"REVOLUTIONIZING TABLET ANALYSIS: CONCURRENT SPECTROPHOTOMETRIC QUANTIFICATION OF BENAZEPRIL HYDROCHLORIDE AND HYDROCHLOROTHIAZIDE"

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Abstract:
A novel analytical technique has been advanced for the concurrent valuation of Hydrochlorothiazide (HCT), and benazepril HCl (BEN) in tablet formulation. This technique, based on the concurrent equation approach, offers simplicity, accuracy, precision, reproducibility, and cost-effectiveness. Utilizing methanol as the solvent and measuring at 240.0 nm and 270.0 nm, the method demonstrates linearity for BEN and HCT in the conc. ranges of 04–14.0 µg/mL, and 02–12.0 µg/mL, respectively, corresponding to their respective λmax. The recovery studies validate the accurateness of the concurrent equation method, with BEN exhibiting recoveries between 100.1% to 100.5% and HCT between 100.0% to 100.1%. This method is recommended for routine analysis due to its speed, simplicity, accuracy, sensitivity, and specificity, making it suitable for practical applications.

Keywords: Benazepril HCl, RP-HPLC, and HCT etc.

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DOI: 10.53555/ecb/2022.11.6.35

Introduction:

Benazepril hydrochloride (BEN) is a compound with the chemical structure "3-[[1-(ethoxycarbonyl)-3-phenyl-(1S)-propyl] amino]-2, 3, 4, 5-tetrahydro-2-oxo-1H-1-(3S)-benzazepine-1-acetic acid mono-hydrochloride" (1(a) Fig.) Its practical method, '$C_{24}H_{28}N_2O_5{\cdot}HCl$', has a mole. wt. of '460.96 gram/mole'. Functionally, it acts as an ACE, and is principally used as an against the hypertensive agent.

HCT is characterized chemical structure as "6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide" (1(b) Fig.) Its practical method, '$C_7H_8ClN_3O_4S_2$', possesses a mole. wt. of '297.73 gram/mol' HCT serves as a diuretic mediator.[1]

Both HCT, and BEN are officially recognized in the BP, and the IP. Although various procedures exist in literature for determining BEN either individually or in mixture with extra drugs, nearby is currently no described UV spectrophotometric technique specifically intended for concurrently estimating HCT, and BEN in pharmaceutical provisions.

The aim of this study is to advance, and validate novel investigative approaches that enable the concurrent resolve of HCT, and BEN in solid dosage approaches, where hydrochlorothiazide was procured from the local market for the experimental procedures.[2, 3.]

Materials and Methods:

For the spectral measurements, "a double-beam Shimadzu UV-visible spectrophotometer 1700 (Pharma spec)" equipped through an accuracy of wavelength ± 0.5 nm was employed. Absorbance readings were taken using a couple of 1 cm coordinated quartz cells.

Precise weighing of substances was carried out using an (Shimadzu BL-220H) electronic balance. Mathematical calculations were conducted using Microsoft Excel 2007 as the analytical tool.

Systematically unadulterated illustrations of HCT, and BEN were obtained as gifted drugs from Intas Pharma. Ltd. and Zydus Cadila Pharma. Pvt. Ltd. based in Ahmadabad, Bharat. Analytical-grade (E. Merck, Mumbai, India) methanol was utilized as the diluents for the solutions.

The tablet formulations are marked with 12.5 mg of HCT, and 10 mg of benazepril hydrochloride branded as Lotensin HCT by Novartis Pharmaceutical Pvt. Ltd. were purchased from the local market for use in this study.[4]

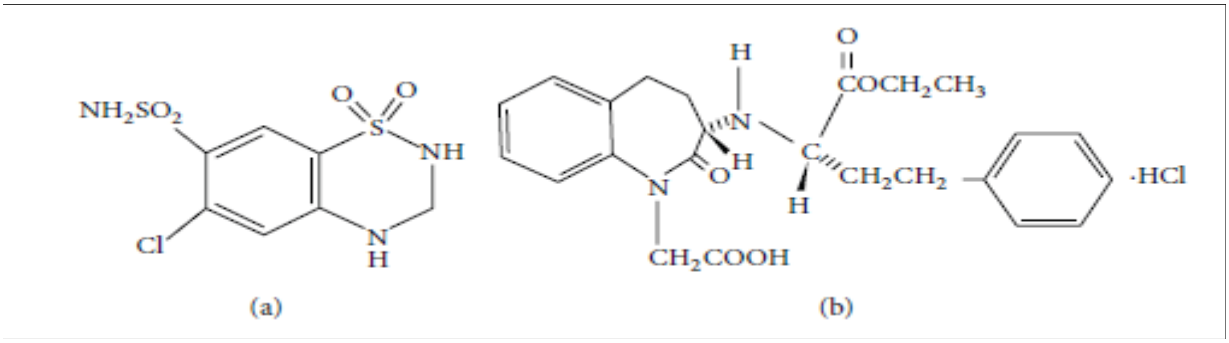


Figure 1: *Chemical structure of (b) HCT and, (a) BEN.*

Formulation of Solutions:

Precisely 100 mg of HCT, and BEN standards were separately shifted to individual 100.0 mL V.F. These substances were liquified in 50 mL of methanol. After thorough shaking, the capacity was adjusted to the spot using CH_3OH, resulting in solutions encompassing 1mg/mL of both HCT, and BEN, respectively.

Procedure:

Investigative wavelengths were determined through separately dissolving unadulterated samples of HCT, and BEN in CH_3OH to produce solutions of 0.0010 mg/mL each. These solutions remained scanned within the wavelength series of 200nm to 400nm. Based on the overlaid spectra shown Fig 2, wavelengths of 270 nm, and 240 nm remained selected for developing concurrent equations.

To construct calibration curves, different concentrations ranging from "04–14.0 µg/mL for HCT, and 02–12.0 µg/mL for BEN" were arranged after their respective standard solutions. Standardization curves remained designed at 270 nm and 240 nm. The absorptivities (1 cm, and A1%) for mutually drugs at these wavelengths remained established as the average values derived from 5 autonomous determinations.

Conc. within the model were considered by means of the subsequent calculations:

$$C_x = \frac{A_1 ay_2 - A_2 ay_1}{ax_1 ay_2 - ax_2 ay_1}$$

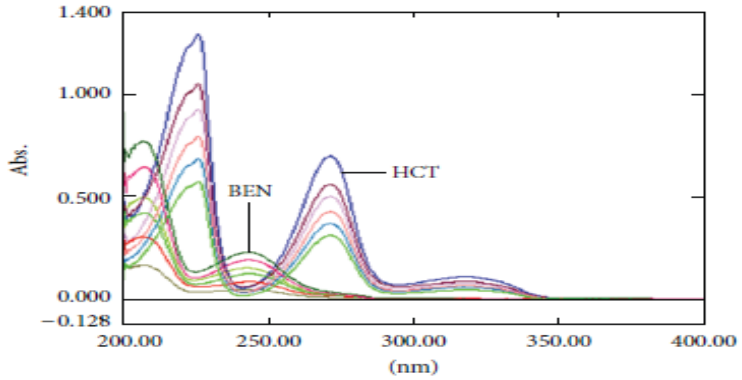
$$C_y = \frac{A_1 ax_2 - A_2 ax_1}{ay_1 ax_2 - ay_2 ax_1},$$

"In the equations:
- A 1 and A 2 represent the absorbance of mixtures at 240 nm and 270 nm, respectively.
- ax 1 and ax 2 denote the absorptivities of BEN at λ 1 and λ 2, respectively.
- ay 1 and ay 2 stand for the absorptivities of HCT at λ 1 and λ 2, respectively.
- $C\ x$ and $C\ y$ represent the concentrations of BEN and HCT, respectively.

The proposed method underwent validation following the guidelines outlined by the International Conference on Harmonization (ICH)."

Linear Relationship and Measurement Range:
The investigative technique established demonstrates a linear response across the concentration range of '0.4 to 14.0 µg/mL for HCT at 270 nm, and 0.2 to 12.0 µg/mL for BEN at 240 nm.'

Precision:
In instruction to evaluate the precision of the anticipated concurrent equation spectrophotometric technique, intraday and interday precision studies were conducted. This involved approximating replies 3 times within a 24 hrs., and across 3 different days (labeled as the 1, second, and 3 days). The concentrations of HCT (08, 10.0, 12.0 µg/mL), and BEN (06, 08, and 10.0 µg/mL) were used for these evaluations. The consequences, expressed in standings of %RSD, were recorded to determine the consistency and reliability of the method.[5, 7.]



***"Figure 2:** Superimposed spectrum of HCT, and BEN in methanol."*

***Table 1:** outline of justification limitations:*

Sr. No.	Limitations	HCT	BEN
1.	LOD	0.025	0.102
2.	LOQ	0.075	0.312
3.	Accuracy (%)	99.8 to 100.20	100.0 to 1005
4.	Precision		
	Intraday (n=3)	0.13 to 0.23 %	0.47 to 0.73 %
	Interday (n=3)	0.18 to 0.41 %	0.31 to 0.80 %
5.	Repeatability (RSD, n=6)	01.96 %	01.33 %
6.	Robustness	Robust	Robust
7.	Specificity	Robust Specific	Specific
8.	System suitability	Appropriate for 1day	Appropriate for 1day

***Table 2:** Arithmetical data of HCT, and BEN:*

Sr. No.	Parameters	HCT at 270 nm	BEN at 240 nm
1.	Linear range	04-14.0 µg/mL	02-12.0 µg/mL
2.	Slope	0.05	0.0180
3.	Intercept	0.034	0.0128
4.	SD Intercept	0.0010	0.0030
5.	SD Slope	0.0018	0.0005
6.	Coefficient of Regression (R^2)	0.9997	0.9998

***Table 3:** 'Approximation of precision for BEN':*

BEN	Conc. µg/mL	Intraday Mean ± SD (n=3)	% RSD	Intraday Mean ± SD (n=3)	% RSD
At 240 nm	6	0.12268 ± 0.00057	0.46	0.124 ± 0.001	0.81
	8	0.15533 ± 0.00116	0.73	0.15533 ± 0.00058	0.37
	10	0.197 ± 0.001	0.51	0.19533 ± 0.00057	0.31
At 270 nm	6	0.03068 ± 0.00059	1.88	0.03068 ± 0.00059	1.88
	8	0.36334 ± 0.00059	1.58	0.03668 ± 0.00059	1.58
	10	0.04368 ± 0.00059	1.33	0.04767 ± 0.00059	1.21

***Table 4:** 'Approximation of precision for HCT':*

BEN	Conc. µg/mL	Interday Mean ± SD (n=3)	% RSD	Intraday Mean ± SD (n=3)	% RSD
At 240 nm	6	0.03433 ± 0.00078	1.69	0.03466 ± 0.00059	0.017
	8	0.04267 ± 0.00059	1.36	0.043 ± 0.001	0.024
	10	0.05433 ± 0.00057	1.08	0.218 ± 0.28233	0.18
At 270 nm	6	0.44467 ± 0.00154	0.32	0.44334 ± 0.00059	0.13
	8	0.52567 ± 0.00207	0.42	0.527 ± 0.001	0.19
	10	0.63333 ± 0.00114	0.19	0.63368 ± 0.00154	0.24

Accuracy:
To assess the accuracy of the technique, standard additions remained employed. Known quantities of HCT (also at 50 percent, 100 percent, and 150 percent), and BEN (at 50 percent, 100 percent, and 150 percent) remained additional to pre-quantified trial solutions. The quantities of HCT, and BEN remained then assessed through determining the responses by the suitable wavelengths. The repossession remained confirmed through conducting estimations of the medications in triplicate measures at individually quantified attentiveness level.

Detection Limit and Quantitation Limit:
The standardization curve was replicated five times, and from these repetitions, the SD of the interrupts remained computed. Subsequently, the determination of the LOQ, and LOD was performed using the following method:

$$LOD = 3.3 \times \frac{\sigma}{S},$$

$$LOQ = 10 \times \frac{\sigma}{S},$$

Where σ represents the SD of the 'y-intercept, and S signifies' the angle of the standardization curve.

Resolution Stability:
The method's solution stability remained investigated through monitoring the constancy of equally drug resolutions at a temperature of 25 ± 2°C for duration of 24 hours.

Investigation of Marketed Preparation:
20 tablets of 'Lotencin HCT', individually encompassing, 0.125 gram of HCT, and 0.0010 gram of BEN as per U.S.P. specifications, were utilized in this study. These tablets were evaluated, and excellently powdered. A precisely evaluated tablet powder corresponding to 0.0010 gram was transferred to a 100.0 mL V.F. A small quantity of CH_3OH remained supplementary, and the combination remained sonicated for 05 minutes. Afterward, the capacity was attuned to the spot using CH_3OH.
After this solution, an aliquot was withdrawn and additional diluted to attain a concluding conc. of 10.00 µg/mL for both HCT, and BEN. The absorbances at their individual wavelengths were recorded. Using the aforementioned methods, the

conc. of individually drug within the tablet formulation was resolute.[8, 9.]

Result, and Conversation:

A concurrent calculation spectrophotometric technique remained industrialized for the precise resolve of HCT, and BET from their collective dosage method. The technique exhibited strong linearity within the concentration ranges of, '04 to 14.0 µg/mL for HCT, and 02 to 12.0 µg/mL for BEN' boasting high correlation coefficients of 0.9987 for HCT, and 0.9998 for BEN (Table 2).

The %RSD standards were notably low, at 1.33% for BEN and 1.96% for HCT, indicating excellent repeatability. In the intraday and interday studies, % RSD values ranged from 0.13% to 0.80%, affirming precision (Tables 3 and 4).

Detection limits were measured at '0.025 µg/mL for HCT, and 0.102 µg/mL for BEN', with quantitation limits at 0.312 µg/mL for BEN and 0.075 µg/mL for HCT. These values indicate the technique's sensitivity in accurately determining nanogram quantities of both drugs.

Accuracy was assessed via the technique of standard additions, yielding recovery percentages between 100.1% and 100.5% for BEN and 100.0% and 100.1% for HCT (Table 5). The technique was successfully practical to determine HCT, and BEN in solid dosage forms, demonstrating consequences comparable to the labeled quantities (Table 6). Not at all interfering from excipients was observed, confirming the method's suitability for repetitive concurrent valuation of HCT, and BEN in pharmaceutical formulations.

Table 5: *Approximations of correctness:*

% level	Amount of drug added (µg/mL)		Recovered amount of drug (µg/mL)		% recovery	
	BEN (µg/mL)	HCT (µg/mL)	BEN (µg/mL)	HCT (µg/mL)	BEN	HCT
50	6	6	6.03	6.01	100.5	100.1
100	8	8	8.01	7.98	100.2	99.99
150	10	10	10.01	9.99	100.1	100.0

Table 6: *Assay consequences of promoted preparation:*

Formulation	Amount of drug added (µg/mL)		Recovered amount of drug (µg/mL)		% recovery	
	BEN (µg/mL)	HCT (µg/mL)	BEN (µg/mL)	HCT (µg/mL)	BEN	HCT
Tab.	4	5	3.93	4.96	98.28	99.30

Conclusions:

A novel, sensitive, and robust UV spectroscopic method has been innovated, thoroughly validated, and aligned with ICH guidelines. Offering precision, accuracy, and cost-effectiveness, this method enables simultaneous estimations of BEN and HCT, making it an ideal choice for routine analysis. The validation, covering "specificity, linearity, accuracy, precision, LOD, LOQ, and robustness, ensures its reliability."

This innovative method not only guarantees accurate assessments but also holds promise for serving as a pivotal tool in the QC evaluate of HCT, and BEN within medicinal dosage forms.

Acknowledgment:

"I am deeply grateful to Dr. R. D. Wagh, an esteemed professor at DCS's A. R. A. College of Pharmacy in Nagaon, Dhule, for his exceptional guidance and unwavering support, pivotal to the success of this venture. My heartfelt appreciation goes to DCS's A. R. A. College of Pharmacy in Nagaon, Dhule, for generously providing vital research facilities, unwavering encouragement,

and steadfast support throughout this rewarding journey."

"Conflict of Interest:"

"The author confirms the absence of conflicts of interest requiring disclosure."

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