RESEARCH PAPER

Nanomaterials in Pharmaceutical Analysis: Current Trend and Future Direction

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ABSTRACT
The nanomaterials have modified pharmaceutical analysis by offering marvellous sensitivity, selectivity, and flexibility in monitoring and characterizing drug formulations, impurities, and delivery systems. Lately, there have been rapid developments in nano-analytical methods, including quantum-based sensoring systems, multimodal imaging, and tools assisted by Al, which have enabled precise drug analysis, impurity identification, and real-time process analysis. The diversity and combination of nanomaterials within pharmaceutical analysis triggered a revolution that continues to expand frontiers within drug detection limits, analysis speed, and transportability. Therefore, the convergence of nanomaterials within pharmaceutical analysis brought about a revolution that continues to expand frontiers within drug detection limits, analysis speed, and transportability. It should be noted that nanomaterials within pharmacy have triggered a revolution that continues to evoke considerable interest within research and analysis, given the precision they offer. The kick-starting review attempts to distil more on current and forthcoming developments within this emerging area. We expose developments within the basics and properties of core nanomaterials, including carbon-based nanostructures, quantum dots, metal/metal oxide nanoparticles, and emerging scaffolding materials including MXenes, making them perfect and more reliable for analyses. Mainly, the review area communicates development within these materials and speaks on their large impact within different fields amplify chromatography and separate biosensing technologies, improve sample preparation methods within nano-sorbents, and develop optimal theranostic imaging tools. We review on recent developments and breakthroughs within nanomaterials assisting POC and wearable drug biosensing tools. Lastly, we forecast on forthcoming developments within multi-tasking "smart" nano-platforms and emerging links with AI within analysis.

Keywords: Nanomaterials, Pharmaceutical Analysis, Biosensors, Theranostics, Point-of-Care testing
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1. INTRODUCTION

After implementation of nanotechnology as an innovative science, there were prodigious swap in its application.[1] Nanomaterials rapidly penetrate a diverse area of biomedicine and pharmaceutical research, including drug development, drug delivery, tissue engineering and medicinal chemistry.[2] Its versatile use helps in alleviating complex difficulties faced with drug administration and absorption, controlled release, targeted delivery and cellular uptake.[3] Due to their distinctive physicochemical properties and ability to form various solid-state formulations, they find increased use in the preparation of new drug formulations, imaging techniques and particularly in medicinal chemistry as catalysts for the sensitive determination of drugs and other biologically active compounds.[4] The role of nanomaterials as catalysts in the preparation of substances with pharmacological properties, the preparation of sensors, or the degradation and removal of medicinal compounds polluting the environment is undeniable.[7]

This special issue aims to cover recent advances in the preparation and application of nanomaterials in the above-

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mentioned fields. Its scope includes the role of nanomaterials in drug delivery and the development of new drug formulations, novel polymorphs and other solid-state forms, the influence of nanotechnology on the physico-chemical properties of importance to adsorption, distribution and metabolism of drugs, tissue and cellular uptake of nanomaterials and their treatment potential and application of nanomaterials as catalysts for the sensitive and selective determination of biologically active compounds. [11]-[13][66]

The history of licensed nanomedicines dates back to 1989, with the introduction of propofol liposomes for anaesthesia and later additional liposomal, colloidal suspensions, and pegylated forms of active ingredients have followed in oncology, infectious disease, and ophthalmology.[14] The Nanomedicines Alliance is an organization of pharmaceutical and biotechnology companies formed in 2010 that occupies a unique place in the global pharmaceutical industry.[14] This group of companies focuses its energy on promoting the scientific development, safe use, regulatory and legislative advancement, and expanding public knowledge of nanomedicines and nanotechnology-enabled medical devices. Members are representative of both large, intermediate, and small companies from the US, Europe, and Japan. The existing regulatory framework allows specific considerations of each candidate on a case-by-case basis.

1.1 The Evolving Landscape of Pharmaceutical Analysis

- Brief context on the increasing demands for analysing complex drug molecules, metabolites, and biomarkers in intricate biological matrices.[1]
- The limitations of conventional analytical techniques in terms of sensitivity, speed, and cost for modern applications like personalized medicine.[2]

Importance of Pharmaceutical Analysis:

Pharmaceutical analysis by definition deals with analysis of drugs, pharmaceutical substances and raw materials.[3] It is devoted to stability testing, comparing related substances determination of impurities and developing, implementing and applying active assays for the pharmaceutical industry.[3] The complex tasks of pharmaceutical analysis may also include development of new pharmacopeial methods, stress testing to validate stability-indicating methods, impurity analysis and identification, herbal or animal material analysis, cleaning validations, degradation tests and stability studies.[3]

All new findings are linked with the use of proper analytical methods.[3] In the past they were mainly various methods of chemical analysis while currently a wide scale of the instrumental analytical methods is preferred. In the frame of the instrumental analytical methods, the spectral, electrochemical and separation methods as well as their combinations are employed the most frequently. Here, hyphenated analytical methods such as high-performance liquid chromatography coupled with mass spectrometry have a unique potential in the analysis of pharmaceutical and biological samples as they combine the sample preparation with the identification and determination of the compounds of interest. In this way, the overall analytical procedure can be simplified and shortened.[31]-[38]

Moreover, the automation of the analysis is beneficial in preventing/reducing errors usually generated during external sample handling. Therefore, an integration of several valuable analytical steps into the single advanced hyphenation is one of the trends in modern analytical chemistry.[31]-[38]

1.2. The Advent of Nanotechnology

- Definition and unique physicochemical properties of nanomaterials. High surface area-to-volume ratio, quantum confinement, tuneable surface chemistry, superior catalytic, optical, electronic properties.[6]
- The rationale for employing nanomaterials in analytical science: signal amplification, enhanced selectivity, miniaturization, and novel recognition mechanisms.[54]

1.3. Scope and Objectives of the Review

- Statement of purpose: to provide a systematic and critical overview of the current state and future potential of nanomaterials in pharmaceutical analysis.[7]
- Outline the structure of the review, detailing the areas of application to be covered and the forward-looking perspective on challenges and opportunities.[7]

2. CLASSES OF NANOMATERIALS AND THEIR FUNCTIONAL PROPERTIES:

2.1 Carbon Based Nanomaterials

Carbon-based nanomaterials such as graphene, graphene oxide, carbon nanotubes (CNTs), fullerenes, and carbon quantum dots (CQDs) are composed mainly of carbon atoms and feature at least one nanoscale dimension (1–100 nm).[16] Their exceptional electrical conductivity, mechanical strength, and thermal stability make them flawless for a broad spectrum of applications.[16]

The latest advances achieved with CNT electrochemical biosensors have significantly improved the sensitivity of immunosensors, enzyme electrodes, and nucleic acid sensors. CNTs act as excellent electron-transfer agents and increase the electrochemical activity of vital biomolecules, NADH and hydrogen peroxide, making them efficient biosensors for oxide-dehydrogenases.[16]

Vertical CNT arrays, so-called ‘forests’, act as molecular wires and sustain direct electron transfer between the electrodes and enzyme redox sites. Biosensors employing enzyme tags benefit from CNT’s signal amplification and

high surface area. Precise control over CNT's structure, functionalization, and surface immobilization leads to successful sensor design.[17]

1. Graphene

Graphene is a single, one atom thick layer of carbon atoms which is arranged as honeycomb lattice.[21] It is examined as thinnest, strongest, and most conductive material known. Scheme of a biosensor is shown in figure 2.1.1

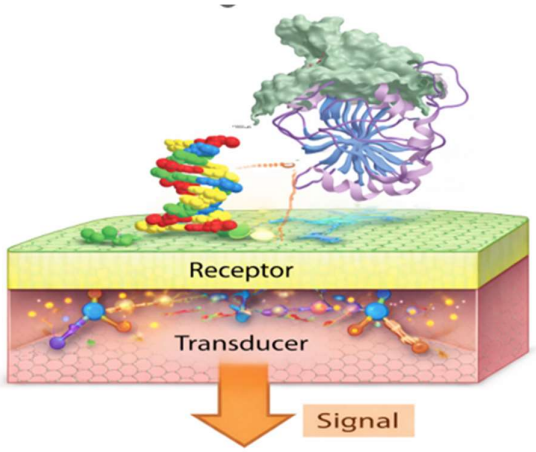

Figure- 2.1.1 Scheme of a biosensor

The characteristics of graphene-based nanomaterials are closely linked to how they are produced.[22] High quality graphene with least deficiency is typically synthesized via chemical vapor deposition (CVD) or mechanical exfoliation of graphite. However, scalable production often involves exfoliating graphite oxide, yielding materials like graphene oxide (GO) or thermally reduced graphene oxide (TRGO).[22]

TRGO, formed through thermal exfoliation, contains countless structural defects in compared to pristine graphene's ideal honeycomb lattice. These imperfections are not a drawback in fact; they increase the electrochemical performance. In sp^2 hybridised carbon systems, electron transfer essentially occurs at defect sites and edges rather than the flat basal plane, making defect-rich graphene materials remarkably valuable for electrochemical applications.[22]

Graphene use in bio-field effect transistors:

The ability of field-effect transistors (FETs) to electrically detect molecular interaction and effortlessly integrate with semi-conductor technologies has led to their increasing use in biosensing. When target biomolecules attach to recognition elements and change the conductivity between the source and drain, these biosensors detect changes in electrical charge in electrical charge at the transistor gate.[44]

Because of its zero-band gap and tuneable electronic characteristics, graphene is particularly well-suited for FET biosensors. It is flawless for detecting charged biomolecule such as DNA, which has a negatively charged phosphate backbone, due to its sensitivity to surface charge. The development of sophisticated, chip-integrated biosensing platforms has piqued the interest of both industry and academic researchers.[68]-[71]

Graphene impedimetric biosensors:

Electrochemical impedance spectroscopy (EIS) is a temperamental technique for biosensing applications. Graphene-based platforms to detect DNA hybridization and single nucleotide polymorphisms (SNPs) using EIS was developed by researcher in trailblazing work.[57] They discovered that few-layer of graphene offered superior sensitivity, during the evaluation of three types of graphene configuration. This dais surpassed fluorescence-based methods, illustrating that impedimetric detection can offers more precise and authenticate results for genetic analysis.[44]

Key properties:

- **High conductivity:** It has better electrical conductivity than copper and better heating ability than any other material.
- **Exceptional strength:** Approximately 200 times stronger than steel.
- **High transparency:** Absorbs only about 2.3% of visible light.
- **Impermeability:** Impermeable to gases, even helium, while allowing water to pass through.[21]
- **High surface area:** Employing it in super-capacitors and batteries because of its high surface area. [21]

Common applications:

- **Electronics:** It is used in flex electronics, super-capacitors, transparent touchscreens, and quicker transistors.[21]-[23]
- **Energy:** Amplify solar panels potential and improve battery capacity and charging time.

- **Composites:** They increase the featheriness and strength of materials used in aeronautics and sports appliances.[21]-[23]
- **Biomedicine:** Targeted drug delivery, biosensors for disease detection, and tissue engineering biomedicine are utilized.

2. Carbon Nanotubes (CNTs):
One or more layer of graphene is rolled into cylinders to create carbon nanotubes (CNTs) which are tube-shaped nanomaterials as shown in figure 2.1.3. Their unique structure offers them a high surface area and customizable characteristic, making them ideal in pharmaceutical applications.[32]

In drug delivery particularly for cancer therapy CNTs can carry medications straight to targeted cells, credit given to their ability to penetrate cell membranes and deliver drugs in a controlled manner. Because of their electrical and optical properties, we can accurately detect illness indicators or track medicine levels which is done by perfect creation of extremely sensitive bio-sensor.[32]

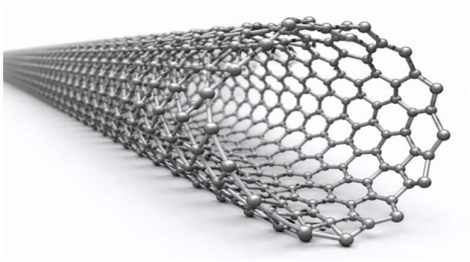

Figure-2.1.3 Carbon Nanotube

Key properties:

- **Extraordinary strength and elasticity:** Exceptionally strong and stiff, with a tensile strength up to 100 times greater than steel.
- **High electrical and thermal conductivity:** Conducts electricity and heat comparable to copper.
- **High aspect ratio:** Extremely long relative to their small diameter, giving them a high surface area.
- **Tunable electronic properties:** Can be either metallic or semiconducting, depending on their structure and "chirality".

Common applications:

- **Composites:** Used as fillers to reinforce polymers, ceramics, and metals.
- **Electronics:** Used in transistors, sensors, and field-emission displays.
- **Energy storage:** Improves the performance of batteries and supercapacitors.
- **Biomedicine:** Potential for use in drug delivery, biosensors, and tissue regeneration.

2.2. Metal and Metal Oxide Nanoparticles:
Metal and metal oxide nanoparticles are broadly used nanomaterials due to their unique properties, which differ significantly from their bulk counter-parts. Enhanced surface reactivity is allowed by high surface-area-to-volume ratios exhibited by them.[24]

- In discipline like biomedical, forensic, and environmental sciences, as well as in the fight against bioterrorism, the identification of chemical and biological agents is essential.
- Advanced technology and expertise in chemistry, biology, and material science are necessary for the creation of efficient sensors.
- Sensors have two main components: a recognition element for binding with target analytes and a transducer for signalling the binding event.
- An efficient sensor's performance depends on these two components, which affect its response time, signal-to-noise ratio, and selectivity.

It includes Magnetic nanoparticles (Fe_3O_4 for separation and MRI), Gold, Silver and Zinc Oxide, nanoparticles (for LSPR, catalysis).

1. Silver nanoparticles (AgNPs):
Depending on their size and shape silver nano-particles are well-known for their powerful antimicrobial and catalytic properties.

AgNPs are particles of silver which ranges from 1 to 100 nano-metres in size that have distinctive electrical, optical, and antimicrobial properties.[26]as shown in 2.2.1. These properties make them advantageous in applications like anticancer agents, medical device coatings, and antimicrobial products. Based on the desired characteristics of the final product synthesis method for silver nanoparticles are selected form several methods of synthesis which includes biological, physical and chemical approaches.

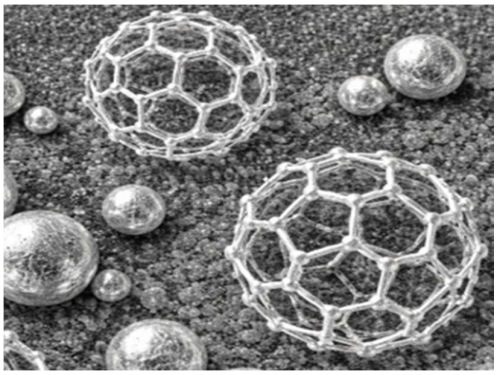

Figure- 2.2.1 Silver Nanoparticle

Key properties:

- **Localized Surface Plasma Resonance (LSPR):** LSPR, by definition, is the resonance exhibited by particles such as AgNPs and AuNPs, usually with an absorption peak around 400 nm for the smaller particles. The LSPR signal of AgNPs is often sharper and more intense compared to that of gold, hence very sensitive for optical biosensing.[26]
- **Strong antimicrobial activity:** Silver nanoparticles are able to interfere with bacterial, viral, and fungal metabolism and cell membranes by releasing silver ions.
- **Catalytic activity:** High surface area and special electronic properties make them useful catalysts in many organic modifications and in environmental remediation.

Common applications:

- **Antimicrobial agents:** Used in wound dressings, medical devices, textiles, and water purification systems to inhibit microbial growth.
- **Optical probes and sensors:** Employed in surface-enhanced Raman spectroscopy (SERS) and fluorescent sensors due to their strong plasmonic properties.
- **Catalysis:** employed for the degradation of environmental pollutants like organic dyes.
- **Biomedicine:** Due to their antimicrobial properties and the induction of oxidative stress, they are under studies for wound-healing applications, bone repair, and cancer therapy.

2. Gold Nanoparticle (AuNPs):

Due to their size-dependent chemical properties, gold nanoparticles (AuNPs), which are derived from the Greek word nanus, which means dwarf, are currently employed in a number of biomedical applications optical and electrical characteristics.[46] The relevant physical characteristics include a high surface-to-volume ratio and biocompatibility. Additionally, the metal nanoparticles' dimensions are similar to those of biomolecules like proteins (enzymes, antibodies) or DNA, whose dimensions range from 2 to 20 nm, giving these two classes of materials structural compatibility.[29][30]

Because AuNPs enzymatic colorimetric assays are straightforward techniques that only need a few steps to detect target molecules, they are posing a challenge to traditional detection systems. Additionally, no They could be developed into appropriate near-patient testing platforms, but sophisticated instrumentation is needed. Controlling AuNP aggregation or dispersion, which is influenced by interparticle attractive and repulsive forces, is the main goal of these assays.[80] The sensitivity of AuNPs-based sensors can be influenced by a number of variables, such as the kind of target molecule or enzyme, the recognition ligand, and the transduction technique. They are appropriate for multiplexed and high throughput detection methods due to their distinct optical characteristics.[29][30]

They are used in colorimetric and fluorescent detection of ions and small organic molecules and also for detection and delivery, but still long way to achieve more and perfect it.

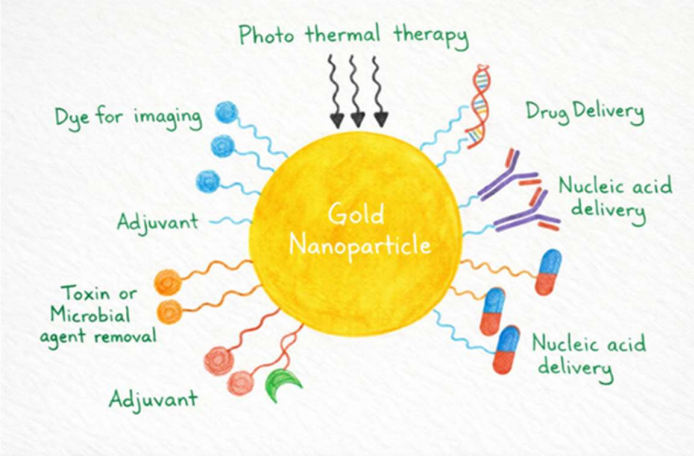

Figure- 2.2.2 Different applications of gold nanoparticles in diagnosis and therapy.

Key Properties:

Surface Plasmon Resonance (SPR): Vibrant colors (red, blue, and purple) that vary with size, shape, and aggregation result from electrons on the surface oscillating when struck by light, causing strong light absorption and scattering.

Low toxicity and biocompatibility: Usually well-tolerated by biological systems, enabling safe use in medicine.

High Surface Area: Extensive functionalization with medications, proteins, or probes is made possible by a large surface-to-volume ratio.

Catalytic Activity: Effective catalysts, even at low temperatures, for particular chemical reactions.

Heat transfer and electrical conductivity are beneficial for thermal control and electronics.

Common Application:

Diagnostics use colorimetric detection for pregnancy tests; colorimetric sensors that detect pathogens/toxins; and highly sensitive biomarker detection for cancer and other diseases.[29][30]

Medical Imaging and Therapy: Microscopy contrast agents for TEM and dark field imaging, Targeted drug and gene delivery, and using photothermal therapy to heat and kill tumour cells.[41][43]

Catalysis in the automotive and fuel cell industries to reduce or eliminate air pollution through oxidation of CO and NOx and make chemical processes more efficient.

Materials and Electronics include building blocks for plasmonic and optical devices, sensors and memory storage.

Antimicrobial agents have unusual properties and biocompatibility and are used to make antibacterial surfaces and products.

3. Magnetic nanoparticles, such as Fe3O4:
Drug delivery, cancer treatment, and MRI contrast agents are just a few of the many uses for magnetic nanoparticles - minuscule magnetic materials, typically smaller than 100 nm. Iron oxides, like superparamagnetic magnetite (Fe3O4), are commonly used to create them due to the special magnetic properties that allow manipulation with an external magnetic field and because of their high biocompatibility as shown in figure 2.2.3.[27][47]

At the nanoscale, magnetic nanoparticles, which are usually composed of iron oxides such as magnetite and maghemite, exhibit superparamagnetic characteristics. That means they possess magnetism only in the presence of an external magnetic field.[47]

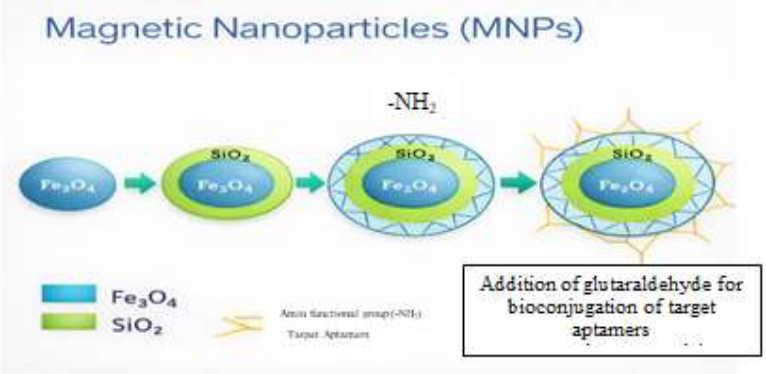

Figure- 2.2.3 Magnetic Nanoparticle

Since all biological molecules are naturally non-magnetic, aptamers can be used to attach these magnetic nanoparticles to ManLAM so that the spin-valve sensor detects them.[81]

Key properties:

- **Superparamagnetism:** This allows them to be manipulated by external magnetic fields for targeted applications, but they do not retain magnetism after the field is removed, preventing aggregation and complications *in vivo*.
- **Biocompatibility and low toxicity:** Iron oxide is generally considered biocompatible and has been approved by the FDA for certain clinical uses.
- **High surface area:** Their large surface area allows for efficient surface modification and drug loading.
- **Tuneable properties:** By adjusting particle size, shape, and surface coatings, the magnetic and physicochemical properties can be adjusted.

Common applications

- **Biomedical imaging (MRI):** SPIONs represent a class of superparamagnetic nanoparticles used as MRI contrast agent for the enhancement of image resolution and targeted imaging of tissue, including the spleen, liver, and lymph nodes.[59][86]
- **Magnetic separation:** This method uses an external magnetic field to extract and purify specific target molecules from complex biological fluids, such as proteins, DNA, or cells.
- **Targeted drug delivery:** Drug can be delivered straight to a target site, like a tumor, by using magnetic field to externally control the movement of MNPs. This lessens adverse effects and improves therapeutic efficacy.[10][15]
- **Hyperthermia:** By producing heat through an alternating magnetic field, MNPs allow for the targeted thermal ablation of cancerous cells.

2.3 Polymeric and Organic Nanostructures:

1. Liposomes

Like cell membranes, they are small, bubble-like structures composed of layers of lipid. Because they can transport hydrophilic drugs inside the liposome and hydrophobic drug inside their outer shell, they represent an effective and adaptable drug delivery system as shown in figure 2.3.1.[14]

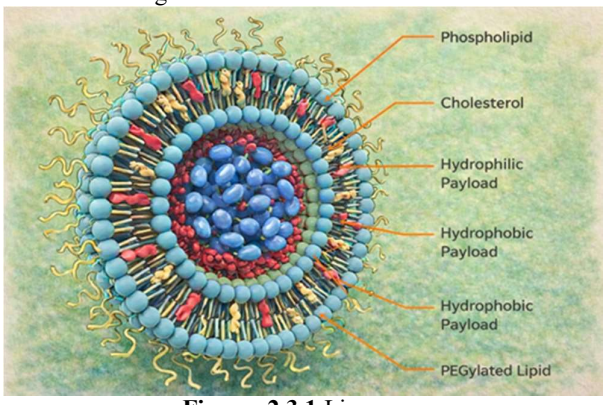

Figure- 2.3.1 Liposome

Key properties

- **Body-Friendly:** Liposome are generally safe and well-tolerated because they are made from natural lipids.[9]

- **Versatile Carriers:** They can hold both water-based and fat-based drugs, along with proteins and genetic therapies.[9]
- **Targeted Delivery:** Their surface can be customized with molecules like antibodies or peptides to direct treatment to specific cells or tissues.
- **Controlled Release:** By tweaking their structure, liposomes can be designed to release their contents at a desired rate, improving treatment precision.

Applications in encapsulation and drug delivery

- **Cancer treatment:** FDA-approved liposomal formulations, such as Doxil (doxorubicin), reduce systemic toxicity while the medication builds up in tumors via the Enhanced Permeability and Retention (EPR) effect.
- **Antifungal and antiviral treatments:** In systemic fungal infections, liposomal formulation enhances the delivery of medications like amphotericin B.
- **Gene therapy:** It can be used to deliver and encapsulate genetic materials like plasmid DNA and small interfering RNA.

Emerging and Hybrid Nanomaterials:

These emerging and hybrid nanomaterials combine different components in nanoscale dimensions to realize advanced properties. They make waves in areas like energy storage, biosensing, and environmental cleanup. Examples include:

1. MXenes for high-performance sensors and electronics

2. MSNs for Targeted Drug Delivery and Imaging

3. Nano-MIPs for Precise Molecular Recognition in Diagnostics [42]

These materials are designed through physical or chemical methods to meet the particular needs, whether in disease detection, cleaning up pollutants, or powering next-generation devices.

1. MXenes

The family of 2D transition metal carbides, nitrides, and carbonitrides known as MXenes is growing very fast. They are produced by selectively etching the "A" layers from precursor "MAX" phases, leaving behind two-dimensional layers of carbon/nitrogen and the transition metal as shown in figure 2.4.1.[42][48]

Synthesis:

- MXenes can be synthesized from MAX-phase precursors through a variety of techniques involving selective etching of the "A" layer by chemical methods.
- The material is delaminated after etching into single or few-layer sheets, often using techniques such as sonication.

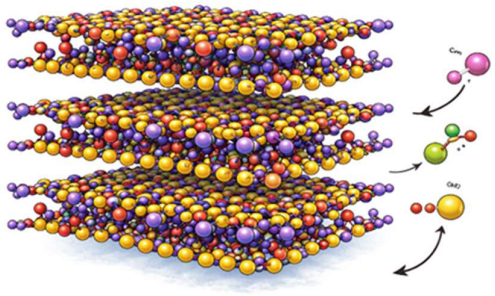

Figure- 2.4.1 MXenes Structure

Key properties:

- **Metallic conductivity:** Possess high electrical conductivity, similar to metals, which is unusual for 2D materials.
- **Hydrophilicity:** The surfaces of MXenes are hydrophilic due to a large amount of terminals (-F, -O, -OH) which allows MXenes to be easily dispersed in water, unlike many 2D materials.
- **Tunable surface chemistry:** The surface can be functionalized with different molecules to control properties and enhance their applications.
- **Large surface area:** The layered structure enables MXenes to have a high specific surface area.

Common applications:

- **Energy storage:** Used in supercapacitors and batteries due to their high conductivity and ion accessibility.
- **Electromagnetic interference (EMI) shielding:** Their conductive layers can effectively block electromagnetic radiation.
- **Biosensors and biomedical applications:** Used in highly sensitive electrochemical and optical biosensors, bioimaging (photothermal and photoacoustic), and therapeutic applications like photothermal cancer therapy.[45]

3. Current Applications in Pharmaceutical Analysis

3.1. Revolutionizing Biosensing Platforms:

Biosensors are analytical devices that are used to detect biological material by combining a biomolecular recognition element (e.g., enzymes or antibodies) with a transducer, which converts biochemical signals into measurable electrical signals.[17] Understanding the meaning of this passage, biosensors find applications in areas such as health, food safety, and environmental monitoring, where they generate both quantitative and qualitative information.

Nano-sensors can be incorporated directly into biomaterials to measure health or quickly identify risks because they function at extremely small scales. They become extremely sensitive and specific when combined with intelligent biological materials.

Nanomaterials are essential parts of these sensors because they serve as a bridge between the biological target and the transducer. Because they can interact at the molecular level while releasing a lot of atoms, they increase sensitivity. Depending on how they identify changes in mass, charge, light, or heat, sensors can be categorized as electrochemical, physical, or optical.

3.1.1 Electrochemical Biosensors:

Electrochemical biosensors are powerful tools for identifying drugs and biomarkers because they convert chemical interactions into electrical signals. They combine the precision of electroanalytical methods with the selectivity of biological components like enzymes or antibodies techniques.[18] When these components bind to or interact with a target molecule, they produce a detectable electrical reaction, such as a change in voltage or current, that shows the analyte's concentration. To make these sensors better, nanomaterials are crucial.[18] They increase sensitivity and selectivity by altering the electrode surface, which facilitates the detection of even minute amounts of substances. These days, industry, agriculture, healthcare, and environmental monitoring all make extensive use of these sensors.[19]

There are primarily two kinds: 1). Biocatalytic sensors: rely on enzyme-driven reactions 2). Affinity sensors: detect binding events between molecules

Essentially, these devices represent a reliable and scalable method to detect chemical changes through signals generated by a redox reaction at the electrode, in either liquids or gases.

1. Key Components

Electrochemical sensors are like tiny laboratories that use electrical signals to detect specific chemicals. Here is how the mechanism works:

- **Sensing (Working) Electrode:** This is where the chemical reaction with the target substance occurs in the sensor. It is commonly made of a reactive metal such as platinum or gold to help the reaction take place.[18][25]
- **Counter (Auxiliary) Electrode:** The partner in crime for the sensing electrode, it completes the electrical circuit performing the opposite reaction, which allows current to flow, if it meets resistance.
- **Reference Electrode:** This acts as a stable voltage reference, which allows for accurate measurements through maintaining a consistent reference, by using materials such as silver/silver chloride.
- **Electrolyte:** This is the ionic highway between electrodes. An electrolyte may be liquid, gel, or solid but maintains electrical neutrality during sensing. It also influences the overall performance and longevity of the sensor.
- **Gas-Permeable Membrane (for gas sensors):** The membrane allows only the target gas to permeate its barrier while sealing off the inner components from the environment. The membrane also allows the analytical method to discriminate between target gas and other potential interference.[20]

2. Main Operational Modes (Transduction Techniques):

Sensors can be classified based on the type of electrical property measured.

- **Amperometric (or Voltammetric):** measures the current produced by a chemical reaction. The stronger the signal, the more of the analyte is present in the sample. Used in glucose monitors, gas detectors, and a variety of types of new sensors testing for analytes in the gas and vapor phase.
- **Potentiometric:** Measures the voltage between electrodes while not taking any current from the sample. The voltage is dependent on concentration these two parameters are generally related by a predictable form, the Nernst equation. Potentiometric sensors are typically used in a pH sensor and an ion selective electrode.
- **Conductometric:** Tracks changes in how well the solution conducts electricity. When the analyte shows up, it tweaks the ion balance, altering conductivity. These are simple, sturdy, but less specific.

3. Advantages and Limitations

Advantages:

- **High Sensitivity and Selectivity:** Can detect very low concentrations (parts-per-million/billion) of specific analytes.
- **Direct Measurement:** Provides a direct electrical signal, simplifying instrumentation.
- **Low Power Consumption:** Especially amperometric sensors, making them ideal for portable and battery-operated devices.

- **Compact Size and Low Cost:** Suitable for mass production and integration into wearable and handheld devices.

Limitations:

- **Cross-Sensitivity:** Can respond to interfering species that undergo similar redox reactions.
- **Limited Lifetime:** The electrolyte can evaporate or degrade, and the electrodes can be poisoned by certain chemicals, leading to signal drift and eventual failure.
- **Environmental Dependence:** Performance can be affected by temperature and humidity, often requiring built-in compensation.
- **Limited Dynamic Range:** Some sensors can become saturated at high analyte concentrations.

4. Applications

Electrochemical sensors have a vast and growing range of applications:

- **Medical Diagnostics:** Glucose meters, lactate sensors, cholesterol tests, and point-of-care testing devices.
- **Environmental Monitoring:** Detection of toxic gases (CO, NO_2, SO_2, O_3) in air quality stations and industrial hygiene.
- **Industrial Safety:** Personal and fixed gas detectors in oil and gas, mining, and chemical industries.
- **Food and Agriculture:** Monitoring freshness (e.g., CO_2 in packaged foods), controlling fermentation processes, and testing for pesticides.
- **Wearable Technology:** Sweat sensors for electrolytes and metabolites in fitness trackers.

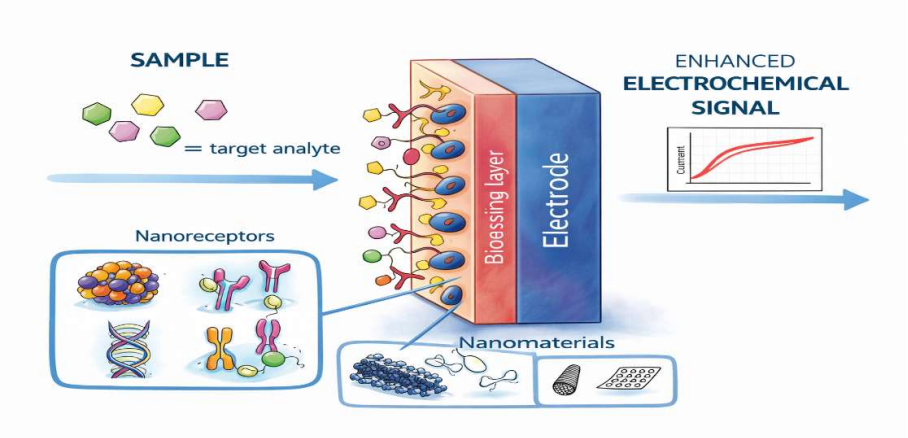

Figure- 3.1.1.1 Main constitution of Nanomaterial based electrochemical biosensor

3.1.1 Optical Biosensors:
LSPR-based sensors using noble metal NPs; fluorescent sensors using QDs and CQDs.

An optical biosensor is an analytical device that integrates a biological recognition element (e.g., enzyme, antibody, DNA, cell) with an optical transducer. The fundamental principle involves the detection of changes in the properties of light when it interacts with the biorecognition element upon binding to the target analyte. Core operation involves following:

1. **Biorecognition:** The target analyte (e.g., a protein, virus, or small molecule) binds specifically to the immobilized biological element.
2. **Transduction:** This binding event causes a change in the optical properties of the sensor surface or the surrounding medium.
3. **Signal Measurement:** The optical transducer converts this change into a quantifiable electrical signal. The magnitude of this signal is proportional to the concentration of the analyte.

1. Key Components

- **Light Source:** Provides the incident light (e.g., LED, laser, halogen lamp).
- **Optical Transducer:** The core of the sensor where the biorecognition event occurs and modulates the light.
- **Biorecognition Element:** Immobilized on the transducer, it provides specificity (e.g., antibodies, enzymes, nucleic acids, aptamers).
- **Photodetector:** Captures the modulated light signal (e.g., photodiode, CCD camera).
- **Signal Processing Unit:** Converts the detected optical signal into a readable output (e.g., concentration).

2. Types and Working Mechanisms:

- Optical biosensors are broadly classified based on the optical property they measure.
- Types: -Fluorescence-based Biosensors, Surface Plasmon Resonance (SPR) Biosensors, Evanescent Wave Biosensors, Chemiluminescence & Bioluminescence Biosensors, Interferometric Biosensors,

- If you had to select one optical biosensor technology as the most important based on its significance to scientific research, commercial success, and foundation for future innovation, Surface Plasmon Resonance (SPR) would be the answer. SPR embodies all of the major benefits of optical biosensors; label-free detection, real-time measurements, and high-quality quantitative data.

1. Surface Plasmon Resonance (SPR) Biosensors:

- **Principle:** Detects changes in the refractive index on a thin metal (usually gold) film surface.
- **Working:**
  - The back of a glass slide covered in a thin layer of gold is exposed to polarized light. The light energy couples with the metal's electrons at a particular resonance angle, producing surface plasmons and a decrease in the intensity of reflected light.
  - When analyte molecules bind to the receptor layer on the gold surface, the mass increases, changing the local refractive index.[25]
  - This change shifts the resonance angle. The shift is measured in real-time and is directly proportional to the mass bound, allowing for label-free and kinetic analysis of biomolecular interactions.
- **Examples:** BIAcore™ systems for drug discovery, protein-protein interaction studies.[56]

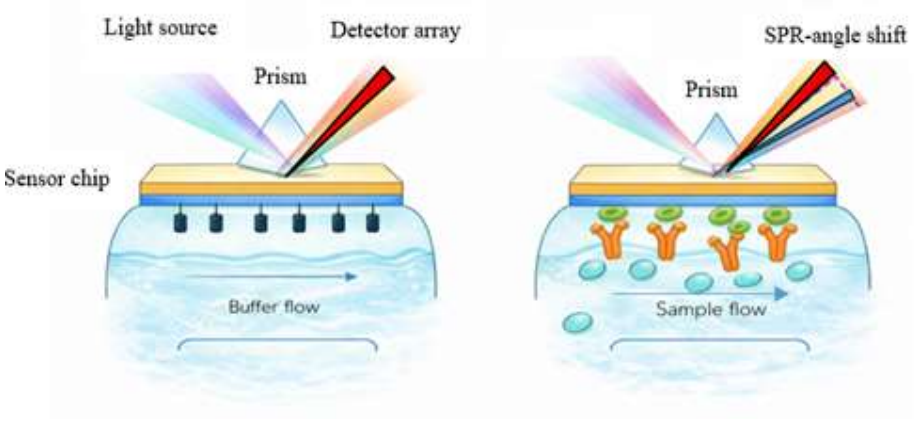

Figure- 3.1.2.1 Surface Plasmon Resonance Biosensors

2. Fluorescence based Biosensors:

- **Principle:** Measures the emission of light from a fluorophore after it is excited by a specific wavelength of light. The binding event alters the fluorescence properties (intensity, lifetime, polarization) as shown in figure 3.1.2.2.
- **Working:**
  - A fluorescent label is attached to the biorecognition element or the target.
  - Upon binding, a change occurs. For example, in FRET (Förster Resonance Energy Transfer) biosensors, binding brings a donor and acceptor fluorophore close, quenching or shifting the emission.
  - The change in fluorescence intensity or wavelength is measured.
- **Examples:** DNA microarrays, immunofluorescence assays, real-time PCR.

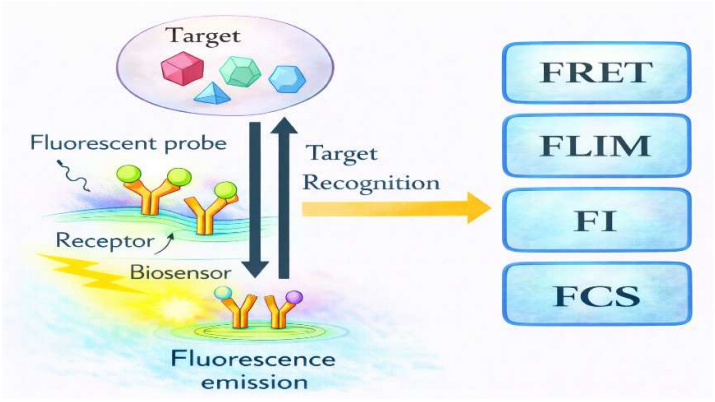

Figure- 3.1.2.2 Fluorescence based Biosensors

3.2 Advanced Separation Science:

3.2.1 Chromatography:

Nanomaterials as stationary phases in HPLC and Nano-LC for improved resolution and peak capacity. Nanomaterials are not merely incremental improvements but offer fundamental advantages due to their unique physicochemical properties.[8] Their chief roles can be classified as follows:

1. Enhanced Efficiency and Resolution

- **High Surface Area-to-Volume Ratio:** In a small volume, nanomaterials offer a remarkably large surface area for interactions with analytes. This makes it possible for:
  - **Higher Loading Capacity:** The ability to handle larger sample amounts without column overloading.
  - **Improved Efficiency:** More theoretical plates per unit length of the column due to a greater number of interaction sites, leading to sharper peaks and better resolution of complex mixtures.

2. Superior and Tunable Selectivity

- **Multiple Modes of Interaction:** Unlike traditional stationary phases, which typically involve one or two main modes of interaction (e.g. hydrophobic), nanomaterials can simultaneously engage in multi-modal interaction. Modes of interaction may include:
  - **π-π Stacking:** Particularly effective with carbon-based nanomaterials (e.g. graphene, carbon nanotubes) for analytes containing aromatic rings.
  - **Hydrophobic and Van der Waals Forces:** With nanomaterial surface.
  - **Electrostatic Forces:** With charged functional groups on modified nanomaterials.
  - **Hydrogen Bonding:** With oxygen-containing functional groups on nanomaterials like graphene oxide.
  - **Size Exclusion:** And molecular sieving, particularly with porous nanomaterials, such as Metal Organic Frameworks (MOFs) or mesoporous silica, to separate molecules based on size and shape.
- Surface Modification: The surface of a nanomaterial enables precise modification with an array of organic, inorganic, or biological ligands (e.g. chiral selectors) to improve selectivity toward particular target analytes (e.g. enantiomers) or isomers

3. Improved Kinetic Performance

Rapid Mass Transfer: Having a nanoscale structure on the stationary phase shortens the diffusion path length for analytes. This allows for faster separations with little loss in efficiency by lowering the mass transfer resistance (the Cterm in the Van Deemter equation). Faster flow rates and shorter run times are made possible by this.

4. Application-Specific Solutions

Advances in some extremely challenging areas of separation have been made possible by nanomaterials:

- **Separation of Complex Biomolecules:** In order to separate or separate peptides, proteins, and metabolites that are typically difficult to separate using traditional separation phases when there is multimodal interaction between the molecules and the interaction is not continuous there needs to be an effective method of separation.
- **Chiral Separations:** Nanomaterials provide excellent support for the immobilization of chiral selectors, which makes it possible to produce chiral stationary phases that have long-term stability and effectiveness.
- **Sample Preparation (Solid-Phase Extraction):** Due to their high affinity and high surface area nanomaterials are great sorbents for pre-concentrating trace analytes and for sample cleanup from complex matrices for enhanced sensitivity.

Table 3.2.1.1 shows summary of nanomaterial class with key contribution in chromatography

Table – 3.2.1.1 Contribution of Nanomaterials in Chromatography

Nanomaterial Class	Key Contribution in Chromatography
Carbon Nanotubes (CNTs)	High hydrophobicity, strong π-π interactions, large specific surface area.
Graphene & Graphene Oxide	Ultra-high surface area, tunable chemistry via oxygen-containing groups, enhanced mechanical strength.
Metal-Organic Frameworks (MOFs)	Extremely high porosity, tunable pore size and chemistry for molecular sieving and specific adsorption.
Mesoporous Silica	Controlled and uniform pore structures, high surface area, easily functionalized.
Polymeric Nanoparticles	High chemical stability, customizable surface functionality for specific applications.

3.2.2 Capillary Electrophoresis:

Recent advances in nanomaterial-based capillary electrophoresis presents a discussion of innovative applications of nanomaterials that provide solutions to capillary electrophoresis's inherent limitations and expand its capabilities. There are many uses of nanomaterials in capillary electrophoresis, often referred to as "nano-capillary electrophoresis," where they are typically used as immobilized substrates or dynamic modifiers. In chromatography, nanomaterials are often used as the stationary phase.

1. Enhanced Separation Efficiency and Selectivity
Nanomaterials create a dynamic or stationary phase that is immobilized within the capillary, resulting in new interactions that enhance the separation of complex or otherwise difficult analytes.

- **Modifying the Capillary Wall:** The capillary's inner surface (generally made of silica) could be modified with nanomaterials, including graphene oxide or gold nanoparticles, which will: **1.** Reduce sticky proteins and peptides from adhering to the negatively charged capillary wall. **2.** Lead to enhance peak shapes and less smearing known as peak tailing.

Increases overall separation efficiency.

Background Electrolyte Modification: Nanomaterials such as carbon nanotubes and metal-organic frameworks (MOFs) can easily be incorporated into buffer solutions. The resulting combination of the nanomaterials together provides a nanoparticle-based pseudo-stationary phase (NPSP) to achieve the following: convert a standard capillary zone electrophoresis (CZE) run into an improved electrokinetic chromatography (EKC) separation; permit interaction of analytes with the nanomaterials in situation by employing hydrophobic, π–π stacking, and chiral interactive forces to result in enhanced resolution compared to the regular CZE process.

2. On-line Preconcentration and Sensitivity Enhancement

A prominent barrier for capillary electrophoresis (CE) is its relatively minimal concentration sensitivity due to small injection volumes and short optical path length. Nanomaterials provide tremendous options for on-line sample preconcentration.

- **Nanomaterial-Assisted Sample Stacking:** Nanomaterials which have a high affinity to particular analytes, can be utilized as concentrating probes. These nanomaterials can be mixed with the sample to adsorb, and pre-concentrate target analytes prior to and/or during injection. Procedures such as field-amplified sample stacking (FASS) or sweeping become remarkably more powerful when analytes are complexed with nanomaterials, as these procedures become based upon relative amount of analyte in a restricted zone, effectively loading much larger amount of analyte into the capillary, translating into tenfold or greater improvements in detection sensitivity.

3. Facilitation of Novel Detection Schemes
Detection systems can be combined with nanomaterials to obtain higher sensitivity and develop new detection modalities.

- **Improved Fluorescent Detection:** Their strong, stable fluorescence and tuneable emission wavelengths allow nanomaterials to be better able to detect multiple analytes than standard dyes with equally great sensitivity.
- **Electrochemical Detection:** The surface of electrodes in CE-EC can be modified with conductive nanomaterials (e.g., graphene, carbon nanotubes) that increase the effective surface area of the electrode, enhance electron transfer rates, and reduce the overpotential required for detection of analytes, which benefits sensitivity and detection limits.

4. Enabling Chiral Separations
The review highlights that nanomaterials are excellent venues for chiral selectors. A chiral selector (such as cyclodextrin or protein) can be immobilized on the surface of a nanomaterial. This functionalized nanomaterial provides a significant surface area where enantioselective interactions can occur upon its use as a capillary coating or in the BGE, and thus is an extremely successful chirality separation material.

3.3. High-Efficiency Sample Preparation:
Nanomaterials as novel sorbents in Solid Phase Extraction (SPE) and Solid Phase Microextraction (SPME) for pre-concentration and clean-up of complex samples.[34]

Preparation of Solid Phase Extraction:
The concept of sol-Gel method is a well-established analytical chemistry technique for extraction of analytes from complex matrices, including biological fluids, environmental samples and food matrices. As Buszewski and Szultka noted, in recent times there have been significant advancements made in the way the techniques used in this area have become more selective for isolating the desired component of interest.

Why SPE Matters in Sample Preparation
Purification of Eluants is achieved through SPE, which eliminates most of the interference from matrices. This leads to improved accuracy and sensitivity for subsequent tests. Furthermore, when utilising SPE instead of LLE there is significantly less solvent consumed, upholding the tenets of Green Chemistry. Another advantage of SPE is its versatility with a variety of different sample types including urine, blood, soil and water.

Key Components of SPE

- Sorbents are the fundamental component of SPE. These materials are designed to retain or selectively capture analytes. There are three main types of sorbents:

1. Silica Base Phases (ex. C18 and C8)
2. Ion Exchange Resin
3. Polymer Base Sorbents

Advances in SPE

- **Miniaturizer of SPE and Online SPE Systems:** Micro-SPE and On-line SPE systems have become popular in high throughput laboratories. [34]
- **Novel Materials:** Carbon Nanotubes, Molecularly Imprinted Polymers (MIPs) and Monolithic Phases

have created a better way to achieve improved selectivity and capacity for these materials. [34] - [38]

- **Automating SPE Steps:** Robotic systems are being developed to automate the processes of SPE, improving reproducibility and reducing the possibility of human error.

3.4. Enabling Theranostics and Bioimaging:

Diagnostic and Treatment Integration. Nanoparticles are a specialized form of Nano vehicles that deliver therapy to specific targets but also give us new imaging technologies such as magnetic resonance imaging (MRI), computed tomography (CT), and fluorescence.[38][43] Nanoparticles are revolutionizing how we perform medical testing and therapy because they allow us to integrate both diagnostics and therapy on a single integrated platform. They are specifically designed to detect, image and treat disease at the same time and at the site of detection, and as such, they represent an invasive diagnostic system as they can provide imaging while treating the patient.[38]

Targeted Delivery Meets Real-Time Imaging:

Spot on targeting: Nanoparticles can be created with ligands that bind specifically to the diseased cells they have targeted (i.e. cancer cells).[5][39]-[40]

Have a diagnostic aspect: Nanoparticles can contain contrast agents that can be used in MRI, PET and fluorescence so that they can be tracked back to the sites where they were delivered.[5]

Target: Nanoparticles also deliver medication directly to the target area, significantly reducing the harmful effects on healthy cells.[5]

Materials That Make It Work:

- **Iron oxide nanoparticles**: Great for MRI contrast and magnetic targeting.
- **Quantum dots**: Bright and stable for optical imaging.[28]
- **Liposomes and dendrimers**: Versatile carriers for both drugs and imaging agents.

Controlled Release & Monitoring:

- Some nanoparticles are designed to release their therapeutic cargo in response to specific triggers like pH changes or enzymes in the tumour microenvironment.
- Real-time tracking of drug delivery and therapeutic response is allowed by imaging, making treatment more adaptive and personalized.[59]

Applications in Cancer and Beyond:

Currently, the main areas in which Theranostic nanoparticles are expected to have a substantial impact when widely adopted will be as follows:

- **Oncology:** With their ability to detect malignancies at an earlier stage than standard imaging techniques and to target only the cells affected by malignant tumors for chemotherapy delivery.[15]
- **Cardiology/Neurology:** New applications with Theranostic nanoparticles include the ability to mark plaques located in arteries and the ability to identify and administer therapy directly into lesions associated with neurodegenerative diseases.
- **MRI/CT:** Nanoparticles will be used as MRI agents made from Iron oxide because of their magnetic properties. Nanoparticles made from both gold and bismuth will enhance CT images because of their extremely high density.
- **Multifunctionality:** Theranostic nanoparticles can be designed for multiple purposes, such as drug delivery, targeting tissues, or reacting to specific stimuli (e.g., changes in pH or temperature). This makes them extremely attractive for use in personalized medicine.
- **Surface Modification:** For biocompatibility considerations, the nanoparticles can be coated with polymers or ligands to enhance biocompatibility for targeting tumors or sites of inflammation.
- **Real-Time Monitoring:** By combining imaging agents with therapeutic composition, clinicians can see drug delivery and assess subsequent therapeutic cohort in real time.

3.5. Analysis of Drug Delivery Systems and Pharmacokinetics:

The use of analytical techniques to study the release rates, distribution patterns, and ultimate fate of newly formulated nano drugs is indicative of how nanotechnology is altering, enhancing and evolving both the way drugs will be delivered through the human body as well as the manner in which these drugs will continue to develop. A picture is being painted indicating that instead of flooding the system with a large amount of drug via traditional means; by using a nanoparticle delivery system, drug is delivered to specific sites at specific times through an intelligent courier approach instead.[79]

Key Features of Stimuli-Sensitive Nanoparticles:

- **Multi-Functionality of Nanoparticles:** These NPs serve not only as drug delivery vehicles, but have other applications as well; for example, the ability to target specific tissues, or respond/react to some external stimulus which triggers their release of medication as well as show the method of delivery, thereby enabling the efficacy of the medication to be observed.[58][82]
- **Stimuli Responsiveness:** This refers to a system that responds to endogenous stimuli, such as pH change, temperature change, or enzyme activity. For example, a nanoparticle may remain intact in the bloodstream but upon encountering the acidity of the tissue of a tumor, will release the drug it is carrying.[58][82]

- **Surface Functionalization:** By modifying the surface of nanoparticles with ligands or antibodies, these particles can recognize and bind to specific cells, i.e., creating an enhanced therapeutic targeting and decreasing off-target effects.

Impact on Pharmacokinetics:
The term "pharmacokinetics" describes a drug's absorption, distribution, metabolism, and excretion throughout the body. This is enhanced by Torchilin's systems in multiple ways:

- **Extended Circulation Time**: Coatings like PEG (polyethylene glycol) help nanoparticles evade the immune system, allowing them to circulate longer and reach their target.
- **Using a Controlled Release Mechanism:** Stimuli-sensitive NP designs can provide time-sensitive or location-based control over drug release, which decreases the need for multiple dosing.
- **Improved Bioavailability**: By protecting drugs from degradation and delivering them straight to the target tissues, these systems increase the amount of drug that actually reaches the site of action.

4. THE RISE OF POINT-OF-CARE (POC) AND WEARABLE SENSORS:

4.1. The Drive Towards Decentralized Testing:

The shift to decentralized testing refers to the movement of testing away from a centralized or traditional location to either a remote or local site, with the testing oftentimes happening closer to the end-user. Technology and operation constraints due to the COVID-19 pandemic have accelerated the concept of decentralized testing. While decentralized testing is significantly recognized for clinical trials labeled as a Decentralized Clinical Trial (DCT), it applies to the software development lifecycle and diagnostic testing. There are several reasons why decentralized testing matters, including:

- **Accessibility:** Many patients live far away from hospitals or laboratories. Decentralized testing allows for testing to occur in one's home, in a clinic, or in the field and eliminates barriers to prompt diagnosis.
- **Timeliness:** When patients have to wait a few days to get lab results, that often means that the treatment is delayed. Point-of-care (POC) diagnostics provide immediate results which benefits the patient but can also be a vital benefit in emergency settings or when a patient has a chronic condition.
- **Empowerment:** Patients have increased power over their health. With devices like glucose monitors or pregnancy tests, a patient can get the information they need without waiting for the doctor to call.
- Using central labs less will reduce healthcare costs in resource-limited areas. Miniaturizing a lab down to the size of a postage stamp is now possible to do using microfluidic or Lab on a Chip technology and these technologies hold promise for many applications.

Technological Drivers:

It involves various technologies has following:

1. Miniaturization: Microfluidics & Lab-on-a-Chip
Think about how incredible it would be to have an entire laboratory shrunk down to the size of a stamp. This is what is being done with microfluidics, or lab-on-chip technology;

- Microfluidics looks at how to move water through pipes that are tiny (generally under 100 microns in diameter), while using incredibly low volumes of both fluid and chemical reagent to complete complex chemical reactions as shown in figure 4.1.1.
- Lab-on-chip devices have multiple functions: they provide everything you need to mix, dilute, prepare, react, and analyse your samples everything happens in one very tiny space.

These improvements enable:

- Rapid testing with minimal sample volumes (e.g., a drop of blood).
- Portability, making diagnostics feasible in remote or resource limited settings.[45]
- Multiplexing, where several tests can be run simultaneously on one chip.

This miniaturization isn't just about size it's about speed, efficiency, and accessibility.

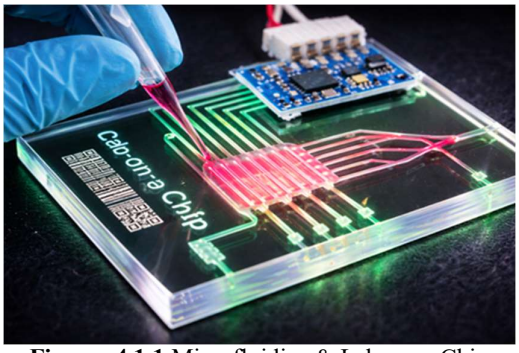

Figure- 4.1.1 Microfluidics & Lab-on-a-Chip

2. Biosensors + Mobile Devices = Smart Diagnostics

- The use of biosensors in conjunction with portable electronics (e.g., smartphones and tablets) represent a new way to collect and evaluate personal health-related data.
- The biological information that a biosensor collects typically includes biological indicators such as glucose levels, pathogens, and/or proteins and is measured through either chemical or physical reactions to the body's biological signals.
- Using a biosensor with a mobile device, one can do the following:
  - Wirelessly send the data almost immediately to providers or the cloud.
  - Enable remote monitoring, especially for chronic conditions like diabetes or heart disease.
  - Support for telemedicine includes allowing patients to receive care without having to make a trip to the doctor's office.

This integration of our services allows users to keep track of their health data in real time; bridging the gap between diagnostic tests and physician decision-making.

3. Materials Science: Disposable, Low-Cost Test Strips

Materials science advancements have made it feasible to create diagnostic instruments that are disposable and reasonably priced, which is essential for widespread use.

Revolution includes:

- Paper-based diagnostics (e.g., lateral flow assays like pregnancy tests).
- Polymer substrates that are flexible, durable, and easy to manufacture.
- Nanomaterials that enhance sensitivity and specificity of detection.

These materials allow for:

- Diagnostic testing that helps prevent contamination risk tests that are Mass-produced and are economically scalable.
- Tests that are designed for use in many climatic or other locations or settings will have greater environmental endurance.
- By using these types of technologies, the diagnostic testing process can be democratized: anyone, anywhere can complete a test.

These technologies represent both engineering innovations and humanitarian advances: They make it possible to transform the process of performing a diagnostic test from a centralized and reactive model to an individualized and proactive approach.

4.2. Nanomaterial-Enabled POC Platforms:

Nanomaterials improve the performance of paper microfluidic devices for their sensitivity, specificity and multiplexing capabilities. In contrast to AI or complicated, costly instrumentation, the paper-based platforms are designed for quick, on-site diagnostics and are typically visible to the naked eye. Nanomaterials are extremely small particles that can only be seen with a strong microscope. Don't let their size fool you. These little guys are very powerful when it comes to detecting biological signals. They act as very sensitive sensors in POC devices, detecting minute amounts of biomarkers of disease in urine, saliva, or blood.[49]-[50]

How they are utilized in point of care (POC) devices.

- **Gold nanoparticles:** These nanoparticles change color when they recognize specific molecules, enabling visually detectable results.
- **Quantum dots:** These dots can also detect multiple conditions at the same time because they emit light when illuminated with the right wavelength.[28]
- **Graphene and carbon nanotubes**: They are implemented in devices that sense electrical signals from biological specimens because they are electrically conductive.
- **Magnetic nanoparticles:** These nanoparticles help to concentrate and isolate target molecules, thus improving the time and accuracy of detection.

These materials are employed on paper-based microfluidic devices. These are similar to high-tech paper strips, directing fluids through tiny channels (in a very precise manner) and providing results quickly.[50]

4.3. Wearable Analytical Devices:

Flexible substrates with embedded nano-sensors for continuous and non-invasive drug and biomarker monitoring.[52] Wearable analytical devices refer to smart sensors embedded in flexible materials that can be worn as patches, as wristbands, or embedded into clothing as shown in figure 4.3.1. These devices combine the ability to monitor using biochemical markers in biofluids (sweat, saliva, tears, interstitial fluid) in real time, without a needle or visit to a lab, provide a glimpse of our health.[51]

Key Technologies and Innovations:

Optical and Electrochemical Biosensors:

The foundation of wearable analytics lies in the electrochemical and optical biosensors which provide doctors and researchers with the ability to monitor patients' health remotely through wearable devices.

Electrochemical Biosensors:

Electrochemical biosensors are the most widely used type of biosensors and have many applications including the detection of glucose, lactate, and various electrolyte levels. Electrochemical biosensors have the following characteristics:

- They provide high sensitivity, rapid response, and low power consumption.
- Electrochemical biosensors are typically found in the form of sweat patches or microneedle arrays.

Optical Biosensors:
- Rely on fluorescence, colorimetry, or surface plasmon resonance to detect biomolecules.
- Ideal for non-contact sensing and visual feedback (e.g., colour changes).
- Can be embedded in contact lenses or skin patches for real-time monitoring.

Multiplexed Sensing: By monitoring several biomarkers at once, sophisticated devices can provide a more complete picture of health. For thorough health insights, the simultaneous detection of several biomarkers is allowed for by multiplexing.

Sensor Arrays:
- Multiple sensing elements tuned to different analytes.
- Integrated with microfluidics to route fluids to specific sensors.

Data Processing:
- The platform for cloud-based technology or on-board electronics.
- The AI algorithm used to identify trends and predict a person's health through complex signals.
- **Microfluidics:** are devices with minute channels that allow for the movement of biofluids from their testing point to the sensors at the base of each device. This allows for exceptionally accurate and precise measurement and assessment of the sample collected.
- **Flexible Electronics**: Materials like stretchable polymers and ultrathin circuits make these devices comfortable and skin-friendly.

A human-based approach to diagnostics is taken (by this technology), because it is game-changing. Rather than waiting for a person to show symptoms or to make an appointment to obtain lab tests, this technology supports people in:

- Track their health in real time like monitoring hydration, stress, or glucose levels.
- Detect early signs of illness before symptoms appear.
- Personalize treatments by observing how their body responds to medications or lifestyle changes

Figure- 4.3.1 Wearable Sensors

5. FUTURE DIRECTIONS AND EMERGING TRENDS:

5.1 Multi-Functional and Stimuli-Responsive "Smart" Nano-systems

1. Multi-Stimuli Responsiveness for Complex Environments

The next generation of Smart Materials are being created as multi-stimuli responsive (pH, temp, magnetic eld) Smart Materials that enable more controlled responses in the dynamic biological/environmental realms.

One of the most exciting applications of these next generation Smart Materials is for targeted drug delivery utilizing a nano-carrier to deliver therapeutic agents selectively (i.e., a therapeutic agent will only be released from the nano-carrier when the nano-carrier encounters the required conditions to warrant therapeutic release).

2. Combining Biosensing with Personalised Medicine

- Smart nano-systems are increasingly embedded into biosensors that detect biomarkers in real time transforming diagnostics from static snapshots to dynamic health monitoring.
- For example, wearable biosensors using stimuli-responsive hydrogels can track glucose, lactate, or cortisol levels in sweat, adapting their sensitivity based on environmental changes.

3. Sustainability and Biocompatibility

- The focus of research into smart nanostructures is now on biodegradable or environmentally-friendly polymer-based systems, creating less risk and a lower environmental burden in the future.

- This change is especially important for the use of smart nanostructures in agriculture, water purification, and implanted medical devices, where the toxicity of the materials and their entire life cycles are significant.

4. Soft Robotics and Actuators

- Materials that respond to external stimulus through movement, shape change, and actuation are referred to as "soft" actuators, and researchers are developing them using smart nano-materials. Soft actuators materialize in new ways with the development of intelligent (i.e., "smart") nanoscale systems; these types of actuators are ideal for adaptive prosthetics, artificial muscle systems, and bio-inspired robotics.
- A future example of the practical application for a smart nanoscale system would be the creation of a nanoscale gripping device that opens or closes depending on the temperature or wavelength of light it meets.

Emerging Trends:

Table- 5.1.1 shows trends of nanomaterials currently developing

Table- 5.1.1 Emerging Trends of Nanomaterials

Trend	Impact
Liquid biopsy-enabled smart biosensors	Real-time, non-invasive disease monitoring
Next-gen SRPs (Stimuli-Responsive Polymers)	Tunable response profiles for complex applications
Hybrid nanosystems	Combining organic/inorganic components for multifunctionality
AI-guided nanosystem design	Accelerating discovery and optimization of smart materials
Environmental sensing and remediation	Smart materials that detect and neutralize pollutants

5.2 The Confluence of AI and Nanotechnology:

The merging of nanotechnology and artificial intelligence (AI), which have complementary strengths, offers a powerful combination. Nanotechnology enables people to control materials at the atomic and molecular levels with great precision; Artificial Intelligence (AI) can analyze large volumes of data and identify complex patterns among otherwise unrelated data.[55] Together these two technologies provide numerous opportunities for furthering our knowledge in medicine, materials engineering, renewable energy, and environmental monitoring/management.[83][85] On the other hand, this integration will also lead to challenges that will require careful consideration and analysis. As artificial intelligence, along with the use of nanotechnology continues to evolve, they will form an alliance that can deliver innovative solutions to global problems and drive the next generation of technological advancements.[67] It is essential for everyone involved to understand the significance of this partnering, including not only those working within the scientific community, but also those responsible for creating and implementing public policy, as well as all members of society.[83][85]

AI Matters in Nanomedicine

Nanomedicine is believed to provide precision with advanced drug delivery systems through sophisticated imaging techniques and personalized therapies; thus, the demand for nanotechnology-based medical solutions is enormous. However, as the biological complexity and the amount of data generated by a nanomedicine-based platform continue to grow, it's been found that conventional analytics cannot keep up. Read on to discover how the development of Artificial Intelligence (AI) can assist in this fast-moving field.[55][72]-[78]

Utilizing Machine Learning (ML) Algorithms, AI can help:

- **Identify patterns** in large, multidimensional datasets
- **Predict outcomes** of nanoparticle-based therapies
- **Optimize formulations** for drug delivery systems
- **Guide clinical decisions** by integrating patient-specific data

Applications Across the Pipeline

- **Drug Development**: AI streamlines the creation of nanoparticle-based therapies by predicting how drugs behave in the body like absorption, distribution, and toxicity making the process faster and more precise than traditional trial-and-error methods.
- **Diagnostics:** AI will enhance the capabilities of nano sensors to diagnose diseases at an earlier stage and with greater accuracy due to AI's capacity to identify complicated patterns in biomarker data that cannot be seen by humans.
- **Personalised Medicine:** By evaluating genetic, protein and clinical information on a patient, AI provides a platform for tailoring nanomedicine to the specific patient, improving the potential for positive response and reducing the risk of side effects.[72]-[74]

5.3 Personalised Medicine and Advanced Concepts:

Function in DNA nanotechnology, 3D nanostructures, pharmacogenomics, and nanozymes.

Pharmacogenomics: The Genetic Blueprint for Safer Drugs

The field of pharmacogenomics studies the relationship between the genetic makeup of an individual and how they process and respond to medications. By identifying

specific genetic variations (e.g., SNPs) associated with specific drugs, we can more accurately predict if an individual will experience an adverse reaction or not respond to a certain drug. This information allows clinicians to optimize dosages and select the most effective medications for a patient based on their genetic information, greatly reducing trial-and-error and improving patient safety.

For example, if a genetic variation (SNP) in the CYP2C19 gene is present in a patient, clopidogrel a common antiplatelet medication may not be effectively metabolized. In such cases, the clinician would likely recommend switching the patient to another antiplatelet medication that the patient would metabolize more effectively.[64]

3D Nanostructures: Smart Scaffolds for Targeted Delivery

Three-dimensional (3D) nanostructured materials created from polymers, lipids or inorganic substances allow precise control over conditions for the release of drugs and interactions with cells. Control of the release of drugs and phage interactions enables the creation of new materials that incorporate multiple agents into a single structure with responsive behaviour to environmental stimuli such as pH or temperature. The structures are designed to mimic biological environments, thereby enhancing the bioavailability of drug products and decreasing the toxicity associated with systemic exposures.

For example, mesoporous silica particles that contain anti-cancer agents can selectively target and release their chemical payloads in the acidic environments of tumours.

DNA Nanotechnology: Molecular Origami for Precision Medicine

Devices made of DNA nanotechnology utilize the programming possibilities of nucleotides to create nanodevices (e.g., aptamers, nanorobots, logic gates etc.) that work against a biological target.[65] DNA nanodevices can detect the presence of a specific biological marker, conduct drug delivery to a specific location within the body, or initiate treatment through the use of molecularly targeted therapies (e.g., precise delivery of drugs). The biocompatibility and flexible architecture of DNA nanodevices make them an excellent choice for individualized diagnostics and the delivery of smart drug therapies.

Example: Nanorobots made of DNA origami have been engineered to open in response to a specific tumor biomarker (tumor-specific antigen) and release thrombin to promote clotting in the blood supply of tumors.

Nanozymes: Catalytic Nanomaterials with Enzyme-Like Activity

Nanozymes can be defined as synthetic materials at the nanoscale that are capable of mimicking the behaviour of natural enzymes, providing a greater degree of robustness and versatility compared to biological enzymes.[64] Nanozymes can also serve as catalysts for the catalysis of a variety of biological reactions (e.g., ROS scavenging and glucose oxidation), which is useful for applications such as biosensing and disease modulation in the context of personalized medicine.[60]-[63] Through these applications, nanozymes can be specifically designed to adapt to an individual's oxidative stress or metabolic state.

For example, cerium oxide nanozymes have been found to have potential therapeutic effects on neurodegenerative diseases, by scavenging reactive oxygen species in a patient-specific manner.

Nanoparticle effect on biological system

Nanoparticle (NP)s' behaviour in biological systems are dictated by their size, shape, and surface chemistry, which determine how NP will interact with cells, proteins, and tissues. The size, shape and surface chemistry of NP also dictate the level to which NP will be distributed in the body and how they are taken up by cells, such as an NP size of 20-30 nm is optimal for uptake by the majority of cancer cells. Smaller NP (<10 nm) are more readily removed through the kidneys, while larger NP typically target the liver and/or spleen. Anisotropic NP shapes (e. g. rods) generally possess greater binding and transport than spherical NP due to their ability to bind and detach from proteins. Surface charge and ligand (hydrophilic vs. hydrophobic) preferences of NP regulate protein binding (i.e., protein corona) and therefore direct NP to specific cells; these factors have a significant impact on the ability of NP to deliver therapeutic agents and/or be visualised as part of diagnostic imaging.[53]

Particle Size: Cellular uptake of nanoparticles is influenced by their size; for instance, cancer treatment studies show that nanoparticles sized between 20-30 nm are typically taken up by cells in greater quantities than smaller (<10 nm) or larger. In addition, larger-sized particles may become trapped in the tissue (without passing through cell membranes). Particle biodistribution is affected by the size of the particle. For example, spheres and rods tend to accumulate in the liver while irregular-shaped particles accumulate in the spleen and discs gather in the heart. Clearance occurs mainly through the kidneys for particles sized less than 6 nm. Drug release is generally faster for smaller sized particles than larger sized particles because smaller-sized particles possess a greater surface area for releasing drugs.[53]

Particle Shape: Cellular interaction with nanoparticles is affected by their shapes; for example, rod-shaped or cylinder-shaped nanoparticles have been shown to produce higher cellular uptake and transport than spherical-shaped nanoparticles, especially when oriented perpendicular to the cell membrane. Also, particle shape affects where the nanoparticles accumulate and how they interact with proteins; e.g., cylindrical-shaped nanoparticles can be delivered to tissues associated with tumors through accumulation in those tissues.[53]

6 CONCLUSION

In this review, it was made clear how nanomaterials are playing a significant role in pharmaceutical analysis; from ultra-sensitive testing in central laboratories, to small portable point-of-care (POC) testing devices, nanomaterials have allowed researchers to conduct more informative, efficient, and cost-effective means of analysis. The field is transitioning from a focus on single-function nanomaterials to an emphasis on more complex, multifunctional, smart systems. Going forward the challenge will be to overcome the major barriers of biocompatibility, manufacturing scalability, and regulatory compliance. The ability to translate the successful implementation of emerging nano-analytical technologies from laboratory-based work into clinical settings will be critical for realising the full potential of personalised and predictive medicine.

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Declaration of interest statement

The authors have declared that there are no conflicts of interest.

Declaration of AI use

During the preparation of this manuscript, the authors used ChatGPT (Open AI) to assist in improving the language quality, grammar, sentence structure, and overall readability. AI was also use to generated some images. No AI tool was used to generate, manipulate, or fabricate research data, results, or references.

Abbreviations:

- **AI** – Artificial Intelligence
- **AgNPs** – Silver Nanoparticles
- **AuNPs** – Gold Nanoparticles
- **BGE** – Background Electrolyte
- **BIAcore** – Biomolecular Interaction Analysis core system (SPR instrument)
- **CE** – Capillary Electrophoresis
- **CE-EC** – Capillary Electrophoresis with Electrochemical Detection
- **CNTs** – Carbon Nanotubes
- **CQDs** – Carbon Quantum Dots
- **CT** – Computed Tomography
- **CVD** – Chemical Vapour Deposition
- **CZE** – Capillary Zone Electrophoresis
- **DCT** – Decentralized Clinical Trial
- **DNA** – Deoxyribonucleic Acid
- **EIS** – Electrochemical Impedance Spectroscopy
- **EKC** – Electrokinetic Chromatography
- **EPR** – Enhanced Permeability and Retention
- **FASS** – Field-Amplified Sample Stacking
- **FET** – Field Effect Transistor
- **FRET** – Förster Resonance Energy Transfer
- **FDA** – Food and Drug Administration
- **GA** – Graphical Abstract
- **GO** – Graphene Oxide
- **HPLC** – High Performance Liquid Chromatography
- **LLE** – Liquid–Liquid Extraction
- **LSPR** – Localized Surface Plasmon Resonance
- **MAX phase** – Layered precursor for MXenes (M = transition metal, A = A-group element, X = C/N)
- **ML** – Machine Learning
- **MOFs** – Metal Organic Frameworks
- **MNPs** – Magnetic Nanoparticles
- **MRI** – Magnetic Resonance Imaging
- **MSNs** – Mesoporous Silica Nanoparticles
- **MXenes** – 2D Transition metal carbides / nitrides
- **NADH** – Nicotinamide Adenine Dinucleotide (Reduced form)
- **Nano-LC** – Nano Liquid Chromatography
- **Nano-MIPs** – Nano Molecularly Imprinted Polymers
- **NPs** – Nanoparticles
- **NPSP** – Nanoparticle-based Pseudo-Stationary Phase
- **PCR** – Polymerase Chain Reaction
- **PEG** – Polyethylene Glycol
- **PET** – Positron Emission Tomography
- **POC** – Point of Care
- **ROS** – Reactive Oxygen Species
- **SERS** – Surface Enhanced Raman Spectroscopy
- **SNPs** – Single Nucleotide Polymorphisms
- **SPE** – Solid Phase Extraction
- **SPIONs** – Superparamagnetic Iron Oxide Nanoparticles
- **SPME** – Solid Phase Microextraction

- **SPR** – Surface Plasmon Resonance
- **SRPs** – Stimuli-Responsive Polymers
- **TEM** – Transmission Electron Microscopy
- **TRGO** – Thermally Reduced Graphene Oxide
- **UV** – Ultraviolet

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