The Linoleic Acid: Dihomo-γ- Linolenic Acid Ratio (LA:DGLA)- An Emerging Biomarker of Zn Status

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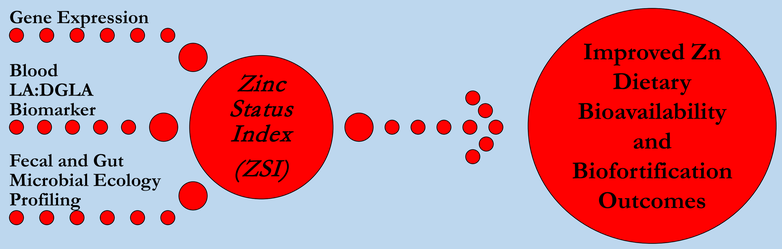
Zinc (Zn) deficiency is a common aliment predicted to affect 17% of the world's population. Zinc is a vital micronutrient used for over 300 enzymatic reactions and multiple biochemical and structural processes in the body. Although whole blood, plasma, and urine zinc decrease in severe zinc deficiency, accurate assessment of zinc status, especially in mild to moderate deficiency, is difficult, as studies with these biomarkers are often contradictory and inconsistent. Hence, as suggested by the World Health Organization, sensitive and specific biological markers of zinc status are still needed.
Here, we provide evidence to demonstrate that the LA:DGLA ratio (linoleic acid: dihomo--linolenic acid ratio) may be a useful additional indicator for assessing Zn status more precisely.

"The need to develop additional robust indicators of zinc status and to further expand the already known clinical markers, for which limited data of reliability exists, is evident" (World Health Organization, 2015).



The Strategy - Development of Zinc Status Index (Tako, 2017)

Research Approach:

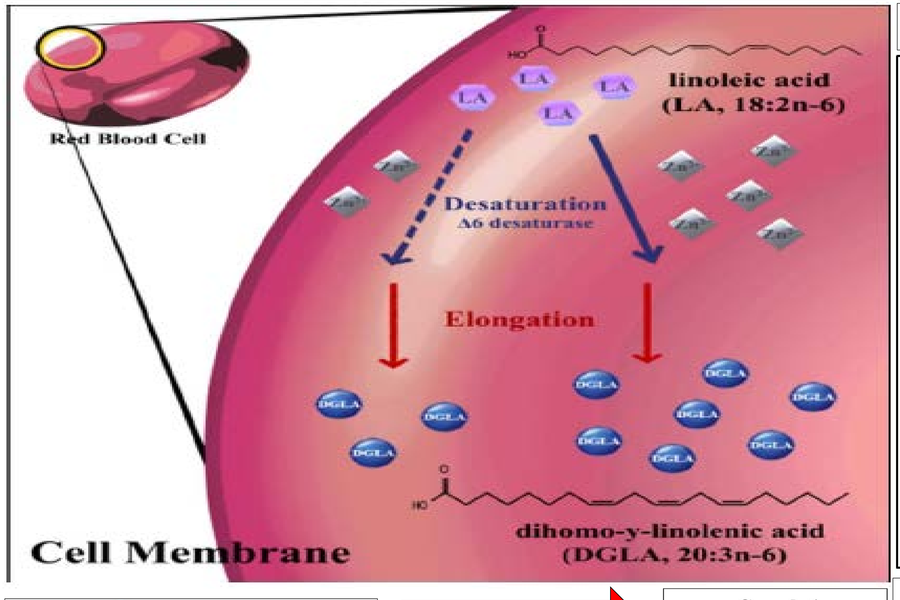
Step 1: LA:DGLA ratio as a potential reactive biomarker of zinc status in vivo (*Gallus gallus*)

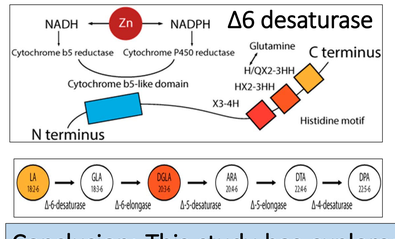
Step 2: LA:DGLA ratio as a reactive biomarker of zinc status in humans

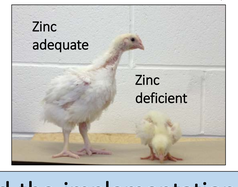
Step 3: LA:DGLA ratio as a biomarker to assess zinc bioavailability in zinc biofortified staple food crops

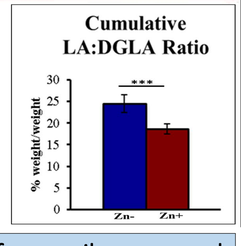
Step 1: Confirmation of LA:DGLA ratio as a reactive biomarker of zinc status *in vivo* (*Gallus gallus*)

Dietary Zinc Deficiency Affects Blood Linoleic Acid: Dihomo-γ- linoileic Acid (LA:DGLA) Ratio; a Sensitive Physiology Marker of Zinc Status in Vivo (Gallus gallus)
Reed S, Qin X, Ran-Ressler R, Brenna JT, Glahn RP, and Tako E.
Nutrients. 2014 Mar 20;6(3):1164-80. doi: 10.3390/nu6031164.







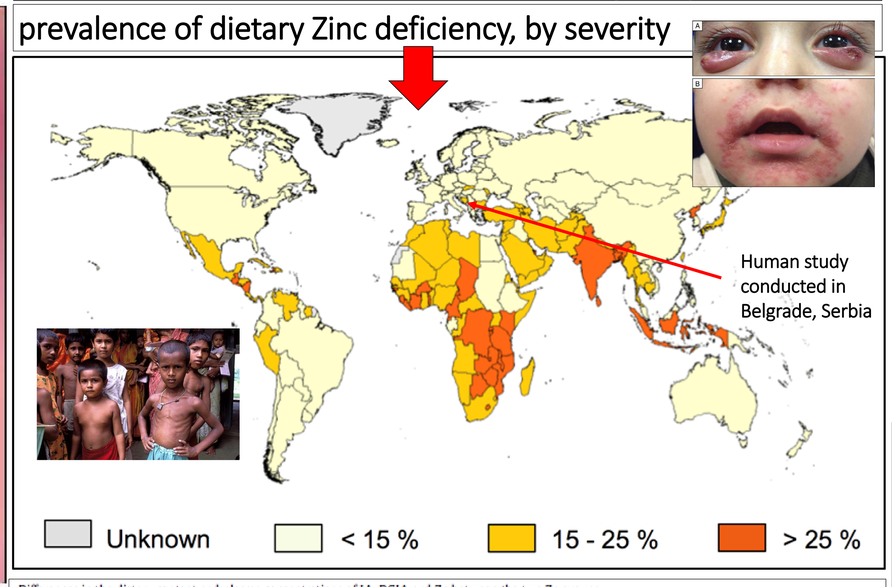


Conclusion: This study has explored the implementation of an easily measured, potential zinc biomarker pertaining to erythrocyte fatty acid composition, the LA:DGLA ratio. These data confirm the responsiveness of the erythrocyte LA:DGLA ratio to dietary zinc manipulation. Among a panel of purported zinc biomarkers, this ratio appears to be sensitive to dietary zinc depletion between bird groups over time.

Step 2: Confirmation of LA:DGLA ratio as a reactive biomarker of zinc status in humans

An initial evaluation of newly proposed biomarker of zinc status in humans- Linoleic Acid: Dihomo-γ- linoileic Acid (LA:DGLA) Ratio
Knez M, Stangoulis J, Zec M, Pavlovic Z,. Martacic J, and Tako E.
Micronutrient Forum 2016,, Cancun, Mexico ;
Clin Nutr ESPEN. 2016 Oct;15:85-92. doi: 10.1016/j.clnesp.2016.06.013

prevalence of dietary Zinc deficiency, by severity



Differences in the dietary content and plasma concentrations of LA, DGLA and Zn between the two Zn groups.

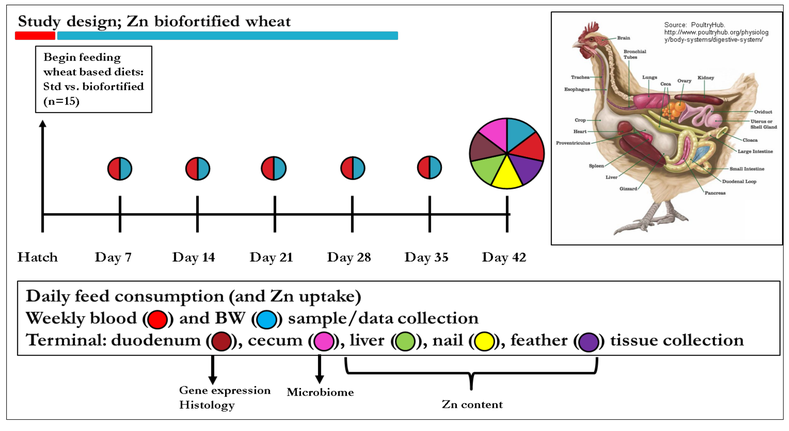
	Group 1 (n = 27)	Group 2 (n = 27)	Significance (2-tailed)
Dietary Zn (mg)	7.01 ± 0.52	12.78 ± 1.54	0.001*
Dietary LA (g)	17.54 ± 3.54	19.75 ± 2.78	0.650
Dietary PUFA (g)	12.61 ± 2.86	12.15 ± 2.17	0.755
Plasma Zn (mg/L)	1.02 ± 0.03	1.07 ± 0.03	0.283
LA (%)	24.01 ± 0.49	24.15 ± 0.54	0.528
DGLA (%)	2.61 ± 0.12	3.14 ± 0.14	0.004*
LA/DGLA	9.53 ± 0.43	8.21 ± 0.47	0.040*

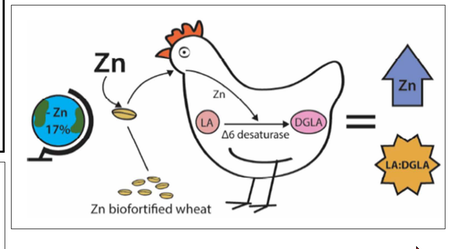
Dietary Zn–Zn content of the diets based on three 24 h recall questionnaires n = 54; 27 in each of the group. LA – linoleic acid; DGLA – dihomo-gamma-linolenic acid; PUFA – poly-unsaturated fatty acid. Values presented are means ± SE (standard errors). *p < 0.05 is considered statistically significant.

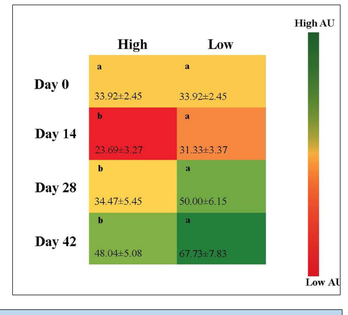
Conclusion: The study correlates Zn related indices with fatty acids and various biochemical, anthropometrical and hematological parameters. This initial study confirms that LA:DGLA ratio responds to dietary Zn manipulations. The study provided new information related to the link between plasma Zn, fatty acid status and dietary Zn intake. In conclusion, additional dietary intervention trials are needed to investigate the efficacy of newfangled biomarker of Zn status fully.

Step 3: LA:DGLA ratio as a biomarker to assess zinc bioavailability in zinc biofortified staple food crops

The linoleic acid: dihomo-γ-linolenic acid ratio predicts the efficacy of Zn biofortified wheat in chicken (Gallus gallus)
Knez M, Tako E, Glahn RP, Kolba N, de Courcy E, Stangoulis J.
J Agric Food Chem. 2018 Jan 23. doi: 10.1021/acs.jafc.7b04905







LA:DGLA (%) Ratio

Conclusion: This study demonstrated that the increased amount of Zn in the biofortified wheat produced a higher dietary bioavailability of Zn and therefore enhanced uptake of Zn by the intestinal enterocytes.. This shows the potential of Zn biofortified wheat varieties in improving the Zn status of consumers. The LA:DGLA ratio responded to dietary Zn manipulations and the consumption of the Zn biofortified wheat lowered the LA:DGLA ratio. Hence, these observations suggest that the LA:DGLA ratio can be utilized as an additional physiological indicator of Zn status.