Supplementary Materials

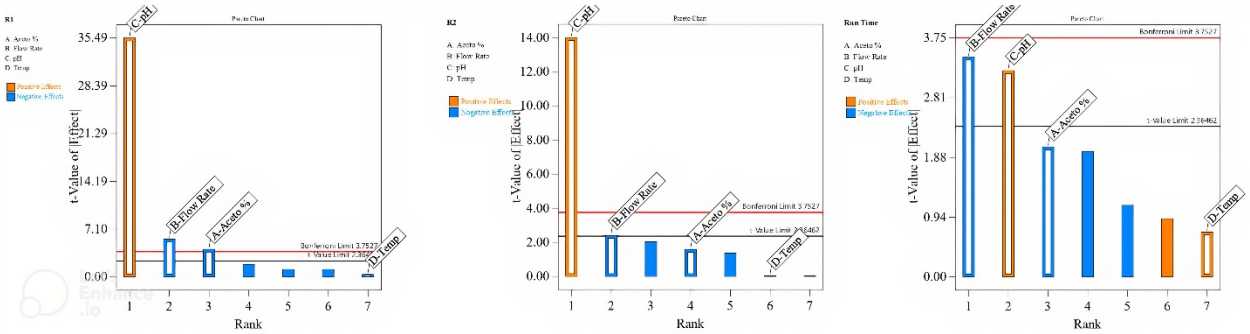


Figure S1. Pareto charts showing the significant factors on each response

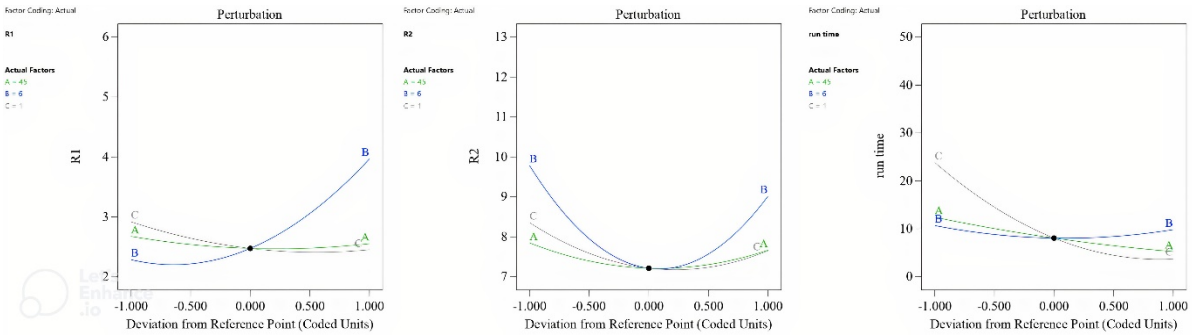


Figure S2. Perturbation charts showing the interaction effects of the studied factors on each response

Table S1. The produced random runs for screening and Optimization

Screening							
Run	**Factors**				**Responses**		
	ACN %	**Flow Rate**	**pH**	**Temp.**	**R1***	**R2****	**Run Time**
1	**70**	**0.5**	**7**	**25**	**4.6**	**13**	**18**
2	**30**	**2**	**7**	**25**	**4.5**	**12**	**10**
3	**50**	**1.25**	**5**	**32.5**	**2**	**8**	**6**
4	**70**	**2**	**3**	**25**	**1.8**	**2.8**	**1.5**
5	**30**	**2**	**3**	**40**	**2.1**	**3**	**4**
6	**50**	**1.25**	**5**	**32.5**	**2**	**8**	**6**
7	**30**	**0.5**	**7**	**40**	**4.8**	**15**	**35**
8	**50**	**1.25**	**5**	**32.5**	**2**	**8**	**6**
9	**30**	**0.5**	**3**	**25**	**2.3**	**3.2**	**10**
10	**70**	**2**	**7**	**40**	**4**	**10**	**4.5**
11	**70**	**0.5**	**3**	**40**	**2.2**	**3.1**	**6**
12	**50**	**1.25**	**5**	**32.5**	**2**	**8**	**6**

Optimization						
Run	**Factors**			**Responses**		
	ACN %	**pH**	**Flow rate**	**R1**	**R2**	**Run Time**
1	**45**	**6**	**1**	**2.5**	**7.3**	**8**
2	**30**	**5**	**1.5**	**2.7**	**12.1**	**9**
3	**45**	**6**	**1**	**2.5**	**7.3**	**8**
4	**45**	**6**	**1**	**2.5**	**7.3**	**8**
5	**19.7**	**6**	**1**	**2.5**	**7.5**	**18**

6	**45**	**6**	**1**	**2.5**	**7.3**	**8**
7	**45**	**6**	**0.15**	**3.1**	**8.9**	**47**
8	**45**	**6**	**1**	**2.5**	**7.3**	**8**
9	**30**	**5**	**0.5**	**2.9**	**12.2**	**28**
10	**45**	**6**	**1**	**2.5**	**7.3**	**8**
11	**45**	**7.7**	**1**	**4.8**	**11.3**	**12**
12	**60**	**5**	**0.5**	**2.9**	**12.5**	**18**
13	**70.2**	**6**	**1**	**2.3**	**7**	**5**
14	**30**	**7**	**1.5**	**4.7**	**11.3**	**10**
15	**45**	**6**	**1.8**	**2.1**	**7**	**4**
16	**60**	**7**	**1.5**	**4.5**	**11**	**6.5**
17	**30**	**7**	**0.5**	**5.2**	**11.8**	**30**
18	**60**	**7**	**0.5**	**5**	**11.5**	**20**
19	**45**	**4.3**	**1**	**2.9**	**12.5**	**19**
20	**60**	**5**	**1.5**	**2.6**	**12**	**5.5**

* Resolution between Pseudoephedrine and Paracetamol
** Resolution between Paracetamol and Loratadine

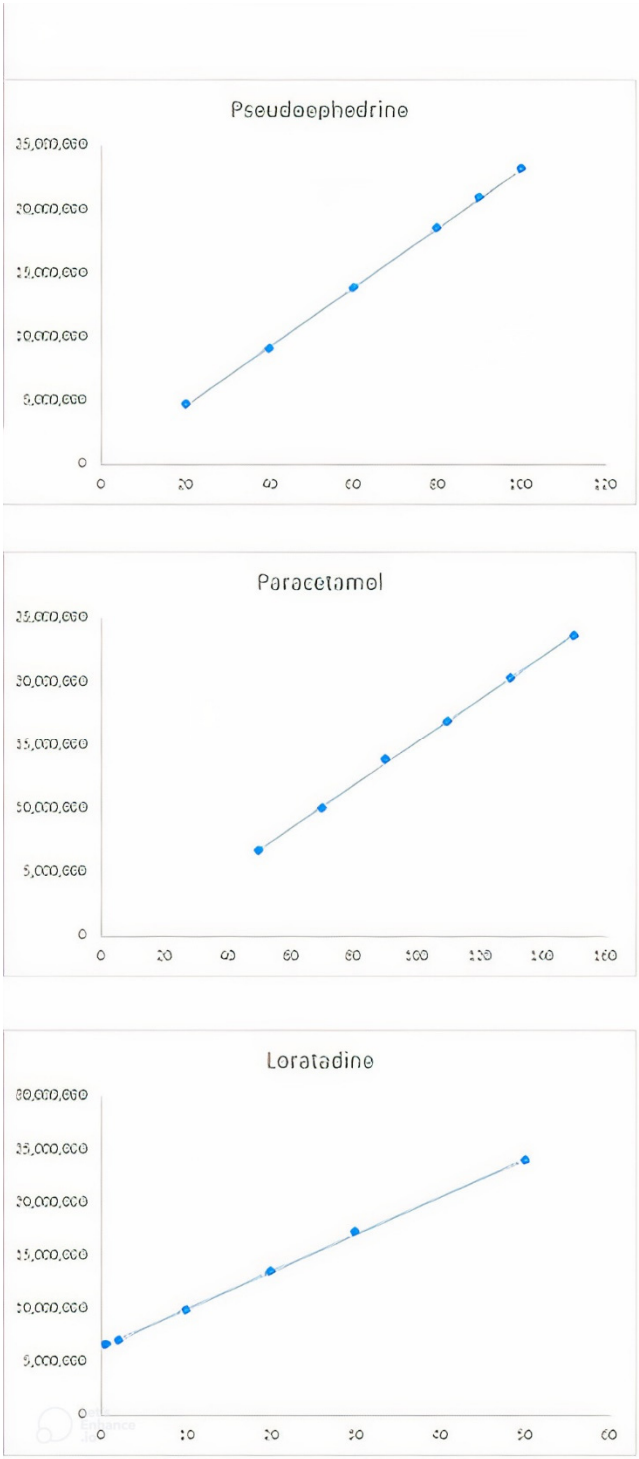
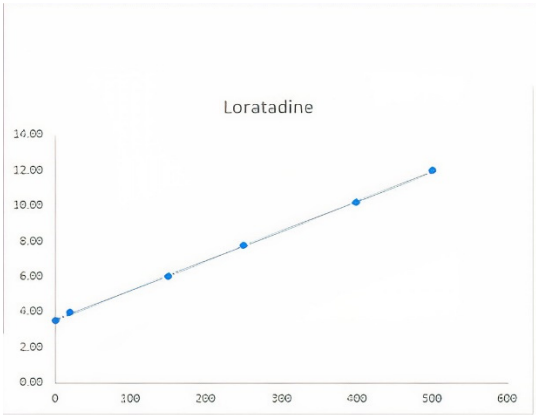
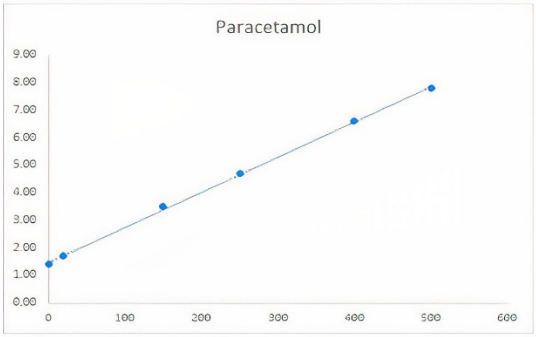
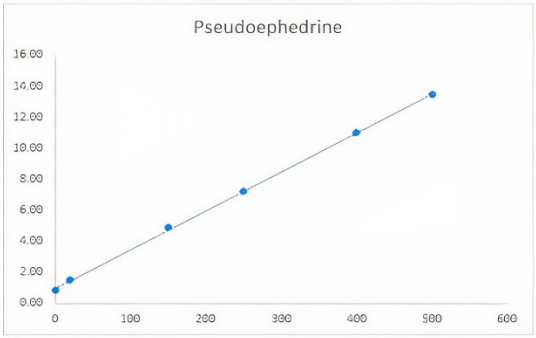


Figure S3. Calibration curves for the analytes for HPLC method







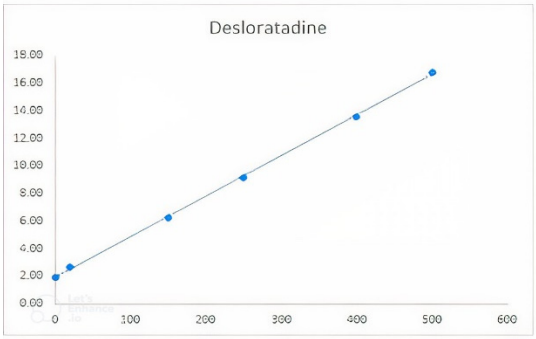


Figure S4. Calibration curves for the analytes for MS method

Table S2. Robustness testing for the developed HPLC method

Parameters	Variations	Run time (min)	R1	R2	Recovery%
Starting Acetonitrile %	55	3.9	2.4	8.5	99.25
	45	4.2	3	10	99.47
Mobile phase pH	5.7	4	2.75	9.25	98.58
	5.3	4	2.76	9.24	100.58
Column Temperature	45	4	2.8	9.2	99.62
	35	4	2.8	9.21	101.18
Flow rate	1.2	3.95	2.25	8.5	99.67
	1	4.15	2.9	9.8	100.66