Stability-Indicating High-Performance Liquid Chromatographic Assay of Buspirone HCl

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Abstract

The *United States Pharmacopoeia* high-performance liquid chromatographic (HPLC) assay method of buspirone is not able to discriminate buspirone from its degradation products. The purpose of this work is to develop a sensitive, selective, and validated stability-indicating HPLC assay for the analysis of a buspirone hydrochloride in a bulk drug. Buspirone HCl and its potential impurities and degradation products are analyzed on an Ultrasphere C_{18} column heated to 40°C using a gradient program that contains monobasic potassium phosphate buffer solution (pH 6.9) and acetonitrile–methanol mixture (13:17) of 35% for 5 minutes, then increased to 54% in 5.5 minutes. The samples are monitored using a photo-diode array detector and integrated at 244 and 210 nm. The stress testing of buspirone HCl shows that buspirone acid hydrochloride is the major degradation product. The developed method shows a separation of buspirone degradation product and its potential impurities in one run. The stability of buspirone HCl is studied under accelerated conditions in order to provide a rapid indication of differences that might result from a change in the manufacturing process or source of the sample. The forced degradation conditions include the effect of heat, moisture, light, acid–base hydrolysis, sonication, and oxidation. The compatibility of buspirone HCl with some pharmaceutical excipients is studied under stress conditions. The linear range of buspirone HCl is between 5 and 200 ng/µL with a limit of quantitation of 2.5 ng/µL. The intraassay percentage deviation is not more than 0.38%, and the day-to-day variation was not more than 0.80%. The selectivity, repeatability, linearity, range, accuracy, sample solution stability, ruggedness, and robustness show acceptable values.

Introduction

8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione monohydrochloride (buspirone HCl) is an antianxiety member of the azaspirone group that is not chemically or pharmacologically related to the benzodiazepines, barbiturates, or other sedative/anxiolytic drugs (1,2).

The recommended storage conditions of buspirone HCl described in the *United States Pharmacopoeia* XXIII (USP 23) are to protect the compound from light, moisture, and heat. Based on these recommended storage requirements, this work was completed to investigate the degradation profile of buspirone HCl under different stress conditions. There are no reports about the stability of buspirone HCl under the conditions described in the USP. Moreover, the stability of buspirone HCl in the presence of common pharmaceutical excipients was studied in this work in order to have an idea about the compatibility of the drug in the presence of other inactive ingredients. Thus, there is a requirement for a sensitive, accurate, and precise analytical method to evaluate the purity and stability of buspirone HCl in bulk drug and in combination with the common pharmaceutical inactive excipients. However, different high-performance liquid chromatography (HPLC) methods for the analysis of buspirone HCl in human blood or rats are described in the published literature. In the literature, the detection methods used were ultraviolet (UV) at 254 nm, electrochemical, coulometric, or mass scanning protocols (3–9).

Described here is a fully validated and developed liquid chromatographic analytical method for the detection and assay of buspirone HCl and its degradation products and the analysis of its potential impurities. A gradient HPLC with photo-diode array detection method was designed to fulfill USP 23 (8,9) and Food and Drug administration (FDA)/International Conference on Harmonisation (ICH) requirements (10–13) regarding the selectivity, peak purity, linearity, suitability, robustness, ruggedness, and sample solution stability.

Experimental

All instruments were qualified and calibrated before use.

Chromatography

The HPLC system consisted of a Beckman (Fullerton, CA) series 126 pump coupled to a Beckman 168 diode-array detector. Samples were injected using a Beckman 507e autosampler with

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a 20-µL sample loop and model 7010-122 Rheodyne (Cotati, CA) injector. The system and data were controlled with Beckman Gold Nouveau software version 1.6. The chromatographic analysis was performed on a 5-µm Ultrasphere ODS column (250 mm × 4.6-mm i.d.) from Beckman, heated to 40°C using a Beckman model 235 block heater. The column was protected with a 5-µm C_{18} precolumn (2 cm × 2-mm i.d.) (Upchurch, Oak Harbor, WA). The mobile phase was delivered from two separate containers. The first container contained monobasic potassium phosphate buffer solution that was prepared by dissolving 1.36 g KH_2PO_4 in 1 L of water adjusted to pH 6.9 with 10% sodium hydroxide. The second solvent reservoir contained filtered and degassed methanol–acetonitrile (17:13). The mobile system was pumped at a flow rate of 1.4 mL/min. A gradient elution program was used to deliver 65% buffer solution for 5 min (t_0 = 0.9 min), decreased to 46% in 5.5 min. The data were collected and integrated at 244 and 210 nm.

The USP 23 HPLC assay method of buspirone HCl was applied using a µBondapack C_{18} column from Waters (Milford, MA) kept at 40°C using an Alltech (Deerfield, IL) column heater.

Chemicals

Buspirone (polymorph P203) was purchased from Flavin (Flavin Pharmaceuticals Inc., Budapest, Hungary) and evaluated and tested for its purity as described in the official monograph of USP 23 (infrared, HPLC, residue on ignition, UV, thin-layer chromatography, mp), matching the buspirone USP reference standard. Buspirone acid HCl (BusAcid, a standard degradation product of buspirone HCl), 8-(4-chlorobutyl)-8-azaspiro-[4,5]decane-7,9-dione (Liq), 1,4-bis(4-(2-pyrimidinyl) piperazine-1-yl)-butane (Bis), and 1,4-bis(8-azaspiro[4,5]decane-7, 9-dione-8-yl)-butane (Dimer) were also supplied by Flavin as buspirone-potential impurities standards (Figure 1). Acetonitrile, methanol, water, and potassium dihydrogen phosphate were HPLC grade. All other chemicals were of analytical grade from Fisher (Fisher Scientific, Springfield, NJ).

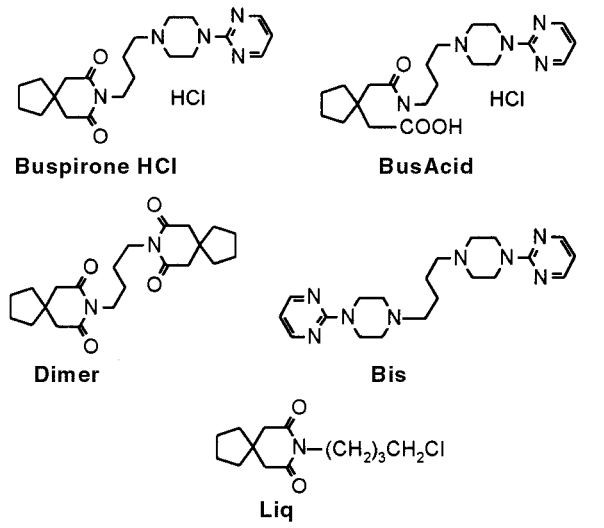

Figure 1. Chemical structures of buspirone HCl, potential impurities, and buspirone acid HCl.

Calibration solutions

Standard solution mixtures consisting of five different concentrations of each substance were prepared (Table I). For HPLC analysis, a 20-µL sample volume was injected three times. The peak area of each was plotted versus concentration (ng/µL), and the calibration curves were constructed using a least-square regression equation for the calculation of the slope, intercept, and correlation coefficient. In all cases, buspirone HCl (BuspHCl), BusAcid, and Bis were integrated at 244 nm, whereas Liq and Dimer were integrated at 210 nm.

Forced degradation

Buspirone HCl was degraded under different stress conditions as follows.

Effect of heat

Three screw-capped, brown, 5-mL reaction vials were used for this experiment (Kimex or Alltech GmbH, Unterhaching, Germany). The first vial contained 20 mg of buspirone HCl, and the second vial contained 20 mg buspirone HCl with 10 µL water as a source of moisture. Both were kept at 60°C for 14 days in a hot-air oven. The contents of the vial were dissolved in water and diluted to 25 mL with the same solvent, and 20 µL was injected for HPLC analysis. Into a third vial, an aliquot of 4 mL of standard buspirone HCl aqueous solution (500 ng/µL) was prepared. This vial was half-inserted into a block heater at 100°C for 1 h and then cooled, and 20 µL was analyzed using HPLC for an estimation of the remaining amount of buspirone HCl in addition to the detection and quantitation of the degradation products.

Effect of acid hydrolysis

In a 5-mL reaction vial, a 4-mL aliquot of standard buspirone HCl solution (500 ng/µL) was prepared in 5N hydrochloric acid. This vial was half-inserted into a block heater at 100°C for 1 h and then cooled, and 20 µL was analyzed using HPLC. This procedure was also repeated using a buspirone HCl (500 ng/µL) solution prepared in 10N HCl, and 20 µL was analyzed by HPLC.

Effect of alkali-hydrolysis

The same procedure as described for acid hydrolysis was followed, except that the buspirone HCl solution was prepared in 0.1N NaOH and 0.1N sodium carbonate basic media. The samples were analyzed after heating times of 1, 5, and 15 min.

Table I. Calibration Levels of Buspirone HCl Solutions Containing the Three Impurities and Buspirone Acid HCl

	Concentration (ng/µL)				
Level	Buspirone HCl	BusAcid	Bis	Liq	Dimer
1	5.06	5.30	5.40	4.10	5.45
2	10.12	10.60	10.80	8.20	10.90
3	50.60	15.90	16.20	12.30	16.35
4	101.20	21.20	21.60	16.40	21.80
5	202.40	31.80	34.40	24.60	32.70

Effect of oxidation

A sample solution of buspirone HCl (2 µg/µL) was prepared in 1% hydrogen peroxide, an oxygen-rich media, and heated in a reaction vial at 100°C for 30 min, followed by HPLC analysis of 20 µL. A blank experiment was prepared parallel with the sample but treated using only hydrogen peroxide. This experiment was repeated, this time using buspirone HCl sample containing copper sulphate (1%).

Effect of sonication

In a 50-mL volumetric flask, a standard buspirone HCl methanolic solution (200 ng/µL) was left in the ultrasonic bath (50 MHz) for 15, 30, 60, and 120 min. At each standing time interval, 20 µL was analyzed by HPLC.

Effect of daylight

In a stoppered, colorless, 2-mL volumetric flask, 20 mg of buspirone HCl was placed. In another flask, 20 mg buspirone HCl and 10 µL water were prepared. The flasks were kept close to the lab window and received daylight for 30 days. The sample content was dissolved in methanol, diluted to volume in a 25-mL brown volumetric flask, and analyzed using HPLC. A control sample was prepared in a 2-mL volumetric flask wrapped in aluminum foil. A 75-Watt LPS-220 xenon lamp (Photon Technology International, Ontario, Canada) was used as a confirmatory in-laboratory experiment (200–850 nm). The lamp was calibrated by quinine hydrochloride dihydrate. A sample film of approximately 0.1-mm thickness in a flat glass dish was exposed to the light source (35-cm distance) for 30 days. A claimed concentration of 500 ng/µL buspirone HCl was prepared, and 20 µL was analyzed by HPLC.

Forced degradation in the presence of inactive ingredients

In this experiment, two sample experiment vials and four blank experiments were prepared.

Blank experiments

The first vial was prepared to contain 20 mg buspirone HCl only. The second vial contained 20 mg buspirone HCl with 10 µL water (as a source of moisture). The third vial contained 20 mg of one type of the inactive ingredients (Avicel, lactose anhydrous, magnesium stearate, hydroxypropylmethylcellulose, Cab-O-Sil, Prosolv SMCC 90, or urea USP). The fourth vial contained one type of the inactive ingredient (20 mg) with 10 µL water.

Sample vials

Two sample vials were used. The first one contained 20 mg buspirone HCl with 20 mg inactive ingredient, and the second vial contained both substances with 10 µL water.

All vials (screw capped) were left to stand at 60°C for 14 days (in a hot-air oven). The contents of all vials were quantitatively transferred into 25-mL brown volumetric flasks, dissolved or suspended in methanol, and diluted to volume. The sample solutions were shaken for 5 min and sonicated for 10 min for the extraction. An aliquot of 5 mL was filtered (with a 0.22-µm syringe filtration disk), and 20 µL was injected, or diluted if necessary, for a suitable HPLC chromatogram.

Results and Discussion

Application of the USP assay method for the separation of buspirone HCl impurities

Flavin-buspirone HCl as a pure substance was verified for its identity and content by applying the HPLC USP 23 assay method. The results were matched upon using the buspirone HCl USP reference standard. The data obtained was in compliance with all USP requirements. However, the synthetic impurities of buspirone HCl could not be separated or estimated in the presence of the major drug (Figure 2). This is in addition to the coelution of buspirone acid HCl with the solvent peak at 0.9 min. The peak purity index of Liq, Bis, Dimer, and BusAcid were found to be less than 0.80. Three-dimensional chromatograms and top-view chromatograms confirmed these results. Based on the incomplete resolution of the major degradation product (BusAcid), the HPLC USP assay method cannot be used as a stability-indicating assay method of buspirone HCl. Several interchangeable parameters were tried to achieve much better resolution, but all trials failed. These trials included pH, flow rate, ratio of acetonitrile–water, and column temperature.

Development of a stability-indicating assay method

The development of a stability-indicating assay of buspirone HCl was necessary, because the assay method described in the USP 23 official monograph is not able to fulfill the requirements. The protocol of the developed method was designed to separate and quantitate the degradation products of buspirone HCl as well as quantitate its potential impurities supplied by Flavin. Six separate degraded buspirone HCl sample solutions were prepared as a result of the effect of heat, boiling, oxidation, acid hydrolysis, base hydrolysis, and light degradation. These samples were injected for HPLC analysis applying several mobile systems and columns. Also, a sample containing buspirone HCl, buspirone acid HCl, and the three potential impurities were also injected, applying several interchangeable chromatographic conditions until the best resolution was achieved. Finally, to obtain the best overall chromatographic conditions, the mobile phase was opti-

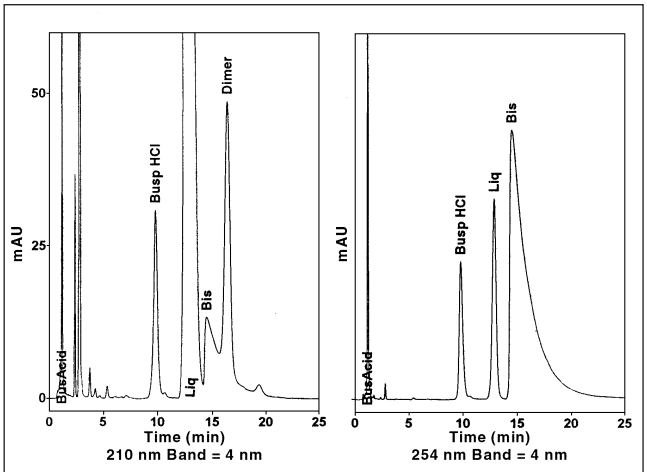

Figure 2. Chromatograms of buspirone HCl and its potential impurities or degradation products using the HPLC USP 23 assay procedure.

mized by examining the effect of pH, column temperature, column type, mobile flow rate, ratio of methanol–acetonitrile to the buffer solution, and the setting of the gradient elution program. The optimal chromatographic conditions were achieved as described in the Experimental section.

Selectivity, precision, and performance parameters

A standard solution mixture of buspirone HCl containing the three impurities and buspirone acid HCl was injected six repetitive times. All peaks showed a complete separation from each other and from the major buspirone HCl peak (Figure 3). Setting and defining the integration parameters of the software calculated the system suitability results according to USP 23 <621> from typical chromatograms. The system was suitable and precise, as shown in Table II.

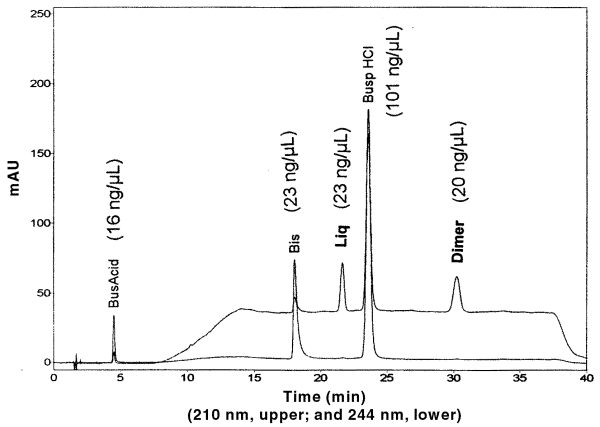

Figure 3. Chromatogram of buspirone HCl and its potential impurities or degradation products using the developed HPLC assay method.

Table II. System Performance Parameters* of Buspirone HCl and its Impurities and Degradation Products

Compound	Parameter (%RSD)				
	k'	μ	*R*	*N*	*As*
BusAcid	2.52 (0.58)	5.75	28.36 (3.11)	4688 (6.12)	1.23 (1.7)
Bis	14.50 (0.41)	1.19	4.52 (2.90)	9276 (7.71)	2.47 (3.5)†
Liq	17.13 (0.41)	1.10	3.06 (2.23)	19277 (4.78)	1.01 (2.1)
Buspirone HCl	18.83 (0.42)	1.30	7.55 (1.98)	18179 (5.24)	1.08 (2.6)
Dimer	24.40 (0.51)	—	—	13122 (4.79)	1.00 (1.3)

* *k'*, capacity factor; μ, selectivity coefficient; *R*, resolution; *N*, number of theoretical plates; and *As*, peak asymmetry.
† Although the As value of Bis relatively exceeds 2, the peak area was precise of not more than 0.40% (RSD), with no overlap with the next peak.

Table III. Calibration Parameters and Retention Time of Buspirone HCl and its Impurities and Degradation Products

Compound	*a**	*b**	*r**	Average RF	%RSD of RF	nm	Retention time
Buspirone HCl	2552	47472	0.9999	47303	1.43	244	23.60
BusAcid	6226	40936	0.9999	41450	0.80	244	4.50
Bis	141735	101853	0.9992	89241	14.56	244	18.10
Liq	2610	43962	0.9994	43872	1.79	210	21.66
Dimer	86152	61579	0.9993	54866	7.41	210	30.20

* *a*, *b*, and *r* correspond the intercept, slope, and the regression coefficient response factor (RF) calculated by dividing the peak area by the concentration (ng/μL).

Peak purity

Peak purity is defined as a peak similarity index value. All chromatographic peaks of the standard substances were UV scanned at peak apex, upslope, and downslope and normalized for estimating the matching percentage. The three-dimensional chromatogram, contour plot, and library search results (of the software) showed a complete separation and peak identity with all standard solutions.

Linearity and range

A linear response in peak area for all compounds was observed (Table III). A relatively higher concentration range of buspirone HCl was used, because we expected to use a higher concentration to be able to detect and quantitate a small amount of any impurities or degradation products, if any. By this method, even if approximately 3 mg/mL of buspirone HCl was injected, one would be able to quantitate the closest peaks to the major drug, which show no overlap.

The lower limit of detection (LOD) was estimated after five repetitive injections. LOD was calculated based on a signal-to-noise (S/N) ratio of 3, also from the chromatogram. The LOD for BusAcid, Bis, Liq, Busp HCl, and Dimer were 0.10, 0.54, 0.41, 0.5, and 0.54, respectively. The limit of quantitation (LOQ) was estimated by satisfying two criteria: the S/N ratio is not less than 10 and the percent relative standard deviation (%RSD) of five replicate injections of the LOQ solution is less than 6% (Table IV).

Accuracy

Analyzing placebo solutions spiked with known amounts of impurities and buspirone acid HCl showed the accuracy of the method. Also, a placebo solution containing BusAcid and the three impurities spiked with buspirone HCl was analyzed. Five concentration levels were used, as shown in Table V. Because the results obtained were within the acceptable range of 100 ± 5%, the method was deemed to be accurate.

Robustness

For the evaluation of the method robustness, one chromatographic parameter was changed while the other parameters were kept unchanged. A standard solution mixture containing BusAcid, Bis, Liq, Dimer, and Busp HCl was injected three times after each change. The chromatographic profile (including capacity factor *k'*, retention time *Rt*, peak asymmetry *As*, resolution, number of theoretical plates *N*, and USP width) was calculated and compared with those of the system suitability. The method robustness was tested after

changing the pH of the phosphate buffer (6.6–7.2), column temperature (25–50°C), and gradient profile (percent of buffer at 10.5 min). The results revealed that the method is robust for these small changes in pH and gradient system, but not for the change in temperature. The column temperature must be maintained at 40 ± 5°C. If the column is maintained at 25 ± 2°C, the resolution value between Liq and BuspHCl will be less than 0.8. Also, if the temperature is adjusted to 50 ± 2°C, a slight overlap between Bis and Liq will be observed.

Ruggedness

The ruggedness of the method was evaluated by applying the HPLC procedure using two different analysts with two different HPLC systems. Both HPLC systems were Beckman series coupled with a diode-array detector and solvent module with two-pump head. The %RSD of *Rt*, *k'*, *As*, and peak areas (*A*) obtained with the two chromatographic systems and operators were NMT 1.3% (Table VI).

Table IV. Estimated Lower Limit of Quantitation and Repeatability of Buspirone HCl and Its Impurities and Degradation Products

Compound	Concentration (ng/µL) Claimed	Found	Found 1	Found 2	Found 3	Found 4	Mean 5	% RSD ± SD
BusAcid	2.65	2.38	2.45	2.44	2.40	2.40	2.42 ± 0.03	1.23
Bis	2.70	2.31	2.32	2.24	2.29	2.31	2.30 ± 0.03	1.40
Liq	4.10	4.44	4.00	3.91	3.88	4.11	4.07 ± 0.22	5.56
Buspirone HCl	2.53	2.59	2.63	2.65	2.69	2.66	2.64 ± 0.03	1.40
Dimer	2.73	2.85	2.67	2.76	2.81	2.47	2.71 ± 0.15	5.57

Table V. Accuracy of the Developed Method

Substance	Claimed (ng/µL)	Found (ng/µL) mean ± SD	% Recovery	%RSD	Mixture number
Buspirone HCl	50.00	50.25 ± 0.19	100.5	0.38	2
	80.00	79.37 ± 0.13	99.2	0.16	3
	101.20	101.01 ± 0.16	99.8	0.16	1
	110.00	110.40 ± 0.19	100.4	0.17	4
	200.00	199.95 ± 0.40	99.9	0.20	5
BusAcid	5.00	4.94 ± 0.02	98.8	0.40	2
	7.00	7.04 ± 0.12	100.6	1.70	3
	10.00	10.03 ± 0.05	100.3	0.50	4
	15.90	16.05 ± 0.11	100.9	0.68	1
	15.00	14.97 ± 0.04	99.8	0.27	5
Bis	10.40	10.44 ± 0.06	100.4	0.57	2
	14.56	14.45 ± 0.16	99.2	1.11	3
	20.80	20.88 ± 0.18	100.4	0.86	4
	23.76	24.04 ± 0.07	101.1	0.29	1
	31.20	31.18 ± 0.04	99.9	0.12	5
Liq	10.70	10.56 ± 0.52	98.7	4.92	2
	14.98	14.97 ± 0.72	99.9	4.81	3
	21.40	21.70 ± 0.40	101.4	1.84	4
	22.96	23.23 ± 0.79	101.2	3.40	1
	32.10	31.95 ± 0.76	99.5	2.38	5
Dimer	10.00	10.09 ± 0.44	100.9	4.36	2
	14.00	13.84 ± 0.69	98.9	4.98	3
	20.00	20.00 ± 0.60	100.0	3.00	4
	19.62	20.05 ± 0.07	102.2	0.35	1
	30.00	30.00 ± 0.40	100.0	1.33	5

* Spiking of impurities was close to the LOQ values, because we expect lower amounts of these impurities. Each level was injected five repetative times.
† Number of determinations $n = 3$.

Sample solution stability

Sample solution stability was tested by a daily injection of calibration solution mixture containing buspirone HCl with BusAcid and its impurities. These sample solutions were prepared in 2 glass vials (in methanol and water). The recovered amount of all substances were approximately 100 ± 1%, except buspirone HCl. The recovered amount of buspirone HCl was approximately 97.5 ± 1% after one day of standing; however, no degradation product was observed. These results are attributed to the adsorption liability of buspirone HCl on glass.

Forced degradation of buspirone HCl

The degradation study of buspirone HCl was conducted until more than 10% was lost and detected. The results of the effect of heat revealed that only BusAcid was detected. The amount of buspirone acid HCl detected was not dependent on the presence or absence of moisture. However, the heating time and temperature were proportional to the amount of BusAcid produced. The boiling of buspirone HCl in 5N HCl showed only 6.2% BusAcid. However, in the case of boiling in 10N HCl solution, both BusAcid and Dimer were detected (19%). On the other hand, if buspirone HCl was boiled or even mixed at room temperature with 0.1N NaOH or 0.1N Na_2CO_3, only BusAcid was generated in a higher concentration (not less than 10%). The boiling of buspirone HCl in a solution containing 1% hydrogen peroxide showed many degradation products (Figure 4A). Most of the detected unknown degradation peaks were matched with those generated from the effect of light (Figure 5A). Also, the degradation of buspirone HCl–H_2O_2 solution was remarkably increased if boiled with 1% Cu(II) ions (Figure 4B). The chromatogram of photodegraded buspirone HCl was characterized by the peak eluted after the major peak at 26.8 min. Buspirone HCl showed not more than 0.05% unknown degradation products after sonication in water for 2 h. In general, the degradation products were optimally detected at 244 nm rather than at 210 nm. Also, the concentration of BusAcid and Dimer were calculated from the corresponding calibration

curve at 244 and 210 nm, respectively. However, the concentrations of the unknown compounds were supposed to have the same response factor of the major drug, according to the FDA/ICH guidelines. In all stress testing, the total amount of the known and unknown peaks were approximately 100 ± 4%. These results confirm that this analytical method is able to efficiently detect and quantitate any degradation products of buspirone HCl.

Table VI. Relative Standard Deviation of the Chromatographic Parameters of Buspirone HCl Analyzed in Two Different Laboratories with Two Different Analysts

System number	Compound (ng/µL)	*Rt* (% RSD)	*k'* (% RSD)	*As* (% RSD)	*A* (% RSD)
1	Buspirone HCl (101.2)	23.803 (0.40)	18.83 (0.42)	1.08 (2.63)	5033750 (0.62)
2	Buspirone HCl (100.4)	23.781 (0.25)	18.82 (0.26)	1.35 (1.43)	4947554 (1.37)

* *As*, tailing factor calculated from the equation cited in USP 23.

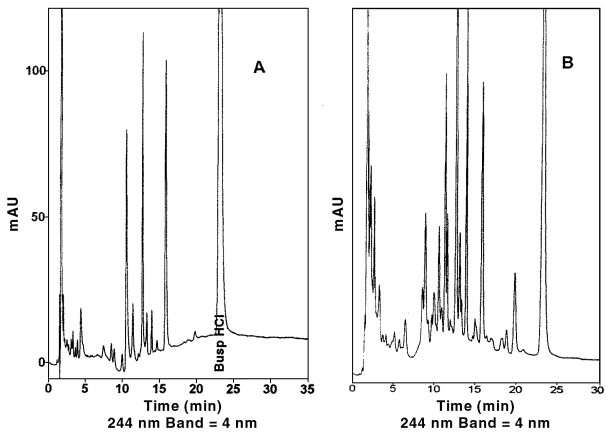

Figure 4. Chromatograms of the forced degraded buspirone HCl sample solution (0.5 mg/mL) with 1% hydrogen peroxide at 100°C for 1 h (A) and 1% copper sulphate solution (B).

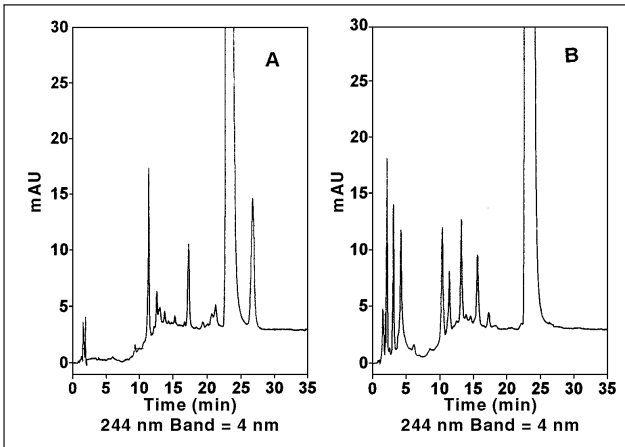

Figure 5. Chromatograms of buspirone HCl solution exposed to daylight (A) and the forced degraded sample powder extract of buspirone HCl incubated at 60°C for 2 weeks with magnesium stearate (B).

Table VII. Compatibility Study of Buspirone HCl with Different Excipients Incubated for 14 days at 60°C

Excipient	Moisture	Degraded %*
—	– or +	0.70
Mg Stearate	– or +	33.00
Urea	– or +	7.70
Cab-O-Sil	– or +	2.65
ProSolv	+	0.00
Avecil	– or +	0.80
HPMC	– or +	0.74
Lactose	–	4.80

* The known degradation % was calculated from the corresponding calibration curve; however, the rest of the detected unknown peaks were calculated as total peak area. All peak areas of the known plus unknown peaks were related to the total amount of Buspirone HCl used.

Forced degradation in the presence of some excipients

The developed method was applied for testing the compatibility of buspirone HCl with some common excipients. This study showed that magnesium stearate and urea were relatively incompatible with the drug (Table VII).

Based on these results, magnesium stearate is not recommended for use (in higher concentrations) in the formulation of buspirone HCl solid dosage forms (Figure 5B). In this study, a high concentration of buspirone HCl (2 mg/mL) was injected for the detection of any degradation products; however, dilution (1:10) was necessary to estimate the remaining amount of the unchanged buspirone HCl. Some of the blank experiments showed unrelated impurities and/or degradation products omitted from the corresponding experiment.

The extraction procedure of buspirone HCl from these excipients together (equal ratios) was validated and compared with the USP method used for buspirone HCl tablets. The extraction method was optimized using methanol as a solvent and sonication for 15 min. With this extraction procedure, the percent recovery of buspirone HCl was found to be equal to 100 ± 0.2%.

Conclusion

The developed method is able to verify buspirone HCl from its impurities (of Flavin) and any possible degradation products. For the proper storage of buspirone HCl, we recommend the use of tight containers. Also, avoid light, heat, and the combination of Mg stearate and urea in the dosage form formulation.

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