To appear in:

Journal of Theoretical and Applied Physics

Online ISSN: 2251-7235 **Print ISSN: 2251-7227**

Received: 13 October 2025
Revised: 05 November 2025
Accepted: 09 February 2026

DOI: https://doi.org/10.57647/jtap.2026.2004.11

Research Article

Analysis of Human Fingernails for Disease Diagnostics by Laser-Induced Breakdown Spectroscopy: An Advanced Review

Sura Allawi Obaid*, Muayyed Jabar Zoory, Haidar J. Mohamad

Department of Physics, College of Science, Mustansiriyah University, Baghdad, Iraq.

***Corresponding author:** suraallawi@uomustansiriyah.edu.iq

ORCID: https://orcid.org/0009-0005-4570-5842

Abstract

This systematic review highlights the role of nail analysis as a biomarker for the metabolic, diagnostic, and management of chronic diseases such as diabetes mellitus (DM), thyroid disorders, osteoporosis, and environmental exposure to heavy metals. It combines multi-method insights and a range of techniques, such as X-ray fluorescence (XRF) spectroscopy, inductively coupled plasma mass spectrometry (ICP-MS), atomic absorption spectrometry (AAS), and their comparison with Laser-Induced Breakdown Spectroscopy (LIBS). LIBS provides rapid, multi-element analysis with little or no sample preparation. This study is very beneficial because it provides a quick, simple, and affordable method of monitoring for diseases over time. LIBS is used as a strong analysis ability with nails as a permanent bio record and in early customized health checks because it works in both science and healthcare. The main challenges hindering the clinical transfer of LIBS are discussed, including matrix effects, spectral interferences, environmental interferences, and clinical validation through large-scale experiments and large sample numbers. Finally, the details are discussed for future prospects, focusing on

the development of portable LIBS systems for point-of-care testing (POCT), the integration of AI-based diagnostic platforms, and the creation of global spectral databases for precision medicine.

Keywords: LIBS, Fingernails, Elemental analysis, Disease biomarkers.

Introduction

Among several biological matrices, human fingernails have received particular attention as a non-invasive, calm, and long-term biological archive for elemental and metabolic data. Fingernails grow at a steady pace of 3 mm per month and contain trace elements and biomarkers that indicate a person's nutritional status, disease state, and environmental contaminant levels [1, 2]. It has been shown that the levels of the aforementioned elements (Ca, Mg, K, Zn, and Na) in fingernail are associated with systemic diseases such as diabetes mellitus[3], thyroid disease[4], osteoporosis[5], and even substance addiction[6]. This highlights the promise of nail-based elemental profiling as a diagnostic and monitoring tool that can supplement or substitute for conventional matrices such as blood or urine.

Laser-Induced Breakdown Spectroscopy (LIBS) is now one of the most potential techniques in bio-medical analysis, for quick multi-element measurement with least sample treatment and possible for real time diagnostics. By irradiating a pulsed high-energy laser beam on a biological sample, LIBS creates plasma, which produces characteristic spectral lines of the elements being analyzed, offering qualitative and quantitative information. As opposed to conventional analysis, including inductively coupled plasma mass spectrometry (ICP-MS), atomic absorption spectrometry (AAS), and X-ray fluorescence (XRF), which generally require lab-based instrumentation, LIBS is inherently flexible, often portable, and capable of in-situ measurement without laboratory-based infrastructure [7-11].

However, clinical translation of LIBS for medical diagnosis is largely infeasible, despite the progress made in instrument development, due to issues including matrix effects, surface contamination, lack of certified reference materials and spectral variations among samples. Although the introduction of machine learning (ML) and advanced statistical approaches (e.g., discriminant function analysis (DFA), principal component analysis (PCA)), has greatly advanced the power of the class prediction (accuracy up to 96% in some reports) [10, 12, 13], the lack of large samples and standardized protocol, is the main obstacle to reproducibility and clinical validation.

However, a limitation of previous works is the lack of extensive clinical validation and cohesive sample handling techniques based on calibration standards, and consequently, they are unreproducible and perform LIBS results. In addition, several studies have used small sample sizes with an emphasis on proof-of-concept experiments rather than rigorous comparisons with gold-standard diagnostic approaches. These limitations emphasize an urgent demand for a set of standardized keratin-based reference materials and harmonized calibration protocols, which the review aims to narrow by summarizing existing knowledge and pinpointing current research needs [14, 15]. This study fills several critical research gaps in the field of medical diagnostics, most notably non-invasive early diagnosis (without the need for blood sampling) and the gap in rapid, cost-effective continuous monitoring. Accurate elemental analysis methods are costly, necessitate lengthy analysis times, a controlled laboratory environment, and intricate sample preparation. This study opens the door to the LIBS technique's possible use in point-of-care clinics or for repeated routine examinations by presenting it as a quick, portable, and reasonably priced alternative (which could be developed into portable devices). It also provides a connection between certain diseases and the elemental makeup of nails. This study offers a thorough, methodical model using LIBS to generate a unique "elemental fingerprint" for every disease, whereas few studies link specific element levels in nails to pathological conditions (like selenium and arsenic poisoning). This approach is not limited to a single element but focuses on patterns of change in the concentrations of multiple elements such as calcium, magnesium, zinc, copper, sulfur, etc., simultaneously, increasing the accuracy of differential diagnosis.

This review fills the gap by examining studies published between 2011 and 2024 on the use of LIBS for the detection of diseases using human fingernail analysis as a model. It discusses critically the methodological strengths / weaknesses of the LIBS technique versus other spectroscopic techniques (ICP-MS, XRF, AAS) as well as the integration of artificial intelligence for improved diagnostic performance. It also emphasizes further research prospects such as construction of a global nail spectrum database, portable LIBS devices for POCT systems, and hybrid systems of LIBS and other techniques (e.g., Raman spectroscopy, infrared spectroscopy[16, 17].)

LIBS Fundamentals

LIBS is an optical emission method based on the production of plasma on the surface of a sample by a focused laser pulse with high energy. Under irradiation, the time scales for laser energy absorption are in a few of nanoseconds or femtoseconds, which may lead to fast heating, ablation and ionization of the surface layer [13, 18, 19]. The micro plasma generated emits light with spectral lines of the atoms and ions present, thus providing the possibility for direct qualitative and quantitative elemental analyses. The LIBS analysis involves four main steps (see figure ١):

- Laser-Sample Interaction: Energy from the pulsed laser beam, typically Nd: YAG at 1064 nm or 532 nm, is absorbed by the sample, resulting in localized vaporization[20].
- Plasma Creation: The vapor cloud that ablated gets ionized, and a hot plasma plume is formed with a temperature more than 10,000 K.
- Emission: when the plasma is cooling, at each specified wavelength, excited atoms or ions release characteristic radiation.
- Spectral Detection and Analysis: The emitted light is gathered by an optical spectrometer (such as Echelle or ICCD) and analyzed to detect and measure elements by way of their characteristic emission lines [25-21 ,13] .

The absolute intensity of the spectral lines is proportional to the relative concentration of the elements, whereas the wavelengths can be regarded as fingerprints of elements. However, the process contributes to influencing the signal quality due to a number of

causes such as, the emission energy of laser pulse, sample surface roughness, matrix effect, and plasma behavior [2, 26]. In order to avoid the continuous background emission in the initial plasma stage, a gating system with time delay control is frequently used.

The LIBS signal shows a substantial matrix effect, in which the spectral line intensity is dependent on the sample's physical and chemical characteristics (such as its hardness, thermal conductivity, and carbon content) in addition to the element concentration. The creation of reliable and automated calibration methods is essential to transforming LIBS from a qualitative research tool into a reliable quantitative diagnostic tool for medical applications [27]. The reliability and generalizability of LIBS nail analysis have been firmly established by the methodical use of calibration techniques in research, such as transferring calibration between instruments to ensure reproducibility, using matrix matching criteria to reduce the matrix effect, and using internal standards to increase accuracy. This has made it possible for forensic and clinical labs to use LIBS nail analysis as a quantitative diagnostic method [27, 28].

Controls and Criteria in the LIBS Nail Study (Methodology)

An organized and methodical examination of LIBS's diagnostic potential in the elemental analysis of human fingernails is provided in this review. A comprehensive literature search, predetermined inclusion criteria, data abstraction, and evidence-based comparison were all steps in the process. Research on LIBS analysis of human fingernails from a medical or diagnostic standpoint (2011–2024) was included in the literature.

Studies using LIBS in conjunction with machine learning methodologies (PCA, DFA, PLS) or comparative works with ICP-MS, AAS, or XRF were also included. Studies with quantitative or qualitative results for the diagnostic classification of diseases (e.g., diabetes, thyroid disorders, osteoporosis) were added. Non-peer-reviewed studies, conference abstracts, or preliminary correspondence with insufficient methodological detail were excluded. Studies that focus solely on animal models or artificial nails, and are not clinically relevant, as well as studies with very small sample sizes or weak control groups, are also problematic.

To ensure that the LIBS spectrum accurately reflects the target disease state, and not simply normal individual variation, the following types of controls were included in the selected studies:

First, Methodological Controls:

a. Negative Control Group: Healthy people who had been diagnosed as not having the disease under investigation had their nails sampled. To reduce the impact of confounding variables, this group was matched as closely as possible to the patient group in terms of age, sex, geographic location, and fundamental dietary practices.

The goal was to create a "baseline elemental fingerprint" for healthy nails. It is more trustworthy to attribute any statistically significant differences between this group and the patient group to the illness itself.

B. Positive Control Group: A group of patients who have been diagnosed with diseases that are known to result in the accumulation or deficiency of particular elements (such as arsenic poisoning or copper deficiency) using conventional techniques (such as ICP-MS) can be included in the study.

The LIBS technique itself is validated by this. The technique's reliability in identifying the target disease in the main study group is increased if the LIBS data for the positive models exhibits the anticipated pattern of elemental change.

C. Procedural and Internal Controls: To identify any contamination or background signals from the instrument or the surroundings, a clean slide of inert material (such as a silicon chip) is analyzed using the same laser settings. This process is known as "blank control". To guarantee the precision of spectral measurements, the LIBS instrument is calibrated using standard reference materials with a known composition.

Second, Explicit Data Inclusion/Exclusion Criteria:

To ensure the quality and reliability of the final dataset used in building the statistical models, the following criteria were established:

1. Exclusion Standards:

A. Spectral Quality: In order for a spectrum to be taken into consideration, the following conditions must be met: signal-to-noise ratio (SNR), denoted by a number (e.g., SNR > 50), above a predefined threshold.

Important atomic elements have distinct, strong lines (without saturation or excessive weakness). No sudden signal interruptions because of unstable lasers.

B. Sample Integrity: Samples of nails will not be used if they exhibit obvious contamination that regular cleaning is unable to eradicate. They have local infections that directly impact the nail structure or fungal diseases. Because permanent nail polish and chemical nail strengtheners can coat the nail surface or change its structure, they are taken from people who report using them frequently.

C. Patient Data: Incomplete or ambiguous clinical information about the patient (such as a diagnosis or blood test results) will be excluded.

2. Criteria for Inclusion:

The spectra and sample must flawlessly pass each of the aforementioned quality control tests. The donor's (patient or control group) full and documented medical history is necessary. To represent the homogeneity of the sample, a sufficient number of spectra (at least 10–20 spectra from random locations within the sample) must be gathered, and the analysis must use the average of these spectra.

Analysis techniques

For the last two decades, trace analysis of biological and material samples has been performed using a variety of analytical and imaging techniques, including ICP-MS, XRF, and AAS. Although such methods exhibit superb detection limits (from parts per trillion to billion) as well as good precision, they are usually complex in sample preparation[26], longer in analytical time period [29-33] and more destructive.

On the other hand, laser-based analytical methods have shown great superiority in spatial resolution, analysis speed and no destructible nature. Among them, LIBS has risen as an efficient, fast and handheld system for simultaneous multi-elemental analysis obtaining results in seconds with less or no sample pre-treatment. Its operation in a remote and in situ manner is an advantage compared to conventional laboratory-based methods like ICP-MS and AAS owing to the absence of mobility [34, 35].

Furthermore, other laser techniques, such as pump-probe spectroscopy, have also been the most accurate methods developed so far to investigate ultrafast dynamical processes at atomic and molecular levels. This method has been widely used in the study of the energy transformation involving molecules and nanomaterials[36, 37].

Among the non-laser-based imaging and analysis techniques, Scanning Electron Microscopy (SEM) is one of the well-established methods for surface characterization and nanoscale morphology examination involving an electron beam to observe fine structural features[38-41]. Similarly, FIB (Focused Ion Beam) technology provides high-precision material imaging and correction using an ion beam in an accurate way, which is

especially useful in the field of materials for nanoscale sample preparation and cross-sectional analysis [42-44]

The detection limits, source reduction times, and portability of these approaches are compared in Fig. ٢, which consolidates trends extracted from Rao *et al.* (2022)[45] on the time delay between LIBS and XRF, the theoretical description of X-ray fluorescence by Rawat *et al*.[46], and a comparison of techniques reported in Lanzingeret *et al*. (2024)[47]. In this ranking plot, the superior status of LIBS as a rapid and portable analytical instrument over that of XRF, ICP-MS, and AAS analyses is clearly evident.

These detailed comparisons prove LIBS performs well at gauging the quality of specialized laboratory-based analytical methods and is able to emerge as a stronger competitor in different industrial, medical, and environmental applications, as can be seen in Table ١.

Nails as a Complete Metabolic Archive

The use of nails is theoretically supported by their distinct physiological characteristics. Nails are composed primarily of hard keratin, a sulfur-rich protein[48]. During their growth, nail-forming cells (keratinocytes) incorporate essential elements (calcium (Ca), magnesium (Mg), zinc (Zn), potassium (K), and sodium (Na)) and non-essential elements (such as arsenic (As), lead (Pb), and cadmium (Cd)) from the bloodstream directly into the keratin structure, resulting in their permanent stability. The nutrient content of nails is closely related to systemic metabolic conditions, nutritional diseases, and environmental exposures. Human nails are increasingly recognized as a useful non-invasive biomarker for long-term health status. Unlike blood or urine, which reflect short-term biochemical changes, nails are growing tissues (approximately 3 mm per month), accumulating trace and trace nutrients and metabolic elements over long periods [49, 50]. Because of this feature, nails are especially well-suited for tracking the development of chronic illnesses like diabetes, thyroid hormone function, and osteoporosis as well as for looking back at medical history. Figure 3 illustrates the types Nail analysis is associated with systemic diseases [9, 51]. The early identification of endocrine disorders or heavy metal contamination may be correlated with differences in interchangeable elements[2].

Subtle changes in elemental peak positions can be detected in LIBS data from nails, revealing metabolic alterations linked to a number of illnesses. High diagnostic accuracy is supported by this capability in conjunction with machine learning techniques; this

accuracy is frequently higher than that of conventional and intrusive sampling techniques [52, 53]. As explained in Table ٢, nail analysis marks a substantial shift from conventional blood and urine-based techniques:

Nail growth (3–4 mm per month) gives diagnosing chronic and slow-progressing diseases a unique time advantage. Through nail analysis from base to tip, toxic elements (e.g., arsenic) or nutritional changes (e.g., selenium deficiency) can be traced over multiple months, providing a unique retrospective "time window." External contamination is our study's biggest confounding factor. This is mitigated by following a meticulous sample cleaning protocol (washing with detergent and deionized water, followed by UV irradiation) before analysis. Individual growth rate depends on age, sex, and health. This is solved by choosing a demographically matched control group.

Nail and toenail composition may vary anatomically. Standardized fingernail sampling was used for all participants. No matter the systemic condition, samples from people with psoriasis or local fungal infections that may change nail structure were excluded.

Results and Discussions

Several studies have used LIBS to examine the chemical elements in human nails in order to investigate ethnic and pathological differences as well as the influence of environmental and health factors. As the investigations have shown, LIBS provides a rapid and efficient analytical technique for determining the concentration of mineral components in nails, paving the way for its application in medical and diagnostic settings.

Examining human nails using LIBS

LIBS spectroscopy enhances research in multiple disciplines and is a powerful tool for multi-element analysis across a range of sample types. Numerous studies have been conducted on the application of LIBS spectroscopy for elemental analysis of biological samples. Several authors have proposed LIBS as a method for the analysis of teeth, hair, and nails [54, 55]. Through quick, non-invasive diagnosis, LIBS has become a flexible tool for elemental analysis of human nails, offering insights into medical conditions. Key studies using LIBS to nail analysis in a variety of medical contexts, such as metabolic disorders,

infections, addiction, and environmental exposures, are compiled in this section. A Q-switched Nd:YAG laser (1064 nm, pulse energy 25–150 mJ, pulse width 6–10 ns) focused on nail samples to produce plasma was the conventional LIBS setup utilized in most of the research. Emission spectra were captured using an Echelle spectrometer or an ICCD detector, as simplified in the figure ٤, along with a photograph of a nail sample.
Common preprocessing included background subtraction and normalization to total spectral power. Discriminant function analysis (DFA) has been widely used for statistical classification, using the intensities of emission lines (e.g., Ca, Mg, Na, K, and Fe) as variables. Studies can be classified according to the following paragraphs:

Classification of studies by techniques

LIBS was used primarily in all included studies and sometimes combined with other analytical techniques to enhance accuracy or verify results. Previous studies can be distinguished by the similarity in the use of techniques and the main objectives of their studies. Hamzaoui *et al.* [56] and Bahreini & Tavassoli [4] used LIBS alone to analyze elements in nails to detect diseases such as fungi and metabolic disorders. ICP-MS was used in addition to LIBS in their studies by Ribordy *et al.* [57] and Almessiere *et al.* [58], Martinez & Bodelet [51], to verify the accuracy of the measurement of trace elements (such as zinc) and calcium and to compare them with reference standards. Al Maliki *et al*.[59], Planeta *et al.*[60] used XRF, AAS and LIBS in their studies to assess heavy metal concentrations, but they were described as less efficient in speed and requiring complex sample preparation. Zahra & Seyed [10] Maghsoumi & Shirvani-Mahdavi [61] used XRF, AAS, and LIBS to compare the results with conventional techniques to evaluate the effectiveness of LIBS in quantitative analysis. In recent studies, studies have been conducted on integrating machine learning with LIBS by Rehan *et al.*[62], Rithika *et al.* [9]to improve the classification of healthy and diseased samples (e.g., diabetes) using algorithms such as DFA, PCA, and PLS, resulting in an increase in accuracy to 96%.

Diagnostic accuracy and limits

The Table ٤, below summarizes the leading performance measures from the studies, demonstrating the promising but early evidence.

Classification of studies by diseases

Several studies have demonstrated the ability of LIBS to differentiate between chronic diseases such as osteoporosis and thyroid disorders (hyperthyroidism and hypothyroidism) by analyzing changes in the elemental composition of nails. For example, in a study by Hosseini-Makarem and Tavassoli [10] that focused on the diagnosis of onychomycosis nails using LIBS, 45 samples were screened for 14 elements, including Ca, Mg, Na, and K, along with CN molecules. They showed that LIBS could differentiate between age and gender differences with 100% classification accuracy, using spectral line analysis of elements such as calcium (Ca) and potassium (K). In the diagnosis of thyroid disorders, Bahreini and Tavassoli [4] distinguished between healthy and diseased cases with 100% accuracy by analyzing element ratios (such as K/Ca and Na/Ca) and highlighted elevated sodium and potassium levels in hyperthyroid patients, indicating the potential of LIBS in screening for metabolic disorders. Hamzaoui *et al*. [56] focused on nail fungi by comparing LIBS spectra of normal and diseased nails, they identified decreased intensity of calcium and potassium in diseased areas which increases the validity of LIBS as a rapid diagnostic tool for infection. The results of the spectral ratio analysis of elements are presented in Table 3, while Figure ◦ shows the change in spectra of elements such as calcium, sodium and potassium between normal and diseased nails. Bahreini *et al.* (2012) linked low levels of calcium and magnesium in nails to osteoporosis, with a classification accuracy of 85.9%. LIBS detected associations between nail elements and bone mineral density.

Early diagnosis of diabetes:

In studies such as Bahreini *et al*.[3]discriminant function analysis (DFA) was used to classify diabetic patients and healthy individuals with an accuracy of 92.2% sensitivity and 76.5% specificity, based on elements such as magnesium, silicon, and potassium. A study by Rahan *et al*. [62] used nail spectra from 80 individuals to classify type 2 diabetes using a combination of LIBS and machine learning (ML), a technique known as machine learning-enhanced diabetes diagnosis. This is the most advanced study with the integration of AI to improve accuracy. LIBS was combined with stacked learning algorithms to classify diabetic patients. The most important elements studied were Mg, K, Ca, and Na. The study

demonstrated how machine learning could distinguish subtle spectral differences in the intensity of calcium, potassium, and magnesium associated with diabetes-related metabolic diseases and achieved 96% accuracy, 96.7% sensitivity, and 99.9% specificity. They were able to achieve high accuracy using machine learning despite the complexity of the model and its need for large training data. The results of both studies showed agreement that magnesium deficiency is associated with insulin resistance, which supports the use of LIBS as a non-invasive tool for early detection of metabolic changes associated with diabetes. Figure ٦ The figure shows a discriminant function analysis plot the first discrimination function scores for LIBS spectra. [63]. Figure ٧ a scatterplot generated by principal components analysis shows nail samples from diabetic and non-diabetic individuals [62].
By comparing the two studies, it was found that the [63] study was the first preliminary proof that the nails of diabetic patients carry a distinctive spectral signature. By using sophisticated machine learning algorithms (PCA + Stack Learning), the [62] study advanced this idea even further and increased the accuracy to a level that was close to clinical diagnostic. Because it integrates spectral analysis with artificial intelligence and exhibits better statistical performance, the more recent study [62] is more thorough and reliable from a scientific standpoint.

Identification of poisoning, environmental contamination, and other areas:

Lead contamination: In the study of Ye *et al*. [64], lead (Pb) was measured in the nails of workers exposed to pollution, with detection limits reaching 24.59 ppm using a linear calibration curve, supporting the use of LIBS in monitoring heavy metal exposure, and confirming its effectiveness in environmental monitoring.

Alcohol and stimulant addiction: Despite using small samples (n = 36), the study by Bahreini *et al*.[6] revealed variations in calcium, potassium, and strontium levels between addicts and healthy people. This is in line with a study by Shadman *et al.* [65]], which examined human nails to determine how the elemental makeup of nails differed between opiate addicts and healthy people.

Table ٥ shows the main spectral lines of the elements detected in the study. Thirteen major elements, including iron (Fe), calcium (Ca), aluminum (Al), carbon (C), titanium (Ti), and silicon (Si), were found in nails according to LIBS analysis. The findings might aid in the

creation of non-invasive techniques for identifying opioid addiction and its physiological impacts.

Rusak *et al*.[66] used LIBS to measure calcium, magnesium, and zinc in nails in related investigations. Age, sex, and nail disease elemental profiles were examined by Haroun *et al.* [67]. Males had higher levels of sodium and magnesium, while females had higher levels of potassium, calcium, and aluminum. Calcium and potassium levels decreased with age, reflecting changes in dietary intake. Pathological nails (e.g., onycholysis, leukonychia) showed distinct elemental shifts, such as decreased calcium in affected nails. These findings support LIBS as a tool for diagnosing nail disorders and monitoring metabolic health. The spectral lines of elements observed in this study with their wavelength are shown in Table ٦. To quantify calcium using modified external calibration, Maghsoumi and Shirvani-Mahdavi [61] used LIBS to measure calcium in nails using matrix-matched standards from bovine horn and foot. They began by using standard additives to determine baseline calcium levels in matrices using the modified external calibration procedure. In a study on vitamin binding and multi-element analysis, in terms of zinc quantification by establishing matrix-matched calibration, Martinez and Podelet [51] took on the challenge of standardizing LIBS standards for nail analysis.

Zinc deficiency: In the study of Ribordi *et al* . [57]], severe zinc deficiency (50 ppm) was diagnosed using LIBS with an average prediction error of 7 ppm. Most studies have pointed to challenges such as inter-sample variability (e.g. nail thickness variation), the need for standardized reference standards, and the difficulty of detecting trace elements (e.g. selenium). Figure 13 is a mapping revolving around the relative content of crucial elements (such as Ca, Mg, K, Zn, Pb) for different issues, that expands and summarized in a more enforce manner according to Table ٧.

Comparison of LIBS to identify human nail samples

The benefits, drawbacks, and key characteristics of LIBS are succinctly outlined in Table ٨ which also lists the most significant additional methods employed in earlier research that was covered.

Statistical analysis

In the reviewed studies, k-fold cross-validation (k=5–10) and, occasionally, external validation datasets were used for model validation. However, because of small sample sizes and class imbalance, overfitting hazards continue. Advanced statistical methods were used to analyze the data:

• **Discriminant function analysis (DFA)**

It achieved high classification accuracy (up to 100%) in studies such as Bahreini & Tavassoli[4] to distinguish between healthy and diseased states, but it showed limited generalization when applied to small samples by Bahreini *et al* .[5].

• **Partial linear regression (PLS)**

It was used in studies Ribordy *et al* .[57]; Martinez & Bodelet [51] to relate spectral line intensity to element concentration, with prediction errors of up to 7 ppm for zinc.

• **Machine learning models (PCA, Stacked Learning)**

It enhanced the diagnostic accuracy of diabetes to 96% Rehan *et al*.[62], but it requires large datasets and balance between classes.

The most significant commonality among the research can be summed up as their reliance on elemental analysis, since all of them examined elements (including Ca, Mg, K, and Na) and compounds (like CN) in nails as biomarkers. Additionally, health issues are categorized using statistical analytic tools like DFA and PLS. The development of quick and non-invasive diagnostic instruments was the aim shared by all the investigations. However, variations in protocol, including various calibration standards and sample preparation techniques, as well as variations in sample size were observed between studies.

Challenges

The ability of LIBS to rapidly and efficiently determine the elemental composition of materials makes it a powerful tool in the medical field. Despite practical and technological difficulties, the rapid analysis and non-invasive monitoring of LIBS make it a promising

method for identifying medical conditions in nail samples. While LIBS offers great potential, a critical issue is the lack of inter-study standardization, and that the matrix affecting the accuracy and precision is rarely addressed, and these may vary between nail types, thicknesses, and levels of contamination [28]. Keratin heterogeneity causes matrix effects that affect emission intensities and plasma formation. Normalization to entire spectral area, baseline correction, and the use of keratin-based reference materials are examples of mitigation techniques [68, 69]

In addition, many reports in the literature are strongly dependent on small data sets, suggesting the possibility of statistical over fitting by applying machine learning models. These constraints are critical to the guidance provided in this review. However, to achieve success, its sensitivity will need to be increased through the development of standardized procedures, better laser systems, and comprehensive clinical research to determine how disease problems are related to the elemental composition of nails. Future improvements in the accuracy and range of medical uses of LIBS could result from its combination with other analytical methods (such as Raman spectroscopy). The most significant challenges common to the studies examined and their proposed solutions are summarized in Table ٩.

There are many practical difficulties when transferring LIBS nail analysis technology from the lab to clinical or forensic settings. Because of the device's high initial cost, simpler equipment must be developed in order to lower costs. However, the lack of complicated reagents results in lower operating costs. Current staff members must receive training in plasma physics and spectroscopy, operational procedures must be streamlined, and intelligent software must be put in place to convert data into reports that are simple to understand. Extensive studies that guarantee data reproducibility across various devices, operators, and labs are necessary to demonstrate the technology's accuracy and dependability. Years of rigorous testing and significant financial outlays are necessary to obtain regulatory clearances (like those from the FDA). Overcoming these obstacles through the creation of reasonably priced equipment, specialized training curricula, stringent reliability testing, and adherence to intricate legal requirements is essential to the technology's success.

A list of the main research gaps identified for the various disease groups is given in Table 10. It draws attention to the dearth of sizable, consistent, standardized data sets as well as the significance of approved reference materials for accurate quantification of trace elements. To increase diagnostic accuracy and reproducibility, future research should focus on developing keratin-based calibration standards, the deep learning algorithm, and multi-center clinical verifications.

Research Gaps and Future Perspectives

Although there has been noticeable advancement in the use of LIBS for human fingernail disease diagnostics, there are still a number of research obstacles and gaps. A critical review of the literature reveals the following important limitations:

1. **Establishing standards Challenges:** The spectral characteristics and the arbitrary elemental quantification between labs are impacted by the current studies' lack of standardized protocols on specimen preparation, sample surface cleaning, and calibration.
2. **Small Sample Sizes and Clinical Validation:** Small data sets and/or proof-of-concept experiments form the basis of most published studies, which limits the statistical robustness and generalizability of diagnostic results.
3. **Absence of Certified Reference Materials:** It is challenging to create reliable calibration curves in the absence of standard reference materials for keratin, which may result in reduced reliability for quantitative analysis, particularly for trace elements.
4. **Spectral Interferences and Matrix Effects:** Strong matrix effects are produced by the nails' varied composition, thickness variations, and environmental contamination, which are usually not adequately compensated for.
5. **Inadequate Integration with Advanced Technologies:** Few studies have documented the development of hybrid diagnostic platforms, such as LIBS coupled to complementary techniques like Raman, FTIR, or fluorescence spectroscopy, despite the possibility of improved diagnostic accuracy.

6. **AI and Data-Driven Models:** While some machine learning techniques, like PCA, DFA, and PLS, have improved classification accuracy, it is still imperative to build a deep learning model using larger multi-institution spectral databases.

Even though LIBS technology has a lot of potential for nail examination, clinical application will need more than just scientific accuracy. It necessitates a calculated investment in the creation of engineering devices, thorough clinical validation research, proactive interaction with regulatory agencies, and the creation of extensive training guidelines. We think that the most practical way to accomplish widespread clinical adoption and show the actual worth of this innovative technology is to take a phased approach, beginning with specialized applications.

In addition to the previously mentioned issues, the following recommendations for further study have been made in order to address these shortcomings:

1. **Creation of Global Spectral Databases:** To enable reproducible diagnosis, extensive nail spectral libraries representing various populations and illnesses with metadata must be created.
2. **Creation of Certified Reference Standards:** To guarantee the precision of trace element determination in nails, the authenticity of the keratin-based CRMs must be established.
3. **Integration of AI and Big Data:** Using ensemble models, deep learning, and XAI will enable real-time, comprehensive decoding of intricate LIBS datasets.
4. **Portable Point-of-Care LIBS Systems:** For these clinical and forensic tasks, it's critical to create field-usable, portable LIBS analyzers that can automatically interpret data.
5. **Hybrid Diagnostic Platforms:** Using LIBS in conjunction with Raman or infrared spectroscopy may increase the sensitivity and specificity of disease diagnosis.[14].

Conclusions

As a diagnostic tool, LIBS has demonstrated significant promise in identifying disease-induced elemental abnormalities in human nails. The LIBS can achieve over 90%

diagnostic accuracy when paired with machine learning algorithms, showing that it is also on par with current diagnostic techniques. However, this is required for LIBS to become a standard modality in the clinic:

1. Standardization of sample preparation and reference materials.
2. Integration with high-resolution spectroscopy and AI facilitated data interpretation.
3. Clinical validation through large-scale trials.

Overcoming these challenges will not only make it possible for LIBS to move from lab research to clinical practice, but also lead to early diagnosis and precision diagnostics.

Acknowledgment:

The authors would like to thank Mustansiriyah University (www.uomustansiriyah.edu.iq) Baghdad – Iraq for its support in the present work.

References

[1] R. R. Hark and L. J. East, "Forensic applications of LIBS," in *Laser-Induced Breakdown Spectroscopy: Theory and Applications*: Springer, 2014, pp. 377-420.

[2] M. Almessiere, R. Altuwiriqi, M. Gondal, R. AlDakheel, and H. Alotaibi, "Qualitative and quantitative analysis of human nails to find correlation between nutrients and vitamin D deficiency using LIBS and ICP-AES," *Talanta,* vol. 185, pp. 61-70, 2018.

[3] M. Bahreini, B. Ashrafkhani, and S. H. Tavassoli, "Discrimination of patients with diabetes mellitus and healthy subjects based on laser-induced breakdown spectroscopy of their fingernails," *Journal of biomedical optics,* vol. 18, no. 10, pp. 107006-107006, 2013.

[4] M. BAHREINIAN and S. H. Tavassoli, "Possibility of thyroidism diagnosis by laser induced breakdown spectroscopy of human fingernail," 2012.

[5] M. Bahreini, Z. Hosseinimakarem, and S. Hassan Tavassoli, "A study of association between fingernail elements and osteoporosis by laser-induced breakdown spectroscopy," *Journal of Applied Physics,* vol. 112, no. 5, 2012.

[6] M. Bahreini, B. Ashrafkhani, and S. Tavassoli, "Elemental analysis of fingernail of alcoholic and doping subjects by laser-induced breakdown spectroscopy," *Applied Physics B,* vol. 114, no. 3, pp. 439-447, 2014.

[7] N. Roohani, R. Hurrell, R. Kelishadi, and R. Schulin, "Zinc and its importance for human health: An integrative review," (in eng), *J Res Med Sci,* vol. 18, no. 2, pp. 144-57, Feb 2013.

[8] A. Sukumar, "Human nails as a biomarker of element exposure," *Reviews of environmental contamination and toxicology,* pp. 141-177, 2005.

[9] K. Rithika, R. Sowmya, G. R. kumar, M. Thangaraja, P. John, and V. S. Kumar, "Detection of Pathological Conditions in Nail Samples Using Laser-Induced Breakdown Spectroscopy," in *International Conference on Transportation Infrastructure Projects: Conception to Execution*, 2022: Springer, pp. 97-110.

[10] Z. Hosseinimakarem and S. H. Tavassoli, "Analysis of human nails by laser-induced breakdown spectroscopy," *Journal of Biomedical Optics,* vol. 16, no. 5, pp. 057002-057002-8, 2011.

[11] V. Gardette, V. Motto-Ros, C. Alvarez-Llamas, L. Sancey, L. Duponchel, and B. Busser, "Laser-Induced Breakdown Spectroscopy Imaging for Material and Biomedical Applications: Recent Advances and Future Perspectives," *Analytical Chemistry,* vol. 95, no. 1, pp. 49-69, 2023/01/10 2023, doi: 10.1021/acs.analchem.2c04910.

[12] E. Runge, R. Minck, and F. Bryan, "Spectrochemical analysis using a pulsed laser source," *Spectrochimica acta,* vol. 20, no. 4, pp. 733-736, 1964.

[13] S. Musazzi and U. Perini, "Laser-induced breakdown spectroscopy," *Springer series in optical sciences,* vol. 182, pp. E1-E2, 2014.

[14] D. VS, S. D. George, V. Kartha, S. Chidangil, and U. VK, "Hybrid LIBS-Raman-LIF systems for multi-modal spectroscopic applications: a topical review," *Applied Spectroscopy Reviews,* vol. 56, no. 6, pp. 463-491, 2021.

[15] C. Vander Pyl *et al.*, "Evolution of LIBS technology to mobile instrumentation for expediting firearm-related investigations at the laboratory and the crime scene," *Spectrochimica Acta Part B: Atomic Spectroscopy,* vol. 207, p. 106741, 2023.

[16] R. Babaei, S. Goli-Haghighi, and H. Savaloni, "Detection of overtone and combined peaks using Mn/Cu helical star-shaped (pine-tree-like) sculptured thin films in surface-enhanced Raman spectroscopy," *Journal of Theoretical and Applied Physics,* vol. 13, no. 4, pp. 305-314, 2019.

[17] M. Kotyagol, J. Tonannavar, and J. R. Tonannavar, "Investigation of D-Glutamine dimer: Characterization of N—H⋯ O bond using experimental-IR, Raman, UV-Vis, ECD spectroscopy techniques, supported by computational-MD, DFT, NBO, AIM, NCI methods," *Journal of Theoretical and Applied Physics,* vol. 19, no. 5, 2025.

[18] D. W. Hahn and N. Omenetto, "Laser-induced breakdown spectroscopy (LIBS), part II: review of instrumental and methodological approaches to material analysis and applications to different fields," *Applied spectroscopy,* vol. 66, no. 4, pp. 347-419, 2012.

[19] S. C. Jantzi, V. Motto-Ros, F. Trichard, Y. Markushin, N. Melikechi, and A. De Giacomo, "Sample treatment and preparation for laser-induced breakdown spectroscopy," *Spectrochimica Acta Part B: Atomic Spectroscopy,* vol. 115, pp. 52-63, 2016.

[20] H. Dehghanpour and P. Parvin, "Glass surface modification using Nd: YAG laser in SF6 atmospheres," *Journal of Theoretical and Applied Physics,* vol. 9, no. 2, pp. 135-140, 2015.

[21] F. Anabitarte García, A. Cobo García, and J. M. López Higuera, "Laser-induced breakdown spectroscopy: fundamentals, applications, and challenges," 2012.

[22] L. J. Radziemski, T. R. Loree, D. A. Cremers, and N. M. Hoffman, "Time-resolved laser-induced breakdown spectrometry of aerosols," *Analytical chemistry,* vol. 55, no. 8, pp. 1246-1252, 1983.

[23] V. Lazic and S. Jovićević, "Laser induced breakdown spectroscopy inside liquids: processes and analytical aspects," *Spectrochimica Acta Part B: Atomic Spectroscopy,* vol. 101, pp. 288-311, 2014.

[24] Y. Cheng *et al.*, "A Stand-Off Laser-Induced Breakdown Spectroscopy (LIBS) System for Remote Bacteria Identification," *Journal of Biophotonics,* vol. 17, no. 11, p. e202400332, 2024.

[25] F. Anabitarte, A. Cobo, and J. M. Lopez-Higuera, "Laser-induced breakdown spectroscopy: fundamentals, applications, and challenges," *International Scholarly Research Notices,* vol. 2012, no. 1, p. 285240, 2012.
[26] K.-Q. Yu, Y.-R. Zhao, F. Liu, and Y. He, "Laser-induced breakdown spectroscopy coupled with multivariate chemometrics for variety discrimination of soil," *Scientific reports,* vol. 6, no. 1, p. 27574, 2016.
[27] V. C. Costa *et al.*, "Calibration strategies applied to laser-induced breakdown spectroscopy: a critical review of advances and challenges," *Journal of the Brazilian Chemical Society,* vol. 31, no. 12, pp. 2439-2451, 2020.
[28] D. S. Ferreira *et al.*, "Laser-induced breakdown spectroscopy (LIBS): calibration challenges, combination with other techniques, and spectral analysis using data science," *Journal of Analytical Atomic Spectrometry,* vol. 39, no. 12, pp. 2949-2973, 2024.
[29] Y. Ke-qiang, Z. Yan-ru, L. Fei, and H. Yong, "Laser-induced breakdown spectroscopy for simultaneous quantitative analysis of multi-elements in soil," *Spectroscopy and Spectral Analysis,* vol. 37, no. 9, pp. 2879-2884, 2017.
[30] K. M. Donaldson and X. T. Yan, "A first simulation of soil-laser interaction investigation for soil characteristic analysis," *Geoderma,* vol. 337, pp. 701-709, 2019.
[31] X. Liu, X. Feng, F. Liu, J. Peng, and Y. He, "Rapid identification of genetically modified maize using laser-induced breakdown spectroscopy," *Food and Bioprocess Technology,* vol. 12, no. 2, pp. 347-357, 2019.
[32] V. Babushok, F. DeLucia Jr, J. Gottfried, C. Munson, and A. Miziolek, "Double pulse laser ablation and plasma: Laser induced breakdown spectroscopy signal enhancement," *Spectrochimica Acta Part B: Atomic Spectroscopy,* vol. 61, no. 9, pp. 999-1014, 2006.
[33] M. K. Hamid, D. A. Ghafoor, and S. A. Obaid, "Characteristic and anticancer activity of silver nanoparticles of graviola (Annona) fruit juice as a reducing agent," *Biochemical & Cellular Archives,* vol. 21, no. 1, 2021.
[34] I. Rehan, M. Gondal, and K. Rehan, "Determination of lead content in drilling fueled soil using laser induced spectral analysis and its cross validation using ICP/OES method," *Talanta,* vol. 182, pp. 443-449, 2018.
[35] R. Nader, M. J. Zoory, and H. J. Mohamad, "Proposed novel relative intensity LIBS approach for quantifying heavy metals in sunscreens, compared with AAS," *Optical Review,* pp. 1-11, 2025.
[36] S. K. Rahi, M. J. Zoory, and A. H. Ali, "Development of probe technology by quantum overlap for controlling spectroscopic behaviors in organic dyes," *Journal of Optics (India),* Article vol. 53, no. 3, pp. 2452-2459, 2024, doi: 10.1007/s12596-023-01365-w.
[37] S. K. Rahi, M. J. Zoory, and A. H. Ali, "Design and develop an optical setup related to the pump-probe technique for spectroscopic study," *Baghdad Science Journal,* Article vol. 21, no. 6, pp. 2137-2145, 2024, doi: 10.21123/bsj.2023.8383.
[38] T. S. Attaa, A. N. Abd, and M. J. Zoory, "Fabrication of Al/Li2O/PSi/ Si/Al heterojunction for photodetector and solar cell applications," in *Materials Today: Proceedings*, 2020, vol. 49, pp. 3607-3614, doi: 10.1016/j.matpr.2021.08.152. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85123437632&doi=10.1016%2fj.matpr.2021.08.152&partnerID=40&md5=da4a4ae10bf5816a1df2ceb30bae52dc
[39] T. S. Atta, M. J. Zoory, and A. N. Abd, "Porous silicon fabrication by electrochemical and photo-electrochemical methods," in *Journal of Physics: Conference Series*, 2021, vol. 1963, 1 ed., doi: 10.1088/1742-6596/1963/1/012153. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85112412674&doi=10.1088%2f1742-6596%2f1963%2f1%2f012153&partnerID=40&md5=bf02881e03b7e8592ec0184aaec4961c

[40] H. S. Hasan, S. A. Obaid, and M. S. Erhayief, "Recent Development-2 of CADTEL Software: The Optimum Conditions of Scherzer Imaging in the Electron Magnetic Lenses," *Iraqi Journal of Science,* pp. 131-148, 2022.
[41] H. S. Hasan, S. A. Obaid, and M. S. Erhayief, "Recent Development-1 of CADTEL Software: The Resolution and Focusing Parameters Affecting at the Properties of Electron Magnetic Lenses," *Iraqi Journal of Science,* pp. 524-537, 2022.
[42] M. J. Zoory, S. F. Madlul, and A. N. Abd, "Review on the effect of ion mirror phenomenon," *NeuroQuantology,* Review vol. 18, no. 1, pp. 91-98, 2020, doi: 10.14704/nq.2020.18.1.NQ20112.
[43] M. J. Zoory and M. M. Abid, "Study a scanning beam current in focusing ion beam device of overcome mirror effect," *Optik,* Article vol. 158, pp. 1470-1477, 2018, doi: 10.1016/j.ijleo.2018.01.051.
[44] S. A. Obaid, J. H. Taha, and S. Abdullah, "Electron lens Optimization for Beam Physics Research using the Integrated Optics Test Accelerator," *Baghdad Science Journal,* vol. 19, no. 6, p. 30, 2022.
[45] A. P. Rao, P. R. Jenkins, J. D. Auxier, M. B. Shattan, and A. K. Patnaik, "Analytical comparisons of handheld LIBS and XRF devices for rapid quantification of gallium in a plutonium surrogate matrix," *Journal of Analytical Atomic Spectrometry,* vol. 37, no. 5, pp. 1090-1098, 2022.
[46] K. Rawat, N. Sharma, and V. Singh, "X-Ray Fluorescence and Comparison with Other Analytical Methods (AAS, ICP-AES, LA-ICP-MS, IC, LIBS, SEM-EDS, and XRD)," 2022, pp. 1-20.
[47] M. Lanzinger, S. Kaufmann, M. Schuster, and N. P. Ivleva, "LIBS as a fast and reliable alternative to μXRF and SEM–EDX for quantitative analysis of aluminium alloy particles in technical cleanliness analysis," *Microchemical Journal,* vol. 207, p. 111782, 2024/12/01/ 2024, doi: https://doi.org/10.1016/j.microc.2024.111782.
[48] T. S. Indi and D. Patil, "A review: Human finger nail image analysis for disease diagnosis," *Journal Emerging Technologies and Innovative Research (JETIR),* vol. 6, no. 5, 2019.
[49] I. Rehan, K. Rehan, S. Sultana, and M. U. Rehman, "Fingernail Diagnostics: Advancing type II diabetes detection using machine learning algorithms and laser spectroscopy," *Microchemical Journal,* vol. 201, p. 110762, 2024.
[50] C. Grover and S. Bansal, "The nail as an investigative tool in medicine: What a dermatologist ought to know," *Indian Journal of Dermatology, Venereology and Leprology,* vol. 83, p. 635, 2017.
[51] M. Martinez and M. Baudelet, "Matrix-matched calibration material for zinc analysis of human nails by laser-induced breakdown spectroscopy," *Spectrochimica Acta Part B: Atomic Spectroscopy,* vol. 163, p. 105732, 2020.
[52] V. K. Singh *et al.*, "application of LIBS to elemental analysis and mapping of plant samples," *At. Spectrosc.,* vol. 42, no. 1, 2021.
[53] A. K. Pathak, R. Kumar, V. K. Singh, R. Agrawal, S. Rai, and A. K. Rai, "Assessment of LIBS for spectrochemical analysis: a review," *Applied Spectroscopy Reviews,* vol. 47, no. 1, pp. 14-40, 2012.
[54] J. Batool, N. Amin, Y. Jamil, N. Shaikh, and S. Al Islam, "Rapid elemental analysis of human teeth using laser induced breakdown spectroscopy," *Physica B: Condensed Matter,* vol. 602, p. 412495, 2021/02/01/ 2021, doi: https://doi.org/10.1016/j.physb.2020.412495.
[55] S. Zhang *et al.*, "Quantitative analysis of mineral elements in hair and nails using calibration-free laser-induced breakdown spectroscopy," *Optik,* vol. 242, p. 167067, 2021/09/01/ 2021, doi: https://doi.org/10.1016/j.ijleo.2021.167067.
[56] S. Hamzaoui, R. Khleifia, N. Jaïdane, and Z. Ben Lakhdar, "Quantitative analysis of pathological nails using laser-induced breakdown spectroscopy (LIBS) technique," *Lasers*

in Medical Science, vol. 26, no. 1, pp. 79-83, 2011/01/01 2011, doi: 10.1007/s10103-010-0821-x.

[57] V. Riberdy, C. Frederickson, and S. Rehse, "Determination of the Zinc Concentration in Human Fingernails Using Laser-Induced Breakdown Spectroscopy," *Applied spectroscopy,* vol. 71, p. 3702816687568, 01/20 2017, doi: 10.1177/0003702816687568.

[58] M. A. Almessiere, R. Altuwiriqi, M. A. Gondal, R. K. AlDakheel, and H. F. Alotaibi, "Qualitative and quantitative analysis of human nails to find correlation between nutrients and vitamin D deficiency using LIBS and ICP-AES," *Talanta,* vol. 185, pp. 61-70, 2018/08/01/ 2018, doi: https://doi.org/10.1016/j.talanta.2018.03.057.

[59] A. Al Maliki, A. K. Al-lami, H. M. Hussain, and N. Al-Ansari, "Comparison between inductively coupled plasma and X-ray fluorescence performance for Pb analysis in environmental soil samples," *Environmental Earth Sciences,* vol. 76, no. 12, p. 433, 2017/06/26 2017, doi: 10.1007/s12665-017-6753-z.

[60] K. Planeta, A. Kubala-Kukus, A. Drozdz, K. Matusiak, Z. Setkowicz, and J. Chwiej, "The assessment of the usability of selected instrumental techniques for the elemental analysis of biomedical samples," *Scientific Reports,* vol. 11, no. 1, p. 3704, 2021/02/12 2021, doi: 10.1038/s41598-021-82179-3.

[61] S. Maghsoumi and H. Shirvani-Mahdavi, "Calcium evaluation of human fingernail using laser plasma spectroscopy by simultaneously applying addition and modified external standardizations," *Journal of Theoretical and Applied Physics,* vol. 12, pp. 319-326, 2018.

[62] I. Rehan, K. Rehan, S. Sultana, and M. Ur Rehman, "Fingernail Diagnostics: Advancing type II diabetes detection using machine learning algorithms and laser spectroscopy," *Microchemical Journal,* vol. 201, p. 110762, 2024/06/01/ 2024, doi: https://doi.org/10.1016/j.microc.2024.110762.

[63] M. Bahreini, B. Ashrafkhani, and S. H. Tavassoli, "Discrimination of patients with diabetes mellitus and healthy subjects based on laser-induced breakdown spectroscopy of their fingernails," *Journal of Biomedical Optics,* 10/01 2013, doi: 10.1117/1.JBO.18.10.107006.

[64] J. Ye, X. Wan, Z. Zhang, Q. Chen, C. Deng, and J. Zhao, "Quantitative Analysis of Pb with Laser-Induced Breakdown Spectroscopy in Human's Nail," in *2012 Symposium on Photonics and Optoelectronics*, 21-23 May 2012 2012, pp. 1-3, doi: 10.1109/SOPO.2012.6270427.

[65] S. Shadman, M. Bahreini, and S. H. Tavassoli, "Comparison between elemental composition of human fingernails of healthy and opium-addicted subjects by laser-induced breakdown spectroscopy," (in eng), *Appl Opt,* vol. 51, no. 12, pp. 2004-11, Apr 20 2012, doi: 10.1364/ao.51.002004.

[66] D. A. Rusak, A. E. Zeleniak, J. L. Obuhosky, S. M. Holdren, and C. A. Noldy, "Quantitative determination of calcium, magnesium, and zinc in fingernails by laser-induced breakdown spectroscopy," *Talanta,* vol. 117, pp. 55-59, 2013.

[67] H. A. Harun, R. Zainal, and Y. M. Daud, "Analysing human nails composition by using laser induced breakdown spectroscopy," *Sains Malaysiana,* vol. 46, no. 1, pp. 75-82, 2017.

[68] M. W. Tehrani, K. X. Yang, and P. J. Parsons, "Development and characterization of reference materials for trace element analysis of keratinized matrices," (in eng), *Anal Bioanal Chem,* vol. 412, no. 8, pp. 1847-1861, Mar 2020, doi: 10.1007/s00216-020-02432-y.

[69] V. Bali *et al.*, "Quantitative analysis of human hairs and nails," (in eng), *Biophys Rev,* vol. 15, no. 3, pp. 401-417, Jun 2023, doi: 10.1007/s12551-023-01069-2.

[70] R. Nader, H. J. Mohamad, and M. J. Zoory, "Comparison of Heavy Metals Concentrations in Toothpaste Using Atomic Absorption Analysis and Laser-Induced Breakdown," *Journal of Optics,* 2024/09/05 2024, doi: 10.1007/s12596-024-02195-0.

[71] Z. J. Kamil, M. J. Zoory, and H. J. Mohamad, "LIBS technique for plant mineral ratio analysis and environmental and agricultural importance: a comprehensive review," *The European Physical Journal D,* vol. 78, no. 3, p. 27, 2024.
[72] L. Kadhim, A. Hussein, M. Zoory, and R. Nader, "Comparison of LIBS and XRF for accurate micronutrient analysis in dried white lemon," *Journal of Optics,* 02/22 2025, doi: 10.1007/s12596-025-02620-y.
[73] N. Sushkov, "Qualitative Classification of Biological Materials by LIBS," in *Laser-Induced Breakdown Spectroscopy in Biological, Forensic and Materials Sciences*: Springer, 2025, pp. 227-281.
[74] I. Sami, M. J. Zoory, and S. H. Lefta, "Quantitative analysis of element calcium using laser-induced breakdown spectroscopy for patients with chronic renal failure," in *AIP Conference Proceedings*, 2025, vol. 3211, no. 1: AIP Publishing LLC, p. 060002.
[75] A. E. Chuprov, "Application of Laser Emission Spectrometry (LIBS) for Identification of Materials within Spent Fuel Cooling Ponds Using LIBSProbe with a Submersible Remote Probe," *Photonics Russia,* vol. 13, pp. 202-205, 01/01 2019, doi: 10.22184/FRos.2019.13.2.202.205.
[76] A. Limbeck *et al.*, "Methodology and applications of elemental mapping by laser induced breakdown spectroscopy," (in eng), *Anal Chim Acta,* vol. 1147, pp. 72-98, Feb 22 2021, doi: 10.1016/j.aca.2020.12.054.
[77] Z. J. Kamil, M. J. Zoory, and H. J. Mohamad, "Application of a new method to estimate micronutrient concentration percentages in dried celery plants using LIBS and XRF techniques," *Journal of Optics,* pp. 1-9, 2024.
[78] M. Zewita, M. M. Shalaby, A. M. Abdlatif, and M. A. Abdalziz, "Renal Function Tests (Blood Urea and Serum Creatinine) Pre-and Post-Operative Treatment for Tubeless Percutaneous Nephrolithotomies and Standard Treatment," *Journal of Pioneering Medical Sciences,* vol. 13, pp. 124-127, 2024.
[79] R. Nader, M. J. Zoory, and H. J. Mohamad, "Quantitative and qualitative analysis of lip balms in the Iraqi market using LIBS and concentration estimation based on electron density," *Journal of Optics,* 2024/10/15 2024, doi: 10.1007/s12596-024-02297-9.
[80] Z. Kamil, M. Zoory, and H. Mohamad, "Estimate of macronutrient concentration in dried flaxseed plants using laser-induced breakdown spectroscopy (LIBS) technique," *Journal of Optics,* pp. 1-7, 07/13 2024, doi: 10.1007/s12596-024-02041-3.
[81] M. Mehdizadeh, A. Omidi, T. M. Ikegwu, C. A. Okolo, E. I. IfedibaluChukwu, and L. C. Ndufeiya-Kumasi, "Laser-Induced Breakdown Spectroscopy (LIBS) for Rapid Food Safety Monitoring: Advancements, Applications, and Future Directions," *Food Safety and Health,* 2025.
[82] I. Sami, M. J. Zoory, and S. H. Lefta, "Implementation of laser-induced breakdown spectroscopy (LIBS) technique in evaluating of renal failure in patients with iron (Fe) deficiency," *Adv Life Sci,* vol. 11, no. 1, pp. 66-77, 2024.
[83] N. M. Dbayh, M. J. Zoory, and A. H. Ali, "Thermal effects in determination of plasma parameters in Fe metal model using LIBS technique," in *AIP Conference Proceedings*, 2025, vol. 3211, no. 1: AIP Publishing LLC, p. 060001.
[84] K. Rawat, N. Sharma, and V. K. Singh, "X-Ray Fluorescence and Comparison with Other Analytical Methods (AAS, ICP-AES, LA-ICP-MS, IC, LIBS, SEM-EDS, and XRD)," in *X-Ray Fluorescence in Biological Sciences*, 2022, pp. 1-20.
[85] A. V. Skalny *et al.*, "Medical application of laser-induced breakdown spectroscopy (LIBS) for assessment of trace element and mineral in biosamples: Laboratory and clinical validity of the method," *Journal of Trace Elements in Medicine and Biology,* vol. 79, p. 127241, 2023.

[86] Z. Mierzyńska *et al.*, "Multi-Elemental Analysis of Hair and Fingernails Using Energy-Dispersive X-ray Fluorescence (ED XRF) Method Supported by Inductively Coupled Plasma Mass Spectrometry (ICP MS)," *Molecules,* vol. 29, no. 4, p. 773, 2024.
[87] A. Triantafillidis, P. Stogiannis, P. Amarantos, I. Kontodimos, C. Ketikidis, and P. Grammelis, "Trace and Major Elements Analysis of Alternative Solid Fuels by Means of Inductively Coupled Plasma Mass Spectrometry: Comparison with Atomic Absorption Spectrometry and X-ray Fluorescence Results," *Engineering Proceedings,* vol. 56, no. 1, p. 238, 2023. [Online]. Available: https://www.mdpi.com/2673-4591/56/1/238.
[88] T. Nurubeyli, N. S. Jafar, and K. N. Ahmadova, "Optimization of ICP-MS Analysis for Studying Matrix Effects in Biological Fluids," *Methods & Objects of Chemical Analysis/Metody & Obekty Himičeskogo Analiza,* vol. 20, no. 1, 2025.
[89] H. Yoon, C. Yoon, C. S. Park, T. Ko, N. S. Kim, and K. N. Han, "Quantitative determination of PGM using ICP-MS, ICP-AES, AAS and XRF," *Mining, Metallurgy & Exploration,* vol. 22, no. 1, pp. 59-64, 2005/02/01 2005, doi: 10.1007/BF03403197.
[90] I. Martinez-Morata, M. Sobel, M. Tellez-Plaza, A. Navas-Acien, C. G. Howe, and T. R. Sanchez, "A state-of-the-science review on metal biomarkers," *Current environmental health reports,* vol. 10, no. 3, pp. 215-249, 2023.
[91] S. Jaramillo Ortiz, M. Howsam, E. H. van Aken, J. R. Delanghe, E. Boulanger, and F. J. Tessier, "Biomarkers of disease in human nails: A comprehensive review," *Critical Reviews in Clinical Laboratory Sciences,* vol. 59, no. 2, pp. 125-141, 2022.
[92] S. Hameed, S. Ashraf, S. Ashraf, N. Nazish, M. Sughra, and A. Ijaz, "Blood, Hair, and Nail as Biomarkers of Arsenic Exposure among Leather Industry Workers in Sialkot," *Journal of Health, Wellness and Community Research,* pp. e702-e702, 2025.
[93] V. A. Riberdy, C. J. Frederickson, and S. J. Rehse, "Determination of the zinc concentration in human fingernails using laser-induced breakdown spectroscopy," *Applied spectroscopy,* vol. 71, no. 4, pp. 567-582, 2017.
[94] S. Zhang *et al.*, "Quantitative analysis of mineral elements in hair and nails using calibration-free laser-induced breakdown spectroscopy," *Optik,* vol. 242, p. 167067, 2021.
[95] Y. Ali and R. Khamis, "Spectroscopic Study of Copper Plasma Produced by Nd: YAG Laser from The Nano and Bulk Copper Targets," *Journal of Physics: Conference Series,* vol. 1818, p. 012008, 03/01 2021, doi: 10.1088/1742-6596/1818/1/012008.

Tables

Table (1). Comparative assessment of LIBS, ICP-MS, AAS, and XRF in relation to type of samples, applications, advantages, and limitations in the field of biomedical diagnostics.

Method	Sample Types	Applications	Strengths	Limitations

LIBS	Biological tissues (toenails, hair, teeth), metals[70-74]	Biomedical diagnostics, environmental/industrial analysis [70-72, 75-83]	Fast, portable, low sample pre-parathion, multi-element analyses [84, 85]	Matrix effects, limited sensitivity relative to ICP-MS
XRF	Solids, powders, metals, ceramics, soils	Elemental and phase analysis, industrial/biomedical samples [71, 72, 77, 84, 86].	non-destructive, inexpensive, high sensitivity trace/main [87].	Needs fairly homogenous samples; its detection limit is higher than that of ICP-MS; has a poor sensitivity for light elements [59].
ICP-MS	liquids, digested solids, environmental samples[88]	Trace element and isotope analysis, toxicology, geology [86, 89].	high sensitivity and accuracy, low detection limits[89].	Samples preparation can be complex, matrix interferences, cost[89].
AAS	Liquids, biological tissues, metals	Single-element analysis [60, 70]	Low-cost, easy-to-operate instruments, widespread availability [60].	Time-consuming for multi-element analysis, detection limit more [87].

Note: LIBS provides better portability and fast multi-element analysis compared to ICP-MS and AAS with lower sensitivity.

Table (2). Illustrates the distinctiveness of nail analysis compared to traditional blood and urine-based approaches.

Property	Nail Analysis	Blood/Urine Analysis
Timeframe	Long-term Integrative: The concentration of elements represents average exposure over weeks to months[50, 90]	Spot/Short-term Measurement: Reflects concentrations at the time of sample collection only (hours to days)[49, 50]
Consistency	A highly stable specimen: the composition does not change after growt[50]h, and it does not require harsh storage conditions (such as deep freezing[91]).	Perishable sample: Requires skillful handling and storage (such as freezing) to allow decomposition or change[91]
Aggregation Method	Completely non-invasive: Sample collection is simple, painless, and carries no risk of infection.[50, 91]	Invasive/Unpleasant: Requires drawing blood with a needle or collecting urine, which reduces the patient's acceptance of repeated examinations[50, 92]

Table (3): Elemental Emission Line Ratios (Ca, Na, K) for Healthy and Diseased Nails Obtained from LIBS Spectra [56].

Analyzed lines (nm)	Intensity ratio				
	Pathological upper face	Inner face yellow region	Inner face brown region	Normal upper face	Normal inner face
Ca 393.37 nm/K 766.49 nm	43.60	26.73	39.57	33.15	14.17
Ca 396.85 nm/K 766.49 nm	42.23	21.05	30.92	23.94	9.51
Na 589.0 nm/K 766.49 nm	13.14	7.74	13.60	5.23	3.46

Na 589.6 nm/K 766.49 nm	10.26	6.07	10.63	3.83	2.63

Table (4).

Source Disease/Analysis	Recorded performance	Study context and sample size	Key limitations
Ribordy et al. (2017)[93] Zinc (Zn) deficiency	The regression model (PLS) predicted zinc concentration within 7 ppm. - The predictions had a standard deviation of 14 ppm, indicating a relative inaccuracy of ~12%. - Nails with a zinc difference of ~50 ppm were identified.	Developing a LIBS protocol to measure zinc in fingernails instead of blood serum. Sample: 5 volunteers (6 fingernails each).	Significant measurement discrepancies arise due to the fibrous and layered nature of the nail plate, resulting in irregular excision. - Uneven nail surface texture increases the discrepancy. - The use of a 1064 nm laser may not be optimal for interaction with keratin.
Maghsoudi & Shirvani-Mahdavi (2018) [61] Calcium (Ca) concentration	Calcium concentrations were measured in three individuals: 10814, 13106, and 14974 parts per million. - The difference between the results of the horn and hoof assays was between 3-5%.	Application of a modified external calibration method using cow horns and hooves as a standard matrix analogous to a fingernail. Sample size: 3 volunteers (their fingernails were analyzed).	- It relies on the assumption that cow horns and hooves are very similar in structure to human fingernails, which may not be entirely accurate. - The study was conducted on a very small sample (only 3 people). - The use of a spectral line (Ca_2I_4 422.673 nm) is subject to self-absorption.
	A strong inverse relationship exists	Investigating the relationship	- The reported relationship is an

Source Disease/Analysis	Recorded performance	Study context and sample size	Key limitations
Almessiere et al. (2018)[2] Vitamin D deficiency	between the intensity of potassium (K) lines in the nails and blood vitamin D levels (Pearson correlation coefficient -0.776). - A weak relationship exists for other elements (Ca, Mg, Na). - Good qualitative agreement with ICP-AES results.	between vitamin D deficiency and nail element intensity using LIBS. Sample size: 71 volunteers (divided by age and vitamin D level).	association, not a cause. - The sample is geographically limited (Saudi Arabia), and the results may not be generalizable. - The mechanism by which low potassium in nails is associated with vitamin D deficiency is unclear and may be related to other factors (such as blood pressure medications).
Zhang et al. (2021)[94] Relative elemental analysis (Ca/Na, Mg/Na)	The relative error between CF-LIBS and ICP-OES results was less than 10% for both hair and nails. (For hair: Ca/Na error 3.7%, Mg/Na error 9.9%).	Application of the CF-LIBS (calibration-free) method supported by a standard reference line for analyzing relative elements in biomarkers (hair and nails). Sample size: Not clearly defined (samples were taken from volunteers).	- The method relies on the assumption of a local kinetic equilibrium (LTE) state in the plasma, which was verified but under specific conditions. - Only the ratios (Ca/Na, Mg/Na) were measured, not the absolute concentrations of the individual elements. - Using a single sodium spectral line (Na_2I 589.00 nm) as a reference may be sensitive to self-absorption.
(Rithika et al.,2022) [9] Detection of various diseases	Successful differentiation of pathological samples based on differences in the intensity of elements	Exploratory study: 27 nail samples (17 healthy samples, 10	The sample size is small, especially among pathological samples (n=10). The results are

Source Disease/Analysis	Recorded performance	Study context and sample size	Key limitations
(diabetes, thyroid, etc.)	such as magnesium (Mg), potassium (K), and calcium (Ca) in the spectra. No numerical performance metrics were reported.	samples from people with various diseases such as diabetes and thyroid disease).	preliminary and need confirmation with larger and more diverse samples.
(Skalny et al., 2023[85]) Clinical validation of LIBS technique (systematic review)	High classification accuracy of 96%, with a sensitivity of 96.7%, a positive prediction accuracy of 99.9%, and an F1 ratio of 96.8%.	Systematic study: 80 samples (40 diabetic patients, 40 healthy individuals). 4800 data were collected. Advanced machine learning algorithms (Stack Ensemble Learning) with principal component analysis (PCA) were used.	The sample size is relatively limited (80 participants). The LIBS technique does not provide molecular information. The experimental setup is complex and costly compared to some conventional diagnostic methods.
Rehan et al., 2024)[49] Type 2 diabetes detection	High classification accuracy of 96%, with sensitivity of 96.7%, positive prediction accuracy (Precision) of 99.9%, and F1 ratio of 96.8%.	Systematic study: 80 samples (40 diabetic patients, 40 healthy individuals). 4800 data were collected. Advanced machine learning algorithms (Stack Ensemble Learning) with principal component	The sample size is relatively small (80 participants). LIBS does not provide molecular information. The experimental setup is complex and costly compared to some traditional diagnostic methods.

Source Disease/Analysis	Recorded performance	Study context and sample size	Key limitations
		analysis (PCA) were used.	

Table (5): Principal spectral lines of the elements identified in human nail samples of drug and alcohol abuse using LIBS[65].

Line ID	Wavelength	Line ID	Wavelength
Ca I	422.672	Ti II	307.865
Ca I	443.568	Ti II	308.804
Ca I	445.588	Ti II	323.451
Ca I	610.272	Ti II	334.94
Ca I	612.2219	Ti II	336.122
Ca I	616.217	Ti II	337.279
Ca I	643.907	Ti II	338.376
Ca I	646.256	Ti II	368.52
Mg I	285.212	Ti II	376.132
Mg II	279.553	O I	777.194
Mg II	280.27	Na I	588.995
Ca II	315.886	Na I	589.5924
Ca II	317.933	K I	766.489
Ca II	370.602	K I	769.896
Ca II	373.69	Si I	250.689
Ca II	396.846	C I	247.586
Al I	308.215	H I	486.136
Al I	309.271	H I	656.285
Al I	394.4	Fe II	259.939
Al I	396.152		

Table (6): Wavelengths and spectral lines of key elements detected in abnormal nails of different pathological groups[67].

Spectrum	Wavelength (nm)	Spectrum	Wavelength (nm)
Ca (I)	422.672	Al (I)	308.215
Ca (II)	317.933	Al (I)	309.271
Ca (II)	393.366	Ti (II)	334.94
Ca (II)	396.846	Ti (II)	376.132
Ca (II)	501.997	O (I)	777.194
Mg (II)	280.270	Na (I)	589.592
K (I)	766.489	K (I)	769.896
P (II)	458.804	P (II)	494.41

Table 7: Summary of the LIBS studies sorted by disease target, main change in elements, and classification accuracy.

Disease	**Main Elements Affected**	**Classification Accuracy (%)**	**Key References**
Diabetes	Ca ↓, Mg ↓, K fluctuations	96	[27,29]
Thyroid Disorders	Na/Ca ratio ↑ or ↓, K/Ca changes	90	[22,28]
Osteoporosis	Ca ↓, Mg ↓, Zn ↓	85.9	[35]
Lead Exposure	Pb ↑ (industrial cases)	-	[30]
Addiction	Ca ↓, K ↓, Sr changes	80–85	[31,32]

Table 8: Chronological summary of LIBS applications (2011–2024) An overview of selected LIBS studies (2011–2024): focusing on methods, sample types, and major findings/publications.

Source & Date	Techniques	Samples	Key Findings
Hamzaoui *et al*. (2011)	LIBS	Pathological vs. healthy nails	Detected Ca, Na, K differences in diseased nails
Bahreini & Tavassoli (2012)	LIBS	Healthy vs. thyroid nails	100% classification accuracy for thyroid cases
Ye et al. (2012)	LIBS	Lead-exposed workers	Pb detection down to 24 ppm

Bahreini *et al*. (2012)	LIBS + ICP-MS	Osteoporosis screening	Correlation between Ca/Mg levels and BMD
Haroun *et al*. (2017)	LIBS	Nail pathologies	Specific elemental shifts in nail diseases
Rehan *et al*. (2024)	LIBS + ML (PCA, Stacked Models)	Diabetic vs. healthy nails	96% classification accuracy with ML

Table 9: Major challenge categories associated with LIBS applications in medical diagnostics along with proposed solutions suggested from studies presented.

Main Challenges	**Affected Studies**	**Proposed Solutions**
Small sample sizes	Bahreini & Tavassoli (2012), Haroun et al. (2017)	Increase sample sizes, conduct multi-center studies
Variability in results	Bahreini et al. (2012), Rithika *et al*. (2023)	Standardize protocols, cross-validate with ICP-MS
Lack of standardized reference standards	Martinez & Bodelet (2020), Maghsoumi & Shirvani (2018)	Develop keratin-based reference materials
Spectral interference and matrix effects	Rusak *et al*. (2013), Ribordy *et al.* (2017)	Use argon environment, advanced background correction
External contamination	Shadman *et al*. (2012), Almessiere et al. (2018)	Adopt rigorous cleaning and sample preparation
Sensitivity and detection limits	Ye *et al*. (2012), Rehan *et al*. (2024)	Use UV lasers, enhance signal processing and ML models

Table 10: Research gaps in the field of LIBS applications for various disease categories and potential future research directions.

Disease/Condition	**Key Research Gaps**	**Recommended Directions**
Diabetes	Limited large-scale datasets; lack of standardized calibration protocols	Multi-center clinical validation; AI-driven modeling with deep learning

Disease/Condition	Key Research Gaps	Recommended Directions
Thyroid Disorders	Small sample sizes; variability in Na/Ca and K/Ca ratios across studies	Standardized protocols and reference materials for reproducibility
Osteoporosis	Lack of correlation studies with gold-standard bone mineral density (BMD)	Joint studies combining LIBS with DEXA scans
Lead Exposure	Inconsistent detection limits; absence of certified nail reference samples	Calibration using keratin-based standards
Addiction (Drugs/Alcohol)	Few studies; low spectral data diversity	Expanded datasets and forensic-level validation

Figures:

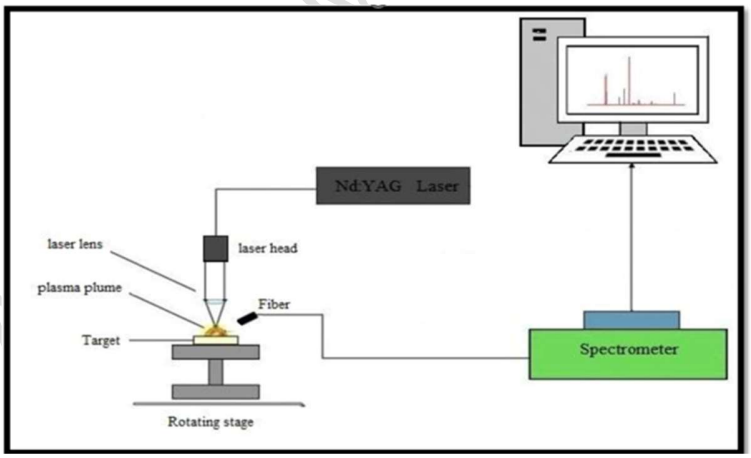

Figure 1: Diagram of a typical LIBS system showing the interaction of the pulsed Nd:YAG laser with the sample, plasma production and emission, and the high-resolution spectrometer [95].

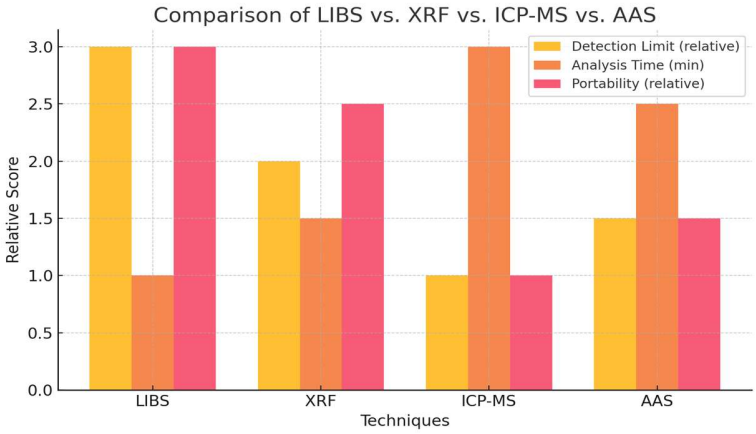

Figure 2: Comparison of detection limits, analysis time, and the portability of LIBS to other analytical methods: XRF, ICP-MS, and AAS[47-45] .

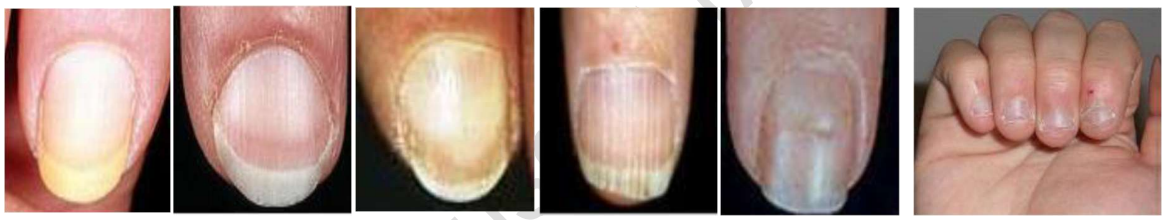

Figure 3: A clinical example of human nails that do not provide the morphological changes and patterns associated with systemic disease (such as diabetes and thyroid disease)[48].

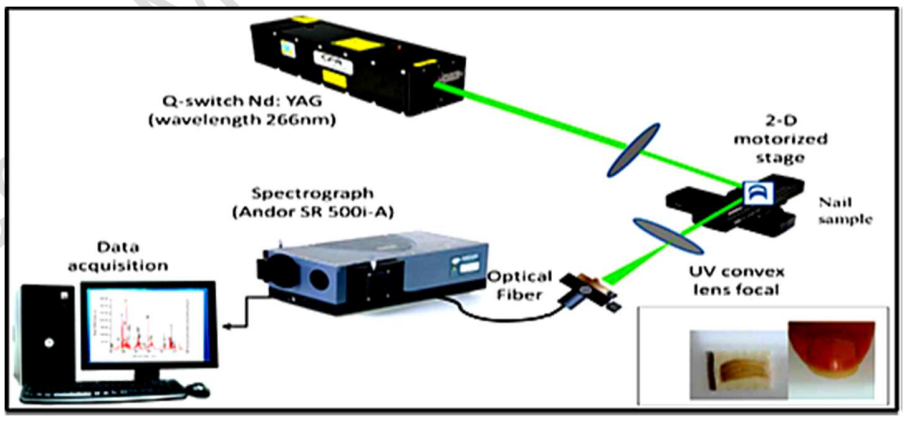

Figure 4: Experimental setup for LIBS fingernail analysis with a schematic diagram of the laser focusing system, spectrometer, and a typical nail sample image [58].

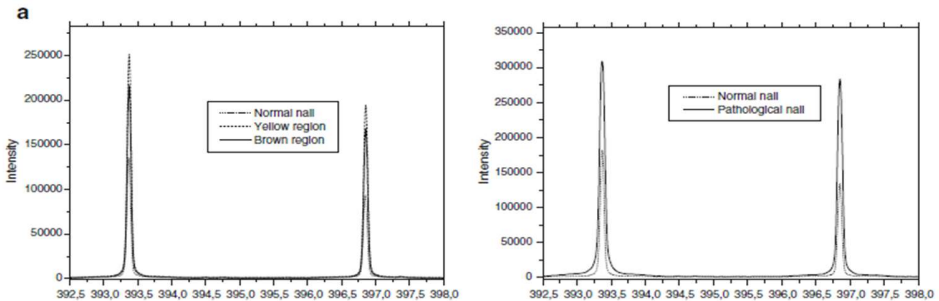

Figure 5: LIBS spectra showing differences in Ca, Na, and K emission lines in healthy nails and infected nails [56].

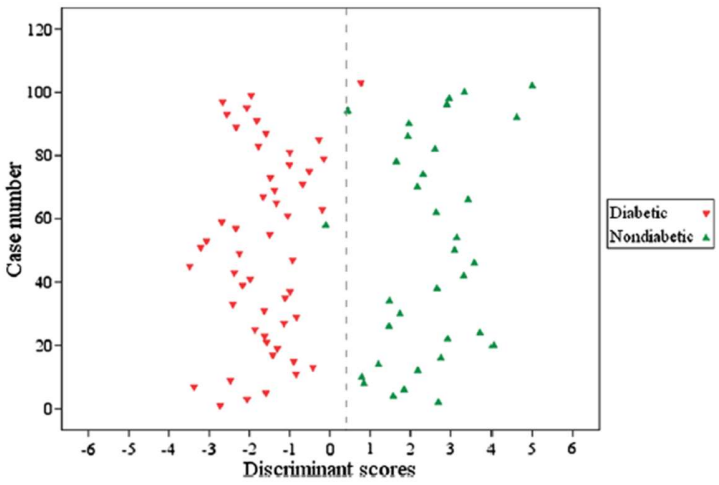

Figure 6: Discriminant function analysis plot showing the first discriminant function scores of LIBS spectra obtained by 82 emission lines of fingernails of diabetic and nondiabetic subjects[63].

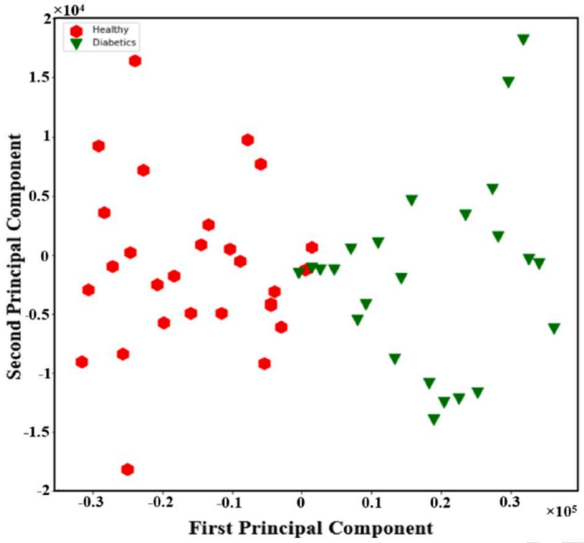

Figure7 : Scatter plot generated by PCA displaying fingernail samples from both controlled diabetic and non-diabetic individuals. [62].

Declarations

- No fund or grant was received for conducting this study.

Competing Interest Declaration:

- The authors declare they have no financial interests.

Author's contribution to the manuscript

The author contributed to experimenting, analyzing the data, and writing the manuscript, and was supervised by the co-authors. wrote the paper with input from all authors.

Data Availability Statement:

- Data sharing does not apply to this article as no data were generated but rather previous study sets were analyzed and conclusions drawn from them during this study.