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Biomarkers of Nutritional Exposure and Nutritional Status in Animals

Pathak S. and Roupesh G.
Nagpur Veterinary College, Nagpur, Maharashtra Animal Fishery Science University, Nagpur
*Corresponding Author: pathaksanket187@gmail.com

Abstract

The emerging public health importance of zinc and selenium and the continuing public health challenges of iron and iodine draw attention to the unmet need for improved biomarkers of trace element status. Currently available biomarkers of these four trace elements are critiqued including the outstanding lack of satisfactory biomarkers for the assessment of zinc intake and status. Other trace elements are reviewed briefly including copper, for which human dietary deficiencies and excesses have been documented, and chromium, which is of possible but unconfirmed public health significance. Evolving strategies of considerable potential include molecular techniques such as the measurement of metallothionein mRNA in lymphocytes as a biomarker of zinc status, an assay that can now be performed with a dried blood spot. The judicious application of tracer techniques also has a role in advancing the quality of zinc biomarkers. Also of special current interest is full definition of the potential of plasma-soluble transferrin receptor concentrations as the biomarker of choice for the detection of early functional iron deficiency.

Introduction

The framework for evolutionary change is variations in physical, physiological, and behavioural features (Kendall, 2009). Causes of individual variation might be extrinsic (such as cultural and environmental factors) or intrinsic (such as genotypic). Expectations of how a species will react to ecological and environmental stimuli may be more accurate if individual variation sources are understood Smiley *et al.*, 2022.

Though variation among individuals is may be well known that gastrointestinal (GI) functionality affects the overall health and wellbeing of animals (Celi et al., 2019, Ziese and Suchodolski, 2021). It also affects fecal characteristics such as consistency and odor, which has an important impact on evaluation of commercial diets. This has prompted an increase in nutritionists' and scientists' interest in this topic: in particular, they want to better understand how ingredients, food additives, and food processing may a. Celi *et al.* (2019) proposed six major domains related to GI functionality: diet, effective digestion and absorption, normal and stable microbiota, effective immune status, gut mucosa, and the neuroendocrine and motor functions of the gut. Of these domains, the gut microbiota and its metabolites have been demonstrated to be potential biomarkers of GI functionality for many species, including dogs. However, considering the complexity of the interactions that occur in the GI tract, individual variations, interactions among dietary components, and variations in analytical methods, it is still a challenge to validate concise biomarkers of GI functionality. Furthermore, in companion animals, most of these potential biomarkers are evaluated in feces because it is easier collected and non-invasive; however, this method leads to greater variation, and thus all such potential biomarkers may not be necessarily good predictors of what happens in the gut.

Diet

The growth and operation of the gastrointestinal tract, including its immune system and the microbiota can be modulated by the composition of the diet (ingredients, nutrients, and additives). It is true that dietary variables can affect inflammation by modifying pro- and anti-inflammatory pathways (Broom and Kogut, 2018). These include a variety of antinutrients that can damage the gut's structural and functional integrity including fiber in the diet, trypsin inhibitors, phytate, lectins, undigested protein in the distal gastrointestinal system, mycotoxins, and many more (Celi et al., 2019). Another important factor in immunonutrition should be included in making up of the diet. In order to improve animal health, welfare and productivity nutrients such macronutrients, vitamins, minerals, and trace elements can be used to modulate the inflammatory response during nutritional and environmental challenges and diseases. A growing amount of research indicates that dietary antioxidant supplements can help cattle and poultry's redox balance. Based on various varieties of diets the most important biomarkers are vitamin and mineral biomarkers. Some of the researchers have also found that anti-oxidants at certain proportion can also act as biomarkers.

Vitamin Biomarker

Various biomarkers that are used to assess nutrient intake from food, non-nutritive food ingredients, or dietary patterns. One such is the nitrogen in urine, which functions as a biomarker for protein consumption. These kinds of biomarkers are quite interesting since their application can enhance the classification of participants based on their exposure to specific nutrients. In intervention studies examining the health impacts of dietary alterations, they also function as an objective measure of adherence to a certain diet plan [Combs, 2015]. The plasma concentration of alkyl resorcinol is thought to be a biomarker of the intake of whole grains, and the combination of sucrose or fructose with erythronic acid is a urinary biomarker for sugar intake [Clarke *et al.*, 2020]. These biomarkers may not only reflect a single nutrient but may also be linked to a dietary pattern or food group. Additionally, biomarkers for soy or soy-based food intake include urine/plasma genistein and daidzein. However, there is currently a dearth of reliable data about markers for other legumes. In this sense a combination of markers may better reflect a food category, for example vitamin C and carotenoids together may be more accurate that either of these fruit and vegetable biomarkers alone (Woodside et al; 2017]. Biomarkers of effects. These are biomarkers that are related to a target function or biological response. Thus, not only do they reflect intake but also nutrient metabolism and, possibly, effects on physiological or disease processes.

Trace organic chemicals need to consume through diet to sustain healthy physiological processes (Martini *et al.*, 2020). Vitamin A (retinol), vitamin B9 (folate), vitamin B12 (cobalamin), and vitamin D were well-established in epidemiological studies. Vitamin A affects cell expression through attaching to the transcription factor p300. Vitamin B is essential for cell metabolism because it is incorporated into CoA. The folate cycle begins with dietary folate being transformed into dihydrofolate (DHF). 5-MTHF to regenerate methionine from homocysteine (Hcy), which is processed by methionine synthase (MS) requires B12 as a cofactor in the form of methyl cobalamin. Vitamin D is bound by vitamin D receptor (VDR), which enhances its translocation into the nucleus.

Table 1: Various vitamin biomarkers in animal nutrition (Woodside et. Al., 2017)

Nutritional biomarker	Sample type	Potential Mechanism
Vitamin A	Serum	Pro inflammatory and inflammatory imbalances
RBP	Blood	Acute phase response is responsible for reduction in vitamin A
Vitamin D (25-(OH)D)	Serum	Stimulates the expression of PDL1 and PDL2 suppressing T cell
Vitamin D (25-(OH)D)	Serum	Activated vitamin D is an inhibitor of RAAS
Folate	Serum	Folate deficiency affects homocysteine level and impaired DNA repair
Vitamin B12 and Folate	Serum	Prevents impaired immune function

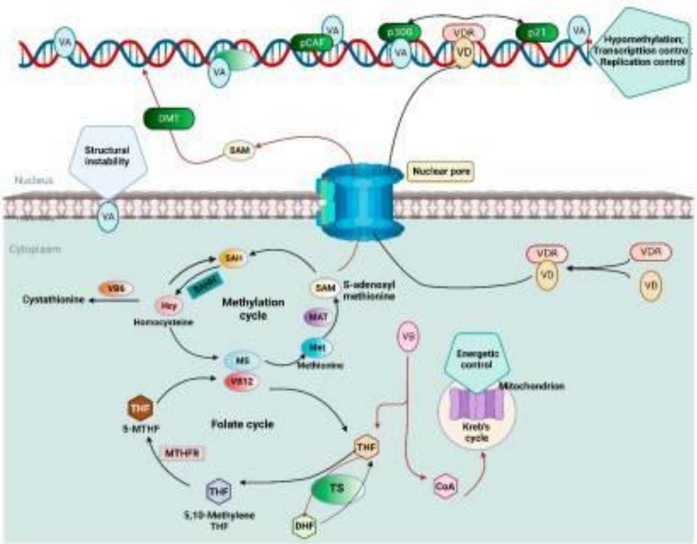

Fig. 1 Schematic representation of Vitamin Biomarker in nutrition (Perera et. al., 2022)

Mineral Biomarker in nutrition

Mineral homeostasis and metabolism

To appreciate the potential value of excretion data and other parameters of mineral homeostasis as biomarkers of intake and status, it is helpful to review, at an organ or system level, the differences in mechanisms by which trace mineral homeostasis is maintained (Table 1).

Iron

Dietary iron as a biomarker is unavailable because of the wide variation in bioavailability. In contrast, a range of biomarkers is available that in combination allows for reliable assessment of iron status. Plasma/serum ferritin is the most sensitive indicator of iron stores. In adults, each 1 mg ferritin/L plasma is proportional to;8 mg of storage iron.

Zinc

Zinc is certainly not unique among the trace minerals for the paucity of adequate biomarkers. As the global public health importance of zinc deficiency has attracted increasing attention during the past decade

zinc has been generally regarded as not readily depleted, although low levels have been reported with some epletion studies (Pereira *et al* 2021) and further evaluation is required. Red cell membrane zinc, in contrast, may be sensitive to zinc depletion in dogs.

Selenium

The quality of biomarkers of dietary intake of selenium and selenium status is quite favorable relative to that of most trace minerals. These biomarkers are in increasing demand principally because of the antioxidant role of this micromineral (Hall et al., 2014).

Copper

Plasma copper and ceruloplasmin levels are the most frequently used biomarkers of copper status. Hepatic synthesis of ceruloplasmin depends on an adequate supply of copper. A high percentage of the copper circulating in plasma is bound to ceruloplasmin.

Ceruloplasmin is an acute phase reactant and is elevated during infections, inflammatory processes and other stress circumstances. No reduction in levels of plasma copper or ceruloplasmin occurred in postmenopausal women that were fed a marginally low (0.57 mg copper/d) copper diet for .3 mo (Chamber *et al*., 2010)

Molybdenum

Apparent human molybdenum deficiency has been reported with Crohn's disease who was on long-term intravenous nutrition (Tallkvist, J., & Oskarsson, A. 2015). Biomarkers for molybdenum deficiency are decreased urinary levels of sulfate and uric acid with elevated sulfite, hypoxanthine and xanthine.

Table 2: Mineral biomarker in animal nutrition

Iron	Serum	Increasing hepcidin activity by inflammation in heart failure
Ferritin/ Creatinine	Urine	Inflammation can stimulate the proliferation and activation of monocyte phagocytic function
Iodine	Urine and Serum	Altered thyroid hormone homeostasis
Zinc	Serum/plasma	Effect on the immune system

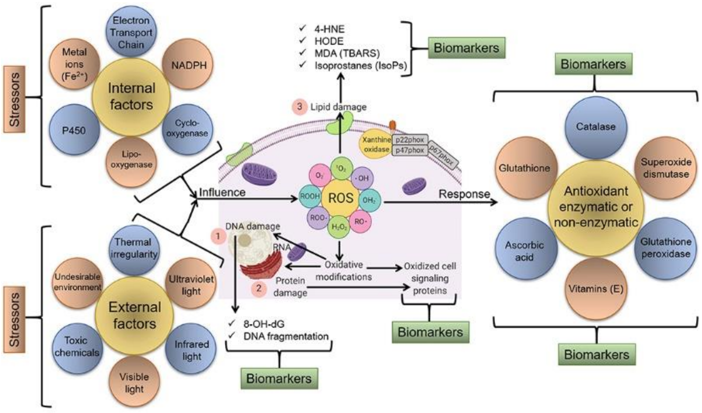

Fig. 2 Oxidative stress on ROS (Dhama et. al., 2019)

References

Celi, P., Verlhac, V., Calvo, E. P., Schmeisser, J., & Kluenter, A. M. (2019). Biomarkers of gastrointestinal functionality in animal nutrition and health. *Animal Feed Science and Technology*, *250*, 9-31.

Chambers, A., Krewski, D., Birkett, N., Plunkett, L., Hertzberg, R., Danzeisen, R., & Slob, W. (2010). An exposure-response curve for copper excess and deficiency. *Journal of Toxicology and Environmental Health, Part B*, *13*(7-8), 546-578.

Chan, L. N., & Mike, L. A. (2014). The science and practice of micronutrient supplementations in nutritional anemia: An evidence-based review. *Journal of Parenteral and Enteral Nutrition*, *38*(6), 656-672.

Clarke, E. D., Rollo, M. E., Pezdirc, K., Collins, C. E., & Haslam, R. L. (2020). Urinary biomarkers of dietary intake: a review. *Nutrition Reviews*, *78*(5), 364-381.

Combs Jr, G. F. (2015). Biomarkers of selenium status. *Nutrients*, *7*(4), 2209-2236.

Dhama, K., Latheef, S. K., Dadar, M., Samad, H. A., Munjal, A., Khandia, R., & Joshi, S. K. (2019). Biomarkers in stress related diseases/disorders: diagnostic, prognostic, and therapeutic values. *Frontiers in molecular biosciences*, *6*, 465402.

Kendall, M., Batterham, M., Obied, H., Prenzler, P. D., Ryan, D., & Robards, K. (2009). Zero effect of multiple dosage of olive leaf supplements on urinary biomarkers of oxidative stress in healthy humans. *Nutrition*, *25*(3), 270-280.

Love, S. T., Di Bona, K. R., Sinha, S. H., McAdory, D., Skinner, B. R., Rasco, J. F., & Vincent, J. B. (2013). Urinary chromium excretion in response to an insulin challenge is not a biomarker for chromium status. *Biological trace element research*, *152*, 57-65.

Martini, L., Pecoraro, L., Salvottini, C., Piacentini, G., Atkinson, R., & Pietrobelli, A. (2020). Appropriate and inappropriate vitamin supplementation in children. *Journal of nutritional science*, *9*, e20.

Pereira, A. M., Maia, M. R., Fonseca, A. J. M., & Cabrita, A. R. J. (2021). Zinc in dog nutrition, health and disease: a review. *Animals*, *11*(4), 978.

Smiley, R. A., LaSharr, T. N., Abernathy, H. N., Shakeri, Y. N., Levine, R. L., Rankins, S. T., Monteith, K. L. (2022). Biomarkers of animal nutrition: From seasonal to lifetime indicators of environmental conditions. *Life*, *12*(3), 375.

Tallkvist, J., & Oskarsson, A. (2015). Molybdenum. In *Handbook on the Toxicology of Metals* (pp. 1077-1089). Academic Press.

Woodside, J. V., McCall, D., McGartland, C., & Young, I. S. (2017). Micronutrients: dietary intake v. supplement use. *Proceedings of the Nutrition Society*, *64*(4), 543-553.

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