Resumo: Um método "spot-test" qualitativo e seqüencialmente quantitativo é proposto para análise de dipirona em fármaco "puro" e em preparações farmacêuticas. A formação de coloração vermelho-violeta indica um resultado qualitativo positivo. Na seqüência, um procedimento quantitativo pode ser realizado no mesmo frasco. Os resultados quantitativos obtidos foram comparados estatisticamente com os resultados obtidos pelo método indicado pela Farmacopéia Brasileira, utilizando o teste ***t*** de Student e o teste ***F***. Considerando a concentração em uma alíquota de 100 µL, o limite qualitativo visual de detecção foi de cerca 5×10^{-6} g; instrumentalmente o limite de detecção foi de LOD $\cong$ 1.4×10^{-4} mol L^{-1} e o limite de quantificação de LOQ $\cong 4.5\times10^{-4}$ mol L^{-1}.

Palavras-chave: dipirona, spot-test, análise, qualitativa, quantitativa

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PRODUCTION OF BIODIESEL FROM BABASSU OIL USING METHANOL-ETHANOL BLENDS

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Abstract: Maranhão state in Brazil presents a big potential for the cultivation of several oleaginous species, such as babassu, soybean, castor oil plant, etc... These vegetable oils can be transformed into biodiesel by the transesterification reaction in an alkaline medium, using methanol or ethanol. The biodiesel production from a blend of these alcohols is a way of adding the technical and economical advantages of methanol to the environmental advantages of ethanol. The optimized alcohol blend was observed to be a methanol/ethanol volume ratio of 80 % MeOH: 20 % EtOH. The ester content was of 98.70 %, a value higher than the target of the ANP, 96.5 % (m/m), and the biodiesel mass yield was of 95.32 %. This biodiesel fulfills the specifications of moisture, specific gravity, kinematic viscosity and percentages of free alcohols (methanol plus ethanol) and free glycerin.

Keywords: Babassu oil, methanol, ethanol, methyl esters, ethyl esters.

I. Introduction

Babassu nut is the main product of the vegetal extractive activities in Maranhão state, Brazil, and one quarter of its territory is covered by such native palm tree (*Orbignya phalerata*). The activities related to the babassu nut generate about 300 thousand jobs, from the collect normally made by the "babassu breakers", up the oil refining [1,2].

Maranhão is the biggest producer of babassu nuts in Brazil. It is responsible for the production of almost 80% of the country output, corresponding to 120 thousand metric tons in the 2005 base year. [3]. The local industries produce about 60 thousand metric tons /year of babassu oil, being most of it transported to other Brazilian states [4].

Babassu oil displays a high percentage of saturated fatty acids, 91%, mainly composed of lauric acid (48%), myristic acid (16%), palmitic acid (10%), stearic acid (2%) and others (5%). It also presents 19% of unsaturated fatty acids, chiefly oleic (14%) and linoleic (5%) acids [5].

Maranhão is also the second biggest soybean producer in Northeastern Brazil, only behind Bahia state. In the 2006/2007 harvest, according to CONAB, the soybean production in Maranhão was of about 0.967 million metric tons, while the whole Brazilian output was of around 56.71 million metric tons [6].

Besides these two cultures, Maranhão displays a big potential for the cultivation of other oleaginous species (castor oil plant, cotton, tame nut, etc.), due to its weather conditions, geogra-

phic location and agricultural tradition. A big part of such production can be transformed in the biodiesel fuel.

Biodiesel is defined as a fuel composed of alkyl esters of long chain fatty acids, derived from vegetable oils or animal fats [7,8]. This fuel can be used in any diesel cycle engine, without the need of adaptations.

Owed to technical and economic reasons, the industries use more often methanol (MeOH) in the biodiesel production process. However, this alcohol presents several drawbacks, such as its high toxicity, being synthesized from non renewable sources, besides the fact that Brazil is not auto-sufficient in its production [9].

Although ethanol has a higher cost per ton, the biodiesel production by means of the ethanol route is attractive under the strategic standpoint, as Brazil is the biggest ethanol producer in the world. As for the environmental aspects, ethanol is not toxic and since it is produced from renewable sources, the whole biodiesel is 100% renewable [10,11].

One of the ways of combining the technical and economic advantages of methanol with the environmental advantages of ethanol is to obtain biodiesel from a blend of these alcohols. Therefore, the proposal of this work was the improvement of the transesterification process of degummed, neutralized and clarified babassu oil, using blends of different proportions of these alcohols with homogeneous catalysis [12].

II. Experimental

The reagents utilized were: commercial clarified babassu oil (OLEAMA), anhydrous ethanol (Petrobrás Distribuidora), methanol P.A. (Quimis) and potassium hydroxide 85 % (Quimis) as catalyst. The raw materials were analyzed following the Standard Methods for the Analysis of Oils, Fats and Derivatives (SMAOFD). For the characterization of the methyl/ethyl biodiesel from babassu were utilized the standards from the Brazilian Association of Technical Standards (ABNT) and the American Society for Testing and Materials (ASTM), indicated in the Resolution number 42 of the Brazilian National Petroleum Agency (ANP) [7].

In the experiments, were utilized a pHmeter Quimis model Q400M2, a mechanical stirrer and a gas chromatograph VARIAN CP 3800.

The procedure for the transesterification reaction starts by dissolving KOH in the methanol/ethanol blend, under stirring at room temperature. Next, add to this solution 100 g of oil under stirring and allow the reaction up to the phase separation. Remove the alcohol excess by distillation under reduced pressure. Transfer the mixture of esters and glycerin to a separatory funnel and allow settling for 12 hours. Afterwards, separate and weigh both phases and wash the biodiesel, using the air bubbling technique. For the first washing, utilize a 0.1 M HCl solution, followed by washings with water until reaching the pH 7.0. Dry the biodiesel in an oven at 100 ºC for 3 hours, allow cooling and weigh, for further physico-chemical tests.

III. Results and discussion

The best reaction conditions to obtain methyl and ethyl babassu biodiesel were determined by Silva and Brandão: oil/methanol molar ratio of 1:4.6, KOH content of 1.5 %, 30 min of reaction time, stirring of 1760 rpm and room temperature [13]. Using the methanol mass as reference, several MeOH:EtOH ratios were investigated, aiming at the optimization of the babassu oil transesterification process. Table 1 presents the percentages and volumes of the alcohols used in the babassu oil transesterification reactions.

Table 1. Methanol/ethanol proportions used for obtaining methyl/ethyl babassu biodiesel

METHANOL			ETHANOL		
% (v/v)	m (g)	V (mL)	% (v/v)	m (g)	V (mL)
100%	21.33	27.0	0%	0	0
90%	19.20	24.3	10%	2.13	2.7
80%	17.06	21.6	20%	4.26	5.4
70%	14.93	18.9	30%	6.39	8.1
60%	12.79	16.2	40%	8.53	10.8
50%	10.66	13.5	50%	11.66	13.5

In order to determine the best methanol/ethanol ratio, the process of spontaneous biodiesel/glycerin separation was analyzed. The produced biodiesel is composed of methyl and ethyl esters of the fatty acids that make up the babassu oil. In the chromatogram of Figure 1, it can be observed that there are two peaks derived from the same fatty acid. This occurs because one peak is obtained from the fatty acid reacting with methanol and the other peak reacting with ethanol. As they display different retention times, it is possible to detect them separately.

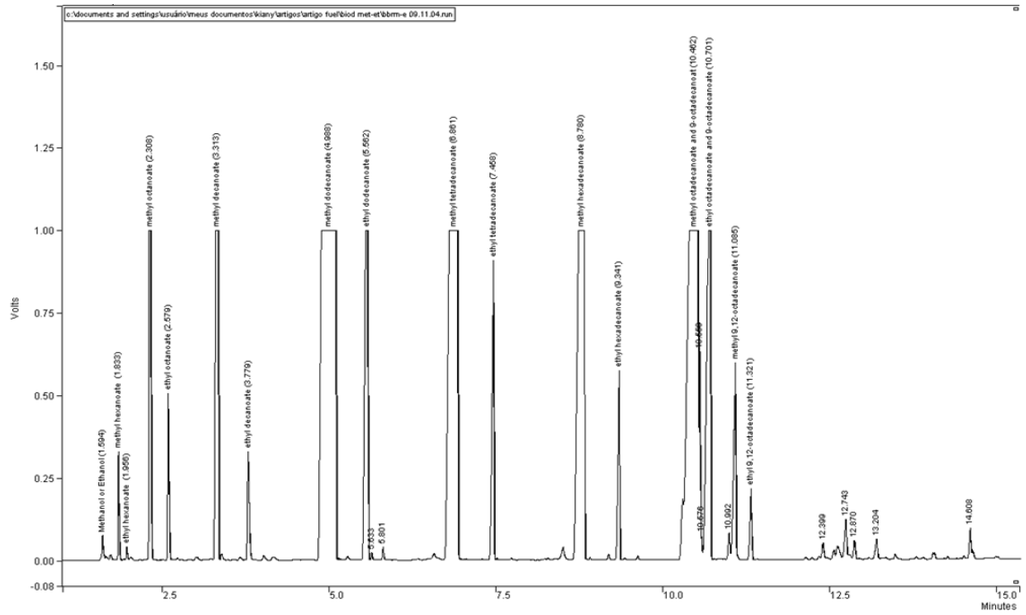

Figure 1. Chromatogram of the babassu methyl/ethyl biodiesel

The ester percentages (E), determined by gas chromatography, are obtained from the sum of all methyl and ethyl esters. The ester percentages and the yield, reported in relation to the mass of pure methyl/ethyl biodiesel (BP), both for the several MeOH/EtOH ratios, are listed in Table 2.

Table 2. Influence of the ethanol/methanol ratio on the yield and ester percentages of babassu biodiesel

$\%_{EtOH}$	$\%_{MeOH}$	$t_{reaction}$	$\%_{mBP}$	$\%_{E}$
0	100	30 min	95.32	98.84
10	90		91.70	97.17
$_{2}0$	80		95.32	98.70
30	70		93.70	98.18
$_{4}0$	60		92.29	98.44
50	50		84.26	96.77

PB: Pure biodiesel E: Ester$_s$
m_{PB}: Mass yield of pure biodiesel m_E: Ester content

The separation of the biodiesel/glycerin mixture does not occur spontaneously using ethanol percentages higher than 50%, even with the removal of the alcohol excess by means of distillation under reduced pressure. It was observed that the mass yield of pure biodiesel tends to diminish with the increase of the ethanol proportion in the blend, due to the difficulty of the biodiesel/glycerin separation.

In Figure 2 shows the influence of the ethanol percentage of the methanol/ethanol blends on the ester content and the mass yield of pure biodiesel, for a fixed reaction time of 30 min.

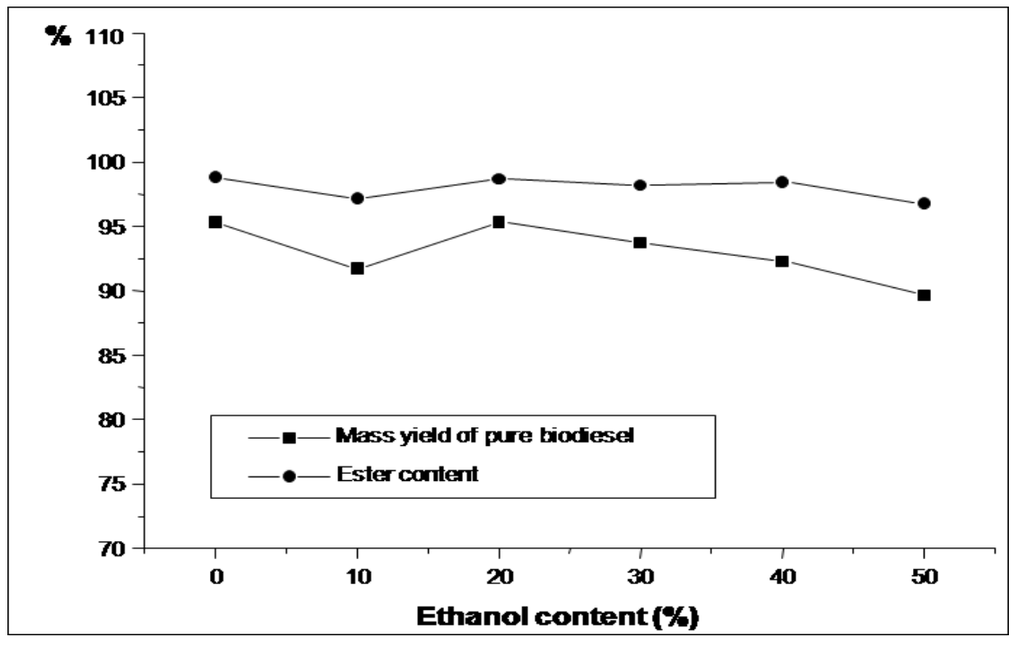

Figure 2. Influence of the MeOH:EtOH ratio on the ester content and on the mass yield of pure biodiesel, for a reaction time of 30 min.

The results point out that, for a fixed reaction time of 30 min, there was no meaningful change in the amount of methyl/ethyl esters with the increase of the ethanol percentage. All the samples presented ester contents in the average of 98%, values above the requirements of the ANP [7], with the exception of the biodiesel obtained with a MeOH:EtOH 50:50 ratio. The mass yields of pure biodiesel obtained do not decrease with the ethanol percentage up to 20% (v/v) ethanol. However, for higher ethanol concentrations, it is shown a tendency of decreasing the mass yield with further ethanol enrichment in the blend. The value for pure methyl ester (95.32%) is higher than the value reported by Oliveira et al. (91%), also for the transesterification reaction of babassu oil with pure methanol [5]. These results point out an optimum methanol/ethanol ratio of 80% MeOH:20% EtOH, with a mass yield of 95.32 % and an ester content 98.70 %, a valor higher than the minimum value required by ANP [7].

The transesterification reaction carried out with 50 % ethanol with a reaction time of 30 minutes displayed the smallest mass yield of pure biodiesel. Nevertheless, it is known that the transesterification reactions with methanol rapidly achieve equilibrium, whereas with ethanol bigger reaction times are needed to reach the maximum conversion of triglycerides into esters. In order to assess if it is possible to obtain higher reaction yields in the reactions employing 50% ethanol, an investigation on the influence of the reaction time was carried out, whose results are presented in Table 3.

Table 3. Babassu oil transesterification reactions with 50% ethanol using different reaction times

$\%_{EtOH}$	$\%_{MeOH}$	$T_{reaction}$ (min)	$\%m_{PB}$	$\%_{E}$
50	50	30	84.26	96.77
		60	83.22	98.13
		90	84.52	99.03

Figure 3 shows that the ester content increases with the reaction time. It was experimentally verified that the biodiesel/glycerin phase separation and the biodiesel washing processes were more efficient, but the mass yield of pure biodiesel did not increase significantly with the increase of the reaction time. It was shown that all the samples obtained with 50% ethanol meet the minimum ester content established in the ANP.

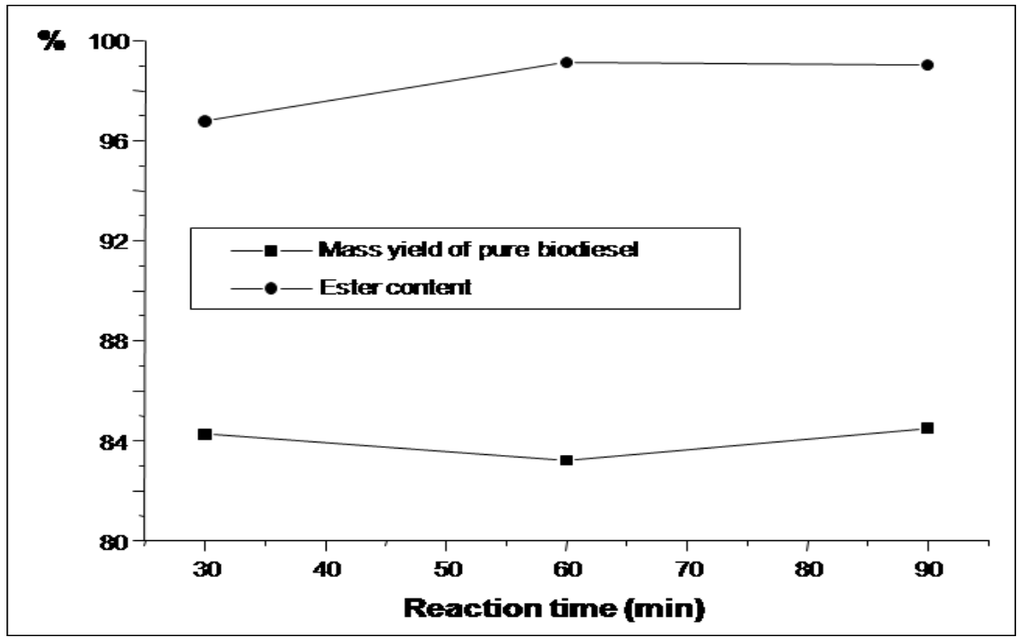

Figure 3. Influence of the reaction time on the mass yield of pure biodiesel and the ester content.

As for the physico-chemical properties, the babassu oil was analyzed utilizing SMAOFD [14] methods and the methyl/ethyl biodiesel analyses employed ASTM and ABNT standards. Table 4 shows the results of some physico-chemical tests of the biodiesel sample obtained with the 80:20 methanol/ethanol blend, as well as the specification limits of the standards.

IV. Conclusions

The following reaction conditions were shown to optimize the biodiesel production from the transesterification of babassu oil with a blend of alcohols: methanol/ethanol ratio of 80% MeOH : 20% EtOH and 30 minutes of reaction time. With these conditions, a biodiesel mass yield equal or higher than 95.32 % was obtained and also an ester content of 98.70 % was achieved, thus meeting the specification of the ANP. It was also observed that it is possible to utilize an ethanol/methanol mass ratio of 50:50, provided that the reaction time is of 60 minutes, in order to obtain satisfactory ester contents (98.13 %). The samples of biodiesel produced with the 80% MeOH:20%EtOH blend meet the specifications required by ANP, taking into account the physico-chemical tests listed in Table 4.

Table 4. Physico-chemical analyses of babassu oil and the biodiesel obtained from a 80:20 methanol/ethanol blend

Tests	Babassu oil	Methyl/ethyl biodiesel	Biodiesel Analysis Method	Biodiesel Limits
Moisture and sediments (% v/v)	0.039	0.028	ASTM D-2709	0.050
Specific gravity at 25ºC (kg/m^3)	923.0	887.2	ASTM D-4052*	860-900
Kinematic viscosity at 40°C (mm^2/s)	34.840	4.830	ASTM D-445*	-
Methanol/Ethanol (% m/m)	-	0.453	ABNT NBR 15343**	0.5 (max.)
Free glycerin (% m/m)	-	0.026	ASTM D-6584*	0.02 (max.)
Esters (% m/m)	-	> 96.500	ABNT NBR 15342**	96.5 (min.)

* Standards from ASTM - American Society for Testing and Materials
** Standards from ABNT – Brazilian Association for Technical Norms

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Resumo: O Estado de Maranhão no Brasil apresenta um potencial grande para o cultivo de várias espécies oleaginosas, como babaçu, feijão-soja, planta de óleo de rícino, etc... Estes óleos vegetais podem ser transformados em biodiesel pela reação de transesterificação em meio alcalino, usando metanol ou etanol. A produção de biodiesel a partir da mistura destes álcoois é uma forma de acrescentar as vantagens técnicas e econômicas do metanol às vantagens ambientais do etanol. A mistura de álcool otimizada foi observada usando a relação de volume metanol/etanol de 80 % MeOH: 20 % EtOH. O teor de ésteres foi de 98.70 %, um valor acima do exigido pela ANP, 96.5 % (m/m), e um rendimento de biodiesel em massa foi de 95.32 %. Este biodiesel cumpre as especificações de umidade, massa específica, viscosidade cinemática e percentagens de álcoois livres (metanol mais etanol) e glicerina livre.

Palavras chaves: Óleo de babaçu, metanol, etanol, ésteres metílicos, ésteres de etílicos.

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SENSITIVE SPECTROPHOTOMETRIC DETERMINATION OF LAMOTRIGINE IN BULK DRUG AND PHARMACEUTICAL FORMULATIONS USING BROMOCRESOL GREEN

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Abstract: Two new, simple, rapid and reproducible spectrophotometric methods have been developed for the determination of lamotrigine (LMT) both in pure form and in its tablets. The first method (method A) is based on the formation of a colored ion-pair complex (1:1 drug/dye) of LMT with bromocresol green (BCG) at pH 5.02±0.01 and extraction of the complex into dichloromethane followed by the measurement of the yellow ion-pair complex at 410 nm. In the second (method B), the drug-dye ion-pair complex was dissolved in ethanolic potassium hydroxide and the resulting base form of the dye was measured at 620 nm. Beer's law was obeyed in the concentration range of 1.5-15 µg mL^{-1} and 0.5-5.0 µg mL^{-1} for method A and method B, respectively, and the corresponding molar absorptivity values are 1.6932 x 10^4 and 3.748 x 10^4 L $mol^{-1}cm^{-1}$. The Sandell sensitivity values are 0.0151 and 0.0068 µg cm^{-2} for method A and method B, respectively. The stoichiometry of the ion-pair complex formed between the dug and dye (1:1) was determined by Job's continuous variations method and the stability constant of the complex was also calculated. The proposed methods were applied successfully for the determination of drug in commercial tablets.

Keywords: lamotrigine; spectrophotometry; ion-pair complex; bromocresol green; pharmaceuticals

Introduction

Lamotrigine, (LMT), [6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine], is an anticonvulsant drug. As an antiepileptic, it has been used successfully to treat epilepsy and bipolar disorder as monotherapy and as an adjunct with other antiepileptics for treatment of partial and generalized toxic-chronic seizures. It is also used to treat neurological lesions and as a tranquilizer [1, 2].

Lamotrigine is not official in any pharmacopoeia. The analysis of LMT in biological samples is abundantly described in the literature. Chromatographic techniques have been widely employed since they are powerful separation techniques. The methods based on the high-performance liquid chromatography (HPLC) [3-10], high-performance thin layer chromatography (HPTLC) [11] and gas-chromatography (GC) [12] have been described. There is an extensive literature on the determination of lamotrigine in pharmaceuticals include planar chromatography [13], TLC and HPLC [14], HPLC and GC [15], capillary electrophoresis [16, 17]. The immunoassay techniques [18, 19] have been developed for