Spectrophotometric Simultaneous Determination of Atorvastatin-Amlodipin and Telmisartan-Hidrochlorothiazide Mixtures by Bivariate and Multivariate Calibrations

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*The bivariate and multivariate spectral calibrations were proposed for the simultaneous quantitative analysis of two different mixtures containing atorvastatin-amlodipine and telmisartan- hydrochlorothiazide combinations in tablets. These methods do not require any separation step of the related compounds in the same mixtures. In the first case, the bivariate spectral calibration (**BC**) was obtained by using four linear regression functions with two single-component regressions for each compound at the two-wavelength sets 218, 260 nm for **ATO-AML** mixture and 224, 236 nm for **TEL-HCT** mixture. In the second case, the multivariate spectral calibration (**MC**) was performed by the simultaneous use of 26 linear regression equations with 26 single-component regression for each compound at a 26-wavelength set from 218 nm to 268 nm with the intervals of $\Delta\lambda$=2 nm for **ATO-AML** mixture and at a 26-wavelength set from 220 nm to 320 nm with the intervals of $\Delta\lambda$=4 nm for **TEL-HCT** mixture. All the methods were validated by analysing the synthetic mixture of two active compounds and by using standard addition technique. The obtained results were successfully compared with each other and both methods were successfully applied to the quantitative evaluation of two different mixtures consisting of **ATO-AML** and **TEL-HCT**.*

Keywords: bivariate and multivariate calibrations; linear regression function; atorvastatin-amlodipine and telmisartan-hydrochlorothiazide tablets

The combination of many active compounds in the same commercial preparation has been used in order to increase pharmacologic activity. The manuscript deals with the tables containing the **ATO-AML** and the **TEL-HCT** combinations. The quality control of the combined pharmaceutical preparations is very important for the pharmaceutical industry and for the human health by using a simple simultaneous analysis method.

As it is known several patients with hypertension require two or more antihypertensive drugs with complementary mechanisms of action to lower their blood pressure. The determination of **ATO** alone and with other active compounds and their metabolites in samples has been performed by HPLC [1-5], spectrophotometric methods [6,7] and **PLS** and **PCR** calibrations [8].

The angiotensin II type 1-receptor antagonist telmisartan and the diuretic hydrochlorothiazide are two antihypertensive agents that have a well-recognized clinical efficacy. Their combination was shown in randomized, controlled trials to be more effective than each agent alone in lowering blood pressure, due to a dual and synergistic mechanism.

The determination of **TEL** in samples was performed by spectrophotometry [9-10], **HPLC** [11-13] and Capillary electrophoresis [14].

It was developed the bivariate calibration method for the resolution of two-component mixtures by spectrophotometry [15-16]. This method is based on the use of the four linear regression calibration equations with two calibrations for each component at two wavelengths selected. The multivariate calibration method based on the multiply-linear regression function was developed for the multiresolution of two-component mixtures and multi-component mixtures [17].

The aim of this work is to present a new, rapid,simple and low cost analytical method for the simultaneous quantitative analysis of **ATO-AML** and **TEL-HCT** tablets without using any separation and graphical procedure. The validity and applicability of both methods were carried out by analysing various synthetic mixtures containing the **ATO-AML** and the **TEL-HCT** combinations and by using the standard addition techniques.

The proposed bivariate and multivariate calibration methods were also applied to two different commercial tablets.

Experimental part

Instruments

In this manuscript a Shimadzu UV-160 double beam UV–VIS spectrophotometer with a fixed slit width (2 nm) was used for the registration of the absorption spectra. This apparatus was connected to a computer loaded with Shimadzu UVPC software and a HP Laser Jet P1005 printer. Microsoft Excel and in Matlab 7.0 was used for calibrations and data process.

Commercial tablet dosage forms

Two different commercial tablet formulations Caduet® Tablets (I) (Pfizer Pharm. Ind., Godecke,Freiburg, Germany) and PRITOR PLUS® Tablet (II) (produced by Glaxo Smith Kline Ind.Pharm.) was marketed in different dosage forms. Commercial tablet formulations (I) and (II) contain 10 mg **ATO** and 10 mg **AML** per tablet and 80 mg **TEL** and 12.5 mg **HCT** per tablet, respectively.

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Standard and calibration solutions

For the analysis of **ATO** and **AML** combination, stock solutions of the active compounds were separately prepared dissolving 50 mg in 100-calibrated flask mL in methanol. Standard series for each compound were prepared between 4.0 - 20.0 μg/mL by using the above stock solutions. A validation set of 20 mixture solutions in the concentration range of 4.0 - 20.0 μg/mL for both compounds was prepared from the prepared stock solutions. In the standard addition assay, the sample solution by adding three concentration levels (4.0, 12.0, 16.0 for both **ATO** and **AML**) to tablet solution were prepared to observe the effect of excipients on the analysis.

Stock solutions for **TEL** and **HCT** were separately prepared dissolving 25 mg of **TEL** and **HCT** in 100-calibrated flask ml within methanol. Calibration solutions of **TEL** and **HCT** in 2.0-14.0μg/mL and 1.0-9.0 μg/mL, respectively were separately prepared from the above stock solutions. For the validation of the proposed calibration methods, an independent set containing the different mixtures of **TEL** and **HCT** in the concentration range of 2.0-14.0 μg/mL and 1.0-9.0μg/mL, respectively was prepared by using the prepared stock solutions.

As mentioned before, for the standard addition procedure, the sample solutions obtained by adding three concentration levels 2.5, 5.0, 7.5 μg/mL for **TEL** and 2.0, 6.0, 9.0 μg/mL for **HCT** to tablet solutions were prepared to observe the effect of excipients on the analysis.

Tablet analysis procedure

In the quantitative analysis of the dosage forms, 20 tablets were accurately weighed and powdered in a mortar. An amount equivalent to one tablet for (I) and (II) was dissolved in methanol in a 100 mL calibrated flask by sonication. The solution was filtered into a 100 mL calibrated flask by using through a membrane filter. This procedure was carried out for Caduet® Tablets (I) and PRITOR PLUS® Tablet (II). Tablet solutions (I) and (II) were diluted to the working calibration ranges, respectively. The proposed methods were successfully applied to the analysis of two pharmaceutical tablet formulations.

Results and discussions

In this study two simple, rapid,reliable and cheap bivariate and multivariate calibration approaches based on the use of the linear regression functions were proposed for the simultaneous quantitative analysis of two different mixtures containing **ATO-AML** and **TEL-HCT** combinations without the use of any separation procedure.

For **ATO-AML** mixture analysis, the UV spectra of the related compounds in the concentration range 4.0- 20.0 μg/mL were recorded between 210-310 nm and the same registration procedure was used for the samples. Figure 1 shows the spectra of calibration series of compounds and their tablet sample.

The UV spectra of **TEL** and **HCT** in the concentration range of 2- 14 μg/mL for **TEL** and 1- 9 μg/mL for **HCT** were recorded in the range of 200-350 nm and the same registration procedure was used for the samples. Figure 2 depicts the spectra of calibration series of compounds together with their tablet sample.

By inspection we observe that we cannot determine simultaneously the above mentioned compounds in their mixtures due to the overlapping spectra by using the traditional methodological approaches. To overcome the above mentioned drawbacks related to the simultaneous evaluation of **ATO-AML** and **TEL-HCT** combinations, the bivariate and multivariate calibrations having simple

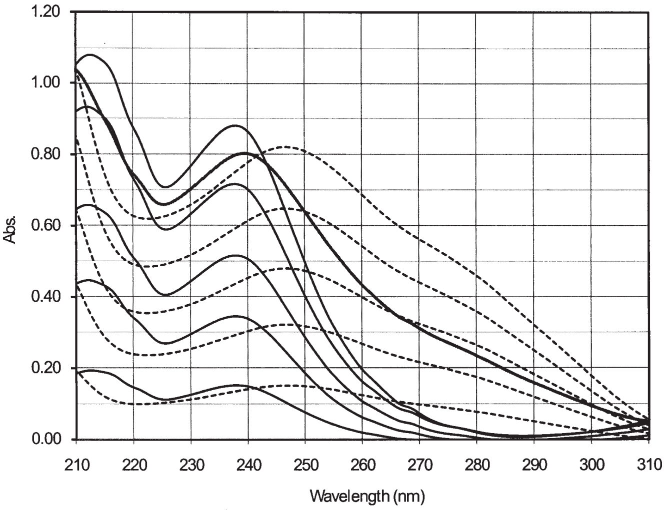

Fig. 1. Absorption spectra of ATO (- - - -) and AML (-+-+-) in the concentration range of 4- 20 μg/ and ATO-AML mixture (–) mL in the methanol

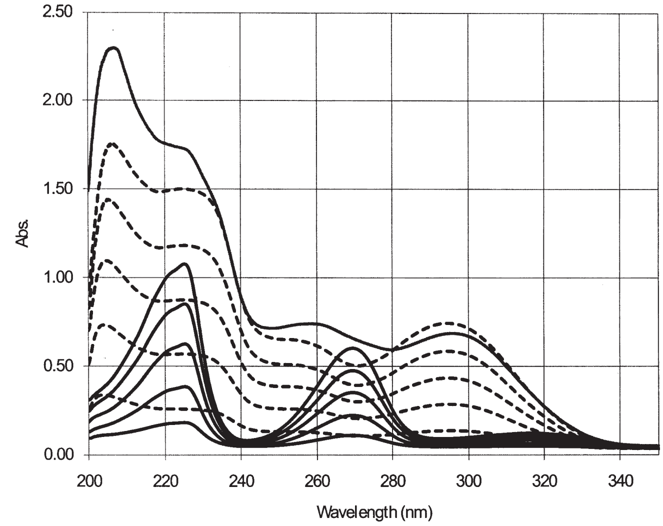

Fig. 2. Absorption spectra of TEL (- - - -) and HCT (-+-+-) in the concentration range of 2- 14 μg/mL for TEL and 1- 9 μg/mL for HCT and TEL-HCT mixture (–) mL in the methanol

application and mathematical algorithm were improved in the overlapping spectral conditions of compounds in the same binary mixtures.

Bivariate spectral calibration method

In this paper 26 wavelength were considered for the binary mixture analysis. The 26 linear regression functions were obtained by using the measurements of the absorbances at 26 wavelengths against the concentrations of standard solution for each compound (table 1). The highest values for the regression coefficients (r) for **ATO-AML** and **TEL-HCT** were obtained for all regression equations. The detection limit (LOD) (signal to noise ratio 3:1) and the quantitation limit (LOQ) (signal to noise ratio 10:1) were computed by using the standard deviation of intercept and slope of the linear regression functions.

In the quantitative spectral evaluation of **ATO** and **TEL** in the linear concentration range of 4.0-24.0 μg/mL, the statistical results and the calibration parameters obtained by the linear regression analysis were shown in table 1 and 2, respectively.

The slope values obtained from the linear regression analysis for each compounds each in the binary mixture of **ATO-AML** and **TEL-HCT** combinations were used to create the sensitivity matrices (table3 and table 4). According to Kaiser's technique [18], the absolute values

Table 1
STATISTICAL RESULTS AT 26 WAVELENGTHS OBTAINED BY LINEAR REGRESSION ANALYSIS FOR **ATO-AML** MIXTURE

	ATO								AML							
λ (nm)	m	n	R	SE(m)	SE(n)	SE(r)	LOD	LOQ	m	n	r	SE(m)	SE(n)	SE(r)	LOD	LOQ
218	0.0341	-0.0320	0.9998	0.0003	0.0046	0.0044	1.15	3.84	0.0492	-0.0266	0.9999	0.0004	0.0056	0.0053	0.96	3.21
220	0.0328	-0.0308	0.9998	0.0003	0.0046	0.0044	1.18	3.95	0.0457	-0.0360	0.9999	0.0003	0.0040	0.0038	0.75	2.49
222	0.0323	-0.0291	0.9998	0.0003	0.0044	0.0042	1.17	3.89	0.0417	-0.0318	0.9998	0.0004	0.0057	0.0054	1.16	3.87
224	0.0323	-0.0277	0.9999	0.0003	0.0042	0.0040	1.11	3.71	0.0379	-0.0332	0.9998	0.0004	0.0053	0.0051	1.20	3.99
226	0.0326	-0.0264	0.9999	0.0003	0.0042	0.0040	1.10	3.68	0.0371	-0.0332	0.9998	0.0004	0.0052	0.0050	1.20	4.00
228	0.0332	-0.0251	0.9999	0.0003	0.0042	0.0040	1.07	3.55	0.0380	-0.0313	0.9998	0.0004	0.0053	0.0051	1.18	3.95
230	0.0340	-0.0245	0.9999	0.0003	0.0040	0.0038	0.99	3.29	0.0399	-0.0304	0.9998	0.0004	0.0053	0.0051	1.13	3.78
232	0.0350	-0.0231	0.9999	0.0003	0.0039	0.0037	0.94	3.13	0.0418	-0.0285	0.9999	0.0004	0.0054	0.0052	1.10	3.67
234	0.0361	-0.0213	0.9999	0.0003	0.0039	0.0037	0.92	3.05	0.0434	-0.0259	0.9999	0.0004	0.0056	0.0054	1.10	3.68
236	0.0374	-0.0209	0.9999	0.0003	0.0037	0.0035	0.85	2.82	0.0449	-0.0253	0.9999	0.0004	0.0057	0.0055	1.09	3.62
238	0.0386	-0.0199	0.9999	0.0003	0.0036	0.0034	0.78	2.62	0.0452	-0.0239	0.9999	0.0004	0.0057	0.0054	1.07	3.56
240	0.0397	-0.0191	0.9999	0.0003	0.0037	0.0035	0.78	2.60	0.0444	-0.0245	0.9999	0.0004	0.0052	0.0050	1.00	3.32
242	0.0408	-0.0184	0.9999	0.0003	0.0036	0.0034	0.74	2.47	0.0422	-0.0255	0.9999	0.0004	0.0051	0.0049	1.03	3.43
244	0.0415	-0.0181	0.9999	0.0003	0.0036	0.0034	0.73	2.43	0.0386	-0.0257	0.9999	0.0004	0.0050	0.0047	1.09	3.63
246	0.0418	-0.0177	0.9999	0.0003	0.0036	0.0034	0.72	2.41	0.0347	-0.0268	0.9999	0.0003	0.0042	0.0040	1.04	3.45
248	0.0417	-0.0175	0.9999	0.0003	0.0035	0.0033	0.70	2.34	0.0304	-0.0275	0.9999	0.0003	0.0035	0.0033	0.97	3.25
250	0.0412	-0.0171	0.9999	0.0003	0.0036	0.0034	0.73	2.45	0.0261	-0.0271	0.9999	0.0002	0.0028	0.0027	0.92	3.07
252	0.0404	-0.0170	0.9999	0.0003	0.0035	0.0033	0.73	2.44	0.0223	-0.0271	1.0000	0.0001	0.0017	0.0016	0.65	2.15
254	0.0393	-0.0172	0.9999	0.0003	0.0035	0.0033	0.75	2.51	0.0187	-0.0268	1.0000	0.0001	0.0013	0.0013	0.60	2.00
256	0.0380	-0.0159	0.9999	0.0040	0.0040	0.0038	0.90	2.99	0.0157	-0.0266	0.9999	0.0007	0.0007	0.0006	0.35	1.17
258	0.0366	-0.0181	0.9999	0.0003	0.0034	0.0032	0.78	2.60	0.0132	-0.0265	0.9997	0.0004	0.0004	0.0004	0.26	0.85
260	0.0352	-0.0182	0.9999	0.0003	0.0035	0.0033	0.83	2.78	0.0110	-0.0259	0.9996	0.0003	0.0003	0.0003	0.21	0.72
262	0.0337	-0.0185	0.9999	0.0003	0.0035	0.0034	0.89	2.96	0.0095	-0.0256	0.9999	0.0004	0.0004	0.0004	0.36	1.20
264	0.0323	-0.0187	0.9999	0.0003	0.0035	0.0033	0.92	3.07	0.0079	-0.0250	0.9994	0.0009	0.0009	0.0008	0.93	3.09
266	0.0310	-0.0189	0.9999	0.0003	0.0037	0.0035	1.01	3.35	0.0065	-0.0245	0.9998	0.0010	0.0010	0.0009	1.25	4.18
268	0.0299	-0.0192	0.9999	0.0003	0.0037	0.0035	1.05	3.48	0.0058	-0.0244	0.9999	0.0006	0.0006	0.0005	0.83	2.77

C = concentration (μg/mL) , A = Absorbance values at selected wavelength for BE and HCT, r = Regression coefficient, Sr = Standard deviation of linear regression, S(b) = Standard deviation of slope, S(a) = Standard deviation of intercept, LOD = Limit of detection, LOQ = Limit of quantification

of the determinant of the sensitivity matrices were calculated to reach the best sensitivity for the application of **BC** method. As a result it was possible to calculate the different 325 pairs of the sensitivity matrices for the selection of optimum two-wavelength set. By using the absolute values of determinants of sensitivity matrices, the application results of Kaiser's method to the selection of

Table 2

STATISTICAL RESULTS AT 26 WAVELENGTHS OBTAINED BY LINEAR REGRESSION ANALYSIS FOR **TEL-HCT** MIXTURE

	TEL								HCT							
λ (nm)	m1	n1	r	SE(m)	SE(n)	SE(r)	LOD	LOQ	m2	n2	r	SE(m)	SE(n)	SE(r)	LOD	LOQ
220	0.1019	0.0552	1.0000	0.0038	0.0038	0.0040	0.32	1.06	0.1031	0.0604	1.0000	0.0026	0.0026	0.0029	0.22	0.72
224	0.1031	0.0526	1.0000	0.0036	0.0036	0.0038	0.29	0.98	0.1118	0.0585	1.0000	0.0025	0.0025	0.0027	0.19	0.63
228	0.1025	0.0513	1.0000	0.0030	0.0030	0.0031	0.25	0.83	0.0896	0.0805	1.0000	0.0029	0.0029	0.0032	0.28	0.92
232	0.0988	0.0496	1.0000	0.0039	0.0039	0.0041	0.34	1.12	0.0360	0.0464	1.0000	0.0009	0.0009	0.0010	0.22	0.73
236	0.0847	0.0470	1.0000	0.0040	0.0040	0.0042	0.40	1.34	0.0121	0.0391	1.0000	0.0004	0.0004	0.0004	0.27	0.90
240	0.0606	0.0441	0.9999	0.0037	0.0037	0.0039	0.53	1.75	0.0052	0.0393	1.0000	0.0001	0.0001	0.0002	0.24	0.81
244	0.0470	0.0440	0.9999	0.0033	0.0033	0.0038	0.60	1.99	0.0061	0.0342	0.9999	0.0002	0.0002	0.0002	0.28	0.95
248	0.0435	0.0455	0.9999	0.0029	0.0029	0.0040	0.57	1.89	0.0092	0.0336	1.0000	0.0003	0.0003	0.0003	0.26	0.86
252	0.0428	0.0463	0.9998	0.0029	0.0029	0.0042	0.58	1.92	0.0160	0.0315	1.0000	0.0005	0.0005	0.0006	0.28	0.93
256	0.0422	0.0469	0.9998	0.0029	0.0029	0.0042	0.58	1.94	0.0252	0.0391	0.9999	0.0010	0.0010	0.0011	0.32	1.08
260	0.0403	0.0462	0.9998	0.0025	0.0025	0.0048	0.52	1.73	0.0381	0.0412	0.9999	0.0014	0.0014	0.0015	0.30	1.00
264	0.0367	0.0467	0.9998	0.0024	0.0024	0.0044	0.56	1.86	0.0503	0.0481	1.0000	0.0011	0.0011	0.0012	0.19	0.62
268	0.0332	0.0445	0.9997	0.0025	0.0025	0.0045	0.65	2.15	0.0608	0.0434	0.9999	0.0021	0.0021	0.0023	0.29	0.96
272	0.0327	0.0425	0.9997	0.0024	0.0024	0.0044	0.62	2.05	0.0596	0.0403	1.0000	0.0009	0.0009	0.0010	0.13	0.43
276	0.0350	0.0394	0.9998	0.0024	0.0024	0.0035	0.59	1.97	0.0427	0.0501	1.0000	0.0010	0.0010	0.0011	0.20	0.65
280	0.0390	0.0371	0.9999	0.0028	0.0028	0.0032	0.61	2.03	0.0247	0.0362	0.9999	0.0010	0.0010	0.0011	0.35	1.18
284	0.0437	0.0362	0.9999	0.0026	0.0026	0.0028	0.51	1.70	0.0124	0.0327	1.0000	0.0003	0.0003	0.0003	0.20	0.66
288	0.0475	0.0354	1.0000	0.0024	0.0024	0.0025	0.43	1.42	0.0074	0.0339	1.0000	0.0002	0.0002	0.0002	0.18	0.60
292	0.0497	0.0361	1.0000	0.0023	0.0023	0.0024	0.39	1.31	0.0064	0.0354	1.0000	0.0002	0.0002	0.0002	0.24	0.82
296	0.0500	0.0369	1.0000	0.0023	0.0023	0.0024	0.39	1.29	0.0067	0.0330	0.9999	0.0003	0.0003	0.0003	0.35	1.15
300	0.0481	0.0376	1.0000	0.0018	0.0018	0.0019	0.31	1.04	0.0066	0.0368	1.0000	0.0002	0.0002	0.0002	0.28	0.92
304	0.0437	0.0387	1.0000	0.0018	0.0018	0.0019	0.35	1.17	0.0075	0.0354	1.0000	0.0000	0.0000	0.0000	0.04	0.12
308	0.0375	0.0377	0.9999	0.0025	0.0025	0.0026	0.56	1.88	0.0085	0.0346	0.9999	0.0004	0.0004	0.0005	0.42	1.39
312	0.0303	0.0371	0.9999	0.0019	0.0019	0.0020	0.54	1.81	0.0099	0.0313	1.0000	0.0003	0.0003	0.0003	0.25	0.82
316	0.0230	0.0371	0.9999	0.0012	0.0012	0.0013	0.46	1.53	0.0096	0.0347	0.9999	0.0004	0.0004	0.0004	0.32	1.06
320	0.0167	0.0361	0.9998	0.0013	0.0013	0.0016	0.67	2.23	0.0095	0.0343	1.0000	0.0003	0.0003	0.0003	0.24	0.78

C = concentration (μg/mL) , A = Absorbance values at selected wavelength for BE and HCT, r = Regression coefficient, Sr = Standard deviation of linear regression, S(b) = Standard deviation of slope, S(a) = Standard deviation of intercept, LOD = Limit of detection, LOQ = Limit of quantification

Table 3

THE OBTAINED SENSITIVITY VALUES OF **ATO** AND **AML** USING SINGLE-COMPONENT REGRESSION ANALYSIS AT 26 WAVELENGTHS

No.	λ (nm)	ATO $Bx10^{-3}$	AML $Bx10^{-3}$
1	218	34.10	49.21
2	220	32.79	45.68
3	222	32.31	41.72
4	224	32.32	37.89
5	226	32.64	37.06
6	228	33.23	38.03
7	230	34.04	39.91
8	232	35.01	41.79
9	234	36.10	43.38
10	236	37.35	44.87
11	238	38.55	45.15
12	240	39.73	44.43
13	242	40.76	42.19
14	244	41.48	38.63
15	246	41.80	34.69
16	248	41.70	30.42
17	250	41.20	26.13
18	252	40.40	22.25
19	254	39.34	18.70
20	256	37.98	15.75
21	258	36.64	13.24
22	260	35.18	11.05
23	262	33.70	9.50
24	264	32.28	7.88
25	266	31.04	6.47
26	268	29.92	5.76

Table 4

THE OBTAINED SENSITIVITY VALUES OF **TEL** AND **HCT** USING SINGLE-COMPONENT REGRESSION ANALYSIS AT 26 WAVELENGTHS

No.	λ (nm)	TEL $Bx10^{-3}$	HCT $Bx10^{-3}$
1	220	101.90	103.05
2	224	103.10	111.75
3	228	102.53	89.55
4	232	98.80	36.05
5	236	84.70	12.09
6	240	60.57	5.20
7	244	47.00	6.06
8	248	43.53	9.25
9	252	42.77	16.00
10	256	42.17	25.20
11	260	40.30	38.15
12	264	36.73	50.33
13	268	33.23	60.80
14	272	32.67	59.56
15	276	35.00	42.66
16	280	38.97	24.69
17	284	43.70	12.35
18	288	47.50	7.36
19	292	49.73	6.40
20	296	49.97	6.75
21	300	48.10	6.65
22	304	43.73	7.52
23	308	37.53	8.54
24	312	30.27	9.85
25	316	23.03	9.58
26	320	16.73	9.51

(B_{TEL} and B_{HCT} denote the slopes of regression equation of TEL and HCT)

the wavelength set for **ATO-AML** and **TEL-HCT** combinations were depicted in tables 5 and 6.

An optimum two-wavelength set, which gives the highest determinant value of the sensitivity matrices, was selected as 218 and 260 nm for **ATO-AML** mixture and as 224 and 236 nm for **TEL-HCT** mixture by the **BC** calibrations.

At these selected two-wavelength set for both binary mixtures, the individual linear regression equations for each compound were separately illustrated in table 7. The following set of equations was created for the **BC** methods:

For the analysis of **ATO-AML** mixture;

$$\lambda_1 = 218.0 \text{ nm}; \quad A_{mix,\lambda 1} = 0.0341 x C_{ATO} + 0.0492 x C_{AML} - 0.0587$$

$$\lambda_2 = 260.0 \text{ nm}; \quad A_{mix,\lambda 2} = 0.0352 x C_{ATO} + 0.0110 x C_{AML} - 0.0441 \qquad (1)$$

Table 5

APPLICATION OF KAISER TECHNIQUE TO THE SELECTION OF THE WAVELENGTH SET FOR **ATO-AML** MIXTURES BY USING THE ABSOLUTE VALUES OF DETERMINANTS SENSITIVITY MATRICES (K . 10^{-3})

λ1/λ2	218	220	222	224	226	228	230	232	234	236	238	240	242	244	246	248	250	252	254	256	258	**260**	262	264	266	268
218	0.0	56.1	167.7	298.5	342.8	338.6	314.4	298.4	297.6	308.1	357.9	440.2	567.4	724.0	874.4	1014.8	1136.6	1229.2	1298.4	1332.3	1351.9	**1354.6**	1334.6	1320.1	1306.8	1276.1
220		0.0	108.1	233.8	275.9	270.9	246.3	229.4	226.7	234.8	280.7	357.9	478.5	627.9	772.0	907.2	1025.1	1115.5	1183.8	1218.7	1239.7	1244.7	1227.9	1216.3	1205.5	1177.8
222			0.0	123.9	164.3	157.5	130.5	110.6	104.5	108.3	149.5	221.7	337.2	482.1	623.0	756.5	874.4	966.1	1036.9	1075.7	1100.8	1110.5	1098.9	1092.1	1085.6	1062.0
224				0.0	39.2	30.1	0.0	-23.6	-34.0	-35.0	1.7	69.4	181.0	323.1	462.8	596.8	716.6	811.4	886.2	930.3	960.5	975.9	969.9	968.6	966.8	947.5
226					0.0	-9.9	-41.3	-66.3	-78.1	-80.6	-45.0	21.9	133.4	276.1	416.8	552.3	673.9	770.6	847.5	893.6	925.8	943.1	938.8	939.2	938.9	920.8
228						0.0	-31.7	-56.9	-68.5	-70.7	-34.1	34.4	148.1	293.6	437.0	574.9	698.5	796.7	874.7	921.2	953.5	970.7	965.9	965.9	965.2	946.4
230							0.0	-24.9	-35.8	-36.8	1.8	73.1	190.6	340.3	487.5	628.6	754.8	854.6	933.5	979.8	1011.7	1027.8	1021.5	1020.2	1018.3	998.0
232								0.0	-10.4	-10.5	30.0	104.3	225.9	380.4	532.0	677.1	806.6	908.7	989.0	1035.7	1067.5	1083.1	1075.5	1073.0	1070.2	1048.5
234									0.0	0.2	42.4	119.3	245.0	404.5	561.0	710.5	843.8	948.9	1031.4	1079.1	1111.5	1127.1	1118.9	1115.9	1112.6	1089.9
236										0.0	43.6	123.2	253.2	418.3	580.1	734.9	872.8	981.5	1066.9	1116.3	1149.8	1166.0	1157.4	1154.4	1151.0	1127.5
238											0.0	80.7	213.8	383.3	550.0	709.9	852.8	965.9	1055.3	1107.8	1144.0	1162.4	1155.3	1153.9	1151.8	1128.8
240												0.0	134.9	308.1	479.2	644.2	792.5	910.8	1005.1	1062.1	1102.2	1124.2	1120.0	1121.4	1121.9	1100.6
242													0.0	175.3	349.7	519.3	673.1	797.2	897.6	960.6	1006.3	1033.9	1034.6	1040.9	1045.6	1027.5
244														0.0	176.1	349.1	507.8	637.5	744.2	814.2	866.5	900.8	907.9	920.4	930.6	916.9
246															0.0	174.8	336.8	471.0	582.9	659.2	717.6	758.4	771.8	790.5	806.0	797.0
248																0.0	163.7	300.9	417.0	498.8	562.6	609.4	629.0	653.5	674.2	669.9
250																	0.0	138.7	257.6	343.7	412.0	464.0	489.2	519.0	544.3	544.4
252																		0.0	120.2	209.1	280.6	336.6	366.2	400.2	429.2	433.1
254																			0.0	90.7	164.3	223.1	256.4	293.7	325.6	332.8
256																				0.0	74.2	134.3	169.9	209.2	242.9	252.3
258																					0.0	60.9	98.1	138.7	173.7	185.0
260																						0.0	38.2	79.6	115.2	127.9
262																							0.0	41.2	76.7	90.1
264																								0.0	35.5	49.7
266																									0.0	14.9
268																										0.0

For the analysis of the **TEL-HCT** mixture;

$$\lambda_1 = 224.0\ \text{nm};\quad A_{mix,\lambda 1} = 0.1031xC_{TEL}+0.1118xC_{HCT}-0.1111$$
$$\lambda_2 = 236.0\ \text{nm};\quad A_{mix,\lambda 2} = 0.0847xC_{TEL}+0.0121xC_{HTC}-0.0861 \qquad (2)$$

The **BC** calibration procedure was achieved by using the linear algebra, also known as matrix mathematics [15-17]. The contents of **ATO-_AML** and **TEL-HCT** mixtures were determined by using the above calibration equations (1) and (2), respectively. The constructed calibration was

Table 6

APPLICATION OF KAISER'METHOD TO THE SELECTION OF THE WAVELENGTH SET FOR **TEL-HCT** MIXTURES BY USING THE ABSOLUTE VALUES OF DETERMINANTS SENSITIVITY MATRICES (K . 10^{-3})

λ_1/λ_2	220	224	228	232	**236**	240	244	248	252	256	260	264	268
220	0.0	-762.9	1440.6	6507.8	7496.4	5711.9	4225.8	3543.2	2777.0	1777.7	265.4	-1343.6	-2771.2
224		0.0	2225.1	7324.1	**8218.7**	6232.6	4627.5	3910.8	3129.9	2114.4	570.3	-1084.4	-2555.0
228			0.0	5151.3	6345.3	4890.9	3587.5	2949.7	2189.6	1192.6	-302.7	-1871.2	-3258.1
232				0.0	1858.9	1669.8	1095.6	655.4	-38.9	-969.5	-2316.4	-3648.5	-4809.1
236					0.0	291.9	54.9	-257.2	-838.1	-1624.6	-2744.1	-3818.9	-4748.0
240						0.0	-122.7	-333.9	-746.7	-1307.1	-2101.2	-2857.5	-3509.9
244							0.0	-171.0	-492.8	-928.9	-1548.8	-2142.9	-2656.2
248								0.0	-300.9	-706.9	-1287.9	-1851.1	-2339.2
252									0.0	-403.1	-986.9	-1564.9	-2068.7
256										0.0	-593.2	-1196.8	-1726.5
260											0.0	-627.1	-1182.5
264												0.0	-560.7
268													0.0

λ_1/λ_2	272	276	280	284	288	292	296	300	304	308	312	316	320
220	-2702.5	-740.3	1499.9	3244.8	4144.9	4472.5	4461.6	4279.1	3740.1	2997.2	2115.6	1397.0	755.
224	-2489.8	-487.0	1809.4	3610.2	4549.3	4897.5	4888.2	4689.6	4111.5	3313.5	2367.1	1585.9	889.
228	-3181.1	-1239.7	958.3	2647.1	3499.0	3797.1	3782.7	3625.5	3145.0	2485.2	1700.8	1080.1	523.
232	-4706.8	-2953.1	-1034.5	355.2	985.2	1160.4	1134.5	1077.0	833.5	509.2	118.1	-116.3	-336.
236	-4649.8	-3190.2	-1620.1	-517.7	-49.1	59.2	32.4	18.3	-108.3	-269.6	-468.3	-533.0	-603.
240	-3437.7	-2401.9	-1292.8	-520.8	-198.8	-129.1	-149.0	-152.7	-228.1	-322.1	-439.2	-460.5	-489.
244	-2601.3	-1792.9	-924.3	-315.6	-58.1	0.6	-14.4	-21.1	-88.4	-174.0	-279.5	-310.7	-345.
248	-2290.4	-1533.2	-714.3	-133.4	119.0	181.4	168.4	155.5	77.2	-24.6	-148.8	-204.0	-259.
252	-2024.7	-1264.6	-432.5	171.0	445.2	522.0	510.8	485.2	378.1	235.2	63.0	-41.3	-139.
256	-1688.4	-917.0	-59.1	580.4	886.6	983.3	974.6	931.7	784.9	585.6	347.4	176.4	20.6
260	-1153.9	-384.0	491.7	1169.5	1515.5	1639.3	1634.3	1567.0	1365.2	1087.6	757.9	492.5	255.
264	-543.4	194.7	1054.5	1745.8	2120.3	2267.8	2267.1	2176.6	1924.7	1575.2	1161.7	807.2	492.
268	7.2	710.4	1548.9	2246.6	2643.4	2810.9	2813.9	2703.5	2408.9	1998.0	1513.1	1081.9	701.
272	0.0	690.9	1514.4	2199.3	2588.6	2752.8	2755.7	2647.6	2358.9	1956.3	1481.1	1058.7	685.
276		0.0	798.3	1432.0	1768.8	1897.5	1895.5	1819.2	1602.3	1302.1	946.6	647.2	380.
280			0.0	597.7	886.0	978.4	970.7	928.4	786.6	593.8	363.5	195.3	42.5
284				0.0	265.0	334.5	322.2	303.4	211.4	90.3	-56.6	-134.2	-209.
288					0.0	62.0	47.2	38.1	-35.3	-129.4	-245.1	-285.6	-328.
292						0.0	-15.9	-22.9	-94.1	-184.5	-296.1	-329.0	-365.
296							0.0	-7.6	-80.6	-173.4	-287.9	-323.3	-362.
300								0.0	-70.9	-161.2	-272.5	-307.7	-346.
304									0.0	-91.2	-203.1	-245.8	-290.
308										0.0	-111.2	-162.9	-214.
312											0.0	-63.1	-123.
316												0.0	-58.7
320													0.0

applied to the analysis of the synthetic mixtures and two commercial tablet formulations.

Multivariate calibration method

This approach is analogous to the **BC** method, but the **MC** method contains *n*-wavelength procedure instead of two-wavelengths [18]. Therefore, the 26-wavelengths set (table 1 and table 2) at the critical points, which correspond to the maximum, shoulder and minimum in the spectral range 210-310 nm for **ATO-AML** combination and 200-350 nm for **TEL-HCT** mixture were selected for the construction of the individual linear regression for the related compounds in the binary mixtures. As indicated in Tables 1 and 2, the 26 linear regression equations of **ATO-AML** and **TEL-HCT**, for each active compound, were obtained by measuring the UV absorbance values at the wavelengths set.

Table 7
SINGLE-REGRESSION EQUATIONS USED FOR THE CONSTRUCTION OF THE BC METHOD AT TWO-WAVELENGTH SET

	ATO	AML
λ (nm)	*A = m x C + n*	*A = m x C + n*
218	A = 0.0341 *x* C -0.0320	A = 0.0492*x* C-0.0266
260	A = 0.0366*x* C-0.0181	A = 0.0132*x* C-0.0265
	TEL	**HCT**
λ (nm)	*A = m x C + n*	*A = m x C + n*
224	A = 0.1031 *x* C -0.0526	A = 0.1118*x* C-0.0585
236	A = 0.0847*x* C-0.0470	A = 0.0121*x* C-0.0391

Table 8
RECOVERY DATA OBTAINED FOR THE DETERMINATION OF **ATO** AND **AML** IN DIFFERENT SYNTHETIC MIXTURES BY USING THE DEVELOPED METHODS

ATO-AML mixture												
			BC		MC		BC		MC			
	Binary mix.		Found		Found		Recovery		Recovery			
	ATO	AML	ATO	AML	ATO	AML	ATO	AML	ATO	AML		
1	4	10	4.05	10.21	4.11	10.27	101.2	102.1	102.7	102.7		
2	8	10	8.07	10.33	8.19	10.21	100.9	103.3	102.3	102.1		
3	12	10	12.04	9.86	12.13	10.0	100.3	98.6	101.1	100.0		
4	16	10	16.04	9.7	16.03	9.85	100.2	97.0	100.2	98.5		
5	20	10	20.47	9.81	20.58	9.85	102.3	98.1	102.9	98.5		
6	10	4	10.37	4.1	10.18	4.1	103.7	102.5	101.8	102.5		
7	10	8	10.57	8.1	10.29	8.19	105.7	101.3	102.9	102.4		
8	10	12	10.61	11.93	10.15	11.97	106.1	99.4	101.5	99.8		
9	10	16	10.47	15.63	10.45	15.78	104.7	97.7	104.5	98.6		
10	10	20	10.48	19.08	10.45	19.48	104.8	95.4	104.5	97.4		
						Mean	103	99.5	102.4	100.2		
						SD	2.28	2.61	1.38	2		
						RSD	2.21	2.62	1.35	1.99		
TEL-HCT mixture												
			Found				Recovery					
	Binary mix.		BC		MC		BC		MC			
	TEL	HCT	TEL	HCT	TEL	HCT	TEL	HCT	TEL	TEL		
1	2	2	2.03	2.06	2.03	2.07	101.5	103.2	101.7	103.4		
2	5	2	5.05	2.05	5.01	2.04	101	102.3	100.1	101.9		
3	8	2	8.33	2.04	7.89	2.04	104.2	102.2	98.6	102.2		
4	11	2	11.07	2.03	11.31	2.02	100.7	101.6	102.9	100.9		
5	14	2	14.54	2.08	14.14	2.03	103.8	104.2	101	101.4		
6	12.8	1	12.53	1.03	13.05	1.01	97.9	102.5	102	101.2		
7	12.8	3	13.04	3.18	12.91	3.09	101.9	105.9	100.8	103.0		
8	12.8	5	13.03	5.29	12.9	5.04	101.8	105.7	100.8	100.8		
9	12.8	7	13.07	7.01	12.9	7.11	102.1	100.1	100.8	101.6		
10	12.8	9	12.41	9.26	12.94	9.16	96.9	102.9	101.1	101.8		
						Mean	101.2	103.1	101	101.8		
						SD	2.29	1.8	1.12	0.85		
						RSD	2.26	1.74	1.11	0.83		

For the analysis of **ATO-AML** mixture we propose the following model;

218 Amix, $\lambda_1 = 0.0341xC_{ATO} + 0.0492xC_{AML} - 0.0587$
220 Amix, $\lambda_2 = 0.0299xC_{ATO} + 0.0058xC_{AML} - 0.0436$
222 Amix, $\lambda_3 = 0.0323xC_{ATO} + 0.0417xC_{AML} - 0.0609$
224 Amix, $\lambda_4 = 0.0323xC_{ATO} + 0.0379xC_{AML} - 0.0609$
226 Amix, $\lambda_5 = 0.0326xC_{ATO} + 0.0371xC_{AML} - 0.0596$
228 Amix, $\lambda_6 = 0.0332xC_{ATO} + 0.0380xC_{AML} - 0.0564$
230 Amix, $\lambda_7 = 0.0340xC_{ATO} + 0.0399xC_{AML} - 0.0548$
232 Amix, $\lambda_8 = 0.0350xC_{ATO} + 0.0418xC_{AML} - 0.0516$
234 Amix, $\lambda_9 = 0.0361xC_{ATO} + 0.0434xC_{AML} - 0.0473$
236 Amix, $\lambda_{10} = 0.0374xC_{ATO} + 0.0449xC_{AML} - 0.0461$
238 Amix, $\lambda_{11} = 0.0386xC_{ATO} + 0.0452xC_{AML} - 0.0438$
240 Amix, $\lambda_{12} = 0.0397xC_{ATO} + 0.0444xC_{AM}L - 0.0436$
242 Amix, $\lambda_{13} = 0.0408xC_{ATO} + 0.0422xC_{AML} - 0.0439$
244 Amix, $\lambda_{14} = 0.0415xC_{ATO} + 0.0386xC_{AML} - 0.0438$
246 Amix, $\lambda_{15} = 0.0418xC_{ATO} + 0.0347xC_{AML} - 0.0445$
248 Amix, $\lambda_{16} = 0.0417xC_{ATO} + 0.0304xC_{AML} - 0.0450$
250 Amix, $\lambda_{17} = 0.0412xC_{ATO} + 0.0261xC_{AML} - 0.0442$
252 Amix, $\lambda_{18} = 0.0404xC_{ATO} + 0.0223xC_{AML} - 0.0441$
254 Amix, $\lambda_{19} = 0.0393xC_{ATO} + 0.0187xC_{AM}L - 0.0439$
256 Amix, $\lambda_{20} = 0.0380xC_{ATO} + 0.0157xC_{AML} - 0.0425$
258 Amix, $\lambda_{21} = 0.0366xC_{ATO} + 0.0132xC_{AM}L - 0.0446$
260 Amix, $\lambda_{22} = 0.0352xC_{ATO} + 0.0110xC_{AML} - 0.0441$
263 Amix, $\lambda_{23} = 0.0337xC_{ATO} + 0.0095xC_{AML} - 0.0442$
264 Amix, $\lambda_{24} = 0.0323xC_{ATO} + 0.0079xC_{AML} - 0.0436$
266 Amix, $\lambda_{25} = 0.0310xC_{ATO} + 0.0065xC_{AML} - 0.0435$
268 Amix, $\lambda_{26} = 0.0299xC_{ATO} + 0.0058xC_{AML} - 0.0436$

	ATO-AML tablet											
	Added (mg/mL)		Found (mg/mL)		SS		RSS (%)		RSE (%)		Recovery (%)	
	ATO	AML	ATO	AML	ATO	AML	ATO	AML	ATO	AML	ATO	AML
BC	4	4	3.99	4.15	0.11	0.02	2.68	0.6	-0.32	3.56	99.7	103.7
	12	12	12.12	11.85	0.03	0.01	0.27	0.05	0.95	-1.31	101	98.7
	16	16	16.39	16.45	0.4	0.49	2.45	2.99	2.31	2.66	102.4	102.8
MC	4	4	4.03	4.07	0.05	0.05	1.23	1.15	0.74	1.6	100.8	101.6
	12	12	11.95	12.08	0.04	0.42	0.36	3.44	-0.46	0.61	99.5	100.7
	16	16	16.18	15.98	0.54	0.25	3.33	1.53	1.05	-0.12	101.1	99.9
	TEL-HCT tablet											
	Added (mg/mL)		Found (mg/mL)		SS		RSS (%)		RSE (%)		Recovery (%)	
	TEL	HCT	TEL	HCT	TEL	HCT	TEL	HCT	TEL	HCT	TEL	HCT
BC	2.5	2	2.56	2.03	0.03	0.04	1.2	2.19	2.37	1.4	102.4	101.5
	5	6	5.1	6.06	0.09	0.06	1.67	0.94	0.51	1.7	101.9	101.1
	7.5	9	7.54	9.03	0.04	0.08	0.58	0.85	0.58	0.36	100.6	100.4
MC	2.5	2	2.54	2.05	0.08	0.04	3.01	2.06	1.67	2.43	101.8	102.5
	5	6	4.97	6.01	0.1	0.05	1.99	0.87	-0.69	0.12	99.3	100.1
	7.5	9	7.53	9.08	0.07	0.16	0.95	1.72	0.34	0.85	100.3	100.9

Table 9
STANDARD ADDITION RESULTS OBTAINED BY **BC** AND **MC** METHODS

	mg/tablet							
	(I)				(II)			
	BC		MC		BC		MC	
No.	TEL	HCT	TEL	HCT	ATO	AML	ATO	AML
1	81.67	12.73	80.00	12.55	10.78	10.13	10.12	9.92
2	80.59	12.60	79.06	12.30	10.51	10.25	10.17	10.06
3	81.59	12.81	80.04	12.64	10.42	10.16	10.38	9.97
4	82.83	12.94	81.39	12.70	10.38	10.25	10.34	10.04
5	82.41	12.66	80.59	12.56	10.39	10.11	10.34	9.94
6	82.78	12.59	80.99	12.51	10.00	10.08	10.36	9.91
7	80.90	13.02	79.52	12.91	10.47	10.23	10.43	10.01
8	82.44	12.96	80.98	12.66	10.52	10.16	10.14	10.00
9	83.43	12.93	81.88	12.87	10.47	10.23	10.43	10.01
10	81.11	12.74	80.37	12.54	10.52	10.16	10.17	10.00
Mean	81.98	12.80	80.48	12.63	10.45	10.17	10.29	9.99
SD	0.94	0.16	0.86	0.18	0.19	0.06	0.12	0.05
RSD	1.15	1.23	1.07	1.4	1.85	0.62	1.2	0.52
SE	0.3	0.05	0.27	0.06	0.06	0.02	0.04	0.02
CL	0.58	0.1	0.54	0.11	0.12	0.04	0.08	0.03

Table 10
RESULTS OBTAINED FOR THE PHARMACEUTICAL SAMPLES BY THE DEVELOPED METHODS

SD= Standard deviation, RSD= Relative standard deviation,

SE= Standard error, CL = Confidential limit (P=0.05)

PRITOR PLUS® Tablet (I) : 80 mg **TEL** and 12.5 mg **HCT** per tablet

Caduet® Tablets (II): 10 mg **ATO** and 10 mg **AML** per tablet

For the analysis of the **TEL-HCT** mixture we propose the following model;

$$^{220}A_{mix,\ \lambda_1} = 0.1019 x C_{TEL} + 0.1031 x C_{HCT} + 0.1156$$
$$^{224}A_{mix,\ \lambda_2} = 0.1031 x C_{TEL} + 0.1118 x C_{HCT} + 0.1111$$
$$^{228}A_{mix,\ \lambda_3} = 0.1025 x C_{TEL} + 0.0896 x C_{HCT} + 0.1318$$
$$^{232}A_{mix,\ \lambda_4} = 0.0988 x C_{TEL} + 0.0360 x C_{HCT} + 0.0960$$
$$^{236}A_{mix,\ \lambda_5} = 0.0847 x C_{TEL} + 0.0121 x C_{HCT} + 0.0861$$
$$^{240}A_{mix,\ \lambda_6} = 0.0606 x C_{TEL} + 0.0052 x C_{HCT} + 0.0834$$
$$^{244}A_{mix,\ \lambda_7} = 0.0470 x C_{TEL} + 0.0061 x C_{HCT} + 0.0782$$
$$^{248}A_{mix,\ \lambda_8} = 0.0435 x C_{TEL} + 0.0092 x C_{HCT} + 0.0791$$
$$^{252}A_{mix,\ \lambda_9} = 0.0428 x C_{TEL} + 0.0160 x C_{HCT} + 0.0778$$
$$^{256}A_{mix,\ \lambda_{10}} = 0.0422 x C_{TEL} + 0.0252 x C_{HCT} + 0.0860$$
$$^{260}A_{mix,\ \lambda_{11}} = 0.0403 x C_{TEL} + 0.0381 x C_{HCT} + 0.0874$$
$$^{264}A_{mix,\ \lambda_{12}} = 0.0367 x C_{TEL} + 0.0503 x C_{HCT} + 0.0948$$
$$^{268}A_{mix,\ \lambda_{13}} = 0.0332 x C_{TEL} + 0.0608 x C_{HCT} + 0.0879$$
$$^{272}A_{mix,\ \lambda_{14}} = 0.0327 x C_{TEL} + 0.0596 x C_{HCT} + 0.0828$$
$$^{276}A_{mix,\ \lambda_{15}} = 0.0350 x C_{TEL} + 0.0427 x C_{HCT} + 0.0895$$
$$^{280}A_{mix,\ \lambda_{16}} = 0.0390 x C_{TEL} + 0.0247 x C_{HCT} + 0.0732$$
$$^{284}A_{mix,\ \lambda_{17}} = 0.0437 x C_{TEL} + 0.0124 x C_{HCT} + 0.0689$$
$$^{288}A_{mix,\ \lambda_{18}} = 0.0475 x C_{TEL} + 0.0074 x C_{HCT} + 0.0693$$
$$^{292}A_{mix,\ \lambda_{19}} = 0.0497 x C_{TEL} + 0.0064 x C_{HCT} + 0.0716$$
$$^{296}A_{mix,\ \lambda_{20}} = 0.0500 x C_{TEL} + 0.0067 x C_{HCT} + 0.0699$$
$$^{300}A_{mix,\ \lambda_{21}} = 0.0481 x C_{TEL} + 0.0066 x C_{HCT} + 0.0744$$
$$^{304}A_{mix,\ \lambda_{21}} = 0.0437 x C_{TEL} + 0.0075 x C_{HCT} + 0.0741$$
$$^{308}A_{mix,\ \lambda_{23}} = 0.0375 x C_{TEL} + 0.0085 x C_{HCT} + 0.0723$$
$$^{312}A_{mix,\ \lambda_{24}} = 0.0303 x C_{TEL} + 0.0099 x C_{HCT} + 0.0684$$
$$^{316}A_{mix,\ \lambda_{25}} = 0.0230 x C_{TEL} + 0.0096 x C_{HCT} + 0.0718$$
$$^{320}A_{mix,\ \lambda_{26}} = 0.0167 x C_{TEL} + 0.0095 x C_{HCT} + 0.0704$$

The **MC** approach here was applied to the resolution of the binary mixture and tablets containing **ATO-AML** and **TEL-HCT** combinations. It was observed that this method is a powerful tool with very simple mathematical content for quantitative resolution of binary and multi mixtures.

Validity and applicability of the proposed calibration methods

The validation and the applicability of the calibration methods were obtained by analysing the synthetic **ATO-AML** and **TEL-HCT** combinations. To check the validity of the calibration models, the simultaneous quantitative analysis of the synthetic mixtures was carried out by the

BSC, MSC and derivative methods. The obtained results were shown in table 8. The means recoveries and the relative standard deviations of the methods were calculated. The output results can be considered satisfactory in the case of spectral overlapping between compounds in the samples.

Standard addition technique was used for the observation of the interference effects of the excipients on the analysis of the active compounds in two commercial dosage forms. The test procedures were carried out as explained in subsection Standard and calibration solutions.No interference for tablet excipients was observed during the analysis of two commercial dosage forms. Essay results obtained by application of standard addition technique were illustrated in table 9.

Analysis of tablet dosage forms

In the application of **BC** and **MC** calibrations at Caduet® Tablets (I) and PRITOR PLUS® Tablet (II), assay results were presented in table 10. It was observed that the results obtained by both methods were found suitable and reliable for the quality control and routine analysis of **ATO-AML** and **TEL-HCT** tablets.

Conclusions

We have developed a simple, cheap, rapid and very easy to apply methodology to characterize the quantity of **ATO-AML** and **TEL-HCT** mixtures**.** The techniques used in this manuscript do not require any separation procedure and graphical procedure as in the case of the derivative spectrophotometry. The calculations and the algorithm of the methods are purely algebraic, therefore these techniques are preferable the most abstract and complicated chemometric methods. In the application of the methods, good accuracy and precision were observed according to the results of recovery studies and the standard addition technique for **ATO-AML** and **TEL-HCT** samples. The obtained results for **ATO-AML** and **TEL-HCT** are comparable with those obtained by HLPC method in [19, 20].

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