The possibility of nuclear quadrupole resonance for distinguishing paracetamol different manufacturers and different forms (parties) from the same manufacturer of the spectral characteristics

Rustem R. Khusnutdinov[1], Irek R. Mukhamedshin[2]

[1]Institute of Electric Power Engineering and Electronics, Kazan State Power Engineering University, Kazan, Russia
[2]Institute of Physics, Kazan Federal University, Kazan, Russia
E-mail: khrr@yandex.ru

Introduction

There is a serious problem of counterfeit (counterfeit) medicines now. In different countries, the percentage of detected counterfeit medicines varies, including because government agencies that control the quality of medicines do not have sufficient laboratory facilities to conduct examinations. For example, in Russia there are only 12 monitoring and analytical laboratories subordinate to the Federal Service for Surveillance in Health Care (Roszdravnadzor) and these laboratories are subject to a check of less than one percent of the LP. According to various sources, the percentage of counterfeit in Russia ranges from 3-4% to 10-15% for some drug groups. In the world, it is estimated that counterfeit medicines represent approximately 10% for a total of 51.6 million pounds sterling [1, 2].

Paracetamol (PCM; IUPAC name: N-(4-hydroxyphenyl) ethanamide, C8H9NO2 or acetaminophen) is a widely used analgesic and antipyretic. It is produced under more than 80 trademarks (Panadol, Tylenol, Lekadol, Plicet, Daleron, Lupocet, etc.) in the form of tablets, capsules, powders and liquid suspensions. Cases of pronounced abuse of counterfeit paracetamol, among other medicines, have been reported in some less-developed countries in the last years [3, 4].

Paracetamol – (acetaminophen) antipyretic and analgesic medicine is one of the most popular drugs in the world. It is produced under more than 50 trademarks in various forms - tablets, capsules, powders, candles, syrups, etc. The great popularity led to the fact that paracetamol, despite the relatively inexpensive price, counterfeited often enough.

Nuclear quadrupole resonance (NQR) spectroscopy is a "fresh" method for detecting counterfeit medicines in a non-destructive way. Besides that it is possible to determine the authenticity of a medicine by comparing its spectrum with a reference ("fingerprint"), the NQR technique makes it possible to distinguish between drugs that contain the same active ingredient produced by different manufacturers (under different trademarks), as well as various batches and a series of medicines of one manufacturer.

NQR of paracetamol

Figure 1 shows the structure of the paracetamol molecule and the fragment of the spectrum. The frequencies of the NQR transitions, relaxation times, and line width parameters are given in Table 1.

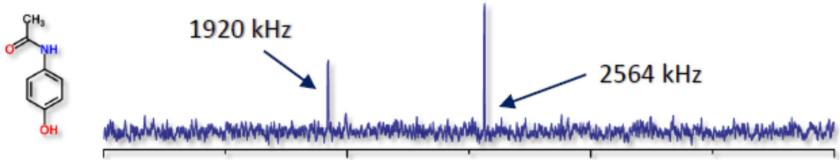

Figure 1. Molecule structure and NQR spectra of paracetamol

Table 1. The frequencies of the NQR transitions, relaxation times, and line width parameters for monoclinic form of paracetamol

NQR frequencies, ν, (MHz)	Δν, linewidth (Hz)	T_1, (s)
2,564	1,400	11
1,921	1,800	5
643		

Experimental

Measurements were performed on a spectrometer Apollo Tecmag. NQR experiments were carried out on *Apollo Tecmag* NQR/NMR console (0.1-100 MHz) with two-channel transmitter and one-channel receiver modules. Two *Tomco BT-00500-Beta* power amplifiers with output power of up to 500 W have been used. The detector unit includes transcoupler, a quarter wave lines π- filter 1,5-3.6 MHz bandwidth, a low-noise single-channel preamplifier Miteq and signal sensor. Using the sensor circuit shown in Fig. 2, where an optimally calculated [5] rectangular solenoid is used as the coil (L), it is possible to distinguish between different manufacturers according to the NQR spectrum.

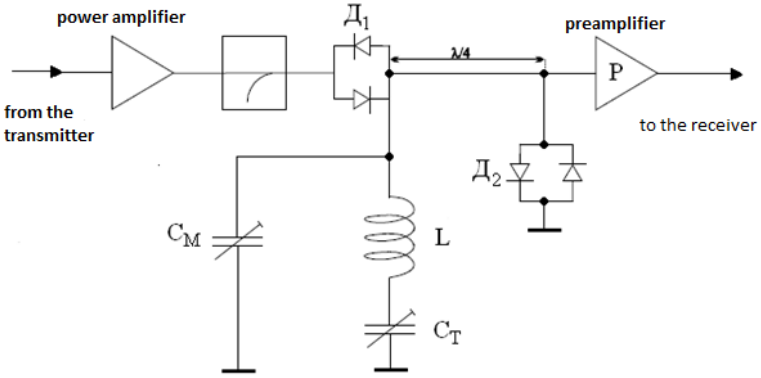

Figure 2. Switching scheme of the NQR signal sensor with the transmitter output and the preamplifier input. Here S_M is an alternating capacitor for matching the circuit, C_T is a variable capacitor for tuning the circuit at the resonant frequency, D_1 and D_2 cross-diodes

The results of the measurements show that, although the resonant frequency is the same for all the measured samples, the line width differs for different manufacturers. For different forms of the same manufacturer, a clear difference in the NQR spectrum for tablets and capsules was also obtained. According to [6] the broadening is the result of a narrow distribution in size of the tensor components of the electric field gradient 14N, mechanical stress caused by compression of tablets at the factory. The broadening differs at different frequencies. On the average, the broadening increases with increasing compaction pressure. The lines of paracetamol spectrum in powders, with a lower pressing pressure, give a narrower width line parameter.

References

1. Martino, R., Malet-Martino, M., Gilard, V., and Balayssac, S. Counterfeit drugs: analytical techniques for their identification. –*Analytical and Bioanalytical Chemistry,* 398(1), 77-92 (2010).
2. Gallagher, J. (2015). *http://www.bbc.co.uk/news/health-33183330*. (accessed January 26, 2018).
3. A.I. Wertheimer, J. Norris. – *Res. Social Admin. Pharm*., 5, 4–16 (2009).
4. Millions of counterfeit drugs seized in the EU, *http://topnews.in/millions-counterfeit-drugs-seized-eu-299089*.
5. Barras J., Katsura S., Sato-Akaba H., Itozaki H., Kyriakidou G., Rowe M. D., Althoefer K. A., and Smith J. A. S., Variable-pitch rectangular crosssection radiofrequency coils for the nitrogen-14 nuclear quadrupole resonance investigation of sealed medicines packets. – *Analytical Chemistry,* 84(21):8970- 8972 (2012).
6. Luznik J., Pirnat J., Jazbinsek V., Lavric Z., Srcic S., and Trontelj Z., The influence of pressure in paracetamol tablet compaction on 14N nuclear quadrupole resonance signal. – *Applied Magnetic Resonance,* 44(6), 735-743 (2013).