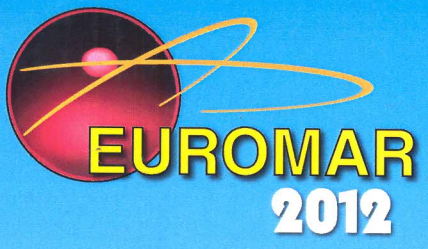

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SIMULTANEOUS QUANTITATIVE AND QUALITATIVE ANALYSES OF COMPONENTS ACTIVES AND EXCIPIENTS IN DRUG FORMULATIONS BY ^{1}H NMR

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The need for effective and reliable quality control in final products and/or raw materials from pharmaceutical becomes the analyses of its actives components and constituents very important to manufacturers, as well as to users of these products. For this purpose, standard methods, such as pharmacopoeia, and from governmental agencies are used. The most commonly used techniques are the chromatographic and spectroscopic, such as UV Visible and Infrared. The Nuclear Magnetic Resonance spectroscopy (NMR), which is an important qualitative analytical tool, is rarely used in quantitative measurements. In this context, the objective of this work was to demonstrate the viability of ^{1}H NMR for simultaneous qualitative and quantitative analyses of active components and excipients in drugs formulations. Two commercial drugs samples were examined in triplicates, using dimethyl sulfone compound (CRM traceable to NIST) 99.65 ± 0.08%, as an internal standard (IS), and deuterated dimethylsulfoxide as a solvent. All analyses were performed in an Inova 400 Varian spectrometer, with the validated ^{1}H qNMR method. From the ^{1}H NMR spectra, it identified three active components (paracetamol, caffeine and chlorpheniramine maleate) and three excipients compounds (ethyl alcohol, propylene glycol and methylparaben) presents in the drug formulations. The content of each compound was obtained using the following equation:

$$Content_X(mg/mL) = \frac{Area_X \times n^o\,of\,nucleus\,absorbents_{IS} \times molecular\ weight_X(g) \times weighed\ mass_{IS}(g) \times Purity_{IS}}{Area_{IS} \times n^o\,of\ nucleus\,absorbents_X \times molecular\ weight_{IS}(g) \times V_{drug}(\mu L)} \times 10^4$$

In one drug we obtained 421 mg/mL of paracetamol and 65.1 mg/mL of caffeine. In the second drug, 96.8 mg/mL of paracetamol and 2.04 mg/mL of chlorpheniramine maleate. These results are reliable because they were obtained by validated ^{1}H qNMR methodology. Furthermore, the active components content determinate from simultaneous quantification is in according to described values in their bulls. Therefore, the same can be done to obtain the content of the excipients identified. It concluded that a single NMR measurement provides structural and quantitative information of active components and excipients in the sample and, thus, contributes to an efficient, simple and fast quality control.

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EVALUATION OF PHASE ALTERNATION STEADY-STATE FREE PRECESSION PULSE SEQUENCES FOR FAST HIGH RESOLUTION NMR ACQUISITION

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Steady State Free Precession (SSFP) sequences have been used to enhance signal to noise ratio in high resolution NMR spectrum but it introduces strong phase and amplitude anomalies. These distortions are essentially caused by the truncation of the signal and the strong interaction between the free induction decay (FID) and echo component. To reduce these distortions we have been testing SSFP sequences with phased alternation. To understanding the effect of the phase alternation in SSFP signals we have compared the experimental results with the numerical simulations using Bloch equations. The ^{1}H and ^{13}C experiments have been performed in an Inova 400 Varian spectrometer. Phase alternation SSFP sequences such as (x –x) and (x x -x –x) has been tested and compared with conventional SSFP sequence, without phase alternation. The FID and echo signals for on resonance signals for x-x sequence have the same phase (fig. 1a), conversely to the conventional SSFP, which are dephased by 180º (fig. 1b). Therefore the addition of the conventional and x -x SSFP signals, can produces a FID without the presence of the echo and consequently, suppressing these anomalies. The SSFP x x-x-x sequence (fig 1c) produces a more complicated results and it varies from maximum to minimum amplitudes depending on the frequency. Theoretical results are in excellent agreement with experimental results.

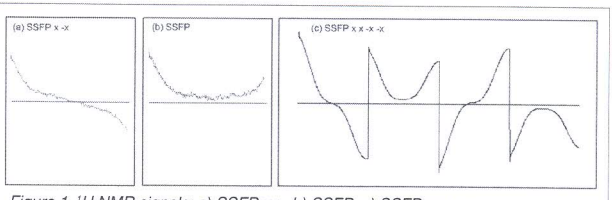

Figure 1. ^{1}H NMR signals: a) SSFP x-x; b) SSFP; c) SSFP x x-x-x.