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IDENTIFICATION AND ANALYSIS OF ELEMENTS IN HUMAN BLOOD SERUM USING 355 NM ND:YAG LASER-INDUCED PLASMA SPECTROSCOPY AT REDUCED PRESSURE OF HE GAS

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ABSTRACT

The human blood serum has often been used as a media for diagnoses of various diseases based on elemental composition. In this present work, identification and analysis of human blood serum has been performed using a standard LIBS technique utilizing 355 nm Nd:YAG laser under He surrounding gas. Experimentally, a human serum was homogeneously poured on a metal copper plate to produce a thin film. The film was then placed in a metal chamber, which was evacuated at a reduced pressure of He surrounding gas. A pulse Nd:YAG laser (355 nm, 10 ns, 70 mJ) was focused on a film to produce a luminous plasma. Major and minor elements in human blood serum from the normal and tuberculosis (TB) patients have successfully been identified including C, H, O, Ca, and Na. The analyte intensities from the human serum of TB patient have good stability with the number of laser shots in different positions. A preliminary test to distinguish the TB patient to normal patient was made based on Ca elements in the blood serum. Namely, the Ca intensities from TB patient is much higher than the case of normal patient.

Keywords: Human blood serum, TB patient, LIBS, Laser-induced plasma spectroscopy, 355 nm Nd:YAG laser

INTRODUCTION

Analysis of elements in human blood serum has become a great of interest for many researchers and medical doctors especially in the medical field [1]. The human serum contains essential elements, which are very important for human life. The essential elements include carbon, hydrogen, oxygen, nitrogen, sulfur, phosphorus, potassium, chlorine, and magnesium, while the essential trace elements are calcium, iron, zinc, manganese, chromium, iodine, silicon, and arsenic. These elements should be present in the human blood in a fair constant concentration. Nutritional elemental deficiency or abundance in the human body including human blood serum leads to susceptibility to infectious diseases. The human serum has often been often used as media for diagnoses of various diseases based on elemental composition [2]. Therefore, sensitive and accurate identification and analysis of elements in human blood serum is indispensable.

Various analytical tools have been commercially available and employed in the study on disease diagnosis based on elemental composition. These include the instrumental neutron activation, the x-ray fluorescence, and especially inductively coupled plasma atomic emission spectroscopy. Such techniques are widely adopted for accurate and sensitive elemental analyses. However, tedious sample pretreatments

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are needed and the techniques suffer from serious spectra interference because of multielements present in the sample target [3-5].

A relatively new spectrochemical method, namely laser-induced breakdown spectroscopy (LIBS), recently grows very rapidly for elemental analysis in various kinds of material including solids, liquids, and gases [6-10]. In this technique, a pulse Nd:YAG laser operated at fundamental wavelength 1064 nm is commonly used as an energy source to excite atoms in the plasma produced on the material surface. In this technique, the excitation mechanism mainly takes place through shock wave excitation process. The applications of LIBS to analysis of elements in human blood have reported in some literature. However, for liquid analysis such as human blood, the technique still has some drawbacks including sample pretreatment and low sensitivity. Furthermore, a standard LIBS technique operated at atmospheric ambient air is very delicate to detect light elements such as H and C, which are main elements in the blood serum, because of the time mismatch effect [11-12].

In this study, laser-induced plasma spectroscopy using 355 nm Nd:YAG laser in reduced pressure of He gas was employed to identify elements of human blood serum including human blood serum from normal patient and tuberculosis patients. The use of He gas in the study is to produce lots of He metastable atoms (He* atoms) in the plasma region. Those He* atoms play an important role in the assisting of excitation process of the analyte atoms including light atoms of carbon and hydrogen. The sample was prepared in the form of thin films placed in a copper metal subtarget. The result certified that the element intensities of C and H in the both human blood serum of normal and TB patients is successfully enhanced with optimum S/N ratio and without any broaden line. Furthermore, the human blood serum of the TB patients can be distinguished from the blood serum of normal patients based on trace element of Ca identified in the spectrum.

EXPERIMENTAL

Basic setup used in this work is shown in Fig. 1. First, a pulse Nd:YAG laser operated at ultraviolet wavelength (355 nm, 10 Hz, energy of 70 mJ) was focused using a quartz lens (f = 150 mm) to initiate and induce a luminous plasma on the sample target. The helium gas (Air Liquid, purity of 6N) was flown in the metal chamber with a flow rate of 10 liter per minute. The experiment was made at a reduced pressure. The emission spectra of analyte atoms are collected by an optical fiber, which has one of its ends positiend from the helium plasma. The other end of fiber connected to the port of detection system consisting an Echelle spectrograph (Mechelle M5000, Andor) and intensified charged couple device (ICCD) detector (Ando, iStar). The gate delay and gate width of the ICCD are fixed at 1 μs and 50 μs, respectively.

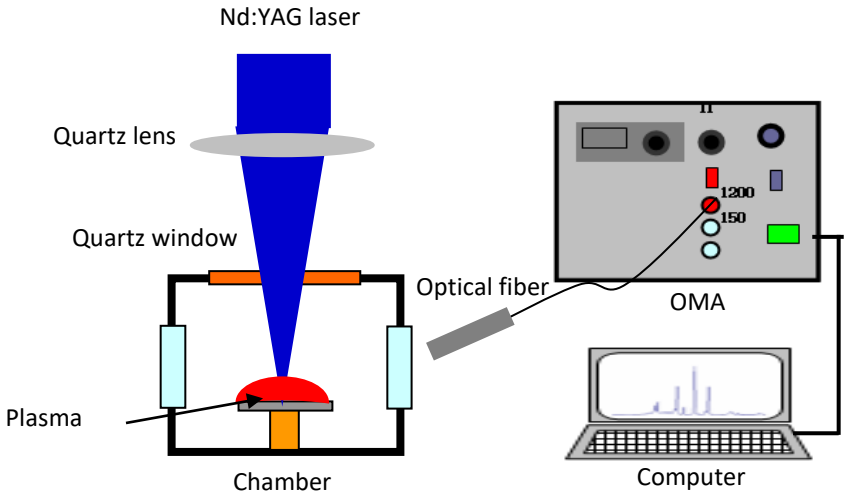

Figure 1. Experimental setup used in this work

The sample used in this work was human blood serum collected from the normal patients and TB patients at Diponegoro National Hospital. Experimentally, 1 ml liquid serum was poured on a copper metal plate

(99.9 % purity) with a dimension of 0.1 x 20 x 20 mm^3. The serum was homogeneously spread on the surface of Cu plate. The serum was then placed in the room temperature for 30 minutes to produce a serum film. During data acquisition, the sample was placed in a metal chamber and was rotated rotated with a rotation rate of 2 rotation per minute (rpm).

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RESULTS AND DISCUSSION

First, identification of elements was made from the pure copper metal plate, which functions as a metal subtarget. Figure 2 shows emission spectrum of Cu metal plate only without any sample of human blood serum obtained by laser-induced plasma spectroscopy operated at reduced pressure of ambient air (5 torr). Typical resonance lines of neutral Cu clearly occur at Cu I 324.7 nm and Cu I 327.4 nm. The other lines of typical neutral Cu are also detected at 510.5 nm, 515.3 nm, and 521.8 nm. These lines are contributed from the Cu plate used as a subtarget. No other elements are identified from the Cu subtarget.

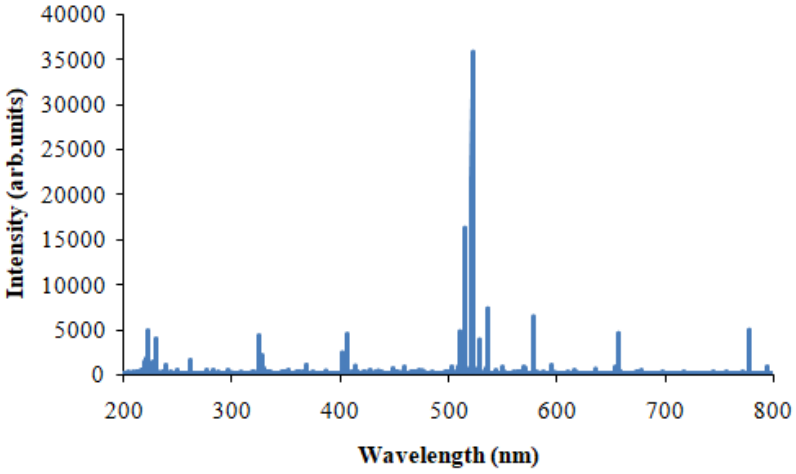


Figure 2. Emission spectrum taken from the pure Cu metal.

The analysis of elements in human blood serum was further made. Figure 3 shows emission spectrum obtained from the human blood serum of normal patient using standard LIBS technique operated at reduced pressure of ambient air (5 torr). The laser energy used was 70 mJ. The analytical lines of C I 247.8 nm, H I 656.3 nm, O I 777.7 nm clearly occurs with high intensity and low background emission. The other lines of neutral sodium Na I 588.9 nm, Na I 589.5 nm, ionic Ca II 393.3 nm and Ca II 396.8 nm appear faintly in the spectrum. Those elements are major and minor elements in the human blood serum as reported here [13]. In addition, typical lines of neutral Cu clearly occur at 324.7 nm, 327 nm, 510.5 nm, 515.3 nm, and 521.8 nm. These lines are contributed from the Cu plate used as a subtarget.

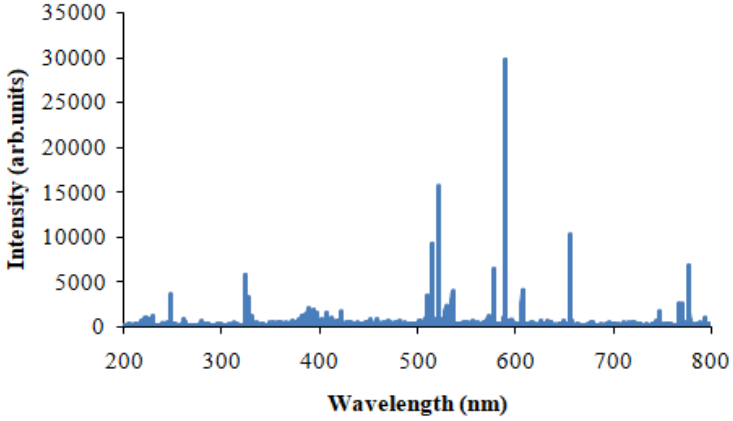


Figure 3. Emission spectrum taken from the human blood serum of normal patient at reduced pressure of ambient air.

To obtain optimum intensity and S/N ratio of analyte, the effect of laser energy to emission intensities of major and trace elements in normal human blood serum was examined. Figure 4 shows the laser energy dependence to emission intensities of C I 247.8 nm, H I 656.3 nm, O I 777.7 nm, and Ca I 393.3 nm. It can clearly be seen that the S/N ratio of all elements increase with increasing the laser energy from 30 mJ to 70 mJ. As reported in the paper [14], the dissociation and excitation of atoms in the sample effectively happens with an increment of laser energy. However, it should be mentioned that the intensities of atoms remain stable when the laser energy was much more increased, which might be due to saturation. Also, when laser energy was more increased, the ablation of the Cu subtarget metal increase, increasing the ablated Cu intensities and thus disturbing the emission lines of analytes. Therefore, in this present work, the laser energy of 70 mJ was selected during experiment for obtaining the optimum emission intensities and S/N ratio of analytical lines.

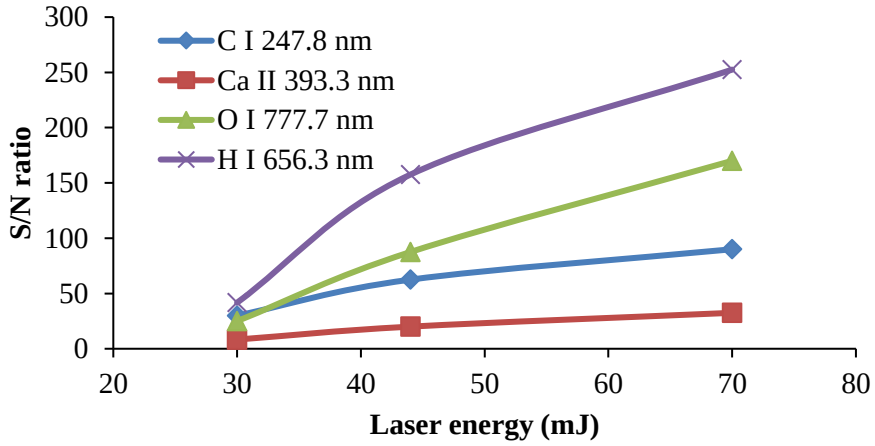


Figure 4. Laser energy dependence of the emission intensities of analyte taken from the the human blood serum of normal patient.

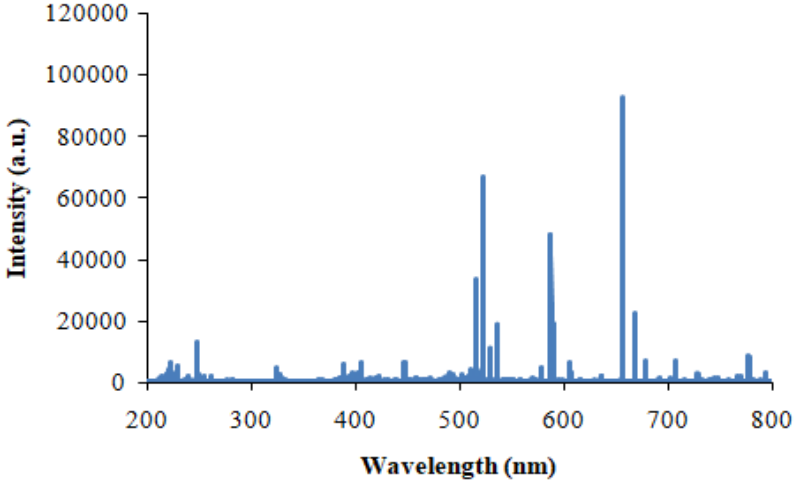
The effect of ambient He gas in the enhancement of emission intensities was also studied. As reported in our previous work [15-16], the use of He as a surrounding gas can produce He metastable atoms, which play role in the excitation process. Figure 5 displays emission spectrum obtained from the human blood serum of normal patient at a reduced pressure of He surrounding gas (30 torr). It appears that total emission intensities of analytical lines in He gas increased almost 4 times compared to the case of ambient air (Fig. 3). All major and trace elements including C I 247.8 nm, Ca II 393.3 nm, Ca II 396.8 nm, H I 656.3 nm, He I 667.8 nm, Na I 588.9 nm, Na II 589.5 nm, and O I 777.7 nm are clearly identified with increasing the intensities compared to the case in ambient air. It is assumed that the increment of the total emission intensities happens in the He plasma due to the different excitation process. Namely, the excitation process in the He plasma region takes place through He metastable atoms (He* atoms) as reported in our previous work [17]. In this process, lots of He metastable atoms, which have very high potential energy of 19.8 eV, produce in the plasma region. He* atoms collide with analyte atoms and by transferring potential energy of He* atoms, the analyte atoms are excited and ionized via penning effect. The ionized analyzed atoms are then recombined to produce atomic emission. All the process follows the question below,

$$He^* + X \longrightarrow He + X^+ + e^- \text{ ; Penning effect} \qquad (1)$$

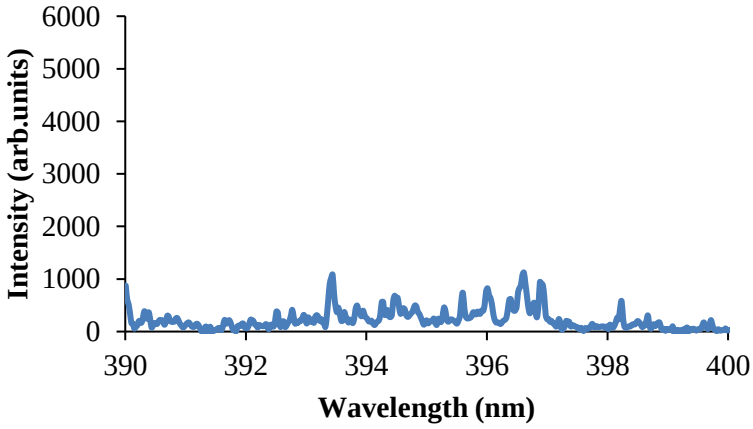
$$X^+ + e^- \longrightarrow X^* \longrightarrow X + h\upsilon \qquad (2)$$

After an X atom is ablated from the metal surface, it collides with a He^* atom present in the He gas plasma induced through the Penning effect. The X atom is then readily ionized and releases a free electron (e^-), as shown in Eq. (1). The energy of this free electron corresponds to the energy difference between the excitation energy of He^* and the ionization energy of the X atom. Multiple collisions

between this electron and ground-state He atoms reduce electron's energy until electron finally recombines with the X atom to form X*, which results in the spectral emission of the X atom, as shown in Eq.(2). Figure 5(b) shows a zoomed area of Fig. 5(a) in the range of 390 nm to 400 nm. It is seen that the emission intensities of Ca II 393.3 nm and Ca II 396.8 nm only faintly occur with quiet noisy.



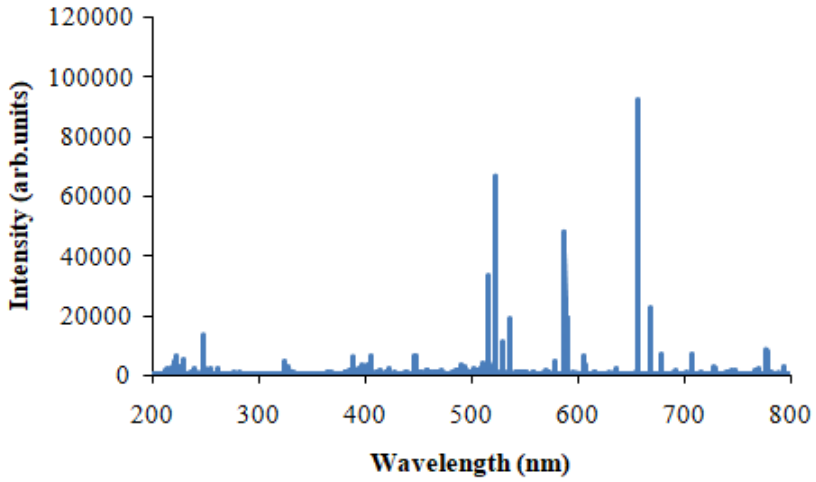
(a)



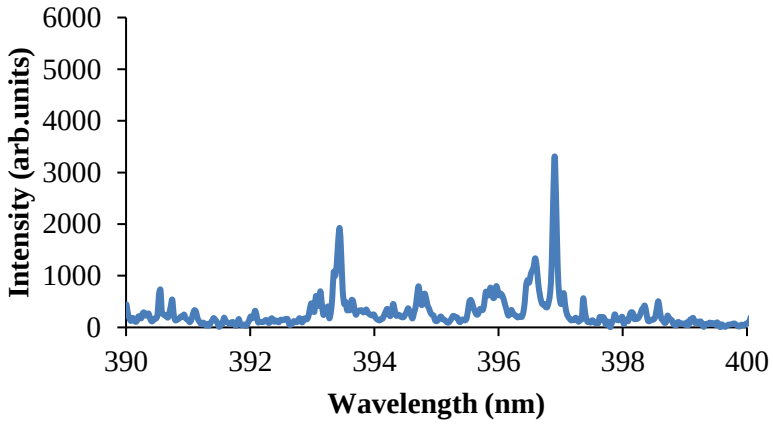
(b)

Figure 5. Emission spectrum taken from the human blood serum of normal patient at reduced pressure of He gas, (a) 200-800 nm and (b) 390-400 nm.

The present technique was then employed to identify and analyze of elements in the human blood serum obtained from the tuberculosis (TB) patient. Figure 6 shows emission spectrum obtained from the human blood serum of TB patient and zoomed area of Fig. 6 in the wavelength region of 390 nm to 400 nm (Fig. 6b). It can clearly be seen that total emission intensities of major and minor elements including C, Na, H, and O obtained from both blood serum of normal and TB patients are almost the same. However, it should be noticed that the intensity of Ca as a trace element in human blood serum of TB patient is significantly different from the normal patient case. Namely, the ionic Ca emission intensity in TB patient is almost four times higher than the case of normal patient. Therefore, the existence of Ca atom in human blood serum can be used to distinguish the serum from the TB patient to normal patient. The human blood of TB patient contains Ca as a trace element [18]. Further detail study on analysis of human blood serum from the TB patients will be carried out in the near future.



(a)



(b)

Figure 6. Emission spectrum taken from the human blood serum of TB patient at reduced pressure of He gas, (a) 200-800 nm and (b) 390-400 nm.

To examine the reproducibility of present technique for human blood serum analysis, the effect of laser shots to the stability of atomic emission intensities was made. Figure 7 shows the laser shot dependence to the S/N ratio of analyte including C I 247.8 nm, H I 656.3 nm, O I 777.7 nm, and Ca II 393.3 nm obtained from the blood serum of TB patients. It clearly appears the emission intensities of C, H, O, and Ca have good stability with the number of laser shots in different position. This result certified that the present technique has good precision in analytical result and thus, it can be employed to analysis of organic liquid material such as human blood serum, which usually difficult to perform using standard LIBS technique.

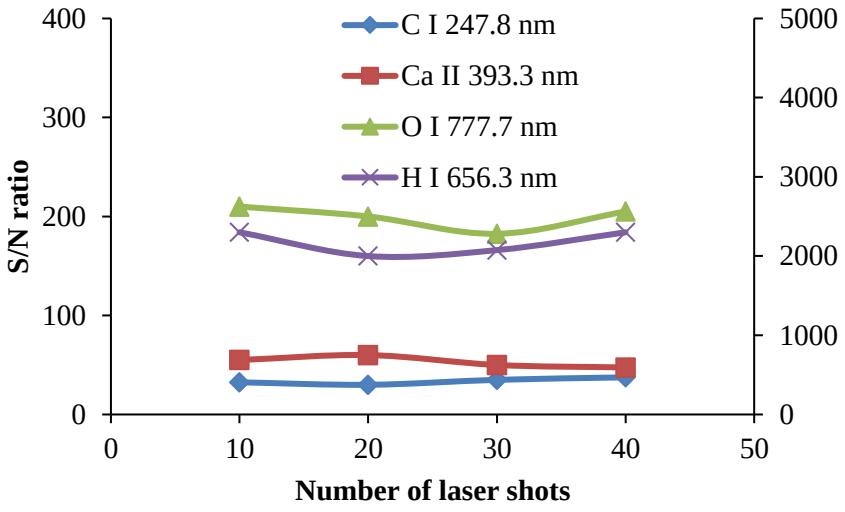


Figure 7. Laser shot dependence of the emission intensities of analyte taken from the human blood serum of TB patient at reduced pressure of He gas.

CONCLUSION

Identification and analysis of human blood serum obtained from normal and TB patients has been conducted by using laser-induced plasma spectroscopy utilizing 355 nm Nd:YAG laser at reduced pressure of He surrounding gas. Identification of major and minor elements including C, H, O, and Na in human blood serum was successfully performed. The intensities of those elements are very stable with the number of laser shots in different positions. It was also found that based on trace elemental identification of Ca, the human blood serum from the TB patient contains higher concentration of Ca compared to the case of normal patient. This present method has high possibility to be applied to analysis of TB patients based on human blood serum as an early diagnosis of TB disease.

ACKNOWLEDGMENT

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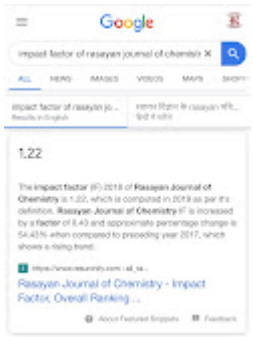

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2. The length of the manuscript should not be more than 08 double spaced A4 pages including all Figures, Tables, Graphs etc and the APCs will be charged as per given on the website.
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6. Especially, References must be strictly as per the format of the Journal. Please mention complete names of the journals in references, not abbreviations. Refer the Sample paper attached.

Best regards,

Prof. Sanjay K. Sharma, FRSC

Editor, RASĀYAN Journal of Chemistry

Note:

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On Mon, Apr 27, 2020 at 11:32 AM Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id> wrote:

> Dear Editor in Chief

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I am Ali Khumaeni from Diponegoro University, Indonesia. We would like to submit a manuscript entitled **Identification and analysis of elements in human blood serum using 355 nm Nd:YAG laser-induced plasma spectroscopy at reduced pressure of He gas** to Rasayan Journal of Chemistry.

Please kindly find the manuscript as in attachment.

Thank you very much for your kindness.

Best regards
Ali Khumaeni

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Best Regards,

Prof. Sanjay K. Sharma, FRSC
Editor-in-Chief, Rasayan J. Chem. (An SCOPUS indexed Journal, Since 2008)

www.rasayanjournal.com | www.rasayanjournal.co.in
Contact: +91 9001699997, +91 9414202678

2 attachments

Revised Manuscript (Ali Khumaeni) RJC 20200504.docx
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RJC paper.pdf
1417K

webmail FISIKA universitas diponegoro

Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

REVISION-1 RJC- 5975/2020

RASĀYAN J. Chem. <rasayanjournal@gmail.com> Mon, May 4, 2020 at 6:52 PM
To: Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

Thank you for your mail.

On Mon, May 4, 2020 at 1:53 PM Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id> wrote:

Dear Editor in Chief
Rasayan Journal of Chemistry

Thank you very much for your kind email. We are very pleased to know that our manuscript passed the quality check.

We would like to send the revised manuscript as your suggestion. We have followed the guideline of the journal and template for writing including references section.

We also would like to send the potential referees for this manuscript as follow,
1. Dr. Rinda Hedwig
Bina Nusantara University, Indonesia
Email: arindaho@yahoo.com

2. Dr. Nasrullah Idris
Syiah Kuala University, Indonesia
Email: nasidain@yahoo.com

3. Prof. Dr. Raja Kamarulzaman
University Teknologi Malaysia
Email: rkamarulzaman@utm.my

Thank you very much for your kindness.

Best regards
Ali Khumaeni

On Sun, May 3, 2020 at 2:18 PM RASĀYAN J. Chem. <rasayanjournal@gmail.com> wrote:

Assigning Manuscript Number and Revision-1

Your Manuscript No. is: RJC- 5975/2020. Please use this number always in any of your future correspondence with us.

Dear Author,

Thanks for submitting your valuable manuscript for the review and subsequent publication in RASĀYAN Journal of Chemistry, which is A SCOPUS (Elsevier) indexed [Since 2008* and the current **CiteScore 2019** is 1.20] international Research Journal of Chemical Sciences. Its also approved by UGC (India) and included in its CARE list.

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5. Please refer the attached **SAMPLE PAPER.** Send your manuscript again in attached Template file ONLY, as **Revision-1** mentioning the assigned Manuscript No. in the subject line of E-mail.
6. Especially, References must be strictly as per the format of the Journal. Please mention complete names of the journals in references, not abbreviations. Refer the Sample paper attached.

Best regards,

Prof. Sanjay K. Sharma, FRSC

Editor, RASĀYAN Journal of Chemistry

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> Dear Editor in Chief
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>
> I am Ali Khumaeni from Diponegoro University, Indonesia. We would like to submit a manuscript entitled **Identification and analysis of elements in human blood serum using 355 nm Nd:YAG laser-induced plasma spectroscopy at reduced pressure of He gas** to Rasayan Journal of Chemistry.
>
> Please kindly find the manuscript as in attachment.
>
> Thank you very much for your kindness.
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> Best regards
> Ali Khumaeni

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4. **Acknowledgment dari Editor (2 September 2020)**

webmail FISIKA universitas diponegoro

Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

REVISION-1 RJC- 5975/2020

RASĀYAN J. Chem. <rasayanjournal@gmail.com> Wed, Sep 2, 2020 at 2:57 PM
To: Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

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The paper shall be published in Vol. 14, No.1, 2021 issue of RASĀYAN Journal of Chemistry.

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5. Submission kedua (21 April 2021)

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Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

Manuscript Submission to Rasayan Journal of Chemistry

Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id> Wed, Apr 21, 2021 at 6:24 AM
To: "RASĀYAN J. Chem." <rasayanjournal@gmail.com>

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I am Ali Khumaeni from Diponegoro University, Indonesia. We would like to resubmit a manuscript entitled **Identification and analysis of elements in human blood serum using 355 nm Nd: YAG laser-induced plasma spectroscopy at a reduced pressure of He gas** to Rasayan Journal of Chemistry.

At the end of last year, this manuscript has been accepted to be published in the Rasayan Journal of Chemistry Vol. 14 No.1 2021. However, due to the budget limit, I could not continue the submission process. Therefore, I would like to resubmit the manuscript to the Rasayan Journal of Chemistry.

Please kindly find the manuscript as an attachment.

Thank you very much for your kindness.

Best regards
Ali Khumaeni

FINAL MANUSCRIPT RJC 20210419.docx
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6. Acceptance letter dari jurnal (30 Juni 2021)

webmail FISIKA universitas diponegoro

Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

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RASĀYAN J. Chem. <rasayanjournal@gmail.com> Wed, Jun 30, 2021 at 3:18 PM
To: Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

Acceptance Letter: Ms. Ref. No. RJC-5975 / 2020

Dear Author,

Greetings from **RASĀYAN Journal of Chemistry,**
Congratulations! Your above-mentioned manuscript has been accepted for the publication in the latest issue of **RASĀYAN Journal of Chemistry,** i.e. **Vol. 14, No.4, 2021 issue.**

Herewith please find attached the **Acceptance Letter and Invoice** for your above-mentioned manuscript.

Also, find **Copyright Transfer Form** and **Letter of Original Work** attached. Please send these duly filled and signed docs as soon as possible.

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I look forward to hearing from you in the near future.
Yours Sincerely,
Best regards,
Dr. Sanjay K. Sharma, FRSC
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3 attachments

5975_Acceptance Letter.pdf
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2_Letter of Original work.doc
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7. Komentar dari Editor dan Reviewer (18 September 2021)

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Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

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RASĀYAN J. Chem. <rasayanjournal@gmail.com> Sat, Sep 18, 2021 at 5:05 PM
To: Ali Khumaeni <khumaeni@fisika.fsm.undip.ac.id>

Demand of Revision-2: Ms. Ref. No. RJC-5975 / 2020

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its Volume No., Page No., Full Name of Journal / Name of Publisher, Year etc. and format according to the Guidelines of the Journal.

7. After revising the manuscript, please send it as **Revision-2, RJC-XXX,** where **XXX** stands for your manuscript Number mentioned above. Please mention your MS Number correctly in the subject line when you send the **Revision-2** version of your manuscript.

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Dr. Sanjay K. Sharma, FRSC

Editor, **RASĀYAN Journal of Chemistry**

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Reviewer's Report

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Abstract, Introduction and Literature Review:	1. The abstract must be brief and concise, one paragraph focusing on the theme of the work. Revise it. 2. The introduction should not be lengthier. It should mention the purpose of the study. 3. Use the latest references in this section.
Research Methodology:	1. Research Methodology/ Experimental should be precise and clear. 2. Do not duplicate the same data in Tables and Figures.
Results and Discussion:	1. This portion must be more precise and connected with the proposed/ used/reported methodology. 2. Use better Quality of Figures, if possible 3. Captions of the Figures and Tables must be rightly placed.
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Originality:	3
Contribution to the Field:	2
Technical Quality:	3
Clarity of Presentation :	3
Depth of Research:	3

SECTION-IV : Recommandation

(Kindly mark with an X)

Accept As it is:	
Requires Minor Revision:	
Requires Moderate Revision:	
Requires Major Revision:	Major Revision Required
Rejected for publication in RJC: (Please give reason)	

SECTION-V: Additional Comments (You may use additional sheet): **No addition Sheet attached**

Signature of the Reviewer

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8. Balasan ke Editor dan Reviewer

Dear Editor in Chief of Rasayan Journal of Chemistry

We are very pleased to receive an information that our paper is acceptable to be published in your journal. Based on the comments from Reviewer, we would like to respond the reviewer comment as below. We have included the revision in the revised manuscript indicated by red letter.

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Best regards
Ali Khumaeni

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Research Methodology:	1. Research Methodology/ Experimental should be precise and clear. 2. Do not duplicate the same data in Tables and Figures.
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Abstract, Introduction and Literature Review:	1. The abstract must be brief and concise, one paragraph focusing on the theme of the work. Revise it. 2. The introduction should not be lengthier. It should mention the purpose of the study. 3. Use the latest references in this section.	**1. We have revised the abstract to be more concise.** **2. We have reduced the introduction. Also, we included the purpose of the study in the revised manuscript.** **3. We have included the latest references in the revised manuscript.**
Research Methodology:	1. Research Methodology/ Experimental should be precise and clear. 2. Do not duplicate the same data in Tables and Figures.	**1. We have revised experimental procedure explanation to be more precise and clearer as in the revised manuscript.** **2. We avoid to make a duplicate of data in Tables and Figures**
Results and Discussion:	1. This portion must be more precise and connected with the proposed/ used/reported methodology. 2. Use better Quality of Figures, if possible 3. Captions of the Figures and Tables must be rightly placed.	**1. We have revised some explanation in the result and discussion to explain and attain the purpose of the study.** **2. We have improved the quality figure by improving their resolution.** **3. We have revised the right caption to be rightly**

Bibliography/ References:	.. References must be cited in the text as per the journal's template and listed with their DOIs as per the journal's style. Please refer to Sample Paper.	**We have added some references and added all papers with their DOI following your sample paper.**

9. Paper setelah proses revisi

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ELEMENTAL CHARACTERIZATION OF HUMAN BLOOD USING LASER-INDUCED BREAKDOWN SPECTROSCOPY UTILIZING 355 NM ND:YAG OPERATED AT REDUCED PRESSURE OF HE GAS

A. Khumaeni[1,*], W. S. Budi[1], A.Y. Wardaya[1], R. Hedwig[2], and K. H. Kurniawan[3]

[1]Department of Physics, Faculty of Science and Mathematics, Diponegoro University, Jl. Prof. Soedharto, S.H., Tembalang 50275, Semarang, Indonesia
[2]Bina Nusantara University, Jakarta Barat 11480, Indonesia
[3]Maju Makmur Mandiri Research Center, Kembangan, Jakarta Barat, Indonesia

✉Corresponding Author: khumaeni@fisika.fsm.undip.ac.id

ABSTRACT

The human blood serum has often been used as a media for diagnoses of various diseases based on elemental composition. In this paper, elemental identification and analysis of human blood serum has been performed using a standard LIBS technique utilizing 355 nm Nd:YAG laser under He surrounding gas. Experimentally, a human serum was homogeneously dropped on a copper metal plate to produce a thin film. The film was then evacuated in a sample chamber, which is filled by He gas at 5-3 torr. A Nd:YAG laser was bombarded on a film to produce a breakdown plasma. Some elements in the serum from the normal and tuberculosis (TB) patients have successfully been identified including C, H, O, Ca, and Na. The analyte intensities from the human serum of TB patient have good stability with laser shot dependence in different positions. A preliminary test to distinguish the TB patient to normal patient was made based on Ca elements in the blood serum. Namely, the Ca intensities from TB patient is much higher than the case of normal patient.

Keywords: Human blood serum, TB patient, LIBS, Laser-induced plasma spectroscopy, 355 nm Nd:YAG laser

INTRODUCTION

Elements deposited in the human blood serum have attracted many doctors and researchers especially in the field of medical researches [1]. The human serum contains essential elements, which are very important for human life. Some imperative elements are nitrogen, oxygen, hydrogen, carbon, potassium, phosphorus, chlorine, and magnesium, while the essential trace elements are calcium, iron, zinc, manganese, chromium, iodine, silicon, and arsenic. These elements should be present in the human blood in a fair constant concentration. Nutritional elemental deficiency or abundance in the human body including human blood serum leads to susceptibility to infectious diseases. The human serum has often been often used as media for diagnoses of various diseases based on elemental composition [2]. Therefore, sensitive and accurate elemental identification and analysis of blood serum is indispensable.

Some imaging and spectroscopic methods have been commercially purchasable and employed in the study on disease diagnosis based on elemental composition. These ICP-OES and NAA spectroscopy. Such methods are widely adopted for accurate and sensitive elemental analyses. However, tedious sample pretreatments are needed and the techniques suffer from serious spectra interference because of multielements present in the sample target [3-5].

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Laser-induced breakdown spectroscopy (LIBS) is a rising-star technique for elemental analysis in many kinds of samples such as gases, liquids, and solids [6-10]. Experimentally, a pulse Nd:YAG laser 1064 nm is used to induce a breakdown plasma, which plays a role as an excitation source of atoms from the material target. The applications of LIBS to elemental analysis of human blood serum have reported in some literature. However, it is known that LIBS has a limitation for the analysis of liquid samples such as blood serum, due to the low sensitivity and delicate sample preparations. Furthermore, a standard LIBS technique operated at atmospheric ambient air is very delicate to detect H and C, which are main elements in the blood serum, because of the time mismatch effect [11-12].

In this work, we proposed laser-induced plasma spectroscopy using 355 nm Nd:YAG laser in reduced pressure of He gas for identification and analysis of elements in the blood serum including human blood serum from normal patient and tuberculosis patients. The use of He gas in the study is to produce lots of He metastable atoms (He* atoms) in the plasma. The He* atoms work assisting a process of atomic excitation of the analyte atoms including light atoms of carbon and hydrogen. The sample was made as a film deposited on a copper metal subtarget. The result certified that the element intensities of C and H in the both human blood serum of normal and TB patients is successfully enhanced with optimum S/N ratio and without any broaden line. Furthermore, the human blood serum of the TB patients can be distinguished from the blood serum of normal patients based on trace element of Ca identified in the spectrum.

EXPERIMENTAL

Figure 1 displays a setup used in this paper. First, an Nd:YAG laser (355 nm, 10 Hz, energy of 70 mJ) was irradiated and focused on a sample target using a quartz lens (f = 150 mm) to initiate and produce a breakdown plasma. Experimentally, the sample target was put in a chamber, in which the helium gas (air liquid, purity of 6N) was used as an environmental gas of sample with a flowing rate of 10 liter per minute and gas pressure of 5 torr.

The human blood serum collected from the normal patients and TB patients at Diponegoro National Hospital were used as sample target. For experiment, 1 ml liquid serum was poured on a copper metal plate (99.9 % purity) with a dimension of 0.1 x 20 x 20 mm^3. The serum was homogeneously spread on the surface of Cu plate. The serum was then placed in the room temperature for 30 minutes to produce a serum film. During data acquisition, the sample was put in a chamber and was rotated with a rotation rate of 2 rotation per minute (rpm).

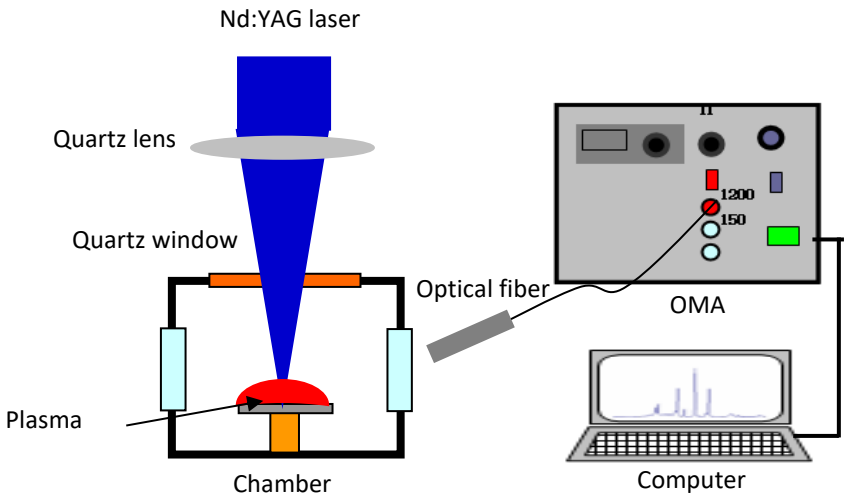


Figure 1. Experimental setup used in this work

The atomic emission spectrum was obtained from the breakdown plasma by using an Echelle spectrograph (Mechelle M5000, Andor) via an optical fiber that is connected to the spectrograph. The delay time and gate width are 1 μs and 5 μs, respectively.

RESULTS AND DISCUSSION

Initially, spectrochemical characteristics of Cu metal plate as a metal subtarget during the study was examined. Figure 2 displays analytical spectrum of Cu taken from the Cu metal plate only. Typical resonance lines of neutral Cu occur at 324.7 nm and 327.4 nm. The other lines of typical neutral Cu are also detected at 510.5 nm, 515.3 nm, and 521.8 nm. These lines are contributed from the Cu plate used as a subtarget. No other elements are identified from the Cu subtarget.

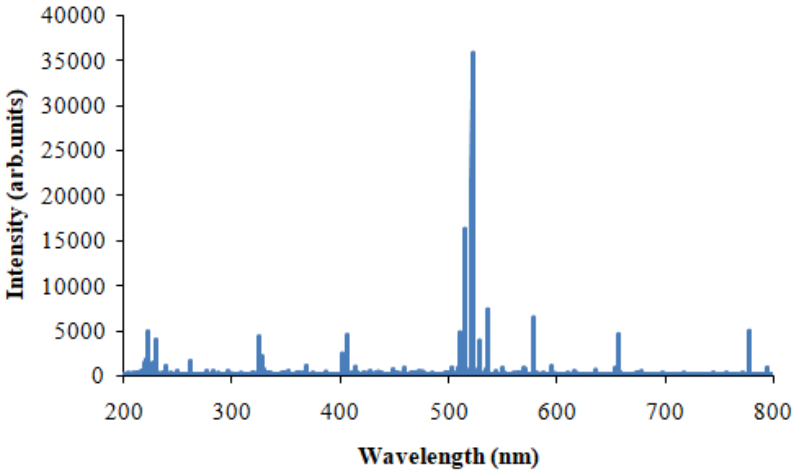


Figure 2. Analytical spectrum taken from the Cu metal.

Further work was identification of elements from the human blood serum. Figure 3 displays an emission spectrum of the human blood serum of normal patient using present LIBS technique. The laser energy used was 70 mJ. The analytical lines of neutral C, H, and O occur clearly at 247.8 nm, 656.3 nm, and 777.7 nm, respectively. The other lines of neutral sodium at 588.9 nm and 589.5 nm, ionic Ca at 393.3 nm and 396.8 nm appear faintly in the spectrum. Those elements are major and minor elements in the human blood serum as reported here [13]. In addition, typical lines of neutral Cu clearly occur at 324.7 nm, 327 nm, 510.5 nm, 515.3 nm, and 521.8 nm. These lines are contributed from the Cu plate used as a subtarget.

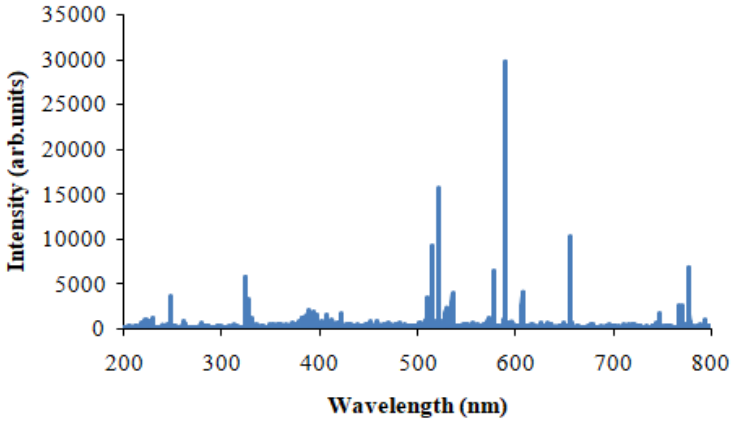


Figure 3. Emission spectrum taken from the human blood serum of normal patient at reduced pressure of ambient air.

To obtain optimum intensity and S/N ratio of analyte, the effect of laser energy to emission intensities of major and trace elements in normal human blood serum was examined. Figure 4 shows the laser energy dependence to emission intensities of C, H, and O at 247.8 nm, 656.3 nm, and O I 777.7 nm, respectively, and Ca I 393.3 nm. It can clearly be seen that the S/N ratio of all elements increase with increasing the laser energy from 30 to 70 mJ. As reported in the paper [14], atomic excitation in the plasma region effectively happens with an increment of laser energy. However, it should be mentioned that the intensities of atoms remain stable when the laser energy was much more increased, which might be due to saturation. Also,

when laser energy was more increased, the ablation of the Cu subtarget metal increase, increasing the ablated Cu intensities and thus disturbing the emission lines of analytes. Therefore, in this present work, the laser energy of 70 mJ was selected during experiment for obtaining the optimum emission intensities and S/N ratio of analytical lines.

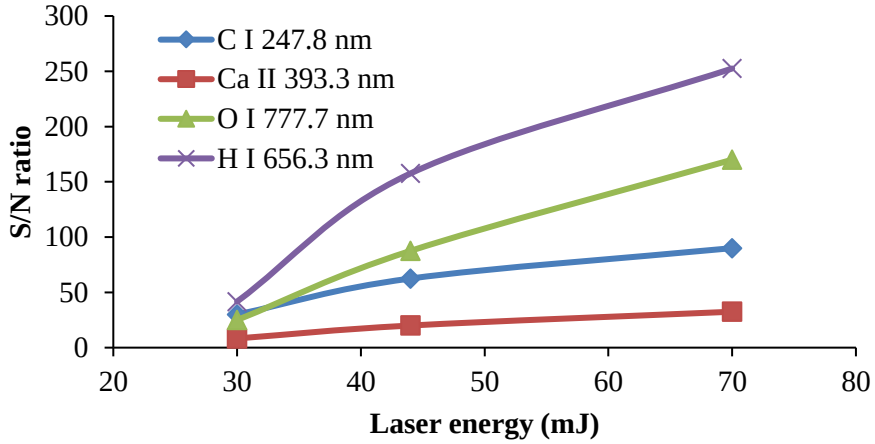


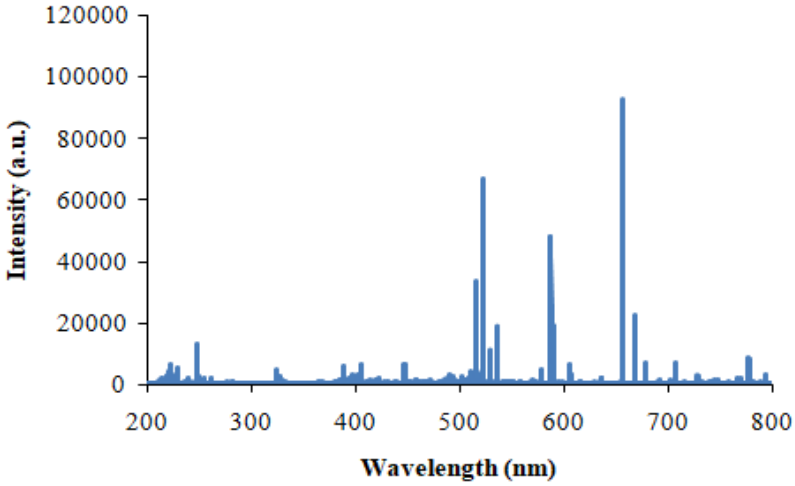
Figure 4. Laser energy dependence of the emission intensities of analyte taken from the the human blood serum of normal patient.

The effect of ambient He gas in the intensity enhancement was also studied. The use of He as a surrounding gas can produce He metastable atoms, which play role in the excitation process [15-16]. Figure 5 displays human blood spectrum of normal patient. It appears that total emission intensities of analytical lines in He gas increased almost 4 times compared to the case of ambient air (Fig. 3). All major and trace elements including neutral C at 247.8 nm, ionic C at 393.3 nm and 396.8 nm, H I 656.3 nm, He I 667.8 nm, neutral Na at 588.9 nm and 589.5 nm, and O I 777.7 nm are clearly identified with increasing the intensities compared to the case in ambient air. It is assumed that the increment of the total emission intensities happens in the He plasma due to the different excitation process. Namely, the excitation process in the He plasma region takes place through He metastable atoms (He* atoms) [17]. In this process, lots of He metastable atoms, which have very high potential energy of 19.8 eV, produce in the plasma region. He* atoms collide with analyte atoms and by transferring potential energy of He* atoms, the analyte atoms are excited and ionized via penning effect. The ionized analyzed atoms are then recombined to produce atomic emission. All the process follows the question below,

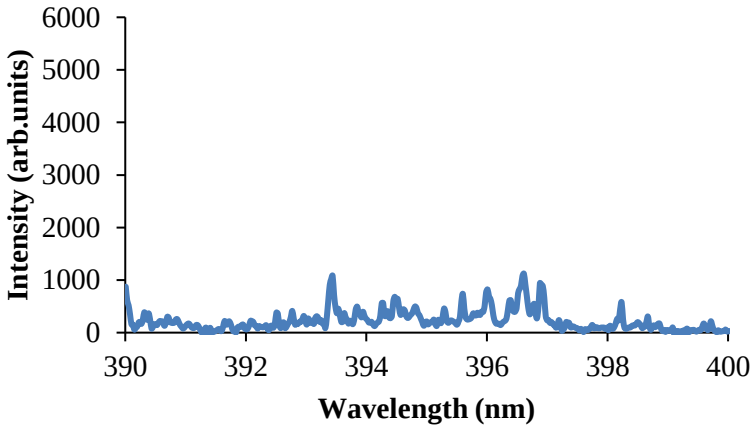
$$He^* + X \longrightarrow He + X^+ + e^- \text{ ; Penning effect} \qquad (1)$$

$$X^+ + e^- \longrightarrow X^* \longrightarrow X + h\upsilon \qquad (2)$$

Ablated X atom from the material target collides via penning effect with the metastable He atoms accumulated in the He gas plasma region, resulting in X ion and free electron (Eq. 1). Multiple collisions among free electrons, He metastable atoms, and other constituents in the plasma region reduce electron's energy and finally electron recombines with the X ion to produce X*, which results in emission of X atom as displayed in Eq. 2. Figure 5(b) shows a zoomed area of Fig. 5(a) in the range of 390 nm to 400 nm. It is seen that the emission intensities of ionic Ca at 393.3 nm and 396.8 nm only faintly occur with quiet noisy.



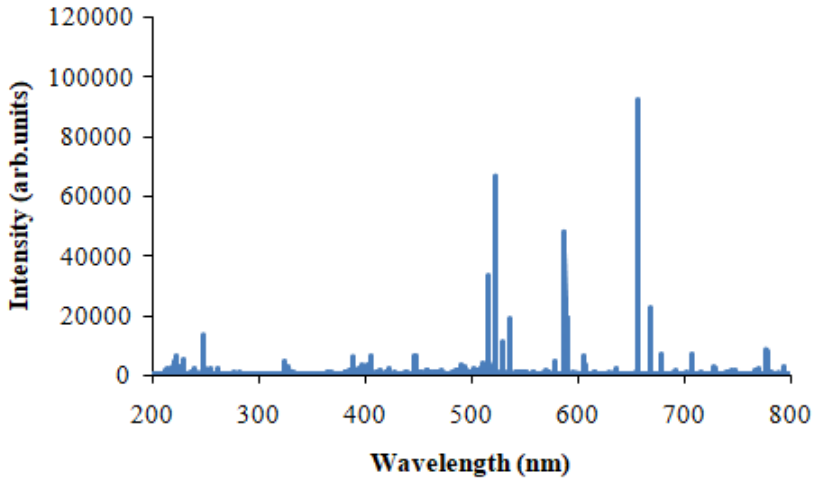
(a)



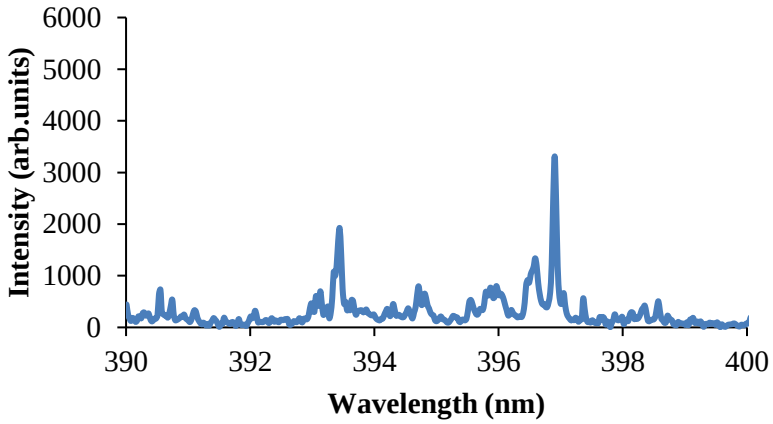
(b)

Figure 5. Emission spectrum taken from the human blood serum of normal patient at reduced pressure of He gas, (a) 200-800 nm and (b) 390-400 nm.

The present technique was then employed to identify and analyze of elements in the blood serum obtained from the tuberculosis (TB) patient. Figure 6 is a spectrum taken from the human blood serum of TB patient and zoomed area of Fig. 6 in the wavelength region of 390 nm to 400 nm (Fig. 6b). Total emission intensities of major and minor elements including C, Na, H, and O obtained from both blood serum of normal and TB patients are almost the same. However, it should be noticed that the intensity of Ca as a trace element in human blood serum of TB patient is significantly different from the normal patient case. Namely, the ionic Ca emission intensity in TB patient is almost four times higher than the case of normal patient. Therefore, the existence of Ca atom in human blood serum can be used to distinguish the serum from the TB patient to normal patient. The human blood of TB patient contains Ca as a trace element [18]. Further detail study on analysis of human blood serum from the TB patients will be carried out in the near future.



(a)



(b)

Figure 6. Emission spectrum taken from the human blood serum of TB patient at reduced pressure of He gas, (a) 200-800 nm and (b) 390-400 nm.

The reproducibility of the analytical intensities obtained from the human blood serum was then examined. Figure 7 shows the laser shot dependence to the S/N ratio of analyte including ionic Ca 393.3 nm, neutral O 777.7 nm, neutral H 656.3 nm, and neutral C 247.8 nm obtained from the blood serum of TB patients. Intensities of Ca, O, H, and C have good stability with the number of laser shots in different position. The present technique has good precision in analytical result and thus, it can be employed to analysis of organic liquid material such as human blood serum, which usually difficult to perform using standard LIBS technique.

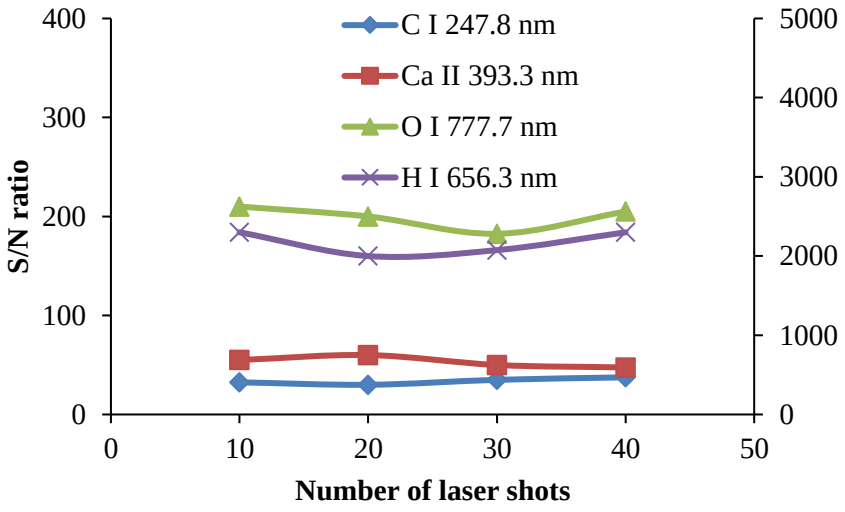


Figure 7. Laser shot dependence of the emission intensities of analyte taken from the human blood serum of TB patient at reduced pressure of He gas.

CONCLUSION

Identification and analysis of human blood taken from the normal and TB patients has been realized by LIBS utilizing 355 nm Nd:YAG laser at reduced pressure of He surrounding gas. Identification of elements including C, H, O, and Na in human blood serum was successfully performed. The intensities of those elements are very stable with the number of laser shots in different positions. It was also found that based on trace elemental identification of Ca, the human blood serum from the TB patient contains higher concentration of Ca compared to the case of normal patient. This present method has high possibility to be applied to analysis of TB patients based on human blood serum as an early diagnosis of TB disease.

ACKNOWLEDGMENT

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