

Supplementary Information

Ethanol Content Determination in Medicine Syrups Using Headspace and Multidimensional Heart-Cut Gas Chromatography Coupled to Mass Spectrometry

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Table S1. Commercial syrups differentiated by active ingredient

Code	Active principle	Treatment (package insert)
S1	ranitidine hydrochloride	healing of gastritis and peptic ulcers of the stomach and duodenum
S2 ^a	levodropropizine	inhibits the cough reflex
S3 ^a	<i>Hedera helix</i> L. (Araliaceae)	symptomatic treatment of acute and chronic inflammatory bronchopulmonary conditions
S4 ^b	calcium phosphate tribasic	prevention and auxiliary treatment in bone demineralization
S5	polyvitamin, polyimeral and lysine	overcoming potential nutrient deficiencies
S6 ^a	ciproptadine hydrochloride	stimulating appetite
S7	ranitidine hydrochloride	indicated in the treatment of duodenal ulcer and benign gastric ulcer
S8 ^a	desloratadine	prevents the action of histamine (allergy-causing substance)
S9 ^c	dipyrone monohydrate	relief from fever and pain
S10 ^a	guaifenesin	guaifenesin increases the elimination of secretions from the respiratory tract and facilitates, expectoration
S11 ^b	bromopride	stimulates digestive tract movement
S12 ^d	ranitidine hydrochloride	treats diseases associated with increased gastric secretion
S13	mikania glomerata	phytotherapeutic product that associates expectorant activity with antitussive activity
S14	dipyrone monohydrate	used in the treatment of painful manifestations and fever
S15	prednisolone sodium phosphate	acts against inflammatory processes, including inflammatory processes in the joints and allergic processes
S16 ^e	ascorbic acid	vitamin supplement
S17	cloperastine phendizoate	symptomatic therapy of all forms of cough

^aAdult and pediatric syrup (children over 2 years of age); ^boral solution for adult and pediatric use (children over 1 year of age); ^coral solution for adult and pediatric use (children over 3 months of age); ^dpediatric use above 1 month of age; ^eadult and pediatric use (above 12 years of age).

Reference syrup cut (first dimension)

Mint essence in 1D

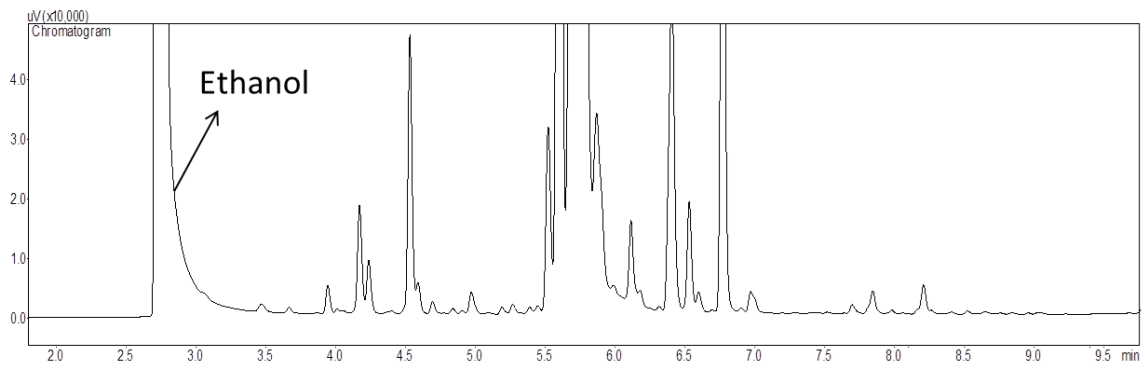


Figure S1. Mint essence.

Reference syrup (1D)

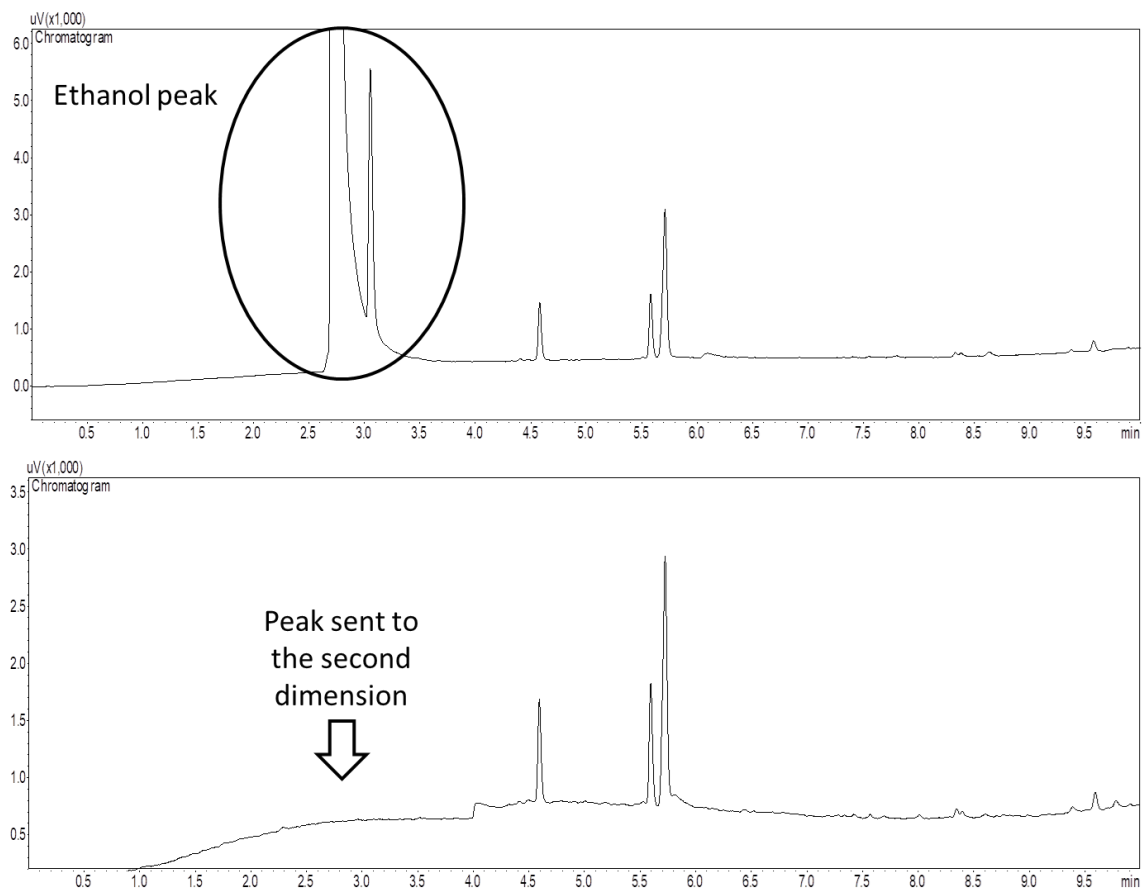


Figure S2. Transfer (heart-cut) of the ethanol peak to the second dimension (GC/MS).

Analytical validation (second dimension)

Selectivity

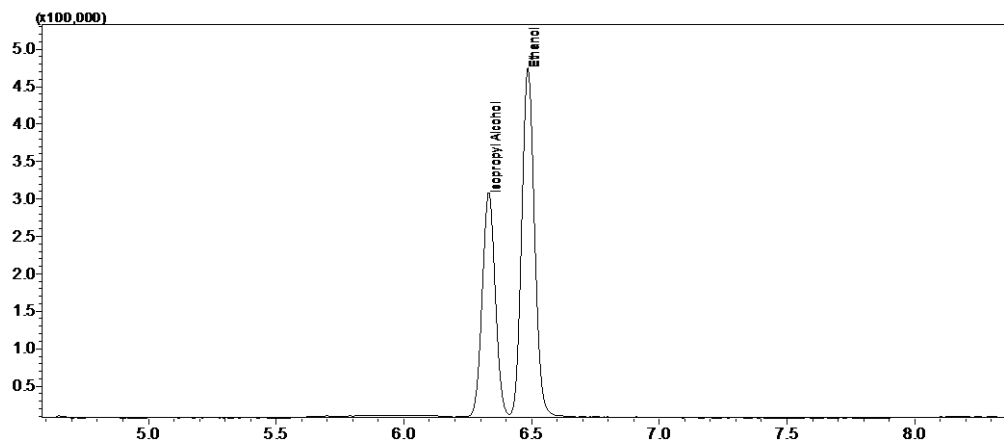


Figure S3. Efficiency in the separation of ethyl and isopropyl alcohols in GC/MS.

Ranitidine hydrochloride (reference syrup)

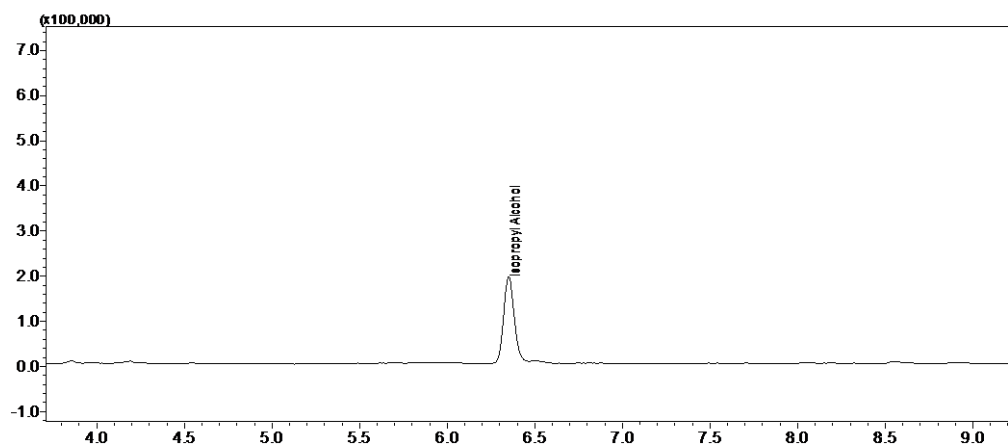


Figure S4. Confirmation of the presence of isopropyl alcohol in the raw material.

Analytical validation

Calibration curve of the best matrix effect condition

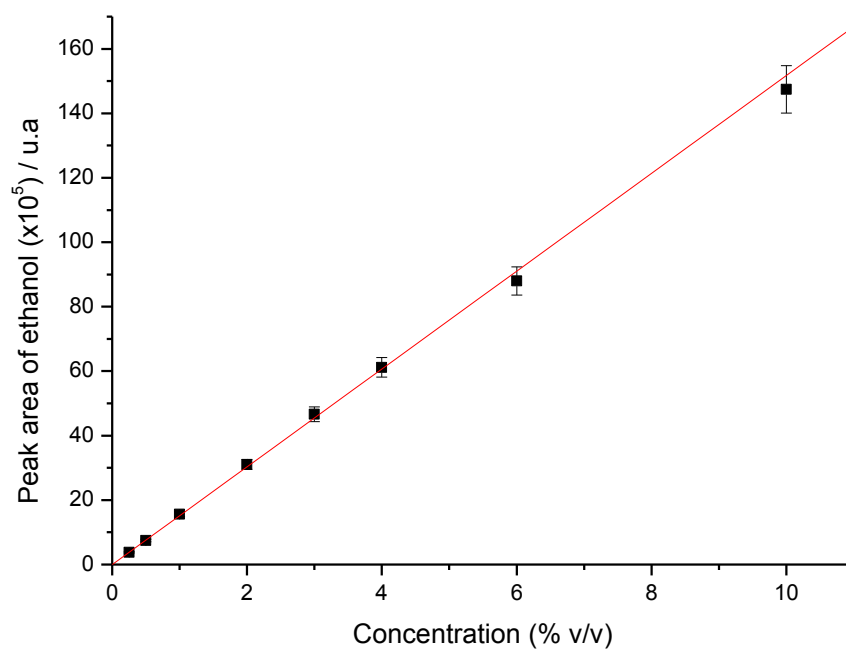


Figure S5. Calibration curve with sorbitol and water.

Linear regression analysis

Table S2. Summary of results of sorbitol curve

Regression statistics	
R multiple	0.997517416
R-square	0.995040994
R-squared set	0.993801243
Default error	417054.8528
Comments	6

ANOVA					
	df	SS	MS	F	Meaning F
Regression	1	1.39602×10^{14}	1.39602×10^{14}	802.6133116	9.23719×10^{-6}
Residue	4	6.95739×10^{11}	1.73935×10^{11}		
Total	5	1.40298×10^{14}			

	Coefficient	Default error	Stat <i>t</i>	<i>P</i> -value	95% lower	95% higher	Lower 95.0%	Higher 95.0%
Intersection	135420.5625	300380.8444	0.450829555	0.675470589	-698570.3628	969411.4878	-698570.3628	969411.4878
Ethanol concentration / %	1617882.563	57107.58766	28.33043084	9.23719×10^{-6}	1459326.48	1776438.645	1459326.48	1776438.645

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

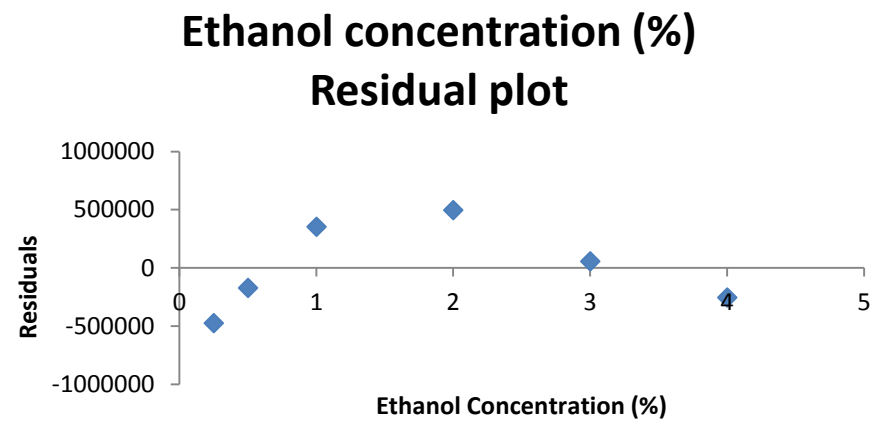


Figure S6. Sorbitol curve residual graph .

Table S3. Summary of results of water curve

Regression statistics	
R multiple	0.999111601
R-Square	0.998223992
R-squared set	0.99792799
Default error	239935.1438
Comments	8

ANOVA					
	df	SS	MS	F	Meaning F
Regression	1	$1.9414 \times 10^{+14}$	$1.94143 \times 10^{+14}$	3372.362551	1.75176×10^{-9}
Residue	6	$3.4541 \times 10^{+11}$	57568873253		
Total	7	$1.9449 \times 10^{+14}$			

	Coefficient	Default error	Stat t	P-value	95% lower	95% higher	Lower 95.0%	Higher 95.0%
Intersection	83469.49385	124778.805	0.66893968	0.528417737	-221853.2426	388792.2303	-221853.2426	388792.2303
Ethanol concentration / %	1589243.699	27366.7591	58.07204621	1.75176×10^{-9}	1522279.652	1656207.746	1522279.652	1656207.746

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

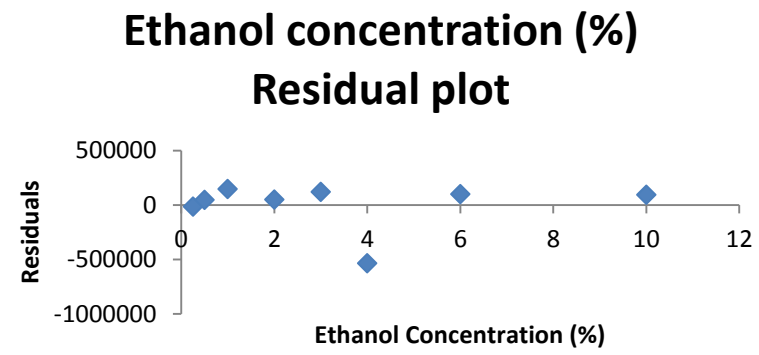


Figure S7. Water curve residual graph.

Table S4. Summary of results of sorbitol and water curve

Regression statistics	
R multiple	0.999756895
R-Square	0.999513848
R-squared set	0.999432823
Default error	115832.4235
Comments	8

ANOVA					
	df	SS	MS	F	Meaning F
Regression	1	$1.65512 \times 10^{+14}$	$1.66 \times 10^{+14}$	12335.83	3.59124×10^{-11}
Residue	6	80502902070	$1.34 \times 10^{+10}$		
Total	7	$1.65592 \times 10^{+14}$			

	Coefficients	Default error	Stat t	P-value	95% lower	95% higher	Lower 95.0%	Higher 95.0%
Intersection	107079.7127	60238.90934	1.777584	0.125797	-40319.58849	254479.0138	-40319.58849	254479.0138
Ethanol concentration / %	1467384.111	13211.72872	111.0668	3.59×10^{-11}	1435056.175	1499712.046	1435056.175	1499712.046

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

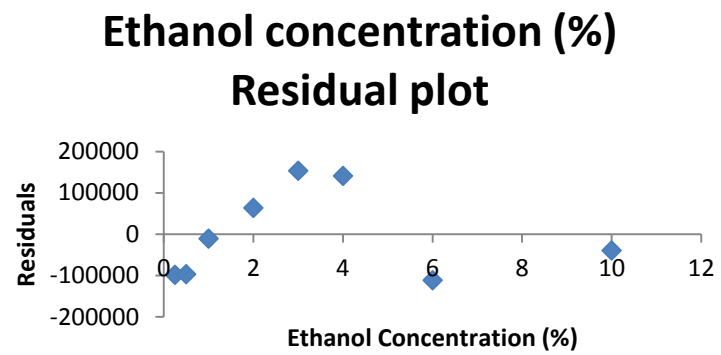


Figure S8. Water and sorbitol curve residual graph.

Robustness

Oven temperature

Table S5. Anova: single factor

Summary						
Group	Score	Sum	Average	Variance		
Peak area at 56 °C	3	20967268	6989089	$4.75 \times 10^{+13}$		
Peak area at 54 °C	3	21876730	7292243	$5.22 \times 10^{+13}$		
ANOVA						
Variation Source	df	SS	MS	F	P-value	F critical
Between groups	$1.38 \times 10^{+11}$	1	$1.38 \times 10^{+11}$	0.002766	0.960575	7.708647
Within the groups	$1.99 \times 10^{+14}$	4	$4.98 \times 10^{+13}$			
Total	$1.99 \times 10^{+14}$	5				

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

Carrier gas velocity

Table S6. Anova: single factor

Summary						
Group	Score	Sum	Average	Variance		
45 cm s ⁻¹	3	20177718	6725906	$4.39 \times 10^{+13}$		
50 cm s ⁻¹	3	20967268	6989089	$4.75 \times 10^{+13}$		
ANOVA						
Variation source	df	SS	MS	F	P-value	F critical
Between groups	$1.04 \times 10^{+11}$	1	$1.04 \times 10^{+11}$	0.002275	0.964245	7.708647
Within the groups	$1.83 \times 10^{+14}$	4	$4.57 \times 10^{+13}$			
Total	$1.83 \times 10^{+14}$	5				

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

Extraction time

Table S7. Anova: single factor

Summary						
Group	Score	Sum	Average	Variance		
15 min	3	19827718	6609239	$4.36 \times 10^{+13}$		
20 min	3	18968368	6322789	$3.84 \times 10^{+13}$		
ANOVA						
Variation source	df	SS	MS	F	P-value	F critical
Between groups	$1.23 \times 10^{+11}$	1	$1.23 \times 10^{+11}$	0.003002	0.958932	7.708647
Within the groups	$1.64 \times 10^{+14}$	4	$4.1 \times 10^{+13}$			
Total	$1.64 \times 10^{+14}$	5				

ANOVA: analysis of variance; df: degrees of freedom; SS: sum of squares; MS: mean square.

