Electronic Supplementary Material (ESI) for Analytical Methods.

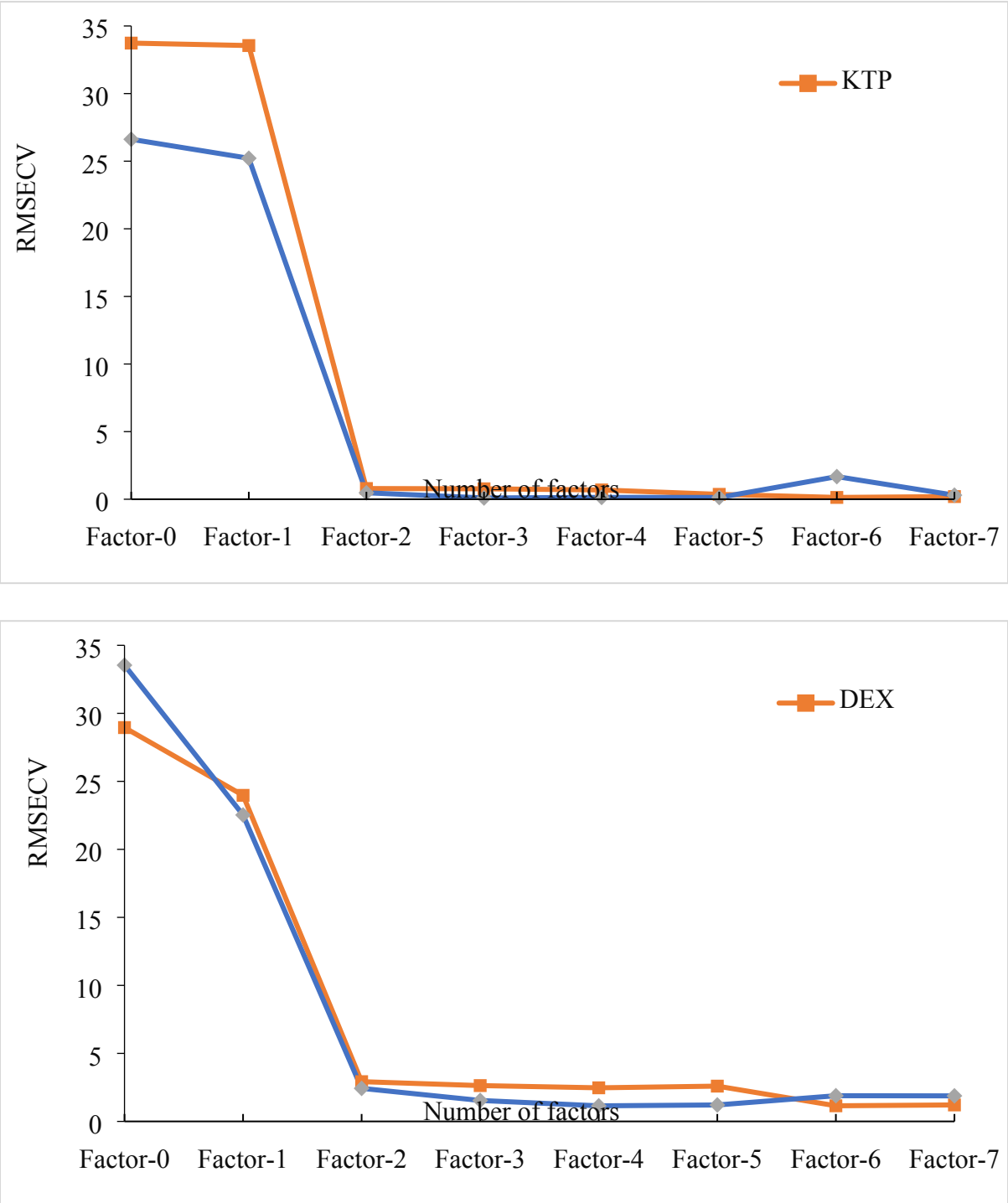
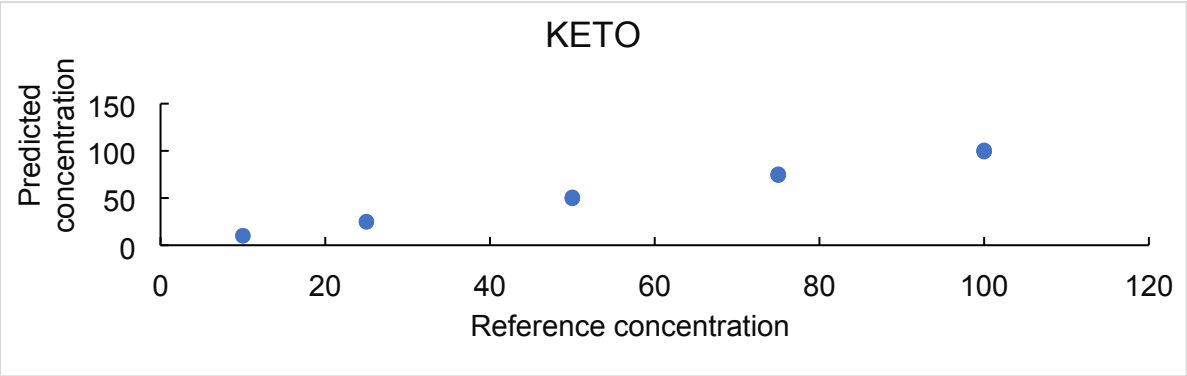
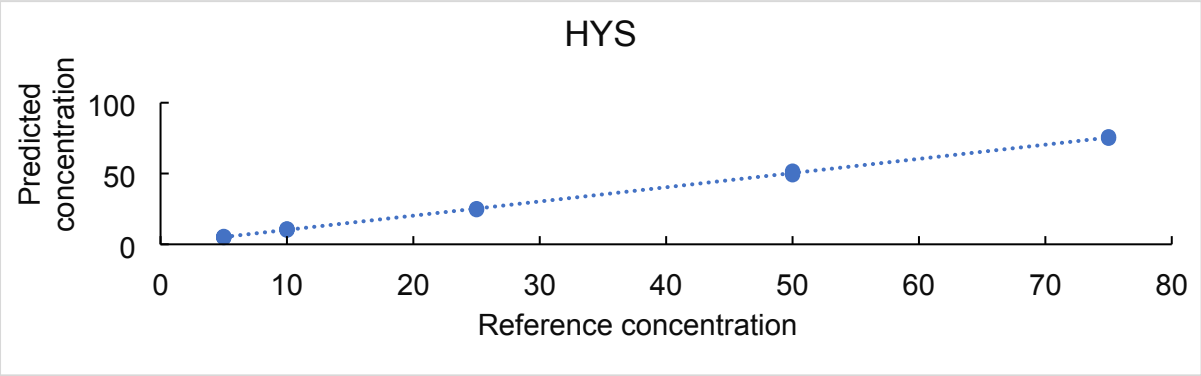
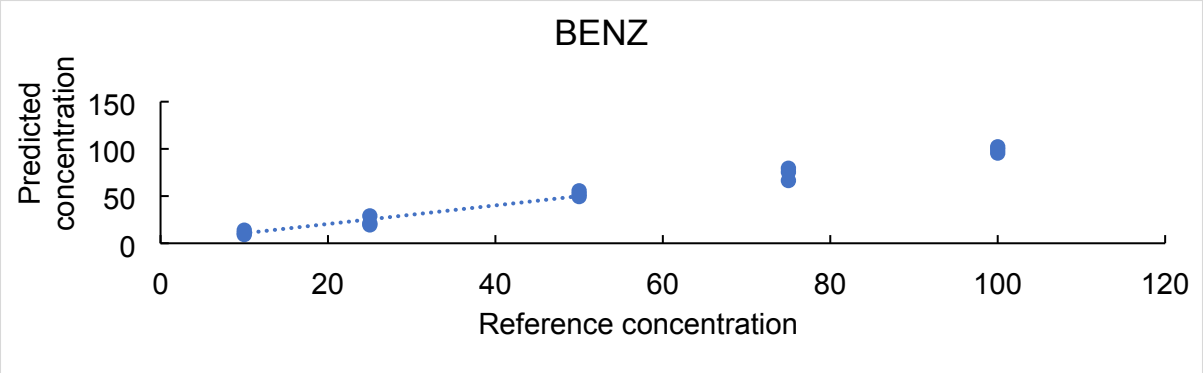


Figure (1S): Plots of RMSECV against the number of factors for calibration set of the binary mixtures using the developed PLSR models for the raw spectral data.







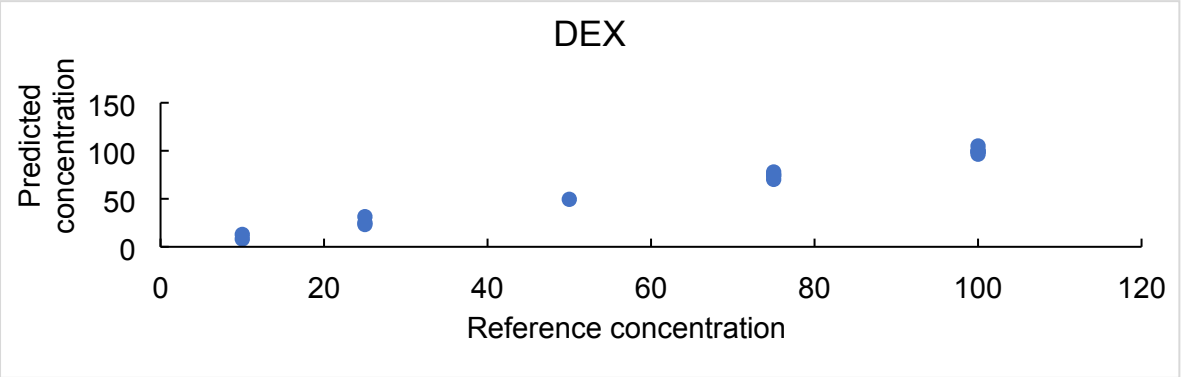


Figure (2S): The analytes reference concentrations against the predicted concentrations

Table 1S: The recovery percent obtained after applying the PLSR model to the test set in the presence of the expected excipients.

Mixture no [#]	***Analytes (R%)***		*Mixture no* [#]	***Analytes (R%)***	
	HYS	*KTP*		*BENZ*	*DEX*
1	97.98	98.87	***4***	102.12	97.82
2	97.88	101.58	***6***	97.54	99.51
9	98.13	99.93	***10***	98.80	101.87
16	98.43	87.11	***12***	99.67	99.86
17	99.76	99.41	***15***	97.09	99.03
19	98.98	98.59	***17***	98.88	98.77
22	97.98	97.79	***18***	101.87	97.66
23	98.55	102.10	***21***	101.65	98.34
24	98.56	97.99	***24***	98.82	100.82
25	99.76	99.69	***25***	97.71	101.92

[#] The concentration levels provided in (Table 1).

Table 2S: *System suitability parameters for the determination of HYS and KTP by the HPLC method.*

Parameters	**Obtained value**		**Reference value**
	HYS	**KTP**	
Resolution (R)	6.78		R > 0.8
Capacity factor (K)	2.85	5.08	1-10 acceptable
Selectivity factor (α)	1.78		> 1
Number of theoretical plates (N)	2002.23	4916.46	Increases with increasing the efficiency of separation
Tailing factor (T)	1.79	1.93	T ≤ 2 T= 1 for a typical symmetric peak
Height equivalent to one theoretical plate (H)	0.12	0.05	The smaller the value, the higher the column efficacy

Table 3S: *Validation parameters of the results obtained by applying the HPLC method for HYS and KTP determination.*

Parameter	***Value***	
	HYS	**KTP**
●Linearity:		
Slope	3760.3	18983
Intercept	-11537	196793
Correlation coefficient (r)	0.9999	0.9998
Range (µg/ml)	10-200	50-1000
●Accuracy *(Mean ± S.D):*	99.63 ± 0.92	99.5 ± 1.4
●Precision (R.S.D%):		
Repeatability	1.13	1.94
Intermediate Precision	1.29	1.98
●Specificity: *(mean ± SD)*	100.33 ±1.67	101.11± 0.73

Table 4S: *System suitability parameters for the determination of DEX and BENZ by the HPLC method.*

Parameters	**Obtained value**		**Reference value**
	DEX	**BENZ**	
Resolution (R)	11.88		R > 0.8
Capacity factor (K)	1.89	4.25	1-10 acceptable
Selectivity factor (α)	2.25		> 1
Number of theoretical plates (N)	4332.89	8613.83	Increases with increasing the efficiency of separation
Tailing factor (T)	1.38	1.20	T ≤ 2 T= 1 for a typical symmetric peak
Height equivalent to one theoretical plate (H)	0.06	0.03	The smaller the value, the higher the column efficacy

Table 5S : *Validation parameters of the results obtained by applying the HPLC method for DEX and BENZ determination.*

Parameter	***Value***	
	DEX	**BENZ**
●Linearity:		
Slope	17638	28580
Intercept	-13938	30915
Correlation coefficient (r)	0.9998	0.9998
Range (µg/ml)	5-100	5-100
●Accuracy *(*Mean ± *S.D):*	100.73 ± 2.03	100.61 ± 1.61
●Precision (R.S.D%):		
Repeatability	2.43	1.70
Intermediate Precision	2.05	1.69
●Specificity: *(mean ± SD)*	99.29 ± 1.20	99.82 ± 1.66