Int J Adv Life Sci Res. Volume 7(2) 68-80
https://doi.org/10.31632/ijalsr.2024.v07i02.005

International Journal of Advancement in Life Sciences Research

Online ISSN: 2581-4877

Journal homepage http://ijalsr.org

Review Article

Artificial Intelligence Powered Insights into Nanotoxicology

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Abstract

The application of nanomaterials in medicine necessitates a thorough assessment of their toxicity to ensure their safe use in living organisms. Advanced technologies like artificial intelligence (AI) and machine learning (ML) are instrumental in processing vast datasets in toxicology, encompassing toxicological databases and image-based screening results. Nanomaterials exhibit significant variability in their physical and chemical properties, making their toxicological assessment unique. The potential adverse effects of these materials, as they find new applications in the consumer market, raise crucial concerns in clinical settings. Understanding the toxicological mechanisms of these substances is vital. Traditionally, the pharmaceutical industry employs animal models to evaluate compound toxicity before human trials, guided by various regulatory legislations. Modern toxicology increasingly relies on computational methods. ML techniques, especially decision tree algorithms, are pivotal for categorizing nanomaterials in nanotoxicology. These algorithms identify essential input parameters and extract meaningful information from extensive datasets. This overview emphasizes the role of AI algorithms in nanotoxicology, quantitative toxicology, nano data collection, predictive models, essential NP properties, image-based databases, and various challenges in the field.

Keywords: *Algorithm Models, Collection of Nano data, Machine learning, PBPK Models, QSAR for Nano toxicology, Toxicology.*

Introduction

AI progress is revolutionizing the way drug discovery and development are approached. Systems biology and bioinformatics efforts aim to evaluate the negative impacts of various chemicals. By leveraging bioinformatics tools and modeling, it becomes feasible to anticipate or clarify the detrimental effects linked to specific chemicals. The physicochemical attributes of nanomaterials play a vital role in quantitative structure-activity relationship (QSAR) modeling. One method of determining QSAR relies on a foundational theoretical model. For instance, analyzing the reactivity of chemicals based on their molecular orbital energies can provide QSAR insights. Alternatively, a statistical approach to QSAR uses pattern recognition to link relevant descriptors with the anticipated effects (Schultz *et al.*, 2003).

The hybrid QSAR model integrates mechanistic insight and statistical accuracy, employing theoretical insights to pinpoint the most likely predictive descriptors (Zhao *et al.*, 2008). Specifically, QSAR are employed at the nanoscale, often called Nano-QSAR. Artificial intelligence (AI) facilitates the integration of text and data mining techniques, augmenting the insights derived from network and systems biology, thereby enhancing our understanding of disease mechanisms and how chemicals operate (Kumari *et al.*, 2023). The critical understanding is that the quantity of a substance determines its toxic impact (Grandjean, 2016). Chemical safety is a significant factor leading to the loss of new chemicals during their discovery phase and even after they've been introduced to the

Received on: 7th February 2024; Revised version received on: 26th March 2024; Accepted: 3rd April 2024

market, especially concerning regulatory matters. The potential side effects of chemicals pose significant challenges in the clinical realm as they find new applications in the consumer market(Fuelle & Lanctin, 2022). Determining how to anticipate these negative chemical/toxicological responses remains crucial. Preclinical animal tests often need to catch up in forecasting human adverse reactions, accurately predicting them in only about 30% of cases (Singh *et al.*, 2022). Understanding the intricate details of chemical toxicological mechanisms is crucial, especially when considering chemical toxicity.

Nanomaterials or nanoforms (NMs) exhibit significant variability in their physical and chemical characteristics, quantum properties, and consequent toxicological effects. This variability makes it challenging to evaluate their risks on an individual basis. Conventional hazard evaluations primarily use invasive tests, which present issues such as reliability in human extrapolation, ethical concerns, and substantial time and financial requirements(Chen *et al.*, 2018). Over the past ten years, various computational models have emerged to forecast the toxicological characteristics or detrimental impacts of NMs. With the rising adoption of these computational methods, this review aims to present the procedural stages involved in these model creations from the past decade, aiming to establish frameworks for constructing more dependable models. The application of nanomaterials in the medical realm hinges on thorough evaluations for the safety of living entities. Leveraging AI and ML can facilitate the analysis of extensive toxicological data, encompassing information from toxicology databases to image-based screenings. Sustainable healthcare leverages AI to optimize resource allocation, enhance diagnostics, and improve patient outcomes. AI algorithms analyze vast datasets to personalize treatments, minimize waste, and streamline operations (Poddar, S. 2022). Nanomaterials, characterized by their minuscule size ranging from 1 to 100 nm, possess distinct physical, chemical, and biological attributes that have propelled advancements in various sectors (Bayda *et al.*, 2019). While nanotechnology and nanomedicines offer numerous advantages, proactively addressing potential adverse effects is imperative. Computational toxicology seeks to identify the elements contributing to harmful interactions through an advanced model. This model considers all possible interactions of the substance to yield relevant outcomes.

The advancements in AI and ML have paved the way for innovative methods in toxicity assessment. In nanomaterials, computational modeling helps establish links between their biological life within the body, the patterns of biological reactions, and their behavior upon reaching the desired organ(Fallah Madvari, 2023). The primary methods examined to evaluate the toxicity caused by nanomaterials include mathematical models based on structure, such as Bayesian techniques and Markov Chain Monte Carlo simulations.

AI in QSAR for Nanotoxicology

Computational modeling techniques include QSAR/nano-QSAR, read-across, and data-driven profiling. The nano-QSAR method establishes a statistical link between independent factors (physicochemical qualities) and dependent variables (toxic effects) (Singh *et al.*, 2019). Four approaches may be employed to interpret the study trends investigation;

- Aggregate graph
- Map illustrating keyword co-occurrence density
- Map based on themes
- Structure map with keyword groupings.

The density visualization map employs a color gradient from yellow to blue to depict focal points in nano-QSAR research. Yellow signifies areas of intense research interest, encompassing topics like QSAR, validation, and cytotoxicity, while blue indicates the opposite trend. This visualization is generated using the "VOSviewer" software (Li *et al.*,2022). Thematic maps categorize subjects into four sectors: foundational, prevalent, emerging/declining, and specialized areas. The prevalent category encompasses extensively explored topics, featuring terms like drug delivery, linguistic choices, and design aesthetics (Di Cosmo *et al.*, 2021).

The conceptual structure map derived from bibliographic clustering classifies topics by red, blue, and green shades, highlighting areas like drug discovery, nanomaterial engineering, and correlation methods (CORAL software). Nano-QSAR is a computational instrument facilitating comprehension of nanomaterials' attributes correlating with their biological effects(Manigrasso *et al.*, 2022). The core objective of nano-QSAR modeling revolves around data acquisition and refinement. Information is sourced from diverse channels, including literature, databases, and experimental studies. This

process entails three pivotal steps: database creation, descriptor identification, and endpoint determination. While traditional QSAR/QSPR approaches rely on consistent, unified datasets, the perturbation method integrates experimental data by introducing slight modifications to enhance predictive accuracy. Hence, an integrated nano-QSAR perturbation approach may offer improved toxicity predictions across diverse experimental scenarios (Wyrzykowska *et al.*, 2019).

Algorithm Models in AI Nanotoxicology

Algorithm regression models are pivotal in nano-toxicology for assessing the potential adverse effects of NP s on biological systems. In ML algorithms, regression techniques, such as linear or polynomial regression, predict toxicity levels based on NP characteristics like size, shape, and surface properties(Singh et al., 2022). These models provide insights into nano-bio interactions by analyzing datasets linking NP attributes to toxicity outcomes. Advanced regression models can account for nonlinear relationships and interactions between multiple NP parameters. Such models aid researchers in optimizing NP designs for safer applications, ensuring the advancement of nanotechnology sustainability and responsibility. While they offer insights into relationships between variables, their transparency is often contingent on the relevance and significance of the descriptors chosen. However, a limitation is their reliance on linear relationships, potentially overlooking nonlinear associations. Furthermore, their susceptibility to outliers can skew predictions, leading to less accurate forecasting(Puzyn *et al.*, 2011). It's essential to interpret regression results cautiously, understanding their strengths in elucidating relationships and vulnerabilities to data anomalies. In ML for Nano toxicology, decision tree algorithms are pivotal models for classifying nanomaterials. They excel in automatically selecting crucial input variables and sifting through large, noisy datasets to pinpoint valuable descriptors. However, a notable limitation lies in their inability to process non-numerical data.

Moreover, their training duration often surpasses other models, making them less efficient in time-sensitive scenarios. Nonetheless, their adeptness in identifying significant features from intricate datasets underscores their importance in nanotoxicology research and their potential to enhance safety evaluations of nanomaterials(Bengio *et al.*, 2010). Support Vector Machines (SVM) is a pivotal algorithmic model in ML for nanotoxicology. They adeptly navigate challenges like collinear descriptors, nonlinear relationships, and datasets of varying sizes. SVM excel in classification and regression tasks, ensuring high precision and reliability. Their versatility allows them to manage intricate problems often encountered in toxicological studies, such as handling small datasets without compromising accuracy. However, their sensitivity to parameter choices, like kernel functions, demands careful calibration. Despite complexities in interpreting SVM decisions, their efficacy in modeling intricate relationships makes them indispensable tools in nanotoxicology research.

In the realm of nanotoxicology, the Artificial Neural Networks (ANN) algorithm model offers a robust model for ML. ANN excel in capturing nonlinear data relationships inherent in intricate structure-activity relationships. They adeptly handle expansive descriptor datasets, even filtering out extraneous variables. However, selecting an optimal complexity remains challenging, with pitfalls such as overfitting. ANN are highly sensitive to parameter fluctuations and changes in network topology, necessitating meticulous tuning. Their capacity to generalize insights from vast and complex datasets makes them indispensable tools in understanding nanomaterial interactions and potential toxicological implications (Sussillo & Barak, 2013,Saini & Srivastava, 2018). The partial least squares (PLS) model is a multivariate statistical method that reduces data's dimensionality by transforming the original descriptors into smaller latent variables. This reduction facilitates more efficient and robust subsequent analyses. PLS is particularly effective in scenarios with multiple noise sources, and the descriptors are highly intercorrelated (Pirouz, D,2006). However, one challenge with PLS is the interpretation of the loadings of the independent latent variables. The distributional properties of PLS estimates are only sometimes well-understood, which can pose challenges in certain applications. Despite these complexities, PLS remains a valuable tool for data analysis.

The principal component analysis (PCA) Model is a statistical technique used for reducing the dimensionality of data (Figure 1). By extracting orthogonal components, PCA eliminates correlations among input variables, such as physicochemical descriptors, while retaining essential information. It aids in preventing overfitting and makes data visualization feasible in lower dimensions. However, interpreting the transformed data becomes challenging as the original variables lose their resolution. Careful selection of the number of principal components is crucial. An inappropriate choice might overlook vital details present in the initial feature set. Thus, PCA offers a balance between simplification and information retention in datasets (Oksel et.al.,2017).

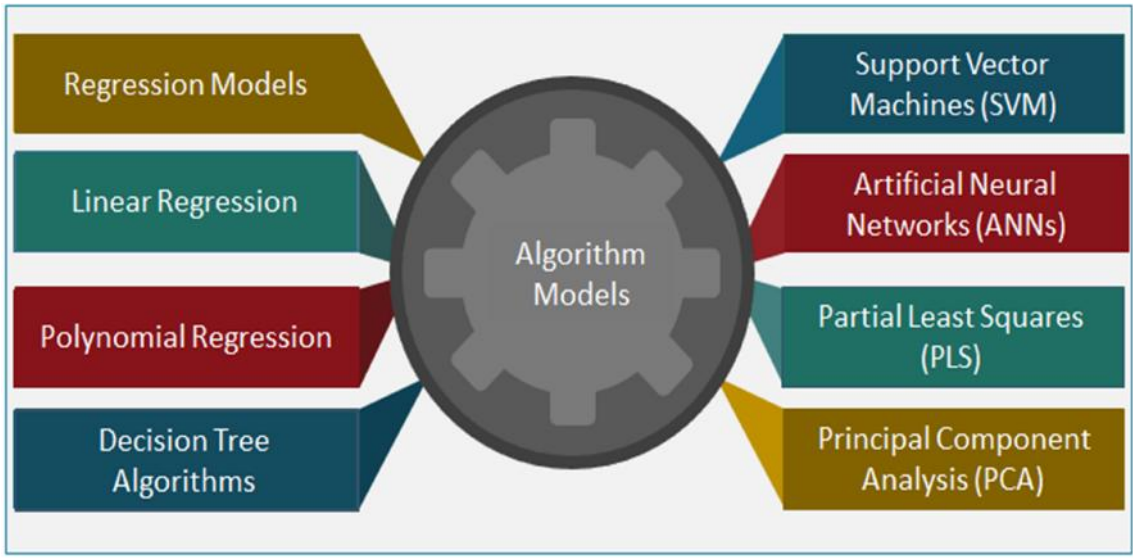

Figure 1: Various Algorithm model for Nano toxicology

Quantitative Toxicology

Quantitative Systems Toxicology (QST) examines the toxic impacts of chemicals and various chemical compounds in the early part of the previous century. It was prompted by numerous deaths attributed to nephrotoxicity, or kidney toxicity, resulting from antibiotic use(Petejova *et al.*, 2019). The pharmaceutical industry traditionally uses animal models to assess the toxicity of compounds before human testing, as mandated by various regulations. However, not all animal models accurately predict human reactions. Recognizing this limitation, computational methods are gaining prominence in contemporary toxicology(Hemmerich & Ecker, 2020). The expense is crucial, given the substantial resources required to validate and create new chemical risk assessments. There is a growing push to minimize the reliance on animal testing across various toxicity assessments(Tornqvist *et al.*, 2014).

Collection of Nano Data

Specific formats and standards are essential for comprehensive data sharing and communication to address the complexities of nanomaterials research and their data effectively, one notable framework developed for this purpose is the ISA-TAB Nano, which stands for Investigation, Study, Assay, and Material in a tab-delimited format(Thomas *et al.*, 2013). ISA-Tab Nano builds upon the foundational ISA-Tab framework, designed for the organized collection and sharing of experimental data. It employs various technologies to gather and relay intricate nanomaterial details systematically (Figure 2). This system categorizes data into four primary files: investigation, study, assay, and materials, each further segmented into distinct fields.

The information, sourced manually from literature using predefined templates, undergoes validation through established rules(Richarz *et al.*, 2015). Moreover, a python tool can transform ISA-Tab Nano files into tab-delimited text files, aiding computational analysis and ensuring database conformity. Challenges arise in potential data revisions, encompassing aspects like reaction rates, chemical constituents, and template structures. Data derived is then organized into relational tables for storage(Kochev *et al.*, 2020).

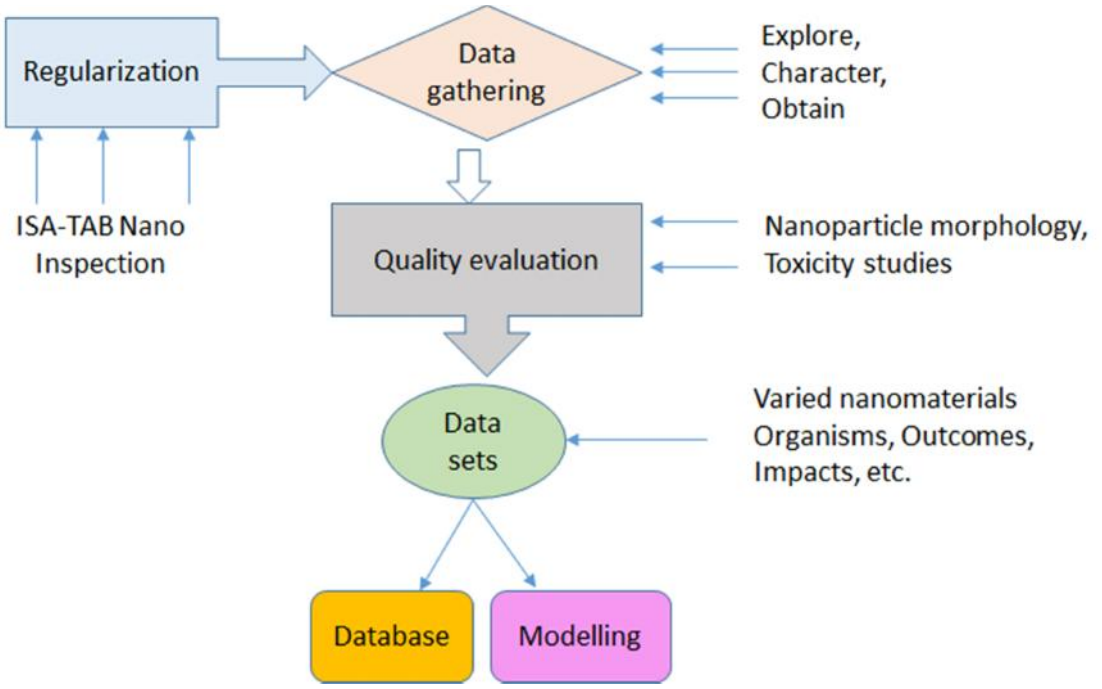

Figure 2: ISA-TAB Nano for collecting Nano data

Nanopredcitors by PBPK Models

The chemical or drugs can produce their desired effects by influencing multiple targets. Certain medications (prodrugs) need to transform into active compounds before they can act on these targets to achieve the intended outcome(Yu *et al.*, 2018). There is a risk that the chemical might lead to adverse effects. These effects could arise from the direct influence of the chemical itself or its breakdown products on the targets. The liver's detoxification processes, like the ADMET profile, convert the chemical's metabolites into substances that can be excreted from the body. Various contemporary tools, including QSAR models, molecular docking methods, and ADMET prediction techniques, are available for predicting chemical toxicity. Both ADMET profilers and Physiologically based pharmacokinetic PBPK models play crucial roles in connecting the toxicity of a substance with its exposure data. These tools help integrate findings from animal studies, laboratory tests, and computational analyses to assess chemicals. With the assistance of QSAR metabolic simulators, it's possible to identify whether a given chemical has recognized or simulated metabolites or breakdown products(Yordanova *et al.*, 2019).

Conjugation with glutathione can inflict direct harm or diminish the cell's capacity to handle oxidative compounds, triggering the body's immune response for healing(Cooper & Hanigan, 2018). The body can manage these reactive substances effectively if they remain balanced or minimal. However, persistent or over-activity can lead to harm at the cellular and tissue levels(Cruz-Migoni *et al.*, 2019). A comprehensive understanding of toxicological processes is vital for predicting adverse chemical reactions in patients. Specifically, for assessing liver toxicity, it's essential to evaluate dynamic biomarkers like transaminase in blood samples and determine the chemical concentration at the liver cell's hepatocyte location (He *et al.*, 2023). Observing dynamic biomarkers, such as variations in ECG or various depolarization patterns, aids in anticipating arrhythmias. Integrating diverse modeling techniques with liver metabolic profiling of chemicals enhances predictions related to cardiac or pulmonary toxicity.

Chemicals undergo absorption, transportation, metabolism, and elimination through PBPK models. Based on existing literature, these models incorporate foundational physiological and mechanical elements to forecast chemical concentrations in plasma and their action sites (Abouir *et al.*, 2021). Emphasizing the modeling of chemical responses, it's crucial to incorporate chemical transformations into metabolic models. Recently, there's been notable research into genome-scale metabolic networks, which simulate human metabolism across cellular, tissue, and organ levels. PBPK models are instrumental in projecting toxic metabolite concentrations in the liver amidst various disturbances,

like prolonged stress from exposure to specific hazardous environments (Maldonado *et al.*, 2017). This approach considers overall body metabolism, liver metabolic processes, and the expression of pivotal enzymes. Utilizing a protein's structural data can depict a response to chemical interaction variances.

Critical Properties of Nanoparticles(NP)

The harmful consequences of nanomaterials are caused by their diverse characteristics. The first step in developing a toxicity prediction model is to identify the features of NP that accelerate their hazardousness. The Organization for Economic Cooperation and Development (OECD) Nanomaterials working group produced a comprehensive list of important physicochemical parameters suitable for toxicological investigations (OECD, N. 2010). As a result, before starting with the QSAR technique, all potential quantifiers must be investigated. NP possess unique properties due to their small size, large surface area, and quantum effects, making them attractive for various applications. However, these distinctive features also raise concerns in nanotoxicology. The physicochemical characteristics, such as size, shape, surface charge, and composition, significantly influence the interactions of NPs with biological systems. For instance, smaller NP can penetrate cells more easily, while specific shapes might induce distinct cellular responses.

Surface modifications can alter NP toxicity, and their ability to generate reactive oxygen species can lead to cellular damage. Understanding these features is crucial for safe nanomaterial design and application. The size of NP, especially for materials like TiO_2 and nano-silver, significantly influences their toxicological impact. Smaller NP often demonstrate enhanced toxicity due to increased surface area per unit mass, facilitating greater interaction with biological systems. The size distribution of NP can affect their behavior within biological environments, influencing uptake, distribution, and potential adverse effects (Park *et al.*, 2011,Pettitt & Lead, 2013). Therefore, understanding the size-related features of NP is crucial for predicting and mitigating potential health and environmental risks associated with their use. NP exhibit shapes such as spherical, rectangular, long, and short rods. Their shape plays a crucial role in nanotoxicology. For instance, when elongated or long in structure, carbon nanotubes (CNT) and Silver NP tend to possess increased toxicity compared to their shorter counterparts. This increased toxicity arises from enhanced cellular interactions and altered biological responses (Monteiro-Riviere, N. A., & Tran, C. L. (Eds.). 2007,Gratton *et al.*, 2008). Thus, understanding the specific features of NP, including their shape, is vital for predicting and managing potential risks associated with nanomaterial exposure in various applications, from medicine to consumer products.

NP possess distinct crystal structure features that significantly impact nanotoxicology. Common structures like tetragonal, orthorhombic, and monoclinic structures are observed in materials such as TiO_2 and nanosilica. The intricate arrangement at the atomic level in these structures can influence how NP interact with biological systems. The toxicity of these NP may vary depending on their specific crystal structure. Understanding these structural nuances is crucial for predicting and managing the potential health and environmental impacts of nanomaterial exposure(Napierska *et al.*, 2010,Jiang *et al.*, 2008). NP exhibit unique properties due to their minuscule size, and one critical feature influencing their biological interactions is the surface charge. The charge of NP, whether positive, negative, weakly negative, or neutral, plays a pivotal role in determining their toxicity. Specifically, studies on Silicon NP and Silica NP have shown that negatively charged NP tend to be more toxic than their neutral or positively charged counterparts. This toxicity is attributed to increased cellular uptake and potential disruption of cellular functions. Understanding these charge-dependent toxicological effects is essential for safe and effective NP-based applications in various fields(Y.-H. Park *et al.*, 2013,Bhattacharjee *et al.*, 2010).

The features of NP significantly influence nanotoxicology, with surface functionality being paramount. NP surfaces can be intentionally functionalized or coated, such as with silver NP (Ag-NPs). This surface customization can modify the NP ' toxicological properties. The toxicity can either increase or decrease depending on the specific coating or modification. Thus, understanding and controlling the surface characteristics of NP is crucial for assessing their potential risks and ensuring safe applications in various fields, from medicine to environmental science(Zhao *et al.*, 2008,Caballero-Díaz *et al.*, 2013). NP possess distinct features influencing nanotoxicology. Depending on their aggregate phase, they can exist as solid, dry, liquid, or suspended entities (Figure 3). Their inherent propensity to interact and cluster together can lead to the formation of larger aggregates. This collective behavior significantly impacts their critical properties, including reactivity, solubility, and bioavailability. Understanding these aggregation dynamics is crucial in nanotoxicology, as it

determines how NP interact with biological systems and potentially influence cellular responses and toxicity outcomes. Hence, the collective nature of NP necessitates meticulous consideration in research and application contexts(Dhawan & Sharma, 2010,Boverhof & David, 2009).

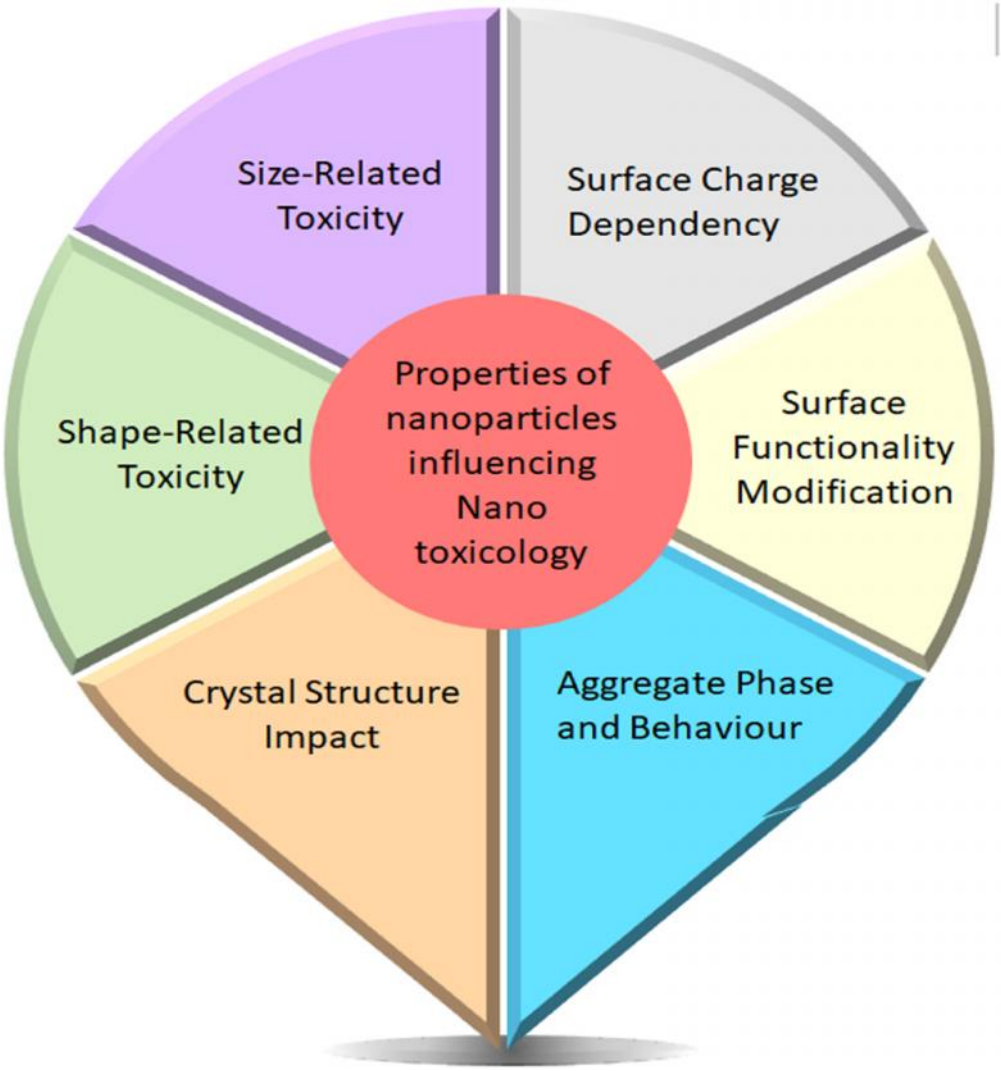

Figure 3: Properties of NP influencing nanotoxicology

Nano descriptor

More than just relying solely on physicochemical properties are required to create an effective computrequired Given the diverse nature of nano features; it's essential to consider nano descriptors (NP Descriptors). NP Descriptors encompass distinct attributes or a combination of a material's various traits(Burello & Worth, 2011). NP descriptors play a crucial role in determining their toxicity. The surface scope of NP refers to the extent of the exposed surface area, influencing interactions with biological entities. Aspect ratio, defining the length versus width of NP, can alter cellular uptake and responses. The shape of NP, whether spherical, rod-like, or irregular, can impact cellular interactions and pathways. Roughness influences surface interactions and potential damage. Additionally, the chemical ordering of NP affects their stability and reactivity, further influencing their toxicological profile(Glotzer & Solomon, 2007). "NP descriptors affecting toxicity" suggests that certain NP characteristics influence their toxicity. The subsequent mention of "Pixels, RGB codes, Grayscale" points to the methods used for image analysis. Pixels represent the smallest unit of a digital image, while RGB (Red, Green, Blue) codes define color. Grayscale refers to images in shades of gray, representing intensity. These descriptors aid in quantifying and understanding the toxicological

implications of NP by analyzing their structural and color attributes in microscopic images(Puzyn *et al.*, 2009).

The Biological Surface Absorption(BSAI) Index emphasizes the significance of molecular properties in biological contexts. Polarity, a key feature, relates to electron density distribution within a molecule, influencing its interactions with biological entities. Lone pair electrons, often present in certain functional groups, play pivotal roles in ligand-receptor interactions and molecular recognition. Molecules acting as hydrogen bond acceptors and donors can engage in essential bonding events within biological systems, influencing processes like protein folding or DNA structure(Xia *et al.*, 2010). These properties underscore the intricate interplay between molecular characteristics and biological responses. NP descriptors affecting toxicity span a wide range of properties.

In the context of the Spectra Category, both Infrared (IR) and Ultraviolet (UV) interactions play pivotal roles. Infrared absorption bands indicate vibrational modes, revealing NP' molecular structure and potential reactivity. On the other hand, UV interactions signify electronic transitions, offering insights into the energy states and potential photoactivity of NP. Together, these spectral analyses provide crucial data for predicting NP toxicity, aiding researchers in designing safer NP with reduced environmental and biological impacts. Understanding these descriptors is vital for advancing nanotechnology's responsible application(Nallappan *et al.*, 2023). The descriptors that influence toxicity within the realm of NPstudies emphasize the methodologies of NPdevelopment, combination, and transformation. These techniques likely play pivotal roles in determining NP' biological and environmental impacts. Understanding these descriptors is crucial for assessing NP applications' potential risks and benefits. It provides a structured approach, ensuring that researchers can systematically evaluate and compare the toxicity profiles of various NPformulations(Epa *et al.*, 2012).

Image-Based Toxicology Database

High-content image-based screening in toxicology involves employing advanced imaging techniques to analyze a vast array of cellular or molecular changes caused by various substances. This method enables comprehensive assessment, examining toxicity effects within biological systems at the molecular level. Capturing and analysing numerous data points from images facilitates precise toxicity evaluations, aiding drug development, environmental assessments, and understanding of chemical impacts on organisms(Lin *et al.*, 2020). Leveraging automated imaging technologies, this approach expedites the identification of toxic compounds or their mechanisms of action. It provides a robust platform for in-depth toxicity studies, offering insights crucial for drug safety assessments and environmental risk evaluations." The high-content image-based screening (HCIBS) is also used in phenotypic drug discovery that utilizes biological images to study specific compounds or details within cells and tissues(Singh *et al.*, 2022). This approach provides visual images of cells or tissues and numerical data regarding the observed cellular characteristics. Such data is gathered from cells or tissues exposed to various substances or environments to pinpoint cell behaviour or genetic activity alterations. Using HCIBS data, researchers can create models that enhance the precision of toxicological forecasts(Kawaguchi *et al.*, 2019).

AI in ADMET Modelling

The compounds that exhibited promising qualities were subsequently analyzed for their pharmacokinetic behaviors, metabolic processes, and possible adverse reactions, with the latter being frequently identified. As biological assessments and chemical production have grown, there's been a significant rise in the need for early insights into absorption, distribution, metabolism, excretion, and toxicity, collectively referred to as ADMET data(Stefaniak, 2015). A growing demand for dependable tools that forecast these properties, addressing primary objectives. Many in vitro tests are automated through robotics and miniaturization due to advancements in high throughput (HTP) technologies. Silico models help choose the right tests and pinpoint specific compounds for screening. Advanced predictive models are emerging, which potentially supplant in vitro tests and in vivo studies.

A deep comprehension of physicochemical attributes and their assessment and anticipation is essential for a thriving nanomedicine initiative(van de Waterbeemd & Gifford, 2003). There are two distinct methods to forecast potential nanotoxicology concerns using in silico models. The initial method relies on models constructed from collecting and structuring human insights and scientific studies(Cohen *et al.*, 2012). The second approach evaluates chemical structure descriptors and examines the connections between these descriptors and nanotoxicological outcomes(Richarz *et al.*,

2015). To simplify the extraction and analysis, there's a need for advanced tools and methods that handle metadata and semantic representation. These can enhance the initial methods used.

Open-source and free software provide platforms for automatically extracting and enhancing various structural and semantic details from scientific data. When comparing different age groups, like adults and children, physiological parameters such as breathing rate and pattern are often considered, but morphological variations within internal organ systems are typically overlooked. Understanding NP effects on cancer stem cells is pivotal for cancer therapy advancement and ADMET modeling (Absorption, Distribution, Metabolism, Excretion, and Toxicity) facilitates predicting a substance's behavior within biological systems, enhancing drug development. Integrating AI-driven ADMET models with nanotoxicology helps ensure safer nanomaterials, potentially revolutionizing cancer stem cell treatment through targeted interventions at the cellular level(Somenath Ghosh *et al.*, 2023,Kanathasan et.al., 2023).

Challenges

Nano QSAR requires significant dedication at each stage, from data preparation to model creation. A primary obstacle is the limited availability of comprehensive experimental data. This scarcity stems from challenges in standardizing toxicity testing techniques and defining NP properties. Properly characterizing NP is crucial for understanding the link between their structure and biological effects and accelerating the analysis of engineered nanomaterial(Mu *et al.*, 2014).

Advancements in modeling interactions between ligands and proteins are paving the way for enhanced nanomaterial design. Utilizing ML techniques is crucial for refining nanomedicine applications. A major obstacle in designing nanomaterial libraries is the limited computational resources to forecast ligand-metal interactions, such as the binding sites between amphiphilic amino acid ligands and gold ions (Singh *et al.*, 2020). These predictions are vital for determining the ultimate structure and dimensions of the resulting nanostructures. The accuracy of any predictive model hinges on its foundational assumptions and often necessitates some level of trade-off. Establishing standardized computational models that gather experimental data and transform it into consistent formats is essential for subsequent predictive modeling.Nanotoxicology has challenges to explores the impact of NP on living organisms.

NPs' unique properties raise concerns about their potential toxicity. Insight into their behavior within biological systems aids risk assessment. Green synthesis, employing eco-friendly methods, ensures safe NP production. This sustainable approach minimizes environmental impact (Sharma *et al.*, 2022). Such advancements herald a new era in medicine, promising more effective and tailored therapies.

Conclusion

In conclusion, the integration of AI into nanotoxicology heralds a transformative era in biomedical sciences, biotechnology, biochemistry, biology, and related fields. This symbiotic relationship between AI and nanotoxicology empowers researchers with unprecedented insights, accelerating our understanding of the complex interactions between NP and biological systems. AI-powered tools facilitate precise predictions of NP behavior, toxicity mechanisms, and potential risks, enhancing safety assessments and guiding the design of safer nanomaterials. This synergy promises breakthroughs in drug delivery, diagnostics, and environmental health. As AI continues to evolve, its influence on nanotoxicology will undoubtedly reshape research paradigms, driving innovation and fostering a safer, more sustainable future.

Acknowledgement

Authors are thankful to the management of Kristu Jayanti College, Bangalore, Karnataka, Guru Nanak Institute of Pharmaceutical Science and Technology, Kolkata and Surya School of Pharmacy, Vikiravandi, Tamil Nadu, India for giving necessary permission to complete the present study.

Conflict of Interest:

Conflict of interest declared none.

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