OPTIMIZATION OF THE N,N,N-TRIMETHYL CHITOSAN (TMC) SYNTHESIS BY FACTORIAL DESIGN

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Talking about chemical processes, words as chemiometry and optimization methods have become very common nowadays owing to the usefulness of the statistical tools in planning experiments [1]. One of these methods is the Factorial Design, largely used for optimization of synthetic routes. Particularly for chitosan, the factorial design was applied to study the processes of cupper ions adsorption [2]; the mechanical properties of films [3] and deacetylation [4]. Regarding chitosan derivatization, there is no published works. In this way, this work applies the factorial design in an attempt to optimize the synthesis of the TMC via dimethylsulfate (DMF) synthetic route [5]. The reaction sequence comprised a suspension of 1.0 g of chitosan (0.005 mol) in 16 cm^3 of DMF and 4 cm^3 of deionized water. Following, 1.2 g of NaOH (0.015 mol) and NaCl were added and the solution mixed over the desired times under magnetic stirrer. The factorial design was arranged for $\alpha = 3$ (temperature, time and NaCl addition) and b = 2 (25/50^{o}C; 3/6 hours and 0/0.44g), resulting in $2^3 = 8$ independent experiments, each done in duplicate. Finally, the TMC was submitted to dialysis in a cellophane membrane (cut-off ~13000 g/mol), precipitated with acetone and dried. The three analyzed responses were weight yield, solubility and degree of substitution (DQ). The factorial design analysis showed that high temperatures, extensive reaction times and presence of NaCl is the worse condition for the weight yield, taking in account the negative value for the global average (Table 1). Indeed, the temperature was the most unfavorable factor to weight yield (negative value for X(T) in Table 1 and normal distribution far from zero and distant from that linear pattern in Fig 1), followed by the reaction time, X(t), and salt addition, X(S). High temperature and presence of H^+ (as byproduct) fast the depolymerization, generating small chains that are washed out during the dialysis thus contributing to weight yield decreasing [5]. The others responses, solubility and DQ, showed similar trend (Table 1), allowing us to conclude that the temperature was the most critical factor influencing the weight yield, solubility and DQ while the NaCl addition was the less one.

Table 1. Statistical analysis for weight yield, solubility and DQ.

Responses	**W. yield**	**Solubility**	$\overline{DQ}$
Global aver.	-21.05	71	29.38
Main effects:			
X(T)	-54.52	-9.5	-7.25
X(t)	-9.84	2.0	4.75
X(S)	4.07	1.0	-1.75
2nd effects:			
X(Tt)	-13.46	-12.5	1.75
X(tS)	11.72	-4.0	-0.75
X(TS)	-6.23	-20.5	1.25
3rd effect:			
X(TtS)	7.79	11.5	9.25

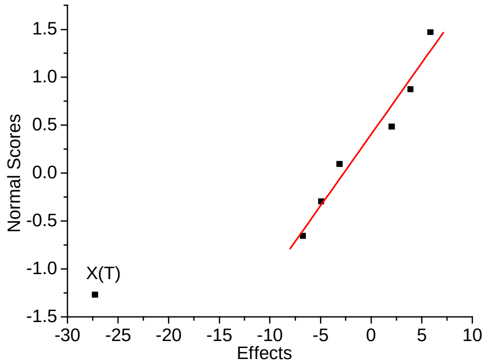

Fig. 1~~1~~. Normal probability versus effects estimative plot concerning the weight yield.

Low intrinsic viscosity and weight-average molecular weight (by GPC) values for TMC obtained at high temperature confirmed the degraded characters of such samples.

ACKNOWLEDGMENTS

The authors are grateful to EMBRAPA, FAPESP and CNPq for financial support, as well for the following researchers: Prof. Dr. José Fabian Schneider (IFSC-USP) and Prof. Dr. Antonio Gilberto Ferreira (DQ-UFSCar) for solid state NMR; Prof. Dra. Telma Teixeira Franco (FEQ-UNICAMP) for GPC and Prof. Dr. Paulo Sérgio Campana Filho (IQSC-USP) for viscosimetry.

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