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Shelf Life Determination of Foods for Special Medical Purposes (FSMP)

Position Paper – Tracers

Summary

- ISDI recommends using nutrients as tracers to determine the nutritional suitability of FSMPs over shelf life.
- Most nutrients (all minerals, all macronutrients, all fatty acids, total nucleotides, some vitamins and most of the amino acids) are stable in all conditions and should be excluded from shelf life tests.
- Shelf-life tests for FSMPs should only require a quantitative analysis of a limited number of identified nutrient markers or tracers (i.e. nutrients with higher rates of degradation during shelf life used as tracers or markers to indicate product nutritional suitability and product shelf life)
- The following nutrients as tracers or markers should be used:

PRODUCT	TRACER
Powder FSMPs	Vitamin A
Non acidified liquid and paste FSMPs	Vitamin C, thiamin (and vitamin D for extensively hydrolyzed protein products)
Acidified liquid and paste FSMPs	Vitamin C, pantothenic acid, folic acid, thiamine and vitamin D

Introduction

In 2019, following a literature review that emphasized the lack of relevant references and studies, the International Special Dietary Industry (ISDI) launched a multiyear project to develop guidance on shelf-life tests for Food for Special Medical Purpose (FSMP).

The major global manufacturers of FSMPs (Abbott, Fresenius, Nestlé Health Science, Nutricia, Reckitt) participated in the Stability Guidelines Task Force. Available stability data on FSMPs were gathered to be analysed and used to provide recommendations on which nutrients should be included in stability tests to determine the shelf-life of foods for special medical purposes[1].

The data collected comprised 32,798 data points and 1,471 datasets (or recipes) covering more than 70 nutrients. The datasets were categorized into 9 categories (physical state, temperature, humidity, pH of the product, level of protein hydrolysis, presence/absence of fat, adult vs infant

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FSMP, type of packaging and protective atmosphere) with 29 subcategories. For each nutrient, statistical analyses were performed to identify which factors among these 29 subcategories were responsible for losses and to which extent.

The recommendations applicable to FSMP would be the same for other Foods for Special Dietary Uses (FSDU) that are manufactured in a similar way, such as for example, infant formula or follow-up formula.

Results

Not all nutrients have the same susceptibility to, or rate of, degradation over shelf life. Temperature, light, oxygen, product pH, degree of protein hydrolysis and product moisture can, to differing extent, affect nutrient stability.

FSMPs typically contain a complex blend of macro- and micro-nutrients. However, the shelf life of FSMPs is primarily defined by the nutrients most prone to degradation. While most nutrients remain stable (Table 1) , other nutrients degrade over time and at different speeds (Table 2). In non-acidified liquid FSMPs, our study identified 3 nutrients that displayed losses much larger than the others. These 3 nutrients are by decreasing amplitude of losses: vitamin C, thiamin and vitamin D (losses only in products with hydrolyzed proteins). In acidified liquid FSMPs, 5 nutrients displayed losses much larger than the others. These nutrients are by decreasing amplitude of losses: pantothenic acid, vitamin C, folic acid, thiamin and vitamin D (losses only in products with intact proteins). In powder the only nutrient displaying losses was vitamin A.

From a nutritional perspective, it is these more labile nutrients that define and reduce the shelf life of FSMPs. Nutrients with higher rates of degradation during shelf life can therefore be used as tracers or markers to indicate product nutritional suitability and help define product shelf life. If the levels of these more unstable nutrients remain adequate at the end of shelf-life, the levels of the other more stable nutrients will be adequate too.

Conclusion

Typically, therefore, shelf life tests for FSMPs should only require a quantitative analysis of a limited number of identified nutrient tracers. Based on the available results from more than 1400 FSMP shelf-life tests conducted by industry and gathered to build this guidance, most nutrients - all minerals, all macronutrients, all fatty acids, total nucleotides, some vitamins and most of the amino acids - are stable in all conditions and should be excluded from shelf life tests.

ISDI recommends to limit the analyses of nutrient in FSMP shelf-life tests to the following most labile tracers or markers (see Table 2 for additional justification):

PRODUCT	TRACER
Powder FSMPs	Vitamin A

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Non acidified liquid and paste FSMPs	Vitamin C, thiamin (and vitamin D for extensively hydrolyzed protein products)
Acidified liquid and paste FSMPs	Vitamin C, pantothenic acid, folic acid, thiamine and vitamin D

Table 1: Lists of nutrients included in the study.

Nutrients in cell highlighted in grey showed no or minimal losses both in the main and complementary analyses. Nutrients in white cells showed losses either in the main analysis or in the complementary analysis or both.

Macronutrients	Minerals	Fatty acids	Amino acids	Vitamins	Other nutrients
Protein	Sodium	Linoleic Acid	Isoleucine	Vitamin A	Choline
Fat	Potassium	Alpha-Linolenic Acid	Leucine	Vitamin D	Inositol
Carbohydrates, Available	Chloride	Arachidonic Acid	Valine	Vitamin E	Carnitine
▪ **Total Sugars**	Calcium	Docosahexaenoic Acid	Lysine	Vitamin K	Taurine
▪ **Glucose**	Phosphorus	Erucic Acid	Methionine	Beta carotene	Total nucleotides
▪ **Lactose**	Magnesium	Eicosapentanoic acid	Phenylalanine	Biotin B7	
	Iron	Saturated fatty acids	Threonine	Niacin B3	
	Zinc	Monounsaturated fatty acids	Aspartic acid/asparagine*	Pantothenic Acid B5	
	Copper	Polyunsaturated fatty acids	Alanine	Riboflavin B2	
	Manganese		Arginine	Thiamin B1	
	Chromium		Glycine	Pyridoxine B6	
	Molybdenum		Proline	Vitamin C	

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Macronutrients	Minerals	Fatty acids	Amino acids	Vitamins	Other nutrients
	Selenium		Tyrosine	Folic acid B9	
	Iodine		Cystine	Cobalamin B12	
	Fluoride		Histidine		
			Tryptophan		
			Glutamic acid/glutamine**		
			Serine		

*Measured as aspartic acid
** Measured as glutamic acid

MB: Observed losses in amino acids, total sugars, glucose and lactose are likely due to Maillard reducing reactions 1, 2.

References:

1. S. Martins, W. Jongen, and M. van Boekel. 2000. A review of Maillard reaction in food and implications to kinetic modelling. Trends Food Sci. Technol. 11: 364-373. Doi:/10.1016/S0924-2244(01)00022-X.
2. M. Wang, X. Yuan, Y. Zheng, Z. Wu, H. Li, H. Li, and J. Yu. 2022. Maillard reaction indicators formation, changes and possible intake in infant formula produced by different thermal treatments during domestic use. Food Chem. 395: 133576.

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Table 2: Average percentage of degradation after one year in liquid FSMPs.

Nutrient	Non-acidified liquid FSMPs		Acidified liquid FSMPs	
	20°C	25/30°C	20°C	25/30°C
Vitamins				
Pantothenic acid (B5)	stable	-10%	-53%	-72%
Vitamin C[1)]	-20% (with flushing) -46% (no flushing)	-55% (with flushing) -65% (no flushing)	-35% (intact protein) -49% (amino acid based/hydr.)	Not enough data (intact protein) -68% (amino acid based)
Folic Acid (B9)	-11%	-16%	-35%	-56%
Thiamin (B1)	-20%	-50%	-20%	-50%
Vitamin D	Stable with intact proteins -33% (extensively hydrolysed proteins)		-28% (with intact proteins)	
Vitamin B12	-11%	-17%	-11%	-17%
Vitamin A	Stable	-15%	stable	
Amino acids				
Tryptophan	stable		-21%	-31%
Cysteine	stable		-20%	
Histidine	stable		-19%	
Sugars				
Glucose	-19%			
Lactose	-10%			
Total Sugars	-7%		-14%	

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Annex – Statistical Analysis

The full statistical analyses of the shared stability data were outsourced to SOCAR Research (SOCAR) a third party statistical provider. As part of this work, a specific statistical analysis was performed on the stability data of affiliated recipes. Affiliated recipes are recipes that only differ by a single parameter such as flavour or the absence or presence of fibre.

The impact of these specific single differences on the degradation rate of nutrients in the affiliated recipes was analysed using a three-level organizational model with a random slope nested by record ID (level 2) and Affiliated ID (level 3). The three-level organizational model enabled the grouping of the data available not only by record ID as the random effect but also by an upper affiliation ID nest.

The affiliation ID identified a group of records from the same recipe code and with the same characteristics related to physical state, age, fat content, type of protein hydrolysis, nitrogen flushed, pH, storage humidity, packaging type and packaging size and storage temperature. This analysis was performed for each nutrient and physical state (i.e. liquid, powder, paste) with sufficient data in at least 10 affiliation IDs. Only data for liquid recipes was used in the analysis of affiliated recipes due to the limited number of available data. This is not seen as an issue, since the main analysis had shown that powder products were generally stable and the only nutrient which was unstable was Vitamin A.

The goal of the analysis of the affiliated recipes was to show the equivalence on degradation rate for different values of the variable of interest. For example, to show equivalence on degradation rate across the different flavours. In order to show no effect of the variable of interest, the 95% confidence interval of the difference was compared with the stability limit (used as the equivalence margin). Nutrients were qualified as stable based on conservative limits. Nutrients were qualified as stable if the losses after one year were lower than 5% for macronutrients; less than 7.5% for fatty acids and less than 10% for vitamins & minerals, amino acids & nucleotides. In order to show equivalence, the 95% confidence interval must have been within the limit of the equivalence margin. In order to show a significantly relevant effect beyond the stability limits, the effect P value must be below 0,05 and the 95% confidence interval must exceed the limit of the equivalence margin.

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