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MODELIZATION OF THE EFFECTS OF A MIXTURE OF PRESERVATIVES IN A TOPICAL EMULSION

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Purpose :

Establishment and statistical validation of mathematical models allowing the modelization of the activity of preservatives within a topic preparation.

Methods :

The selected preparation is an emulsion containing 70% water, characterized by an Aw superior to 0.96 and a pH of 6,5. An experimental design D-optimal was adopted to select the concentration of preservatives to be studied in order to model the antimicrobial effect of the preservatives. The responses analyzed for these experiments were the survival of the germs of the challenge test according to European Pharmacopea.

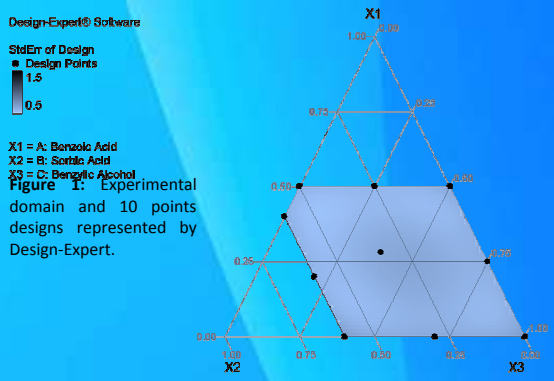

Figure 1: Experimental domain and 10 points designs represented by Design-Expert.

Table I: Criteria of acceptance for the preparations for local application according to the European Pharmacopeia

		Logarithmic reduction			
		D2	D7	D14	D28
Bacteria	A	2	3		NI
	B			3	NI
Fungus	A			2	NI
	B			1	NI

NI : no increase

Results :

Polynomial equation were established to model the efficacity of the selected preservatives. The validation of each model was made with the results of the Analysis of Variance (ANOVA). Initially the statistical analysis defined that six of the eleven adopted models were statistically significant. An optimization of the significance was carried out with the assistance of the software Design-Expert. This step made it possible to make significant four additional models so ten of the eleven models were regarded as significant

Table II: Significativity of the results and Mathematical model retained

	Species	$F_{0,1}$	p	Significativity for alpha at 10%	Mathematical model	R-Squared (R2)
D2	*E. coli*	12,50	0,01	Significant	Quadratic	0,94
	S. aureus *	3,70	0,08	Significant	Quadratic	0,64
D7	*E. coli*	5,40	0,06	Significant	Quadratic	0,87
	S. aureus *	5,38	0,04	Significant	Quadratic	0,73
	P. aeruginosa	3,50	0,09	Significant	Linear	0,50
D14	*E. coli* *	4,02	0,07	Significant	Quadratic	0,67
	S. aureus *	4,77	0,05	Significant	Quadratic	0,70
	P. aeruginosa	5,49	0,04	Significant	Linear	0,61
	C. albicans	3,97	0,07	Significant	Linear	0,53
	A. niger	14,03	0,03	Significant	Cubic	0,96

*: Significativity obtained after optimization

Exemple: The response of *A. niger* at D14 was expressed by cubic equations

$$A.niger_{D14} = -0{,}49X_1 + 7{,}77X_2 + 0{,}67X_3 - 15{,}45X_1X_2 + 1{,}36X_1X_3 - 9{,}32X_2X_3 + 63{,}94X_1X_2X_3$$

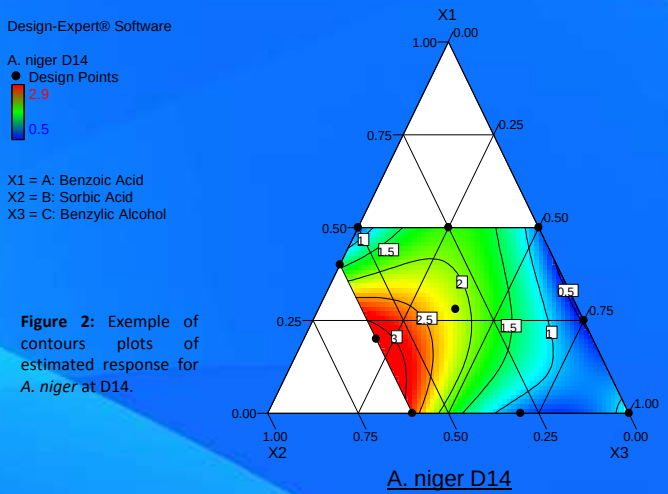

Figure 2: Exemple of contours plots of estimated response for *A. niger* at D14.

Conclusions :

The efficiency of preservatives within a topic preparation has been modelled by polynomial equations. The statistical significance of these models was optimized, thus improving their aptitude to predict the results of the preservative effect.

Références :

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