

## ***Bioavailability and Bioactivity of NutraLac®***

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### **Definition and Results from the Lactating Mothers and Breastfed Infants Study in Guatemala**

#### **Definition**

Bioavailability relates to the rate and extent to which a nutrient or pharmacological isolate reaches the site of action within the body (the gastrointestinal absorption rate) to achieve efficacy. Most vitamins and minerals consumed orally are inorganic in nature and subsequently, have low rates of gastrointestinal absorption. Natural nutritional supplements possessing high levels of bioavailable phytonutrients and phytochemicals characteristically have high rates of gastrointestinal absorption and are subsequently more bioactive and efficacious for mitigating specific health conditions.

NutraLac® is comprised of a complex of all-natural vitamin, mineral, and antioxidant isolates (nutraceutical phytonutrients) extracted from the bran and germ layers of rice which possess high pharmacological values, thus making NutraLac highly bioavailable and efficacious in the human gastrointestinal tract once enzymatically hydrolyzed using our Nutra-Iso® proprietary technology (ref. USPTO Patent Number 8,945,642 B2). NutraLac embodies naturally occurring phospholipids, phytosterols, tocotrienols and tocopherols that have been scientifically documented in playing important roles in mitigating certain chronic health conditions.

#### **SUMMARY OF NUTRALAC NUTRITIONAL SUPPLEMENTATION FOR LACTATING MOTHERS AND THEIR BREASTFED INFANTS**

Infant chronic malnutrition affects 1 out of every 2 children under 5 years of age in Guatemala and over 165 million children worldwide. The nutritional impact of NutraLac®, a rice bran extract formulation (85%) supplemented with 7 natural vitamins and minerals (15%) to comply with World Health Organization (WHO) standards, was evaluated on lactating mothers (LM) and their exclusively breastfed infants (BI). The nutritional supplement (in a beverage presentation) was consumed daily by LMs living in rural villages of the municipality of Comapa, in the Eastern Department of Jutiapa, republic of Guatemala in Central America. The nutritional intervention window had a duration of 4.5 months, starting when the BIs were approximately 40-45 days old until the age of 6 months, at the end of the exclusive breastfeeding period. Determining the nutritional impact of NutraLac on lactating mothers was one objective of this study, and adequate baseline weight data can only be obtained after the mother's uterus has returned to normal size (post-puerperium) and they have regained their normal pre-pregnancy weight. This regeneration period is known as puerperium and lasts approximately 40 days. The nutritional impact of NutraLac on the BIs was determined by length, weight, and cephalic perimeter measurements, transformed to Z- scores and compared to WHO growth indicators and reference curves. The five growth indicators measured included: (1) weight-for-length (ZWL), (2) weight-for-age (ZWA), (3) length-for-age (ZLA), (4) cephalic perimeter-for-age (ZCPA) and (5) body mass

index-for-age (ZBMIA). In LMs the nutritional impact was determined by BMI prior to consumption and at the end of the 4.5-month intervention period. Anemia prevalence among MLs was determined via micro-hematocrit test before and at finalization of the nutritional window.

Prior to the intervention at 1.5 months old, 43% of BIs were chronically malnourished and 7.2% suffered from moderate or severe acute malnutrition, while 25% and 18.4% showed delayed cerebral growth (ZCPA) and moderate or severe thinness (ZBMIA), respectively. At the end of the consumption period, no acute malnutrition was detected among the BI participants. Statistical analysis with student "T" test for independent samples determined that a highly significant improvement was observed among BIs in the ZWL, ZWA and ZBMIA growth indicators at the end of the consumption window. A statistically significant improvement ( $p \leq 0.05$ ) was observed in ZCPA, while ZLA exhibited only a slight improvement.

No statistically significant differences were found between BMIs exhibited by LMs before and at the end of the nutritional intervention; however, the prevalence of anemia was reduced from 21.2% to 11.4% among participants. LMs also showed a statistically significant ( $p \leq 0.05$ ) increase in their micro-hematocrit results and important increases in their breast milk production. Subsequent trials have shown that NutraLac provided to the LMs immediately prior to birth, and throughout the breastfeeding period, significantly enhances their milk production to benefit neonate nutritional health and wellness. This result is particularly important for neonates born prematurely whose LMs have low levels of breast milk at the time of birth (nearly 10% of all births in the United States alone). In conclusion, NutraLac provided a significant nutritional contribution to both mothers and infants, when consumed daily by LMs during the exclusive breastfeeding period. Since rice bran is present in almost all developing countries in the world, NutraLac has a potentially global impact when our innovative rice bran stabilization and enzymatic hydrolyzation technology is incorporated into worldwide chronic malnutrition mitigation and prevention programs. In its natural state rice bran is not readily digestible in the human intestinal tract, and it is our NutraLac formulations and technology (Nutra-Iso®) that achieve the bioavailability of the phytonutrients embodied in the bran and germ layers of rice. (ref. the attached Patent for Humanity Award)

#### **DISCUSSION ON BIOACTIVITY AND BIOAVAILABILITY**

Results show a statistically significant improvement in the exclusively breastfed infants' nutritional status during the intervention window. Since maternal milk (MM) represented the sole food source that these infants received during the nutritional intervention period, the improved growth exhibited by the BIs was a direct result of either an increased consumption of MM, increased quality in the composition of the MM or a combination of both factors. The only significant change in the mothers' diets was the daily addition of the NutraLac supplement, as determined by 24-hour dietary recall interviews and food frequency surveys among LMs. The claim that NutraLac consumption resulted in increased MM production is further supported by the evidence provided by the lactating mothers in follow-up interviews at the clinic. As a result of NutraLac, they were able to increase the daily frequency and length of time at which their infants could breastfeed. These results show increased galactopoietics and are clear evidence of NutraLac's bioavailability and bioactive efficacy.

As Table 1 shows, statistically significant improvement in the nutritional status of the participating BIs was initially detected in the weight-for-age results in the range between 30 days (Group 1) and 67 days (Group 2) into the intervention window. No significant difference in the nutritional status of BIs was detected during the first 30 days of the study. It is interesting to observe that in the second half of the intervention period (from day 67 to day 135) the overall weight-for-age mean continued to improve among the group of infants but not at a statistically significant pace. This is understandable because infants had reached a weight-for-age status that placed them within the normal limits of the international WHO growth standards.

Table 1. Summary of T student test results for weight among participating breastfed infants in the NutraLac® trials conducted in rural Eastern Guatemala, 2012- 2014. Infants were between 40 and 50 days old at the start of the nutritional intervention.

Weight measurement <sup>1</sup> (W)		WEIGHT-FOR-AGE GROWTH INDICATOR					T	p-value
		n(1)	n(2)	Mean(1)	Mean(2)	Mean(1)- Mean(2)		
Group (1)	Group (2)							
0	1	153	114	-1.6	-1.33	-0.27	-1.73	0.0846
0	2	153	128	-1.6	-0.94	-0.66	-4.41	<0.0001
0	3	153	124	-1.6	-0.89	-0.71	-4.98	<0.0001
0	4	153	129	-1.6	-0.78	-0.81	-5.85	<0.0001
1	2	114	128	-1.33	-0.94	-0.39	-2.55	0.0115
1	3	114	124	-1.33	-0.89	-0.44	-2.98	0.0032
1	4	114	129	-1.33	-0.78	-0.54	-3.8	0.0002
2	3	128	124	-0.94	-0.89	-0.05	-0.32	0.7488
2	4	128	129	-0.94	-0.78	-0.15	-1.1	0.2722
3	4	124	129	-0.89	-0.78	-0.11	-0.81	0.4163

1 Exclusively breast fed infants were measured five times during the nutritional intervention window. Weight 0 (W0) was the baseline measurement prior to consumption of Nutra-Iso™ by their mothers, W1 was at 30 days after the start of the nutritional intervention and W2, W3, W4 and W5 were weight measurements taken at days 67, 97 and 135 (final) of the nutritional window.

The results mentioned above correlate with the observations reported by the lactating mothers in terms of increased MM production, which by their own account was markedly noticeable somewhere within the first 20 to 30 days after having started the daily consumption of NutraLac®. Therefore, it is understandable that an increased nutritional status among BIs was detected approximately 30 days after the mothers were capable of increasing the frequency and duration of breastfeeding, given the increased MM production.

Similar results were obtained with the other 4 growth indicators, as Table 2 shows. With the exception of length-for-age, the 4 growth indicators showed an improvement throughout the duration of the nutritional study, but only statistically significant during the first half of the nutritional intervention window (Table 3).

Table 2. Descriptive statistics for growth indicators of infants participating in the NutraLac® clinical trials conducted in the dry corridor of Eastern Guatemala, 2012-2014.

Anthropometric Measurement	Growth Indicator	n	Z score			
			Mean	S.D.	Percentile	Median
0 (basal)	weight-for-length	153	0.17	1.3	56.75	0.32
2 (67 days)	weight-for-length	128	0.63	1.11	73.53	0.68
4 (135 days)	weight-for-length	129	0.53	0.99	70.19	0.46
0 (basal)	length-for-age	153	-1.9	1.21	2.87	-1.85
2 (67 days)	length-for-age	128	-1.72	1.25	4.27	-1.72
4 (135 days)	length-for-age	129	-1.76	1	3.92	-1.72
0 (basal)	cephalic perimeter-for-age	153	-1.3	1.14	9.68	-1.16
2 (67 days)	cephalic perimeter-for-age	124	-1.05	1.18	14.69	-1.14
4 (135 days)	cephalic perimeter-for-age	128	-1.02	0.91	15.39	-1.11
0 (basal)	body mass index-for-age	153	-0.82	1.33	20.61	-0.63
2 (67 days)	body mass index-for-age	128	0.14	1.14	55.57	0.13
4 (135 days)	body mass index-for-age	129	0.32	1.01	62.55	0.19

After running a T student test on these 4 growth indicators, it was clear that the main effect of the nutritional intervention with NutraLac came within the first 67 days of the trials (Table 3) as highly significant differences ( $p < 0.0001$ ) were found in the indicators weight-for-length, weight-for-age and Body mass index-for-age, whereas significant differences ( $p < 0.05$ ) were found in the cephalic perimeter for age indicator, during the same time window.

The last indicator (Cephalic perimeter for age) is an important result. Scientific studies have clearly documented that the size of the cerebral circumference is directly correlated with brain growth and development. The results obtained in this study regarding brain development support the results from other studies in which delays in brain development can be reversed through timely nutritional intervention.

The fact that LMs noticed an increased MM production within 20 to 30 days after the start of the intervention window seems to indicate that NutraLac was readily assimilated by the participating mothers. Since current guidelines recommend exclusive breastfeeding during the first 180 days into the life of infants, a supplement like NutraLac® which evidences enhancement of MM galactopoiesis (lactogenesis stage 3) would prove to be immensely valuable for nutritional programs worldwide, as current intervention guidelines for the initial 6 months of a child's life are entirely focused on exclusive breastfeeding and on the training of LMs in infant care and hygiene. While nutritional supplements that

benefit lactating mothers are indeed available, there is little information regarding the existence of bioactive nutritional supplements that directly benefit the nutritional status of both the mother and the breastfed infant.

*Table 3. Summary of T student test results for five growth indicators among breastfed infants in the NutraLac® trials conducted in rural Eastern Guatemala, 2012- 2014. Infants were between 40 and 50 days old at the start of the nutritional intervention.*

Growth indicator (z score)	Group 1	Group 2	n(1)	n(2)	Mean(1)	Mean(2)	Media(1) - Media(2)	T	p-value
weight for length	M0	M2	153	128	0.17	0.63	-0.46	-3.15	0.0018
weight for length	M0	M4	153	129	0.17	0.53	-0.36	-2.64	0.0087
weight for length	M2	M4	128	129	0.63	0.53	0.1	0.75	0.4549
length for age	M0	M2	153	128	-1.9	-1.72	-0.18	-1.25	0.2133
length for age	M0	M4	153	129	-1.9	-1.76	-0.14	-1.05	0.2926
length for age	M2	M4	128	129	-1.72	-1.76	0.04	0.32	0.7524
weight for age	M0	M2	153	128	-1.6	-0.94	-0.66	-4.41	<0.0001
weight for age	M0	M4	153	129	-1.6	-0.78	-0.81	-5.85	<0.0001
weight for age	M2	M4	128	129	-0.94	-0.78	-0.15	-1.1	0.2722
BMI <sup>1</sup> for age	M0	M2	153	128	-0.82	0.14	-0.96	-6.44	<0.0001
BMI for age	M0	M4	153	129	-0.82	0.32	-1.13	-8.12	<0.0001
BMI for age	M2	M4	128	129	0.14	0.32	-0.17	-1.29	0.199
CP <sup>2</sup> for age	M0	M2	153	124	-1.3	-1.05	-0.24	-1.73	0.0841
CP for age	M0	M4	153	128	-1.3	-1.02	-0.28	-2.26	0.0243
CP for age	M2	M4	124	128	-1.05	-1.02	-0.03	-0.26	0.7978

<sup>1</sup> BMI:body mass index, <sup>2</sup> CP:Cephalic perimeter. Exclusively breast fed infants were measured five times during the nutritional intervention window. Measurement 0 (M0) was the baseline measurement prior to consumption of Nutra-Iso™ by their mothers, while M2 and M4 were weight growth measurements taken at days 67 and 135 (final) of the nutritional window.

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# **Patent for Humanity Awarded to Intermark Partners Strategic Management for Nutra-Iso Nutrient Extraction Technology**

**Award Recipient:** Dr. Glenn H. Sullivan

**Award Presentation:** U.S. Senator Patrick Leahy and U.S. Department of Commerce Undersecretary Teresa Stanek Rea

The Nutra-Iso™ technology embodies a unique multiphase process that utilizes specific enzyme combinations under precise time and temperature conditions to optimally extract the bioactive phytonutrient isolates from rice bran and other cereal grains. This method achieves a significantly enhanced protein, carbohydrate, micronutrient, and antioxidant complex, thereby increasing the overall nutritional values of the derivative as a functional nutraceutical food ingredient for nutritional supplementation in chronically malnourished populations worldwide.

Rice bran is a by-product of the rice milling process and is exceptionally high in natural phytonutrients and phytochemicals which have been scientifically documented to have potentially significant health benefits when properly extracted, isolated and concentrated, thereby providing a sustainable and low-cost nutritional ingredient for meeting the needs of undernourished populations in nutrient deficit regions. Rice is the most widely produced cereal grain worldwide, with over 40 million tons of rice bran available annually for human nutrition when properly stabilized and the bioactive phytonutrients scientifically extracted to enhance bioavailability in the human gastrointestinal tract.

What was lacking in prior attempts to develop a commercially viable extraction process is that such attempts produced derivatives that were not competitive in their nutritional profiles when compared to commercially available substitutes like whole milk, whey and soy protein. Yet rice bran itself possesses a nutritional profile superior to these alternatives. The problem is that rice bran itself is not readily available for human consumption due to rapid enzyme oxidation activity that most often renders it to livestock feed, and the fact that rice bran is not readily digested in the human digestive system.

The Nutra-Iso technology overcomes this problem through strategically integrated enzyme, time, temperature, and centrifuging regimes that result in a commercially superior and nutrient-rich bioavailable extract for human consumption. It is this nutrient-rich extract that is being formulated into supplements for pregnant mothers, lactating mothers, and infants up to twenty-four months of age; a time when an infant's physical, mental, and metabolic processes are developed, and a life stage when chronic malnutrition can be remediated. Moreover, rice bran is hypoallergenic, gluten-free and low glycemic.

The Nutra-Iso™ formulations are currently being administered in Guatemala for a collaborative program with the Government of Guatemala to eradicate chronic malnutrition at an early stage in the life of infants, thereby enhancing the overall physical and socio-economic wellbeing of the population and reducing food welfare costs at the national level over time.

See [www.sustainable-nutrition-intl.org](http://www.sustainable-nutrition-intl.org); or contact Dr. Glenn H. Sullivan, Founding Member of Intermark Partners and Nutraceutical Technologies International at [gsullivan@ntiassoc.com](mailto:gsullivan@ntiassoc.com) or phone 317-815-5871.