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Original article

Comparative Quality Evaluation of Three Commercial Brands of Candesartan Cilexetil/Hydrochlorothiazide (16/12.5 mg) Tablets Using HPLC and UV-Spectrophotometric Methods: A Study from Tripoli, Libya

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Keywords.
Candesartan cilexetil, Hydrochlorothiazide, Fixed-dose combination, Tablet quality, HPLC, Libyan market.

Abstract

The fixed-dose combination of candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) remains a first-line option in managing essential hypertension, owing to its complementary antihypertensive mechanisms. This study evaluated the physicochemical quality and drug content of three commercially available brands of this combination marketed in Tripoli, Libya. Three brands, coded A (Atacand Plus®, Sweden; innovator/reference), B (Atacand Plus, Turkey), and C (Hytacand, Algeria), were evaluated for weight variation, friability, hardness, thickness/diameter uniformity, and disintegration time in accordance with USP procedures. Drug content was determined using a previously validated HPLC method, with re-verification for system suitability, precision, and specificity under local analytical conditions of this study. A UV-spectrophotometric method was additionally validated in terms of linearity, limit of detection (LOD), and limit of quantitation (LOQ). All brands complied with pharmacopoeial limits, showing friability values of 0.054–0.197%, disintegration time of 3.41–5.17 minutes, and weight variation within the ±7.5% limit. Tablet hardness ranged from 10.41 to 11.78 kgf, without adversely affecting friability or disintegration. The UV method showed acceptable linearity for candesartan cilexetil (R^2 = 0.9960) and hydrochlorothiazide (R^2 = 0.9997). HPLC assay results ranged from 99.01–100.85% for candesartan cilexetil and 100.52–102.48% for hydrochlorothiazide, all within the 90–110% acceptance criterion. These findings confirm consistent drug content across the three brands despite differences in manufacturing origin. System precision showed low variability, with %RSD values of 0.107% for candesartan cilexetil and 0.138% for hydrochlorothiazide. Chromatographic specificity, confirmed by a resolution value of 4.46, further supported method reliability. All three brands met the pharmacopoeial and analytical requirements assessed, indicating comparable pharmaceutical performance among the tested products. Given the observed compliance of all tested brands, routine post-marketing quality monitoring remains warranted to ensure sustained therapeutic equivalence among multisource candesartan/hydrochlorothiazide products in the Libyan market.

Introduction

Hypertension remains a major modifiable risk factor for cardiovascular disease and premature mortality worldwide. An estimated 1.4 billion adults aged 30–79 years worldwide had hypertension in 2024, representing approximately one-third of the population in this age range, with two-thirds of affected adults living in low- and middle-income countries [1]. The WHO Eastern Mediterranean Region, which includes Libya, has the highest estimated prevalence of hypertension among WHO regions, at 38% [2]. Candesartan cilexetil (Fig. 1a) is an ester prodrug that is hydrolysed to its pharmacologically active form, candesartan, during absorption from the gastrointestinal tract [3].

Candesartan is a selective angiotensin II type 1 (AT1) receptor antagonist used, alone or in combination with a thiazide diuretic, for the management of hypertension and heart failure [4]. Pharmacologically, candesartan blocks the AT1 receptor, which inhibits the vasoconstrictor and aldosterone-secreting effects of angiotensin II [5]. Hydrochlorothiazide (Fig. 1b) is a thiazide diuretic that lowers blood pressure primarily by inhibiting sodium and chloride reabsorption in the distal convoluted tubule, thereby promoting natriuresis and reducing extracellular fluid volume [6]. The fixed-dose combination of candesartan cilexetil and hydrochlorothiazide (16/12.5 mg) integrates complementary antihypertensive mechanisms, with an additive blood pressure-lowering effect compared with either component alone [7].

Multiple generic (multisource) brands of candesartan cilexetil/hydrochlorothiazide tablets have become available in pharmaceutical markets worldwide, including that of Libya. Several spectrophotometric [8,9] and HPLC [10,11] methods have been reported for the determination of candesartan cilexetil and hydrochlorothiazide individually or in combination; however, published data comparing multiple brands of this combination marketed in Libya against USP-NF specifications appear to be limited.

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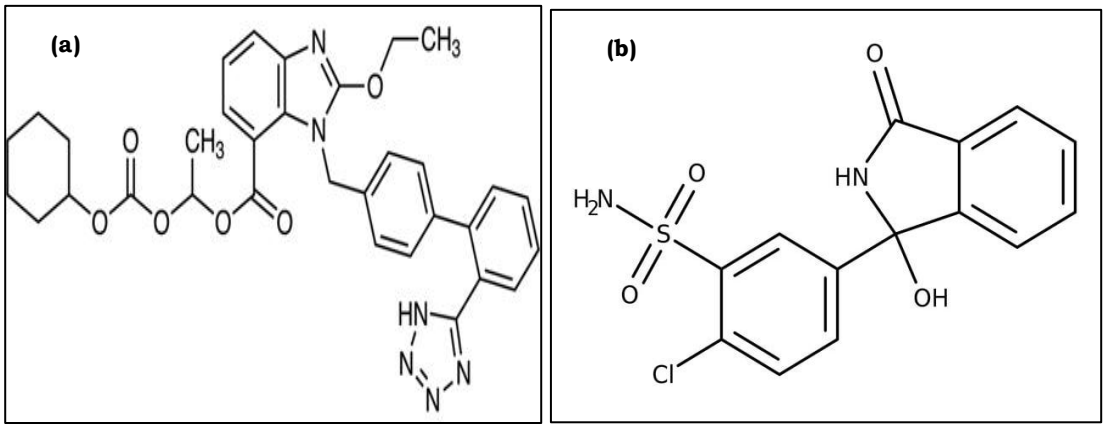

Fig 1. Chemical Structure of (a) Candesartan Cilexetil and (b) Hydrochlorothiazide

An estimated 10.5% of medical products circulating in low- and middle-income countries, where regulatory oversight is often constrained, are substandard or falsified, based on a WHO analysis of over 48,000 medicine samples from 88 countries [12]. This highlights the importance of systematic quality assessment of marketed medicines. Generic brands of a given medicine may differ in manufacturer, raw material source, and formulation. Systematic quality control testing against pharmacopoeial standards, such as USP-NF, therefore provides an objective benchmark for verifying that all marketed brands meet the required specifications for identity, potency, and physical performance [13]. Reliable quantification of the active ingredients also depends on the use of appropriately validated or verified analytical procedures, in accordance with internationally harmonised standards, such as ICH Q2(R1) [14]. The present study aimed to evaluate and compare the physicochemical quality and drug content of three commercial brands of candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) tablets marketed in Tripoli, Libya. Standard pharmacopoeial quality-control tests were performed, HPLC and UV spectrophotometric methods were used for analytical assessment, with the innovator product serving as the reference.

Materials and Methods

Materials

Three commercial products of candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) tablets, coded as A, B, and C, were purchased from a licensed retail pharmacy in Tripoli, Libya. All tested tablet samples were analysed before their stated expiration dates.

Chemicals and reagents

High-performance liquid chromatography (HPLC) grade reagents, including Acetonitrile (ACN), Methanol (MeOH), and Monopotassium phosphate (KH_2PO_4), were all obtained from Rankem and used for mobile-phase and buffer preparation. The chemical supplies were sourced through the Food and Drug Control Centre, Tripoli, Libya.

HPLC Instrumentation and Analytical Conditions

Chromatographic analysis was performed using a Shimadzu UFLC system (VP series, Shimadzu Corporation, Japan). The chromatographic conditions for the HPLC method, including column specifications, mobile phase composition, and detection parameters, are summarized in (Table 1) [15].

Table 1. Summary of Optimised Chromatographic Conditions

Parameter	Condition
Mobile phase	HPLC-grade mixture of (80% MeOH, 18% ACN and 2% KH_2PO_4 buffer)
Pump	LC-10AT
Detector	SPD-20AV UV-visible
Column	C18 reverse-phase column (250 mm × 4.6 mm internal diameter and 5µm particle size).
Wavelength	272 nm
Flow rate	1 mL/min
Injection volume	10 µL
Runtime	10 min
Column Temperature	Ambient temperature (25°C).

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Preparation of Standard Solutions

Standard stock solutions of candesartan cilexetil and hydrochlorothiazide were prepared separately. Accurately weighed quantities of each reference standard, equivalent to 25 mg of the respective drug, were transferred separately into 25 mL volumetric flasks. Each standard was dissolved in mobile phase and sonicated for 5 minutes. Each solution was diluted to volume with the same solvent to obtain a stock concentration of 1 mg/mL (1000 µg/mL). A working standard solution of 50 µg/mL was prepared by transferring 5 mL of the 1 mg/mL stock solution into a 100 mL volumetric flask and diluting to volume with the mobile phase. All prepared solutions were mixed thoroughly and filtered through a 0.45 µm membrane filter before use.

Preparation of Sample Solutions

Twenty tablets of each brand were weighed and crushed to a fine powder. For each active pharmaceutical ingredient (API), a separate quantity of powder was accurately weighed such that it contained an amount of the target analyte equivalent to approximately 25 mg of the respective API and transferred into a 25 mL volumetric flask. A volume of mobile phase was added, and then the mixture was sonicated for 30 minutes using a Sonorex ultrasonic bath (Bandelin, Germany). The resulting solution was then centrifuged at 3000 rpm for 30 minutes using a Heraeus centrifuge (Model D-37520, Germany). The supernatant was collected and filtered through an Ultipor N66 Nylon membrane filter (0.45 µm). An aliquot of 5 mL of the filtered solution was transferred into a 100 mL volumetric flask and diluted to volume with the mobile phase to obtain an approximate concentration of 50 µg/mL. The resulting solution was mixed thoroughly, and 10 µL was injected into the HPLC system. The peak areas were recorded at a wavelength of 272 nm, and the samples were determined [15].

Assay Drug Content Calculation

The percentage assay of each API was calculated by comparing the mean peak response of the sample solution with that of the corresponding reference standard solution, taking into account their respective concentrations. The nominal concentration of each API in the sample solution was calculated based on the labelled amount, average tablet weight, weight of powdered tablets taken, and the dilution factors. The percentage assay was calculated using the following equation:

$$\textit{Final concentration (CU)} = \frac{(W_t \times LC \times V_a)}{(AW \times V_1 \times V_2)} \qquad \text{Eq. 1}$$

Where:
Wt = weight of powdered tablets taken (mg)
LC =labelled amount of the respective API per tablet (mg/tablet)
AW = average tablet weight (mg)
V_a = aliquot volume transferred for the final dilution (mL)
V_1 = first dilution volume (mL)
V_2 = final dilution volume (mL)

$$\textit{Assay (\%)} = \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times 100 \qquad \text{Eq. 2}$$

Where:
r_U = mean peak area of the sample
r_S = mean peak area of the corresponding reference standard
C_S = concentration of the reference standard solution (µg/mL)
C_U = concentration of the sample solution (µg/mL)

Acceptance Criterion

In accordance with the official USP monograph for candesartan cilexetil and hydrochlorothiazide tablets, the assay of each active ingredient should contain not less than 90% and not more than 110% of the labelled amount [13].

Analytical Method Validation

The chromatographic method employed in this study (Table 1) was based on the verification of a previously validated HPLC procedure [15]. Accordingly, the present study focused on verifying key method performance parameters relevant to the local analytical conditions for the three commercial brands, rather than performing full method re-validation. The UV spectrophotometric method was evaluated for linearity, limit of detection (LOD), and limit of quantitation (LOQ), in accordance with ICH Q2(R1) guidelines [14]. Concurrently, the HPLC method was assessed for system suitability [16] and for precision and specificity in accordance with the same guidelines.

System Suitability

System suitability was evaluated before sample analysis by injecting standard solutions into the HPLC system. The monitored parameters included retention time, peak area, per cent relative standard deviation (%RSD), and

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chromatographic resolution (R_s) between candesartan cilexetil and hydrochlorothiazide peaks .System suitability was assessed in accordance with USP Chapter ⟨621⟩ [17]. Chromatographic resolution (Rs) was calculated using the following equation:

$$R_s = \frac{2(t_{R2} - t_{R1})}{(W_1 + W_2)} \quad \text{Eq. 3}$$

Where t_{R2} and t_{R1} are the retention times of hydrochlorothiazide and candesartan cilexetil, respectively, and W_1 and W_2 are the corresponding peak widths at the baseline.

Acceptance Criterion

The chromatographic resolution (Rs) between the two analyte peaks was required to be ⩾1.5.

Precision (Repeatability)

The precision study was performed in terms of repeatability (intra-day precision) by five replicate injections of the standard solution derived from two independently prepared standard solutions for candesartan cilexetil and hydrochlorothiazide into the chromatographic system under the same operating conditions over a short time interval. Precision was expressed as the per cent relative standard deviation:

$$\%RSD = \frac{Standard\ Deviation}{Mean} \times 100 \quad \text{Eq. 4}$$

Acceptance Criterion

In accordance with the official USP-NF monograph, the method was considered precise if the %RSD values were not more than (NMT) 1.0% for the assay [13].

Specificity

Specificity was assessed by comparing the chromatograms of the standard solutions with those of the tablet sample solutions under the established chromatographic conditions. The separation of the target analytes from potential interferences was assessed based on chromatographic peak separation and the absence of interfering peaks at the analyte retention times. Overlay chromatograms were visually inspected to determine whether any co-eluted peaks arising from excipients or other matrix components were present at retention times of the principal drug peaks [18].

Calibration Curve Construction (Linearity)

Linearity of the UV spectrophotometric method was evaluated by preparing five concentration levels for both candesartan and hydrochlorothiazide. Aliquots of 0.5, 1.0, 1.5, 2.0, and 2.5 mL from the working standard solution (50 µg/mL) were transferred into a series of 5mL volumetric flasks. The volume was made up to the mark with 0.02 M potassium phosphate buffer solution (pH 6.5) to yield final concentrations of 5, 10, 15, 20, and 25 µg/mL. The absorbance was measured using a UV spectrophotometer (Jenway 6305, UK) at 272 nm. A calibration curve was obtained by plotting the absorbance against the concentration, and the regression equation was calculated. The linearity was assessed using least-squares linear regression analysis, and the coefficient of determination (R^2) was calculated.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The detection limit (LOD) and quantitation limit (LOQ) of the UV-spectrophotometric method were estimated from the standard deviation of the response and the slope of the calibration curve using the following equations [19]:

$$LOD = 3.3 \times \frac{\sigma}{S} \quad \text{Eq. 5}$$

$$LOQ = 10 \times \frac{\sigma}{S} \quad \text{Eq. 6}$$

Where
σ is the standard deviation of the y-intercept and
S is the slope of the calibration curve.

Quality Control Test

The physicochemical properties of the tablets were evaluated according to USP procedures. The following tests were conducted:

Weight Variation Test

According to the USP weight variation test, twenty tablets from each brand were individually weighed using a calibrated analytical balance (Mettler Toledo AL104, Greifensee, Switzerland; precision: ±0.1 mg). The average weight was calculated, and the percentage deviation of each tablet from the mean value was determined. Weight variation was determined using the following equation:

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$$\% \text{ Deviation} = \frac{\text{Individual tablet weight} - \text{Average weight}}{\text{Average weight}} \times 100 \quad \text{Eq. 7}$$

Acceptance Criterion

In accordance with USP guidelines, the weight variation limits depend on the average tablet weight: ±10% for tablets weighing ⩽ 130 mg, ±7.5% for tablets weighing 130–324 mg, and ±5% for tablets weighing >324 mg. The batch complies with the test if no more than two of the individual tablet weights deviate from the average weight by more than the allowed percentage limit, and no individual tablet deviates by more than twice that percentage [20].

Hardness and Tablet Dimensions Test

The mechanical strength of the tablets was evaluated using a hardness (breaking force) test, while thickness and diameter measurements were conducted to assess dimensional consistency. A total of ten tablets from each brand were randomly selected and analysed using a calibrated multi-parameter tablet testing instrument (Model PTB311E "3-in-1", Pharma Test, Germany). Each tablet was positioned between the measuring jaws of the instrument, and dimensional readings (thickness and diameter) were recorded in millimetres (mm). Tablet hardness (crushing strength) was determined as the force required to fracture the tablet along its diameter and was expressed in kilogram-force (kgf) [21].

Acceptance Criterion

Individual thickness and diameter values should not deviate by more than ±5% from the calculated mean value [22, 23]. As tablet hardness is not a compendial parameter with a universally mandated numerical limit, target ranges are instead derived from standard pharmaceutical manufacturing practice: a hardness of 4–8 kgf is generally considered acceptable for conventional uncoated tablets, while 5–10 kgf is typically targeted for coated tablets to withstand downstream handling and packaging operations [24]. Mean values and standard deviations (Mean ± SD) were calculated for all parameters.

Friability Test

The friability was determined using a calibrated Pharma Test friability tester (PTF 20E/20ER, Pharma Test, Germany) to assess the tablets' resistance to mechanical shock and attrition. Twenty tablets randomly selected from each brand were carefully dedusted and accurately weighed to obtain the initial weight (W_0). The tablets were then placed in the friabilator's drum and rotated at 25 rpm for 4 minutes (equivalent to 100 revolutions). After completion of the test, the tablets were removed, dedusted, and reweighed to obtain the final weight (W_1) [25].

The percentage weight loss was calculated using the following equation:

$$\% \text{ Weight Loss} = \left(\frac{W_0 - W_1}{W_0}\right) \times 100 \quad \text{Eq. 8}$$

Where W_0 is the initial weight of the tablets before rotation, and W_1 is the final weight of the tablets post-rotation.

Acceptance Criterion

In accordance with USP standards, a maximum mean weight loss of not more than 1.0% of the initial mass is considered acceptable. Additionally, no individual tablet should show signs of capping, cleaving, or breaking during the test [26].

Disintegration Test

Tablet disintegration time was evaluated using a USP disintegration testing apparatus (PTZ AUTO 1, Pharma Test, Germany. The apparatus consists of a basket rack holding six open-ended glass tubes with a 10-mesh stainless-steel wire screen at the bottom. One tablet was placed into each of the six tubes (n=6), and the apparatus was operated using 900 mL of distilled water maintained at 37 ± 2 °C as the immersion medium. The time required for all six tablets to break down completely, leaving no palpable core or solid residue on the mesh screen, was recorded automatically in minutes. Mean values and standard deviations (Mean ± SD) were calculated for each brand.

Acceptance Criterion

According to USP standards, conventional uncoated tablets comply with the test if all six units disintegrate completely within 15 minutes, whereas plain film-coated tablets must disintegrate completely within 30 minutes [27].

Results and Discussion

Physical and Physicochemical Characterization

Three commercial brands of candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) tablets were evaluated for their physical and physicochemical properties. All samples were within their stated shelf life at the time of testing. A summary of their physical attributes is presented in Table 2. The evaluated products exhibited comparable physical and visual

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characteristics, including colour, shape, and presence of scoring.

Table 2. Description of Different Brands of Candesartan Cilexetil/Hydrochlorothiazide Tablets

Brand Code	Brand Name	Country	Manufacturer	Color	Shape	Scoring
A	Atacand Plus®	Sweden	AstraZeneca	Peach	Oval, biconvex	Scored
B	Atacand Plus	Turkey	AstraZeneca	Peach	Oval, biconvex	Scored
C	Hytacand	Algeria	AstraZeneca	Peach	Oval, biconvex	Scored

The physicochemical quality attributes, including weight variation, friability, and disintegration time, are presented in Table 3. All three brands complied with the USP acceptance criterion for weight variation (±7.5% for tablets weighing 130–324 mg). These results indicate acceptable weight uniformity among the tested units. The friability values ranged from 0.054% to 0.197%, remaining below the acceptance limit of 1% for all brands [27], indicating adequate resistance to mechanical abrasion. All tablets disintegrated within 3–5 min, well below the USP disintegration time limit of 30 min for film-coated tablets [28], indicating rapid disintegration under the test conditions.

Table 3. Physicochemical Quality Evaluation of Different Brands of Candesartan Cilexetil / HCTZ Tablets: Weight Variation, Friability and Disintegration Time

Brand Code	Average weight (mg) n=20	Weight variation (%) n=20	Friability (%) n=20	Disintegration time (min) n=6
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
A	130.29 ± 0.0015	0.079 ± 0.116	0.138 ± 0.320	3.41 ± 0.120
B	130.98 ± 0.0013	1.076 ± 0.722	0.054 ± 0.110	4.05 ± 0.054
C	132.18 ± 0.002	0.985 ± 0.572	0.197 ± 0.157	5.17± 0.009

Hardness and Tablet Dimensions Uniformity

The physical and mechanical parameters of the evaluated candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) tablet brands, including thickness, diameter, and crushing strength, are summarised in Table 4. As the evaluated products are film-coated tablets, the relevant target hardness range is 5–10 kgf, typically applied to withstand downstream handling and packaging operations. The mean hardness across all brands, which ranged from 10.41 to 11.78 kgf, exceeded this upper limit, indicating a formulation compressed to a higher than typical mechanical strength. Importantly, this did not compromise friability or disintegration performance, as all samples complied fully with pharmacopeial limits for both parameters. Furthermore, the minimal percentage variation observed in tablet thickness (⩽0.21%) and diameter (⩽0.13%) indicates good consistency in tablet dimensions.

Table 4. Thickness, Diameter and Hardness of Different Brands of Candesartan Cilexetil / Hydrochlorothiazide Tablets

Brand Code	Thickness Variation (%) n=10	Diameter Variation (%) n=10	Hardness (kgf) n=10
	Mean ± SD	Mean ± SD	Mean ± SD
A	0.21 ± 0.021	0.044 ± 0.019	10.41± 0.265
B	0.030 ± 0.007	0.087 ± 0.009	10.92 ± 0.716
C	0.065 ± 0.0105	0.130 ± 0.011	11.78 ± 0.589

Analytical Method Validation

Linearity

The calibration data are presented in Table 5 and the corresponding Fig. 2 for candesartan cilexetil and hydrochlorothiazide. Phosphate buffer at pH 6.5 was used as the diluent for preparing the calibration standards. Both analytes demonstrated good linearity over the studied concentration range, with coefficients of determination (R^2) of 0.9960 for candesartan cilexetil and 0.9997 for hydrochlorothiazide.

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Table 5. Calibration Curves of Candesartan Cilexetil / Hydrochlorothiazide Drug in Phosphate Buffer (pH 6.5)

Concentration (µg/mL)	Absorbance (AU) of Candesartan Cilexetil	Absorbance (AU) of Hydrochlorothiazide
5	0.189	0.179
10	0.375	0.339
15	0.502	0.519
20	0.637	0.690
25	0.798	0.852

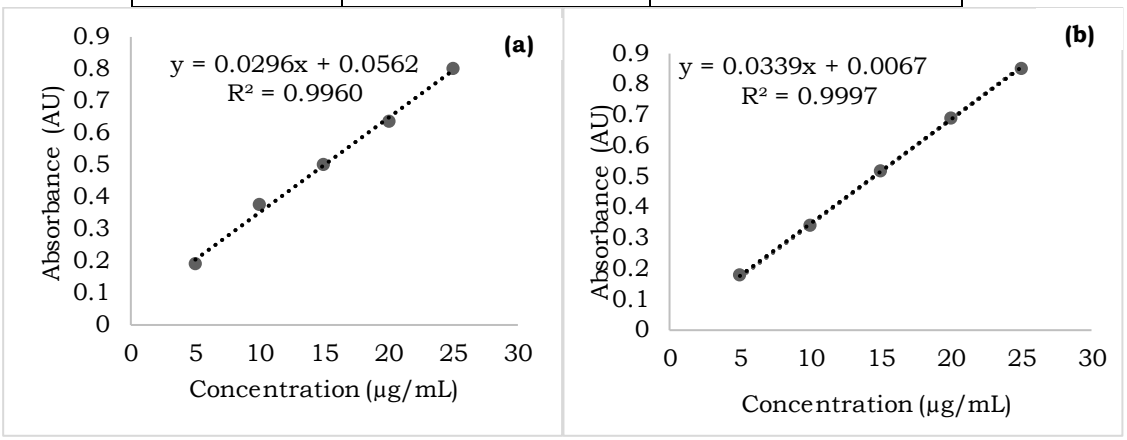

Fig 2. Calibration Curve of: (a) Candesartan Cilexetil and (b) Hydrochlorothiazide in Phosphate Buffer (pH 6.5)

Sensitivity (LOD and LOQ)

LOD and LOQ were estimated from the standard deviation of the y-intercept (σ) and slope (S) of the calibration curves according to ICH Q2(R1) guidelines. The LOD values were 0.039 µg/mL for candesartan cilexetil and 0.041 µg/mL for hydrochlorothiazide, while the LOQ values were 0.118 µg/mL and 0.124 µg/ mL, respectively, as shown in Table 6. The low LOD and LOQ values indicate that the method has adequate analytical sensitivity for determining both analytes at the investigated concentrations.

Table 6. Sensitivity Parameters (LOD and LOQ)

Name of drug	LOD(µg/ml)	LOQ(µg/ml)
Candesartan Cilexetil	0.039	0.118
Hydrochlorothiazide	0.041	0.124

Quantitative Determination by HPLC (Assay Results)

The assay results for candesartan cilexetil and hydrochlorothiazide in the three studied brands are summarised in Tables 7 and 8. The assay results for both active ingredients in all three brands were within the acceptance criteria specified (90–110% of the label claim) for the tested products [13]. Candesartan content was consistent within specification across all brands, ranging from 99.01% to 100.85% of the label claim (Table 7), indicating close agreement with the labelled amount in all three brands. Hydrochlorothiazide ranged from 100.52% to 102.48% of the label claim (Table 8) across the three brands, indicating satisfactory drug content under the conditions of the present analysis.

Table 7. HPLC Assay Results of Candesartan Cilexetil in Different Brands of Tablets

Brand code	Label claim (mg)	Wt* (mg)	Peak area (Mean ± SD*)	Calculated concentration (mg/mL)	Assay (% of label claim)
A	16	204.58	618108 ± 97.6	0.0496102	100.85
B	16	204.79	613372 ± 30.4	0.0500250	99.22
C	16	206.29	611909 ± 77.8	0.0500249	99.01

Table 8. HPLC Assay Results of Hydrochlorothiazide in Different Brands of Tablets

Brand code	Label claim (mg)	Wt* (mg)	Peak area (Mean ± SD*)	Calculated concentration (mg/mL)	Assay (% of label claim)
A	12.5	262.11	1914638 ± 139.5	0.0496571	100.52
B	12.5	263.47	1940362 ± 651.2	0.0502805	100.59
C	12.5	263.97	1965985 ± 183.8	0.0500095	102.48

SD = Standard deviation and Wt*=Powder weight taken*

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Precision (Repeatability)

Precision was evaluated by injecting each of two independently prepared standard solutions five times (n=5). The relative standard deviations (%RSD) of peak areas were 0.107% for candesartan cilexetil and 0.138% for hydrochlorothiazide (Table 9). These results satisfy the acceptance criterion of %RSD ⩽1.0%, confirming good instrumental repeatability.

Table 9. System Precision (Repeatability) for Candesartan Cilexetil and Hydrochlorothiazide

Injection (n=5)	Peak Area of Candesartan Cilexetil	Peak Area of Hydrochlorothiazide
Injection-1	616794	1920497
Injection-2	617258	1918860
Injection-3	618328	1917721
Injection-4	618039	1915312
Injection-5	618177	1913964
Mean	617719.2	1917270.8
Standard Deviation	661.6628295	2641.421341
%RSD	0.107113852	0.137769862

Chromatographic Analysis

Method specificity was confirmed by comparing the chromatographic profiles of standard mixture solutions and commercial tablet formulations (Fig. 3). No interfering peaks from tablet excipients or matrix components were observed at the retention times of candesartan cilexetil (t_{R1} = 3.52 min) or hydrochlorothiazide (t_{R2} =2.45 min). Furthermore, baseline resolution (Rs = 4.46) far exceeded the minimum acceptance criterion of 1.5, indicating excellent chromatographic separation.

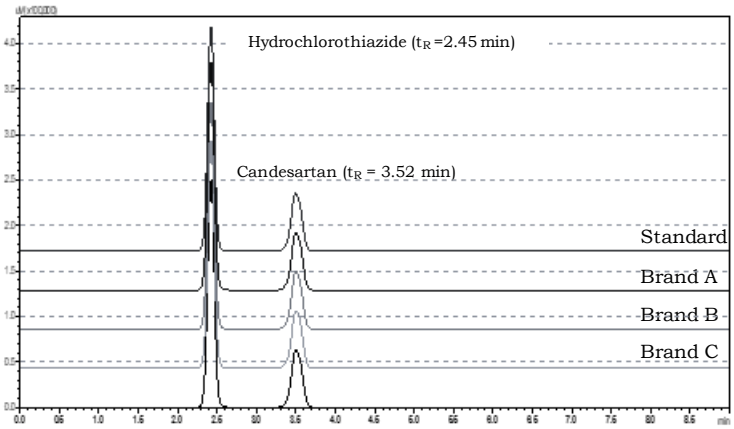

Fig 3. Typical Chromatograms Overlay of Three Tested Brands.

Conclusion

This comparative evaluation showed that the three commercially available brands of candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) tablets marketed in Tripoli, Libya, met USP-NF compendial standards across most physicochemical and analytical parameters assessed. Specifically, weight variation, friability, and disintegration results were within compendial limits for all brands. Although hardness values exceeded the target range typically reported for film-coated tablets [24], this did not compromise friability or disintegration performance, indicating that increased tablet hardness did not translate into impaired drug release behaviour. Drug content determination by HPLC confirmed that both active ingredients in all three brands fell within the %110–90 acceptance criterion specified in the USP-NF monograph. The HPLC method demonstrated adequate system precision and specificity, while the UV spectrophotometric method showed strong linearity and acceptable detection/quantitation limits for both analytes, confirming the suitability of both analytical approaches for routine quality assessment. Collectively, these findings indicate that the three brands are comparable in the physicochemical and content-related attributes assessed, reflecting acceptable and consistent pharmaceutical quality among the products available in the Libyan market. Given the demonstrated compliance of all three brands in this study, sustained post-marketing surveillance remains warranted to ensure long-term batch-to-batch consistency of multisource candesartan/hydrochlorothiazide products circulating in the Libyan pharmaceutical market.

Conflict of interest. Nil

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