20 *Egypt. J. Chem.* **58**, No. 3 pp. 349 -364 (2015)

Spectrophotometric Determination of Gemifloxacin Mesylate, Moxifloxacin.HCl and Gatifloxacin Sesquihydrate in Pure and in Pharmaceutical Preparations

M.A. Zayed* **and Heba A. Dakhly**
Chemistry Department, Faculty of Science, Cairo University, Gamaa Str., 12613, Giza, Egypt.

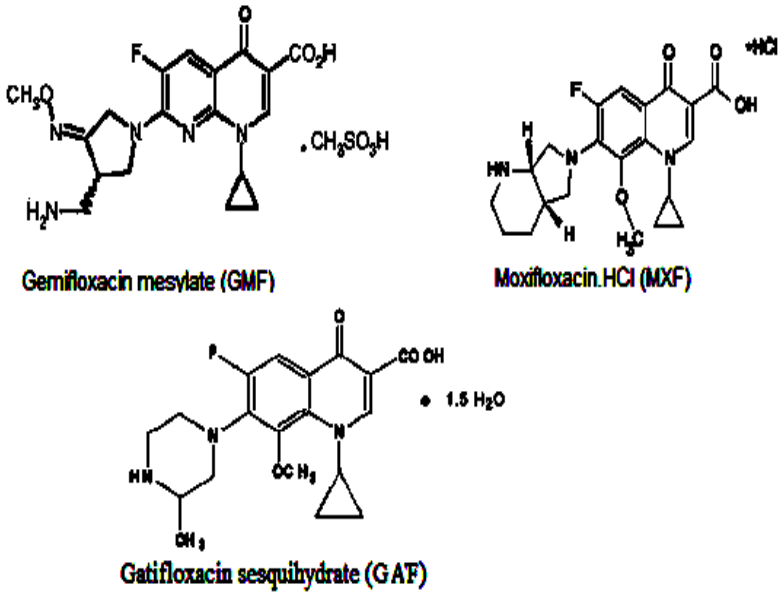
SIMPLE, rapid and sensitive spectrophotometric method was developed for the determination of gemifloxacin mesylate (GMF), moxifloxacin.HCl (MXF) and gatifloxacin sesquihydrate (GAF) in pure and pharmaceutical preparation. This method is based on ion pair formation reaction between GMF, MXF and GAF and rosebengal indicator in universal buffer of pH 5.The formed ion pair is measured at λ_{max} = 575 nm. All optimum conditions are established. The calibration graphs are rectilinear at concentration ranges 9.71 – 53.40, 8.758 – 52.55 and 8.048– 48.29 µg ml^{-1} for GMF, MXF and GAF, respectively. The sandell sensitivity (S) = 0.0263 , 0.0244 and 0.0263 µg cm^{-2} , molar absorptivity = 1.861x 10^4, 1.835x 10^4 and 1.561x 10^4 L mol^{-1} cm^{-1}, correlation coefficient 0.9998 and LOD = 01.90, 1.607 and 1.876 µg ml^{-1} and LOQ = 05.74, 0.2036 and 5.684 µg ml^{-1} are calculated for GMF, MXF and GAF, respectively. The values of SD are = 0.0218 - 0.0297, 0.02 - 0.0377 and 0.0216 - 0.0282 and RSD are = 0.0554 - 0.3075, 0.0380 - 0.4344 and 0.0537 - 0.3497 % for GMF, MXF and GAF. The method is applied for the assay of investigated three drugs in pharmaceutical dosage forms. The results are in good agreement with those obtained by the official methods.

Keywords: Gemifloxacin mesylate, Moxifloxacin. HCl, Gatifloxacin sesquihydrate, Ion pair formation and Spectrophotometry**.**

Over the last twenty years, fluoroquinolones have emerged as one of the most important classes of antibiotics [1-2]. Fluoroquinolones are the second-generation members of quinolone antibiotics fluorinated in position 6 and bearing a piperazinyl moiety at position. They are considered to be the most effective Gram-positive and Gram-negative pathogens to combat infection caused by microorganisms that are resistant to other microbials, such as tetracyclines. Also, they have some activity against mycobacteria, mycoplasmas and the protozoan *Plasmodium falciparum* [2– 5]. There is a substantial body of literature related to both the mechanism of their action as DNA gyrase inhibitors and the

*Corresponding author: mazayed429@yahoo.com;
Tel: 002-01005776675, Office: 002-02-35676624

influence of systematic structural modifications on their biological activity [6, 7]. Gemifloxacin mesylate (GFX) is [(R,S)-7-[(4Z)-3-(aminomethyl)-4-(methoxyimino) -1- pyrrolidinyl] -1- cyclopropy l-6- fluoro- 1,4- dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acidmesylate[9] Moxifloxacin (MXF) is 1-cyclopropy l-7- [2,8- diazobicyclo (4.3.0) nonane] -6- fluoro -8- methoxy -1,4 dihydro-4-oxo-3-quinolone carboxylic acid. Gatifloxacin sesquihydrate(GAT) is (1-cyclopropy l-6-fluoro -8- methoxy -7- (3-methylpiperazin -1-yl) -4 oxo-1,4-dihydro-quinoline-3-carboxylic acid).GMF,MXF and GAT are fourth-generation synthetic broad-spectrum 8-methoxy fluoroquinolone antibacterial drug derivatives used for the treatment of pneumonia and bronchitis and sinusitis [8-10], GMF,MXF and GAT are also used for treatment of urinary tract infection [11, 12]. GMF, MXF and GAT are receiving a great interest due to their clinical advantages and there was an increase in number of their pharmaceutical dosage forms in the market recently. The chemical structures of the studied fluoroquinolones are shown in (Scheme 1).No official (pharmacopoeia) method has been found for the assay of GMF, MXF and GTF in their pharmaceutical formulations. Several methods have been reported for the determination of fluoroquinolones either in pure forms, dosage forms, or biological fluids like chromatography [13 – 17], capillary zone electrophoresis [18 – 19], electrochemistry [20 – 23], atomic absorption spectrometry [24, 25], and spectrofluorimetry [25 – 27]. However, these methods are expensive and not available at most quality control laboratories. For routine analysis of the studied drugs, a simple, rapid, and cost effective analytical method was required. The spectrophotometric technique continues to be the most preferred method for the assay of different classes of drugs in pure, pharmaceutical formulations and in biological samples, for its simplicity and reasonable sensitivity with significant economical advantages. Spectrophotometric methods are reported for the assay of GMF, MXF and GAF [13, 28 – 32], these methods were associated with some major drawbacks such as decreased selectivity due to measurement in ultraviolet region and/or decreased simplicity of the assay procedure (*e.g.*, tedious precipitation, heating, or liquid-liquid extraction steps in the ion pair formation-based methods). For these reasons, it was worthwhile to develop a new simple and selective spectrophotometric method for the determination of the studied drugs in their pharmaceutical dosage forms. In the present work, we report the development of accurate and precise spectrophotometric method based on formation of ion pairs between the studied fluoroquinolone antibiotics (GMF, MXF, and GAF) and rosebengal organic reagent. The absorbance measurements were measured at optimum wavelengths. The proposed methods were applied successfully for the determination of the studied drugs in pure and dosage forms. The methods provide rapid, economic procedures and more sensitive compared to the previously reported spectrophotometric methods. These methods were validated by the statistical data.



Scheme 1. The chemical structure of the studied fluoroquinolones .

Experimental

Materials and solutions

All chemicals and reagents used were of analytical reagent grade. They included GMF reference standard provided by El-Obour Modern Pharmaceutical Industries Co., El-Obour city, Kaliobeya, Egypt, its potency was 99.99±0.39%.MXF reference standard was provided by Sabaa, Kahira Company, Cairo, Egypt, its purity was 100.01 ± 0.71%.GAF reference standard was provided by EPCI, Egyptian Company for Pharmaceutical and Chemical Industries, S.A.E., Beni Suef, Egypt, its potency was 99.65 ± 0.74%. Reagent is rosebengal disodium salt supplied from BDH Chemicals. Ltd (Poole, England).Absolute ethanol supplied from El Salam for Chemical Industries – Egypt, Assay: 95%, sodium hydroxide supplied from El Salam for Chemical Industries - Egypt, phosphoric acid supplied from Chemicoke El Tabbin – Egypt, Assay: 88%, acetic acid supplied from El Salam for Chemical Industries - Egypt, Assay: 99%, boric acid from El Nasr Pharmaceutical Chemical Co – Egypt, Assay: 99.5% .Distilled water was usually used in all preparations. Fresh stock solutions were prepared by dissolving the accurately weighed amounts 0.0486, 0.0438 and 0.0402 g of GMF, MXF and GAF, respectively in 100 ml of distilled water, dilute solutions were prepared by accurate dilution from the stock solution to get desired concentrations. Series of universal buffer solutions covering the range of pH values from 2.0 to 11.0 were prepared as recommended by Britton and Robinson [33]. The Stoichiometric ratio between drugs and reagent in the ion-pair complexes was determined by the molar ratio method (MRM). In this method to constant reagent concentration of

Rb (1-1.2 X 10^{-4}M), variable concentrations (0.1 – 2.8) X 10^{-4}M of GMF, MXF and GAF were added [34]. A mixture of 0.04 M phosphoric, acetic and boric acids was titrated with 0.1 N NaOH to adjust the desired pH into the required value in 100 ml of the acid mixture using pH – meter. Quinabiotic tablets were obtained from Medizen Pharmaceuticals Industries, Borg Elarab – Alexandria – Egypt, labelled to contain (320 mg GMF $tablet^{-1}$). Moxifloxacin tablets were obtained from Sabaa International Company for pharmaceuticals and chemical industries, S.A.E. labelled to contain (400 mg MXF $tablet^{-1}$). Gatiflox tablets were obtained from (EPCI, Egyptian Company for Pharmaceutical and Chemical Industries, S.A.E., Beni Suef, Egypt labelled to contain (400 mg GAF $tablet^{-1}$).

Apparatus

The spectrophotometric measurements were carried out using the Thermo Fisher Scientific, Model: EVO 60 in the wavelength range from 190-800 nm. The pH measurements were performed by using HANNA pH/ mV/Temperature meter, Model pHS – 3CW. Weights measurement was performed by using Radwag Wagi Elektroniczne Sensitive analytical balance 0.0001g, Model: AS 220/C/1.Stirring and heating were performed by using ARE Heating Magnetic Stirrer Theromostated Hot Plate, Model: VELP-Europe. Automatic Micropipettes, Model: Accupipette USA, Volume range 100-1000 µLwere used to measure the small volumes.

Procedure for determination of Gemifloxacin (GMF), Moxifloxacin (MXF) and Gatifloxacin (GAF) using rosebengal disodium salt reagent (Rb)

a. General procedure

Aliquots of GMX, MXF and GAF (0.2-1.2) x 10^{-3}M were transferred into a 10 ml calibrated measuring flasks, treated with 1.2 x 10^{-3} M Rb solution, then 0.5 ml of universal buffer of pH 5 was added, diluted to volume with distilled water and allowed to stand for 12, 15 and 15 min for GMX, MXF and GAF, respectively at 20-30 ^{0}C. The absorbance was measured at 575 nm against a reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

b. Procedure for the tablets analysis

Each ten tablets of Quinabiotic (320 mg GMF $tablet^{-1}$), Moxifloxacin (400 mg MXF $tablet^{-1}$) and Gatiflox (400 mg GAF $tablet^{-1}$), were weighed and powdered well separately. Equivalent amount of powder to one tablet of each separate drug was weighed and dissolved in sufficient amount of distilled water, with gentle warming. The resulting solutions were filtered using filter paper and then the filtrate of each drug was transferred into separate 250 ml volumetric flasks and the volume completed to the mark with distilled water. The procedure was continued as mentioned under general procedure and calibration graphs. The procedure mentioned above was followed where different concentrations of GMX, MXF and GAF in the range, respectively 9.71 – 53.40,

8.758 – 52.62 and 8.048– 48.29 μg ml^{-1}, respectively were added for Rb reagent. The drug concentrations were calculated from the standard calibration graph prepared under identical conditions.

Results and Discussion

Absorption spectra

This method based on the formation of ion pairs between drugs and rosebengal disodium salt reagent as the nitrogenous drugs are present in positively charged protonated forms [35 , 36] and rosebengal disodium salt reagent present mainly in anionic form at acidic pH. So when treated drugs with an acid dye rosebengal at pH range 2.0–5.0 of acidic universal buffers solutions, a rose ion-pair complex is formed. The absorption spectra of the ion-pair complexes, which were formed between GMF, MXF, or GAF and reagent Rb, were measured in the range 350 – 600 nm against the blank reagent solution. The ion-pair complexes of GMF, MXF, or GAF and reagent Rb show maximum absorbance at 575 nm (Fig 1).

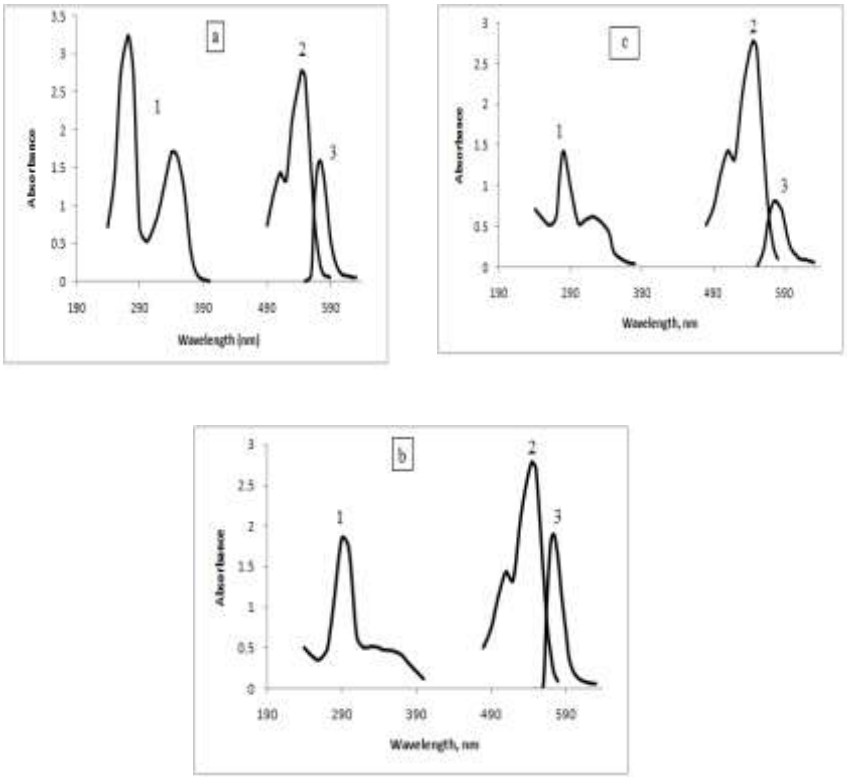


Fig . 1. Absorption spectra of (a) 1.GMF, 2.Rb disodium salt, 3.GMF-Rb ion pair. (b)1. MXF, 2.Rb disodium salt, 3.MXF-Rb ion pair. (c)1. GAF, 2.Rb disodium salt, 3.GAF-Rb ion pair.

Optimum reaction conditions for complex ion pair formation

Optimum conditions of the methods were carefully studied to achieve complete reaction formation, highest sensitivity, and maximum absorbance.

Effects of pH on ion-pair formation

The effect of pH on the drug-reagent ion pair complex was studied by measuring absorbance of the reaction ion pair product of GMF, MXF, and GAF with reagent Rb at λ_{max} = 575nm, the highest absorbance value was observed at pH 5.0 as showed in Fig .2.

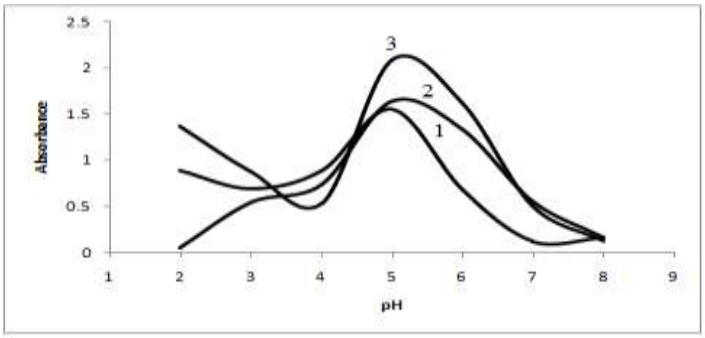


Fig. 2. Effect of pH on the ion pair reaction product of 1.GMF-Rb, 2.GAF-Rb, 3.MXF-Rb at λ_{max} = 575nm.

Effect of time and temperature

The optimum reaction time effect on the drug-reagent ion pair complex was studied by measuring absorbance of the reaction ion pair product of GMF, MXF and GAF with reagent Rb at 575 nm and pH 5.0, time was investigated from 0.5 to 60 min. From the obtained results, the absorbance is increased gradually with time increased until 12, 15, 15 min for GMF, MXF and GAF, respectively then remains almost unchanged (Fig 3).

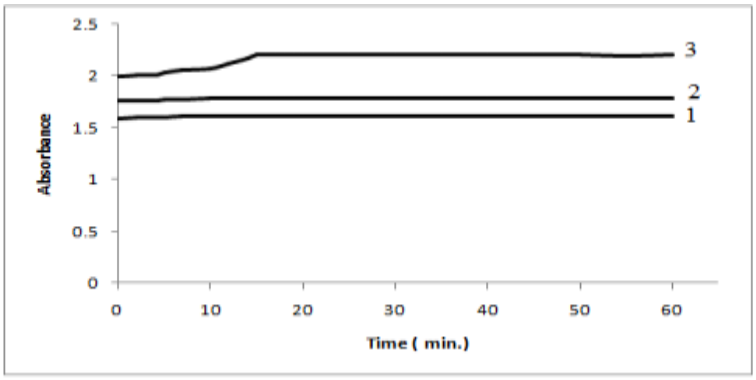


Fig .3. Effect of time on the ion pair reaction product of 1.GMF-Rb, 2.GAF-Rb, 3.MXF-Rb at λ_{max} = 575nm.

From these data it is clear that, the optimum time for ion – pair formation between GMF, MXF and GAF and Rb reaction product is found to be 12, 15, 15 min, respectively.

The effect of temperature on the drug-reagent ion pair complex was studied by measuring absorbance of the reaction ion pair product of GMF, MXF and GAF with reagent Rb at 575 nm and pH 5.0 to select the optimum temperature suitable for the ion- pair formation (Fig. 4).

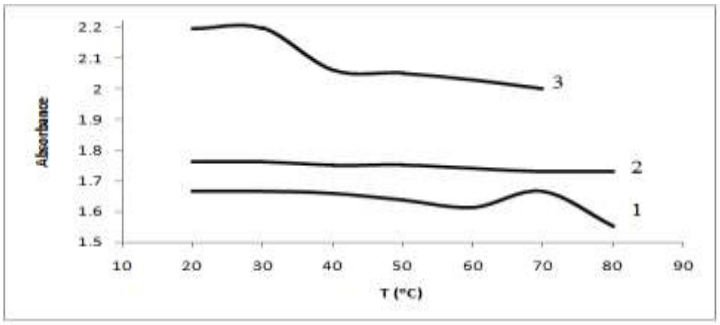


Fig. 4. Effect of temperature on the ion pair reaction product of 1.GMF-Rb, 2.GAF-Rb, 3.MXF-Rb at λ_{max} = 575nm.

The optimum temperature from the obtained results was found to be 20-30 ^{o}C, which gave maximum absorption.

Stoichiometric relationship

The Stoichiometric ratio between drugs and reagent in the ion-pair complexes was determined by the molar ratio method (MRM). In this method to constant reagent concentration of Rb (1-1.2 X 10^{-4}M), variable concentrations (0.1 – 2.8) X 10^{-4}M of GMF, MXF and GAF were added. The spectrophotometric measurements of these solutions were recorded at λ_{max}= 575 nm (Fig. 5).

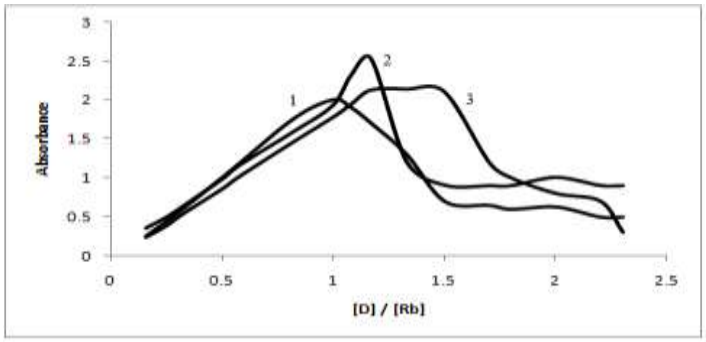
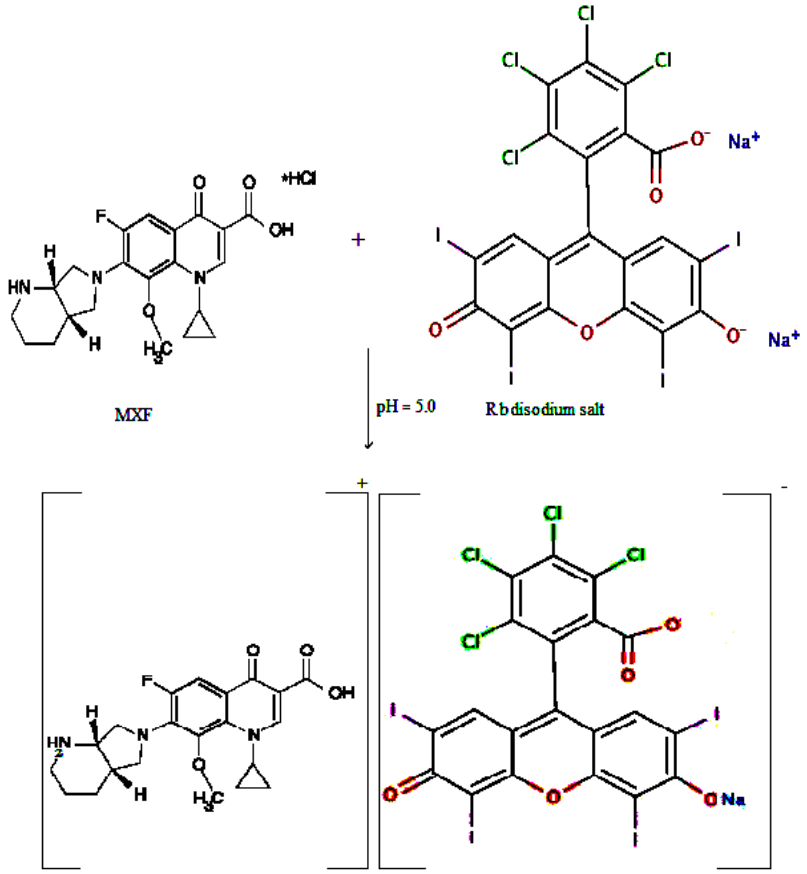


Fig . 5. Stoichiometric ratio of the reaction product 1-GMF-Rb, 2-MXF-Rb and 3-GAF-Rb ion pairs at λ_{max} = 575nm using molar ratio method.

The results indicate that 1: 1 (drug : reagent) ion-pairs are formed through the electrostatic attraction between positive protonated GMF+, MXF+, or GAF+ and negative Rb^- as example the ion pair of MXF-Rb (Scheme 2).



Scheme 2. Proposed mechanism of the reaction between MXF and Rb .

Validity of Beer's law

Standard calibration curves for GMF, MXF, and GAF with reagent were constructed by plotting absorbance versus concentration at optimum described experimental conditions. Beer's law was valid over the concentration range 9.71 – 53.40, 8.758 – 52.62 and 8.048– 48.29 μg ml^{-1} for GMF, MXF, and GAF using Rb, respectively. Table 1 shows the different analytical parameters obtained such as slope, intercept, correlation coefficient, Sandell sensitivity, molar absorptivity, standard deviation, and relative standard deviation, limit of quantification and limit of detection.

TABLE 1. The different analytical parameters .

Drug / Parameters	GMF	MXF	GAF
Reagent	Rose Bengal	Rose Bengal	Rose Bengal
Temperature (C^o)	20-30 ^oC	20-30 ^oC	20-30 ^oC
λ max (nm)	575	575	575
pH	5	5	5
Beer's law ($\mu g.ml^{-1}$)	09.71 – 53.40	8.758 – 52.55	8.048– 48.29
LDL ($\mu g\ ml^{-1}$)	09.71	8.758	8.048
HDL ($\mu g\ ml^{-1}$)	53.40	52.55	48.29
LOD ($\mu g\ ml^{-1}$)	01.90	1.607	1.876
LOQ ($\mu g\ ml^{-1}$)	05.74	4.870	5.684
R^2	0.9999	0.9999	0.9998
Regression equation (Y)*	y = 0.038x - 0.117	y = 0.041x - 0.007	y = 0.038x - 0.079
Molar absorptivity ($L\ mol^{-1}\ cm^{-1}$)	$1.861x\ 10^4$	$1.835x\ 10^4$	$1.561x\ 10^4$
SD	0.0218 - 0.0297	0.0200 - 0.0377	0.0216 - 0.0282
RSD %	0.0556 - 0.3075	0.0380 - 0.4344	0.0537 - 0.3497
Sandell sensitivity ($\mu g\ cm^{-2}$)	0.0263	0.0244	0.0263
Recovery %	99.23 - 100.77	99.18 - 100.7	99.54 - 100.9

The small value of Sandell sensitivity indicates the high sensitivity of the proposed method in the determination of the drug under investigation. The assay of GMF, MXF, and GAF were validated with respect to linearity, limit of detection, and quantitation, repeatability and reproducibility.

Linearity

The linearity of calibration graphs was proved by the high values of the correlation coefficient (r^2).

Sensitivity

The limits of detection (LOD) and quantitation (LOQ) for the proposed methods were calculated in Table 1; their values confirm the sensitivity of the proposed method.

Accuracy and precision

The accuracy and precision of the proposed methods were established by measuring the content of GMF, MXF and GAF in pure form at different

concentration levels five replicate. The results of standard deviation (SD), relative standard deviation (RSD) and recoveries by the proposed methods are presented in Table 2. The inter-day precision of the proposed methods is performed by carrying out five replicate experiments at each concentration level within 6 hr (Table 2).

TABLE.2. Within – day precision of the determination of GMF, MXF, GAF using Rb reagent .

Compound	[Drug], Taken µg mL^{-1}	[Drug], Found µg mL^{-1}	Percentage Recovery (%)	SD*	RSD (%) *
GMF	10.71	10.68	99.68	0.0248	0.2323
	28.13	27.96	99.40	0.0238	0.0851
	32.98	32.77	99.36	0.0195	0.0595
	47.55	47.58	100.1	0.0232	0.0488
	52.40	52.46	100.1	0.0232	0.0442
MXF	12.14	12.15	100.1	0.0291	0.2395
	16.52	16.53	100.1	0.0291	0.1760
	20.9	20.93	100.2	0.0721	0.3443
	42.79	42.53	99.39	0.0220	0.0517
	51.55	51.63	100.2	0.0227	0.0439
GAT	9.048	9.068	100.2	0.0238	0.2625
	15.10	15.09	99.93	0.0260	0.1723
	23.15	23.08	99.73	0.0236	0.1023
	39.24	39.21	99.94	0.0206	0.0526
	47.29	47.07	99.53	0.0238	0.0506

* Five replicate experiments at each concentration level within 6 hr.

The intra- day precision of the proposed methods is performed by carrying out five replicate experiments at each concentration level within 6 days (Table 3).

The analytical results for accuracy and precision show that the methods proposed have good repeatability and reproducibility. Thus the proposed methods are very effective for the assay of GMF, MXF and GAF.

TABLE 3. Between – day precision of the determination of GMF, MXF, GAF using Rb reagent .

Compound	[Drug], Taken µg mL^{-1}	[Drug], Found µg mL^{-1}	Percentage Recovery (%)	SD*	RSD (%) *
GMF	11.71	11.65	99.45	0.0273	0.2344
	30.13	29.93	99.33	0.0274	0.0916
	34.98	34.72	99.23	0.0266	0.0766
	49.55	49.54	99.97	0.0265	0.0535
	51.40	51.4	99.98	0.0218	0.0424
MXF	14.14	14.12	99.86	0.0269	0.1903
	18.52	18.50	99.89	0.0304	0.1643
	22.90	22.81	99.61	0.1467	0.6431
	44.79	44.51	99.37	0.0224	0.0503
	50.55	50.61	100.12	0.0204	0.0403
GAF	10.05	10.04	99.90	0.0291	0.2898
	17.10	17.05	99.71	0.0332	0.1947
	25.15	25.06	99.64	0.0296	0.1181
	41.24	41.21	99.93	0.0261	0.0633
	46.29	46.06	99.50	0.0249	0.0541

* Five replicate experiments at each concentration level within 6 days.

Analytical applications

The applicability of the proposed methods for the determination of GMF, MXF and GAF has been tested on commercially available pharmaceutical formulations. The results of the proposed methods were compared with those obtained by the official method [37, 38] (Table 4).

These results were compared with those obtained from the reference spectrophotometric methods for GMF, MXF and GAF dosage forms by statistical analysis with respect to the accuracy (by student's t-test) and precision (by F-test) [39]. No significant differences were found between the calculated and theoretical values of t- and F-tests at 95% confidence level proving similar accuracy and precision in the determination of the studied drugs by the proposed and references methods .

TABLE 4. Application of the proposed method to the determination of the studied drugs in its pharmaceutical preparations .

Sample		Proposed method	Reported method
GMF			
Quinabiotic	X ± SD[a]	99.63± 0.4000	99.2± 0.9833
	t-Value[b]	0.91 (2.57)**	
	F-Value[b]	6.043 (6.388)**	
MXF			
Moxifloxacin	X ± SD[a]	99.94 ± 0.3200	99.90 ± 0.8800
	t-Value[b]	0.204 (2.31)**	
	F-Value[b]	7.5625 (6.388)**	
GAF			
Gatiflox	X ± SD[a]	99.93 ± 0.6600	101.73 ±1.36
	t-Value[b]	1.982 (2.45)**	
	F-Value[b]	4.246 (6.388)**	

*Mean values for five replicates, **the values between brackets are the tabulated F- and t-values at P = 0.05.

Conclusion

The data given above reveal that the proposed method is simple, accurate and sensitive with good precision and accuracy. Also, the reagent utilized in the proposed method is cheaper, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. Thus, this proposed spectrophotometric method can be successfully applied for the determination of GMF, MXF and GAF in the pure form and in pharmaceutical preparations.

References

1. **Rosentiel, V.N. and Adam, D.,** Quinolone antibacterial. An update of their pharmacology and therapeutic use. *Drugs.* **47** (6), 872 – 901 (1994).

2. **Owens, R. J. and Ambrose, P.G.,** Clinical use of the fluoroquinolones. *Med. Clin. North Am.* **84** (6), 1447 - 69 (2000).

3. **Bolon, M.K.,** The newer fluoroquinolones. *Infect. Dis. Clin. N. Am.* **23** (4), 1027 – 51 (2009).

4. **Hohl, A.F., Frei, R., P¨unter, V., Graevenitz, A.V., Knapp, C. and Washington, J.,** Significant bacteriuria in infants and young children and relation to bacterial species and pyuria. *Clin. Microbiol Infect.* **4**, 280 - 4 (1998).

5. **Anquetin, G., Greiner, J., Mahmoudi, N., Hayat, M.S., Gozalbes, R., Farhati, K., Derouin, F., Aubry, A., Cambau, E. and Vierling, P.,** Design, synthesis and activity against *Toxoplasma gondii, Plasmodium spp* and *Mycobacterium tuberculosis* of new 6-fluoroquinolones. *Eur. J. Med. Chem.* **41**, 1478 – 493 (2006).

6. **David, C.H.,** Emerging mechanisms of fluoroquinolone resistance. *Emerging Infectious Diseases.* **7** (2), 337 - 41 (2001).

7. **John, S.W. and David, C.H.,** The fluoroquinolones structures mechanisms of action and resistance, and spectra of activity in vitro. *Antimicrob*. *Agents Chemother.* **28** (4), 581- 86 (1985).

8. **Ebraheem, S.A.M., Elbashir, A.A. and Aboul-Enein, H.Y.,** Spectrophotometric methods for the determination of gemifloxacin in pharmaceutical formulations. *Acta Pharm. Sini. B.* **1**(4), 248 - 53 (2011).

9. **Tood, A.D., Lind, A.M.K., Dianne B.H., Lois, M.E., Catherine, L.C., Saralee, B., Michael, R.J. and Peter, C.A.,** Activities and postantibiotic effects of gemifloxacin compared to those of 11 other agents against *Haemophilus influenza* and *Moraxella catarrhalis*. *Antimicrob. Agents Chemother*. **44** (30), 633 - 39 (2000).

10. **Jivcu, C. and Gotfried, M.,** Gemifloxacin use in the treatment of acute bacterial exacerbation of chronic bronchitis. *Int. J. COPD.* **4**, 291- 300 (2009).

11. **Dwight, H., Daniel, A., Lionel, A.M. and Coleman, R.,** Comparative *in vitro* activities of ciprofloxacin, gemifloxacin,grepafloxacin, moxifloxacin, ofloxacin, sparfloxacin, trovafloxacin and other antimicrobial agents against bloodstream isolates of gram-positive Cocci. *Antimicrob. Agents Chemother.* **44** (3), 802 - 5 (2000).

12. **Kurt, G.N.,** Which fluoroquinolones are suitable for the treatment of urinary tract infections. *Int. J. Antimicrob. Agents.* **17**, 331 – 41 (2001).

13. **Ramzia, I., Nisreen, F.A. and Badawi, M.,** Validated stability indicating assay of gemifloxacin by different chromatographic and spectrophotometric methods of analysis. *J. Chem. Pharm. Res.* **3** (6), 562 – 70 (2011).

14. **Badraddin, M.H., Adnan, A.K. and Gamal, A.E.,** Validated liquid chromatographic-fluorescence method for the quantitation of gemifloxacin in human plasma. *Talanta*, **83**, 110 - 16 (2010).

15. **Sultana, N., Arayne, M.S., Akhtar, M., Shamim, S., Gul, S. and Khan, M.M.,** High-performance liquid chromatography assay for moxifloxacin in bulk, pharmaceutical formulations and serum: application to in-vitro metal interaction. *J. Chin. Chem. Soc.* **57**, 708 - 17 (2010).

16. **Salem, M.Y., El-Guindi, N.M., Mikael, H.K. and Abd-El-Fattah L.S.,** Stability indicating methods for the determination of some fluoroquinolones in the presence of their decarboxylated degradates. *Chem. Pharm. Bull.* **54** (12), 1625 -32 (2006).

17. **Santoro, M.I., Kassab, N.M., Singh, A.K. and Kedor-Hackmam, E.R.,** Quantitative determination of gatifloxacin, levofloxacin, lomefloxacin and pefloxacin fluoroquinolonic antibiotics in pharmaceutical preparations by high-performance liquid chromatography. *J. Pharm. Biomed. Anal.* **40**, 179 – 84 (2006).

18. **Faria, A.F., de Souza, M.V.N., de Almeida, M.V. and de Oliveira, M.A.L,** Simultaneous separation of five fluoroquinolone antibiotics by capillary zone electrophoresis. *Anal. Chim. Act.* **579,** 185 - 92 (2006).

19. **Elbashir, A.A., Saad, B., Salhin, A., Ali, A.S.M., Al-Azzam, K.M.M. and Aboul-Enein, H.Y.,** Validated stability indicating assay of gemifloxacin and lomefloxacin in tablet formulations by capillary electrophoresis. *J. Liq.. Chromatogr. Relat. Technol.* **31**, 1465 – 77 (2008).

20. **Abdel Ghani, N.T., El-Ries, M.A. and El-Shall, M.A.,** Validated polarographic methods for the determination of certain antibacterial drugs. *Anal. Sci.* **23**, 1053 – 58 (2007).

21. **Radi, A.E., Wahdan, T., Anwar, Z. and Mostafa, H.,** Electrochemical and spectroscopic studies on the interaction of gatifloxacin, moxifloxacin and sparfloxacin with DNA and their analytical applications. *Electroanalysis*, **22** (22), 2665 - 71 (2010).

22. **Radi, A.E., Wahdan, T., Anwar, Z. and Mostafa, H.,** Electrochemical determination of gatifloxacin, moxifloxacin and sparfloxacin fluoroquinolones antibiotics on glassy carbon electrode in pharmaceutical formulations. *Drug Test. Analysis.* **2**, 397 – 400 (2010).

23. **Erk, N.,** Voltammetric behavior and determination of moxifloxacin in pharmaceutical products and human plasma. *Anal. Bioanal. Chem.* **378** (5), 1351 - 56 (2004).

24. **Al-Ghannam, S.M.,** Atomic absorption spectroscopic, conductometric and colorimetric methods for determination of some fluoroquinolone antibacterials using ammonium reineckate. *Spectrochim. Acta. A.* **69** (4), 1188 – 94 (2008).

25. **Salem, H.,** Spectrofluorimetric, atomic absorption spectrometric and spectrophotometric determination of some fluoroquinolones. *Am. J. Appl. Sci.* **2** (3), 719 - 29 (2005).

26. **Tekkeli, S.E.K. and Önal, A.,** Spectrofluorimetric methods for the determination of gemifloxacin in tablets and spiked plasma samples. *J. Fluoresc.* **21** (3), 1001 -07 (2011).

27. **Ula, S.T.,** Rapid and sensitive spectrofluorimetric determination of enrofloxacin, levofloxacin and ofloxacin with 2, 3, 5, 6-tetrachloro-p-benzoquionoe. *Spectrochim. Acta. Part A.* **72** (5), 1038 - 42 (2009).

28. E**l Sheikh, M.G., Gouda, A.A. and Taleb, S.A.,** Kinetic Spectrophotometric determination of some fluoroquinolone antibiotics in bulk and pharmaceutical preparations. *Bull. Chem. Soc. Ethiop.* **27** (3), 329 - 46 (2013).

29. **Ebraheema, S.A.M., Elbashira, A. and Aboul-Enein, H.Y.,** Spectrophotometric methods for the determination of gemifloxacin in pharmaceutical formulations. *Acta. Pharmaceutica. Sinica. B.* **1**(4), 248 - 53 (2011).

30. **Misra, M., Misra, A.K., Zope, P., Panpalia, G.M. and Dorle, A.K.,** Simple and validated UV-spectroscopic method for estimation of moxifloxacin.hcl in bulk and formulation. *Journal of Global Pharma. Technology.* **2** (6), 21 - 27 (2010).

31. **Charan, D.C. and Satyabrata, S.,** Simple and rapid spectrophotometric estimation of gemifloxacin mesylate in bulk and tablet formulations. *Inter. J. Pharm. Res.* **3** (1), 133 - 35 (2011).

32. **Sayed, R.A., Hassan, W.S., El- Mammli, M.Y. and Shalaby, A.A.,** A new extractive spectrophotometric method for the determination of gatifloxacin and cefotaxime sodium in pure and pharmaceutical dosage forms. *Orient. J. Chem.* **28** (2), 639 - 50 (2012).

33. **Britton, H.T.S.,** *Hydrogen Ions,* 4th edition. Chapman and Hall, London (1952).

34. **Yoe, J.H. and Jones, A.L.,** Colorimetric determination of Fe with disodium. 1,2-dihydroxybenzene-3,5 disulfonate. *Indust. Eng. Chem. Analyst. Edit.* **16**, 111 - 16 (1944).

35. **Gouda, A.A., Amin, A.S.A., El-Sheikh, R. and Yousef, A.G.Y.,** Spectrophotometric determination of gemifloxacin mesylate, moxifloxacin hydrochloride, and enrofloxacin in pharmaceutical formulations using acid dyes. *Journal of Analytical Methods in Chemistry.* 1 - 16 (2014).

36. **Sahu, S., Patro, S.K., Narayan, U.L. and Garnaik, B.,** Ion-pair spectrophotometric estimation of gemifloxacin. *Pharmaceutical Methods,* **3** (1), 26-30 (2012).

37. **El Sheikh, R., Amin, A.S., Gouda, A.A. and Youssef, A.G.,** Utility of oxidation-reduction reaction for determination of gemifloxacin mesylate and moxifloxacin HCl in pure form and in pharmaceutical formulations using n-bromosuccinimide. *Pharm. Anal. Acta.* **4** (5),1- 9 (2013).

38. **Venugopal, K. and Saha, R.N.,** New, simple and validated UV spectrophotometric methods for the estimation of gatifloxacin in bulk and formulations. *Il Farmaco,* **60**, 906 - 12 (2005).

39. **Miller, J., Miller, J. and Saeed A.,** *Statistics and Chemometric for Analytical Chemistry.* 6th ed. (2010).

(*Received* 14/12/2014;
accepted 25/ 3/ 2015)

التقدير الطيفي لأدوية الچيميفلوكساسين ميثيلات والموكسيفلوكساسين هيدروكلوريد و الجاتيفلوكساسين سيسكويهيدرات فى صورتها النقية وفى مستحضراتها الصيدلانية

محمد عبد الجواد زايد و هبه على داخلى على سالم
قسم الكيمياء – كلية العلوم – جامعة القاهرة – شارع الجامعة – الرقم البريدى 12613– الجيزة – القاهرة .

اقتراح طريقة تحليلية طيفية بسيطة وسريعة وحساسة للتقدير الدقيق لأدوية الچيميفلوكساسين ميثيلات، والموكسيفلوكساسين هيدروكلوريد والجاتيفلوكساسين سيسكويهيدرات فى صورتها النقية وفى مستحضراتها الصيدلانية ، حيث يتم التفاعل من خلال تكوين الزوج الأيونى بين الأدوية المختارة وكاشف الروزبينجال العضوى عند الرقم الهيدروجيني 5 ، يتم قياس الزوج الأيونى عند الطول الموجى 575 نانومتر. تم اختيار الظروف المثالية. الخطوط المستقيمة لمنحنيات المعايرة تقع فى نطاق تركيز 9.71 – 53.4 و 8.758 – 52.55 و 8.048 – 48.29 ميكروجرام/ ميليلتر لأدوية الچيميفلوكساسين ميثيلات، والموكسيفلوكساسين هيدروكلوريد والجاتيفلوكساسين سيسكويهيدرات على التوالى. الامتصاصية المولارية تساوى 1.861 ×10 ^{4}و 1.835 × 10^4 و 1.561 × 10^4 لتر/ مول × سنتيمتر لأدوية الچيميفلوكساسين ميثيلات، والموكسيفلوكساسين هيدروكلوريد والجاتيفلوكساسين سيسكويهيدرات على التوالى. تم حساب الإنحراف القياسى والإنحراف القياسى النسبى لكل من الأدوية المختارة، كما تم تطبيق الطريقة المقترحة على الأدوية المختارة فى مستحضراتها الصيدلانية ومقارنتها بالطرق القياسية.