Qualitative and semi-quantitative analysis of health-care pharmaceutical products using laser-induced breakdown spectroscopy

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A B S T R A C T

Laser-induced breakdown spectroscopy (LIBS) is a sensitive optical technique that is capable of rapid multi-elemental analysis. The development of this technique for elemental analysis of pharmaceutical products may eventually revolutionize the field of human health. Under normal circumstances, the elemental analysis of pharmaceutical products based on chemical methods is time-consuming and complicated. In this investigation, the principal aim is to develop an LIBS-based methodology for elemental analysis of pharmaceutical products. This LIBS technique was utilized for qualitative as well as quantitative analysis of the elements present in Ca-based tablets. All the elements present in the tablets were detected and their percentage compositions were verified in a single shot, using the proposed instrument. These elements (e.g., Ca, Mg, Fe, Zn, and others) were identified by the wavelengths of their spectral lines, which were verified using the NIST database. The approximate amount of each element was determined based on their observed peaks and the result was in exact agreement with the content specification. The determination of the composition of prescription drug for patients is highly important in numerous circumstances. For example, the exploitation of LIBS may facilitate elemental decomposition of medicines to determine the accuracy of the stated composition information. Moreover, the approach can provide element-specific, meaningful, and accurate information related to pharmaceutical products.

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1. Introduction

Laser-induced breakdown spectroscopy (LIBS) is a rapidly evolving analytical technique based on optical emission spectroscopy of laser-produced plasma. In LIBS, a high-energy laser output is focused on a small volume of sample (10^{-8} to 10^{-5} cm^3) of solid, liquid, or gas, which results in the generation of plasma due to stimulation of the sample [1-3]. The process results in the emission of an optical signal that is detected and analyzed using a spectrometer. The resulting spectral lines are recorded by this instrument, which is typically connected to a PC. When a typical measurement is performed, the observed spectral lines are compared with those in the database of the National Institute of Standards and Technology (NIST) to facilitate the identification of the elements [4,5]. LIBS is widely applied in numerous areas including process monitoring due to its rapidity, ability to perform noncontact optical measurement, minimal sample preparation requirement, and potential to perform real-time in-situ measurements for laboratory or industrial use. The application of LIBS for quantitative elemental analysis has been demonstrated in metallurgy, mining, environmental analysis and several other fields [1,6,7].

In the pharmaceutical sector, there has been recent interest in LIBS. To date, the application of this technique in the pharmaceutical field has been exclusively in the analysis of solid dosage forms, such as quantitating active pharmaceutical ingredient (API). The analysis is then based on an element specific to the API (e.g., chlorine, sulfur, fluorine, or bromine) [1,7,8]. The same analytical scheme is applied in principle to liquid formulations. However, the analysis of pharmaceutical products in solution by LIBS has not been reported. Compared to available techniques for the analysis of pharmaceutical liquids (colorimetric or potentiometric titration, chromatography, and spectrometric methods), LIBS is a direct and
rapid method that does not require sample preparation. The technique also has several advantages such as high specificity (analysis versus other preparation) and the possibility of avoiding sample transfer. It is therefore an efficacious instrument in the rapidly evolving field of process analytics [2,9]. LIBS is equally effective for liquids, solids, and gasses. It is a non-destructive technique for the essential arrangement of a variety of gasses, solids, and liquids. In the technique, a laser can be utilized in the laboratory for element analysis and for quantitative assessment of elements. LIBS is an extremely flexible technique and has several important benefits. These benefits include rapid analysis, no sample preparation for the majority of samples, responsiveness to a large range of essentials as well as the option of immediate multi-essential investigation [10–12].

Usually, standard samples are required prior to qualitative analysis using LIBS to calibrate the system. However, several calibration-free LIBS techniques have been developed [13–16].

In this investigation, we determined the elements present in pharmaceutical tablets including metals and some non-metals using LIBS. By utilizing a single incident pulse of LIBS on the tablet, we identified the elemental compositions, which were further confirmed by comparing the results with those in the NIST database. In this case, we used calcium-based tablets for the analysis of Ca (as an active agent) and other elements (as passive agents). Moreover, the percentage of Ca and some other elements was also determined via quantitative analysis.

In the pharmaceutical industry, tablets are composed of a powder mixture containing active and inactive agents. Some constituents are also mixed to keep the tablets in a condensed form, but these are present in very small amounts on the order of 0.5–3%. The substances which are used as active agents can constitute relative amounts as low as 1%–2% and as high as 50%–80% of the mass of the tablet. Strict rules are often implemented for quality control in pharmaceutics. By utilizing LIBS analysis, compliance will be very simple and reliable. The purpose of this investigation was to identify the elements present in pharmaceutical salts. This technique will be useful for pharmaceutical industry to differentiate the genuine and counterfeit medicine [3,7,17].

The tablet samples used in this research contained Ca as an active element and many other elements such as Fe, Mg, F, Zn, Cu, Ni, P, and Vitamin-D as passive agents. These medications are used to prevent low blood pressure, bone loss (osteoporosis), weak bones (Osteomalacia /Rickets), decreased activity of the parathyroid gland, and a certain muscle disease. The samples may also be used by specific groups of patients to ensure that their dietary needs in regard to Ca and vitamins are being met. This sample was also purchased from a local market for the elemental analysis. Prior to the investigation, the composition of the tablets was carefully examined to ensure that elements would be accurately detected with little uncertainty.

In this study, the LIBS technique was utilized for the identification of the elements present in pharmaceutical tablets. A Q-switched Nd: YAG pulsed laser (PULSED LASER / SOLID-STATE / INFRARED / LPSS BRILLIANT, Quantel, France) was used as an excitation source in this investigation [18]. The lasing medium of this laser was an Nd: YAG (neodymium-doped yttrium aluminum garnet; Nd: Y3Al5O12) crystal. A spectrometer with a wide spectral range and high sensitivity, fast response rate, with a time-gated detector was also utilized. It was connected to a computer for rapid processing and interpretation of the acquired data [19] as shown in Fig. 1A.

2. Experimental procedure

For the elemental analysis, medicine tablet-samples (OMC-D, Osnate-d, and Hectoral) were purchased from a local market. LIBS was used to investigate Ca and other elements present in different samples of medicines. The Q-switched Nd: YAG laser with a pulse duration of 5 ns, a wavelength of 1064 nm and energy of 300 mJ, was used to irradiate the surface of the target sample (Ca-tablets) using a 10 cm quartz lens [20]. The laser ablation region is shown in the scanning electron microscope (SEM) image in Fig. 1B. In the process of data acquisition, we optimized many experimental parameters to improve the resolution and sensitivity of LIBS to minimize measurement fluctuation and problems due to the heterogeneity of the sample [21]. The region of the laser spot on the sample was calculated using the Gaussian beam profile of the focused beam. The target was mounted on the sample stage. Moreover, the region between the focusing lens and the target sample was less than the central thickness of the lens in order to avoid signal acquisition from the ambient gas on the surface of the sample [22]. Emission from the trail was registered using an HR4000 finding system in combination with a visual thread (high-OH, center width: 600 μm) with a collimating lens (0–45 playing field of sight) located at 90° to the path of plasma development. Output data was averaged for 10 laser shots. The data acquired by the spectrometer was stored on a PC for subsequent elemental analysis [23]. The emission spectra were analyzed by comparing the wavelengths in the spectra with NIST data to identify the optical spectral signature of Ca and the other elements present.

3. Results and discussion

The acquired data was obtained using a pulsed laser with a spectrometer to investigate the spectral lines associated with different elements on the basis of wavelength and energy. Specifically, the emissions produced by plasma were utilized to identify the constituent particle. The LIBS method involves a focused high-energy laser beam which is used to produce plasma and to stimulate the sample. Generally, dual-pulse or high-power laser operations are used to produce the necessary plasma. Improved
plasma radiation can be created by dual-pulse operations where the interval between the first and second pulse, and the laser beam geometry play a key role in optimizing the produced signal [24].

The first investigated sample was OMC-D which contained Ca as an active agent and additional elements as passive agents. The spectra obtained by LIBS was used to identify the elements present in these pharmaceuticals tablets. A laser operating at 1064 nm with 61 mJ per pulse was focused on the Cra film tablet. The Q-switched Nd:YAG (Quantel Brilliant) laser beam with an FL-Q-switch delay of 280 μs in a spectral range of 300–700 nm was used to ablate the sample. The emission spectrum was recorded using an Avantas Spectrometer placed at an angle of 90° with respect to the surface of the sample, regardless of the direction of the laser beam. The spectrum was recorded using a continuous beam of the Nd:YAG laser with a first harmonic of 1064 nm. The spectrum data for each sample was recorded two to three times to minimize the uncertainty or the errors. The emission spectrum consists of singly or doubly ionized spectral lines of Ca, Fe, Mg and other elements such as Ni, Zn, P and Cu as shown in Fig. 2. The specified results of OMC-D tablet described in Table 1 accurately match the NIST database results. The transition from the upper level to the lower level was expressed in each table for each sample individually.

The intensity (I) of the spectral lines was calculated by using the following equation [24].

Fig. 2. The LIBS data obtained for OMC-D tablet is plotted in the range of 300–700 nm wavelength. (A) The elements observed in the range of 300–700 nm wavelength. (B) The elements observed in the range of 385–425 nm wavelength. (C) The elements observed in the range of 580–600 nm wavelength. (D) The elements observed in the range of 600–630 nm wavelength. (E) The elements observed in the range of 635–675 nm wavelength.
The width of the spectral line is estimated by the equation [24] given by

\[ \Delta \lambda_{1/2} = 2\alpha \left( \frac{N_e}{10^{16}} \right) \]

where \( N_e \) denotes the electron number density and \( \alpha \) denotes the electron-impact broadening parameter.

Calcium carbonate is the most commonly used form of Ca supplement and it is available as capsules, tablets, oral suspension, and chewable tablets. Moreover, the elements identified in Osnate-d and Hectoral tablets are expressed with their transition states shown in Table 2 and Table 3, respectively. In the Osnate-d tablets, Ca, Mg, Fe, and other elements were traced and their peaks were obtained by utilizing the LIBS technique as presented in Table 2, and verified by comparison with the NIST database results [24,25]. The elements traced in the Hectoral tablets are expressed in Fig. 4 using LIBS. Further, a quantitative-based analysis of each tablet was performed and the results were compared with the prescription provided by each medical company. The estimated amount for Ca, Fe, Mg, and other elements are 29%, 20%, 10%, and 41%, respectively, which is precisely comparable to the prescriptions provided by medical companies. It is observed from Figs. 2–4 that Ca is relatively abundant in all samples as compared to other elements. The approximate quantity of Ca, Fe, and Mg with some other constituents is determined by their observed peaks [26], which are in accordance with the indicated prescription of the tablets.

4. Conclusion

We concluded that LIBS is an important technique that can be used to characterize samples in liquid, solid, and gaseous forms. A portable version of an LIBS device has been designed and used in
this investigation. In this research, LIBS was used to detect the elements present in pharmaceutical products (Calcium tablets) which contain Ca and numerous other elements. The LIBS approach yielded accurate and precise results which were obtained in a short time from a small sample volume. All the elements (Ca, Mg, Fe, Zn, and others) were determined by the wavelengths of their spectral lines, which were verified using the NIST database. The approximate amount of element was determined by their observed peaks, which are in exact agreement with the prescription. We believe that in the future LIBS may revolutionize the pharmaceutical industry because of its rapid and accurate analysis.

Conflicts of interest

All authors declare that there are no conflicts of interest.

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