

ICIC Express Letters
(An International Journal of Research and Surveys)

Author's Warranty and Assignment of Copyright

Dear Contributor(s),

We are pleased that you are contributing a paper to the **ICIC Express Letters** -- *An International Journal of Research and Surveys* (ICIC-EL). State the complete title and all authors of the contribution, read the agreement, sign and return it to the ICIC-EL Office on the online submission system.

Paper ID: ICICEL-2104-017

Full title of paper:

Anticancer Compound Identification Model of Rodent Tuber's Liquid Chromatography-Mass Spectrometry Data

Author(s) (Full names):

Iwan Binanto
Harco Leslie Hendric Spits Warnars
Nesti Fronika Sianipar
Widodo Budiharto

Your submission of this work and our acceptance for publication are contingent upon your warranty of the following conditions which constitute the Agreement between the author(s) and the ICIC International.

You warrant that the above titled contribution is original, has not been published elsewhere or has not been submitted for publication elsewhere. You warrant that it does not contain libelous material. You agree to transfer copyright to the ICIC International upon acceptance for publication. If the article contains material copyrighted by others, the author warrants that written permission has been obtained from copyright holders who agree to transfer copyright to the extent allowable.

Please indicate your agreement with these terms by signing and dating below.

Author(s) Signature:



Date: 20 May 2021

Please sign and return this form promptly

It is necessary to sign and return this Author's Warranty and Assignment of Copyright in order to publish your contribution

Return Copyright form on the submission system



Iwan Binanto <binanto.iwan@gmail.com>

Acceptance Letter: ICICEL-2104-017

1 pesan

office@icicel.org <office@icicel.org>

12 Mei 2021 11.13

Kepada: binanto.iwan@gmail.com

Cc: spits.hendric@binus.ac.id, nsianipar@binus.edu, wbudiharto@binus.edu

Dear Mr. Iwan Binanto,

It is my great pleasure to inform you that your contribution to ICIC Express Letters,

Reference No.: ICICEL-2104-017

Title: Anticancer Compound Identification Model of Rodent Tuber's Liquid Chromatography-Mass Spectrometry Data

Author(s): Iwan Binanto, Harco Leslie Hendric Spits Warnars, Nesti F. Sianipar and Widodo Budiharto

has been accepted for the publication with the following conditions. Also, please use the ICIC-EL style files <http://www.icicel.org/ell/information.html> (either LaTeX source files, or Word with PDF files) for preparing your paper (no more than 8 pages) for the publication.

The paper is generally well written and organized. The results presented in the paper seem correct, and potentially useful in practice. The techniques employed to tackle the problems are generally standard with some novelties. The paper can be accepted for publication subject to some necessary minor changes as below:

Comments:

- 1) This study proposes an anticancer compound identification model from liquid chromatography-Mass spectrometry data of Rodent Tuber. In Introduction, the research contributions should be stated clear. And a brief organizational overview is suggested to be added in the end of Introduction to facilitate readers.
- 2) More details of reviewed literature and corresponding discussion should be added in Section 2 to make the research motivations clear.
- 3) Section 3 is too short as an independent section, which may be combined with Section 4.
- 4) What is the number of sampling, 18,000 or 18,275?
- 5) Figure quality should be improved; for example, in Figure 2, please recheck "Otomated" and "webscropping".
- 6) In consideration of monochrome print, to use color like "blue dots" and "red dots" for identification in Figure 5 is not effective.
- 7) More explanation should be added on Table 1 to present the effectiveness of the identification model, for example, what does the number of "identified count" show?
- 8) The manuscript should be greatly improved regarding language presentation. For example, in Abstract, the 4th and the last sentences in Abstract are ill-formed; "This combination namely LC-MS" in Paragraph 2 of Introduction is not a complete sentence.
- 9) The following research is suggested to be cited to enrich the current study: Yunna Kim and Heasoo Hwang, Approximate Consistent Weighted Sampling for Efficient Top-k Search, International Journal of Innovative Computing, Information and Control, vol.16, no.3, pp.1125-1132, 2020, DOI: 10.24507/ijicic.16.03.1125.

Please note that if the paper is not revised satisfactorily complying with the conditions above, ICIC-EL reserves the right to reject the paper from the journal.

Please submit your Final Version, Revision Note, the Publication Page Charges and Copyright Form (<http://www.icicel.org/ell/information.html>) to us within Three Weeks' Time (from the date of this message) at our online submission system <http://www.icicel.org>. Thank you for your understanding and cooperation.

ICIC-EL has been indexed in Scopus (Elsevier), and INSPEC (IET). We would like you to refer to ICIC-EL publications especially your own works in your future research. We believe it will help you promote your article and enhance its visibility.

Please feel free to contact me if you have any questions about your paper.

Best Regards,
Dr. Yan SHI
Editor-in-Chief, ICIC-EL
Professor, School of Industrial and Welfare Engineering, Tokai University
9-1-1, Toroku, Kumamoto 862-8652, Japan
Tel.: 81-96-386-2666, Fax: 81-96-386-2666
E-mail: office@icicel.org



Iwan Binanto <binanto.iwan@gmail.com>

Invoice-Letter (ICICEL-2104-017)

1 pesan

office@icicel.org <office@icicel.org>

12 Mei 2021 11.14

Kepada: binanto.iwan@gmail.com

Cc: spits.hendric@binus.ac.id, nsianipar@binus.edu, wbudiharto@binus.edu

ICIC Express Letters**An International Journal of Research and Surveys**

2021-05-12

INVOICE (No. ICICEL-2104-017)

Mr. Iwan Binanto
Sanata Dharma University
Indonesia
binanto.iwan@gmail.com

Publication Page Charges for:

Reference No.: ICICEL-2104-017

Title: Anticancer Compound Identification Model of Rodent Tuber's Liquid Chromatography-Mass Spectrometry Data

Author(s): Iwan Binanto, Harco Leslie Hendric Spits Warnars, Nesti F. Sianipar and Widodo Budiharto

in (ICIC Express Letters -- An International Journal of Research and Surveys, ISSN 1881-803X) as a publication, which will generally be published within 6 months thereafter.

Amount due: JPY48,000 (no more than 8 pages)

Please complete the following form and return it to the ICIC-EL Editorial Office together with your final version on the submission system.

Credit Card: ☐ Visa ☐ MasterCard

Credit Card No.: _____/_____/_____/_____

Expiry Date: _____month/_____year

Card Holder's Name: _____

Authorized Signature: _____

Note that the item is Journal Fee by IJICIC. If you would like to get the Receipt for the payment, please notify us via office@icicel.org and indicate the detailed Receipt Information as the following sample at the same time.

Name: ****

Organization: ****

Paper Title: ****

Yan Shi, Editor-in-Chief
ICIC-EL Editorial Office
Tokai University, Kumamoto Campus
9-1-1, Toroku, Kumamoto 862-8652, Japan
Tel: +81-96-386-2666; Fax: +81-96-386-2666
E-mail: office@icicel.org

ANTICANCER COMPOUND IDENTIFICATION MODEL OF RODENT TUBER'S LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY DATA

IWAN BINANTO^{1,2,*}, HARCO LESLIE HENDRIC SPITS WARNARS¹
NESTI FRONIKA SIANIPAR^{3,4} AND WIDODO BUDIHARTO¹

¹Computer Science Department, BINUS Graduate Program – Doctor of Computer Science

³Food Technology Department, Faculty of Engineering

⁴Research Interest Group Biotechnology

Bina Nusantara University

Jl. K. H. Syahdan No. 9, Kemanggisan, Palmerah, Jakarta 11480, Indonesia
email?

²Informatics Department

Sanata Dharma University

Yogyakarta, Indonesia

*Corresponding author: iwan@usd.ac.id

Received April 2021; accepted July 2021

ABSTRACT. *Chemical compounds identification of Liquid Chromatography-Mass Spectrometry data is challenging, especially anticancer compound identification from the Rodent Tuber sample. This paper proposed a novel model for anticancer compound identification of a sample of Liquid Chromatography-Mass Spectrometry Rodent Tuber data. Data sampling was done by linear systematic sampling. The model begins with data labeling which was giving a name to the compound followed by data labeling of the status anticancer compound or not utilizing webscrapping technique. After the data was labeled, the anticancer compound was identified from the data. This model was successfully identifying the most dominant anticancer compounds contained in the sample of Liquid Chromatography-Mass Spectrometry Rodent Tuber data.*

Keywords: Chemical compound identification, Liquid Chromatography-Mass Spectrometer data, Rodent Tuber, Anticancer compound identification, Linear systematic sampling

1. Introduction. Research in the field of chemical compounds interpretation and identification from the Liquid Chromatography-Mass Spectrometry data is challenging. Mass Spectrometry (MS) is used to determine the mass of particles, to determine the elemental composition of a sample, and to describe the chemical structure of molecules, such as peptides and other chemical compounds [1]. When combined with Liquid Chromatography (LC), more comprehensive information can be obtained. It will consist of hundreds of thousands of mass per charge (m/z), retention time, and intensity [2]. This combination called Liquid Chromatography-Mass Spectrometry (LC-MS). It is also widely utilized to examine extracts of medicinal plants.

This paper will present and explain our model to identify anticancer compounds from LC-MS data of Rodent Tuber. It contributed to the development of a method of chemical compound identification in LC-MS. As a case study, we use one of the LC-MS data of Rodent Tuber from the studies of Sianipar et al. [3-8]. Their studies resulted in 10 datasets which are proprietary raw data. This means, only the instrument that produced them can read. The dataset should be converted to a format that is human-readable and easier to analyze. There are two steps, which are 1) convert the raw data to .mzXML which

is an open format by an open-source software developed by Chambers et al. [9], namely Proteowizard version 3 for Windows, and 2) convert .mzXML to .xlsx, by our software, developed by Python programming. Only one dataset of ten is used in this paper and it is randomly selected.

Using huge native data would be costly. So, data sampling will be carried out. LC-MS data of Rodent Tuber in this case is time-series data [10], and it is necessary to get samples per period time to obtain a representative sample that represents the actual dataset. We use a sampling technique called Linear Systematic Sampling (LSS) as Algorithm 1, because it is simple and produces a sample that represents the actual dataset [11,12] compared to Kim and Hwang [13]. In this case, the number of samples which is about 18,000 and 18,275 was generated. The sample data from the result of Algorithm 1 will be used in this paper.

Algorithm 1. LSS

- 1: Get data from the dataset.
 - 2: Create a list that contains the "Retention Time" column without duplication with the pivot feature.
 - 3: Find the skip (s) value with a sample size (y), while the number population of elements (X) is the actual data list:
 $s = \text{len}(\text{list})/18000$
 - 4: Create a list of indexes with the first index as a random integer Rd in range 1 to s , which determines the sample to be the units numbered Rd , $Rd + s$, $Rd + 2s$, and so on.
 - 5: This index is used to retrieve data in the actual data list and put it on the temporary list.
-

This paper is categorized as follows: Section 2 describes the related works, Section 3 describes the research method and the proposed model, Section 4 describes the result and discussion, and Section 5 focuses on conclusions and future work.

2. Related Works. The back-to-nature trend by using natural ingredients including plants for treatment is increasing. This plant needs to be examined for its chemical content so that it is used more optimally. One of the plants studied intensively in its ingredients is Rodent Tuber [4,14-19]. Apart from the study of chemical compound content, breeding and its effect on chemical compound content were also investigated [3-8], but they still manually identify the chemical compounds that exist through Gas Chromatography-Mass Spectrometry and Liquid Chromatography-Mass Spectrometry data. This identification is assisted by an online database. It takes a lot of time because of done manually.

The more advanced technology, the greater data generated, and the greater challenges. Done manually becomes impossible. There are already many software tools for this, such as XCMS [20-22] which aim to facilitate interpretation of metabolomic data by scientists with limited background in bioinformatics or statistics; MAVEN [23,24] which provide interactive processing of LC-MS-based metabolomics data; CAMERA [25] which is designed to postprocess XCMS feature lists and to collect all features related to a compound into a compound spectrum; **MetaboAnalystR [26]; and the one which is also summarized by Binanto et al. [27].** Almost all of them do not have the feature for identifying anticancer chemical compounds; they discuss more about preprocessing, signal processing, or whole identification of chemical compounds.

3. Research method. Our research method directly uses the proposed model as shown in Figure 1. The first stage of this method is an initial stage by implementing Algorithm 1. This algorithm produces a representative sample of the whole dataset which is 18,275

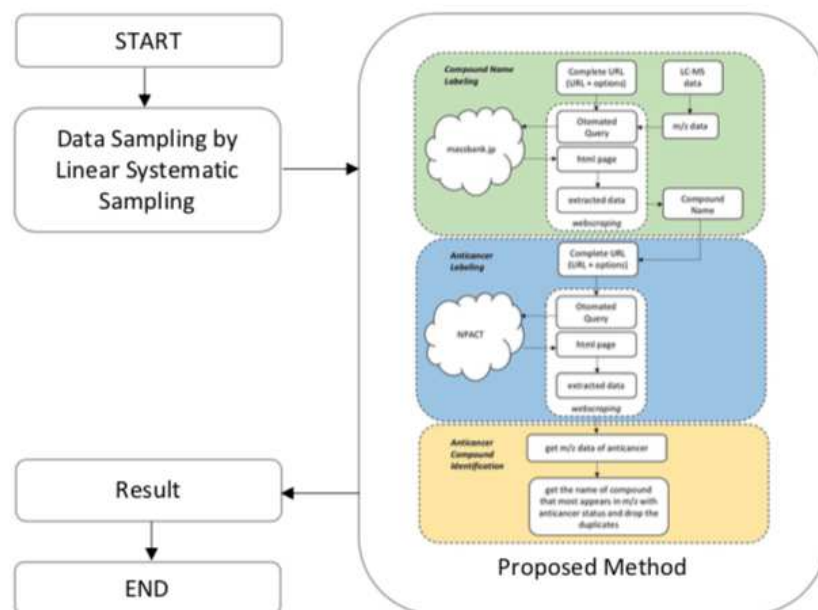


FIGURE 1. Research method

records out of 985,925 records. Then this sample was processed using the proposed model depicted in Figure 2.

3.1. Proposed model. The proposed model has three main stages, which are 1) labeling the name of the compound and its real mass and formula; 2) labeling of compound status: anticancer or not; 3) identification of anticancer compounds. This proposed model is illustrated in Figure 2. Data sampling is not included in this model because for actual conditions, it does not use sample data, but original data.

Labeling is the main thing that must be done in this model because it will be used to retrieve other data from the online database. We utilize an existing online database, namely massbank.jp [28] and NPACT (Naturally occurring Plant-based Anticancerous Compound-Activity-Target database) at <http://crdd.osdd.net/raghava/npact/> [29] for labeling. Unfortunately, there is not any piece of information about the Application Programming Interface (API) on those websites. Hence, we use webscraping technique.

Webscraping technique was originally developed for business purposes in the private sector. It is used to get content from websites to analyze certain structured or unstructured data. However, it offers great benefits for those looking for specific information [30-32]. In this case, it will be used for getting compound names from massbank.jp and anticancer status from NPACT.

3.1.1. Compound name labeling. There are input forms for m/z and formulas that can be filled in one of them on massbank site, to get the compound name. So, m/z value is entered into the form to be queried to massbank. There are a lot of options, but we just used the default options.

The first step to do webscraping is to get a complete URL. To get the name of the compound in masbank.jp, the m/z value is used. Manually, m/z value entered into the “Exact Mass” filling form’s massbank.jp and the search button clicked; since then, there emerged the complete URL with its options in the browser’s address bar as shown in Figure 3. This complete URL will be used for webscraping.

To get the preferred data, we must understand the structure of the HTML page generated by the query. Webscraping technique can run well and get the preferred data by

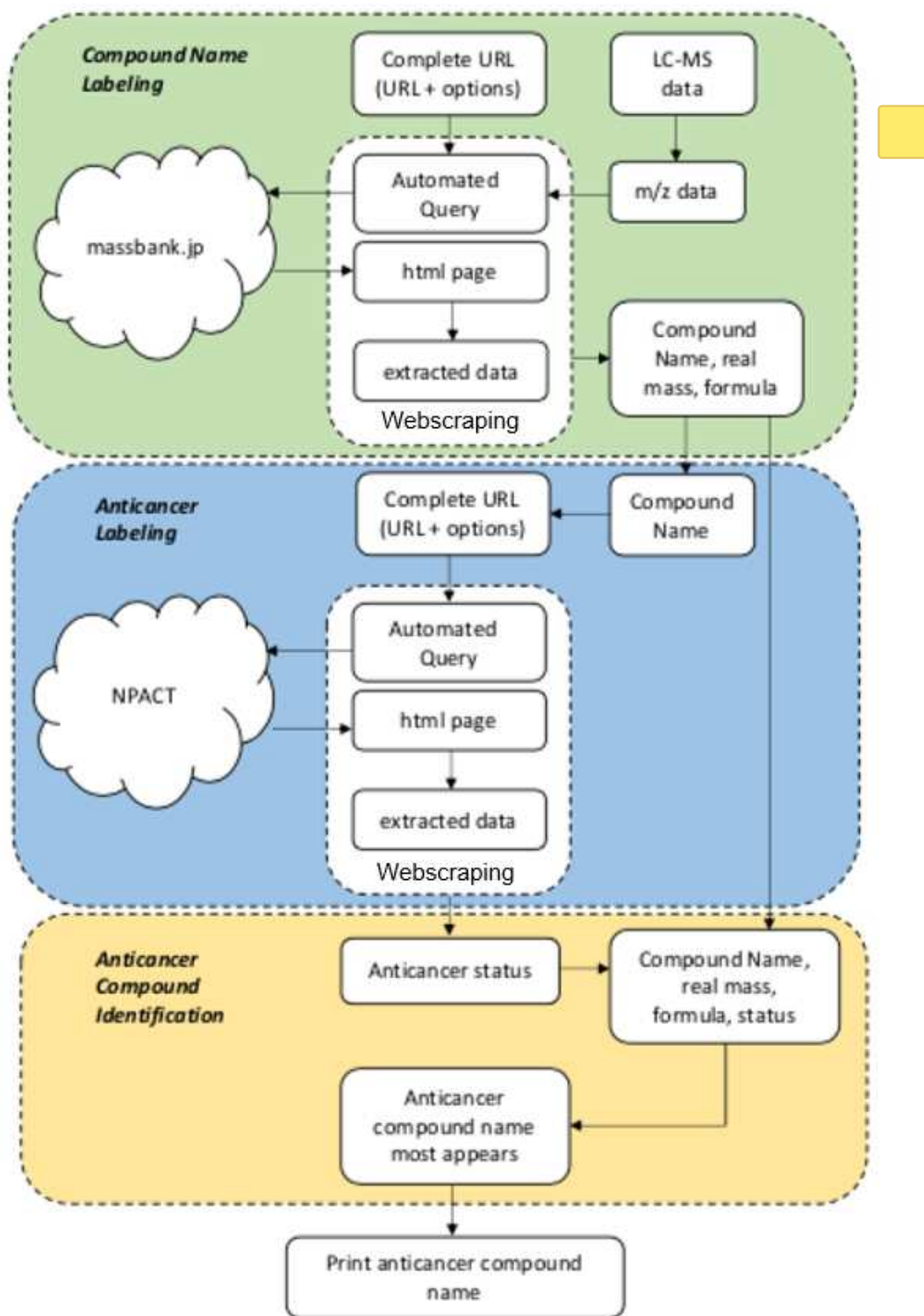


FIGURE 2. The model

http://www.massbank.jp/Result.jsp?compound=&op1=and&mz=68.78610229&tol=0.3&op2=and&formula=&type=quick&searchType=keyword&sortKey=not&sortAction=1&pageNo=1&exec=&inst_grp=ESI&inst=CE-ESI-TOF&inst=ESI-ITFT&inst=ESI-ITTOF&inst=ESI-QIT&inst=ESI-QTOF&inst=ESI-TOF&inst=LC-ESI-IT&inst=LC-ESI-ITFT&inst=LC-ESI-ITTOF&inst=LC-ESI-Q&inst=LC-ESI-QFT&inst=LC-ESI-QIT&inst=LC-ESI-QQ&inst=LC-ESI-QQQ&inst=LC-ESI-QTOF&inst=LC-ESI-TOF&ms=MS2&ion=0

FIGURE 3. Massbank's complete URL

python programming with its library. The preferred data are compound name, compound formula, and real m/z in massbank.jp.

The value of real m/z is the value closest to the input, because, during the experiment, no m/z values were retrieved the same. In our opinion, it was because signal processing is not carried out and the mass itself is a float number not an integer; upon this, we call it a brute force process.

3.1.2. Compound status labeling. This stage aims to label chemical compound whether it is an anticancer compound or not. To do this, the Naturally occurring Plant-based Anticancer Compound-Activity-Target (NPACT) database is used [29]. It does not provide an application programming interface, so webscraping technique is utilized.

This stage is similar to the compound name labeling stage, and the difference is the detailed steps, such as the complete URL and how to extract data from the obtained HTML page. It is simpler than the compound name labeling stage above.

Using a compound name to get the status of the compound in NPACT. Manually, the compound name entered into the filling form's field provided in NPACT and the search button clicked; since then, there emerged the complete URL in the browser's address bar as shown in Figure 4. This complete URL will be used for webscraping.

`https://webs.iiitd.edu.in/raghava/npact/search_cmpnd.php?cmpnd=sanguinarine`

FIGURE 4. NPACT's complete URL

Bold text in Figure 4 is the actual variable that will be replaced with a compound name from the previous stage.

The result of this stage is to obtain the status of the compound name as an anticancer compound (labeled with 1) or not anticancer compound (labeled with 0). Based on this label, the most dominant anticancer compounds will be identified.

3.1.3. Identification. This stage aims to identify the dominant anticancer chemical compounds in the sample of LC-MS Rodent Tuber data. The way it works is to find the most detected anticancer compounds in the sample of LC-MS Rodent Tuber data over the retention time. The algorithm is shown in Algorithm 2.

Algorithm 2. Identification Anticancer Compound

- 1: Get data from the dataset.
 - 2: Get the compound labeled "1" (anticancer) and place it in a new array.
 - 3: Find and count the occurrence of each anticancer compound already in the array.
 - 4: Print the finding which is the most occurrence anticancer compound.
-

The detected anticancer compound is the most appearing anticancer compound and could be said it is dominant. It caused this compound have strong chemical bonds so from the early time it is detected to the last time.

4. Result and Discussion. The use of webscraping for labeling really speeds up and simplifies the task, both for labeling name compounds and for the status of anticancer compounds or not. The data sample contains anticancer and non-anticancer chemical compounds, detected from the early retention time. All the anticancer compounds appear as it is shown in Figure 5. It can be seen that many anticancer compounds were detected at the early retention time. However, not many were detected at the end of the retention time.

Algorithm 2 is used to identify anticancer compounds and successfully identify anticancer compounds contained in the data sample. After the algorithm was run, the results showed the 10 most identified anticancer compound in Table 1. It has been sorted from

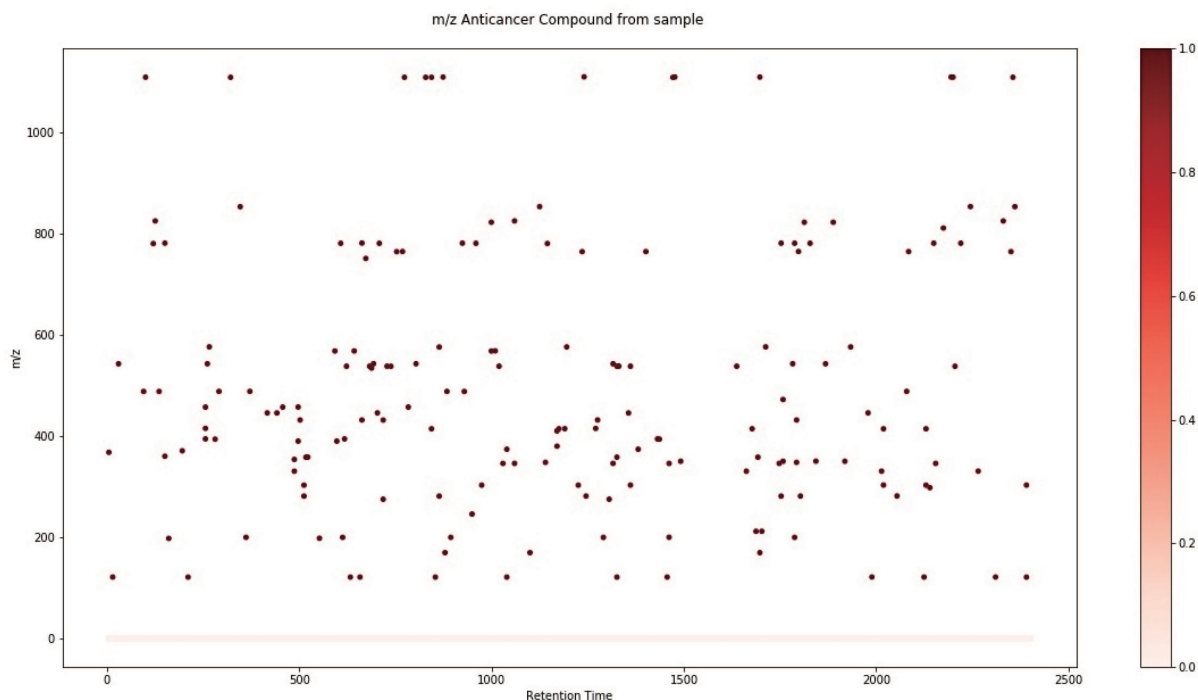


FIGURE 5. (color online) Anticancer compounds from sample based on m/z

TABLE 1. The ten most anticancer compound detected

No.	Compound name	Real m/z	First detection in retention time in second	Last detection in retention time in second	Identified count
1.	Benzoic acid	122.03678	15	2390	12
2.	Saikosaponin a	780.99298	150	2220	11
3.	Amentoflavone	538.09003	622	2205	10
4.	Ginsenoside Rb1	1108.60291	100	2355	8
5.	Doxorubicin	543.17407	30	1868	7
6.	Asiatic acid	488.35019	95	2079	7
7.	Digitoxin	764.43469	753	2350	7
8.	Harmalol	200.241	361	1788	6
9.	Pseudobaptigenin	282.0528	512	2054	6
10.	Diosgenin	414.634	843	2129	6

the most identified compound. “Identified count” represents the number of the same compounds identified.

Table 1 shows benzoic acid with m/z is 122.03678 identified earliest at the 15th second of the retention time and longest at the 2390th second and detected 12 times. This shows benzoic acid has a strong bond so it remains intact from the beginning to the end of the retention time.

5. Conclusion. The proposed model has succeeded in identifying existing anticancer compounds and providing information on the dominant anticancer compounds which is benzoic acid with m/z 122.03678. Followed by “Saikosaponin a” as the second dominant, and so forth.

This study uses sample data, so it is still a reflection of the actual data. For future work, the real data will be used and will be compared with the processing results with sample data. In addition, the model will be tested on other LCMS datasets.

REFERENCES

- [1] P. R. Kumar, S. R. Dinesh and R. Rini, LCMS – A review and a recent update, *World Journal of Pharmacy and Pharmaceutical Sciences*, vol.5, no.5, pp.377-391, DOI: 10.20959/wjpps20165-6656, 2016.
- [2] F. Fernández-Albert, *Machine Learning Methods for the Analysis of Liquid Chromatography-Mass Spectrometry Datasets in Metabolomics*, Universitat Politècnica de Catalunya, 2014.
- [3] N. F. Sianipar, D. Laurent, R. Purnamaningsih and I. Darwati, Genetic variation of the first generation of rodent tuber (*Typhonium flagelliforme* Lodd.) mutants based on RAPD molecular markers, *HAYATI Journal of Biosciences*, vol.22, no.2, pp.98-104, DOI: 10.4308/hjb.22.2.98, 2015.
- [4] N. F. Sianipar, R. Purnamaningsih, D. L. Gumanti, Rosaria and M. Vidiанти, Analysis of gamma irradiated-third generation mutants of rodent tuber (*Typhonium flagelliforme* Lodd.) based on morphology, RAPD, and GC-MS markers, *Pertanika J. Trop. Agric. Sci.*, vol.40, no.1, pp.185-202, 2017.
- [5] N. F. Sianipar, R. Purnamaningsih, I. Darwati, D. Laurent and Chelen, The effects of gamma irradiation and somaclonal variation on morphology variation of mutant rodent tuber (*Typhonium flagelliforme* Lodd.) LINES, *The 3rd International Conference on Biological Science*, pp.637-645, 2015.
- [6] N. F. Sianipar and R. Purnamaningsih, Enhancement of the contents of anticancer bioactive compounds in mutant clones of rodent tuber (*Typhonium flagelliforme* Lodd.) based on GC-MS analysis, *Pertanika J. Trop. Agric. Sci.*, vol.41, no.1, pp.305-320, 2018.
- [7] N. F. Sianipar, R. Purnamaningsih and Chelen, Effect of gamma irradiation on protein profile of rodent tuber (*Typhonium flagelliforme* Lodd.) in vitro mutant based on 1D and 2D page analyses, *Jurnal Teknologi*, vol.78, no.10-4, pp.35-40, 2016.
- [8] N. F. Sianipar, R. Purnamaningsih and Rosaria, Bioactive compounds of fourth generation gamma-irradiated *Typhonium flagelliforme* Lodd. mutants based on gas chromatography-mass spectrometry, *The 2nd International Conference on Agricultural and Biological Sciences*, DOI: 10.1088/1755-1315/41/1/012025, 2016.
- [9] M. C. Chambers, B. Maclean, R. Burke, D. Amodei, D. L. Ruderman, S. Neumann, L. Gatto, B. Fischer, B. Pratt, J. Egerton, K. Hoff, D. Kessner, N. Tasman, N. Shulman, B. Frewen, T. A. Baker, M.-Y. Brusniak, C. Paulse, D. Creasy, L. Flashner, K. Kani, C. Moulding, S. L. Seymour, L. M. Nuwaysir, B. Lefebvre, F. Kuhlmann, J. Roark, P. Rainer, S. Detlev et al., A cross-platform toolkit for mass spectrometry and proteomics, *Nature Biotechnology*, vol.30, no.10, pp.918-920, DOI: 10.1038/nbt.2377, 2012.
- [10] I. Binanto, H. Leslie, H. Spits, N. F. Sianipar and W. Budiharto, Understanding LCMS data for identification of chemical compounds contained in rodent tuber: Timeseries or not, *Systematic Reviews in Pharmacy*, vol.12, no.1, pp.648-654, 2021.
- [11] S. L. Lohr, *Sampling: Design and Analysis*, 2nd Edition, Brooks/Cole, Cengage Learning, Boston, 2010.
- [12] R. Arnab, Systematic sampling, in *Survey Sampling Theory and Applications*, Academic Press, DOI: 10.1016/B978-0-12-811848-1.00004-2, 2017.
- [13] Y. Kim and H. Hwang, Approximate consistent weighted sampling for efficient top-k search, *International Journal of Innovative Computing, Information and Control*, vol.16, no.3, pp.1125-1132, 2020.
- [14] C. Y. Choo, K. L. Chan, K. Takeya and H. Itokawa, Cytotoxic activity of *Typhonium flagelliforme* (Araceae), *Phytotherapy Research*, vol.15, no.3, pp.260-262, DOI: 10.1002/ptr.717, 2001.
- [15] C. Y. Chee, L. C. Kit, W. S. Teng, Y. Hitotsuyanagi and K. Takeya, The cytotoxicity and chemical constituents of the hexane fraction of *Typhonium flagelliforme* (Araceae), *Journal of Ethnopharmacology*, vol.77, no.1, pp.129-131, DOI: 10.1016/S0378-8741(01)00274-4, 2001.
- [16] S. Mohan, A. Bustaman, S. Ibrahim, A. S. Al-Zubairi and M. Aspollah, Anticancerous effect of *Typhonium flagelliforme* on human T4-lymphoblastoid cell line CEM-ss, *Journal of Pharmacology and Toxicology*, vol.3, no.6, pp.449-456, DOI: 10.3923/jpt.2008.449.456, 2008.
- [17] A. Bustaman, S. Mohan, S. Ibrahim, A. S. Al-Zubairi, M. Aspollah, R. Abdullah and M. M. Elhassan, In vitro ultramorphological assessment of apoptosis on CEMss induced by linoleic acid-rich fraction from *Typhonium flagelliforme* tuber, *Evidence-Based Complementary and Alternative Medicine*, vol.2011, DOI: 10.1093/ecam/nej010, 2011.
- [18] E. Purwaningsih, Y. Suciati and E. Widayanti, Anticancer effect of a *Typhonium flagelliforme* L. in raji cells through telomerase expression, *Indonesian Journal of Cancer Chemoprevention*, vol.8, no.1, pp.15-20, 2017.

- [19] R. Purnamaningsih and N. F. Sianipar, Analysis of bioactive compounds and morphological traits in Indonesian rodent tuber mutant clones of pekalongan accession using GC-MS, *Jurnal Teknologi*, vol.80, no.2, pp.131-136, 2018.
- [20] C. A. Smith, E. J. Want, G. O. Maille, R. Abagyan and G. Siuzdak, XCMS: Processing mass spectrometry data for metabolite profiling using nonlinear peak alignment, matching, and identification, *Analytical Chemistry*, vol.78, no.3, pp.779-787, DOI: 10.1021/ac051437y, 2006.
- [21] H. P. Benton, D. M. Wong, S. A. Trauger and G. Siuzdak, XCMS2: Processing tandem mass spectrometry data for metabolite identification and structural characterization, *Analytical Chemistry*, vol.80, no.16, pp.6382-6389, DOI: 10.1021/ac800795f.XCMS, 2009.
- [22] H. Gowda, J. Ivanisevic, C. H. Johnson, M. E. Kurczy, H. P. Benton, D. Rinehart, T. Nguyen, J. Ray, J. Kuehl, B. Arevalo, P. D. Westenskow, J. Wang, A. P. Arkin, A. M. Deutschbauer, G. J. Patti and G. Siuzdak, Interactive XCMS online: Simplifying advanced metabolomic data processing and subsequent statistical analyses, *Analytical Chemistry*, vol.86, no.14, pp.6931-6939, DOI: 10.1021/ac500734c, 2014.
- [23] E. Melamud, L. Vastag and J. D. Rabinowitz, Metabolomic analysis and visualization engine for LC-MS data, *Analytical Chemistry*, vol.82, no.23, pp.9818-9826, DOI: 10.1021/ac1021166, 2010.
- [24] M. F. Clasquin, E. Melamud and J. D. Rabinowitz, LC-MS data processing with MAVEN: A metabolomic analysis and visualization engine, *Current Protocols in Bioinformatics*, DOI: 10.1002/0471250953.bi1411s37.LC-MS, 2012.
- [25] C. Kuhl, R. Tautenhahn and S. Neumann, LC-MS peak annotation and identification with CAMERA, pp.1-14, 2010.
- [26] J. Chong, M. Yamamoto and J. Xia, MetaboAnalystR 2.0: From raw spectra to biological insights, *Metabolites*, vol.9, no.3, DOI: 10.3390/metabo9030057, 2019.
- [27] I. Binanto, H. L. H. S. Warnars, N. F. Sianipar and B. S. Abbas, LC-MS analysis: Mini review frequently used open source, *2019 6th International Conference on Information Technology, Computer and Electrical Engineering (ICITACEE)*, Semarang, Indonesia, pp.1-5, 2019.
- [28] H. Horai, M. Arita, S. Kanaya, Y. Nihei, T. Ikeda, K. Suwa, Y. Ojima, K. Tanaka, S. Tanaka, K. Aoshima, Y. Oda, Y. Kakazu, M. Kusano, T. Tohge, F. Matsuda, Y. Sawada, M. Y. Hirai, H. Nakanishi, K. Ikeda, N. Akimoto, T. Maoka, H. Takahashi, T. Ara, N. Sakurai, H. Suzuki, D. Shibata, S. Neumann, T. Iida, K. Tanaka et al., MassBank: A public repository for sharing mass spectral data for life sciences, *Journal of Mass Spectrometry*, vol.45, no.7, pp.703-714, DOI: 10.1002/jms.1777, 2010.
- [29] M. Mangal, P. Sagar, H. Singh, G. P. S. Raghava and S. M. Agarwal, NPACT: Naturally occurring plant-based anti-cancer compound-activity-target database, *Nucleic Acids Research*, vol.41, no.D1, pp.1124-1129, DOI: 10.1093/nar/gks1047, 2013.
- [30] M. Herrmann and L. Hoyden, Applied webscraping in market research, *The 1st International Conference on Advanced Research Methods and Analytics*, Valencia, DOI: 10.4995/carma2016.2016.3131, 2016.
- [31] M. Shreesha, S. B. Srikara and R. Manjesh, A novel approach for news extraction using webscraping technique, *The 3rd National Conference on Image Processing, Computing, Communication, Networking and Data Analytics (NCICCNDA2018)*, pp.359-362, DOI: 10.21467/proceedings.1.56, 2018.
- [32] R. McAlister, Webscraping as an investigation tool to identify potential human trafficking operations in Romania, *Proc. of the 2015 ACM Web Science Conference*, DOI: 10.1145/2786451.2786510, 2015.

ICIC Express Letters
An International Journal of Research and Surveys

May 12, 2021

INVOICE (No. ICICEL-2104-017)

Dr. Iwan Binanto
Sanata Dharma University
Indonesia
E-mail: binanto.iwan@gmail.com

Publication Paper Charges for:

Reference No.: ICICEL-2104-017

Title: Anticancer Compound Identification Model from Liquid Chromatography-Mass Spectrometry Data of Rodent Tuber

Author(s): Iwan Binanto, Harco Leslie Hendric Spits Warnars, Nesti Fronika Sianipar, Widodo Budiharto

in **(ICIC Express Letters** --- *An International Journal of Research and Surveys*, ISSN 1881-803X) as a publication, which will generally be published within 6 months thereafter.

Amount due: JPY48,000 (no more than 8 pages)

Amount due: JPY48,000 should be sent to the ICIC-EL.

Beneficiary: ICIC-EL
Account No.: 1549727
Bank name: Toroku Branch, The Higo Bank
SWIFT Code: HIGOJPJT
Bank address: 3-2-25, Toroku, Kumamoto 862-0970, Japan

Note: 1. The payment sent by bank transfer must be free of charges for ICIC-EL.
2. After you completed the page charges through the bank, please send a copy of the payment receipt (from your bank) with Reference No.: ICICEL-2104-017 to ICIC-EL submission system together with the final version.
3. If you would like to get the Receipt for the payment, please notify us via office@icicel.org and indicate the detailed Receipt Information as the following sample at the same time.

Name: ****
Organization: ****
Paper Title: *****



Yan Shi, Editor-in-Chief
ICIC-EL Editorial Office
Tokai University, Kumamoto Campus
9-1-1, Toroku, Kumamoto 862-8652, Japan
Tel: +81-96-386-2666; Fax: +81-96-386-2666
E-mail: office@icicel.org

Dear Editor of ICIC Express Letters

We would like to thank you for the Acceptance, and the opportunity to resubmit a revised copy of this manuscript. We would also like to take this opportunity to express our thanks to the reviewers for the positive feedback and helpful comments for correction or modification.

We believe have resulted in an improved revised manuscript, which you will find uploaded alongside this document. The manuscript has been revised to address the reviewer comments, which are appended alongside our responses to this letter.

We very much hope the revised manuscript is accepted for publication in Journal.

Sincerely yours,

Iwan Binanto
on behalf of the authors

REVISION NOTE (ICICEL-2104-017)

No.	Reviewer Notes	Comments
1.	This study proposes an anticancer compound identification model from liquid chromatography-Mass spectrometry data of Rodent Tuber. In Introduction, the research contributions should be stated clear. And a brief organizational overview is suggested to be added in the end of Introduction to facilitate readers.	The revision is: <ul style="list-style-type: none"> <i>It contributed to the development of a method of chemical compound identification in LC-MS.</i> <i>This paper is categorized as follows: section 2 describes the related works, section 3 describes the research method and the proposed model, section 4 describes the result and discussion, and section 5 focuses on conclusions and future work.</i>
2.	More details of reviewed literature and corresponding discussion should be added in Section 2 to make the research motivations clear.	The revision is: <i>Add more detail of reviewed literature to make the research motivations clear</i>
3.	Section 3 is too short as an independent section, which may be combined with Section 4.	The revision is: <i>Combining Section 4 to Section 3 as subsection 3.</i>
4.	What is the number of sampling, 18,000 or 18,275?	The revision is: <i>In this case, the number of samples is about 18,000 and 18,275 were generated</i>
5.	Figure quality should be improved; for example, in Figure 2, please recheck “Otomated” and “webscropping”.	We revised: “webscropping” to webscraping “otomated” was not revised because it passive
6.	In consideration of monochrome print, to use color like “blue dots” and “red dots” for identification in Figure 5 is not effective.	Eliminate Figure 5 and also to reduce the page to 8 pages
7.	More explanation should be added on Table 1 to present the effectiveness of the identification model, for example, what does the number of “identified count” show?	The revision is: <i>It has been sorted from the most identified compound. “Identified Count” represents the number of the same compound identified</i>
8.	The manuscript should be greatly improved regarding language presentation. For example, in Abstract, the 4th and the last sentences in Abstract are ill-formed; “This combination namely LC-MS” in Paragraph 2 of Introduction is not a complete sentence.	We revised ill-formed expressions.

9.	The following research is suggested to be cited to enrich the current study: Yunna Kim and Heasoo Hwang, Approximate Consistent Weighted Sampling for Efficient Top-k Search, International Journal of Innovative Computing, Information and Control, vol.16, no.3, pp.1125-1132, 2020, DOI: 10.24507/ijicic.16.03.1125.	We agree to added the paper suggested by reviewers as a reference.
----	--	--