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Automated diagnosis and treatment by lasers employing Raman spectroscopy and catheter with optical fibers

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Abstract. Raman spectroscopy is considered a very powerful tool for biochemical characterization, especially regarding biological samples. This technique allows the diagnosis of several diseases, such as cancer and atherosclerosis. In this context, the non invasive or minimally invasive character of the spectroscopic resources is an auspicious clinical advancement when compared with conventional procedures, which are associated to significant trauma and possible decrease in the quality of life of patients. Recently, the use of catheter with optical fibers associated to Raman spectroscopy has significantly minimized the invasive character of several clinical procedures. It is important to notice that this optical sensor already presents flexibility due to the employment of optical fibers to applications of lasers. Nowadays, this kind of device possesses autonomy of use and can be coupled to an optic fiber in order to permit the treatment with lasers. In this way, it is possible to develop an electronic automated optic system that achieves a diagnosis through catheter with optic fiber connected to a Raman spectrometer in order to analyze a certain organ and, considering the diagnosis obtained, to develop the adequate optical treatment can be automatically selected and applied to the respective organ. In the present work, the structure of this device will be presented with the more suitable optical techniques available to the laboratories. The minimum intervals of time involving each step of the sequence are evaluated and the efficiency of the spectroscopic system is discussed in details in agreement with the literature.

Keywords: Raman spectroscopy, catheter, optical fiber, laser, diagnosis

1. Introduction

Raman spectroscopy is an optical technique that allows a very accurate biochemical analysis of several biological tissues [5,17,20]. This kind of analysis propitiates the clinical diagnosis of several pathologies, being that the results obtained from this procedure have a high degree of confidence due to the inherent

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characteristics of the Raman spectroscopy, which are associated to an excellent ability of structural characterization.

However, the optical phenomenon of Raman scattering is associated to a lower probability of occurrence when compared with physicochemical processes as the absorption. As consequence of this lower intensity of Raman signal, the Raman spectroscopy is considered an instrumental technique of relatively low sensitivity. In this context, in order to improve the signal to noise ratio associated to the Raman scattering, it is necessary to employ the laser radiation on the near infrared region [1,21,22].

Furthermore, the employment of Raman spectroscopy for diagnosis purpose has been limited by the impossibility to access the internal organs. However, the use of optical fiber catheter allows this access with minimal degree of invasiveness, implying in a lower trauma and, consequently, in a improvement of the life quality during the treatment, promoting a better rehabilitation to the patient [13].

The catheter of optical fibers applied to biomedical analysis via Raman spectroscopy already represents advancements that allow the employment of the great ability of structural characterization of Raman spectroscopy in biological systems. Furthermore, this device has significant autonomy of use as function of its direct insertion in the biological tissue, without requirement of any additional device [16]. In addition, this optical sensor already presents developments that permit its utilization with suitable signal-to-noise ratio in order to be applied with Raman spectroscopy [3,7,11,12,19].

It is also important to notice that together with the advantages mentioned above, a very interesting property of catheters is the possibility of application of the optical fiber inserted in the own catheter for “optoclinical” therapies via lasers sources [14]. In fact, there is not a significant decrease of the signal-to-noise ratio due to the lower number of optical fibers (decrease of one optical fiber) of the system of signal collection. Electronic techniques of signal acquisition and treatment associated to specific softwares to signal analysis allow obtaining a conclusive result in terms of diagnosis through Raman spectroscopy [18]. Indeed, the Raman spectrum collected of biological sample represents a versatile source of physicochemical data of compounds present in the respective tissue, which can be analyzed in a short interval of time [18].

This advancement implies in a lower time for diagnosis acquisition, favoring the rapid clinical treatment. In fact, this kind of analysis consists in a less traumatic methodology, which decrease the stress associated to the clinical procedures, favoring the efficacy of the treatment and propitiating a higher quality of life to the patients.

In this context, the control of some parameters of the system itself, such as the variation of the width of slit or the time interval of exposition of the photodetector CCD in order to improve the signal-to-noise ratio constitutes in a relevant resource to improve the sensitivity and/or selectivity of the application of this kind of analytical methodology [9,10].

In this way, it has been suggested the development of an automatic system that becomes possible the transmission of laser through optical fiber of the own catheter to realize the treatment of the diseases diagnosed in the analysis. Figure 1 presents a scheme that illustrates the organization of the system of spectroscopic analysis, which can involve a second laser to act in ablation (Fig. 1). Indeed, from the obtaining of the diagnosis, the system of analysis begins the process that guides the laser to the removal of the biological material. Concomitantly, the spectroscopic system continues collecting the Raman signal until the moment in which any signal from the substance considered in this process can be detected, implying that the emission of the laser radiation to the procedure of ablation is finalized.

In agreement with Fig. 1, the system acts through the laser emission of the diode in the near infrared spectral region. This infrared diode laser is connected to the catheter of optical fibers, which, with the control of this own device, allows the distal extremity to access the internal organ of the patient through

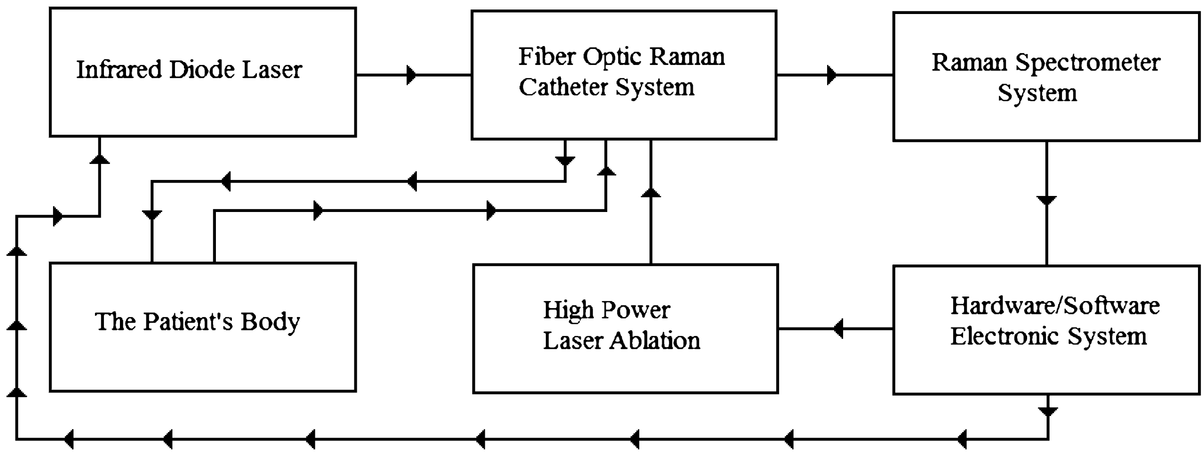

Fig. 1. Diagram of blocks evidencing the automatic system of diagnosis and treatment in patients via lasers, Raman spectroscopy and catheter with optical fibers.

the control performed by the clinical analyst. These procedures are performed through the control of the distal mobility of the catheter with the use of the system of mechanical operation and visualization of the guide process of this optical sensor via analysis by X-ray system [15]. Indeed, when the distal tip of the catheter touches the biological tissue, the "Hardware/Software System" liberates the radiation of the laser diode to the coupling to the catheter of optical fibers. Thus, the signal is guided until the biological sample, which is excited, producing the inelastic retro-scattering effect, which allows that the other optical fibers of the own catheter collect the Raman signal generated by the tissue.

In this way, the Raman signal is conduced to the Raman spectroscopic system by the distal tip of the catheter. Thus, this signal is transformed in spectral data, arriving to the software system, which, through assignment of the spectral peaks, allows the precise diagnosis of the respective biological tissue. In fact, this system has excellent potential to permit the accessibility to the clinical diagnosis that involves a specific biological tissue. The software system sends an electronic signal to the high potency laser to generate ablation with controlled removal of the tissue, which usually occurs in cases as, for example, cardiopathy, in order to treat obstructed coronary vessel [2,23], or urologic diseases involving acute symptoms associated to the kidney [4,24].

This proposal of biochemical analysis, diagnosis and treatment involving a spectroscopic system must to consider the aim of minimum trauma to the patient. Thus, it is very important to decrease the interval of time of each step, in agreement with scheme demonstrated in Fig. 1. Indeed, the lower time of analysis propitiates a lower risk of accidents and collateral effects to the patient.

In this Raman spectroscopic system, the devices that act optically present very short time intervals of response, since the transmission involves the own light. The unique device that requires a higher interval of time is the called "Hardware/Software electronic system", since this device is responsible for acquisition and treatment of the Raman signal originated by the sample. These attributions imply in a very lower interval of time (maximum of 0.1 s) [26].

To the ablation or removal of the biological material, it is necessary to know the specific time of response of the Raman spectroscopic system. The "Hardware/Software electronic system" allows that the signal of electronic pulse to the laser perform the ablation of the biological material. However, it is not known with significant precision, the time of response presented by the respective electronic system of laser. In this context, several measurements were evaluated in order to verify the time of delay of the electronic device of the ablation laser. In addition, the analysis of some important parameters of this system was carried out. The data are discussed in details in agreement with the state of art in the literature involving employment of Raman spectroscopy and catheters with optical fibers in biomedical applications.

2. Material and methods

In order to achieve the measurement of the action times of the system, the following assemblage was performed (Fig. 2): A digital oscilloscope (Tektronix TEK TDS 724) was coupled to a system that simulates the electronic signal generated when the diagnosis of atheroma is confirmed. The ablation laser is habilitated at the moment in which the sign is generated. This assemblage is also constituted by an Excimer laser (Lambda Physic Compex 102) and a photodetector (silicon MRD500 with time response Ins).

In order to allow a precise estimation, it is important to know the minimum time necessary to perform all the cycle of automation of the system of diagnosis/treatment by ablation laser.

3. Results

Figure 3 shows the oscilloscope screen when the measurement of the electric pulse is generated by the hardware/software system that identifies the sign of the disease. The pulse verified by this instrument was of 18.68 µs, which means a discrepancy of 6.6%. This measurement can be transmitted to the excimer laser, since the TTL pattern accepted by this gadget varies from 10–100 µs with electric tension of 3.4 V.

The second measurement verified the response time of the optic-electronic excimer laser system, starting from the habilitation electric pulse. Figure 4 demonstrates the oscilloscope screen indicating the presence of the laser pulse from the photodetector (see channel 2 of the oscilloscope). Considering the point of electric tension of the pulse in 3.4 V, the response time of the system excimer laser is 1.19 µs

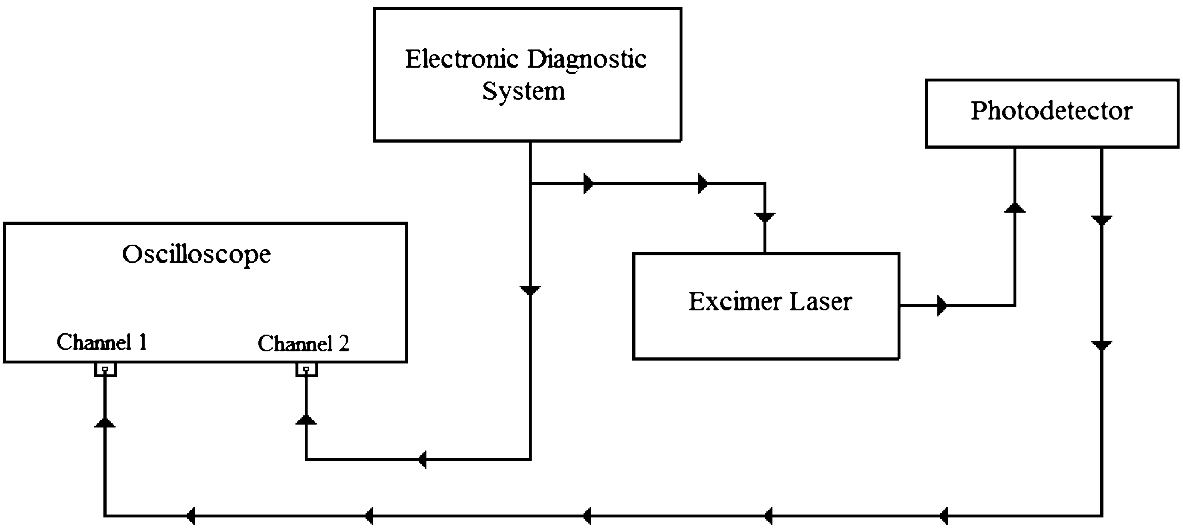

Fig. 2. Assemblage for measurement action times of electric signs that act on the automated optic-electronic system with lasers.

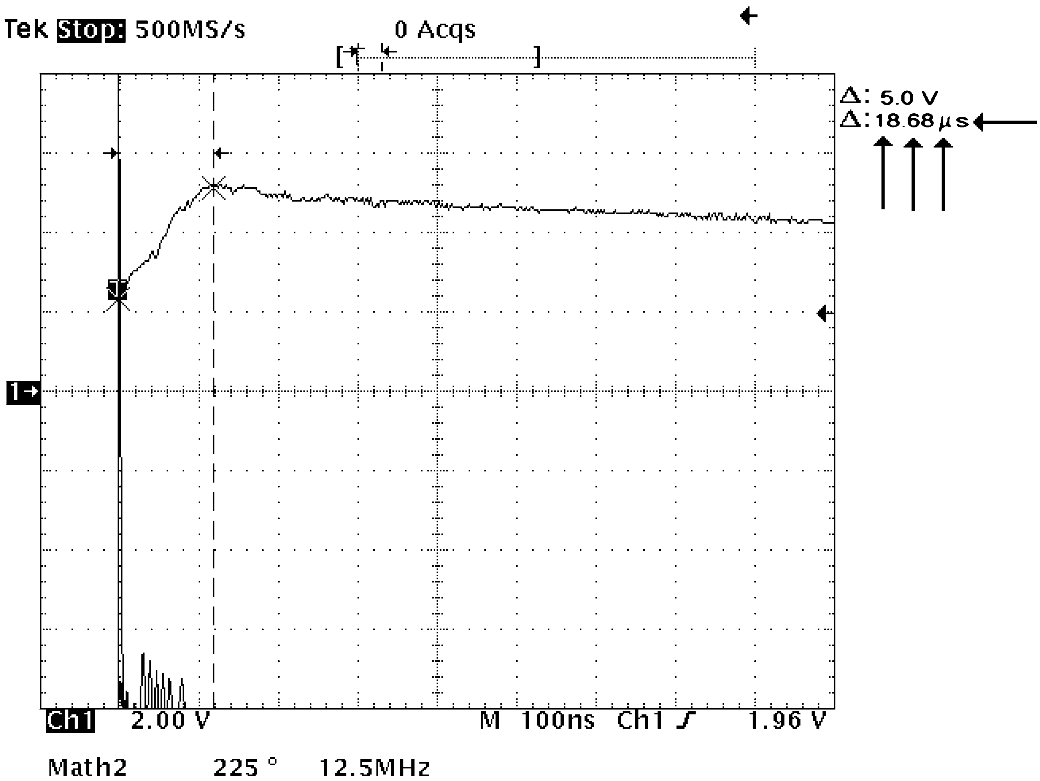

Fig. 3. Time measurement of the initial electric pulse for the excimer laser of ablation. The time is indicated by the arrows and the sign is evidenced in the oscilloscope screen.

(see channel 1 of the oscilloscope), i.e., starting from the habilitation for liberating the ablation laser. Only after this time, the radiation will be available for removal of the material.

Figure 5 shows the time measurement of the pulse of the high potency laser excimer. The time obtained (14.7 ns) is not significant in relation to the total time necessary for the automation of the system of diagnosis/treatment by light.

4. Discussion

The present work denotes the viability of developing an automated system, which allows a precise *in vivo* diagnosis using a Raman spectrum obtained from a specific organ. This is possible due to the employment of an optic fiber catheter, because this device has some characteristics as flexibility, small diameter, autonomy and significant potential to access several organs of the body. Since Raman spectroscopy provides a precise diagnosis of the pathological condition investigated, the creation of an automated system that allows the treatment through laser guided by the optic fiber itself is reliable.

In this context, the present work aimed to analyze the viability of this modality of diagnosis and treatment in cases for which the removal of biological material is necessary. Among these conditions, we can mention cardiopathic diseases, in which the unblocking of the coronary artery is the indicated procedure, since the removal of calcified material formed in cardiac valves as well as the ablation for the treatment of heart arrhythmias constitutes suitable procedures.

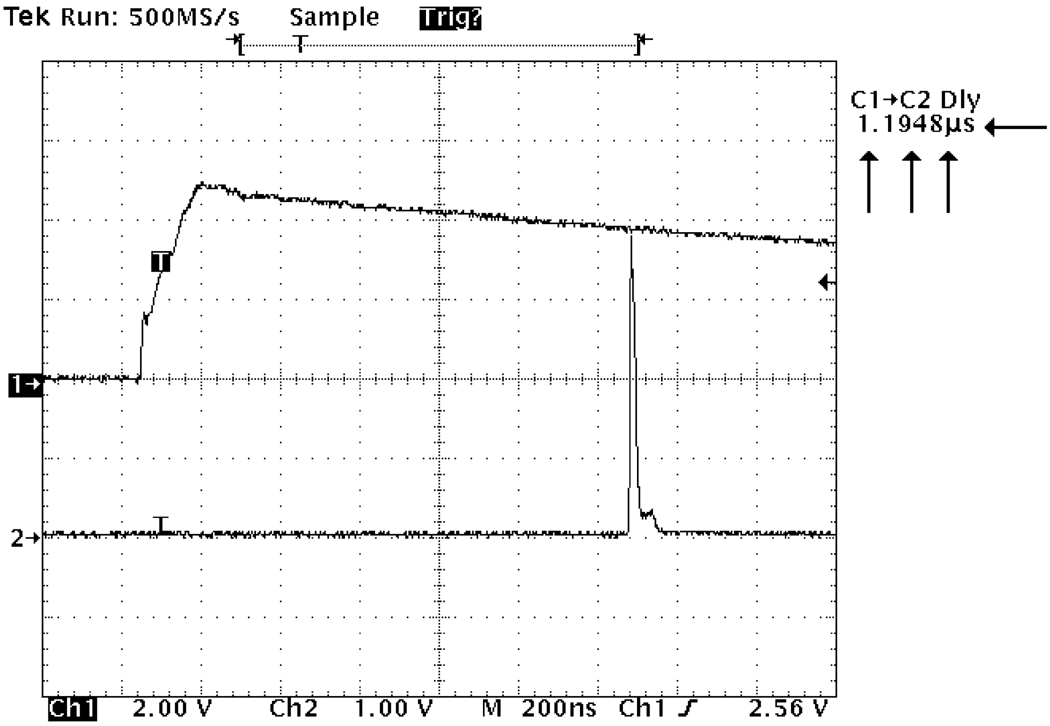

Fig. 4. Oscilloscope measurement of the response time of the excimer laser system, using the electric tension of 3.4 V in TTL pattern as reference.

The automated system proposed in the present work has also a great potential to be employed in urologic diseases, such as renal calculus or prostate conditions. It is evident that each case must have a clinical characteristic that allows monitoring all the procedure. In the specific case of the coronary treatment as well as in the urologic employment, this same kind of optical fiber can be guided through an endoscope with video sign. For all the clinical conditions mentioned, it is relevant to consider that the time of response of the system must be as short as possible in order to benefit the patient. In this way, the stages of insertion and guidance of the catheter to the organ to be analyzed as well as the specific procedures of spectrographic calibration should require a minimum interval of time. Indeed, the calibration in wavelength and Raman sign intensity, cosmic radiation rejection, removal of fluorescence curve, etc., must be as brief as possible in order to avoid increase in the inherent risks of the clinical procedure.

With the improvement of computational performance, the time spent in each of these procedures is minimal, being of approximately 0.1 s from the moment that the catheter is positioned in the tissue to be diagnosed and treated [26]. In this context, it would be necessary to know the total time when we consider the start of the electric pulse released by the automated system and the delay of the optic-electronic ablation laser. In fact the measured values demonstrated to be very short in relation to the total time measured. However, it is important to register that after the release of the ablation laser pulse, there is a generation of a photoelastic physic effect that usually possess time of hundreds of microseconds [6, 25]. Thus, the total cyclic time for the next acquisition of Raman spectrum from the automated system will take a greater time, depending on the kind of tissue analyzed.

The configuration of the automated system proposed can also be employed in the treatment of certain kinds of cancer by photodynamic therapy (PDT). Raman spectroscopy furnishes the differentiation be-

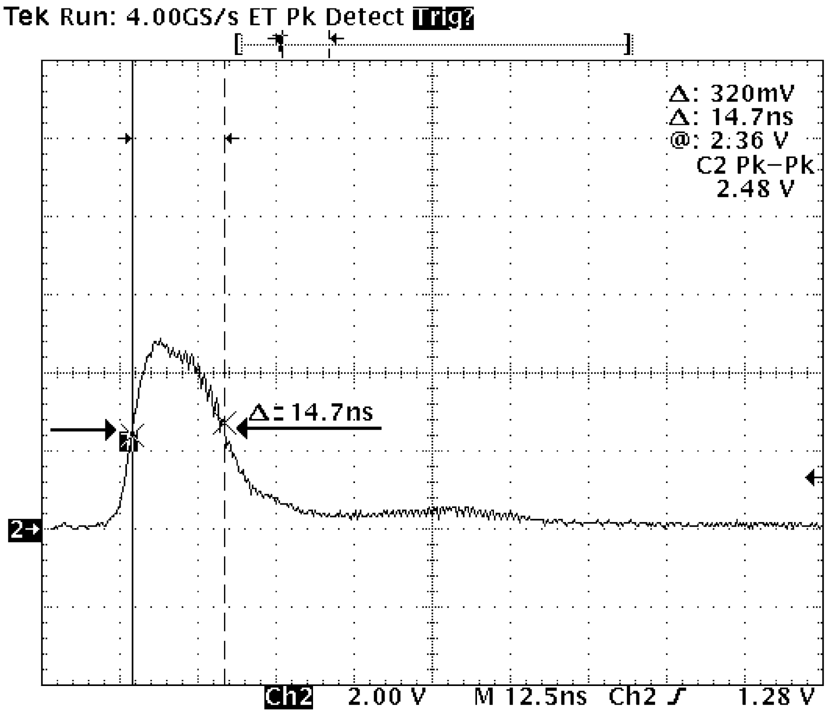

Fig. 5. Time measurement of the excimer laser pulse employing the silicon photodetector and digital oscilloscope.

tween normal and cancerous tissues, because the photosensitizer applied in PDT is more concentrated in cancerous cells. This allows that the routines of program can emit laser on the adequate wavelength by the optic fiber, aiming the generation of singlet oxygen and, consequently, eliminating cancer cells in a selective manner.

In the area of dermatology, one of the major issues of concern is the removal of tattoo pigments impregnated on the skin. Traditional clinical procedures, such as surgery or abrasion are significantly traumatic and may result in the formation of scars. Considering this, the ablation through potency laser has been increasingly employed for this procedure. However, one of the limitations of this technique is the use of a specific laser, which is adequate to interact with the kind of pigment impregnated to the skin [8]. The option of using the automated Raman spectroscopic system with lasers could represent a viable solution for this problem because the precise identification achieved by Raman allows the selection of a laser with wavelength compatible with the pigment analyzed, and the removal would be more effective through elective ablation.

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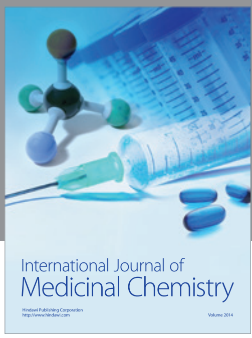
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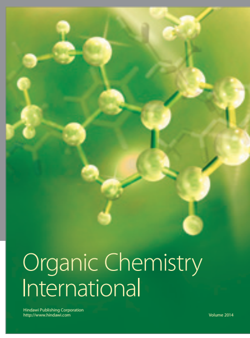
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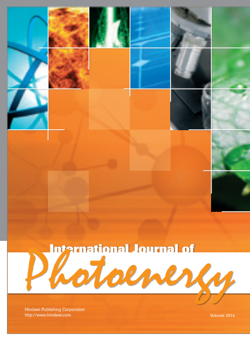
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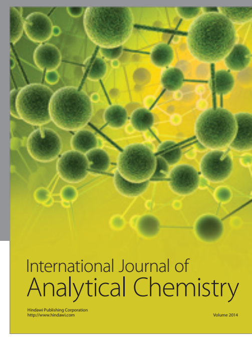
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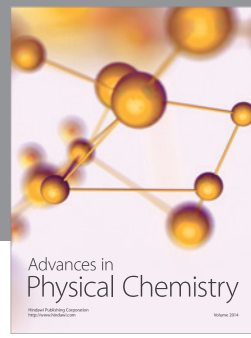
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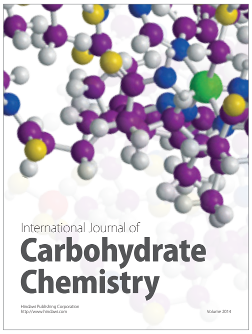
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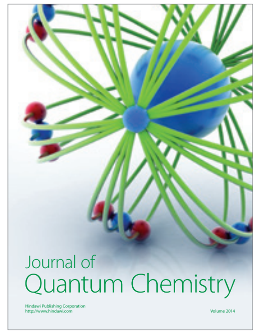
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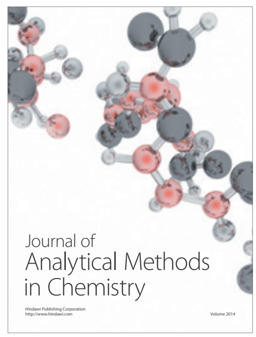
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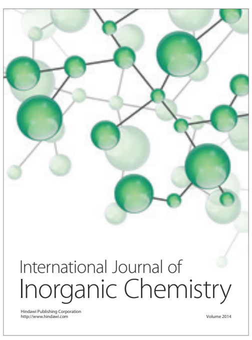
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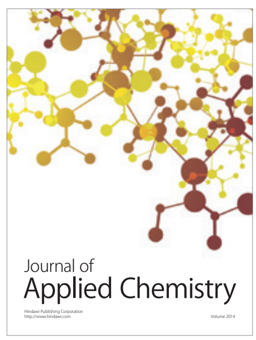
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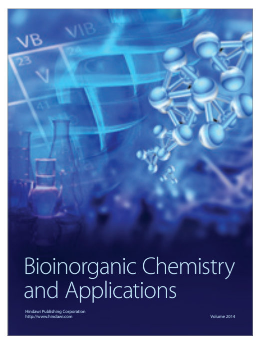
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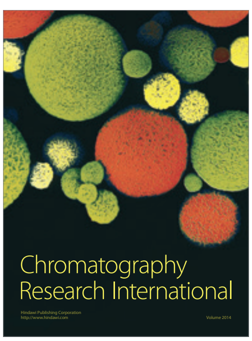
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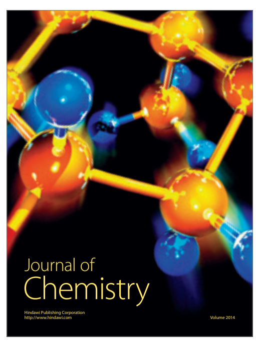
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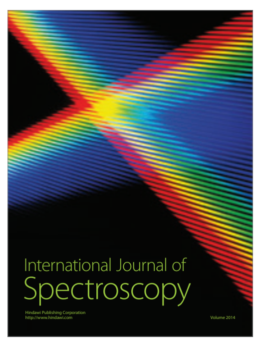
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