IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)
An International Open Access, Peer-reviewed, Refereed Journal

Biomedical Applications of Plant Mediated Multimetallic Nanoparticles

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Abstract: Innovative multimetallic nanoparticles (NPs), comprising two or more metals arranged in alloy or core–shell configurations, have gained considerable attention for their distinctive functionalities. The synergistic interplay between various metals enhances their multifunctionality and efficacy. With the growing need for versatile and efficient nanoparticle agents, multimetallic NPs are particularly gaining popularity. These integrate various functional materials to achieve tailored size, structure and multiple functionalities. Compared to monometallic counterparts, bimetallic and trimetallic NPs often demonstrate improved chemical, optical, biomedical applications due to the synergistic effects. These applications span various medical fields such as antibacterial treatments, anticancer therapies, biological imaging and drug delivery. This review presents a focused look at bimetallic nanoparticles (BNPs) and trimetallic nanoparticles (TNPs) synthesised from plant extract and their biomedical applications—antimicrobial, anticancer, wound healing and diabetes management—showing significant feature enhancements over monometallic nanoparticles and other current biomedical nanomaterials.

Keywords: Green synthesis, plant-based synthesis, bimetallic nanoparticles, trimetallic nanoparticles, bio medical applications

I. INTRODUCTION: The past few decades have seen significant synthesis and investigation of metallic nanoparticle (NP) based systems, with a strong emphasis on their biomedical applications [1,2]. Metallic nanoparticles are classified by their composition, including single-metal (monometallic) and multiple-metal types (multimetallic such as bimetallic, trimetallic or tetrametallic). Beyond monometallic nanoparticles, bimetallic nanoparticles (BNPs) and trimetallic nanoparticles (TNPs) have garnered significant research interest due to their modifiable high surface to volume ratio and biocompatibility [3,4]. These biocompatible multimetallic nanostructures are utilized in numerous biomedical applications, functioning as antibacterial agents [5,6], anticancer treatments [7], improved drug encapsulation [8], drug delivery systems [9], imaging tools [10] and sensing [11]. That's why the number of nanotechnology publications has seen a remarkable increase, reflecting the high expectations that mastering this technology will lead to advancements across all facets of modern life, particularly in medicine. Beside these, comparing to their monometallic counterparts, BNPs and TNPs often exhibit superior catalytic activity [12,13], enhanced antimicrobial effects [14,15], diverse morphologies [16,17], highly selective and sensitive detection capabilities, good stability and enhanced chemical transformation abilities. These advantages arise from the synergistic or multifunctional effects of the two or three metals within the BNPs and TNPs [18]. The presence of multiple metals also allows for various morphologies and structures, including core-shells [16], alloys [17], Janus [19], heterostructured [4], doped NPs [20]. Nanomedicine exemplifies the use of nanotechnology in biomedical research, aiming to enhance diagnosis, treatment and monitoring—ideally with greater accuracy, fewer side effects and non-invasive evaluation [21]. Nanotechnology offers both improvements to existing methods and innovative tools. By manipulating drugs at the nanoscale, their properties—such as solubility [22], bioactivity [23] and release profiles—can be precisely controlled. This enables targeted delivery, extended circulation time and environment-responsive release. Additionally, the high surface area of nanoparticles can be leveraged for increased functionality in therapeutic and diagnostic applications. BNPs and TNPs have generated significant research interest for their promising role in diagnosing and treating serious diseases, leading to potential biomedical applications [24]. Recent emphasis in the biomedical field on early disease diagnosis for improved human health has positioned BNPs and TNPs systems as a foundation for early cancer detection. The anticancer and antibacterial effectiveness of these nanomaterials is closely linked to their shape, size and composition. Enhancements in these activities are achieved through optimized composition, conjugation with appropriate ligands, suitable shape/size, and interactions at the metal interfaces. Nanoparticles enhance drug absorption and delivery in pharmaceuticals, often alongside medical devices. Nanoparticles can target chemotherapy drugs to specific cells, such as cancer cells. Superparamagnetic iron oxide nanoparticles (SPIONs) and ultrasmall superparamagnetic iron oxide (USPIO) are also significant for targeted drug delivery [25]. With cancer deaths projected to reach 13.1 million by 2030 (IARC), the low survival rate highlights the critical need for advanced drug delivery systems [26]. The issue isn't a lack of effective antitumor agents, but rather their inadequate delivery. Therefore, developing carriers for targeted and efficient delivery of chemotherapeutics, minimizing systemic side effects, is crucial [27].

Traditionally, nanoparticles were synthesized using harsh chemicals and energy-intensive processes. However, increasing environmental concerns have led to the growing adoption of greener synthesis approaches that are more sustainable and eco-friendlier. Green synthesis of nanoparticles offers an eco-friendly, cost-effective alternative to traditional methods by utilizing renewable plant extracts as both reducing and stabilizing agents [28]. These extracts transform metal ions into stable nanoparticles with controlled size, shape and surface properties, while avoiding harmful chemicals and excessive energy use. This biocompatible approach is ideal for biomedical and environmental applications and it supports scalability and property customization for various uses. This review outlines biomedical applications of bimetallic and trimetallic nanoparticles in medical field.

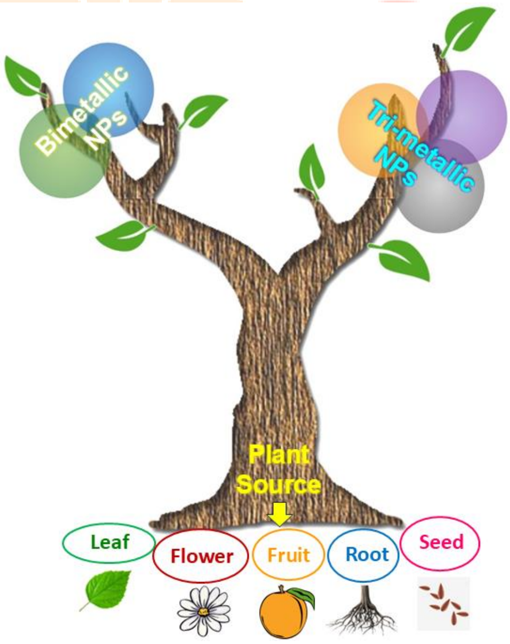

Figure 1. Plant extracts mediated bimetallic nanoparticles (BNPs) and trimetallic nanoparticles (TNPs) from different plant source

II. BIMETALLIC NANOPARTICLES: Bimetallic nanoparticles (BNPs) composed of two metals, are increasingly vital in biomedicine. Their unique properties arise from synergistic effects [29], allowing researchers to combine metals for enhanced functionalities over single-metal NPs. Designed as alloys [30] or core-shells [16], BNPs offer precisely tunable physical, chemical and biological behaviours, leading to improved catalytic [12], antimicrobial [14], optical and magnetic properties [31]. Their adjustable features enable optimization for specific biomedical uses, including multifunctional applications like drug delivery and imaging. Certain noble metal combinations exhibit good biocompatibility and low toxicity for in vivo applications.

In recent years, bimetallic nanoparticles (NPs) with alloy or core-shell structures have gained significant attention for their diverse uses in catalysis, biomedicine, and environmental applications. To synthesize these nanomaterials in a green, non-toxic and cost-effective manner, utilizing natural resources, particularly plants, has become crucial. Environmentally friendly methods for producing Ag-Au and Au-Ag NPs, which combine silver (Ag) and gold (Au) in core-shell or alloyed forms, are notable examples. These structural variations enhance their optical, catalytic and biocompatible properties, making them highly suitable for biomedical applications, catalysis, and sensing technologies. Table 1 showcases a range of bimetallic systems, including Ag-Pt, Ag-Pd, Au-Pd, Au-Pt, and Pt-Co, highlighting studies on their green synthesis and potential applications.

Table 1: Plant Mediated Synthesis of Bimetallic Nanoparticles

Nanomaterials type & Morphology	Plant Source	Size (nm)	Applications	References
Ag-Au Spherical, triangular, rod	Solidago canadensis (Canada goldenrod) Leaf Extract	Av. size ~15	Cytotoxic against rat hepatoma cells and HuTu-80 (human intestinal) cell	Botha *et al.* [32]
Ag-Au Triangular	Stigmaphyllonovatum (amazonvine) Root Extract	9.1-20.4 Av. size ~15	Anticancer potential	Elemike *et al.* [33]
Ag-Au Spherical	Asparagus racemosus (Shatavari) Root Extract	10-50	Antibacterial and Immunomodulatory Potentials	Amina *et al.* [34]
Ag@Au Spherical	Artocarpus heterophyllus (jackfruit) Latex Extract	Average size ~15	Antibacterial and antioxidant activity	Sundarrajan *et al.* [35]
Ag/Au Spherical	Gloriosa superba (flame lily) Leaf Extract	Average size ±10	Antibacterial and antibiofilm activity	Arumuga *et al.* [36]
Au-Ag Spherical	Antigonon leptopus (Coral vine) Plant Extract	10-60	Biological activity	Abbasi *et al.* [37]
Au-Ag Spherical	Madhuca longifolia (Butter Tree) Seed Extract	34–66	Wound healing bio-efficacy	Sharma *et al.* [38]
Au-Ag Spherical, rod, triangular	Commelina nudiflora (carolina dayflower) Plant Extract	10-50	Antibacterial against oral pathogens	Kuppusamy *et al.* [39]
Au-Ag Spherical	Ocimum basilicum (Basil) Leaf Ectract	3-25	Antidiabetic and antimicrobial properties	Anand *et al.* [40]
Au-Ag Spherical	Trigonella foenum Graecum (Fenugreek) Seed Extract	Av. Size ~73.18	Antidiabetic Effect	Virk *et al.* [41]
Ag-Pt Spherical	Vernonia mespilifolia (Blue bitter tea) Plant Extract	Av. size 35.5 ± 0.8	Antioxidant, antimicrobial, and cytotoxic activities	Oladipo *et al.* [42]
Ag/Pt Spherical	Crocus sativus (saffron) Plant Extract	Average size ~36	Cytotoxic activities against pathogenic microbes & MCF-7 breast cancer cell	Fakhri *et al.* [43]
Ag-Pd Spherical	Terminalia chebula (Haritaki) Fruit Extract	Average size ~20	Anticancer and antimicrobial activity	Suganthy *et al.* [44]
Au-Pd NPs on reduced graphene oxide (RGO)	Ziziphus ziziphus (Chinese date) Leaf Extract	----	Photothermal killing activity against HNE-1 tumour cells	Henglei *et al.* [45]
Ag-Pt Spherical	Vernonia mespilifolia (blue bitter-tea)	Average size 35.5±0.8	Anticancer and antimicrobial activity	Oladipo *et. al.* [14]
Ag-Cu/Ag-Zn	Annona muricata (soursop) Leaf Extract	____	Anti-diabetic activity	Baadhe *et. al.* [46]

Au-Pt Spherical shape, triangular, rod	Phragmites australis (Common Reed) Leaf Extract	Average size 35.1 ± 2.71	Cytotoxic activities Catalytic activity	Oladipo *et. al.* [47]
Ag/Ni Pseudo-Cubic	Senna occidentalis (Coffee Weed) Leaf Extract	10.25 ± 4.19	Optical activity for medical purpose	Akinsiku *et. al.* [48]
Pt-Pd Irregular shape	Dioscorea bulbifera (air potato) Tuber Extract	20-25	Anticancer and antioxidant activity	Ghosh *et al.* [49]
Ag–Cu Spherical	Aerva lanata (mountain knotgrass) Plant Extract	7-12, average size ~9.5	Cytotoxic and antimicrobial activities	Thirumoorthy *et al.* [50]
Pt-Co Spherical core-shell	Sechium edule (Chayote) Fruit Extract	13.2–26.4	Antibacterial activity	Golder *et al.* [51]
ZnO-Ag Spherical	Mirabilis jalapa (Four-o'clock plant)	19.3 - 67.4	Antibacterial and antileishmanial properties	Zia *et al.* [52]

III. TRIMETALLIC NANOPARTICLES: Trimetallic nanoparticles (TNPs), composed of three metals at the nanoscale, are emerging as promising materials for various biomedical applications, offer enhanced physicochemical properties due to synergistic effects [53] that outperform mono- and bimetallic systems. They exhibit improved catalytic activity [13], stability, optical and electronic characteristics. TNPs typically form alloy [54] or core-shell structures [55]. Alloys ensure uniform metal distribution, maximizing synergy, while core-shell configurations—especially triple core-shells—allow for independent tuning of each layer, with the outer shell often enhancing functionality or protecting the core. Plant extracts rich in compounds like flavonoids and phenolics act as reducing, stabilizing and capping agents for green synthesis of TNPs and alloys [4]. This bio-renewable approach offers faster synthesis and better control over nanoparticle size and shape, eliminating the need for bacterial cultures. While promising, challenges remain in understanding formation mechanisms, scaling up production, and ensuring consistency. Various plant parts (leaves, buds, gum, seeds, roots, tubers, fruit peels) have been successfully used (Table 2). Plants offer a readily available, cost-effective and scalable source for stable, well-characterized TNP production due to their diverse secondary metabolites and purifying potential.

Table 2: Plant Mediated Synthesis of Trimetallic Nanoparticles

Nanomaterials type & Morphology	Plant Source	Size (nm)	Applications	References
Au/Pt/Ag Nanoparticles Spherical	Lamium album (White dead nettle) Leaf Extract	Average size ~40	Antimicrobial activity	Dlugaszewska *et al.* [56]
Ag−Au−Pd Nanoparticles Quasi Spherical	Aegle marmelos (bael) and Syzygium aromaticum (clove) leaf and bud Extract	8.1 and 11.61	Antimicrobial activity against E. coli	Paria *et al.* [57]
Ag-Cu-Co Nanoparticles Spherical	Salvia officinalis (common sage) Leaf Extract	Average size 3.25 ±0.75	Fungicidal activity	Malik *et al.* [58]
Au/ZnO/Ag Spherical, triangular	Meliloti officinalis (yellow sweetclover) Plant Extract	Average size ± 20	Cytotoxic activity	Dobrucka *et al.* [59]
Au/ZnO/Ag Nanoparticles Spherical	Glechoma hederacea (ground ivy) Leaf Extract	Size range 50-70	Cytotoxic activity against leukemia	Dobrucka *et al.* [60]

Au/CuO/ZnO Nanoparticles Spherical	Verbena ofcinalis (Common Verbena) Plant Extract	Average size 35	Cytotoxic activities against Jurkat cell line	Dobrucka *et al.* [61]
Cu-Ag-Ru Nanoparticles Spherical, flakes	(Green chiretta) Leaf Extract	Size range 25-60	Antibacterial and photocatalytic activity	Radhakrishnan *et al.* [62]
Cu/Cr/Ni Nanoparticles Cubic, plate-like structure	Eryngium campestre (E. campestre) and Froriepia subpinnata (F. subpinnata) Leaf Extract	Size range 100-200	Antimicrobial activity	Vaseghi *et al.* [15]
Co-Zn-Ni Oxide nanoparticles Spherical	Cicer Arietinum (Chickpea) Leaf Extract	Average size ± 25.72	Antibacterial activity	Mohammed *et.al.* [63]
Ni/Cr/Cu Nanoparticles Spherical	Coriander sativum (coriander) Leaf Extract	___	Antimicrobial activities	Kumar K *et al.* [64]
Ru/Ag/Pd Nanocomposites Spherical	Allium sativum (garlic tunicate) Leaf extract	Size range 50-90	Antimicrobial activities	Hussein *et al.* [65]
CuO/Ag/ZnO Nanocomposites Spherical	Ziziphus spina-christi (Christ's thorn jujube) Leaf extract	Average size 7.11± 0.67	Antibacterial activities	Kamoun *et al.* [66]
ZnO-MgO-CuO Spherical	Artemisia abyssinica (chikugn) Leaf extract	Average size ~15.13	Antibacterial activities	Orshiso *et al.* [67]
CuO-Se-ZnO Nanoparticles Tetragonal pyramid	Aspergillus niger Fungi	Average size ~26.3 5.4	Antifungal activity against fungi causing mucormycosis	Hasanin *et al.* [68]
ZnO@ TiO_2@SiO_2 Nanocomposites Spherical	Lecanora muralis (LM) lichen Fungi	Average size ~53	Antibacterial acitivities	Sajadi *et al.* [69]
Cuo-Ag-Au Nanoparticles Spherical	Vossia cuspidata (Roxb.) Griff. (hippo grass) Leaf extract	Size range ~19	Anti-inflammatory, anti-cancer, wound-healing activities	El-Haziz *et al.* [70]

IV. FACTORS AFFECTING NANOPARTICLES SYNTHESIS: Nanotechnology is a rapidly growing field with nanoproducts finding increasing applications across electronics, healthcare, cosmetics, and medicine. However, the safety of nanomaterials remains a critical concern, with cytotoxicity evaluations requiring testing under varied cell culture conditions like temperature, pH and nutrient levels [71]. In the biological synthesis of BNPs and TNPs, key factors such as pH, temperature, reaction time, and metal ion concentration significantly impact the final product. The size and shape of the synthesized nanoparticles are largely dependent on these chemical and physical parameters. Consequently, precise optimization of metal ion concentration, pH, and temperature in the reaction mixture is essential for achieving controlled and efficient nanoparticle synthesis [72].

4.1 pH Effect: pH is a critical factor in the green synthesis of nanoparticles, influencing their size and texture. By adjusting the pH of the solution, nanoparticle size can be controlled. As a key experimental parameter in nanoparticle growth dynamics, pH affects most equilibrium processes involved. For instance, at the isoelectric point, the surface charge becomes zero. Multiple studies confirm pH's significant role in controlling the size and formation of synthesized nanoparticles. Abbasi manifested the effect of optical density on increasing in pH, in the synthesis of Au-Ag nanoparticles from Antigonon leptopus [37]. Initially, at a pH of around 4, the bimetallic nanoparticle (BNP) synthesis showed two absorption peaks (500-550 nm and 400-420 nm). This pattern persisted up to pH 6. However, at pH 7 or above, these two peaks merged into a single peak near 490 nm. For the synthesis of, Pt@Co Core-Shell NPs from sechium edule zeta potential decreased as the pH increased from 2 to 12. At higher pH levels, the nanocrystal surface might become more passivated [51].

4.2 Temperature Effect: Temperature plays a crucial and multifaceted role in the synthesis of nanoparticles, significantly influencing their nucleation, growth, size, shape, crystallinity, and stability. Temperature, a crucial physical parameter, significantly influences the spatial arrangement and size distribution of nanoparticles, in the synthesis of Ag-Au BNPs from golden rod [32]. Optimizing experimental parameters, including temperature, in the biosynthesis process is essential. Researchers monitor changes in the UV–VIS spectrum to determine the ideal conditions for controlled nanoparticle formation. In the case of Au–Ag nanoparticles from Antigonon leptopus [37] as the temperature of the reaction mixtures increased from 29 ± 3 °C to 70 °C, a single spectral peak was consistently observed across all pH levels, accompanied by a rise in optical density. The presence of a single peak indicates that higher temperatures promote the formation of alloy nanoparticles. Additionally, the notable increase in optical density at pH 4 suggests that elevated temperatures accelerate the synthesis of bimetallic nanoparticles under acidic conditions.

4.3 Time Effect: The duration of biosynthesis is a key factor, as the reduction process, irrespective of the plant extract used, requires time to complete. Crucial changes during NPs biosynthesis are influenced by temperature predominantly [73]. At pH 4, Au–Ag NPs concentration (indicated by SPR band OD) peaked gradually over time. Conversely, at pH 10, BNP formation was rapid, reaching near completion within minutes, with only minor optical density increases afterward. The stable spectral shape throughout indicated consistent BNP monodispersion and isotropy [37].

V. APPLICATIONS: Nanoparticles have revolutionized the biomedical field due to their small size, high surface area and customizable properties. Their unique physicochemical properties, stemming from their small size and large surface area-to-volume ratio, enable them to interact with biological systems at the cellular and molecular level, leading to innovative solutions for diagnosis, treatment and prevention of diseases. The following section highlights the effective use of bimetallic and trimetallic nanomaterials in biomedical applications, showcasing their potential in addressing cancer, bacterial infections and diabetes.

5.1 Antimicrobial Activity: The increasing prevalence of multi-drug-resistant against microorganisms across different microbial systems underscores the critical need for novel antimicrobial agents. Currently, metallic nanoparticles are proving to be powerful antimicrobials effective against bacteria, fungi and viruses. The escalating challenge of antibiotic resistance has spurred the exploration of nanotechnology, particularly BNPs and specially TNPs. TNPs as a novel antimicrobial strategy. Since long, noble metal nanoparticles like gold and silver have long been recognized for their antibacterial properties, bacteria are beginning to develop resistance. BNPs, combining two different metals, offer a promising avenue to overcome these limitations through synergistic antibacterial effects [14, 42, 52, 62]. For instance, Ag-Au bimetallic alloy NPs [34], AgPd NPs [44], Ag–Cu NPs [50], Co-Zn-Ni trimetallic oxide NPs [63] exhibited the greatest inhibitory effect against *Pseudomonas aeruginosa, Staphylococcus aureus* bacteria frequently involved in co-infections, especially in chronic wounds and the lungs of cystic fibrosis patients. Ag@Au nanoparticles [35], Ag/Au bimetallic NPs [36], Au/Pt/Ag NPs [56], ZnO–MgO–CuO [67] exhibit strong antibacterial activity against the Gram-negative strain and Gram-positive strains. Au–Ag alloy NPs demonstrated significant minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) against selected oral pathogenic bacteria [39]. PtCo coreshell NPs [51], Au-Ag NPs [40] showed antibacterial activity against Bacillus subtilis and Escherichia coli bacteria while CuO/Ag/ZnO nanocomposite [66], ZnO–MgO–CuO [67] inhibited Escherichia coli and Staphylococcus aureus bacteria. In essence, bimetallic nanoparticles represent a significant step forward in the fight against antibiotic resistance. Similarly, Ni/Cr/Cu nanoparticles inhibited four species of pathogens including Escherichia coli, Staphylococcus aureus, Aspergillus flavus and Penicillium [64]. (Ru/Ag/Pd)-NPs showed potent antimicrobial activity against Aspergillus flavus, Aspergillus niger, Candida albicans, Candida glabrata, Escherichia coli and Bacillus cereus bacteria [65]. Furthermore, Trimetallic copper–selenium–zinc oxide NPs have promising antifungal activity against Mucor racemosus, Rhizopus microsporus, Lichtheimia corymbifera, and Syncephalastrum racemosum [68].

5.2 Anticancer Activity: Cancer refers to a group of diseases characterized by the uncontrolled proliferation of abnormal cells, which can invade and destroy surrounding healthy tissues. These cells can originate from any tissue in the body and may occur in various organs. In 2018, the global cancer incidence reached 18.1 million new cases, with 9.6 million cancer-related deaths. In the United States alone, an estimated 1,735,350 new cases and 609,640 deaths were reported the same year [74]. As survivorship increases, the projected cost of cancer treatment is expected to reach $157.77 billion by 2020 (Mariotto et al. 2011) [75].

Surgery was an early approach to cancer treatment, but the current era is dominated by chemotherapy (chemical drugs targeting cancer cells via bloodstream delivery) and radiotherapy (ionic radiation damaging tumor DNA). Often used together, both methods face limitations like variable patient response and significant side effects including anemia, organ damage, hair loss and vomiting [76]. To overcome these drawbacks, newer treatments such as immunotherapy (boosting the body's immune system), hyperthermia (using heat to damage cancer cells) [77] and gene therapy (modifying genes to fight cancer) [78] have emerged in recent decades.

BNPs and TNPs have shown promise in cancer therapy, functioning as chemotherapeutic agents. They can also enhance the efficacy of conventional chemotherapy by exerting a synergistic effect, making them a valuable tool in anticancer strategies. They have demonstrated a cytotoxic effect against various cancer cell types like H4IIE-luc and HuTu-80 cells [Ag-Au NPs [32]], Human cervical carcinoma (HeLa) cells (Ag-Au NPs [33], Pt–Pd NPs [49], Ag–Cu NPs [50]), MCF-7 breast cancer cell line (Ag/Pt alloy NPs [43], CuO-Ag-Au NPs [70]), AuPt Nps [47]), Human lung cancer cell line A549 (AgPd NPs [44], AuPt Nps [47]), Leukemia cell line (Au/ZnO/Ag NPs [60]), Jurkat (human T lymphocyte cells) (Au/CuO/ZnO NPs [61]). Similarly, AgPt NPs have greater cell-killing ability (cytotoxic potency) towards MCF-7 breast cancer cell line compared to HEK 293 normal cell line [43]. Au–Pd/RGO manifested effectiveness of photothermal therapy in killing HNE-1 tumor cells [45], K562 leukaemia cancer cell (Ag-Cu, Ag-Zn NPs [46]).

5.3 Wound-healing Efficacy: A wound is a disruption of the skin's surface and underlying tissue structure and function. The healing process involves three overlapping phases: inflammation, cell proliferation and tissue remodeling. Delayed or impaired wound healing can cause significant illness and prolonged hospital stays. Consequently, there's a constant need for effective wound treatments that accelerate healing and reduce the likelihood of complications [79]. Au–Ag bimetallic NPs manifested wound-healing efficacy [38,70].

5.4 Anti-Diabetic Activity: Type 2 diabetes mellitus (DM-2) is a widespread chronic metabolic disease characterized by high blood sugar (hyperglycemia) and abnormal lipid levels (dyslipidemia). It's also known for serious complications like kidney, nerve, and eye damage (diabetic nephropathy, neuropathy, and retinopathy) as well as liver damage [80]. These complications contribute significantly to illness and death in individuals with DM-2. The World Health Organization (WHO) considers DM a growing global epidemic that could be a major cause of disease and disability in the coming decades. Currently affecting around 230 million people globally, this number is projected to rise to approximately 366 million by 2030. Consequently, managing DM-2 presents a significant challenge for both patients and healthcare professionals. Au-Ag BNPs from ocimum basilicum manifested potential antidiabetic effect [40, 46] whereas Au/Ag nanocomposite from trigonella seed extract [41] proposed a groundbreaking nanomedicine solution for diabetes.

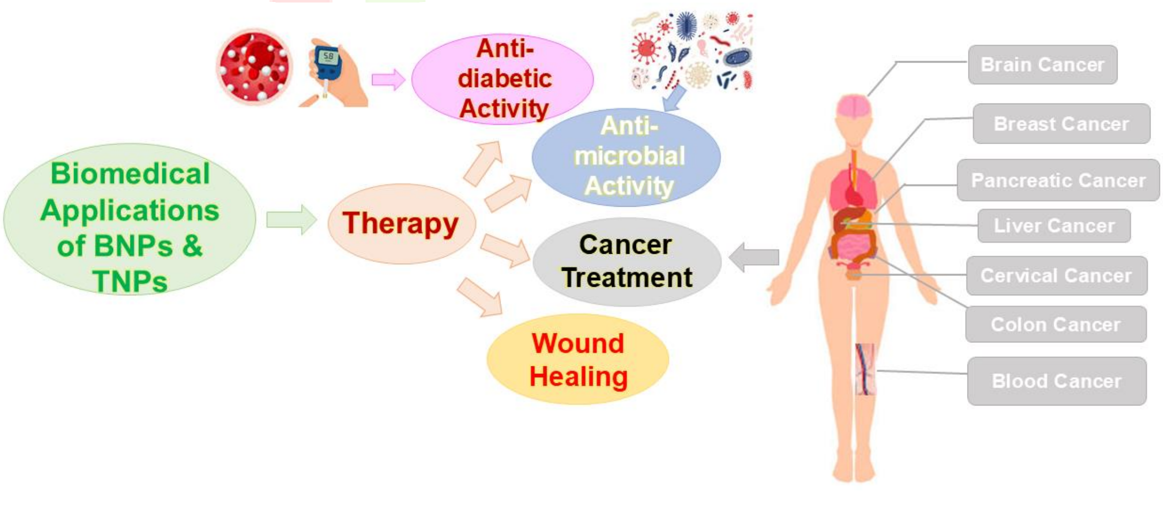

Figure 2. Applications of bimetallic nanoparticles (BNPs)and trimetallic nanoparticles (TNPs) mediated by plant extracts

VI. CHALLENGES, FUTURE PERSPECTIVE AND CONCLUSIONS: Despite progress in BNPs and TNPs development for biomedicine, challenges remain. Precise control over particle size during synthesis is limited, yet size significantly impacts cytotoxicity, as seen with Au and AgNPs. Notably, size-

dependent cytotoxicity in noble metal-based BNPs, TNPs with consistent composition is understudied. Efficient transport of NPs across biological barriers like cell membranes and the intestinal wall is crucial, where their biological affinity plays a key role. BMNPs can potentially enhance this affinity. The development of predictive mathematical and computer models for BNP and TNP interactions is also needed, proving more complex than for monometallic NPs, though initial theoretical models show promise in explaining phenomena like BNP, TNP penetration through bacterial layers.
The application of bimetallic and trietallic formulations in medical nanotechnology is still a nascent field requiring further research, particularly focusing on in vivo studies to evaluate excretion and off-target effects. More investigation is needed to link BNP, TNP biosynthesis with bioactivity and elucidate their mechanisms of action. Finally, while natural extracts used in green synthesis are generally considered safe, more comprehensive toxicological data are necessary. Overall, BNPs and TNPs synthesized from natural extracts show potential for antioxidant, antimicrobial and anticancer activities and have broad applications across various industries, necessitating continued research into their biological interactions and safety.
But overall nanotechnology is a rapidly transforming field with increasing economic impact across healthcare, environment and agriculture. While nanoparticles are revolutionizing biomedicine, the full potential of BNPs and TNPs formulations in realizing nanotechnology's promise for a better future remains largely untapped, with many unanswered questions and potential uses yet to be discovered to fully realize nanotechnology's promise of a better world for humanity.

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