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Isolation and structure elucidation of photodegradation products of fexofenadine

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Abstract

The photostability of the antihistamine fexofenadine hydrochloride is described. The stress studies revealed the photostability of the drug as the most adverse stability factor. The main photodegradation products were isolated and its structures were elucidated by ^{1}H, ^{13}C, COSY, HSQC, HMBC NMR and mass spectrometry techniques. The drug was exposed to UVC light at 254 nm in methanolic solutions and the degradation was followed by HPLC and TLC. The photostability of fexofenadine tablets was studied and the same degradation products were observed. The two photodegradation products isolated were characterized as the isopropyl derivative, obtained by decarboxilation of fexofenadine, and a benzophenone compound, which was obtained by rearrangement of aromatic rings and oxidation reactions. The results show the importance of appropriate light protection during the drug development process, storage and handling.

Keywords: Fexofenadine hydrochloride; Quality control; Photodegradation; Fexofenadine photostability; Fexofenadine photodegradation products

1. Introduction

Fexofenadine, α,α-dimethyl-4-[1-hydroxy-4-[4-(hydroxydiphenyl-methyl)-1-piperidinyl] butyl]-benzene acetic acid [1] (Fig. 1) is the active carboxylic acid analog of the antihistamine terfenadine. It shares the histamine H_1 receptor antagonist and non-sedative properties of the parent compound but does not affect the cardiovascular events. Fexofenadine is a second generation antihistamine drug useful to available treatments of allergic diseases as allergic rhinitis and chronic urticaria, with a wide margin of safety [2–5]. Besides, fexofenadine may prove a safer alternative in the treatment of asthma [6] and atopic dermatitis [7] and is rapidly absorbed with a long duration of action, making it suitable for once daily administration. Thus, fexofenadine fulfils the essential and desirable characteristics of an ideal antihistamine, being responsible for the improvement in quality of life of the patients with allergic diseases [8].

There are some HPLC methods reported in the literature for the determination of fexofenadine in biological fluids with mass spectrometry detection [9], ionspray tandem mass spectrometry detection [10,11], electronspray tandem mass spectrometry detection [12] and fluorescence detection [13]. Recently a HPLC method to separate the enantiomers of fexofenadine was reported [14]. Few methods reported the quantitation of fexofenadine in pharmaceutical dosage forms using spectrophotometric methods [15], HPLC methods with ultraviolet detection [16,17], and capillary electrophoresis [18,19]. In addition, dissolution tests were developed for fexofenadine in capsules and coated tablets [20]. In spite of its importance in the therapy of allergic diseases, there is just one report concerning the stability of fexofenadine [21], but the isolation and characterization of its degradation products was not performed.

The International Conference on Harmonization (ICH) guideline requires that stress testing be carried out to elucidate the inherent stability characteristics of the active substance in a pharmaceutical preparation. The light testing should be an integral part of stress testing [22–24]. The drug photostability constitutes an important current subject of investigation because

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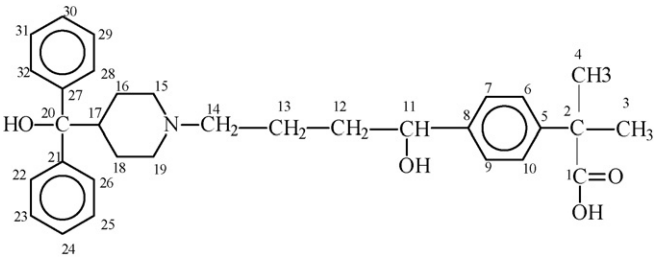

Fig. 1. Chemical structure of fexofenadine.

the photodegradation process can result in a loss of the potency of the drug and also in adverse effects due to the formation of minor toxic degradation products. In preliminary forced stress testing, we have observed the photostability of fexofenadine, and the determination of this kinetic of photodegradation in methanolic and water solutions were studied [25]. Considering the importance of this frequently prescribed drug and the non-existent of reports concerning the isolation and characterization of its degradation products, a more completed study was performed. The present work describes the photostability testing of fexofenadine, under stress condition, isolation and characterization of the main photodegradation products of the drug.

2. Experimental

2.1. Materials

Fexofenadine hydrochloride substance reference (99.60%) was obtained from Aventis Pharma (São Paulo, Brazil). Fexofenadine hydrochloride bulk substance was obtained from lazar (Buenos Aires, Argentina). Allegra® coated tablets for oral administration, containing fexofenadine hydrochloride (120 mg/tablet), and pregelatinized starch, croscarmellose sodium, and microcrystalline cellulose, magnesium stearate, colloidal anhydrous silica, hydroxypropyl methylcellulose, povidone, titanium dioxide, polyethylene glycol, pink iron oxide blend, yellow iron oxide blend as excipients, were commercially available.

Analytical reagents grade chemical (Merck, Darmstadt, Germany) were used. TLC aluminium sheets 20 × 20 silica gel 60 F_{254}, silica gel 60 GF_{254} for TLC, and silica gel 60 (0.063–0.200 mm) for column chromatography (Merck, Darmstadt, Germany) were used.

A Milli-Q® (Millipore, Buenos Aires, Argentina) water purification system was used to obtain the purified water for HPLC analysis.

HPLC experiments were performed on a Hewlett-Packard (now Agilent Technologies) 1100 consisting of an HP-G1311A Quat pump, HP 61315A UV detector, and reversed phase semi-preparative column Thermo Electron Corporation (250 × 10 mm × 5 μm) (Winsford, UK). Data acquisition and treatment were performed by a Hewlett-Packard HP-G2170AA Chem Station software (Avondale, PA).

Mass spectra were recorded on a VG Trio-2 mass spectrometer (Manchester, UK). High-resolution mass spectra were measured on a ZAB-SEQ4F mass spectrometer (Manchester, UK). The ionization method was electron impact at 70 eV.

Nuclear magnetic resonance (NMR) ^{1}H, ^{13}C, COSY (correlation spectroscopy), HSQC (heteronuclear single quantum correlation), HMBC (heteronuclear multiple bond correlation) spectra were recorded on a Bruker AM-500 spectrometer (Karlsruhe, Germany) equipped with 3 mm gradient inverse detection. NMR samples were dissolved in methanol-d_3 (Aldrich, Milwaukee, WI).

2.2. Photostability studies

Considering the sensibility of fexofenadine to light, demonstrated in preliminary studies, the photostability of the drug was study in this work.

Two light sources were tested: an UV fluorescent lamp Philips®, 15 W, emitting radiation at 254 nm; and a medium-pressure metal halide lamp HPA-400 W Philips®, both fixed to a chamber in a horizontal position, each time. The chamber was internally coated with mirrors, in order to distribute the light uniformly. The effect of light was studied exposing methanol sample solutions in 1 cm quartz cells, in a distance of 5 cm of each of the lamps. The temperature was controlled into the chamber and was always below 30 °C.

2.3. Stress degradation

Stock solutions (4.8 mg mL^{-1}) of fexofenadine hydrochloride in methanol pH 6.0 and pH 11.0 (adjusted with NaOH 0.1N) were prepared. The stress degradation study was performed exposing the solutions contained in quartz cells in the chamber. The samples were positioned horizontally, to provide maximum area of exposure to the light source [26]. The irradiation was carried out for 6 h in each lamp. In order to evaluate the contribution of thermally induced change to the total change, protected samples, wrapped in aluminium foil, were used as dark controls. The effect of the pH, as well as the different light source in the photodegradation of the drug were evaluated by HPLC and TLC techniques.

Tablets and powder of tablets were irradiated at UV 254 nm at different time intervals (0, 7, 15, 20, 30, 45 and 50 days). After each time the tablets and powder of the tablets were dissolved in methanol, filtered, diluted with the mobile phase to 800 μg mg mL^{-1}, and evaluated by HPLC to verify the content of remaining fexofenadine hydrochloride and the formation of photodegradation products.

2.4. Isolation of the photodegradation products

In order to isolate the photodegradation products, fexofenadine hydrochloride in methanol (9.6 mg mL^{-1}) pH 11.0 were irradiated for 18 h at 254 nm. After irradiation, the content of the quartz cells were collected in a vessel with an amount of 1 g of silica gel for column chromatography and the methanol was evaporated to dryness under reduced pressure. This sample was used to isolate the degradation products, employing the tech-

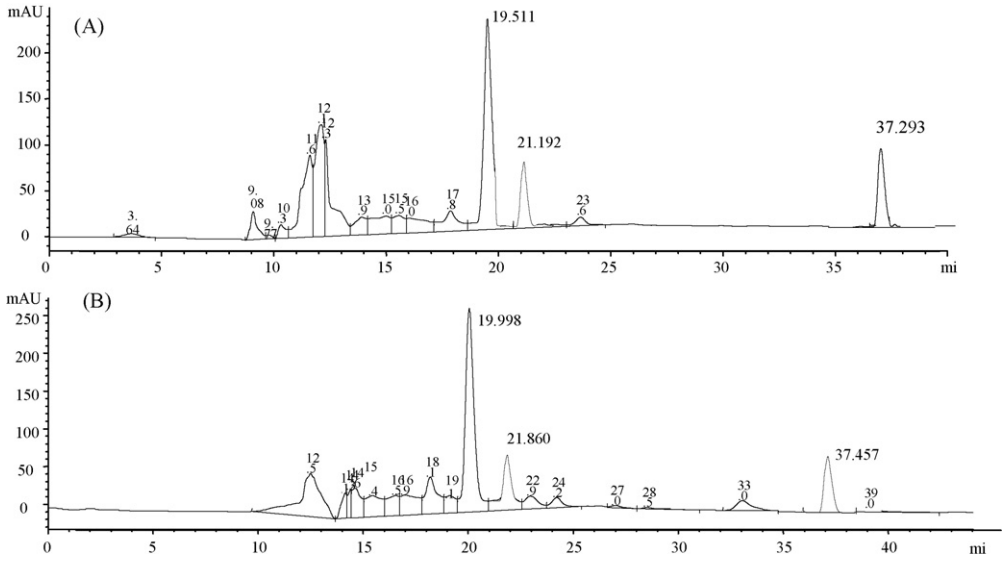

Fig. 2. Typical chromatograms of fexofenadine in methanol pH 6.0 after 6 h of exposure to metal halide HPA 400 W lamp (A) showing fexofenadine at 19.511, DP-1 at 37.293 min and DP-2 at 21.192 min; and fluorescent UV 254 nm lamp (B), showing fexofenadine at 19.998 min, DP-1 at 37.457 min and DP-2 at 21.860 min. Chromatography conditions: acetonitrile–water (50:50, v/v) at pH 3.0 mobile phase; flow rate of 1.0 mL min^{-1}; semi-preparative column Thermo Electron Corporation (250 × 10 mm × 5 μm) stationary phase; ultraviolet detection at 220 nm; injection volume of 20 μL.

nique of column chromatography. The separation was carried out using chloroform and methanol gradients from (100:0, v/v) to (75:25, v/v). Two degradation products – designed as DP-1 and DP-2 – could be isolated through this method of separation. All fractions were analyzed by HPLC and TLC. The fractions containing DP-1 were successively purified by preparative TLC using methylenechloride:methanol (90:10, v/v), while the fractions containing DP-2 were purified by the same technique using chloroform:methanol (80:20, v/v). The samples were always protected from light exposure and the collected fractions were immediately stored in the dark. Solvent was removed by evaporation under reduced pressure, and the fractions were stored in a dessicator protected from light, prior to further manipulations and analyses. The purity of the products was evaluated by HPLC and TLC techniques. For the HPLC method, a mixture of acetonitrile:water (50:50, v/v) pH 3.0 (adjusted with hydrochloride acid 0.1N) as the mobile phase in a flow rate of 1 mL min^{-1} and UV detection at 220 nm were employed. The TLC was performed with chloroform:methanol (85:15, v/v) as eluent for both products.

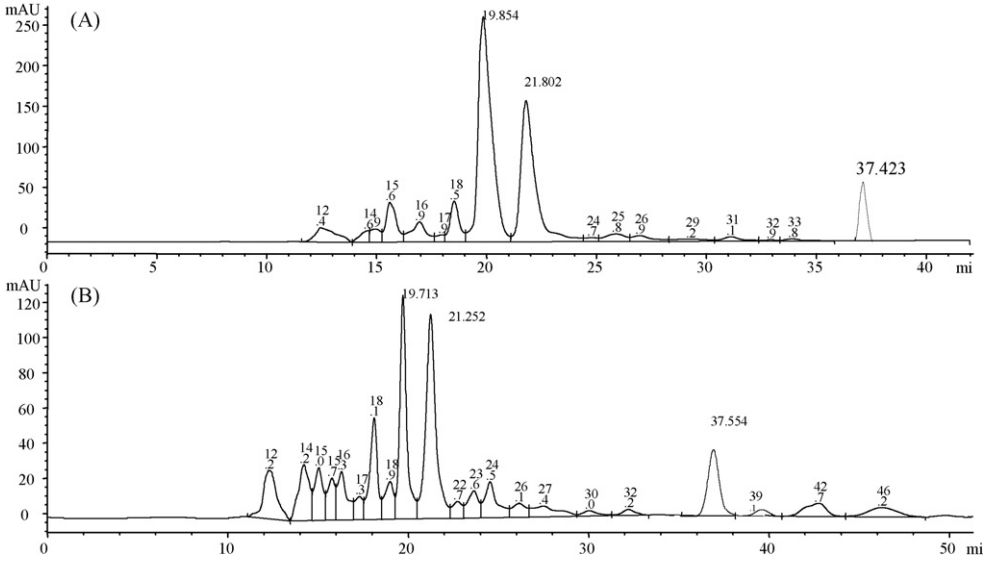

Fig. 3. Typical chromatograms of fexofenadine in methanol pH 11.0 after 6 h of exposure to metal halide HPA 400 W lamp (A), showing fexofenadine at 19.854 min DP-1 at 37.423 min and DP-2 at 21.802 min; and fluorescent UV 254 nm lamp (B), showing fexofenadine at 19.713 min DP-1 at 37.554 min and DP-2 at 21.252 min. Chromatography conditions: acetonitrile–water (50:50, v/v) at pH 3.0 mobile phase; flow rate of 1.0 mL min^{-1}; semi-preparative column Thermo Electron Corporation (250 × 10 mm × 5 μm) stationary phase; ultraviolet detection at 220 nm; injection volume of 20 μL.

2.5. Identification of the photodegradation products

After confirmation of the purity of the photodegradation products, by HPLC and TLC analyses, the spectroscopic techniques of NMR – ^{1}H, ^{13}C, COSY, HSQC, HMBC – using methanol-d_3 as solvent, and mass spectrometry were performed to allow characterization of the impurity structures. Fexofenadine standard substance was evaluated for the same NMR and mass spectrometry methods in order to compare its spectrums with those of the degradation products.

3. Results and discussion

The purpose of photostability testing is to provide evidence on how the quality of a drug varies with the time under the influence of the light. Drug photodecomposition results in loss of potency and adverse effects due to the formation of minor degradation products [27]. The stress testing is the first part of the stability evaluation and can help identify the likely degradation products, establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedure used [28,29].

Stress study on the photostability of the antihistamine fexofenadine hydrochloride was performed using a medium-pressure metal halide lamp HPA-400 W and a UV light at 254 nm in order to verify which of the light source was proper to degrade fexofenadine in methanol solutions pH 6.0 and pH 11.0. Different pH values were tested since the photodegradation process is strongly dependent on the ionization form of the molecule [30]. The medium-pressure metal halide lamp HPA lamp has a close resemblance to sunlight, and present the output spectrum rather uniform across the 350–650 nm region. The fluorescent UV 254 nm lamp is useful in stability studies, since it provides the exposure of many samples at the same time and is low cost [31]. The accelerated tests show that two main photodegradation products were formed with the exposure of fexofenadine in methanol pH 6.0 (Fig. 2) and pH 11.0 (Fig. 3) to both lamps. It was observed around 70 and 80% of fexofenadine degradation in the UV 254 nm and metal halide lamp, respectively. However, it was observed that the pH 11.0 provides high formation of one of the degradation products (DP-2) in both light sources. Then, in order to isolate the main photodegradation products, fexofenadine methanolic solutions pH 11.0 were exposed at UV 254 nm for 18 h. The degraded samples were collected in a vessel with silica gel, and the methanol was evaporated to dryness under reduced pressure. This mixture was applied to the column chromatography. Two main photodegradation products could be isolated through this technique, followed by preparative TLC. The purity of the products DP-1 and DP-2 was evaluated by HPLC (Fig. 4) and TLC. The peak purity tool was employed and shows that the obtained peaks were 100% pure. Besides, each photodegradation product applied in TLC present only one spot, showing the purity of the products. The structures of the two major photodegradation products were characterized by NMR and mass spectrometry techniques. The obtained spectrums were compared to those of fexofenadine. The results of ^{1}H NMR and ^{13}C NMR of fexofenadine evaluated to correlate each sign

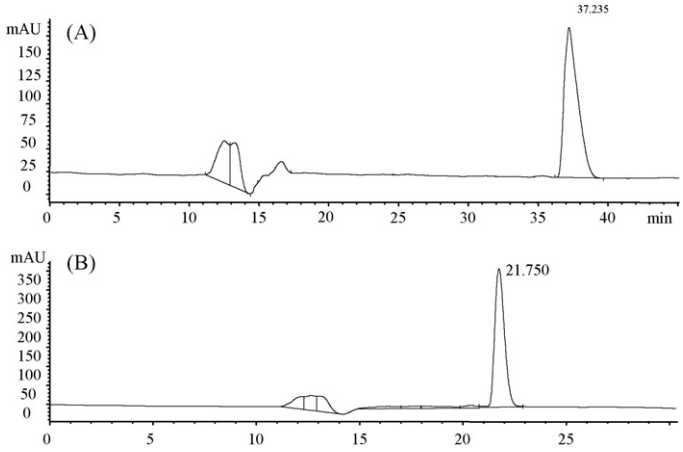

Fig. 4. Chromatograms of the main photodegradation products of fexofenadine: DP-1 (A) and DP-2 (B). Chromatography conditions: acetonitrile–water (50:50, v/v) at pH 3.0 mobile phase; flow rate of 1.0 mL min^{-1}; semi-preparative column Thermo Electron Corporation (250 × 10 mm × 5 μm) stationary phase; ultraviolet detection at 220 nm; injection volume of 20 μL.

to the hydrogens or carbons of the structure [32,33]. Besides, Table 1 shows chemical shifts (δ) ppm, multiplicities and coupling constants (J), number of hydrogens, and the corresponding hydrogen, as well as the chemical shifts (δ) ppm of the carbons and the corresponding carbon following the numeration of the molecule of fexofenadine presented in Fig. 1. The bidimensionals NMR spectrums (not shown), COSY, HSQC and HMBC, revealed important correlations, which were of high importance to confirm the attributions. Table 2 presents the obtained correlations in bidimensionals NMR for fexofenadine hydrochloride, DP-1 and DP-2.

The mass spectrum of fexofenadine shows the molecular ion (m/z 501) and the base peak (m/z 280). The mass spectrum presents the principal ions at m/z 501, 280, 183, 147, 105, 85 and 77, which were described in the literature [34].

The ^{1}H NMR of DP-1 shows a doublet at δ 1.20 ppm, assigned to six hydrogens, which was attributed to the two methyl groups. This multiplicity means that the methyl groups have neighbor hydrogen, which proves the loss of the acid group. The presence of a multiple at δ 2.85 ppm with an integration value of one hydrogen was attributed to the hydrogen bonded to the carbon which loses the acid. This sign was absent in the NMR ^{1}H spectrum of fexofenadine, where there was no hydrogen in this position. All the other hydrogen observed to fexofenadine spectrum were also verified to DP-1 (Table 1).

The ^{13}C NMR of DP-1 was lack of the carbon at δ 180 ppm, which was attributed to the acid group in fexofenadine. All the other carbons observed to fexofenadine spectrum were also verified to DP-1 spectrum (Table 1).

The COSY spectrum shows correlation between the hydrogen at δ 2.85 ppm and the hydrogen of the methyl groups at δ 1.20 ppm, confirming the attributions.

The HSQC spectrum shows correlation between the hydrogen at δ 2.85 ppm and the carbon at δ 35.06 ppm, which was assigned to the CH of the isopropyl group. The HMBC spectrum shows correlation between the hydrogens at δ 1.20 ppm and the carbon at δ 35.06 ppm (Table 2).

Table 1
Chemical shifts (δ ppm), multiplicities and coupling constants (J), number of hydrogen, corresponding hydrogen to NMR ^{1}H spectrum, chemical shifts (δ ppm), corresponding carbon to NMR ^{13}C spectrum of fexofenadine, DP-1, and DP-2, obtained in BRUKER (500 MHz) spectrometer and methanol-d_3 as solvent

Fexofenadine						DP-1						DP-2					
NMR ^{1}H (δ) ppm	M* and (J) Hz	H**	H (Fig. 1)	NMR ^{13}C (δ) ppm	Carbon (Fig. 1)	NMR ^{1}H (δ) ppm	M* and (J) Hz	H**	H	NMR ^{13}C (δ) ppm	Carbon	NMR ^{1}H (δ) ppm	M* and (J) Hz	H**	H	NMR ^{13}C (δ) ppm	Carbon
1.51	s	6	3, 4	21.75	C13	1.20	d	6	3, 4	C13	23.70	1.44	s	6	3, 4	C13	23.05
1.73	m	8	12, 13, 16, 18	25.71	C16, C18	1.45	m	8	12, 13, 16, 18	C16, C18	24.00	1.56	m	8	12, 13, 16, 18	C16, C18	28.00
2.83	t	1	17	27.09	C3, C4	2.05	m	2	15	C3, C4	24.47	2.14	m	1	17	C3, C4	28.32
2.95	m	2	15	36.84	C12	2.35	t	2	14	C2	35.06	2.23	t	2	14	C12	32.97
3.03	t	2	14	42.74	C17	2.50	t	1	17	C12	38.70	2.76	m	2	15	C17	37.90
3.47	m	2	19	47.23	C2	2.85	m	1	2	C17	45.17	3.62	m	2	19	C2	47.92
4.65	t	1	11	53.96	C15 or C19	2.90	m	2	19	C15 or C19	54.86	4.51	t	1	11	C15 or C19	53.20
7.15	t 7.32, 7.33	2	24, 30	54.06	C19 or C15	4.55	t	1	11	C19 or C15	55.11	7.17, 7.33	AA′BB′ 8.15	2, 2	6, 10, 7, 9	C19 or C15	53.33
7.27	t 7.79, 7.55	4	23, 25, 29, 31	58.27	C14	7.10	t 7.26, 7.56	2	24, 30	C14	59.68	7.28	m	2	28, 32	C14	58.89
7.28–7.36	AA′BB′ 8.40	4	6, 10, 7, 9	73.81	C11	7.12–7.21	AA′BB′ 7.88	4	6, 10, 7, 9	C11	74.73	7.38	m	2	29, 31	C11	74.34
7.50	d 7.80	4	22, 26, 28, 32	79.76	C20	7.23	t 7.56, 7.57	4	23, 25, 29, 31	C20	80.28	7.40–7.44	AA′BB′ 7.44	4	21, 22, 24, 25	C6, C10	126.46
				126.92	C22, C26, C28, C32	7.46	d 7.57	4	22, 26, 28, 32	C22, C26, C28, C32	127.15	7.53	m	1	30	C7, C9	126.93
				129.18	C23, C25, C29, C31					C23, C25, C29, C31	128.89					C29, C31	128.60
				127.03	C7, C9					C7, C9	127.20					C21, C25	129.03
				126.85	C6, C10					C6, C10	127.01					C28, C32	129.84
				127.64	C24, C30					C24, C30	127.22					C22, C24	129.94
				144.13	C8					C8	143.73					C30	131.80
				145.65	C21, C27					C21, C27	147.89					C23	141.05
				147.11	C5					C5	149.01					C27	141.25
				180.42	C1					C13	23.70					C20	141.84
																C8	143.26
																C5	148.47
																C1	184.93
																C26	196.03

M* = multiplicities (s = singlet, d = doublet and m = multiplet); H** = number of hydrogen.

Table 2
Correlations observed in COSY, HSQC and HMBC spectrums of fexofenadine and its degradation products DP-1 and DP-2 obtained in BRUKER (500 MHz) spectrometer, and methanol-d_3 as solvent

	COSY ^{1}H –^{1}H (δ) ppm	HSQC ^{1}H–^{13}C (δ) ppm	HMBC ^{1}H–^{13}C (δ) ppm
Fexofenadine	1.73–2.83	1.51–27.09	1.51–27.09
	1.73–2.95	1.73–21.75	1.51–47.23
	1.73–3.03	1.73–25.71	1.51–147.11
	1.73–3.47	1.73–36.84	1.51–180.42
	1.73–4.65	2.83–42.74	4.65–36.84
	7.15–7.27	2.95–53.96	4.65–127.03
	7.27–7.50	3.03–58.27	4.65–144.13
		3.47–54.06	7.15–126.92
		4.65–73.81	7.27–126.92
		7.15–127.64	7.27–145.65
		7.27–129.18	(7.28–7.36)–47.23
		(7.38–7.36)–126.85 and 127.03	(7.28–7.36)–126.85
		7.50–126.92	(7.28–7.36)–147.11
			7.50–79.76
			7.50–145.65
DP-1	1.20–2.85	1.20–24.47	1.20–24.47
	1.45–2.05	1.45–23.70	1.20–35.06
	1.45–2.35	1.45–24.00	1.45–74.73
	1.45–2.50	1.45–38.70	2.35–23.70
	1.45–2.90	2.05–54.86 or 55.11	4.55–38.70
	1.45–4.55	2.35–59.68	4.55–127.20
	7.10–7.23	2.50–45.17	4.55–143.73
	7.23–7.46	2.85–35.06	7.10–128.89
		2.90–54.86 or 55.11	(7.12–7.21)–35.06
		4.55–74.73	(7.12–7.21)–74.73
		7.10–127.22	7.23–127.22
		(7.12–7.21)–127.01 and 127.20	7.23–147.89
		7.23–128.89	7.46–80.28
		7.46–127.15	7.46–145.65
DP-2	1.56–2.14	1.44–28.32	1.44–47.92
	1.56–2.23	1.56–23.05	1.44–148.47
	1.56–2.76	1.56–32.97	2.14–141.84
	1.56–4.51	2.14–37.90	2.23–53.20 or 53.33
		2.23–58.89	4.51–32.97
		2.76–53.33 or 53.20	4.51–126.93
		3.62–53.20 or 53.33	4.51–143.26
		4.51–74.34	7.17–47.92
		7.17–126.46	7.28–141.25
		7.28–129.84	7.33–74.34
		7.33–126.93	7.28–196.03
		7.38–128.60	(7.40–7.44)–196.03
		(7.40–7.44)–129.03 and 129.94	(7.40–7.44)–141.84
		7.53–131.80	7.53–129.84

The mass spectrum of DP-1 shows the molecular ion at *m/z* 457, which confirm the mass of the molecule without the acid group (isopropyl derivative) and the base peak at *m/z* 280, the same value of the molecular ion observed to fexofenadine, upholding the structure interpretation of DP-1.

Thus, the photodegradation product DP-1 was identified as the isopropyl derivative of fexofenadine (Fig. 5), with a chemical name of 4-[4-(hydroxydiphenyl-methyl)-1-piperidinyl]-1-(4-phenylisopropyl)butanol.

The ^{1}H NMR and ^{13}C NMR of DP-2 spectrums show many changes, when comparing to those of fexofenadine. First a ketone group at δ 196.03 ppm in the NMR ^{13}C spectrum was observed. Besides, the quaternary carbon at δ 79.76 ppm, observed to fexofenadine, was absent in the DP-2 spectrum.

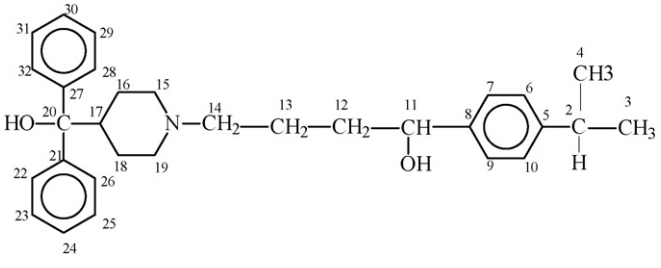

Fig. 5. Chemical structure of DP-1, the isopropyl derivative of fexofenadine, 4-[4-(hydroxydiphenyl-methyl)-1-piperidinyl]-1-(4-phenylisopropyl)butanol.

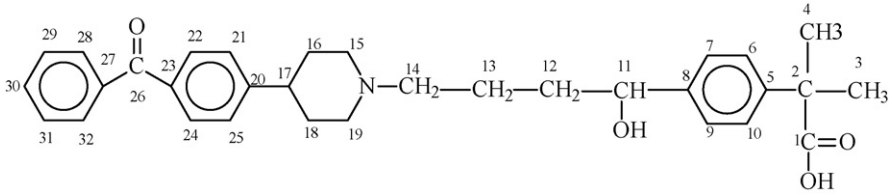

Fig. 6. Chemical structure of DP-2, the benzophenone derivative of fexofenadine, α,α,-dimethyl-4-[1-hydroxy-4-[4-(benzophenone)-1-piperidinyl]butyl]-benzene acetic acid.

It means that it occurred a modification in the region of the aromatic zone and the tertiary alcohol.

The secondary alcohol was not modified to ketone, since the C at δ 74.43 ppm and the H at 4.50 ppm are still present. This way the oxidation to ketone occurred in the OH of the tertiary group after modification in the aromatic rings.

It was verified the presence of seven aromatic carbons in the region of δ 125–132 ppm, instead of five observed for fexofenadine and DP-1. There are five quaternary aromatic carbons in the region of δ 141–149 ppm in DP-2, when compared to three observed to fexofenadine and DP-1. It means that the molecule of DP-2 loses the symmetry presented by fexofenadine and DP-1. This could be seen in the aromatic zone in NMR ^{1}H of DP-2, which shows many changes. There are a multiple at δ 7.53 ppm with integration to one H, attributed to H30, which was not presented at fexofenadine. There are also two para-substituted rings in DP-2, following the lines observed in the aromatic zone.

The mass spectrum shows a molecular ion at *m*/*z* 499 and a base peak at *m*/*z* 278, which means that the molecule of DP-2 differs of fexofenadine only in two mass units.

The HMBC spectrum shows that the ketone group correlate to aromatic carbons (7.28–196.03 and (7.40–7.44)–196.03 ppm). Thus, this group must be bonded to aromatic ring. The chemical shift of the ketone confirms it. Besides, the COSY, HSQC and HMBC results show that the structure since C1 to C17 was preserved, when compared to fexofenadine (Table 2).

Thus, the photodegradation product DP-2 was identified as the benzophenone derivative of fexofenadine (Fig. 6), with a chemical name of α,α,-dimethyl-4-[1-hydroxy-4-[4-(benzophenone)-1-piperidinyl]butyl]-benzene acetic acid.

The tablets and powder of tablets, which were exposed for UVC 254 nm lamp for 50 days, were evaluated by HPLC. The results demonstrated the presence of the same degradation products presented in solutions.

4. Conclusion

In this work, photostability study of fexofenadine in two different lamp sources and pH values was performed. Two majority photodegradation products of the antihistamine fexofenadine hydrochloride were isolated and characterized by NMR and mass spectrometry techniques. The products were shown to be an isopropyl and benzophenone derivatives of fexofenadine, which were not described in literature till now. Considering the obtained results, it is very important to protect the antihistamine from light in all stages of drug development process, handling and storage.

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