"Advancing Genetic Drug Safety and Efficacy Using ICP-MS: A High-Sensitivity Analytical Approach".

1. N.Pujitha, 2.k.Maneesh kumar Reddy, 3. C.T.Manjunath, 4.M.Mohan Reddy, 5.P.Mounika, 6.Dr.K.Vinod kumar*

12345 Department of pharmacy, Raghavendra institute of pharmaceutical education and research, K. R. Palli cross, Cheyyadu post, Anathapur-525721

6Assistant professor, Department of pharmaceutical Analysis, Raghavendra institute of pharmaceutical education and research, K R. palli, Cheyyadu post, Ananthapur -525721.

Corresponding author: Dr. K.Vinod Kumar, Professor, Raghavendra institute of pharmaceutical education and research, K.R.alli cross,Anathapur-515721

Phone No: 9989071070

Abstract:

Genetic drugs, including mRNA vaccines, siRNA therapies, and CRISPR-based treatments, are transforming modern medicine by offering precise interventions at the molecular level. However, ensuring the quality, safety, and efficacy of these drugs requires advanced analytical techniques. Inductively Coupled Plasma (ICP) Spectroscopy, comprising ICP-Optical Emission Spectroscopy (ICP-OES) and ICP-Mass Spectrometry (ICP-MS), has emerged as a vital tool for the elemental analysis of genetic drugs. ICP methods are instrumental in quality control, impurity detection, bioavailability studies, nanoparticle-based drug delivery research, and stability testing. They provide high sensitivity, multi-element analysis, rapid throughput, and regulatory compliance, making them indispensable for pharmaceutical applications.

Despite its advantages, ICP analysis faces challenges such as high operational costs, complex sample preparation, and spectral interferences. However, technological advancements, including portable ICP systems, AI-driven data processing, and integration with chromatographic techniques, are enhancing its capabilities. As genetic drugs continue to evolve, ICP **spectroscopy** will remain crucial for ensuring their purity, stability, and regulatory compliance, ultimately advancing the field of personalized medicine.

Keywords:

Genetic drugs, Inductively Coupled Plasma (ICP) Spectroscopy, ICP-Optical Emission Spectroscopy (ICP-OES) ,ICP-Mass Spectrometry (ICP-MS) ,Elemental analysis

Introduction:

Genetic drugs represent a revolutionary advancement in medicine, targeting genetic material to treat or prevent diseases at a molecular level. Unlike traditional drugs that interact with proteins or metabolic pathways, genetic drugs modify DNA, RNA, or gene expression to achieve therapeutic effects. Examples include mRNA vaccines, small interfering RNA (siRNA) therapies, CRISPR-based gene editing, and antisense oligonucleotides (ASOs).

As these therapies gain prominence, stringent quality control and analytical techniques are required to ensure their efficacy and safety. Inductively Coupled Plasma (ICP) Spectroscopy has emerged as a powerful tool for elemental analysis in genetic drug research. ICP methods help in detecting metal contaminants, monitoring drug stability, and assessing the purity of genetic drugs.

Elemental impurities in genetic drugs can arise from raw materials, manufacturing processes, or storage conditions. Even trace amounts of heavy metals such as arsenic, mercury, or lead can have toxic effects, making precise analytical methods essential. ICP-based techniques, including ICP-Optical Emission Spectroscopy (ICP-OES) and ICP-Mass Spectrometry (ICP-MS), provide highly sensitive and accurate measurements of elemental content in pharmaceutical formulations.

This article explores the role of ICP spectroscopy in genetic drug analysis, detailing its principles, applications, advantages, and challenges. By leveraging ICP methods,researchers and pharmaceutical industries can ensure the safety and efficiency of genetic drugs, paving the way for advanced personalized medicine.

Understanding Inductively Coupled Plasma (ICP) Methods

Inductively Coupled Plasma (ICP) Spectroscopy is a powerful analytical technique used to determine the elemental composition of a sample with high precision and sensitivity. It works by ionizing the sample using a high-temperature plasma, typically composed of argon gas, and then analyzing the emitted light or ionized particles to identify and quantify elements present in the sample.

Principle of ICP Spectroscopy

The core principle of ICP methods revolves around plasma generation and atomic excitation. The process involves the following steps:

1. Sample Introduction: The sample is usually converted into a liquid form and nebulized into fine droplets. These droplets are introduced into the plasma for ionization.
2. Plasma Generation: The plasma, which operates at temperatures between 6,000 and 10,000 Kelvin, excites the atoms in the sample, causing them to emit characteristic wavelengths of light or ionize into charged particles.
3. Detection: The emitted light (for ICP-OES) or the ionized particles (for ICP-MS) are detected and analyzed to determine the type and concentration of elements present.

Types of ICP Methods

1. **ICP-Optical Emission Spectroscopy (ICP-OES)**

ICP-OES, also known as ICP-Atomic Emission Spectroscopy (ICP-AES), measures the light emitted by excited atoms in the plasma. Each element emits a unique set of wavelengths, allowing for simultaneous detection of multiple elements. ICP-OES is widely used for routine elemental analysis and is particularly effective for detectingmetals and minerals in pharmaceutical samples.

2. **ICP-Mass Spectrometry (ICP-MS)**

ICP-MS is a more advanced technique that detects ionized elements based on their mass-to-charge ratio. It is highly sensitive and capable of detecting elements in extremely low concentrations, down to parts per trillion (ppt). This makes it ideal for tracing impurities, metal contaminants, and isotope analysis in genetic drugs.

Importance of ICP in Genetic Drug Analysis

ICP methods are essential in pharmaceutical quality control, toxicology, and bioavailability studies. Genetic drugs often rely on metal-based components (such as nanoparticles for drug delivery), making ICP a crucial tool for ensuring product consistency and safety. The ability to detect even the slightest variations in elemental composition helps in improving the efficacy and stability of genetic therapeutics.

Application of ICP Methods in Genetic Drug Analysis

The development and commercialization of genetic drugs require rigorous analytical techniques to ensure their safety, purity, and efficacy. ICP spectroscopy plays a critical role in this process by enabling precise elemental analysis at trace levels. The following are key applications of ICP methods in genetic drug analysis.

1. **Quality Control and Elemental Purity Testing**

One of the primary applications of ICP in genetic drug analysis is ensuring elemental purity. Genetic drugs, including mRNA vaccines, CRISPR-based gene therapies, and RNA interference (RNAi) treatments, require extremely pure raw materials. Even trace metal contaminants can lead to instability, toxicity, or reduced therapeutic effects.

Heavy Metal Testing: Contaminants such as lead (Pb), mercury (Hg), cadmium (Cd), and arsenic (As) can enter genetic drug formulations through water, reagents, or packaging materials. ICP-MS is particularly useful in detecting these metals at parts-per-trillion (ppt) levels.

Raw Material Verification: Reagents used in genetic drug synthesis, such as buffers, nucleotides, and polymerases, must be tested for elemental impurities before formulation. ICP-OES and ICP-MS provide rapid and precise analysis.

Regulatory Compliance: Agencies like the FDA and EMA have set strict limits on elemental impurities in pharmaceutical products (ICH Q3D guidelines). ICP methods help ensure that genetic drugs meet these regulatory standards.

2. **Bioavailability and Pharmacokinetics**

Bioavailability refers to the extent and rate at which a drug enters systemic circulation, while pharmacokinetics involves the absorption, distribution, metabolism, and excretion (ADME) of the drug. ICP-MS plays a crucial role in studying these factors by:

Tracking Elemental Markers: Some genetic drugs incorporate metal-based tags or nanoparticles to track their movement in the body. ICP-MS allows researchers to monitor these elements with extreme sensitivity.

Studying Drug Distribution: By analyzing blood, urine, and tissue samples, scientists can determine how a genetic drug is distributed and metabolized. This information helps optimize drug formulations for better efficacy.

Nanomedicine Research: Many genetic drugs use metallic nanoparticles (e.g., gold or silver nanoparticles) for targeted delivery. ICP-MS helps quantify nanoparticle concentration and assess their interaction with biological systems.

3. **Nanoparticle-Based Genetic Drug Delivery**

Nanotechnology is revolutionizing the delivery of genetic drugs, with lipid nanoparticles (LNPs) and metallic nanoparticles playing a significant role in mRNA vaccines and siRNA-based therapies. ICP methods assist in:

Nanoparticle Characterization: ICP-OES and ICP-MS can determine the composition and purity of nanoparticles used in drug carriers.

Monitoring Degradation: Over time, nanoparticles may degrade or accumulate in unintended tissues. ICP analysis helps track their stability and potential toxicity.

Optimizing Formulations: By precisely measuring metal content, researchers can fine-tune nanoparticle properties to enhance drug delivery efficiency.

4. **Stability Studies and Degradation Analysis**

Genetic drugs must remain stable throughout their shelf life to maintain effectiveness. ICP methods are used to:

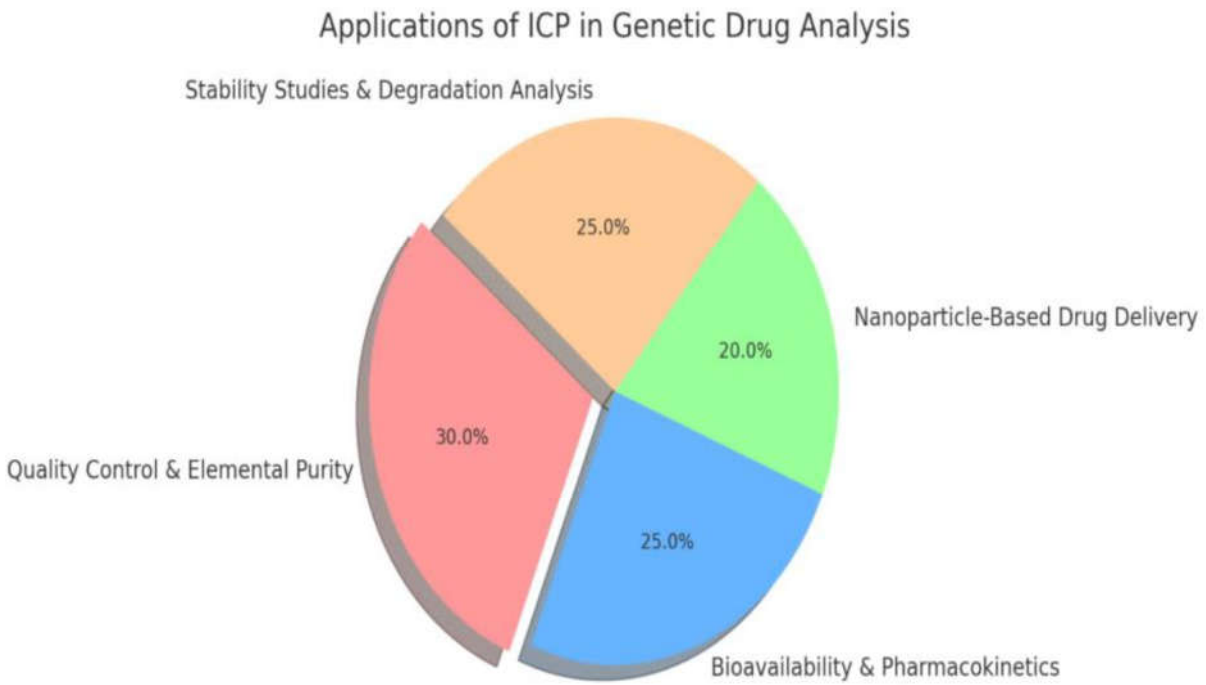
Monitor Elemental Changes Over Time: By regularly testing genetic drug formulations, ICP can detect changes in elemental composition that may indicate degradation.

Assess Metal Ion Leaching: Some genetic drug formulations are stored in metal-based containers, which may leach trace metals over time. ICP-MS helps assess potential contamination.

Ensure Long-Term Drug Safety: By studying how genetic drugs interact with storage materials and environmental factors, ICP techniques help extend drug shelf life while maintaining purity.

Conclusion of Applications

The use of ICP methods in genetic drug analysis is essential for quality control, pharmacokinetic studies, nanoparticle characterization, and stability testing. These techniques provide highly accurate, reliable, and sensitive elemental analysis, making them indispensable in the development of next-generation gene-based therapies.



Advantages of Using ICP for Genetic Drug Analysis

Inductively Coupled Plasma (ICP) methods have become a cornerstone of genetic drug analysis due to their high sensitivity, accuracy, and ability to detect trace elements. These advantages make ICP an essential tool for pharmaceutical research and regulatory compliance. Below are the key benefits of using ICP techniques in genetic drug analysis.

1. **High Sensitivity and Detection Limits**

ICP-MS, in particular, offers exceptional sensitivity, capable of detecting elements at parts-per-trillion (ppt) levels. This is crucial for genetic drug analysis because:

Even trace amounts of metal contaminants can alter drug stability or cause toxicity.

The precise measurement of elemental markers allows for detailed pharmacokinetic and bioavailability studies.

It enables the detection of extremely low concentrations of nanoparticles used in drug delivery.

2. **Multi-Element Analysis**

One of the most significant advantages of ICP methods is the ability to analyze multiple elements simultaneously.

ICP-OES can detect dozens of elements in a single run, making it efficient for screening raw materials, drug formulations, and biological samples.

ICP-MS provides isotopic analysis, allowing for advanced tracking of labeled elements in drug metabolism studies.

3. **Speed and High Throughput**

ICP techniques are fast and efficient, which is vital for large-scale pharmaceutical testing.

ICP-OES: Provides results within minutes, making it ideal for routine quality control checks.

ICP-MS: Offers rapid scanning of multiple elements with high throughput, allowing researchers to process numerous samples efficiently.

4. **Accuracy and Reproducibility**

Pharmaceutical research requires highly accurate and reproducible results. ICP methods provide:

Minimal interference: Advanced ICP-MS instruments have collision/reaction cell technology that reduces spectral interferences, leading to more reliable measurements.

Consistent results: ICP ensures that repeated measurements yield the same outcomes, which is crucial for regulatory compliance.

5. **Wide Elemental Range**

ICP techniques can analyze almost the entire periodic table, from alkali metals to transition metals and rare earth elements.

This capability is essential in genetic drug research, where metal-based nanoparticles, enzyme cofactors, and buffer components need precise quantification.

6. **Non-Destructive Nature**

ICP analysis does not require chemical modification or destruction of the genetic drug sample, allowing researchers to preserve valuable materials while conducting in-depth analysis.

7. **Regulatory Compliance**

Global regulatory agencies, including the FDA, EMA, and ICH, impose strict guidelines on elemental impurities in pharmaceuticals. ICP methods are:

Fully compliant with ICH Q3D guidelines, ensuring drugs meet safety standards.

Essential for Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) in drug development.

Challenges and Future Perspectives

While inductively coupled plasma (ICP) methods offer numerous advantages in genetic drug analysis,they also present certain challenges that must be addressed.Addtionally,continuous advancements in technology are shaping the future of ICP techniques, making them even more effective for pharmaceutical applications.

1. **Challenges of Using ICP for Genetic Drug Analysis**
    a) **High Instrumentation and Operational Costs**

ICP-MS and ICP-OES instruments are expensive, requiring significant investment for purchase, installation, and maintenance. Consumables such as high-purity argon gas, nebulizers, and standards add to operational costs.

Skilled personnel are needed to operate and maintain ICP systems, further increasing expenditure.

b) Sample Preparation Complexity

Genetic drug formulations, especially nanoparticle-based or biologic drugs, require complex sample preparation steps, such as:

Digestion with strong acids for effective dissolution.

Filtration to remove interfering biological matrices.

Improper sample preparation can lead to inaccurate readings and sample loss.

c) Interference and Matrix Effects

Spectral interferences occur when signals from different elements overlap, leading to false-positive or inaccurate readings.

Matrix effects arise when components in the sample suppress or enhance the signal, affecting quantification.

Advanced techniques like collision/reaction cell technology in ICP-MS help minimize these interferences, but they require careful optimization.

d) Regulatory and Standardization Challenges

While ICH Q3D and FDA guidelines provide impurity limits, standardizing ICP protocols across different laboratories remains challenging.

Variation in sample digestion methods and instrument calibration procedures can lead to discrepancies in results.

2. Future Perspectives in ICP-Based Genetic Drug Analysis

a) Integration with Advanced Separation Techniques

Combining ICP methods with chromatographic techniques (such as LC-ICP-MS) allows for elemental speciation, helping differentiate toxic vs. non-toxic forms of metal contaminants in genetic drugs.

This integration is especially useful for studying metal-based drug formulations, enzyme cofactors, and degradation products**.**

b) Miniaturization and Portable ICP Instruments

Advances in microplasma and compact ICP-MS technologies are making ICP systems more portable and cost-effective.

Portable ICP-MS units could enable on-site drug testing in manufacturing plants or research facilities, reducing turnaround time for analysis.

c) Automation and AI-Driven Data Processing

Automated sample introduction systems can reduce human error and improve reproducibility in ICP-based drug analysis.

Artificial intelligence (AI) and machine learning are being explored to enhance data interpretation, trend analysis, and predictive modeling for impurity control.

d) Expanding Applications in Personalized Medicine

As personalized genetic therapies become more common, ICP-MS could be used to track individual patient responses to metal-based drug components.

Elemental analysis may also play a role in developing targeted drug delivery systems, optimizing biocompatibility of metal-based nanoparticles.

Conclusion of Challenges and Future Perspectives

Despite its challenges, ICP spectroscopy remains a critical tool for genetic drug analysis. Ongoing advancements in instrumentation, automation, and integration with separation

techniques will further enhance its applications. As genetic medicine evolves, ICP methods will continue to play a pivotal role in ensuring drug safety, quality, and effectiveness.

Conclusion

The field of genetic drugs is transforming modern medicine, offering revolutionary treatments for genetic disorders, cancer, and rare diseases. However, ensuring the safety, stability, and efficacy of these drugs requires precise analytical techniques, and Inductively Coupled Plasma (ICP) Spectroscopy has emerged as an indispensable tool in this domain.

ICP methods, including ICP-OES and ICP-MS, provide highly sensitive, accurate, and multi-element detection capabilities that make them ideal for genetic drug analysis. These techniques play a crucial role in:

Quality control by detecting heavy metal impurities and ensuring regulatory compliance.

Pharmacokinetics and bioavailability studies by tracking elemental markers in drug metabolism.

Nanoparticle-based drug delivery research, helping optimize metallic drug carriers for enhanced therapeutic effects.

Stability testing and degradation analysis, ensuring long-term drug safety.

Despite its advantages, ICP methods face challenges such as high operational costs, sample preparation complexity, and interference issues. However, technological advancements, including portable ICP systems, AI-driven data analysis, and integration with chromatographic techniques, are addressing these limitations, making ICP more accessible and efficient.

As genetic drugs continue to evolve, ICP-based elemental analysis will remain a cornerstone of pharmaceutical research and development. The combination of precision, sensitivity, and regulatory compliance makes ICP spectroscopy a powerful tool for advancing personalized medicine and ensuring the success of next-generation genetic therapies.

References:

1.Hamdy NM, Basalious EB, El-Sisi MG, Nasr M, Kabel AM, Nossier ES, Abadi AH. Advancements in current one-size-fits-all therapies compared to future treatment innovations for better improved chemotherapeutic outcomes: a step-toward personalized medicine. Current Medical Research and Opinion. 2024 Nov 1;40(11):1943-61.

2.Sparmann A, Vogel J. RNA-based medicine: from molecular mechanisms to therapy. The EMBO Journal. 2023 Nov 2;42(21):e114760.

3.Decosterd LA, Widmer N, André P, Aouri M, Buclin T. The emerging role of multiplex tandem mass spectrometry analysis for therapeutic drug monitoring and personalized medicine. TrAC Trends in Analytical Chemistry. 2016 Nov 1;84:5-13.

4.Douvris C, Vaughan T, Bussan D, Bartzas G, Thomas R. How ICP-OES changed the face of trace element analysis: Review of the global application landscape. Science of The Total Environment. 2023 Dec 20;905:167242.

5.Michalke B. Review about powerful combinations of advanced and hyphenated sample introduction techniques with inductively coupled plasma-mass spectrometry (ICP-MS) for elucidating trace element species in pathologic conditions on a molecular level. International Journal of Molecular Sciences. 2022 May 29;23(11):6109.

6.Geigert J. Complex process-related impurity profiles. in the Challenge of CMC Regulatory Compliance for Biopharmaceuticals 2023 Jun 16 (pp. 339-379). Cham: Springer Nature Switzerland.

7.Nageswaran G, Choudhary YS, Jagannathan S. Inductively coupled plasma mass spectrometry. InSpectroscopic methods for nanomaterials characterization 2017 Jan 1 (pp. 163-194). Elsevier.

8.Bettmer J, Bayón MM, Encinar JR, Sánchez ML, Medel AS. The emerging role of ICP-MS in proteomic analysis. Journal of proteomics. 2009 Aug 20;72(6):989-1005.

9.Omenogor CE, Adeniran AA. Advancing Precision Healthcare: The Integration of Nanotechnology, Millimeter Wave Sensing, Laser Technology, Fibre Bragg Grating, and Deep Learning Models. International Journal of Research Publication and Reviews. 2024

10.Wilschefski SC, Baxter MR. Inductively coupled plasma mass spectrometry: introduction to analytical aspects. The Clinical Biochemist Reviews. 2019 Aug;40(3):115.

11.Thompson M. Handbook of inductively coupled plasma spectrometry. Springer Science & Business Media; 2012 Dec 6.

12.Aras N, Yeşiller SÜ, Ateş DA, Yalçın Ş. Ultrasonic nebulization-sample introduction system for quantitative analysis of liquid samples by laser-induced breakdown spectroscopy. Spectrochimica Acta Part B: Atomic Spectroscopy. 2012 Aug 1;74:87-94.

13.Boulos MI, Fauchais PL, Pfender E. The plasma state. InHandbook of thermal plasmas 2023 Feb 21 (pp. 3-55). Cham: Springer International Publishing.

14.Van de Wiel HJ. Determination of elements by ICP-AES and ICP-MS. National Institute of Public Health and the Environment (RIVM). Bilthoven, The Netherlands. 2003 Sep:1-9.

15.Rollinson HR, Rollinson H, Pease V. Using geochemical data: to understand geological processes. Cambridge University Press; 2021 May 6.

16.Ash KO, Komaromy-Hiller G. Analysis of clinical specimens using inductively coupled plasma mass spectrometry. InHandbook of Analytical Therapeutic Drug Monitoring and Toxicology (1996) 2017 Nov 22 (pp. 107-125). CRC Press.

17.Ghazal H, Waqar A, Yaseen F, Shahid M, Sultana M, Tariq M, Bashir MK, Tahseen H, Raza T, Ahmad F. Role of nanoparticles in enhancing chemotherapy efficacy for cancer treatment. Next Materials. 2024 Feb 28:100128.

18.Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nature reviews drug discovery. 2021 Feb;20(2):101-24.

19.Riley CM, Nguyen KL, editors. Specification of drug substances and products: development and validation of analytical methods. Elsevier; 2024 Sep 22.

20da Silva AB, Arruda MA. Single-cell ICP-MS to address the role of trace elements at a cellular level. Journal of Trace Elements in Medicine and Biology. 2023 Jan 1;75:127086.
21.Shekhar S. Fundamental study of silicate substituted nanostructured calcium phosphates (NanoSiCaPs) and 3-D scaffolds for non-viral gene delivery (Doctoral dissertation, University of Pittsburgh).
22.Georgiou CA, Danezis GP. Elemental and isotopic mass spectrometry. InComprehensive analytical chemistry 2015 Jan 1 (Vol. 68, pp. 131-243). Elsevier.
. .23.Beauchamp CR, Camara JE, Carney J, Choquette SJ, Cole KD, DeRose PC, Duewer DL, Epstein MS, Kline MC, Lippa KA, Lucon E. Metrological tools for the reference materials and reference instruments of the NIST material measurement laboratory. NIST Special Publication. 2020;260:136.

24.Khalikova M, Jireš J, Horáček O, Douša M, Kučera R, Nováková L. What is the role of current mass spectrometry in pharmaceutical analysis?. Mass Spectrometry Reviews. 2024 May;43(3):560-609.

25.Alston AB, Digigow R, Flühmann B, Wacker MG. Putting square pegs in round holes: Why traditional pharmacokinetic principles cannot universally be applied to iron-carbohydrate complexes. European Journal of Pharmaceutics and Biopharmaceutics. 2023 Jul 1;188:6-14. 26.Doble PA, de Vega RG, Bishop DP, Hare DJ, Clases D. Laser ablation–inductively coupled plasma–mass spectrometry imaging in biology. Chemical reviews. 2021 May 21;121(19):11769-822.

27.Di L, Kerns EH. Drug-like properties: concepts, structure design and methods from ADME to toxicity optimization. Academic press; 2015 Dec 17.

28.Rónavári A, Igaz N, Adamecz DI, Szerencsés B, Molnar C, Kónya Z, Pfeiffer I, Kiricsi M. Green silver and gold nanoparticles: Biological synthesis approaches and potentials for biomedical applications. Molecules. 2021 Feb 5;26(4):844. 29.Zhang Y, Almazi JG, Ong HX, Johansen MD, Ledger S, Traini D, Hansbro PM, Kelleher AD, Ahlenstiel CL. Nanoparticle delivery platforms for RNAi therapeutics targeting COVID-19 disease in the respiratory tract. International journal of molecular sciences. 2022 Feb 22;23(5):2408.

30.Zanoni I, Crosera M, Pavoni E, Adami G, Mauro M, Costa AL, Lead JR, Larese. Filon F. Use of single particle ICP-MS to estimate silver nanoparticle penetration through baby porcine mucosa. Nanotoxicology. 2021 Sep 14;15(8):1005-15.

31.Abbas Q, Zia-ur-Rehman M, Ullah H, Munir MA, Ali MU, Ali A, Pikon K, Yousaf B. Recent advances in the detection and quantification of manufactured nanoparticles (MNPs) in complex environmental and biological matrices. Journal of Cleaner Production. 2024 Aug 22:143454.

32.Patel PR, Haemmerich D. Review on electrospray nanoparticles for drug delivery: Exploring applications. Polymers for advanced technologies. 2024 Jul;35(7):e6507.

33.Comanescu C, Racovita RC. An Overview of Degradation Strategies for Amitriptyline. International Journal of Molecular Sciences. 2024 Mar 29;25(7):3822. 34Pinheiro FC, Nobrega JA. An overview of sample preparation procedures for determination of elemental impurities in medicines. Microchemical Journal. 2022 Apr 1;175:107189.. 35.Petersen EJ, Henry TB, Zhao J, MacCuspie RI, Kirschling TL, Dobrovolskaia MA, Hackley V, Xing B, White JC. Identification and avoidance of potential artifacts and misinterpretations in nanomaterial ecotoxicity measurements. Environmental science & technology. 2014 Apr 15;48(8):4226-46.

36.Seoane-Viano I, Ong JJ, Basit AW, Goyanes A. To infinity and beyond: Strategies for fabricating medicines in outer space. International Journal of Pharmaceutics: X. 2022 Dec 1;4:100121.

37.Muyumba NW, Mutombo SC, Sheridan H, Nachtergael A, Duez P. Quality control of herbal drugs and preparations: The methods of analysis, their relevance and applications. Talanta Open. 2021 Dec 1;4:100070. 38.Camp CL. Combining elemental and molecular mass spectrometry to study 3 types of biologically important compounds: DNA, phosphopeptides and anticancer drugs (Doctoral dissertation, Loughborough University).

39.Timerbaev AR. Recent progress of ICP-MS in the development of metal-based drugs and diagnostic agents. Journal of Analytical Atomic Spectrometry. 2014;29(6):1058-72.

40 .De La Rica R, Aili D, Stevens MM. Enzyme-responsive nanoparticles for drug release and diagnostics. Advanced drug delivery reviews. 2012 Aug 1;64(11):967-78.

41.Grochowski C, Blicharska E, Krukow P, Jonak K, Maciejewski M, Szczepanek D, Jonak K, Flieger J, Maciejewski R. Analysis of trace elements in human brain: its aim, methods, and concentration levels. Frontiers in chemistry. 2019 Mar 5;7:115.

42.Patriarca M, Barlow N, Cross A, Hill S, Robson A, Tyson J. Atomic spectrometry update: review of advances in the analysis of clinical and biological materials, foods and beverages. Journal of Analytical Atomic Spectrometry. 2024. 43.Carter S, Fisher A, Garcia R, Gibson B, Lancaster S, Marshall J, Whiteside I. Atomic spectrometry update. Review of advances in the analysis of metals, chemicals and functional materials. Journal of Analytical Atomic Spectrometry. 2015;30(11):2249-94.

44..Meermann B, Nischwitz V. ICP-MS for the analysis at the nanoscale–a tutorial review. Journal of Analytical Atomic Spectrometry. 2018;33(9):1432-68. 45.Whale AS, Jones GM, Pavšič J, Dreo T, Redshaw N, Akyürek S, Akgöz M, Divieto C, Sassi MP, He HJ, Cole KD. Assessment of digital PCR as a primary reference measurement procedure to support advances in precision medicine. Clinical chemistry. 2018 Sep 1;64(9):1296-307. 46.Bush L. Analysis of the State of the Art: ICP-MS. 47.Sargent M, Goenaga-Infante H, Inagaki K, Ma L, Meija J, Pramann A, Rienitz O, Sturgeon R, Vogl J, Wang J, Yang L. The role of ICP-MS in inorganic chemical metrology. Metrologia. 2019 Apr 25;56(3):034005. 48.Carter S, Clough R, Fisher A, Gibson B, Russell B. Atomic spectrometry update: review of advances in the analysis of metals, chemicals and materials. Journal of Analytical Atomic Spectrometry. 2021;36(11):2241-305. 49.Hu H, Xu Q, Mo Z, Hu X, He Q, Zhang Z, Xu Z. New anti-cancer explorations based on

metal ions. Journal of nanobiotechnology. 2022 Oct 23;20(1):457. 50. Van Heuveln F, Meijering H, Wieling J. Inductively coupled plasma-MS in drug development: bioanalytical aspects and applications. Bioanalysis. 2012 Aug 1;4(15):1933-65.

51.Maithani M, Raturi R, Gupta V, Bansal P. Evolution of regulatory aspects of genotoxic impurities in pharmaceuticals: Survival of the fittest. Journal of Liquid Chromatography & Related Technologies. 2017 Sep 14;40(15):759-69.

52.Thompson S, Lewen N, Cook G, Teasdale A, Ulman K, Smallshaw L, Lee C, Rockstroh H, Glennon J, Powell S, Chéry C. Implementation of ICH Q3D Elemental Impurities Guideline: Challenges and Opportunities.

53.Shepherd AJ. Good laboratory practice in the research and development laboratory. Gene Therapy Technologies, Applications and Regulations: From Laboratory to Clinic. 1999 Sep 17:375-81.

54.Pröfrock D, Prange A. Inductively coupled plasma–mass spectrometry (ICP-MS) for quantitative analysis in environmental and life sciences: a review of challenges, solutions, and trends. Applied spectroscopy. 2012 Aug;66(8):843-68.

55.Thomas R. Practical Guide to ICP-MS and Other Atomic Spectroscopy Techniques: A Tutorial for Beginners. CRC Press; 2023 Sep 29.

56.Gray AR. Geochemical analysis by inductively-coupled plasma optical emission spectroscopy using slurry atomization.

57.Vora LK, Gholap AD, Jetha K, Thakur RR, Solanki HK, Chavda VP. Artificial intelligence in pharmaceutical technology and drug delivery design. Pharmaceutics. 2023 Jul 10;15(7):1916.

58Rosenthal PB, Henderson R. Optimal determination of particle orientation, absolute hand, and contrast loss in single-particle electron cryomicroscopy. Journal of molecular biology. 2003 Oct 31;333(4):721-45.

59.Offringa AR, Adebahr B, Kutkin A, Adams EA, Oosterloo TA, Van Der Hulst JM, Dénes H, Bassa CG, Lucero DL, Blok WJ, Hess KM. An interference detection strategy for Apertif based on AOFlagger 3. Astronomy & Astrophysics. 2023 Feb 1;670:A166.

60.Furey A, Moriarty M, Bane V, Kinsella B, Lehane M. Ion suppression; a critical review on causes, evaluation, prevention and applications. Talanta. 2013 Oct 15;115:104-22.

61.Balaram V. Strategies to overcome interferences in elemental and isotopic geochemical analysis by quadrupole inductively coupled plasma mass spectrometry: A critical evaluation of the recent developments. Rapid Communications in Mass Spectrometry. 2021 May 30;35(10):e9065.

62.Finotti Cordeiro C, Lopardi Franco L, Teixeira Carvalho D, Bonfilio R. Impurities in Active Pharmaceutical Ingredients and Drug Products: A Critical Review. Critical Reviews in Analytical Chemistry. 2024 Jul 23:1-21.

63.Mao Z. Evaluation and Impact of Measurement Uncertainty in Laboratory Instruments and Analytical Methods: A Comprehensive Study of Volumetric, Chromatographic, and Gravimetric Techniques. International Journal of Chemistry and Materials Science. 2024 Oct 2;1(1):10-70088.

64.Dressler VL, Antes FG, Moreira CM, Pozebon D, Duarte FA. As, Hg, I, Sb, Se and Sn speciation in body fluids and biological tissues using hyphenated-ICP-MS techniques: A review. International Journal of Mass Spectrometry. 2011 Oct 1;307(1-3):149-62.

65.Claudel M, Schwarte JV, Fromm KM. New antimicrobial strategies based on metal complexes. Chemistry. 2020 Oct 16;2(4):849-99.

66.Mahmud MS, Hasan MM, Islam MB. Advances In Heavy Metal Detection: From Traditional To 3D-Printed And Smartphone-Based Methods. Journal of Next-Gen Engineering Systems. 2024 Dec 22;1(01):11-34.

67.Adesina KE, Burgos CJ, Grier TR, Sayam AS, Specht AJ. Ways to Measure Metals: From ICP-MS to XRF. Current Environmental Health Reports. 2025 Jan 27;12(1):7.

68.Resano M, Vanhaecke F, de Loos-Vollebregt MT. Electrothermal vaporization for sample introduction in atomic absorption, atomic emission and plasma mass spectrometry—a critical review with focus on solid sampling and slurry analysis. Journal of Analytical Atomic Spectrometry. 2008;23(11):1450-75.

69.Houhou R, Bocklitz T. Trends in artificial intelligence, machine learning, and chemometrics applied to chemical data. Analytical Science Advances. 2021 Apr;2(3-4):128-41.

70.Zang Z, Liu X, Wang M, Wang Z. The Application of Inductively Coupled Plasma Mass Spectrometry in Cancer Research. Critical Reviews in Analytical Chemistry. 2025 Feb 4:1-25.

71.Chandrakala V, Aruna V, Angajala G. Review on metal nanoparticles as nanocarriers: Current challenges and perspectives in drug delivery systems. Emergent Materials. 2022 Dec;5(6):1593-615.

72.Thirumdas R, Janve M, Siliveru K, Kothakota A. Determination of food quality using atomic emission spectroscopy. InEvaluation technologies for food quality 2019 Jan 1 (pp. 175-192). Woodhead Publishing

73.Meermann B, Nischwitz V. ICP-MS for the analysis at the nanoscale–a tutorial review. Journal of Analytical Atomic Spectrometry. 2018;33(9):1432-68.

74..Katakam LN, Aboul-Enein HY. Elemental impurities determination by ICP-AES/ICP-MS: A review of theory, interpretation of concentration limits, analytical method development challenges and validation criterion for pharmaceutical dosage forms. Current Pharmaceutical Analysis. 2020 Jun 1;16(4):392-403.

75.Stielow M, Witczyńska A, Kubryń N, Fijałkowski Ł, Nowaczyk J, Nowaczyk A. The bioavailability of drugs—the current state of knowledge. Molecules. 2023 Dec 11;28(24):8038.