A Method for Content Uniformity Determination of Atenolol and Losartan Potassium in Combined Tablet Dosage Form

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A simple, accurate, rapid, specific and reproducible UV spectrophotometric method was developed for estimation of content uniformity of atenolol and losartan potassium in its combined tablet dosage form. The method involves formation and solving the simultaneous equation using 226.4 and 254 nm as two wavelengths for atenolol and losartan, respectively. Developed method was employed to determine the atenolol and losartan content in ten individual tablet units of five market formulations. Methanol was used as solvent. The method was validated. From the results, it was concluded that all brands are within the content uniformity limit, 85-115%.

Key words: Atenolol, content uniformity, losartan potassium, simultaneous equation method

Atenolol (ATN), 4-[2-Hydroxy-3-[(1-methylethyl) amino]propoxy]phenylacetamide is a selective β_1-adrenoceptor antagonist applied in the treatment of numerous cardiovascular disorders such as hypertension and angina pectoris[1]. Several analytical methods reported for the quantitative determination of ATN individually in pharmaceutical formulations or in combination or in biological fluids, are HPLC[2,3], HPTLC[4], LC-MS-MS[5] and UV spectrophotometry[6].

Losartan potassium (LSR), a monopotassium salt of 2-butyl-4-chloro-1-[p-(o-1H-tetrazol-5-ylphenyl)benzyl] imidazole-5-methanol, represents the first of a new class of orally active non-peptide angiotensin II (Type AT_1) receptor antagonists employed in the management of essential hypertension[7]. Determination of LSR has been carried out by HPLC[8], UV spectrophotometry[9], HPTLC[10] and spectrofluorometry[11].

As it is established that content uniformity determination should be performed for the product to be tested contains 50 mg or less of active ingredient [12], this test is applied to ATN –LSR combination. The present study describes development and validation of a simple, accurate and precise simultaneous equation method for content uniformity determination of ATN and LSR in combination tablet.

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ATN and LSR were obtained as gift samples from Torrent Pharmaceutical Ltd., Ahmedabad, India. Methanol (A.R. grade) was purchased from Shraddha Chem., Vadodara, India. Five brands of ATN and LSR combination tablets (50-50 mg) (Repalol, Sun Pharma; Losar-Beta, Unichem Laboratories; Nusar-ATN, Emcure Pharmaceuticals; Angizaar-AT, Microlab Ltd.; and Covance, Emcure) were purchased from the local market. Analysis was performed on double beam UV/Vis spectrophotometer (Shimadzu, model 1700) having two matched quartz cells with 1 cm light path. For weighing, electronic analytical balance (Shimadzu AUX 220) was used. Sonicator (Sonica 2200 MH) and sintered glass filter (G_3) were also used.

Standard stock solutions of ATN and LSR (1000 µg/ml) were prepared by dissolving and diluting 25 mg of both the drugs in separate 25 ml volumetric flasks using methanol (standard stock solution) and were further diluted with methanol to obtain final concentration of 100 µg/ml (working standard solution). Sample solution was prepared by dissolving ten tablets individually in 30 ml of methanol by sonicating them for 15 min and diluting up to 50 ml with methanol. Solution was filtered using sintered glass filter (G_3). Filtrate was diluted to obtain 100 µg/ml which was further diluted to obtain 16 µg/ml solution.

For selection of analytical wavelength for simultaneous equation method, standard solutions of ATN (16 µg/ml) and LSR (16 µg/ml) were scanned in the UV range. fig. 1 represents the overlain spectrum of both drugs. Wavelengths 226.4 and 254 nm i.e.the λ_{max} of ATN and LSR respectively, were selected for formation of the simultaneous equations.

Working standard solutions (100 µg/ml) of both the drugs were diluted to prepare solutions having the concentration 8, 12, 16, 20 and 24 µg/ml of ATN and LSR. All solutions were measured at both the wavelengths and four calibration curves (ATN and LSR at 226.4 and 254 nm) were plotted. Absorptivities at each wavelength for ATN and LSR were determined and used to form the equation. The absorbance and absorptivity values at particular wavelengths were substituted in the following Eqns to obtain concentration. $C_{ATN}=(A_2a_{Y1}-A_1a_{Y2}) / (a_{X2}a_{Y1}-a_{X1}a_{Y2})\ldots 1$; $C_{LSR}= (A_1a_{X2}-A_2a_{X1})/(a_{X2}a_{Y1}-a_{X1}a_{Y2})\ldots 2$, where, C_{ATN} and C_{LSR} are the concentration of ATN and LSR respectively, A_1 is absorbance of sample at 254 nm, A_2 is absorbance of sample at 226.4 nm, a_{X1} is the absorptivity of ATN at 254 and a_{X2} is the absorptivity of ATN 226.4 nm, a_{Y1} the absorptivity of LSR at 254 and a_{Y2} is the absorptivity of LSR at 226.4 nm.

Linearity was obtained in the range of 8-24 µg/ml for both the drugs. The developed method was validated by determining accuracy, precision, and repeatability. For determination of intraday precision, solutions containing ATN and LSR in the range of 8-24 µg/ml were analyzed 5 times on the same day and % CV was calculated. For interday precision, same range was analyzed on 5 different days and % CV was calculated. Repeatability was determined by analyzing three concentrations of the calibration curve, prepared in triplicate and % CV was calculated. Accuracy of analysis was determined by calculating percentage recovery of combination of ATN and LSR by standard addition method. To a fixed amount of sample solution, increasing aliquots of mixture of standard stock solution (0.4, 0.8 and 1.2 ml) was spiked and diluted to 10 ml with methanol. The solutions were measured at 226.4 nm and 254 nm and % recovery of ATN and LSR was calculated.

Absorptivity of ATN at 254 nm (a_{X1}) and at 226.4 nm (a_{X2}) was found to be 21 and 413 respectively. Absorptivity of LSR at 254 nm (a_{Y1}) and at 226.4 nm (a_{Y2}) was 321 and 620 respectively. Validation parameter of proposed method is summarized in Table 1. The developed simultaneous equation method is simple, precise and accurate. It was applied for content uniformity determination of ATN and LSR in its tablet dosage form.

Five different brands of ATN and LSR combination were analysed for their content uniformity. Content of individual tablet unit (10 replicates) for all formulations were calculated using formulated equations. None of the results fall outside the prescribed range i.e. 85–115 %[13]. The results for all five brands complied with pharmacopoeial requirements. The corresponding data along with % content of both the drugs for each formulation are given in Table 2. The method can be used for routine quality control of dosage form in industry.

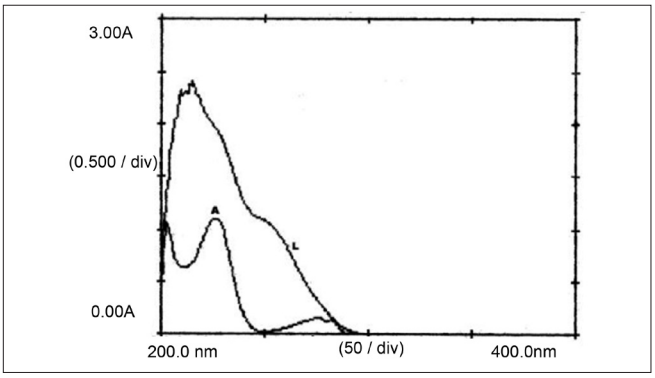

Fig. 1: Overlain spectra of atenolol and losartan potassium
A is atenolol spectrum and L is losartan spectrum

TABLE 1: VALIDATION PARAMETERS FOR ATN AND LSR ESTIMATION

Parameter	Results of ATN		Results of LSR	
	226.4 nm	254 nm	226.4 nm	254 nm
Correlation coefficient, r	0.9980	0.9998	0.9999	0.9999
	226.4 nm		254 nm	
Linearity range (µg/ml)	8-24		8-24	
Precision				
Repeatability (n=3)(% CV)	0.49-1.23		0.88-2.11	
Intraday (n=5) (% CV)	0.93-1.94		0.67-1.24	
Interday (n=5) (% CV)	1.04-2.52		1.79-2.92	
Mean % Recovery	100.53-101.67		101.33-102.00	

TABLE 2: PERCENTAGE CONTENT OF ATN AND LSR IN DIFFERENT BRAND FORMULATIONS

Tablet no.	A		B		C		D		E	
	ATN	LSR	ATN	LSR	ATN	LSR	ATN	LSR	ATN	LSR
1	89.88	92.44	92.25	94.69	92.19	91.88	103.31	101.25	91.56	93.06
2	90.50	92.38	98.81	98.44	92.69	100.19	101.13	98.06	93.06	92.81
3	91.38	95.63	100.19	95.38	90.75	96.63	105.50	103.25	93.63	85.56
4	89.13	94.19	111.00	110.88	93.25	89.69	103.56	108.25	94.94	87.63
5	89.13	94.38	96.06	95.69	92.50	92.00	99.44	100.38	90.69	95.44
6	90.19	92.56	100.25	97.94	93.75	90.38	103.44	100.50	91.00	100.50
7	89.88	93.38	100.00	98.75	89.75	96.13	106.06	101.88	90.88	89.44
8	92.56	92.56	95.50	94.44	91.88	93.00	101.44	102.94	89.88	96.50
9	90.38	95.25	97.13	96.19	90.38	96.06	103.94	105.50	91.69	89.19
10	92.19	92.24	97.81	96.75	90.25	95.88	99.75	100.69	89.06	99.44
Average*	90.52	93.50	98.90	97.92	91.74	94.18	102.76	102.27	91.64	92.96
SD*	1.18	1.27	4.94	4.79	1.38	3.31	2.25	2.90	1.78	5.03
% CV*	1.30	1.36	4.99	4.89	1.50	3.51	2.19	2.84	1.94	5.41

*n=10; SD – Standard deviation; CV – Coefficient of variation

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