	1.73	602	102.1
MAF11	100±0.34	98.80±0.13	96.44±0.70	94.48±0.61	6.5	6.5	6.5	6.4	1.56	668	100.8
MAF12	100±0.88	97.69±0.45	95.47±0.57	93.43±0.77	7.2	7.2	7.2	7.0	1.86	558	103.1
MAF13	100±0.10	98.54±0.28	96.80±0.62	94.79±0.63	7.2	7.2	7.2	7.0	1.47	709	100.2
MAF14	100±0.42	99.27±0.28	98.45±0.11	97.11±0.58	7.2	7.2	7.2	7.1	0.80	1294	95.4
MAF15	100±0.33	98.27±0.16	96.42±0.40	94.15±0.54	7.2	7.2	7.2	7.0	1.65	630	101.5
MAF16	100±0.33	96.89±0.54	95.90±0.54	94.46±0.74	7.2	7.2	7.2	6.9	1.56	666	100.9
MAF17	100±0.33	98.36±0.48	94.06±0.48	92.38±0.58	7.2	7.2	7.2	7.0	2.17	479	105.4
MAF18	100±0.33	98.19±0.21	93.69±0.51	92.85±0.50	7.2	7.2	7.2	6.9	2.03	512	104.4

*Values are mean ± SE (*n*=3), D: days,, M: months , * K_{calc}: calculated first-order degradation rate constant, t_{90}: time to reach 90% of initial drug concentration, Int_{calc}: calculated initial drug concentration for shelf life (t_{90}) of 2 years.

Stability studies on moxifloxacin aqueous ophthalmic solutions pH 7.2 of different concentrations (0.1-0.5 % w/v) revealed that among all the formulations, MAF5 showed least degradation under accelerated storage for 6 months and room temperature storage for one year. Stability study on moxifloxacin aqueous ophthalmic solutions (0.5 % w/v) of different pH suggest that stability of moxifloxacin is favored by pH around 7.2. Addition of buffer in the formulations favored stability of drug at room temperature up to 12 months. Formulation containing benzalkonium chloride (BAK) and EDTA showed maximum stability followed by formulation with BAK, THM and BA. The degradation of drug followed first order kinetics and the former could provide two years shelf life at room temperature. Rest of the formulations might need some overage to ensure 2 year shelf life at room temperature, and the same is shown in the last column of Table 4. Permeation studies with excised cornea, conducted earlier, showed maximum permeation of moxifloxacin from formulation with BAK and EDTA. Thus formulation with BAK and EDTA appears ideal from both stability and permeation point of view.

Table 5 and 6 present the results of accelerated and long-term stability studies conducted on oily moxifloxacin ophthalmic formulations. All formulations showed more than 90% moxifloxacin content both under accelerated as well as room temperature storage conditions for 6 months. No change in appearance of any of the oily formulations was observed. Formulation containing 0.05 % (w/v) moxifloxacin in castor oil without or with benzyl alcohol (0.5% v/v) (MOF3 and MOF4) showed least degradation. Addition of benzyl alcohol favored stability.

Table 5: Stability of Moxifloxacin in Oily Ophthalmic Solutions under Accelerated Storage Conditions.

Formulations	Moxifloxacin content			
	0 D	6 W	3 M	6M
MOF1	100±0.33	98.44±0.51	96.78±1.11	93.39±1.13
MOF2	100±0.55	99.05±0.42	97.12±0.61	95.35±0.66
MOF3	100±0.88	98.74±0.53	97.31±0.56	94.23±0.50
MOF4	100±0.11	99.16±0.40	98.64±0.66	96.5±0.47
MOF5	100±0.10	98.07±0.55	96.79±0.15	93.71±0.60
MOF6	100±0.10	99.03±0.32	97.13±0.51	95.89±0.70
MOF7	100±0.68	98.69±0.45	96.91±0.56	92.11±0.01
MOF8	100±0.03	98.53±0.38	97.26±0.77	95.46±0.60
MOF9	100±0.42	98.27±0.98	95.33±0.70	92.96±0.62
MOF10	100±0.03	99.00±0.25	96.89±0.99	94.26±0.55
MOF11	100±0.33	98.68±0.17	96.06±0.56	92.29±0.71
MOF12	100±0.07	99.32±0.19	97.85±0.51	95.23±0.75
MOF13	100±0.33	97.97±0.58	95.17±0.56	92.69±0.62
MOF14	100±0.57	98.41±0.60	96.37±0.45	94.75±0.66

*Values are mean ± SE (*n*=3), D: days, W: weeks, M: months

Oily solutions of poorly water soluble drugs have earlier been reported to prolong the pre-corneal residence and promote the ocular bioavailability of drugs. So formulations of moxifloxacin in different food grade refined vegetable oils were formulated. *In vitro* corneal permeability studies, conducted earlier, showed enhanced permeability of moxifloxacin from ophthalmic solution in castor oil without benzyl alcohol (0.05%,v/v) (MOF3) while formulation in sesame oil (MOF) provided least permeability through all mammalian corneas(goat, sheep, buffalo). The degradation of moxifloxacin from oily drops also followed first order kinetics. The formulations might need overage to ensure a 2 year shelf life at room temperature, resulting in higher initial drug concentration, which is shown in the last column of the Table 6. Moxifloxacin (0.05%, w/v) ophthalmic solution in castor oil without benzyl alcohol appears ideal taking both stability and corneal permeability in view.

Table 6: Stability of Moxifloxacin in Oily Ophthalmic Solutions under Room Temperature Storage.

Formulations	Moxifloxacin content				$k_{cal(day^{-1} \times 10^{4})}$	t_{90} days	Int_{calc} 2 years
	0 D	6 W	3 M	6 M			
MOF1	100±0.33	99.07±0.50	98.46±0.49	94.45±0.66	3.17	328	113.4
MOF2	100±0.55	99.62±0.21	98.09±0.60	96.23±0.66	2.14	487	105.2
MOF3	100±0.88	99.72±0.70	98.32±0.56	96.72±0.34	1.85	561	103.0
MOF4	100±0.11	99.66±0.76	98.78±0.46	97.08±0.47	1.65	632	101.5
MOF5	100±0.10	99.67±0.06	98.12±0.16	94.12±0.58	3.37	309	115.1
MOF6	100±0.10	99.63±0.14	97.73±0.48	96.36±0.70	2.06	505	104.6
MOF7	100±0.68	99.45±0.37	98.25±0.26	94.35±0.72	3.23	322	113.9
MOF8	100±0.03	99.63±0.21	97.56±0.19	95.86±0.60	2.35	443	106.8
MOF9	100±0.42	99.56±0.19	97.71±0.58	93.23±0.77	3.90	267	119.6
MOF10	100±0.03	99.58±0.19	98.43±0.84	95.78±0.55	2.40	434	107.2
MOF11	100±0.33	99.42±0.15	98.45±0.63	95.75±1.14	2.41	431	107.3
MOF12	100±0.07	99.58±0.32	98.5±0.727	96.56±0.75	1.95	535	103.7
MOF13	100±0.33	99.36±0.22	98.23±0.58	95.78±0.53	2.40	434	107.2
MOF14	100±0.57	99.54±0.26	97.87±0.15	96.24±0.66	2.13	488	105.1

*Values are mean ± SE (*n*=3), D: days, W: weeks, M: months, * K_{calc}: calculated first-order degradation rate constant, t_{90}: time to reach 90% of initial drug concentration, Int_{calc}: calculated initial drug concentration for shelf life (t_{90}) of 2 years.

CONCLUSION:

The accelerated and long term stability studies conducted on aqueous ophthalmic solutions of moxifloxacin indicate that moxifloxacin (0.5%, w/v) formulation of pH 7.2, containing sodium chloride as tonicity modifier, preserved using BAK and EDTA could provide a shelf life (t_{90}) of 2 years, and the formulations appear promising from corneal permeation point of view. Similarly, among the oily formulations, moxifloxacin (0.05%, w/v) ophthalmic solution in castor oil, with adequate overage, containing benzyl alcohol (0.5%, v/v) appears ideal from both stability and corneal permeability point of view. However, further studies are needed to comment more in this respect.

CONFLICT OF INTERESTS:

There is no conflict of interests regarding the publication of this paper.

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