Investigating Metabolite-Diet Relationships to Diagnose Nutrient Deficiencies

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Abstract

Calcium deficiencies threaten bone health in adults and proper development in growing children; furthermore, they contribute to the risk of diseases including osteoporosis and hypocalcemia. Recognizing dietary calcium deficiencies is important to addressing calcium shortages in toddlers and the elderly in Asia, however, studies have shown that current health monitoring methods for calcium intake are inefficient; personal monitoring methods are often incorrect and professional methods are often sparse and unavailable to many. Problems with recall include mislabeling, inaccurate measurements, and ethnic diets; for example, in some countries, milk is watered down. Comparing dietary tests to individuals' dietary recall showed that dietary patterns identified by the former were up to 38% more inaccurate. Through literature review, it is seen that urine tests which measure the health of an individual's diet through metabolites can make calcium intake monitoring more efficient and available to the masses, therefore preventing calcium deficiencies. Metabolites in urine are the waste byproducts of foods that are "metabolized" by the body. Results from a US cohort reveal that a general test measuring multiple metabolites can accurately relay health patterns. The mapped metabolic activity of bioanalytical markers can give insight into nutrient intake such as calcium. With such testing made available to the masses, calcium deficiencies can be addressed with appropriate prevention and intervention strategies. Beyond testing for calcium deficiencies, metabolite testing can help diagnose and treat an array of diseases; for example, modified testing can help monitor diets of those afflicted by diabetes via glucose metabolite tracking. However, current impediments include economic concerns such as mass production and pricing, as well as further human trials.

Case Study Comparison of Recommended and Average Calcium Intakes in Adults

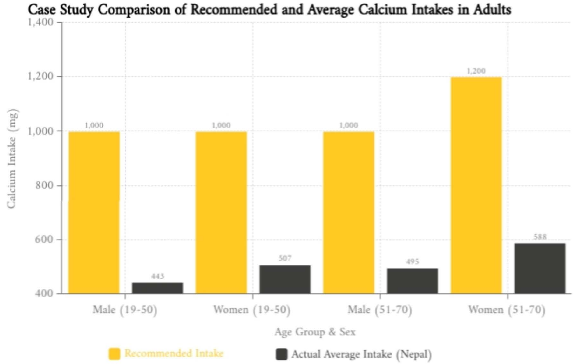

Figure 1: Graph comparing recommended daily calcium intakes from the NIH and actual daily calcium intakes collected from FFQs (Food Frequency Questionnaires) in Nepal. Compiled from NIH ODC & Balk, E. M., et al (2017).

Conclusions

- Many biomarkers have been identified using metabolites; each are associated with the consumption of fruits, vegetables, and other foods. For example, proline and betaine were identified as biomarkers of citrus intake to monitor various phytochemicals. Applied mass spectrometry or NMR (nuclear magnetic resonance) in blood plasma and urine are used to extract metabolite profiles
- These metabolite profiles are unique to each individual and can give insight into a person's diet. Citrate and formate have been found in higher concentrations in urine produced by diets high in calcium. Testing for these can reveal calcium deficiencies in diets.
- Urinary spectroscopic characterization objectively captures the end-products of metabolism, therefore overcoming the problem of reporting bias in dietary records. The characterization is easily scalable as the H-NMR spectrum can measure hundreds of metabolites in a mere five minutes.
- The individual metabolomic profiles produced by these tests findings suggest that these urinary metabolic profiles can be used as an objective measure to classify people's dietary patterns. In tests, for each nutrient-metabolite association, the variable with the most significant correlation was recorded (the higher the peak, the higher the occurrence and vice versa as depicted in figure 2).
- 24-hour recall compared to 24-hour urine testing revealed that urine testing produced a more accurate phenotype of dietary intake testing over 60 nutrients.

Future Directions

- Current impediments to making such testing available to the masses include economic concerns such as mass production and viable pricing. Spectrometry is required to analyse urine. Therefore, although a more efficient and personalized testing option, metabolome profiles still require a central testing location. In order to address this, further testing is required.
- Beyond testing for calcium deficiencies, metabolite testing can help diagnose and treat an array of diseases; for example, modified testing can help monitor diets of those afflicted by diabetes via glucose metabolite tracking.
- Current test results need to be modified so it is easier for patients to comprehend and monitor diet.

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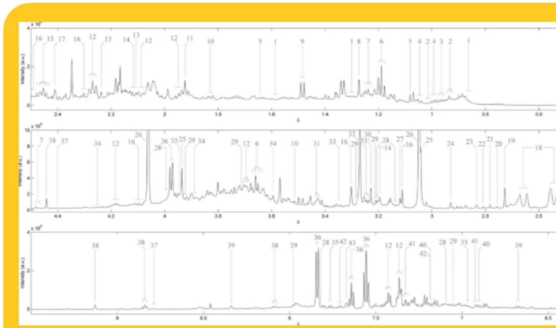

Figure 2: 600 MHz 1H-NMR spectra of human urine depicting quantities of different metabolites. From Posma, J. M., et al (2020).

1 – fatty acids (C5-C10)
2 – pantothenate
3 – isoleucine
4 – leucine
5 – valine
6 – 2-hydroxy-2-(4-methylcyclohex-3-en-1-yl)propoxyglucuronide
7 – ethanol
8 – ethyl glucuronide
9 – 3-hydroxyisovalerate
10 – alanine
11 – unknown 1
12 – acetate
13 – phenylacetylglutamine
14 – glutamine
15 – O-acetylcarnitine
16 – acetone
17 – proline betaine
18 – succinate
19 – citrate
20 – dimethylamine
21 – S-methyl-cysteine-sulfoxide metabolite
22 – N-acetyl-S-methyl-cysteine-sulfoxide
23 – S-methyl-cysteine-sulfoxide metabolite
24 – S-methyl-cysteine-sulfoxide
25 – dimethylglycine
26 – creatine
27 – creatinine
28 – N6,N6,N6-trimethyllysine
29 – histidine
30 – 1-methylhistidine
31 – carnitine
32 – taurine
33 – trimethylamine-N-oxide
34 – 4-hydroxyproline betaine
35 – unknown 2
36 – 4-hydroxyhippurate
37 – hippurate
38 – N-methylpyridinium
39 – N-methylnicotinate
40 – N-methylnicotinamide
41 – N-methyl-2-pyridone-5-carboxamide
42 – tyrosine
43 – 3-hydroxymandelate
44 – 2-furoylglycine
45 – pseudouridine
46 – formate.

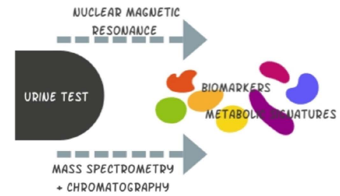

Figure 3: Metabolite-Diet Relationship Process. Metabolic signatures and biomarkers found in urine can give insight into dietary patterns. Testing can reveal different metabolic signatures via nuclear magnetic resonance or mass spectrometry paired with chromatography (example: Figure 2). Figure designed from Posma, J. M., et al (2020); Guasch-Ferre, M., et al (2018).

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