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Formulation and characterization of an O/W/O multiple emulsion with a sunscreen

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Introduction

Multiple emulsions are complex dispersion systems which have significant potential in pharmacy and cosmetics. In cosmetics, a high capacity of entrapment compared to other systems, the protection of fragile substances, the possibility of coexistence of two immiscible agents in the same product and the possibility of providing prolongation of drug release by including drugs in the innermost phase were reported.

The objective of this study was to formulate and characterize an $O_1/W/O_2$ multiple emulsion, of second order and three components, containing a sunscreen agent¸ 3-(4-methylbenzylidene)camphor¸ Eusolex 6300, an UVB filter). An optimization procedure was used in order to find the best preparation conditions for the multiple emulsions.

Experimental methods

Emulsion preparation
A two-step procedure was used to prepare the multiple emulsions.

Experimental Design.
Box Behnken experimental factorial plan with three factors and three levels.
Software**:** Modde 6 software, (Umetrics, Umea, Sweden).

Screening procedure.
In a previous study, a screening study for the preparation conditions for the O/W/O multiple emulsion was performed, using a Plackett-Burman fractional experimental design with nine variables and two levels The studied variable were: the homogenizer type, the stirring time for the first and second emulsification step, the stirring rate for the first and for the second emulsification step, the ratio of hydrophilic and lipophilic surfactant, the percent of lipophilic phase in the primary emulsion and the percent of aluminium stearate in the multiple emulsion. The responses variables were: the particle size and the polydispersion index (Y_2) for the internal oil drop drop, the particle size and the polydispersion index for the water drop and the viscosity of the multiple emulsions. The most important factors which influenced the emulsion drops size and homogeneity were the stirring rate for the primary and secondary emulsion and the concentration of lipophilic surfactant. These factors were selected for the

Emulsion characterization
***Microscopic analysis*. O**ptical microscope (Optika, Italy) with a videocamera (Optikam 3 digital camera). The droplet size was measured using the microscope software.

Optimization procedure

Table I . Variables

Formulation variables		Levels		
	Symbol	-1	0	+1
Stirring rate for first emulsification step	X_1	1000	3000	5000
Stirring rate for second emulsification step	X_2	500	850	1200
Ratio of lipophilic surfactant	X_3	1	3	5

Responses variables	Symbol
Particle size of water drops	Y_1
Polydispersion index for water drops (I.P.) =+/-	Y_2
Particle size of internal oil drops	Y_3
Polydispersion index for internal oil drops (I.P.) =+/-	Y4

Table I. Matrix of experimental design.

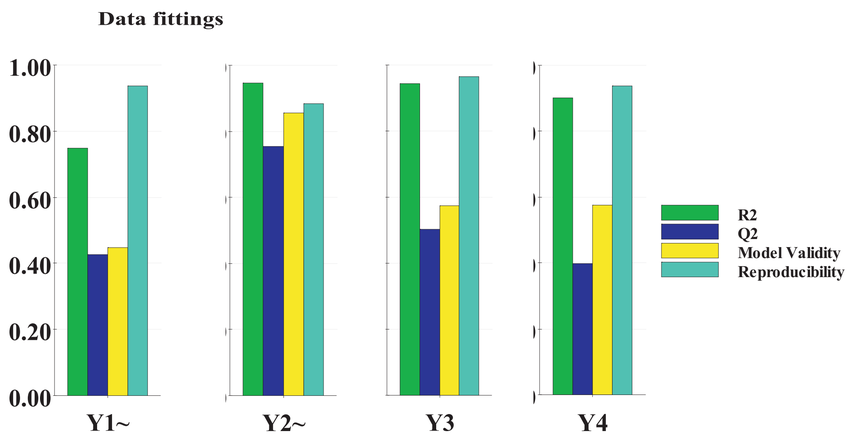
Exp. Name	X_1 (rpm)	X_2(rpm)	X_3(rpm)
N1	1000	500	3
N2	5000	500	3
N3	1000	1200	3
N4	5000	1200	3
N5	1000	850	1
N6	5000	850	1
N7	1000	850	5
N8	5000	850	5
N9	3000	500	1
N10	3000	1200	1
N11	3000	500	5
N12	3000	1200	5
N13	3000	850	3
N14	3000	850	3
N15	3000	850	3

Results

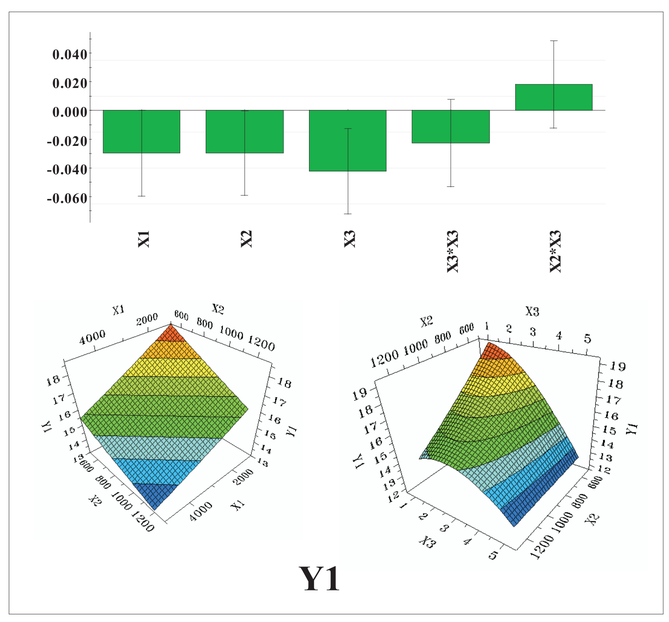
Experimental design analysis

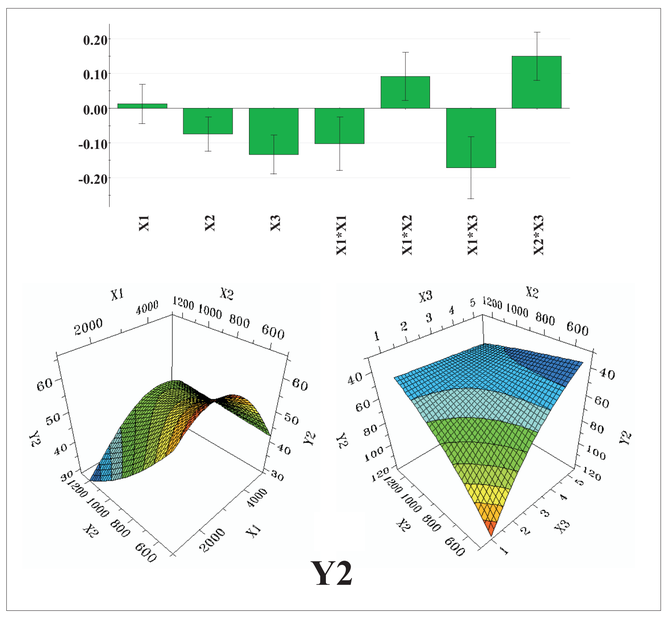
Table II. Matrix of studied responses

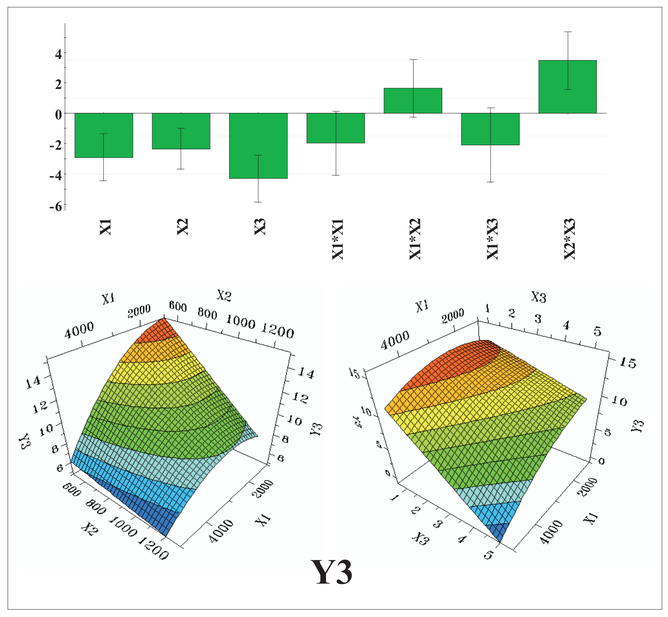
Exp.Name	Y1 (m)	Y2	Y3 (m)	Y4
N1	20.85	63.57	16.03	59.57
N2	14.19	41.64	5.08	31.53
N3	16.85	30.69	9.12	55.67
N4	11.93	46.58	4.76	41.54
N5	16.45	34.89	12.52	58.67
N6	17.76	86.28	12.73	79.08
N7	12.32	42.41	7.12	60.50
N8	14.61	48.20	9.43	76.52
N9	18.18	60.49	20.26	69.62
N10	13.82	46.36	7.54	56.01
N11	12.68	35.85	5.65	32.52
N12	12.90	49.04	6.81	60.13
N13	16.11	51.90	11.35	66.49
N14	16.14	53.53	10.65	67.61
N15	16.01	42.09	10.69	69.38

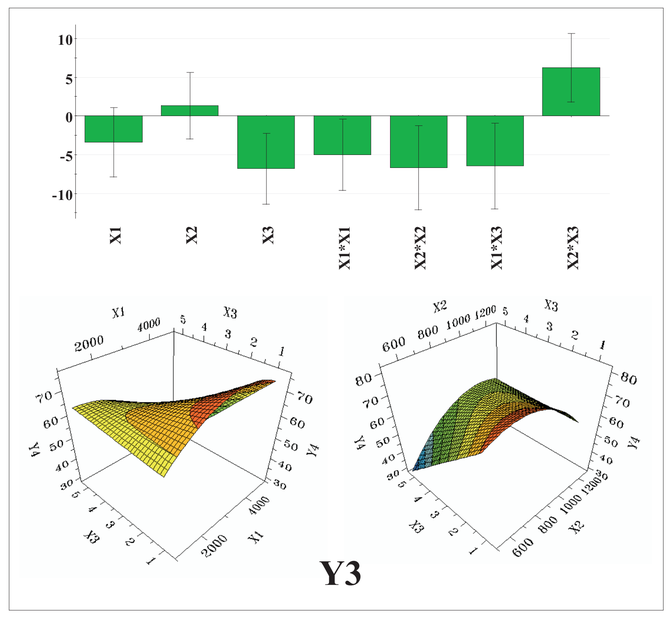


Formulation factor analysis









Optimal formulation		
Variables	Symbol	Value
Stirring rate primary emulsification step	X_1	4999.66
Stirring rate secondary emulsification step	X_2	501.383
Ratio lipophilic surfactant	X_3	4.9906

Responses for optimal forulation		Prevision	Obtained	± S.D.
Y_1	Particle size of water drops (Xa) =	10.8737	11.2349	3.44
Y_2	Polydispersion index for water drops (I.P.) =+/-	14.8486	17.5846	0.508
Y_3	Particle size of internal oil drops (Xa) =	1.9965	2.2531	0.2631
Y_4	Polydispersion index for internal oil drops (I.P.)=+/-	4.2296	4.8479	0.280

Conclusions

The optimal conditions for multiple emulsions preparation are obtained using a 5000 rpm value as stirring rate for the primary emulsification step, a 500 rpm value as stirring rate for the secondary emulsification step and using maximum value for the lipophilic surfactant. The responses obtained when studying the multiple emulsion founded optimal with this procedure were very close from those predicted by te model, thus the experimental plan is validated.