KBMO
DIAGNOSTICS

Metabolic Insights Profile (MIP)
Clinical Significance Guide

- MICROBIAL METABOLITES
- DETOXIFICATION MARKERS
- METABOLISM & MITOCHONDRIAL MARKERS
- NUTRITION & OXALATES
- NEUROTRANSMITTER MARKERS

METABOLIC INSIGHTS PROFILE
NEXT GENERATION ORGANIC ACIDS

Fungal metabolites

Arabitol
Candida can produce Arabitol which is then converted to arabinose, before excretion from the body. High Arabitol could indicate a Candida infection or another fungal species (1, 2).

Citramalic
Sources have been shown to come from multiple species of yeast. High values can indicate a fungal overgrowth (3).

5-Hydroxymethyl-2-furoic
Produced by Penicillum species (4). Elevations in this marker correlate with elevations in urine mycotoxins (5).

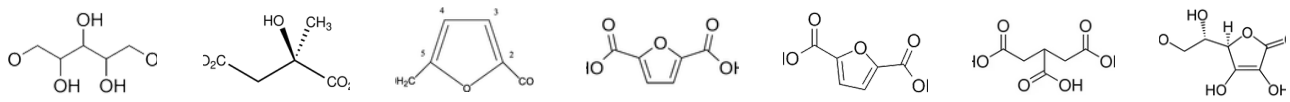
Furancarbonylglycine
Elevations in this marker correlate with elevations in urine mycotoxins (5).

Furan-2,5-dicarboxylic
Metabolite of Aspergillus. Could indicate an overgrowth of aspergillus in the body (6).

Tricarballylate
Produced by Fusarium during the production of the toxin fumonisin (7). Can also be produced by a strain of aerobic bacteria (8).

Ascorbic / Erythorbic (vitamin C and fungi)
Also known as vitamin C. Low amounts do not necessarily mean the patient needs additional vitamin C. Some patients show elevated amounts without supplementation. This could be attributed to yeast or other microbiota in the gut producing their own ascorbic acid (9).

In patients who routinely supplement vitamin C, the half-life of the vitamin significantly reduces to about 30 minutes - 2 hours. The greater the deficiency state the longer the half life of the nutrient, which is largely preserved at the level of the kidney (not excreted in urine). Subsequently it can be summised that high levels of ascorbic acid in the urine after an overnight fast are likely related to yeast and fungal species. The vast majority of eukaryotes (with the exception of primates) can produce ascorbic acid, including nearly all yeast and fungal species. Saccharomyces boulardii can produce ascorbic acid the most easily and readily from simple sugars (10,11).



Microbial Metabolites

Clostridia metabolites

HPHPA
Produced by Clostridia difficile. Found in higher amounts in adults with recurrent diarrhea. Metabolite of m-tyrosine. Inhibits the enzyme dopamine-beta-hydroxylase (12, 13).

m-Cresol-sulphate
Produced by several families of bacteria. Can be harmful to intestinal cells and decreases mitochondrial oxygen consumption. Can be increased in chronic kidney disease (14).

3-Indoleacetic
Produced by Clostridium and several other bacterial species. 3-Indoleacetic is the product of the metabolism of tryptophan by bacteria (15).

Bacterial metabolites

Benzoic
Common food preservative in packaged foods, also present naturally in some fruits. Elevated benzoate could indicate an inadequate amount of glycine or pantothenic acid for conjugation reactions (16). Can be produced by intestinal bacteria but other elevations should be present to confirm (17).

Hippuric
Hippuric Acid is a metabolite of gut bacteria metabolism of phenylalanine. It can also result from the hepatic glycine conjugation of benzoic acid (18).

4-Hydroxybenzoic
Strains of E.coli can produce p-hydroxybenzoate from glucose (19).

4-Hydroxyphenylacetic
The detection of large amounts of p-Hydroxyphenylacetate is associated with Giardia lamblia infestation as well as other anaerobic bacterial overgrowths (20).

4-Hydroxyphenyllactic
Patients with high amounts of p_Hydroxyphenyllactic could have a bacterial overgrowth in their gut (21).

Miscellaneous microbial metabolites

Tartaric
Tartaric acid can be elevated from wine, grape, apple, or several other fruit ingestions or produced by some fungi (22-24). There is no evidence that Tartaric is a metabolite of any species of Candida.

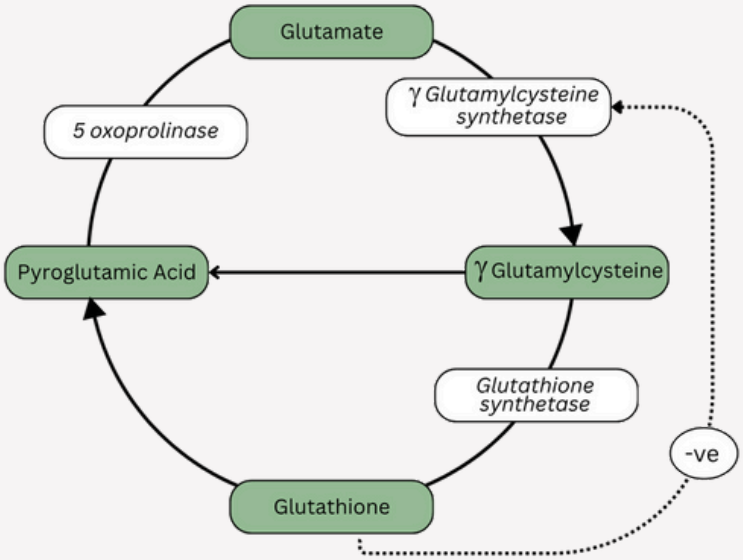
Detoxification markers

L-Pyroglutamic acid
Pyroglutamate is an intermediate in glutathione recycling. High pyroglutamate could be an indicator of overabundance of glutathione usage, or a lack of precursors in the recycling, such as glycine, cysteine, or glutamine (25).

Depletion could be caused by external toxins.

Pyroglutamic acid is also increased by consuming a vegetarian or low protein diet (26).

Low amounts of pyroglutamic acid could indicate deficiencies in glutathione, its precursors, or problems with the methylation cycle (27).



N-Acetylcysteine (NAC)
Mostly used as a precursor for glutathione. Can also have anti-bacterial and anti-biofilm properties. If the patient is supplementing with NAC and values go up considerably, that could indicate a problem in glutathione production. Supplementation with glutathione may be necessary (28, 29).

8-Hydroxy-2-deoxyguanosine (8-OHdG)
Produced when guanine bases are subjected to oxidative damage and positively correlates with inflammation. Toxin exposure could lead to increased amounts of 8-OHdG. Green tea and exercise have been shown to decrease 8-OHdG levels (30).

2-Hydroxybutyric (2-HB)
A marker for oxidative stress. Byproduct of glutathione synthesis, thus increased demand for glutathione could lead to an increase of 2-HB in urine.

Higher amounts of 2-HB in urine is correlated with insulin resistance and prediabetes (31).

2-Hydroxyhippuric
Produced during the detoxification of salicylic acid in the liver. Salicylic acid can be found in aspirin, stomach-relief aids and food preservatives (32).

Metabolism & Mitochondrial Markers

Citric Acid Cycle

Citric acid
Low levels could indicate calcium stone disease. Low values could be caused by kidney disease, excessive muscle activity, hypoparathyroidism, or the use of ACE inhibitors.

High levels could indicate a high carbohydrate diet, estrogen therapy, or excess vitamin D (33).

Cis-Aconitate
Produced during the citric acid dehydration during the Krebs Cycle and is a marker for mitochondrial activity. Activates the NRF2 pathway which leads to the production of glutathione (34).

Isocitric
Elevated levels may reflect mitochondrial nicotinamide adenine dinucleotide phosphate (NADP) isocitrate dehydrogenase inactivity. May correlate with elevated risk for myocardiopathy (35).

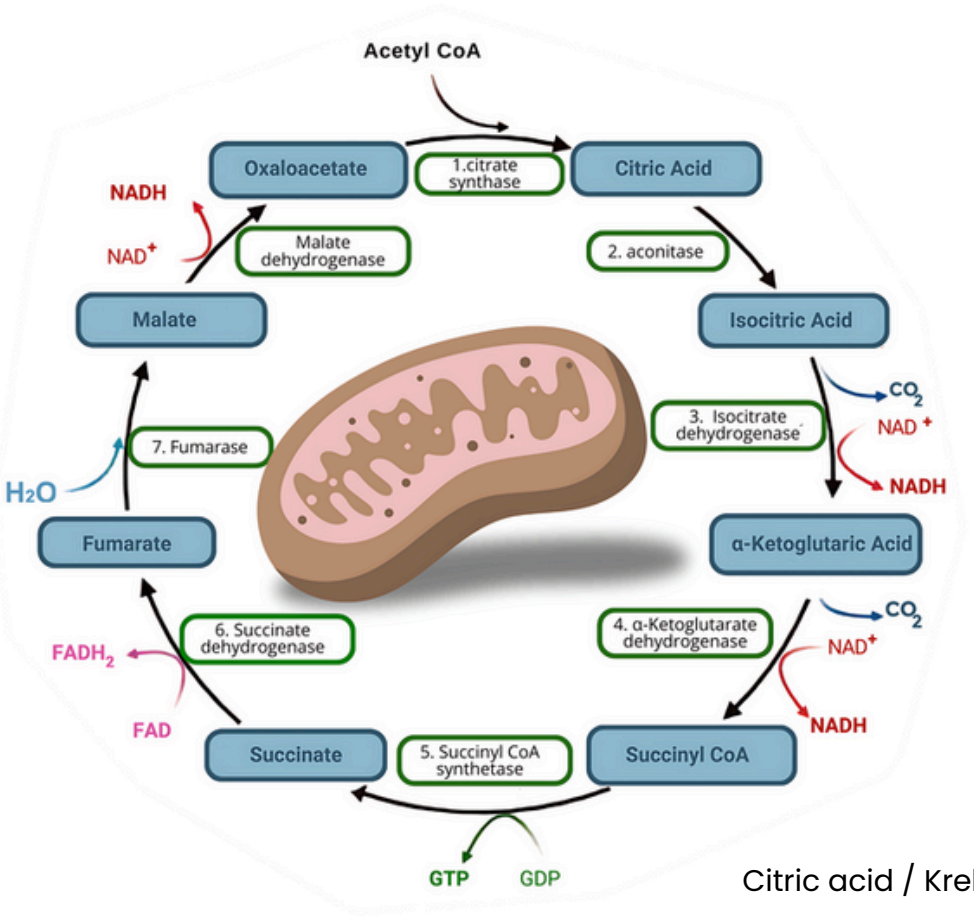
2-Oxoglutaric
This is a rate-determining intermediate in the Krebs Cycle. Low levels may indicate deficiencies in Citric Acid, Isocitric acid, Manganese, or Iron. Much smaller accumulations could be from a deficiency in calcium (37).

High levels could indicate a deficiency in B1, B2, or B3. Higher levels could indicate a mitochondrial oxidative phosphorylation disorder (38). Very large amounts could indicate the presence of L-2-hydroxyglutaric aciduria which is an inborn error in metabolism (36).

Succinic acid
Succinate is converted to Fumarate by the enzyme Succinate4 dehydrogenase. This enzyme can be inhibited by pesticides and other environmental toxins. This inhibition can lead to a buildup of succinate in the body (39). Low levels could be caused by poor dietary intake or poor absorption of branched-chain amino acids. One other possible cause is a deficiency of B12 which would lead to a decrease in the precursor succinyl-CoA (40) or from autoimmune disease (41).

Fumarate
Extremely high values are uncommon. Can lead to developmental delay, hypotonia, and microcephaly (42). Extremely low values are seen with patients with autoimmune disease (41).

Malic acid
Is converted to oxaloacetate by malate dehydrogenase. If this conversion is inhibited by lack of NAD or vitamin B3, it can lead to elevated levels. Is present in many fruits and vegetables, as well as being a preservative in beverages (43). Patients with autoimmune disease may see decreased amounts (41).



Citric acid / Krebs cycle

Glycolysis metabolism / Lactic acid cycle

Pyruvic acid
High Pyruvate could mean that the pathway to form Acetyl-Co-A is inhibited. This could be caused by mutations or a deficiency in cofactors such as vitamins B1, B2, B3, and B7. Magnesium deficiency could also pay a role in high levels of pyruvic acid. Patients that are consuming a high amount of carbohydrates could also have high amounts of pyruvate in their urine.

Low Levels of pyruvate could indicate that the patient is ingesting a low carbohydrate diet (44).

L-Lactic acid
High Lactate can occur when the body produces energy through anaerobic respiration. This often happens when tissues are deprived of oxygen. This can occur from excessive exercise but can also occur from toxins such as mycotoxins (45).

2,4-dihyroxybutanoic acid
Elevations in this marker could indicate early development of Alzheimer's disease. Elevations are often caused by cerebral hypoxia which are distinctly linked to Alzheimer's disease, brain tumors, or normal pressure hydrocephalus (46, 47).

Metabolism & Mitochondrial Markers

Fatty acid metabolism

Suberic acid
Elevated levels could indicate ketosis undergoing in the body (48).

Ethylmalonate
Elevated levels could indicate glutaric aciduria type II with B-ketothiolase deficiency when seen with excessive amounts of other organic acids such as dicarboxylic acids (49).

3-Hydroxybutyric
One of three ketone bodies which are produced by ketosis. This process can be triggered by fasting, diabetes, or alcoholism (50).

Acetoacetic
Elevations in urine indicate the body is using fat for energy which could be the result of a ketogenic diet. Symptoms associated with high levels include: increased thirst, increased urination, fatigue, fruity-smelling breath, and confusion (51).

Methylsuccinic
Elevated levels could indicate glutaric aciduria type II with B-ketothiolase deficiency when seen with excessive amounts of other organic acids such as dicarboxylic acids (49).

Sebacic
Elevations in urine indicate the body is using fat for energy which could be the result of a ketogenic diet. Symptoms associated with high levels include: increased thirst, increased urination, fatigue, fruity-smelling breath, and confusion (51) .

Nutrition and Oxalates

Nutrients

Xanthurenic acid
Xanthurenic is a product of the kynurenine pathway which is one of the routes of tryptophan catabolism. When B6 is low xanthurenate could build up in the body and be excreted in urine. Conditions that are correlated with high xanthurenate include inflammatory diseases and immune suppression (52).

4-Pyridoxic (B6)
Correlated with B6 intake. Low values could indicate the patient is deficient in B6 (53).

Pantothenic (B5)
Pantothenic, which is also known as B5, is an essential vitamin. It is found in some foods and is vital in the synthesis of coenzyme A (CoA) (54).

Glutaric (B2)
Produced from the breakdown of both lysine and tryptophan. Elevations could indicate an insufficiency of B2. Very large buildups could indicate a rare organic aciduria. This is caused by deficiency of glutaryl-CoA dehydrogenase (55).

Formiminoglutamic acid (FIGLU)
Elevated levels of FIGLU could indicate folate, vitamin B12, or a rare genetic disorder FTD deficiency (56).

Methylmalonic (MMA)
High values of MMA could indicate B12 deficiency. Patients taking B12 typically lowers MMA (57).

Pyrimidine metabolites

Uracil
Elevated urinary uracil concentrations are characteristic of genetic deficiencies of enzymes catalyzing the first two steps of the pyrimidine degradative pathway (58).

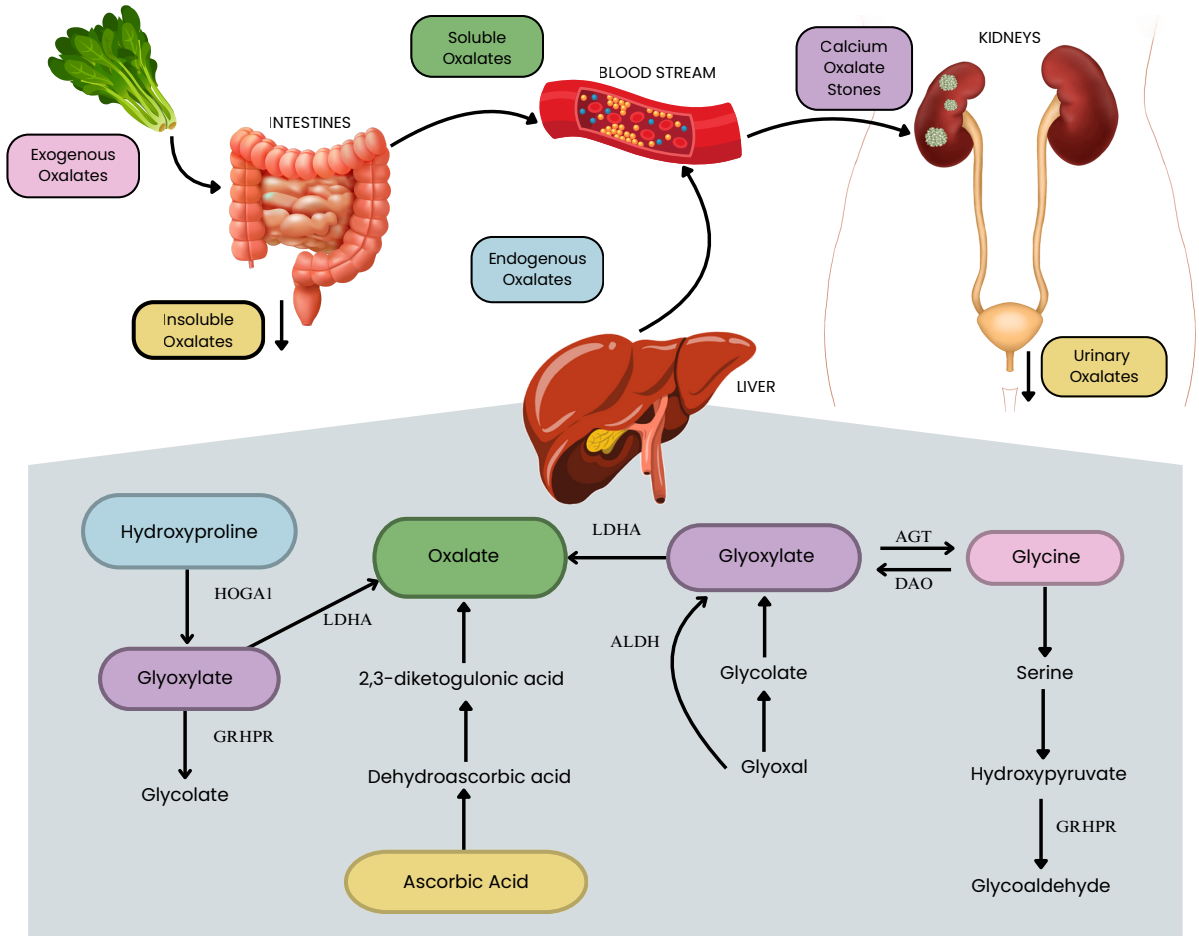
Thymine
In patients with pyrimidine degradation defects thymine can increase in several different body fluids. This can cause neurological issues because of built up toxicity (59).

Oxalates

Oxalic
Oxalate elevations can come from three different areas. The most common is from diet. Many leafy greens and fruits are high in oxalates. The second is from yeast and other microbiota that form oxalates in the gut. The third reason for buildup are genetic polymorphisms that could lead to enzymes that are less efficient at clearing out oxalates. This would potentially also lead to buildups in glycolic and glyceric (60, 61).

Glycolic
Glycolic acid is a metabolite of the oxalate pathway. Deficiencies in either enzyme efficiency or inadequate amounts of B6 could lead to a buildup of glycolic acid. When seen in tandem with high oxalic acid, this could indicate a genetic predisposition to oxalate buildup (62). It could also indicate a predisposition to forming primary hyperoxaluria I (63).

Glyceric
Glyceric acid is a metabolite of the oxalate pathway. When seen in tandem with high oxalate it could indicate a genetic predisposition to oxalate buildup. Could indicate a predisposition to form the disease primary hyperoxaluria II (63).



Inborn errors of metabolism

3-Methylglutaconic
Large buildups of this intermediate could indicate the patient has 3-MGA-uria type I. This is caused by the disruption of the metabolism of leucine (64).

2-Oxoisovaleric
Increased in patients with mutations in enzymes that are involved in the metabolism of branched chain amino acids. These include the amino acids leucine, isoleucine, and valine (65).

Malonic
Malonic acidemia is an inherited condition in which the body is unable to break down certain proteins.

2-Oxoisocaproic
Elevated in ketoacidosis and acquired organic acidurias in newborns (66). Is elevated in patients with propionic acidemias (67).

2-Oxo-4-methiolbutyric acid
Elevated levels may indicate an inborn error of methione metabolism. This can occur due to a number of genetic diseases such as SAH and MTHFRD.

3-Hydroxy-3-Methylglutaric (CoQ10)
Patients with elevations in this marker cannot produce ketone bodies. They are unable to break down certain proteins (68). High levels may reflect inadequate endogenous synthesis of CoQ10. CoQ10 may help prevent heart ailments, inhibition of LDL oxidation, and progression of atherosclerosis (69).

Mandelic
Elevated with patients with inborn error of metabolism. Patients with an elevated amount could be at risk of developing PKU.

3-Phenyllactic
Elevated in patients with inborn error of metabolism. Patients with an elevated amount could be at risk of developing PKU.

Homogentisic
Elevated in people at risk for alkaptonuria.

Nutrition and Oxalates

Inborn errors of metabolism

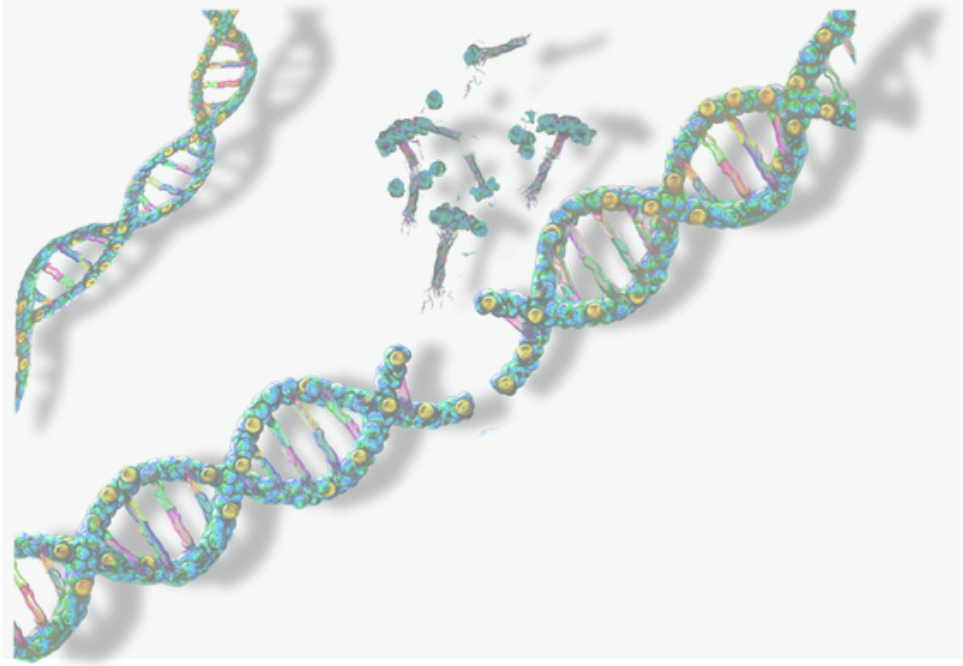
Orotic acid
Orotic acid is an intermediate in the pyrimidine biosynthetic pathway. Excessive excretion could indicate the presence of inborn errors of the urea cycle. Disorders involving arginine metabolism could also lead to high amounts of orotate in the urine (70).

4-Hydroxybutyric
High levels may be indicative of succinic semialdehyde dehydrogenase deficiency. Patients with this disorder typically have values 100-3000 times the normal range. Catheter use can lead to the increase of this marker (71).

2-Hydroxyisovaleric
Minor elevations could be caused by ketoacidosis. Larger elevations could be indicative of patients with dihydrolipoyl dehydrogenase (E3) deficiency (72).

2-Hydroxyisocaproic
Extremely elevated values could indicate metabolic disorders such as maple syrup urine disease. This disorder usually is diagnosed in early childhood (73).

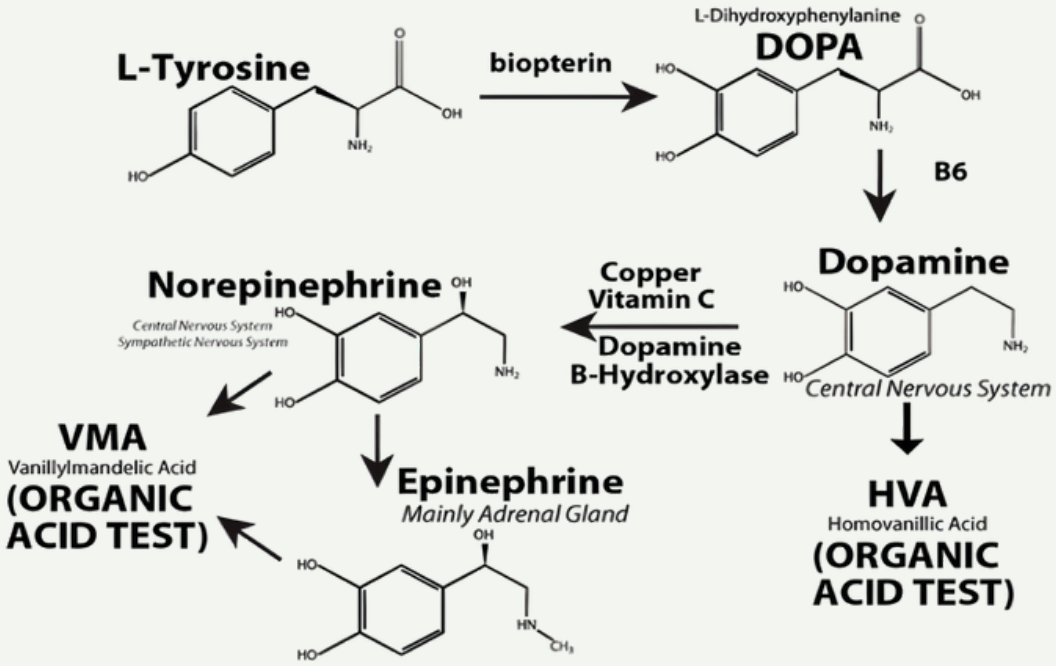
3-Methyl-2-oxovaleric
Used in the diagnosis of cobalamin deficiency (not enough B12) or maple syrup urine disease (74).



Neurotransmitter markers

Homovanilate (HVA)
Dopamine metabolite that can increase with stress or deficiency of dopamine conversion to epinephrine. Could also result in the taking of L DOPA (75).

Vanilmandelate (VMA)
A metabolite of epinephrine and norepinephrine. Can show up low in urine samples if patients have a copper deficiency, enzyme deficiency, or inhibition from pathogenic bacterial metabolites in the gut (76).



HVA/VMA ratio
This ratio indicates how well dopamine is converted to epinephrine. A high ratio is seen in people with copper deficiencies, mutations to enzymes, or inhibitions to the enzymes by toxins.

5-Hydroxyindoleacetate (5-HIAA)
5-Hydroxyindoleacetate (5-HIAA) is a metabolite of serotonin. Exercise, certain foods and medications may increase 5-HIAA levels. Other medications can also decrease 5-HIAA.

Supplements such as Tryptophan and 5-HTP can increase 5-HIAA levels (77).

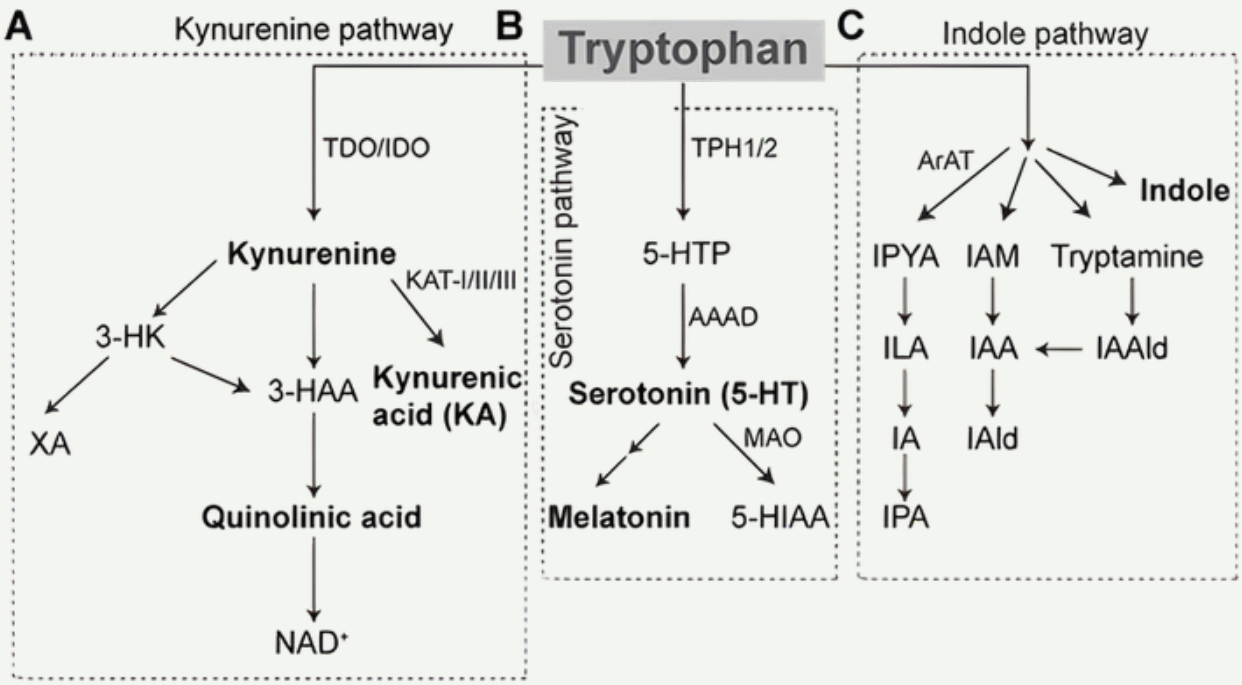
Neurotransmitter Markers

Neurotransmitter markers

Kynurenic acid
A metabolite of tryptophan. Kynurenic acid has some neuroprotective properties in the brain. It has the ability to stimulate NMDA receptors (78).

Quinolinic acid
A metabolite of tryptophan, can be both inflammatory and neurotoxic. Quinolinate can lead to neuronal dysfunction and cell death, by over-exciting NMDA receptors. It also activates resident microglia and macrophages. Elevations can be caused by B6 deficiency (79).

Kynurenic acid / Quinolinic acid ratio
High value in this ratio could indicate that tryptophan is being metabolized through the kynurenine pathway rather than the serotonin pathway (80). Higher values have been seen in patients with depression (81).



Miscellaneous metabolism marker

Creatinine
Most individuals' creatinine excretion is inverse to their hydration status. Patients with low urinary creatinine are well hydrated, while patients with high creatinine are not well hydrated. Patients with kidney ailments may have high creatinine values independent of hydration status (82).

METABOLIC INSIGHTS PROFILE

NEXT GENERATION ORGANIC ACIDS

CONTACT INFORMATION

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SCAN FOR MORE INFORMATION

SAMPLE REPORT

COLLECTION INSTRUCTIONS

COLLECTION INSTRUCTIONS VIDEO

KBMO'S MIP CAN HELP IN IDENTIFYING:

- Microbiome Imbalances
- Fungal Colonization
- Malnutrition
- Autoimmune Diseases
- Metabolic Disorders
- Detoxification Processes
- PANS / PANDAS
- Neurological Disorders
- Memory Retention
- Depression /Anxiety
- Cardiovascular Disease
- Oxidative Stress
- Energy Production
- ... and much more

SAMPLE INFORMATION

Requirements: 5 ml first morning urine

Turn around time: 7-10 business days

Reporting method: Practitioner's portal, interactive report, printable PDF

KBMO Diagnostics is scientist developed and owned, and committed to providing the highest quality testing services to ensure your patients receive the best care possible.

KBMO DIAGNOSTICS