RESEARCH PAPER

Integrating Pharmacogenomics with Green-Synthesized Nanoparticle Platforms for Personalized Cancer Therapy

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ABSTRACT

Background

Nanoparticles (NPs) synthesized with green reagents are an innovative concept of individualized cancer treatment in precision nanomedicine that links eco-friendliness and design for therapy. They use phytochemicals, microbial metabolites and biopolymers to replace the traditional reducing and capping agents of these NPs; and such nanoparticles have proven to be biocompatible and very stable with no harm to nature.

Methods

A systematic review of the literature was conducted according to PRISMA standards using PubMed, ScienceDirect, and Frontiers databases over 2018-2025. Discussion centered on green synthesis techniques (to achieve sustainable harmony of nanostructure, function and materials) and their functionalization towards personalized drug delivery results with a focus on biological characteristics of the structurally modified receiver system as well as receptor-based current pharmacogenomic judgments.

Results

Nanoparticles synthesized by green routes show in comparison with conventional methods greater receptor (folate, transferrin and HER2) overexpressing tumor cell-targeting selectivity and significantly improved effectiveness in vivo. Functionalized nanovehicles carrying siRNA or miRNA into being multi-targeting agents to many of the major genetic mutations in cancer, such as p53, EGFR and Caspase-3, underscore their potential application in genotype-tailored nanotherapy.

Conclusion

Green nanotechnology offers a new hope for genomics-based personalized medicine needs to be further built upon. It will require the standardization of synthesis processes, the introduction of AI-based optimization systems, and expansion into toxicogenomics databases, in addition to building a model to help with personalized clinical trials so that materials are safe and regulatory compliant across all patients.

Keywords: Pharmacogenomics, Green-synthesized nanoparticles, Personalized cancer therapy, Targeted nanomedicine, Gene-specific delivery, Sustainable nanotechnology, Precision oncology, siRNA / miRNA therapeutics

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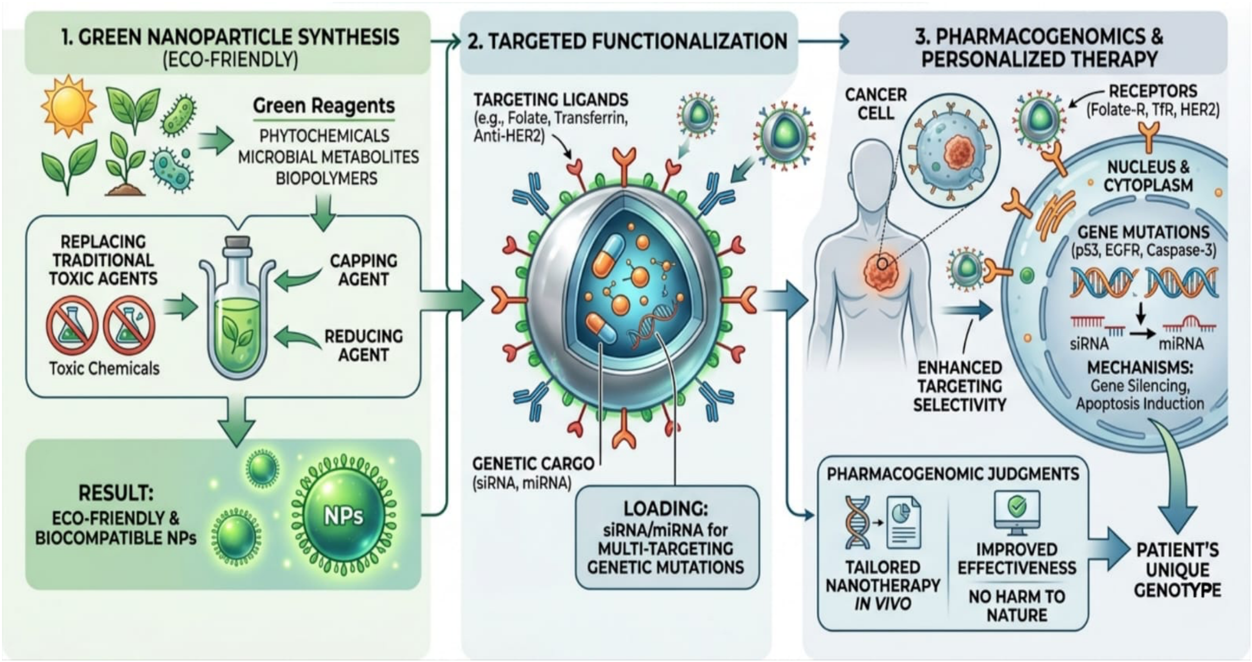

1. Introduction

Nanoparticle (NP)-mediated material delivery has fundamentally changed therapeutic tactics, offerin controlled release of drug or contrast agents and the possibility to increase bioavailability as well as site-specific targeting of these agents and others through the use of higher molecular weight recognition elements, thus increasing effectiveness while lowering side effects [1],[2]. Conventional physical and chemical synthesis strategies often involve toxic reagents, high energy input, as well as the production of toxicity by-products, which may pose environmental and biocompatibility issues when translate into clinical applications [3]. Green synthesis, involving a biologically mediated reduction of nanoparticles through plant extracts, microbes or other biological sources instead provides environmentally friendly approach by utilizing natural reducing and capping agents such as flavonoids, polyphenols, proteins and others to fabricate biocompatible nanomaterials at mild conditions [4],[5][6].

Plant-mediated nanoparticles synthesis is particularly appealing due to the ability of large-scale production, low cost, and intrinsic functionality conferred by phytochemical capping agents that may enhance colloidal stability and biological interaction [7][8][9]. The recent achievement of plant-made nanocarriers and exosome-like nanoparticles derived from plant origins is presenting emergent promising functions in targeted delivery, controlled release, and immunomodulation that could be adapted for patient-specific solutions [10][11][12].

Incorporation of green-synthesized nanoparticles into personalized drug delivery entails tailoring nanoparticle size, surface chemistry and ligand conjugations according to personal disease biomarkers or microenvironmental triggers (e.g., tumor pH and receptor expressions) to achieve improved targeting ability with a reduction in off-target effects [13][14][15]. Here, green nanocarriers responding to stimuli and ligand-conjugated biogenic nanoparticles have exhibited promising preclinical results in the field of oncology and antimicrobial applications, suggesting a potential to translation [16][17][18].

However, there exist numerous obstacles for clinical translation: the variability of plant growth and a long maturation period of plants across batches makes reproducibility difficult; scale-up under precise regulations remains problematic; and full in vivo toxicology or ultimate fate studies on biogenic NPs are limited [19][20][21].

2. What Constitutes a Nanoparticle?

Nanoparticles (NPs) are defined as materials with a size of 1 to 100 nm in at least one dimension that demonstrate physicochemical, optical and mechanical properties distinct from those of larger bulk components, and which fall under the submicrometer category [23],[24]. The large surface-area-to-volume ratio and control of surface chemistry of NPs gives rise to increased reactivity, and enables the NPs to interact selectively with biological systems [25],[26]. Nanoparticles are metallic, oxide-metallic, polymer-lipid or hybrid depending on its composition and these possess unique characteristic properties in regards to medical applications [27].

Biological sources including plant extracts, microorganisms and biomolecules in green synthesis serve as biogenic reducing and stabilizing agents ultimately leading to the formation of biological friendly nanoparticles with a high degree of biocompatibility for less environmental consequence [28],[29]. Phytochemicals: Here comes another important part, that is, phytochemicals isolated from the plants plus. These plant derived phytochemicals such as flavonoids., polyphenols., terpenoids and proteins have dual function like reduction of metal ions (active functional groups) along with natural capping agent for controlling size, shape as well as surface charge of nanoparticles[30],[31].

Physicochemical characteristics of NPs, including size, zeta potential, and surface ligands are critical factors in biodistribution, cellular uptake and pharmacokinetics [32] [33]. Smaller size NPs (<100 nm) can be better penetrate biological barriers, while surface charge influence serum protein adsorption and circulation half-life [34],[35]. Surface functionalization with biocompatible polymers or ligands for targeting, receptor-mediated uptake at pathological site provides a tool to customize and target drug delivery [36], [37]. Such design principles are especially important in sustainable nanomedicine, where plant produced NPs can be designed to match individual patient's genetic and metabolic profiles, thereby enhancing therapeutic precision and reducing side effects [38][39] [40].

3. Methods for Nanoparticle Fabrication

Traditionally, processing of nanoparticles was based on physical (e.g., laser ablation, evaporation–condensation) and chemical (e.g., sol–gel, chemical reduction) processing methods in order to obtain materials with controlled morphology and size [41],[42]. Even though these traditional routes can produce homogeneous NPs, they usually suffer from toxic solvents, high cost of energy, and aggressive reducing agents, which are not suitable for clinical application [43], [44]. In comparison, green (or biogenic) synthesis has recently been developed as an efficient, cheap, and biocompatible alternative that involves biological systems to reduce and stabilize nanoparticles [45].

3.1 Green and Biogenic Nanoparticle Synthesis

Green synthesis refers to the process that involves using plants, microorganisms, algae, or biomolecules as environmentally friendly reducing agent and capping agents for synthesizing metal or metal oxide nanoparticles [46]. During plant mediated synthesis, phytochemicals such as polyphenols, flavonoids terpenoids and proteins serve as electron donor reducing metal ions (e.g., Ag^{+}, Au^{3+}, Zn^{2+}) into inherent nanoparticulate forms catalysis [47][48] and natural encapsulating agents for stabilization. Microorganisms (e.g., bacteria and fungi) are a resourceful means for the production of enzymatic and metabolic agents that enable intracellular or extracellular formation of NPs in an eco-friendly, solvent-free manner at mild conditions [49].

These biogenic nanoparticles present superior biocompatibility, low cytotoxicity, and natural functionalization making them suitable for medical applications at individual level [50][51]. The natural 'biomolecular corona' enveloping green-synthesized nanoparticles provides selective intracellular internalization as well as better pharmacokinetic profiles compared to their chemically fabricated counterparts [52][53]. In addition, biogenic synthesis offers the potentiality to reproduce nanoparticles in a cost-effective greener method under ambient conditions with less ecological footprint meetng green nanotechnology and susta inable healthcare [54].

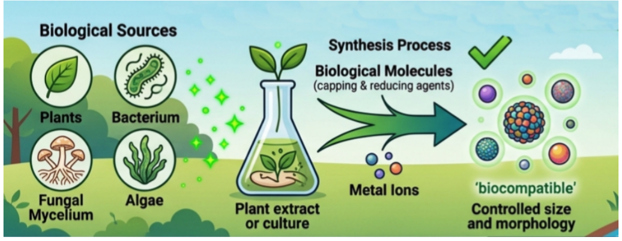

Figure -1: Green and Biogenic Nanoparticle Synthesis

3.2 Surface Modification and Functionalization

One of the significant benefits of green-based synthesized nanoparticles is that their surfaces are directly modified to bind targeting peptides or ligands and/or those antibodies, which leads to site-specific drug delivery [55][56]. The phytochemicals-induced functional groups on the nanoparticles (e.g., hydroxyl, carboxyl and amine) are reactive for the conjugation with biomolecules including folic acid, HER2 or EGFR antibody that enable the nanoparticle to selectively target cancer cells that overexpress these receptors [57][58]. This approach maximizes treatment benefit with reduced systemic toxicity or offsite effects.

Surface engineering can additionally be used to make nanoparticles responsive to physiological stimuli, including pH, temperature, and redox state, for controlled drug release at the site of disease [59].

4. Biological Pathways for Green Synthesis

Green synthesis is the production of nanoparticles from natural materials, such as plant extracts. Compared to traditional chemical approaches, biological routes are generally conducted at mild conditions that reduce toxic byproducts and provide nanoparticles with biomolecules adsorbed on surface for better biocompatibility as well as functionality[60][61]. A number of organisms such as Bacteria, Fungi, Yeast, Algae and Plants have been studied for green synthesis of metal and metal oxide nanoparticles.

4.1 Bacteria-Mediated Nanoparticle Synthesis

Depending on the reaction between the metal ions and bacterial enzymes, bacteria may biosynthesize nanoparticles intracellularly or extracellularly. Enzymes including nitrate reductase, de-hydrogenase, hydrogenase etc., reduce ionic metals (Ag^+, Au^{3+} and Pd^{2+}) to stable devic-es often in assistance with chemicals as biomolecules from the secretions form natural capping [62][63]. The as-obtained nanoparticles exhibit high stability and tunable morphology.

Recent investigations have reported that certain bacterial strains such as Bacillus subtilis and Pseudomonas aeruginosa are capable of synthesizing silver and gold nanoparticles having antimicrobial and anticancer activity [64][65].

These biologically produced NPs possess surface functional groups, which can even be further modified to employ for receptor-targeted drug delivery [66].

4.2 Fungi-Mediated Nanoparticle Synthesis

Fungi have high metal tolerance, large biomass and enzyme or metabolite secretion for reduction and stabilization (8) that make them efficient biofactories of nanoparticulate production. The species such as A. niger, F. oxysporum and P. chrysogenum have received much attention due to their ability to extracellular synthesis of silver (Ag), gold (Au) and zinc oxide (ZnO) nanoparticles [67][68].

The fungal proteins and polysaccharides provide the resulting colloids with stability and biofunctional groups for biomedical conjugation.

These myconanoparticles have biomolecule-coated surfaces, which can be further modified for receptor-specific or ligand-directed drug delivery.

4.3 Yeast-Mediated Nanoparticle Synthesis

Another environmentally benign biological method is the yeast-mediated synthesis, which utilizes the metabolic and enzymatic systems of the organism. Yeast such as Saccharomyces cerevisiae can sequester and transform metal ions by utilizing NADH-dependent reductases to transfer electrons, resulting in NP particles with a fairly homogenous distribution [69].

In this context, path via S. Typhimurium seems to have advantages in terms of homogeneous and size-controlled particles with narrow distribution and better reproducibility than with other microbial systems.

The yeast-based nanoparticles are coated with biomolecules, which can be programmed for site-specific targeting via antibody/peptide conjugation [70].

4.4 Algae-Mediated Nanoparticle Synthesis

The algae serve as reducing and capping agent due to the presence of proteins, polysaccharides and secondary metabolites. Marine and freshwater algae, e.g., Sargassum muticum, Chlorella vulgaris and Spirulina platensis have been used for the biosynthesis of Au-NPs, Ag-NPs as well as ZnO molecules [71][72].

Extraction of algae allows accelerated bioreduction and results in NPs with interesting optical and catalytic features.

Nanoparticles formulated using algal-mediated route and with naturally functionalized surface are reactive sites, which can be exploited for targeted or receptor-based drug delivery systems[73].

4.5 Plant-Mediated Nanoparticle Synthesis

For green nanoparticle synthesis, plants are the most studied biological system because of their rich storehouse of bioactive phytochemicals. Phenolics, flavonoids, terpenoids and alkaloids are reducing and stabilizing agents that allow the synthesis of NPs at room temperature [74]. This method is fast, scalable and nontoxic, which is desirable for the application of biomedicine. Nanoparticles of plant origin have shown significant antioxidant, antimicrobial and anticancer activities and may be included in drug delivery systems. The surface phytochemicals of these plant-synthesized nanoparticles can act as natural linkers between antibodies, ligands or peptides that could improve targeted therapeutic delivery [75].

5. Synthesis and Characterization

The synthesis of green nanoparticles typically involves the bioreduction of metal salts by plant extracts, microbial metabolites, or other natural agents containing polyphenols, flavonoids, terpenoids, and proteins that act as both reducing and stabilizing agents [76][77][78]. The selection of biological source and reaction parameters—such as pH, temperature, precursor concentration, and extract composition—directly influences nanoparticle morphology, particle size distribution, and surface chemistry [79][80]. These factors are critical because the resulting physicochemical characteristics determine not only material stability but also biological compatibility and drug-loading efficiency [81].

Characterization plays a pivotal role in linking synthesis conditions to biomedical functionality, especially for personalized and targeted drug delivery. A comprehensive understanding of nanoparticle properties enables prediction of in-vivo behavior and optimization of therapeutic performance. Dynamic light scattering (DLS) is widely employed to determine hydrodynamic diameter and polydispersity index, parameters closely associated with biodistribution, circulation half-life, and clearance pathways [82][83]. Zeta potential analysis provides information on surface charge, which governs colloidal stability and influences electrostatic interactions with cell membranes, plasma proteins, and target tissues [84].

Fourier transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS) confirm the presence of functional groups or biomolecular coatings derived from green synthesis, which can be exploited for further conjugation with targeting ligands such as folic acid, antibodies, or aptamers [85][86]. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) provide detailed visualization of particle shape, crystallinity, and size uniformity, while energy-dispersive X-ray (EDX) spectroscopy validates elemental composition [87].

Beyond structural confirmation, characterization data increasingly inform precision-medicine design. Understanding how nanoparticle size, charge, and surface chemistry modulate cellular uptake and intracellular trafficking allows researchers to tailor nanocarriers for specific disease phenotypes or genetic signatures [88][89]. For instance, nanoparticles optimized for passive tumor targeting through the enhanced permeability and retention (EPR) effect may be modified to incorporate ligands recognizing receptors overexpressed only in certain molecular subtypes of cancer [90]. Likewise, assessing nanoparticle–cell interactions using flow cytometry or confocal microscopy can reveal selective uptake in genetically distinct cell populations [91].

6. Applications of Green Nanoparticles in Personalized and Targeted Therapy

6.1 Personalized and Targeted Drug Delivery

Green nanoparticles can also be functionalized for receptor-mediated targeting to selectively target and internalize cells over-expressing particular receptors (e.g., folate receptor, transferrin receptor, HER2). For example, plant-based gold or silver NPs prepared by green approaches can be functionalized with folic acid or antibodies which target tumour-specific markers, to trigger selective delivery. Recent reports for green synthesized metal NPs indicated potential in targeted cancer therapy with the use of tumor-targeting ligands for increased specificity [92].

Specifically, in a pharmacogenomic context the MDR is determined by genetic polymorphism of target receptors, transporters or metabolic enzymes altering the import, intracellular trafficking and metabolism of NPs. Therefore, the nanocarrier design could be adapted to patient genotype. For instance, a green-synthesized NP functionalized with anti-HER2 ligands may allow targeted delivery of therapeutic payloads to such cells but not the normal ones in the case when the tumor is overexpressing HER2 because of gene amplification.

For instance, green-produced silver nanoparticles (AgNPs) have been investigated in colon cancer treatment and present selective cytotoxic effect when compared to AgNPs produced by chemical methods that can be exploited for targeted delivery on genetically predisposed cancers [93]. Another example of ARNPs are green NPs loading curcumin or anticancer drugs plus stimuli (such as ultrasound) to realize tumor site targeted release [94].

Therefore, green NPs platforms offer an environmentally sustainable template enabling to tailor patient-specific ligand selection, dosage regimens and combination of payloads in precision medicine.

6.2 Cancer Nanotherapy and Gene-Specific Targeting

In addition to targeting, nanoparticles synthesized with green methods can be internalized and used to deliver gene-silencing agents like siRNA or miRNA for gene-specific treatment. Bioengineered nanomaterials are currently being studied for carrying siRNA to suppress oncogenes or drug resistance genes in cancer cells. 4, 26 For instance, stimulus (pH, redox)-responsive multifunctional NPs have been applied to the targeted gene silencing in cancer therapy using chemotherapeutic and siRNA for resistance overcoming[94].

Green NP systems may incorporate this gene therapy idea. As an example, green synthesized AuNP or AgNP could be surface-functionalized with the help of siRNA for harboring gene such as EGFR, p53 or Caspase-3 (mutant) cancer cell. Such a system could release the gene-silencing payload systemically in only tumor cells and potentially restore aberrant pathways depending on genotype. Such an integration is also supported by recent work on stimuli-responsive multifunctional nanoparticle systems for gene silencing [95].

6.3 Toxicity and Biocompatibility in a Personalized Context

With personalized treatment, interindividual variability in metabolism, immune response, and handling of clearance must be taken into account. Patients how have different reticuloendothelial systems, renal clearance or enzymatic degradation systems Thus the fate and toxicities of NPs are different. The green synthesis procedure possesses some benefits such as the capping of the green NPs by natural biomolecules that could lead to diminution against unpredicted immune responses, oxidative stress or genotoxic side effects that would be due to chemically synthesized particles.

Furthermore, green-synthesized NPs have shown superior biocompatibility and lower cytotoxicity in comparative studies as well. For instance, in colon cancer models, green-synthesis AgNPs exhibited more desirable safety profiles compared to chemical-synthesis AgNPs . A different study on the green metal NPs for wound healing also points the relatively safety and reduced cytotoxic byproducts [96].

Nevertheless, individual susceptibility remains a factor contributing to personalized nanomedicine – for instance, an individual with renal dysfunction patients have already been demonstrated to clear NPs more slowly than those with normal function and may also experience inflammation or harbor genetic polymorphisms in detoxifying enzymes (such as glutathione S-transferases) that might affect their response(s) following NP exposure. Genotype-stratified in vivo studies should hence be included in toxicity testing. By virtue of reducing un-reacted toxic reagents or harsh stabilizer, green synthesis supports safer clinical translation in different patient populations.

7. Future Perspectives and Challenges

The intersecting point of green nanotechnology and personalised medicine is considered one of the potential frontiers of sustainable healthcare. Although considerable advances have been made in regards to the biogenic synthesis of NPs, a number of scientific, regulatory, and translational challenges need to be overcome before these materials can seamlessly find their place in precision drug delivery applications.

7.1 Integration with Pharmacogenomics and AI-Driven Personalization

The next level of this development will clearly depend on the integration of pharmacogenomic data, along with nanocarrier design considering patient's genetic polymorphisms in terms of drug metabolism, receptor availability or immune recognition. Machine learning algorithms incorporating artificial intelligence (AI) and machine learning (ML), processes patient data DNA/genome, transcriptome/proteins, the metabolome can predict the individual therapeutic response to a therapy and thereby guide optimization of nanoparticle parameters like size, charge, ligand type or release kinetics [97].By predicting NP–cell interactions using AI, orogenetic heterogeneity among NP–cells could be modeled in silico in a dataset-independent fashion which would render targeted treatment safer and more effective prior to clinical investigation [98].

7.2 Personalized Toxicity and Biocompatibility Assessment

Although green synthesis minimizes toxic chemicals use, the individual toxicity is still a major issue. Differences between individuals' oxidative stress responses, immune activation and clearance pathways can modify nanoparticle safety. Standard cytotoxicity tests may not reflect in vivo responses between different genetic backgrounds. Novel models such as organ-on-a-chips devices or genome-edited cell lines can be used to simulate patient-specific adaptation, and the capacity of these technologies may contribute to further validate nanotoxicogenomic signatures [99].

7.3 Standardization, Scale-Up, and Regulatory Barriers

The batch-to-batch variation is one of the bottlenecks in bringing green nanoparticles to clinics. Variations in the nature of biological source (determination from plant's age, season, and extraction protocol) may reduce reproducibility of its physicochemical properties [6]. Preparation of standardised extraction protocols, nanoparticle purification and surface characterisation are necessary to achieve reproducibility and regulatory acceptability. Furthermore, green nanocarriers need to be prepared in compliance with Good Manufacturing Practice (GMP) for mass clinical translation.

There is no mature regulatory system with regard to personalized nanomedicine. Near future strategies should integrate sustainability criteria, assessment of biogenic material safety and patient-specific streamlined approval procedures which recognize the dynamic nature of biologically produced nanomaterials.

7.4 Predictive and Smart Nanocarrier Design

For the future, bio-safe intelligent next-generation nanocarriers will incorporate sensing/receptive materials that can interact with patient biomarkers in real time [100]. Green-synthesized NPs functionalized with biosensing ligands or responsive coatings (e.g. pH, redox and enzyme-sensitive) may dynamically tailor drug release based on the molecular context of the disease microenvironment [101]. The integration of these materials with AI-powered predictive modeling will enable clinicians to predetermine personalized treatment courses, reducing the guesswork in dosing and increasing therapeutic accuracy.

7.5 Translational Outlook

Clinical adoption will require the collaboration of material scientists, clinicians, computational biologists and regulatory authorities. Green nanotechnology offers an eco-friendly approach to the development of biocompatible, low-cost and patient-specific nanomedicine. But if this vision is to be realized the field needs to evolve from proof-of-concept studies into integrative clinical pipelines that combine green chemistry, systems biology and digital health solutions.

8. Conclusion

Their biogenic coatings are enriched with natural ligands for receptor-specific targeting and improved pharmacokinetics but reduced systemic toxicity. Green synthesis of nano coatings, researchers combine in vitro methods of drug development with what they find by looking at metabolic cycle genes when studying these kinds of nanoparticles, managing sourcing and manufacture process problems. Genomic technologies make it possible to then identify every person who undergoes drugs built from green nanocarriers according not only to his or her own molecular signature but also in terms Of phenotypic information. Running clean green technology extract process instruments requires both consistent and reproducible synthesis as well as comprehensive toxicogenomic validation. Despite the considerable challenges, injection of these particles into the human body remains inherently uncertain. AI-driven design and Pharmacogenomics in combination promise safe and precise dosing. Reinventing the brakes for green nanotechnology makes it both sustainable and ethical. It combines integrated pharmacogenomics with an existing branch of science that's on the brink of revolutionizing both personalized drug delivery and precision oncology.

Conflicts of interest –Author declare there are no Conflicts of interest

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