
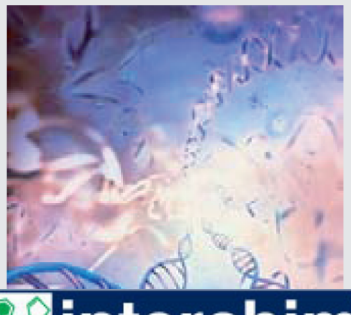

NEW!

interchim®

jasem

44+1 AMINO ACIDS & 17 ORGANIC ACIDS

Analysis of HUMAN SERUM, URINE and DRY-BLOOD-SPOTS by LC-MS/MS

Jasem® Method: Highest Sensitivity – Highest Accuracy – Highest Speed – Simplicity in New Dimensions !

® Patent pending

There may be no commerical kit available to determine amino acids and organic acids together in the same run. This unique Jasem® Combo-kit in the **first combined kit in the world** for metabolic disorders.

Quantitative free amino acid analysis has applications in the diagnosis of inherited metabolic disorders, and nutritional studies of neonates (M. Armstrong et. al., Rapid Commun. Mass Spectrom., 2007, 21, 2727). Newborn screening is originated with an amino acid disorder-phenylketonuria (PKU) - which is a metabolic genetic disorder characterized by a mutation in the gene for the hepatic enzyme phenylalaline hydroxy-lase (PAH) in 1960s.

17 ORGANIC ACIDS

Newborn secreening most of the time includes testing for a panel of acylcarnitines. In some cases, an elevated level of a particular acylcarnitine may indicate the possibility of one of several different organic acid disorders; the specific disorder cannot be de-termined without further testing. It has been demonstrated that the following organic acids disorders may be detected using this panel:

Aminoacid disorders are:
Argininosuccinic acidemia(ASA), Citrullinemia(CIT), Homocystinuria(HCY), Maple syrup(urine) disease(MSUD), Phenylketonuria(PKU), Tyrosinemia(TYR), Argininemia(ARG), Bening Hyper phenylalaninemia(H-PHE) and Hypermethioninemia(MET).

ORGANIC ACIDS:
list of compounds determined with Jasem® sample prep method

COMPOUNDS			
1	Glutaric acid	10	Ethylmalonic acid
2	Methylmalonic acid	11	Homogentisic acid
3	Adipic acid	12	N-Acetylaspartic acid
4	Alpha-hydroxyisovaleric acid	13	3-Hydroxyisovaleric acid
5	Malonic acid	14	Pyruvic acid
6	Alpha-ketoglutaric acid	15	Succinylacetone
7	Succinic acid	16	Fumaric acid
8	Malic acid	17	Lactic acid
9	3-Methylglutaric acid		

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JASEM LABORATUVAR SISTEM VE COZUMLERI SANAYI VE TICARET A.S.
Inonu Mah. Kartal Cd. No:55 Kat:2, Kayisdagi-Atasehir-Istanbul/TURKEY
T: +90 216 469 70 65 - 66, F: +90 216 469 70 67

The aim of analysis is to identify and quantify

In the Jasem® method:

2 main methods for in total 44 aminoacids have been developed by Jasem® :

one is a gradient application (7.5 min.), the other method is isocratic (2.5 min.) – both methods can be used directly one after the other in one go, by using the

same sample preparation procedure,
same column,
same mobile phase,
same source parameters,
same injection volume

39 aminoacids are analysed by Method 1:

	COMPOUND	RT	prec.	prod
1	L-Tryptophan	1.820	205.1	188.1
2	Taurine	1.977	126.1	44.3
3	L-Phenylalanine	2.025	166.1	120.1
4	L-Tyrosine	2.069	182.1	165
5	L-Leucine	2.187	132.2	43.3
6	L-isoleucine	2.281	132.2	69.2
7	L-Methionine	2.297	150.1	104.1
8	Gamma amino butyric acid	2.313	104.0	87.1
9	3-Aminoisobutyric acid	2.390	104.1	86.2
10	L-Norvaline	2.466	118.1	72.1
11	L-Cysteine	2.522	122.1	59.1
12	L-2-aminoadipic acid	2.537	162.0	98.0
13	Beta-Alanine	2.698	90.1	72.1
14	Ethanolamine	2.757	62.1	44.2
15	L-Aspartic acid	2.829	134.1	74.1
16	L-2-aminobutyric acid	2.884	104.2	58.3
17	L-Threonine	3.000	120.2	74.2
18	L-Serine	3.065	106.2	60.2
19	L-Alanine	3.072	90.2	44.2
20	L-Glycine	3.207	76.2	30.1

	COMPOUND	RT	prec.	prod
21	L-Asparagine	3.261	133.1	74.2
22	Trans-4-hydroxy-L-proline	3.267	132.2	68.2
23	L-Glutamine	3.356	147.1	84.2
24	Sarcosine	3.384	90.1	44.2
25	L-Proline	3.402	116.2	70.2
26	L-Homocitrulline	3.450	190.0	173.1
27	L-Citrulline	3.541	176.2	159.3
28	DL-Homocystine	3.680	269.0	136.0
29	L-Cystine	3.920	241.1	74.2
30	L-Cystathionine	3.950	223.0	134.0
31	L-Arginine	3.960	175.2	70.2
32	L-Histidine	3.991	156.1	110.1
33	L-Ornithine	4.041	133.2	70.3
34	DL-5-Hydroxy lysine	4.044	163.1	128.1
35	L-Lysine	4.078	147.1	84.2
36	L-Carnosine	4.190	227.1	110.1
37	3-Methyl-L-Histidine	4.320	170.1	126.2
38	1-Methyl-L-Histidine	4.340	170.1	124.1
39	L-Anserine	4.490	241.1	109.1

5 aminoacids are analysed by Method 2:

	COMPOUND	RT	prec.	prod
1	Argininosuccinic acid	1.73	291.0	70.2
2	Ortho phospho-L-Serine	1.63	186.0	88.1
3	Ortho phosphoryl ethanolamine	1.74	142.0	44.2
4	L-Valine	1.73	126.1	80.2
5	L-Glutamic acid	1.65	148.1	84.2

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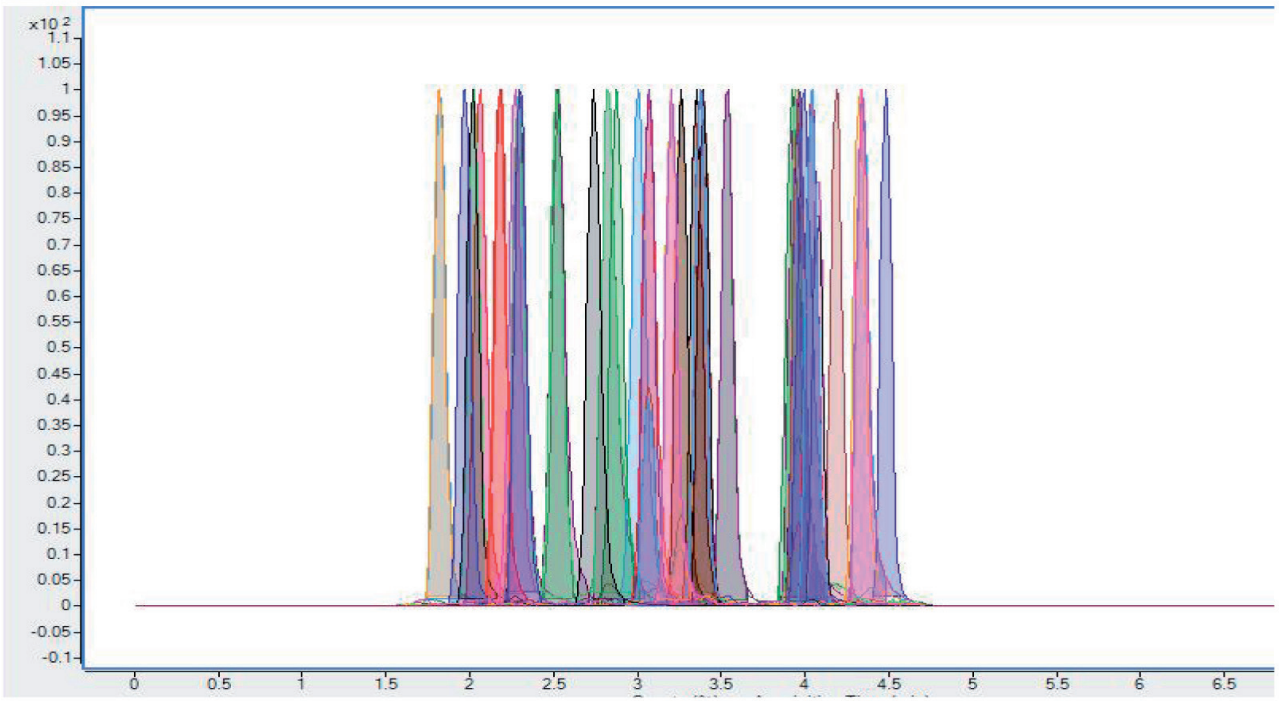
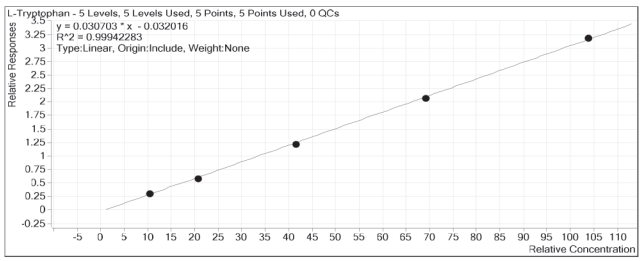
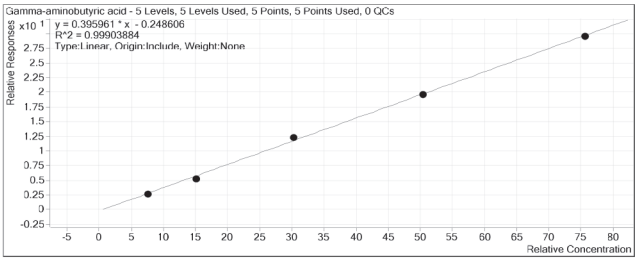


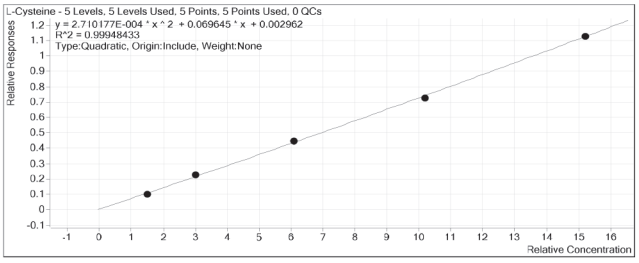
Normalized chromatogram of amino acids



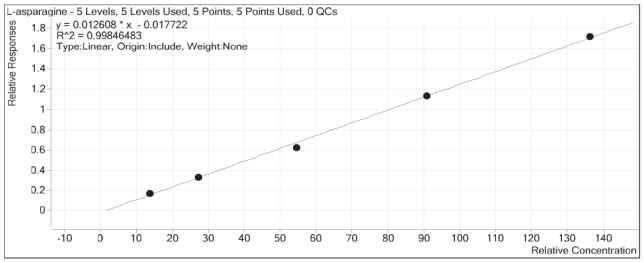
L-Tryptophan calibration curve from 13.8 nmol/ml to 138 nmol/ml



Gamma amino butric acid calibration curve from 10 nmol/ml to 100 nmol/ml



L-Cysteine calibration curve from 3 nmol/ml to 30 nmol/ml



L-Asparagine calibration curve from 17 nmol/ml to 170 nmol/ml

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Compound	R^2	LOQ nmol/ml	LOD nmol/ml
L-Trypthophan	0.9994	0.57	0.19
Taurine	0.9939	0.45	0.15
L-Phenylalanine	0.9998	0.15	0.05
L-Tyrosine	0.9968	0.77	0.26
L-Leucine	0.9979	0.14	0.05
L-Isoleucine	0.9984	0.15	0.05
L-Methionine	0.9983	0.03	0.01
Gamma amino butyric acid	0.9990	0.05	0.02
3-Amino isobutyric acid	0.9985	0.08	0.03
L-Norvaline	0.9950	0.11	0.04
L-Cysteine	0.9994	0.45	0.15
L-2-aminoadipic acid	0.9979	0.11	0.04
L-Glutamic acid	0.9990	0.38	0.13
L-Valine	0.9985	0.05	0.02

Compound	R^2	LOQ nmol/ml	LOD nmol/ml
Beta-Alanine	0.9987	0.35	0.12
Ethanolamine	0.9953	0.06	0.02
L-Aspartic acid	0.9982	0.29	0.10
L-2-amino butyric acid	0.9917	0.12	0.04
L-Threonine	0.9967	0.53	0.18
L-Serine	0.9928	0.23	0.08
L-Alanine	0.9989	0.16	0.05
L-Glycine	0.9921	3.20	1.06
L-Asparagine	0.9984	0.22	0.07
L-Glutamine	0.9992	0.04	0.01
Sarcosine	0.9948	0.12	0.04
L-Proline	0.9992	0.21	0.07
L-Homocitrulline	0.9989	0.31	0.10
L-Citrulline	0.9960	0.43	0.16
L-Homocystine	0.9991	0.23	0.08

Traditionally, free amino acids in plasma have been analyzed by ion chromatography (IC-UV) using ninhydrin post-column derivatization or by cation-exchange solid-phase extraction followed by derivatization and analysis by gas chromatography/ mass spectrometry (GC/MS).

Present Reference Method: Ion-exchange chromatographic methods are widely used as reference method and chemical derivatization of amino acids is required for detection. Very long run times due to ion-exchange chromatography (1.5-2 hours per sample)

Jasem® Method: 4 sample prep steps only and done within 5 minutes and 10 minutes run time for 44 amino acids!

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Why is all over the world medical interest in Amino acidsanalysis so rapidly growing ?

The first disorder detected by modern newborn screening programs was phenylketonuria, a metabolic condition in which the inability to degrade the essential amino acid phenylalanine can cause irreversible mental retardation unless detected early. With early detection, and dietary management, the negative effects of the disease can be largely eliminated.

Note

Regulatory Label Consideration

The age that symptoms start and the types of symptoms that a person has vary. Many babies with these conditions will appear normal at birth. Some of the disorders will cause developmental delay or mental retardation if not treated promptly. Other newborns may develop symptoms such as poor appetite, sleepiness, vomiting, or irritability. If the condition is not treated promptly, babies can develop more serious problems including breathing problems, seizures, swelling of the brain, or even coma or death (Department of Health and Environment, Kansas, www.kdheks.gov).

Example of Metabolic Disorders: Phenylketonuria (PKU)

- Approximately 0,1% of babies are born with an inherited metabolic disorder called Phenylketonuria
- If Phenylketonuria is NOT detected and treated, the levels of Phenylalanine in the child's blood will increase
- The increase in Phenylalanine will result in brain damage and mental retardation
- The cost of care over the 30 year life expectancy of such an untreated person is huge!
- The treatment simply involves restricting the amount of Phenylalanine in the person's diet

BENEFITS & ADVANTAGES of JASEM® METHOD

- Sample Preparation takes only 5 minutes.
- Much lower cost than ref. method
- High analysis efficiency: very short run time of only 10 minutes for all 44 amino acids (ref. method: 85-120 min.) + 17 Organic Acids
- High sensitivity nmol/ml.
- No source contamination
- Cost savings method compared to existing methods
- Very easy & fast sample preparation
- Monitoring also alloisoleucine for maple syrup urine disease
- Excellent repeatability: RSD typically lower than 1%
- No need for on-line SPE
- Column life extended (>15.000 injections)
- No matrix effect / no ion suppression

ANALYTICAL SCIENCES
interchim
211 bis, avenue JF Kennedy
BP 1140 - 03100 Montluçon
Fax 33 4 70 03 82 60
Hotline +33 4 70 03 73 09
interchrom@interchim.com