Stabilization of fish oil emulsions rich in ω-3 for topical use

Mirian SANCHEZ [1] and Mariana LANDIN [1]

[1]*Department of Pharmacology, Pharmacy and Pharmaceutical Technology, I+D Pharma Group, Faculty of Pharmacy, University of Santiago de Compostela, Spain.*
e-mail : mirian.sanchez.fernandez@usc.es

Introduction and objetives

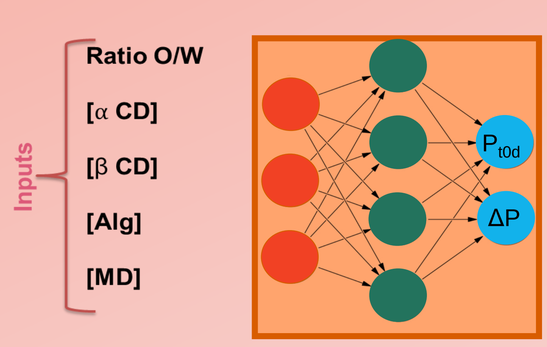
The use of fish oils is of great importance due to its high content of ω-3 fatty acids, substances that play a fundamental role as components of cell membranes in the brain, retina and other organs, being necessary for proper functioning [1]. This has generated interest in its incorporation into solid and semi-solid formulations, whose high contents in DHA and EPA (ω-3) would be suitable as nutraceuticals or therapeutic adjuvants. However, its development faces problems related to its stability, which leads to its oxidation and the production of highly volatile products [2] with a characteristic bad smell and taste.

The objective of this work is to evaluate the usefulness of the addition of cyclodextrins and other excipients in semi-solid systems containing fish oil, to modulate their stability and rheological characteristics [3].

Materials and methods

Materials:
Fish oil rich in ω-3 as an organic phase (O), provided by Biomega SL, was stored at 5°C. As the aqueous phase, solutions of alpha (αCD) and beta (βCD) cyclodextrins, maltodextrin (MD) and alginate (Alg) were used.

Methods:
- ✓ Balanced experimental design for 5 variables (DataForm® Software v3.1, Intelligensys Ltd, UK).
- ✓ Variables or inputs: Quanty of O, αCD, βCD, MD and Alg.
- ✓ Preparation of 18 semi-solid systems. Modeling the database using FormRules® v4.03.
- ✓ Characterization of the organoleptic and rheological properties through the use of PT & GC-MS and TA TX plus Texturometer.




TA TX plus Texturometer


PT & GC-MS

Results

Table 2. Inputs included by FormRules® for each output, together with the quality parameters (coefficient of determination (R^2) and statistical significance from the ANOVA results) for the models carried out using the results of freshly prepared formulations. α<0.05 indicates statistical significance of the model.

	Output	Submodel	Inputs FormRules®	R^2	α
P_0 days	Hardness	Submodel 1	O×αCD	91.60	<0.01
		Submodel 2	βCD		
	Adhesion	Submodel 1	βCD×MD	95.48	<0.01
		Submodel 2	O×αCD		
	Consistency	Submodel 1	O×αCD	87.42	<0.01
	1-penten-3-one	Submodel 1	O×αCD	94.67	<0.05
		Submodel 2	Alg.		
	Hexanal	Submodel 1	O×Alg.	75.32	<0.05
		Submodel 2	αCD		
	Heptanal	Submodel 1	O×Alg.	82.41	<0.05
	Octanal	Submodel 1	O×Alg×βCD	98.67	<0.19 (n.s)

Table 3. Inputs included by FormRules® for each output, together with the quality parameters of the models (coefficient of determination (R^2) and statistical significance from the ANOVA results) for the models stored at 40ºC. α<0.05 indicates statistical significance of the model.

	Output	Submodels	Inputs FormRules®	R^2	α
ΔP	ΔHardness	Submodel 1	O×αCD	91.40	<0.01
		Submodel 2	βCD		
	ΔAdhesion	Submodel 1	βCD×MD	78.51	<0.01
		Submodel 2	O		
	ΔConsistency	Submodel 1	O×αCD	71.06	<0.01
	Δ1-penten-3-one	Submodel 1	O×βCD	95.94	n.s
		Submodel 2	αCD × MD		
	ΔHexanal	Submodel 1	O×MD	71.78	<0.01
	ΔHeptanal	Submodel 1	O×βCD	95.92	<0.05
		Submodel 2	βCD ×MD		
		Submodel 3	αCD		
	ΔOctanal	Submodel 1	O×MD	72.97	<0.05
	Δ(*E*,*E*)-2,4-heptadienal	Submodel 1	O×MD	71.02	<0.05
		Submodel 2	αCD		

Discussion

Fresh formulations: The predictability of the models is over 70% and the models are statistically significant (α<0.05), except for the octanal and the (*E, E*)-2,4-heptadienal.

➢O/W, CDs and MD condition the texturometric properties of semi-solids systems. O and Alg condition the volatiles elimination.

The rules **IF… THEN…** obtained by FormRules® we can state that:

➢High proportions of O and αCD give highest values texturometric properties of fresh formulations.

➢Alg reduced the release of volatile compounds and facilitates large quantities of oil.

➢αCD modulates:1-penten-3-one and hexanal, βCD reduces the octanal.

Formulations stored at 40ºC: The predictability of the models are high but not all statistically significant.

➢O/W, CDs and MD condition the texturometric properties and volatiles elimination.

The rules **IF… THEN…** obtained by FormRules® allow us to state that:

➢Smallest variations in texturometry occur with high incorporation of CDs and a reduced incorporation of MD.

➢Both CDs reduced the release of 1-penten-3-one, (*E, E*)-2,4-Heptadienal and Heptanal.

➢Low proportion of MD modulates the release of volatile compounds such as Heptanal, Octanal and (*E, E*)-2,4-Heptadienal.

➢Alg does not contribute to the reduction of volatiles in stored formulations.

Conclusions

✓The emulsification of fish oils with alginate dispersion give rise to creams of suitable texturometric properties to be used on the skin.

✓Alpha and beta CDs modulate the texturometric properties of the emulsions together with the evaporation of volatiles related to the degradation of fatty acids, reducing them in both, fresh and stored formulations. This suggests that both CDs incorporate the fatty acid chains in their hydrophobic cavity, reducing their degradation and thus correcting their characteristic bad smell.

✓The generated knowledge allows to select the composition of semisolid systems of adequate rheological and organoleptic properties to produce prototypes based on fish oil for different applications in skin pathologies.

References

[1] W. E. Connor, *Am. J. Clin. Nutr.*, *71*(1), 171S-175S, 2000.
[2] G. Venkateshwarlu, M. B. Let, A. S Meyer, C. Jacobsen, *J. Agric. Food Chem.*, *52*(2), 311-317, 2004.
[3] D. Duchêne, A. Bochot, S. C.Yu, C. Pépin, *Int. J. Pharm*. *266*(1-2), 85-90, 2003.

Financial support: V-A POCTEP Program Interreg España-Portugal (0302_CVMAR_I_1_P) EU, (FEDER).