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Nanotechnology-based herbal medicine: Preparation, synthesis, and applications in food and medicine

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ABSTRACT

Nanotechnology has instigated profound developments among herbal medicineregarding bioavailability, stability, and therapeutic efficacy. This review deals with nano-herbal formulations' preparation, applications, and therapeutic capabilities for medical problems and foods like food packaging and preservation. The formulations are developed using advanced nanotechnology techniques, such as solvent evaporation, nanoemulsion formation, and encapsulation. Phytosomes, liposomes, nanocapsules, and nanoemulsions have ensured that bioactive ingredients' stability has been secured, bioavailability and targeted administration have been improved, and negative side effects have been cut considerably. The ability of nanoherbal formulations to deliver drugs to tumor cells in an improved permeability and retention manner, such as, cancer therapy while minimizing tissue damage, has been largely practiced in many laboratories. Enhanced drug solubility, distribution to the site of interest, and successful therapeutic outcomes have had a major impact on inflammatory disorders, cardiovascular diseases, diabetes, skin problems, and neurodegenerative diseases. Dendrimers and solid lipid nanoparticles transport anti-inflammatory and antioxidant substances, whereas polymeric nanoparticles protect against Alzheimer's and Parkinson's diseases. Nanocarriers increase the absorption of curcumin and resveratrol, decreasing oxidative stress and improving cardiac function. Nanotechnology has used such reinforcing materials to improve the performance of protective food packages and, consequently, ensure their longer service time. On the one hand, antimicrobial and antioxidant herbal nanoparticles will prevent spoilage and degradation during storage.

On the other hand, nanoemulsions form a medium for vitamins, minerals, and antioxidants to be bioavailable in fortified meals. The following practices have contributed to preserving food products' nutritional and functional attributes. Nonetheless, nanotechnology has found its way into these chemical compositions, bringing about the issues of scaling up, cost-efficiency, regulatory compliance, and safety concerns. Biodistribution, metabolism and the coccion of long-term effects studies must confirm safe and sustainable usage. To stimulate

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full utilization of nanotechnology in medicine and food science, further study must be undertaken to clear the existing drawbacks and discover other fields of the most appropriate applications of nanotechnology. Nanotechnology and herbal medicine join forces and form a potent medical and nutritional solution to various diseases, food production, and conservation. Such advancements would modify treatment and nutritional strategies, allowing a more secure, effective, and long life.

Abbrivation

BBB Blood-Brain Barrier
EPR Enhanced Permeability and Retention
NPs Nanoparticles
QD Quantum Dots
ROS Reactive Oxygen Species
SLN Solid Lipid Nanoparticles
NP Nanoprecipitation
PDI Polydispersity Index
LBNPs Lipid-Based Nanoparticles
SLN Solid Lipid Nanoparticles
NLC Nanostructured Lipid Carriers
LBNP Lower Body Negative Pressure
PVA Polyvinyl Alcohol
PEO Polyethylene Oxide.
PVP Polyvinylpyrrolidone
PLA Polylactic Acid
PCL: Polycaprolactone
PU Polyurethane
PLLA Poly(L-lactic acid)
PLGA Poly(lactic-co-glycolic acid)
DLS Dynamic Light Scattering
TEM Transmission Electron Microscopy
SEM Scanning Electron Microscopy
AFM Atomic Force Microscopy
XRD X-ray Diffraction
NIPAAM N-isopropylacrylamide
VP Vinyl Pyrrolidone
PEG-A: Polyethylene Glycol Acrylate
NFκB Nuclear Factor Kappa-light-chain-enhancer of Activated B cells
IL-6, IL-8 Interleukins 6 and 8
TNFα Tumor Necrosis Factor Alpha
DAOY Medulloblastoma cell line
D283 Med Medulloblastoma cell line
HSR-GBM1, JHH-GBM14 Glioblastoma neurosphere lines
STAT3 Signal Transducer and Activator of Transcription 3
CA Camptothecin Analog
NCI-H460 Non-small cell lung cancer cell line
HeLa Human Cervical Cancer Cell Line
B16F10 Murine Melanoma Cell Line
DNA Topoisomerase Enzyme targeted by certain cancer drugs
NCTC2544 Human Keratinocyte Cell Line
DMBA 7,12-Dimethylbenz[a]anthracene
PCNA Proliferating Cell Nuclear Antigen
mPEG2000 Methoxy Polyethylene Glycol 2000
4T1 Mouse Breast Cancer Cell Line
NCI-H460 Non-small Cell Lung Cancer Cell Line
t1/2 Plasma Half-life
G2/M Gap 2/Mitosis Phase of the Cell Cycle
STAT3 Signal Transducer and Activator of Transcription 3
ACG-NSps Annonaceous Acetogenins Nanocrystals
HepG2 Human Liver Cancer Cell Line
ICTN Icaritin Nanocrystals
TMP-NS Tetramethylpyrazine Dihydroxynaphthalenate Nanocrystals
BN-PEG-NLC Baicalin-Loaded PEGylated Nanostructured Lipid Carriers
HK-NSps Honokiol Nanocrystals
HMGR 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase
TPGS D-α-Tocopheryl Polyethylene Glycol Succinate
VNME Vitex Negundo Methanol Extract
BSA Bovine Serum Albumin
Cmax Maximum Plasma Concentration
MCF-7 Human Breast Cancer Cell Line
H9C2 Rat Cardiomyoblast Cell Line
TEWL: Transepidermal Water Loss
MMPs Matrix Metalloproteinases
NLC Nanostructured Lipid Carrier
SPF Sun Protection Factor
GPx Glutathione Peroxidase
GSH Glutathione
ZEO Zataria multiflora Essential Oil
BEO Bunium persicum Essential Oil
EGCG Epigallocatechin Gallate
QC Quercetin
RSV Resveratrol

1. Introduction

Nanotechnology is gaining ground as the main impact factor in the development of food and pharmaceutical sectors. The use of Nano-herbal formulations in this field is entirely like merit. The main things are nano-herbal formulations, which enhance the efficacy and delivery of therapeutic agents through nanotechnology, facilitating the integration of traditional herbal medicine and technological advances. These formulations directly addressed the drawbacks inherent in conventional herbal medication, for example, the use of components with low bioavailability and the instability of the preparations. By optimizing its solubility, protecting active compounds from speedy degradation, and targeting this drug to the part of the human body that requires it, nano-herbal formulations are designed as a unique platform for therapy and appetite. Application. Plant-based nanoparticles have a great deal of cancer therapy potential because they can isolate cancer cells and reduce side effects, a common outcome of classical chemotherapy. Non-herbal preparations like phytosomes, liposomes, nanocapsules, and nanoemulsions were studied to improve gastric absorption as well as the effectiveness of phytotherapy [1]. These advanced delivery systems guarantee that the components are slowly released, well distributed, and protected from metabolism, thus leading to increased therapeutic efficacy [2]. Nanoherbal formulations have improved pharmacokinetics, which are the main characteristics of these formulations, including better solubility and stability; therefore, the drug is better absorbed and stays longer in the body. These formulations are easier to deliver to specific targets; thus, the drug is released only in the affected areas. Precision therapeutics like that help reduce systemic side effects and increase the chances of getting well [3]. In cancer treatment, nanoparticles, for example, exploit the enhanced permeability and retention

(EPR) effect, enabling them to build up selectively in tumor cells. In this way, the use of cancer drugs will not only be more effective but will also cause less injury to the healthy tissues of the body [4]. Nanoherbal formulations, operating in the food sector, are deeply concerned with the nutritional quality and functional aspects of food particles. By encapsulating bioactive compounds such as vitamins, minerals, and antioxidants, nanotechnology prevents these substances from being damaged during processing and storage. Thus, their positive features are still present even when consumed. For example, nanoemulsions have been used to infuse essential oils and other herbal extracts into food products. Nanoemulsions exhibit high stability and bioavailability and are carried away to the target organs to produce health-promoting effects on consumers [5]. Nanoherbal drugs can be helpful in different ways. However, their safety is a big worry. Their tiny size might change how they react in our bodies. So we need to test them very carefully. For example, some nano-herbal drugs made from Rhodomyrtus tomentosa are great at stopping rust but are only slightly harmful. Still, they can hurt important body parts, which we must study more about [5]. Integrating nanotechnology with herbal medicine represents success rates in healthcare and nutrition, offering innovative solutions to long-standing challenges. Nevertheless, it can only be used if carefully designed programs and detailed safety checks ensure the customer is safe. Still, evolving in this area can reshape treatment and nutrition strategies, thus creating less hazardous and more efficient avenues. Nano-based herbal medicine and food applications are promising yet not fully explored due to the wide variety of other problems that can set up desert areas instead of green fields worldwide. The aspect of toxicity and safety is only one side of these problems. As the development, registration, and commercial introduction of nanoformulations are not yet bound by clear frameworks and standards, there are still thorny regulatory issues. Differing legislative regimes in different nations, in turn, hinder entry into markets and make it hard for global corporations to comply. Another concern is economic feasibility. Nanotechnology-based formulations are costly as they range from raw material acquisition to complex synthesis [6]. The necessity for modern equipment and knowledge makes large-scale production expensive. Thus, many inventions languish in academic research or pilot-scale development without becoming cost-effective, market-ready products. Scalability in manufacturing is difficult. Nanoparticle size, content, and stability must be precisely controlled to replicate lab results in high-volume production. This is especially difficult with natural extracts, whose bioactive components vary by location, season, and processing. These variations can impair nanoherbal formulation repeatability and efficacy, requiring considerable standardization [7].

This review examines the synergy between nanotechnology and herbal medicine in creating nano-herbal formulations for food and therapeutic purposes. It explores their potency, stability, bioavailability, targeted delivery, and therapeutic efficacy in cancer treatment, dermatology, and culinary enhancement. The potential of these formulations to advance healthcare and nutrition is discussed alongside the critical need for thorough safety evaluations.

2. Nanoherbals

Nanotechnology has been increasingly applied to enhance the effectiveness of herbal medications, addressing key challenges such as poor solubility, low bioavailability, and limited therapeutic efficacy. Thus, nanoscale drug delivery systems are used through polymeric nanoparticles, solid lipid nanoparticles, and nanostructured lipid carriers, and the active ingredients are protected, stabilized, and released subsequently. These systems have demonstrated substantial potential in treating chronic diseases, enhancing the therapeutic effects of herbal remedies, and expanding their applications across healthcare and the food industry.

2.1. Benefits of nanoherbals

Nanoherbal formulations have the key benefits of low solubility and low bioavailability in herbal medicines by being well absorbed and directly getting into the body's bloodstream with the active compounds. The new pharmaceutical carriers, which include polymeric nanoparticles, liposomes, and micelles, increase the active agents' solubility and are more effective in treating cancer [8]. For instance, some of the plant representatives of flavonoids and lignans, which are naturally affected by their poor absorption, are the ones that show a very high level of bioavailability when delivered through nanotechnology [9]. Additionally, nano-herbal systems also provide controlled and specific delivery possibilities, which allow for the prolonged release of the active ingredients to the target sites of the body. The approach of precision medicine leads to lower systemic exposure and toxicity, which increases the safety and efficacy of the treatment and, at the same time, minimizes damage to healthy tissues. Nanoherbals reduce the required dosages of the active compounds, which lowers the risk of side effects, and the administration becomes simple and thus improves the patients' adherence [10]. Furthermore, Nanostructured systems enhance the stability and durability of plant extracts by protecting them from environmental degradation caused by exposure to light, heat, and oxygen, which increases their reliability and lengthens their shelf life. Nano-herbal formulations are new products for medicine, foods, and cutting-edge technologies. In healthcare, they assist the treatment of chronic diseases such as cancer, cardiovascular disorders, and diabetes by increasing solubility, thus allowing the release in a controlled manner and targeting specific sites; the curcumin and resveratrol-based compounds result in better therapeutic outcomes through nanocarriers [11]. With their antimicrobial and antioxidant qualities, plant-based nanoparticles enhance preservation, packaging, and nutrient delivery in the food industry, thus enriching product stability and safety. The following section tackles innovative developments in food-related nano-herbal technology [12]. Fig. 1 depicts the specific areas where the different nanoherbal techniques are used in food and pharmaceuticals.

2.2. Safety and toxicity

Recent studies show that nano-herbal formulations are both a therapeutic opportunity and a potential safety risk. The toxicity of these formulations is due to particle size, surface charge and chemical composition. For instance, the polyherbal formulation study reported no acute toxicity but warned of possible kidney and liver damage at higher doses, with reversible injury if treatment is stopped [13]. Besides, other research about nano-herbal medicine indicates that nanoparticles initiate oxidative stress, which would probably cause mitochondrial damage, reactive oxygen species (ROS) production, and cell apoptosis. This is true when the metrology is poorly optimized [14]. Additionally, quality can be ensured by the right manufacturing process. Impurities during the synthesis of nanocarriers or their functionalization can result in higher degrees of cytotoxicity. For instance, lipid-based nanocarriers, though usually compatible with the body, might be toxic systematically in cases of too low or too high doses and when the characterization process is inadequate [15]. Another study on the use of β-cyclodextrin nanosponge-based formulations showed no notable toxicological changes in acute and subchronic studies, thus indicating their safe use under controlled conditions [16]. Methods for in vitro and in vivo testing of toxic substances are important in determining the product's safety. Training combining cellular and animal studies in a computer simulation has been constantly employed to predict toxicological outcomes. For example, machine learning models have been applied to assess the toxicity of nanoparticles regarding their concentration and physicochemical properties, and the high accuracy in toxicity classification thus obtained has assisted in the optimization of the dose [17]. Histological studies confirm organ-specific toxicity further. A study of the nano-herbal harmonizing showed radiation changes in liver, kidney,

Fig. 1. Application Nano herbals in Food and Drug.

and heart tissues; an emphasis on dose-dependent evaluations and long-term safety through all three organs were the backbone of this study [18]. In the same way, research on polyherbal gold nanoparticle conjugates in cancer therapy shows rare side effects. It indicates the need for deep toxicity profiling to avoid off-target effects [4].

3. Synthesis techniques for nanoherbals

Nanoformulations are advanced systems engineered at the nanometer scale, exhibiting unique physical and chemical properties that make them ideal for diagnostic and therapeutic applications [19]. Nanocarriers are particles with diameters ranging from 10 to 1000 nm that can dissolve, encapsulate, or attach therapeutically active substances for delivery purposes. Nanocarriers typically consist of a polymer shell on the outside and an inside core for medication transportation [20]. The outer core governs the particle's circulation time and interaction with the cell surface. Additionally, this imparts stability to the nanoformulation. The dimensions of these carriers typically range from 1 to 300 nm and are transported to a specified target together with a therapeutic medication [21]. Oral nanocarriers provide targeted drug delivery to specified sites and allow for controlled release. These agents can deliver active substances to specific tissues since they are smaller and can change shape and charge. Nanocarriers are consistently defined as having at least one dimension within the scale of 1–300 nm [22]. Nano strategies are employed in treating neural diseases, namely in drug formulation, due to the inherent inability of pharmaceuticals to traverse the blood-brain barrier independently [23]. Various classes of nanoparticles are employed in the pharmaceutical industry to facilitate drug

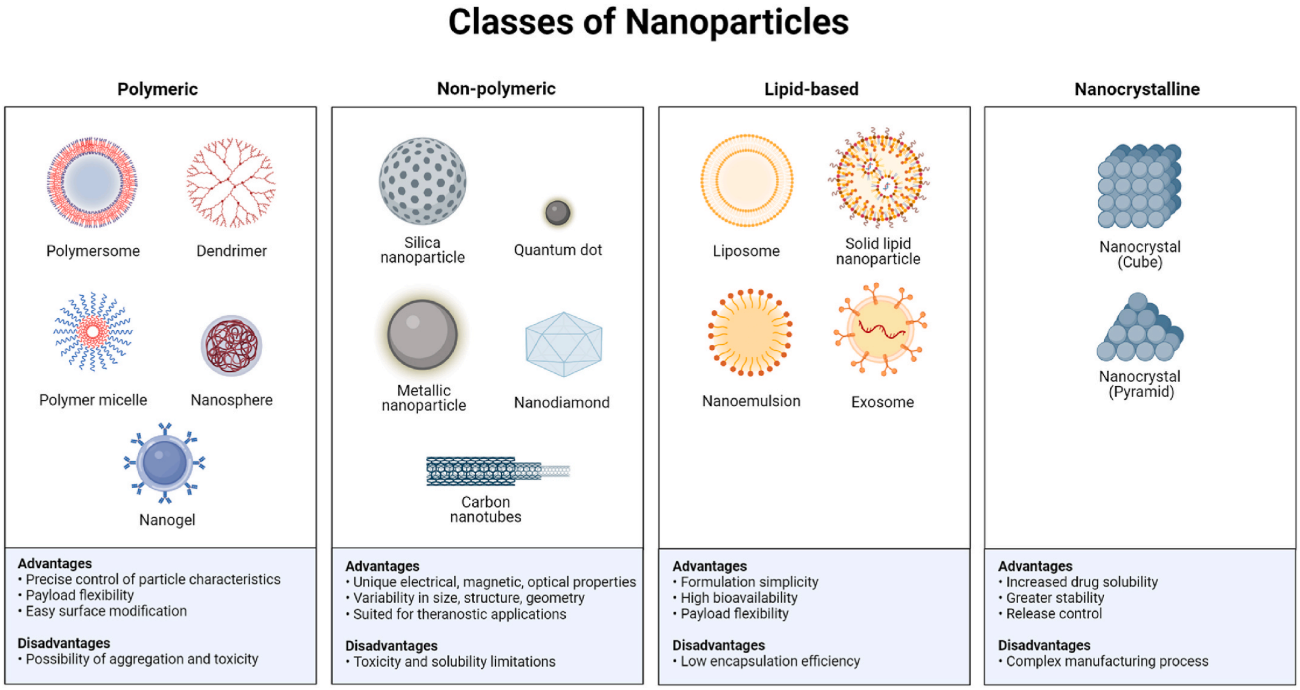

Fig. 2. Classes of nanoparticles are employed in the pharmaceutical industry to facilitate drug delivery [31].

delivery Fig. 2. Iron oxide, gold, zinc, and other metallic complexes create inorganic nanocarriers [24]. Metal and inorganic nanoparticles were made by changing functional groups and adding ligands, drugs, and antibodies. The potential applications in biotechnology include targeted drug delivery, gene and drug carriers, and magnetic separation [25]. Diagnostic and therapeutic uses of gold, silver, and magnetic nanoparticles (NPs) were widespread [26]. Quantum dot crystals (2–20 nm) were used as herbal active ingredient carriers due to their exact regulation. They were known for their optical properties, exact density of states, and high-quality transport [27]. Semiconductor quantum dots on a nanometer scale exhibit characteristics of a highly stable photovoltage, show broader absorption spectra and have tunable emission wavelengths. Quantum dots embody precise and long-term stable bioimaging imaging, biosensing, and diagnostics [28]. Quantum dots, aside from liposomes, also do the work of diagnosis and cure and thus can be used for theranostic purposes. Colloidal methods are one of the ways to produce very stable and size-tunable nanoparticles from the precursors, which are heated to high temperatures in a controlled setting [29].

On the other hand, Dendrimers are extremely precise at the structure's surface due to the highly branched, tree-like macromolecule structure with a well-defined morphology, exact molecular weight, and numerous functional groups. Dendrimers can, one way or another, gather several drugs and pass them to their destination or be soluble in hydrophobic chemicals. Their multiple valences help them in the biological target interactions, enhancing the treatment efficacy. While liposomes rely on lipid bilayers, dendrimers' structural flexibility and functionalization give them the power to regulate drug release and adjust surface characteristics. Dendrimer production employs divergent and convergent strategies for controlling branching and functionalization [30]. Table 1 shows nanoformulation methods. Nanoprecipitation is fast for encapsulation. Dendrimers target delivery. Quantum dots' glowing aids diagnosis but may be harmful. This helps pick the best methods.

Moreover, lipid nanocarriers were chosen for their biocompatibility and versatility [32]. Pharmaceutical researchers developed these nanocarriers to transport oral, pneumonic, and parenteral drugs. Lipid nanoformulations were tailored to disease conditions, delivery routes, product stability, toxicity, and cell viability. This improved immunization, diagnostics, and medication safety and efficacy [33]. Nanoemulsions, liposomes, dendrimers, and carbon nanocarriers are organic nanoformulations. Liposomal phospholipid bilayers form spherical liposomes, and this spherical structure's aqueous phase contains pharmaceuticals [34]. Their endurance makes them essential carriers of vaccines, steroids, and genetic elements [35]. Nanoemulsions, which are 20–200 nm in size, are less prone to creaming and settling, improving medication delivery. Solid-lipid nanoparticles (NPs) overcome the constraints of liposomes and emulsions by enhancing drug release with a solid matrix. Small carrier particles solubilize lipophilic compounds, improving cellular absorption. Polymorphic chemicals in solid lipid nanoparticles can cause instability. However, their composition of physiologically significant lipids reduces toxicity, making them promising anti-cancer drug delivery vehicles [36]. Colloidal nanoparticles have high thermal stability, a surface area-to-volume ratio, and surface reactivity. Nanoparticles are uniformly distributed in a solution. Due to their unique physicochemical properties, they are used in pharmaceutical administration, cancer therapies, diagnostics, and optical imaging [37]. Moreover, polymeric nanoparticles make biodegradable natural and artificial polymers. Depending on the encapsulated molecule, these drugs release their active contents gradually and are stable [38]. Dendrimers are hyperbranched polymeric molecules with a single atom or molecule in the center and numerous peripheral groups that form a spherical configuration. Enclosing the molecule in the center allows them to carry herbal drugs and create a diverse medication structure. Amphiphilic compounds form 10–100 nm micelles [39]. These entities have two cores that reject and attract water and transport long-lasting medications into the bloodstream. Polymers nanospheres and nanocapsules are efficient medication carriers. They increase herbal medicine water solubility and control drug release. Therapeutic nanoparticles

Table 1
Comparative analysis: Properties, benefits, and limitations of nanoformulation techniques.

Technique	Properties	Benefits	Limitations	References
Nanoprecipitation	Produces nanoparticles through solvent-antisolvent interaction. Particle size: 50–500 nm.	Simple, scalable, high encapsulation efficiency (up to 90 %), suitable for hydrophilic and hydrophobic compounds.	Requires optimization to avoid aggregation; solvent residue removal is essential.	[79,80]
Liposomes	Spherical vesicles with lipid bilayers. Particle size: 50–200 nm. Encapsulation efficiency: 50–60 %.	Biocompatible, versatile for both hydrophilic and hydrophobic drugs, and widely used for drug delivery.	Prone to instability, limited drug loading capacity, and high production costs.	[81]
Dendrimers	Highly branched, monodisperse macromolecules. Size: 1–10 nm. Functional groups available for drug conjugation and targeting.	High drug loading capacity, precise targeting, controlled drug release, and versatile functionalization.	Complex synthesis, potential cytotoxicity, and high cost of raw materials.	[82]
Quantum Dots	Semiconductor nanocrystals. Size: 2–10 nm. Tunable fluorescence emission for imaging and diagnostics.	Exceptional for diagnostics and bioimaging due to high fluorescence stability and tunable optical properties.	Potential cytotoxicity due to heavy metals; expensive synthesis processes.	[83]
Solid Lipid Nanoparticles (SLN)	Lipid-based systems solid at room temperature. Particle size: 50–300 nm. Encapsulation efficiency: 60–80 %.	High stability, controlled release of drugs, and biocompatibility.	Limited drug loading capacity and potential lipid degradation during storage.	[84,85]
Polymeric Nanoparticles	Nanoparticles made from biodegradable polymers like PLGA or PEG. Particle size: 100–500 nm.	Customizable release profiles, suitable for targeted delivery, and high encapsulation efficiency.	Complex fabrication processes, potential residual solvent toxicity, and high cost.	[86]
Nanoemulsions	Thermodynamically unstable emulsions stabilized by surfactants. Particle size: 20–200 nm.	High solubility for hydrophobic drugs, enhanced bioavailability, and easy production methods.	Stability issues over time, surfactant-related toxicity, and limited scalability.	[87]
Micelles	Amphiphilic carriers that self-assemble in aqueous solutions. Size: 10–100 nm.	Excellent for solubilizing hydrophobic drugs, high stability, and extended drug circulation times.	Limited loading for hydrophilic drugs and requires careful optimization to ensure stability.	[88]
Nanofibers	Ultrafine fibers with high surface area-to-volume ratio. Diameter: 10–500 nm. Fabrication via electrospinning or self-assembly.	High drug loading, controlled release, excellent for wound healing and tissue scaffolds.	Mechanical fragility and potential defects during fabrication.	[89]
Nanohydrogels	Cross-linked hydrophilic polymer networks with high water content. Tunable mechanical properties.	Mimics extracellular matrix (ECM), localized and sustained delivery for hydrophilic drugs, highly biocompatible.	Limited drug loading capacity for hydrophobic drugs and potential mechanical instability in physiological conditions.	[90]

are biodegradable or non-biodegradable solid particles with a diameter of less than 100 nm [40]. These nanoparticles can be nanocapsules or nanospheres. Nanocapsules contain a polymeric membrane enclosing the medicine and distributing active ingredients in a nanosphere matrix. Most of the components found in herbal remedies are utilized for their medicinal properties, and converting these components into nanoparticles ensures enhanced absorption and increased bioavailability. Fig. 3 shows active constituents found in herbal remedies and their medicinal uses.

3.1. *Herbal nanosuspensions*

Nanosuspensions are aqueous colloidal dispersions consisting of solid nanoparticles, which are stabilized by surfactants or polymers. They are employed to enhance the rate at which herbal extracts dissolve and their capacity to be absorbed by the body, particularly when these extracts have limited solubility and low bioavailability [41]. Herbal extract nano-suspensions can be created utilizing many techniques such as nanoprecipitation, antisolvent precipitation, and high-pressure homogenization. These techniques are designed to decrease the size of the particles in herbal extracts, which in turn increases the amount of exposed surface area and improves the rate at which they dissolve [42]. Ultimately, this enhances the ability of the extracts to be absorbed by the body Fig. 4.

3.2. *Nano-polymerization in herbal medicine*

Nanopolymerization in herbal utilizes nanotechnology to improve the bioavailability and bioactivity of herbal substances. The efficacy of plant extracts can be enhanced by encapsulating, entrapping, or adsorbing them into nano-sized systems composed of biodegradable and biocompatible polymers [43]. This approach reduces dosage requirements, decreases side effects, and improves overall activity. Nanotechnology-based delivery methods are essential for addressing the constraints of herbal medicines, including their limited solubility, bioavailability, and durability. This makes them highly promising for use in clinical applications. Researchers are currently developing polymeric nanoparticles, solid lipid nanoparticles (SLNs), and other nanosystems to enhance the bioactivity of phytochemical substances included in herbal medicines and use some polymers to formulate nano-herbals [44]. Fig. 5 shows polymers utilized in the production of nano-herbal formulations.

3.3. *Herbal nanofibers*

Nanofiber preparation in herbal medicine entails employing several processes, such as electrospinning, bubble electrospinning, and centrifugal electrospinning, to fabricate nanofibers derived from plant extracts [45]. Nanofibers can transport herbal bioactive components, enhancing their solubility and bioavailability and mitigating negative effects. Herbal extracts are frequently transported via natural polymers such as chitosan, hyaluronic acid, cellulose acetate, and guar gum. The nanofibers that are produced imitate the natural extracellular matrix, improving the ability of cells to connect, move, and carry nutrients [46]. This methodology has been extensively examined to facilitate the healing of wounds and the administration of drugs. In vivo investigations have demonstrated encouraging outcomes compared to wound healing solutions already available on the market [47]. This method employs electrostatic forces to continuously produce electrofibers with a diameter ranging from 10 nm to a few micrometers. Several research investigations have been undertaken on the electrospinning method since 1999 [48]. To initiate the process of electrospinning, the necessary components are a high-voltage power supply, a syringe fitted with a metallic needle, and a collector. The active component undergoes exposure to a high-voltage power supply, resulting in its liquefaction and the formation of small spherical particles [49]. Electrostatic repulsion in the fluid causes the droplet to change into a conical shape near the tip of the needle to control surface tension. The electrostatic force induces the ejection of a charged polymer solution from the needle tip, resulting in an interplay between the electric field and the surface tension of the fluid. The solvent vaporizes and condenses in the grounded collector, creating a homogeneous fiber [50]. In addition, electrospinning improves drug delivery, wound healing, tissue regeneration, and food packaging by incorporating herbal medicine into nanofibers. Nanofibers with high porosity, mechanical strength, and flexibility use natural and synthetic polymers. Nanofibers mimic the extracellular matrix, helping cells proliferate and attach [51]. Researchers combine natural and biological synthetic polymers to improve cell adhesion and

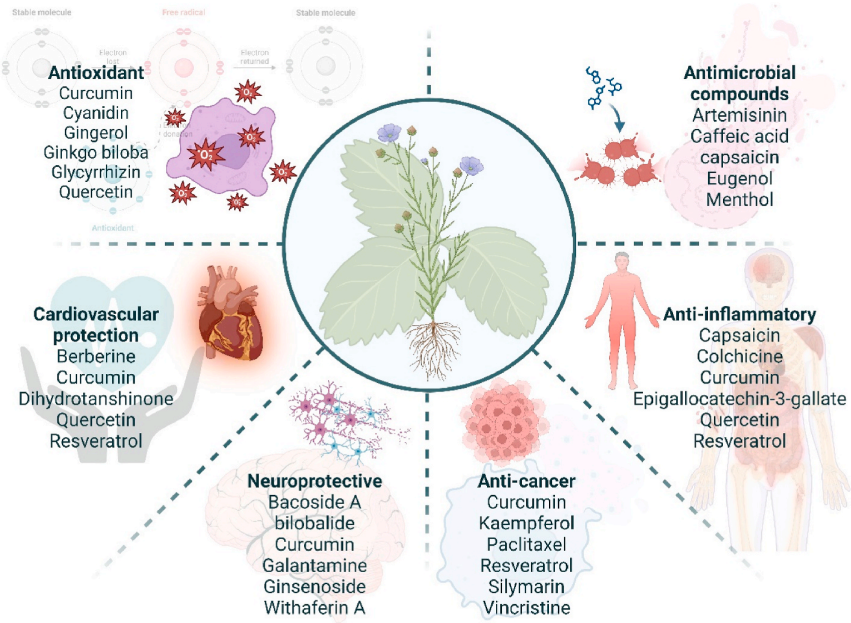

Fig. 3. Active constituents found in herbal remedies and their medicinal uses.

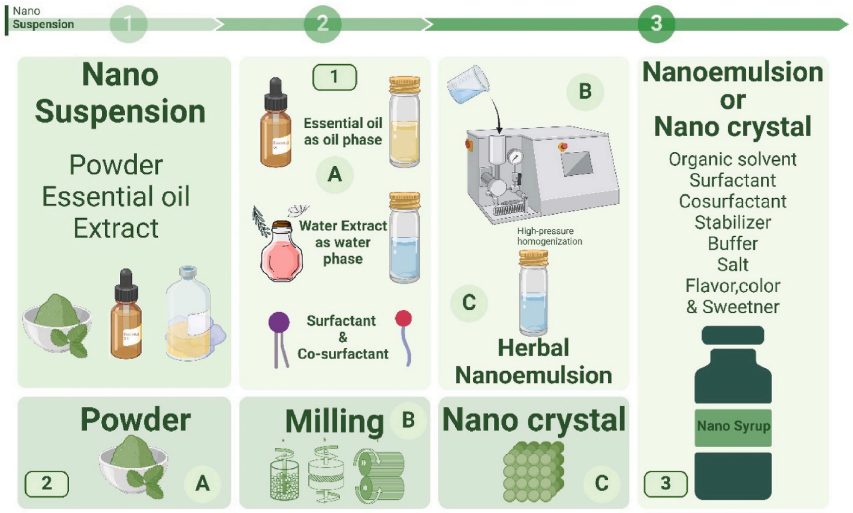

Fig. 4. Techniques for producing nano-suspensions from herbal substances involve the utilization of essential oils, as well as their aqueous extracts and powders.

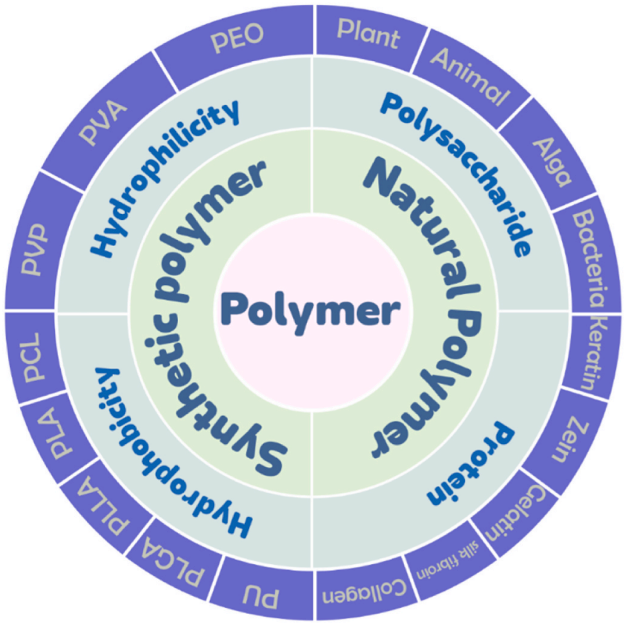

Fig. 5. Polymers are utilized in the production of nano-herbal formulations based on their inherent characteristics, both natural and synthetic, as well as their affinity for water (hydrophilicity) and oils (lipophilicity).

proliferation, ensuring durability and regulating biodegradability. Fig. 6 illustrates the method for preparing three types of nanofibers.

3.4. Lipid-based nanoparticles

Lipid-based nanoparticles (LBNPs) show great potential as a technique for delivering drugs, especially in cancer treatment [52]. Nanoparticles, such as liposomes, solid lipid nanoparticles (SLN), nanoemulsions and nanostructured lipid carriers (NLC), have several benefits, including a large capacity for holding substances, easy preparation, and low costs of manufacture [53]. They can transport hydrophobic and hydrophilic molecules, demonstrate low toxicity, and release regulated medication. Lower body negative pressure (LBNP) has demonstrated considerable promise in improving therapeutic outcomes by improving medication bioavailability, reducing toxicity, and increasing drug concentrations in tumor tissues while decreasing them in healthy tissues [54].

3.4.1. Herbal nanoemulsions

Nanoemulsions are highly advantageous for efficiently delivering herbal extracts in diverse applications. They are prepared using various techniques, such as low-energy and high-energy emulsions. These emulsions offer reduced droplet size, increased surface area, and enhanced ingredient penetration [55]. Herbal nanoemulsions have been used in medication delivery systems, gene therapy, and the food sector because they are stable and easy to prepare. The utilization of plants in nanotechnology has become important, as numerous medicinal plants, such as fenugreek (Trigonella foenum-graecum) are being investigated for their therapeutic characteristics in nanoemulsion formulations [56]. Nanoemulsions are essential for encapsulating active chemicals, improving their bioavailability, and preventing degradation. In summary, the advancement of herbal nanoemulsions presents favorable prospects for enhancing the transportation and effectiveness of herbal extracts in diverse applications. Fig. 7 illustrates the various methods used to produce herbal nanoemulsions.

3.4.1.1. Nanoemulsification of herbal extracts via solvent evaporation method. The process of nanoemulsification of herbal extracts using the solvent evaporation method entails dissolving the herbal oil in a water-immiscible organic solvent, such as cyclohexane or chloroform, and then emulsifying it in an aqueous phase that contains surfactants. During the process of emulsification, the organic solvent undergoes evaporation, resulting in the lipids being precipitated. This approach is employed to produce stable nanoemulsions for drug delivery systems and herbal remedies, improving the bioavailability and effectiveness by overcoming challenges such as inadequate absorption and large molecular sizes of active chemicals [57].

3.4.1.2. Nanoemulsification of herbal extracts through homogenization. Homogenization is a frequently employed technique in nanoemulsification for extracting herbal compounds. High-pressure homogenization is a vigorous technique that utilizes severe homogenization to reduce the size of droplets in nanoemulsions. This approach has extensively developed nanoemulsions for culinary, pharmaceutical, and biotechnological ingredients. It allows precise manipulation of the emulsion's particle size, stability, rheology, and color [58]. For best performance, small-molecule surfactants as emulsifiers in high-pressure

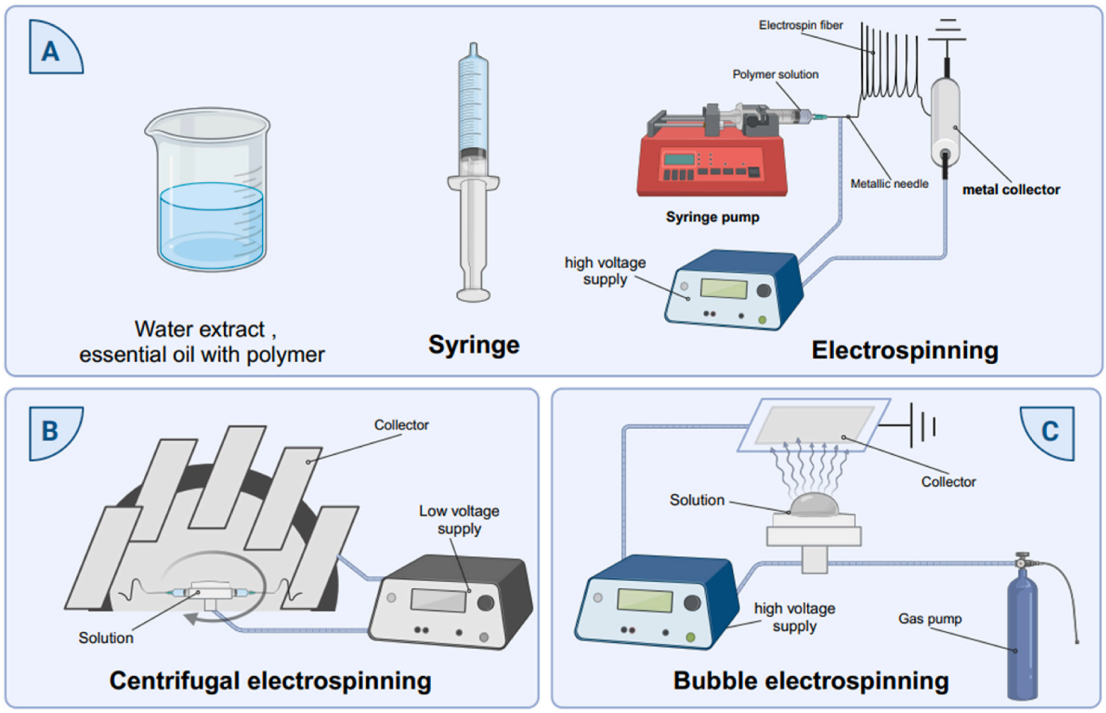

Fig. 6. There are three techniques for producing nano fibers from top (A) electrospinning, (B) centrifugal electrospinning, (C) bubble electrospinning.

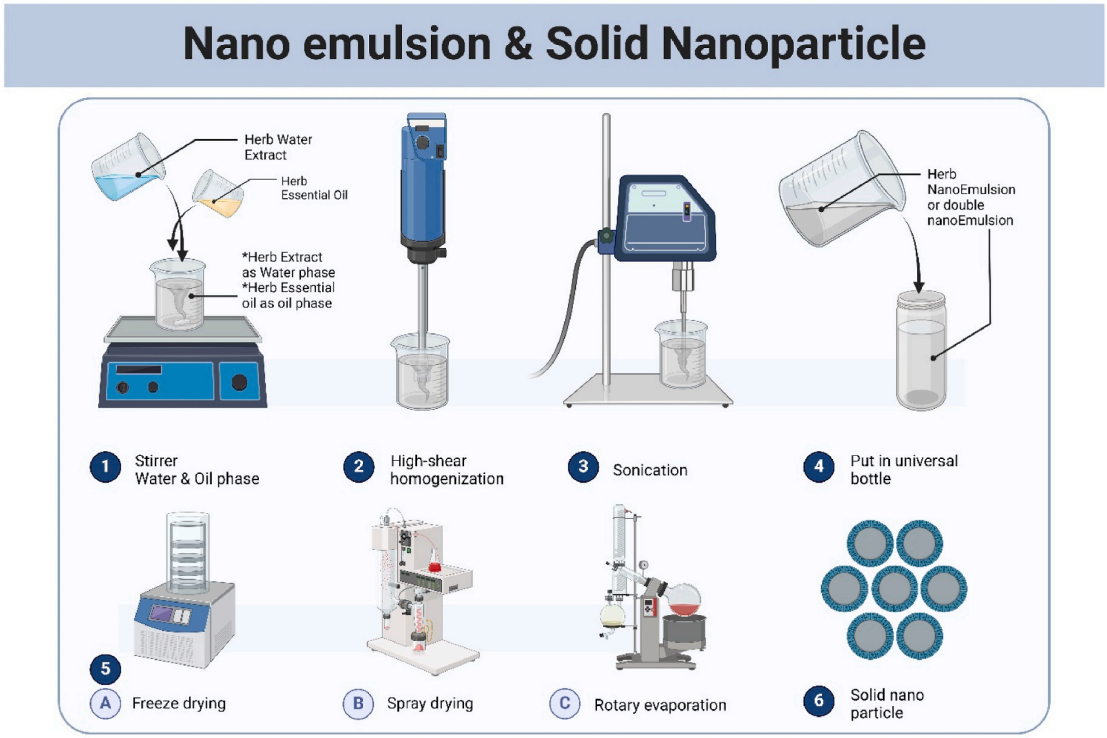

Fig. 7. Illustrates the various methods used to produce Herbal Nanoemulsion.

homogenizers are recommended. High-pressure homogenizers play a vital role in producing extremely small particle sizes and guaranteeing uniformity in nanoemulsions. In addition, low-energy approaches, such as phase inversion and self-nano emulsification, employ internal chemical energy and moderate churning to produce nanoemulsions [59]. These technologies are characterized by higher energy efficiency

and cost-effectiveness compared to high-energy approaches [60]. Nevertheless, food-grade emulsions are not frequently made using them since they necessitate larger concentrations of surfactants, which can hurt taste and safety. Low-energy techniques are favored due to their effectiveness and decreased energy demands, which makes them appropriate for delivering hydrophobic compounds with limited bioavailability.

3.4.2. Nanoprecipitation in herbal medicine

Nanoparticles made from herbal extracts use a process called nanoprecipitation. This improves how well the body can absorb the herbs and how well they work. First, the bioactive chemicals or herbal extracts are dissolved in a solvent that mixes with water. Then, non-solvent-like water is added while stirring to make nanoparticles. This sudden change in conditions causes particles to form and grow. To keep the particles from sticking together and ensure they are all the same size, stabilizers like PVA or PEG-PLGA are added [61]. Nanoprecipitation is good for the industry because it is easy to use and produces small particles. The particles' size, stability, and effectiveness depend on how much solvent is used, how fast it is stirred, and how much polymer is added. Making the particles stable and not clumping together is possible using special substances or quick cooling methods. By enclosing curcumin and resveratrol, their effects and stability were also improved [62]. Nanoprecipitation can encapsulate a wide range of herbal extracts due to their compatibility with hydrophilic and hydrophobic components. Soft supercritical fluid techniques incorporating nanoprecipitation are utilized for nanoparticle extraction and up-scale production. Combinations of various methods have resulted in more active plant components and decreased solvent consumption. Research has discovered that nanoprecipitation can create nanoparticles that exhibit improved pharmacokinetics, meaning they show the results of prolonged release and more absorption in the case of curcumin and β-carboline alkaloids [63]. Fig. 8 shows the preparation process for nanoprecipitation.

3.4.3. Solid lipid nanoparticles in herbal medicine

Solid lipid nanoparticles (SLNs) are becoming increasingly popular due to their ability to transport herbal extracts effectively. The nanoparticles, with sizes ranging from 50 to 1000 nm, consist of biocompatible and biodegradable lipids. This makes them well-suited to transporting different chemicals [64]. The preparation of SLNs incorporates emulsification-hot melt homogenization and ultrasonication to produce stable particles ideal for delivering drugs [65]. SLNs provide benefits such as increased drug bioavailability, regulated release of active components, enhanced intracellular permeability, and precise drug administration through surface changes [66]. The lipophilic matrix of these substances can efficiently encapsulate medicines with hydrophilic and hydrophobic properties. SLNs are renowned for their exceptional physical stability, biocompatibility, and absence of biotoxicity, rendering them a highly promising choice for drug delivery systems. The utilization of SLNs, including plant extracts such as Hibiscus rosa-sinensis, has demonstrated potential in addressing concerns associated with inadequate absorption in the oral route and inconsistencies among individuals [67]. The SLNs are formulated by employing lipids such as GMS and beeswax, utilizing a technique that involves homogenization and ultrasonication to achieve particles with a size below 500 nm. Fig. 9 illustrates the process of synthesizing SLNs and nanostructured lipid carriers.

3.4.4. Nanostructured lipid carriers in herbal medicine

Nanostructured lipid carriers (NLCs) have become a promising drug delivery system for herbal formulations. The method of incorporating herbal actives into NLCs involves specific techniques and considerations. In addition, the production of NLCs for herbal preparations typically entails utilizing a melt-emulsification technique employing solid lipids, liquid oils, and emulsifiers. The size of NLCs can vary from 100 to 1000 nm, contingent upon the precise formulation and preparation procedure. Using NLCs in herbal preparations enhances herbal actives' solubility, stability, and bioavailability, thereby augmenting their therapeutic efficacy [68] for synthesizing NLCs Fig. 9.

3.4.5. Liposomes

Liposomes are being investigated as versatile nano-carriers for herbal and natural therapeutic compounds to tackle limited solubility, stability, and targeted distribution. Lipid-based systems can encapsulate bioactive molecules with varying solubilities, reducing oxidation and improving bioavailability [69]. Liposomes offer several benefits, including their composition of natural substances, inclusion of aqueous compartments, and protection against ingredient oxidation caused by free radicals. Adding herbal extracts to liposomes can improve stability, controlled release, and bioavailability, enhancing the pharmacological benefits at lower doses and minimizing toxicity [70]. Research has demonstrated that liposomes, microspheres, and phytosomes are employed in drug delivery by enclosing or trapping pharmaceuticals [71]. In summary, liposomes present a hopeful natural framework for precise medication delivery systems that involve herbal and natural components. Fig. 10 (A) illustrates synthesizing liposomes, nanohydrogels, and biosynthesis methods.

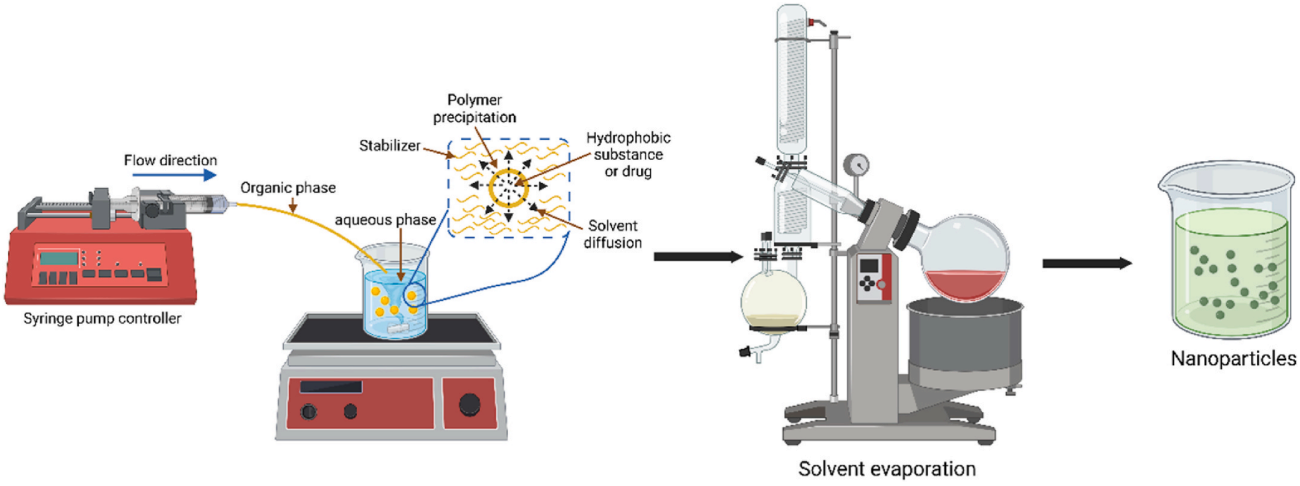

Fig. 8. Nanoprecipitation process: synthesis of herbal nanoparticles via solvent diffusion, polymer precipitation, and solvent evaporation.

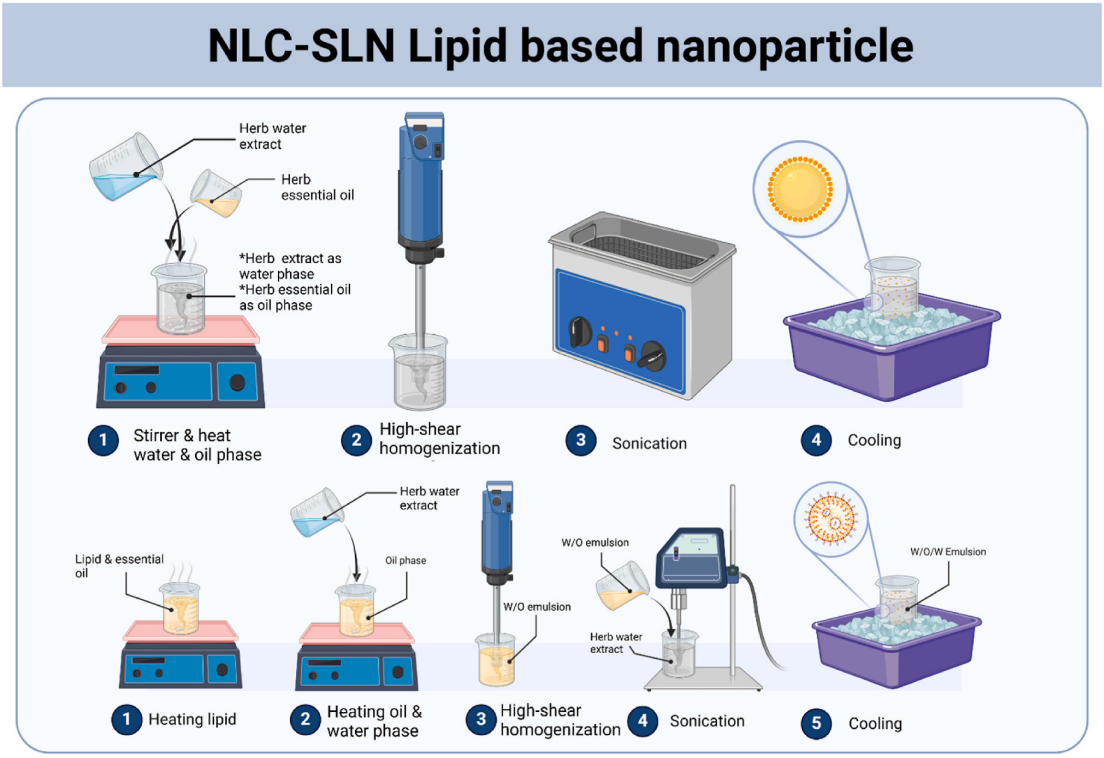

Fig. 9. Both solid liquid nanoparticles and nanostructured lipid carriers are briefly demonstrated as one of the synthesis methods.

3.5. Biosynthesis of nanoparticles loaded with herbal extracts

Researchers have recently become interested in the use of herbal extracts for the synthesis of nanoparticles. This method has several advantages, including a biocompatible stabilization procedure, fast synthesis, and achieving desired morphologies [72]. Biomolecules facilitate the reduction of metal ions throughout the preparation process. Thus, biosynthesis has been regarded as more advantageous than alternative chemical and physical approaches [73]. Synthesizing nanoparticles utilizing plants as a reducing agent involves a bottom-up approach and a top-down approach [74]. The biosynthesizing nanoparticles using plant extract involves washing and boiling the extract, filtering it, and then adding the appropriate salt solution to create the desired nanoparticles. Over time, the solution undergoes a color shift, indicating the creation of nanoparticles. These nanoparticles can then be isolated, cleaned, and dried for future applications [75]. Fig. 10 (C) preparation of three types of nanoformulations based on herbal.

3.6. Nanohydrogels in herbal medicine

Advanced delivery technologies like herbal nanohydrogels use nanotechnology to improve herbal chemical solubility, activity, and dispersion for numerous therapeutic uses [76]. These nanogels improve herbal drug efficacy and absorption. Drug delivery is ideal for nanogels, tiny crosslinked polymer networks that absorb water. They can deliver medications orally, pulmonary, nasally, parenterally, or intraocularly. Nanogels can encapsulate herbal components for controlled release, improving medication efficacy. In pharmaceuticals, herbal nanogels show potential for treating cancer, skin diseases, and diabetes. Chitin, chitosan, PLGA, PEG, and other polymers make nanogels [77]. These polymers enable skin-applied medicine delivery with fewer side effects than oral pharmaceuticals. Herbal nanogels use nanotechnology to turn natural chemicals into effective medicines, improving patient adherence and safety [78]. Fig. 10 (B) illustrates the process of synthesizing nanohydrogel.

4. Analytical techniques for assessing properties and composition of nanoherbal formulations

To effectively create nanoherbal formulations for use in biomedicine, it is essential to have a comprehensive understanding of their features. Despite the validation and acceptance of numerous characterization methodologies, obtaining a comprehensive characterization profile of nanoparticles in solution continues to be challenging. Observation is employed to ascertain specific attributes, such as dispersion, swelling, agglomeration, and aggregation. Some assessments need the use of advanced tools. Table 2 presents the characteristics of the attributes and the corresponding methods used to assess them.

Dynamic light scattering is vital for nanoparticle and colloidal solution analysis. DLS measures laser light dispersion in colloidal solution. The intensity of scattered light over time can be used to assess solution particle size [91]. XRD is a technique employed to determine the crystallographic configuration of a material [92]. Zeta potential measures colloidal nanoparticle electrostatic stability. This gadget measures nanoparticle surface charge. A nanoparticle's net surface charge is offset by a higher concentration of negatively charged ions nearby. Surface charge of nanoparticles changes with pH. At the pH isoelectric point, the surface charge is zero. Sandwiching the nanoformulation solution between two gold electrodes measures zeta potential. Particles tend to cluster at 0–5 mV. Their stability is low (5–20 mV), moderate (20–40 mV), and extreme (>40 mV). Test stability next [93]. Drug substance and product stability testing is often conducted on a range of substances and items as part of the product development process. Accelerated stability testing is conducted initially to identify any degradation products that may form during extended storage periods. Products undergo rigorous testing in conditions of high temperature and humidity. Herbal product shelf life and expiration dates are assessed in less strict environments, such as those recommended for longer storage on shelves at

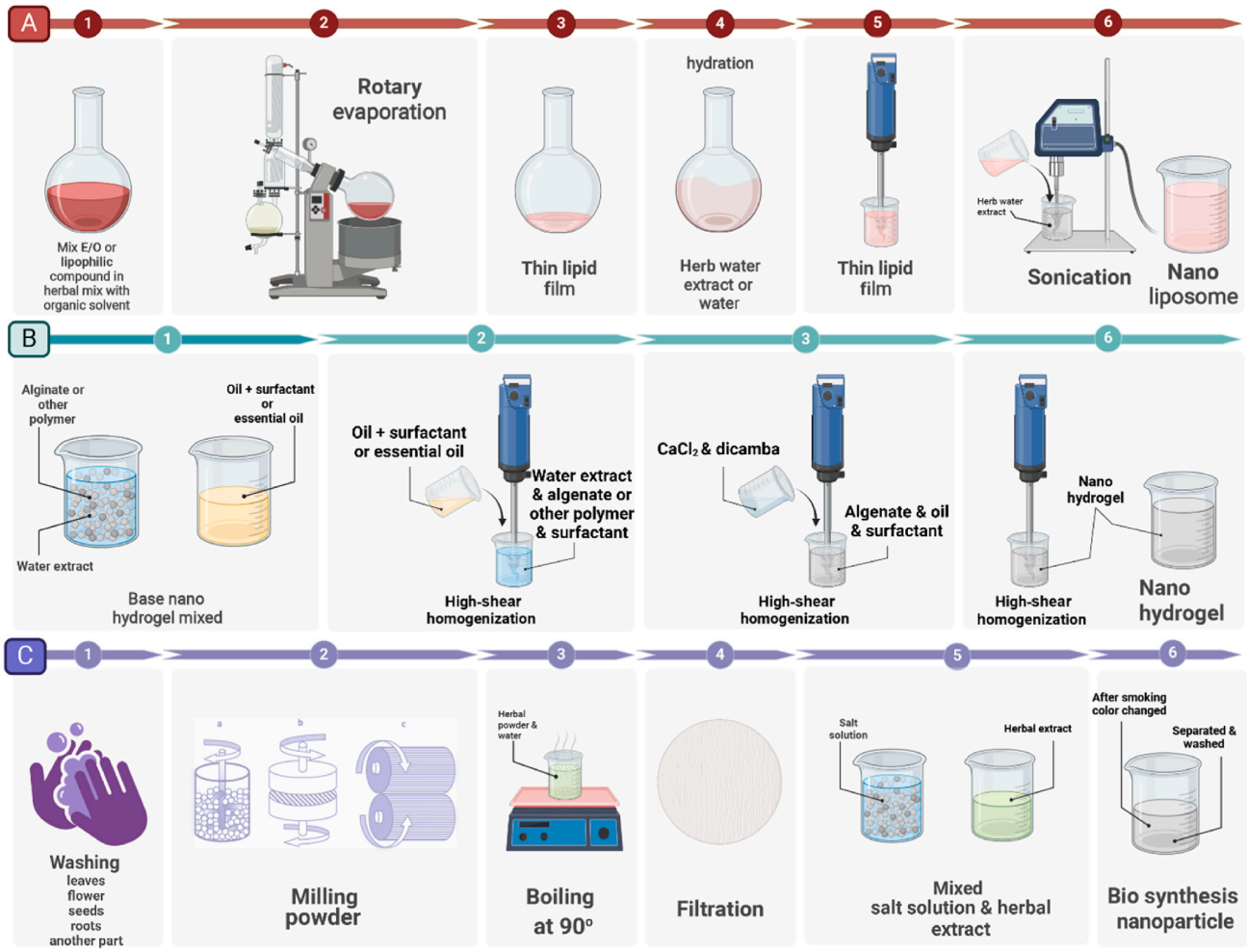

Fig. 10. Method of preparation of A. Nano liposomes, B. Nanohydrogels, C. Nano Biosynthesis.

Table 2
Characteristics of nanoherbal compositions from a physicochemical perspective.

Characteristics	Methods and tools utilized
Particle morphology, dimensions, and dispersion	DLS, TEM, SEM, AFM
Particle roughness, topography, surface area, and surface chemistries	XRD
Electric charge on the surface	Zetasizer
Consistency	Method stability chamber
Purity	HPLC/LC-MS

slightly elevated temperatures. The objective of stability testing is to ensure a fair level of confidence that the quality of the product will remain consistent and unchanged over a period of time [94]. The nanoherbal formulation may be quantified by LC-MS. Liquid chromatography-mass spectrometry (LC-MS) is a method that integrates the physical separation capabilities of liquid chromatography, commonly referred to as high-performance liquid chromatography (HPLC), with mass spectrometry (MS) [95]. Liquid chromatography is used to separate mixtures with several components, while mass spectrometry is performed to determine the structural identification of individual components that have been separated, using high molecular specificity and detection sensitivity [96].

5. Nanoherbal drugs: advancements in medical applications

Drug delivery methods have been transformed by nanotechnology, particularly in the field of herbal remedies. Nanotechnology in herbal medicines entails creating nanoscale drug delivery systems to improve efficiency and solve problems related to conventional plant medicines [97]. Because of their small size, these nanocarriers can maximize medication delivery by ensuring that the drug reaches the affected area at the lowest effective dose, avoiding liver metabolism, and boosting drug circulation in the blood. Many medicinal plant species' effectiveness depends on active compounds' availability [98]. These phytoconstituents show promise as a preventive mechanism against various diseases, including cancer, diabetes, cardiovascular disease, and neurodegenerative disorders. They are efficacious in a range of medicinal formulations. However, due to their poor bioavailability, there are major barriers to the therapeutic application of phytochemicals. In the upcoming sections, we shall explore the ability of nanoherbals to resist illnesses [99]. Fig. 11 illustrates the arrangement of herbals using nanocarriers.

5.1. Nanotechnology applications in herbal medicine for cancer treatment

Nanotechnology is employed in herbal medicine to treat cancer by utilizing nano-drug delivery systems to enhance the efficacy of natural bioactive compounds against cancer [100]. Researchers are

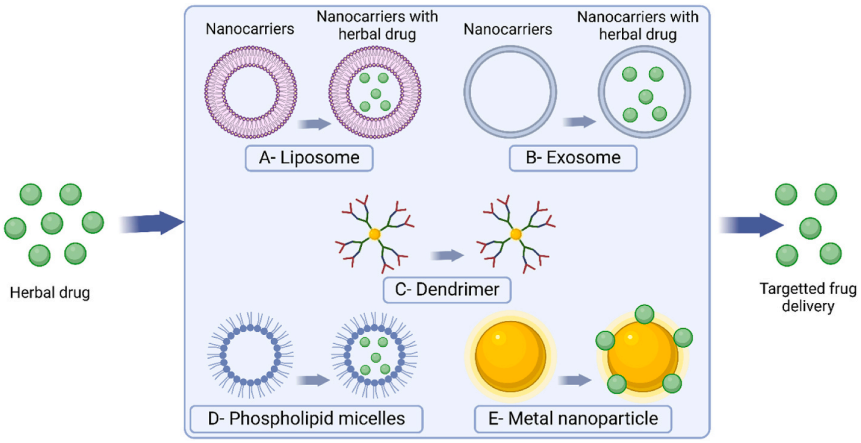

Fig. 11. The illustration depicts the structure of herbal nanocarriers.

investigating the use of nanocarriers, such as liposomes, dendrimers, and biopolymer-based carriers, to encapsulate powerful plant-based anticancer drugs like curcumin, quercetin, and resveratrol [101]. This approach aims to address issues such as limited solubility in water, low effectiveness in the body, and lack of specificity in delivering the drugs to the intended site. Furthermore, the utilization of biogenic nanoparticles produced from plant extracts presents a hopeful strategy for cancer treatment [102]. Phytochemicals can be added to these nanoparticles to boost their ability to fight cancer and increase the rate at which cancer cells die [103]. Biogenic nanoparticles have demonstrated promise in precisely targeting cancer cells, minimizing adverse effects, and enhancing treatment results by directly transporting medications to tumor locations [104]. In the study producing a water-soluble extract from the *Solanum melongena* involves a concentration of between 60 and 90 % solasonine and solamargine. This extract contains nanoparticles with a size smaller than 1 μm. These nanoparticles may readily dissolve in water, forming a clear and transparent yellowish aqueous phase. The solubility range of this extract is 2–20 mg or higher. Extract is utilized as an active ingredient in medicine formulations to treat or inhibit the growth of tumor or cancer cells, specifically in the liver, lungs, and breast [105]. Liposomal curcumin is utilized for the treatment or prevention of breast cancer, carcinoma, and pancreatic cancer in humans or other mammals [106]. Studies have demonstrated that it can hinder the development of cancer cells in a controlled environment and prevent the occurrence of cancer in animals when given through injection as a liposomal drug delivery system in the form of nanoparticles or nanocapsules [107]. By subjecting cells to a liposomal drug delivery system that contains curcumin encapsulated inside it, it is possible to prevent the growth of cancer in a laboratory environment [108]. Then the reported ratio of curcumin to lipid mixture (by weight) varied from 1:75 to 1:10. The study revealed that liposomal curcumin exhibited a significantly greater effect on tumors compared to normal curcumin [109] In another study, nanocurcumin, a yellow polyphenol from turmeric (Curcuma longa) rhizomes, was synthesized. This formulation encapsulates curcumin with micellar aggregates of cross-linked and random copolymers of NIPAAM, VP, and PEG-A. Particle dispersion from 50 nm. Nanocurcumin disperses better in water than free curcumin. Nanocurcumin works as well as free curcumin against human pancreatic cancer cell lines in the lab. In soft agar studies, cell viability and clonogenicity were assessed. Like free curcumin, nanocurcumin impacts pancreatic cancer cells through comparable processes. This involves initiating cellular apoptosis, suppressing NFκB activation, and lowering pro-inflammatory cytokines (IL-6, IL-8, and TNFα) [110]. On the other hand, some researchers also used Indian turmeric curcumin in nanoparticles to cure medulloblastoma and glioblastoma cells and reduced the proliferation of embryonal tumor-derived lines DAOY and D283 Med, as well as glioblastoma neurosphere lines HSR-GBM1 and JHH-GBM14, depending on dosage. G2/M arrest and apoptosis led to the viable cell mass drop. Curcumin also suppressed cell development without attachment and decreased CD133-expressing stem-like cell populations. Downregulation of the insulin-like growth factor pathway in DAOY medulloblastoma cells may explain the observed changes. Lower STAT3 levels. Hedgehog signalling was blocked in DAOY cells, whereas Notch signalling was unaltered. The study found that curcumin nanoparticles can slow malignant brain tumor growth by affecting cell division, survival, and stem cell properties [111]. In addition, camptothecin, a cytotoxic alkaloid derived from *Camptotheca acuminata*, was encapsulated within superparamagnetic nanoparticles (NPs) composed of iron oxide, with a particle size of 14 nm. In the H460 lung cancer cell line, the NPs that were generated exhibited proapoptotic activity [112]. A different investigation was conducted to tackle the issue of limited solubility of camptothecin analog (CA) by developing a nanoparticulate system based on polyethylene glycol (PEG) through the utilization of high-pressure homogenization technology. In human tumor xenografts (NCI-H460 cell lines) established in athymic nude mice, the nanoparticulate formulation exhibited comparable anticancer activity to that of regular irinotecan [113]. Despite extensive research on the antitumor activity of camptothecin over the past six decades, recent progress in drug delivery systems has significantly enhanced the effectiveness of this medicine. This improvement is mostly attributed to the creation of nanosized dosage forms of camptothecin-derived pharmaceuticals. DNA topoisomerase is a target for drugs used in cancer therapy. Camptothecin is a botanical alkaloid that is obtained from the Chinese tree *Camptotheca acuminate*. Camptothecin, an alkaloid, induces DNA damage by selectively binding to DNA topoisomerase, resulting in the significant destruction of a wide range of tumors [114]. The work employed nanodiamonds conjugation to enhance the antiproliferative effects of citropten and quercetin on HeLa and B16F10 cancer cells. Naradidamonds were created through the processes of oxidation, chemical reduction, and plasma reduction. The nanodiamond adduct included 0.5 mmol of citropten and quercetin per milligram. Nevertheless, citropten samples produced through plasma reduction exhibited significantly elevated drug concentrations. Exposing HeLA cells to treatment for 48 and 72 h resulted in significant inhibition of cell growth. The citropten adduct, resulting from the process of oxidation and plasma reduction, exhibited a greater inhibitory effect on cell proliferation compared to pure citropten. Nanodiamonds that were functionalized with quercetin exhibited a reduction in growth comparable to pure quercetin. Both cell lines exhibited enhanced bioactivity of citropten following conjugation with nanodiamonds produced through oxidation and plasma reduction. The antiproliferative activities of quercetin were enhanced when it was combined with chemical and plasma reduction

nanodiamonds. The presence of nanodiamond adducts can potentially activate biological processes such as cell cycle differentiation and arrest, which could provide an explanation for the observed behavior [115]. Moreover, an investigation of solid lipid nanoparticles (SLNs) containing trans-resveratrol was conducted by Teskac and Kristl (2010). The internalization, shape, proliferation, metabolic activity, and genetic material of keratinocytes were assessed by comparing the impacts of the generated solid lipid nanoparticles (SLNs) using the NCTC2544 cell line. It was noted that small lipid nanoparticles (SLNs) less than 180 nm migrate quickly across the cell membrane, spreading throughout the cytoplasm, and ultimately settling in the perinuclear region without causing any harm to the cells. SLNs of resveratrol exhibited enhanced solubility, stability, and intracellular delivery, with resveratrol being released in a biphasic manner. Resveratrol solid lipid nanoparticles (SLNs) were observed to accumulate in the vicinity of nuclei and consistently release resveratrol, thereby demonstrating its cytostatic properties through a significant stop of the cell cycle at the S stage and a substantial decrease in the G2/M phase [115]. In addition, nanoparticles loaded with naringenin were tested for their chemopreventive effects in Syrian hamsters with experimental oral carcinogenesis caused by 7, 12-dimethylbenz [a]anthracene (DMBA). Oral naringenin-loaded nanoparticles suppressed tumor growth better than free naringenin. It also significantly reduced histopathological lesions. Sulfikkarali et al. found that nanoparticles (NPs) decreased PCNA and p53 expression in mice's buccal mucosa after DMBA treatment. Compared to free naringenin, NPs had stronger anti-lipid peroxidative and antioxidant effects [116]. Moreover, for salidroside and paeonol Peng et al. developed an innovative nanosphere gel to administer salidroside and paeonol in a sequential manner, with the aim of achieving anti-melanogenic effects. A dual drug-releasing nanosphere gel was created by incorporating nanospheres carrying both paeonol and salidroside into a carbomer hydrogel. The optimal nanoparticles, with a particle size of 275 nm and a low PDI index of 0.208, were obtained by combining Dynasan 116 with Miglyol 812 at a ratio of 6:4. The nanosphere gel facilitated the expeditious liberation of salidroside from the hydrogel, subsequently leading to a sustained release of paeonol from the nanosphere. The evaluation of the anti-melanogenesis effects was conducted by assessing melanogenesis in guinea pig skin that had been exposed to UVB

Table 3
Summary of the phytochemicals employed in cancer therapy.

Phytochemicals	Source	Type of Nano carrier	Therapeutic attributes	References
Curcumin	 Rhizome *Curcuma longa*	Hybrid nanoparticles, SLNs, NLCs, PLGA nanoparticles, Micelles, Liposomes, Nanoemulsion, Double nanoemulsion,	Cancer (Cervical Liver, Breast, Ovarian)	[127]
Podophyllotoxin, Etoposide, Teniposide	 *Podophyllum peltatum*	Lipid nanoparticles, Magnetic Nanoparticles, Albumin Nanoparticles, Polymeric nanoparticles	Cancer (Brain, Small cell lung, Testicular, Lymphoblastic, Breast)	[128,129]
Taxol	 *Taxus brevifolia*	Polymeric nanoparticles, gold nanoparticle, PLGA nanoparticles	Cancer (Breast, ovarian, and lung, prostate)	[130,131]
Vinblastine	 *Madagascarn periwinkle*	Chitosan/hyaluronan nanoparticles (CS/HY NPs), quantum dots, and vinblastine-loaded meso-porous silica nanoparticles functionalized with folic acid.	Cancerous red blood cells, Hodgkin's lymphoma, non-Hodgkin's lymphoma, cancer cells, Breast and Pancreatic Cancer Cells	[129,132]
Homoharringtonine	 Cephalotaxus	Lipid nanoparticles, phytosomes, dendrimers, magnetic Fe3O4 nanoparticles	Chronic myeloid Leukemia,	[133]
Camptothecin, Topotecan, Irinotecan	 *Camptotheca acuminata*	Liposomal Nanoparticles, Silica nanoparticles,	Cancer (Lung, ovarian, cervical, Colorectal)	[134]
Apigenin	 Chamomile	Gold nanoparticles, PLGA nanoparticles,	Cancer (Breast, colon , lung cancer, skin)	[135,136]

radiation. In the initial hour, salidroside exhibited a high release efficiency of 36.9 %, with a subsequent release of over 91 % throughout a span of 12 h. Similarly, paeonol shown a sustained release of 67 % over a duration of 72 h within the nanospheres [117]. Table 3 provides a summary of the phytochemicals employed in cancer therapy. The anticancer properties of annonaceous acetogenins (ACGs) are well-known and are derived from the seeds of the Annonaceae family [118]. Their anticancer efficacy against a range of cancer cell lines, such as A549, MCF-7, L1210, SMMC7721, HeLa, MKN-45, and HepG2, has been found to be substantial Although ACGs are effective, they can lead to acute toxicity when taken orally, such as liver and kidney damage [119]. In order to augment the anticancer efficacy of ACGs while minimizing their toxicity, Hong et al. employed an antisolvent sonoprecipitation approach to synthesize an ACG nanocrystal (ACG-NSps). The ACG-NSps, when stabilized with mPEG2000 PCL2, had particle diameters of around 126 nm and a zeta of near 20 mV. The aforementioned formulation exhibited heightened cytotoxicity against 4T1, MCF-7, and HeLa cells, surpassing that of the unbound drug. It is worth mentioning that ACG-NSps demonstrated effective tumor accumulation and produced improved therapeutic effectiveness with a significantly reduced dosage of only 1/10th compared to the drug oil solution [120]. Garcinia hanburyi contains gamogenic acid, which has a wide range of anticancer properties against breast cancer, lung cancer, and multiple myeloma [121]. It has the ability to counteract P-gp-mediated multidrug resistance and impact apoptosis via activating IRE1γ/JNK through ROS-dependent activation [122]. In order to improve the bioavailability and effectiveness of Gambogenic acid in treating tumors, Gambogenic acid nanocrystals (GNA-NSs) were synthesized by Yuan et al. using PVP K30 and PEG2000 as stabilizers. The resultant particles had a size of near 184 nm and a zeta potential of near −23 mV. The AUC and $t_{1/2}$ values of GNA-NS exhibited a significant increase of 2.63- fold - 1.77- fold, respectively, when compared to the reference formulation. Additionally, the GNA-NSs demonstrated heightened cytotoxicity in HepG2 cells [123]. Subsequently, the alkaloid hydroxycamptothecin is derived from the seeds or roots of *Camptotheca acuminata* Decne. It has the ability to specifically hinder topoisomerase I, hence disrupting the process of DNA replication [124]. Prior to entering the bloodstream, the phytoconstituents present in herbal drugs encounter a significantly acidic pH in the stomach. Additionally, some of these phytoconstituents undergo hepatic metabolism. Consequently, the optimal amount of biologically active compounds fails to reach the bloodstream, resulting in diminished or insignificant therapeutic effects of the drug. The utilization of nanocarriers in conjunction with herbal medications facilitates the transportation of an ideal dosage of the drug to the intended site of action. This approach overcomes many obstacles such as acidic pH and hepatic metabolism, hence enhancing the sustained circulation of the drug in the bloodstream [125]. Bioactive compounds in natural sources used for anticancer are summarized in Fig. 12. Nanosized delivery systems offer several advantages in comparison to conventional drug delivery systems. Here are a few examples: the unusual size and large loading capabilities of these entities enable them to effectively transport high drug concentrations to infected regions. Administer the medication in a reduced particle size, thereby enhancing the drug's surface area and facilitating improved dispersion in the bloodstream. The medication exhibits prolonged persistence at active sites, leading to improved permeation and retention outcomes. These outcomes encompass

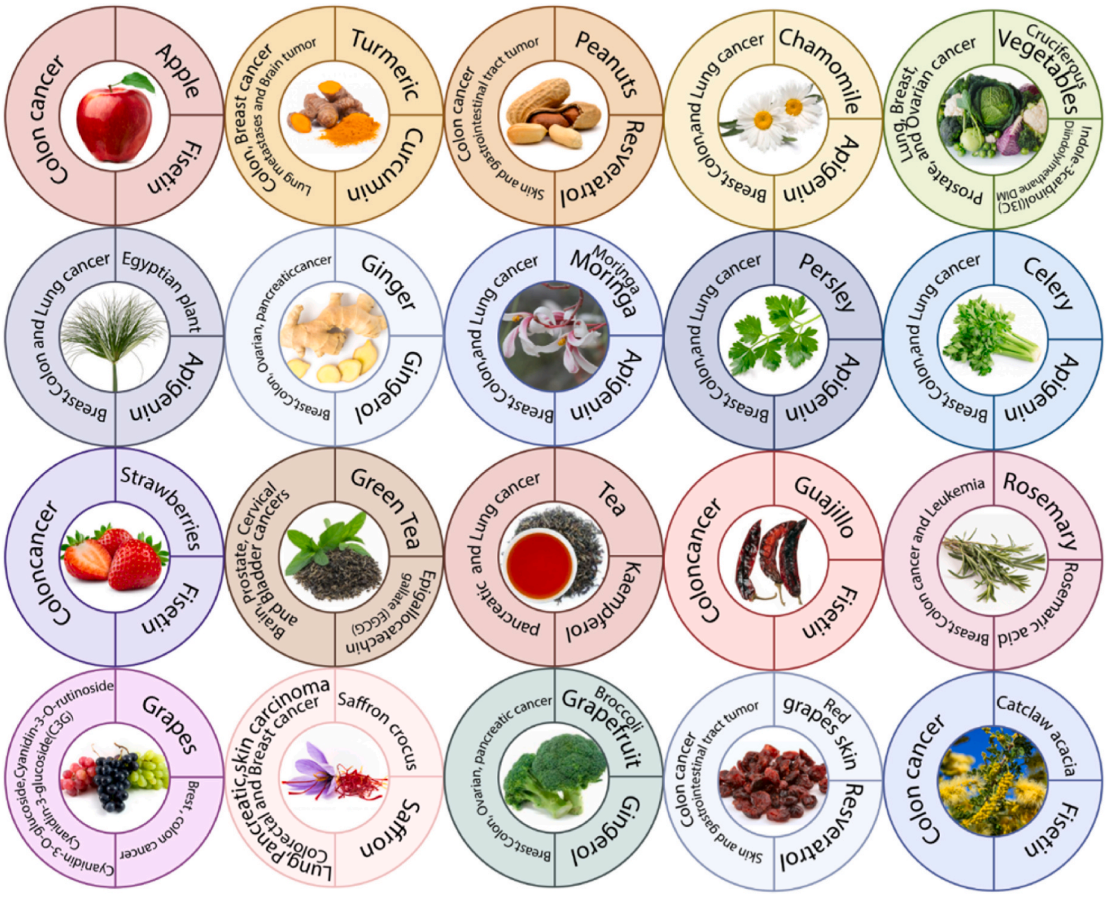

Fig. 12. Bioactive compound in natural source use for anticancer.

enhanced permeation through barriers resulting from reduced size and improved retention due to inadequate lymphatic drainage in tumor-affected tissues [126]. Novel drug delivery methods demonstrate the ability to passively target the location of action without requiring a specific ligand component. The utilization of innovative drug delivery systems leads to a decrease in adverse effects. The reduction in the dosage of the pharmaceutical formulation.

5.2. Nanotechnology in herbal medicine for anti-inflammatory effects

Research on using nanoherbal technology to treat inflammation has made encouraging progress recently. Anti-inflammatory treatments, such as those for rheumatoid arthritis, osteoarthritis, and inflammatory bowel disease, have used drug delivery systems mediated by nanoparticles [137]. A study investigated the potential of two herbal plants, Plectranthus amboinicus and Hemigraphis colorata, for developing a nano-encapsulated antimicrobial ointment formulation. These botanical specimens possess antimicrobial, anti-inflammatory, and anti-oxidant characteristics. Both Gram-positive and Gram-negative bacteria, as well as various fungal species, exhibited antimicrobial properties. The expedited wound healing can be attributed to the anti-inflammatory properties, while the anti-oxidant properties facilitate scavenging free radicals from the skin [138]. The SLN synthesized using a ratio of 1:25 and 1:30 were found to be in the optimal nano-range, specifically between 1:30 and 77.63 nm and between 1:25 and 48.51 nm. Combining leaf extracts from both plants resulted in a wide range of ointments. The formation of SLN through nano-encapsulation further improved the drug's penetration into the system, leading to efficient delivery with minimal side effects [139]. In a separate investigation, the potential anti-inflammatory benefits of the homegrown gel detailing formulation may be attributed to the presence of luteolin and apigenin in methanol leaf concentrates derived from Vitex negundo and Cardiospermum halicacabum. The definition F4 that was developed exhibited potential as a natural gel for treating joint inflammation in the skin. The composition consisted of 2 % CHME and VNME each and 1.5 % carbopol 934. Implementing this plan for persons with joint provocative infections can be supported by additional clinical assessment [140]. In another study, lavender, an essential oil, was found to be incorporated into solid lipid nanoparticles (SLNs) and produced as a gel to address localized inflammation. Solid lipid nanoparticles (SLNs) were synthesized utilizing cocoa butter as the solid lipid and Tween 80 % as the surfactant. Encapsulating lavender in solid lipid nanoparticles (SLNs) can address its limitations of low water solubility and limited bioavailability. The ex-vivo approach was employed to evaluate the anti-inflammatory activity using the carrageenan-induced edoema technique. The edoema inhibition percentage of 1 % lavender-based solid lipid nanoparticles (SLNs) was determined to be 28 ± 0.1 %, while the anti-inflammatory properties of diclofenac gel were discovered to be 33.6 ± 0.05 % [141]. SLNs are a novel approach to deliver curcumin into inflamed joints. The lipid hydration approach was employed to load curcumin into liposomes. The liposome that was synthesized underwent characterization to assess its anti-inflammatory effectiveness. The study focused on examining pro-inflammatory markers, including IL-6 TNFα and IL-8. The formulations containing curcumin demonstrated enhanced encapsulation efficacy and suppression of pro-inflammatory indicators compared to the positive control group, which received treatment with liposomes loaded with salbutamol [142]. The other study used nanoemulsion to administer capsaicin in vivo via topical therapy. The optimized formulation, stable for over 8 months, was tested in a skin irritation investigation. The nanoemulsion showed no edoema or erythema, reduced rat paw edoema inflammation, and demonstrated good thermal pain resistance. It showed excellent potential for topical capsaicin delivery [143]. The metabolite curcumin, derived from the rhizome of Curcuma longa, exhibits a range of beneficial qualities, including anti-inflammatory, antioxidant, anticancer, antidiabetic, antiarthritic, antiangiogenic, antipsoriasis, and antibacterial effects [144]. It has shown impressive efficacy in reducing inflammation at the targeted site by absorbing free radicals through several mechanisms, such as inhibiting nuclear factor-B and decreasing IL-1, IL-6, and TNF-κ levels. Ultimately, this results in the inhibition of psoriatic and skin inflammation [145]. Nevertheless, curcumin, a substance with limited solubility and bioavailability, can treat persistent inflammatory conditions like psoriasis and acne vulgaris. A nano delivery system was prepared using hot emulsification and probing sonication, with a particle size of 96.2 nm and 70.5 % entrapment efficacy. The gel showed a 48-h release time and 3.24 times superior skin retention compared to free curcumin [146]. On the other hand, herbal medicine nanocrystals are used to treat In their study, Gera et al. documented the synthesis of naringenin nanocrystals (NRG-NS) using antisolvent sonoprecipitation. The resultant nanocrystals exhibited a particle size of 117 ± 5 nm. The nanocrystals displayed increased levels of alkaline phosphatase (ALP) in comparison to nitrogen-rich graphene (NRG) and exhibited enhanced structural healing of the cortical and trabecular bone architecture [147]. NRG nanocrystals were synthesized using the wet media milling approach with TPGS in a distinct investigation to treat postinfectious cough. Compared to the blank model and crude NRG, the NRG nanocrystal demonstrated improved antitussive properties, resulting in a threefold and 1.6-fold decrease in cough frequency, respectively. The oral absorption of icariin, a flavonoid glycoside belonging to the BCS IV class, is impeded by solubility and membrane permeability restrictions. Icaritin, a bioactive aglycone version of icariin, is a significant metabolite in the intestines. It belongs to the class of BCS II compounds and has superior efficacy to icariin in promoting osteoblast differentiation and proliferation. Li et al. synthesized icaritin nanocrystals (ICTN) by the antisolvent precipitation technique, resulting in rod-shaped particles forming 216.6 ± 12.4 nm in size and a reduction in crystallinity of around 50 %. Research on bioavailability has revealed a notable increase in Cmax (4.7-fold higher) and AUC0–12 (2.0-fold higher), as well as a decrease in Tmax, compared to unformulated ICT. The research on anti-osteoporosis action additionally showed that ICTN enhanced the growth and specialization of osteoblasts, but ICT did not provide such stimulation [148]. In their study, Li et al. developed tetramethylpyrazine dihydroxynaphthalene nanocrystals (TMP-NS) to administer them intra-articularly to address osteoarthritis [149] specifically. Applying TMP-NS resulted in a retention period that was five times longer within the articular cavity. Additionally, it led to increased concentrations of TMP in the joints and demonstrated a more significant anti-osteoarthritic effect when compared to the TMP solution.

5.3. Nanotechnology applications in herbal medicine for cardiovascular health

The utilization of nanotechnology in herbal medicine for the treatment of cardiovascular diseases (CVDs) has witnessed a notable increase. The amalgamation of nanotechnology with herbal medicine presents auspicious therapeutic avenues owing to heightened efficacy in drug administration and diminished adverse reactions. Nanoformulation techniques have been shown to enhance the solubility, bioavailability, and therapeutic effectiveness of curcumin, quercetin, and resveratrol, which are frequently employed in the management of (CVDs) [150]. The recognized benefits of isoflavones, QUE, catechin, resveratrol, carotenoids, and sulforaphane include their ability to protect the heart and reduce the risk of cardiovascular disease. These chemicals demonstrate antioxidant, antiangiogenic, antiischemic, antihypercholesterolemic, platelet aggregation inhibition, and anti-inflammatory effects. Additionally, it has provided a succinct overview of current advancements in the realm of natural product-derived nanodrugs for the management of cardiovascular diseases (CVDs) [151]. In their study, Rachmawati et al. conducted an in *vitro* evaluation of the antihypercholesterolemic and antihypertensive properties of curcumin nanoemulsion. The researchers employed

acetylcholinesterase (ACE) and 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) assay kits for this purpose. The findings of the study indicate that the inhibitory impact of nanoemulsified curcumin on ACE was marginally enhanced in comparison to pure curcumin. In addition, the curcumin nanoemulsion demonstrated an enhanced inhibition of HMGR, indicating its potential as an antihypercholesterolemic agent [152]. In a separate investigation, the water solubility, biological effectiveness, and dispersion of curcumin in water-based solutions were improved in a model of diabetic cardiomyopathy by enclosing curcumin within a multipolymer known as PBLG-PEG-PBLG, which consists of poly (gamma-benzyl -L-glutamate) and poly (ethylene glycol). Curcumin injection in *vivo* led to an increase in the blood levels of H2S and Ca2+i content in cardiac cells. Additionally, the expression of cystathionine β-lyase, calmodulin, and calcium-sensing receptor was elevated. Furthermore, the administration of curcumin and curcumin/P resulted in a notable decrease in diabetic cardiomyopathy, along with the alleviation of clinical and morphological harm to cardiac cells [153]. Monocrotaline-induced pulmonary arterial hypertension in rats was treated with curcumin nanoparticles (NPs). Curcumin nanoparticles (50 mg/kg intraperitoneally) reduced right ventricular hypertrophy development, weight-to-bodyweight ratio, TNF-κ and IL-1β mRNA expression, and oxidative stress [134]. In another study, Li et al. found that curcumin nanoparticles reduced cell apoptosis, ROS levels, and Rac1 activation in cardiomyocytes. Curcumin nanoparticles also inhibited palmitate-induced $gp91^{phox}$, $p22^{phox}$, $p47^{phox}$, and $p67^{phox}$ expression. Curcumin nanoparticles increased cardiomyocyte Bcl-2/Bax ratio, glucose-regulated protein 78, and C/EBP homologous protein expression. Cardiomyocytes received curcumin nanoparticles, which inhibited apoptosis, reduced ROS and MDA, increased SOD activity, and decreased NADPH oxidase isoforms. The study found that endoplasmic reticulum stress signalling likely suppressed NADPH-induced oxidative damage. Due to lipid toxicity, curcumin nanoparticles (NPs) have been suggested as pharmaceuticals to enhance heart damage [154]. For the Naringenin, using a naringenin-cyclodextrin or liposome combination or integrating it into chitosan core-shell nanoparticles coated with alginate can improve its pharmacokinetics. PEGylated lipid nanoemulsions include anti-inflammatory naringenin and hesperetin and a vascular cell adhesion molecule 1 recognizing peptide. This combination improves endothelial cell function and reduces inflammation. Monocyte attachment and movement were inhibited, NF-κB movement was reduced, MCP1 production was increased, and endothelial inflammation was reduced [155]. By the other hand Phosphatidylcholine liposomes (PCLs) loaded with quercetin have been observed to exhibit protective effects against myocardial injuries caused by peroxynitrite. This protective mechanism involves the direct scavenging and decomposition of endogenously produced peroxynitrite ions. Consequently, PCLs have the potential to restore the normal contractility of the myocardium in both anesthetized animals and isolated tissues [156]. A study on polymeric micelles containing resveratrol and quercetin demonstrated their effectiveness in mitigating cardiotoxicity, both in *vivo* and in *vitro*, against doxorubicin-induced cardiotoxicity [157]. In addition, Giannoulia et al. employed an electrohydrodynamic atomization approach to produce polymeric PLGA nanoparticles loaded with quercetin, with the aim of addressing its limitations and mitigating the risk of atherosclerosis. Quercetin has shown great promise in reducing atherosclerosis and other (CVDs) due to its biphasic release from nanoparticles (24 h and 59 days, respectively) [158]. Quercetin-loaded PLGA nanoparticles were given to H9c2 cells, which led to the preservation of mitochondrial activity and ATP generation under hypoxia-reoxygenation conditions. The preservation was associated with the suppression of oxidative stress [159]. Furthermore, Carlson et al. employed a polymeric micellar co-delivery system to mitigate the cardiotoxic effects caused by doxorubicin. This was achieved by mixing curcumin and resveratrol. Encapsulation of a substance led to an increase in its solubility, which in turn improved the protection of cardiomyocytes in H9C2 cells by removing reactive oxygen species [160]. In a separate investigation, the treatment of solid lipid nanoparticles loaded with resveratrol resulted in a notable elevation in heart rate, ejection fractions, and fractional shortening in mice with doxorubicin-induced cardiotoxicity. The arrangement of cardiac fibers exhibited regularity, and a limited number of vacuole degenerations were observed within the myocardial cell [161]. Finally, several nanosized formulations have been used to address baicalin's limited hydrophilicity, short half-life, and poor oral absorption in the acute myocardial infarction model, baicalin-loaded PEGylated nanostructured lipid carriers (BN-PEG-NLC) had longer plasma circulation, better delivery to the ischemic heart, and smaller infarcts. PEG-NLC may be a biocompatible carrier for heart-targeted baicalin delivery [162]. Table 4 summarized Physicochemical Characteristics of NPs Loaded for the Treatment of CVDs and Fig. 13 depicts the ways by which nano herbs phytomedicines exert their effects. Nanocrystals have been utilized to improve the bioavailability and therapeutic effectiveness of insoluble active substances. One example of a compound with platelet aggregation inhibitory properties is honokiol, which is obtained from the stem bark of *Magnolia officinalis* Rehd. et Wils. This compound functions as a selective antagonist of collagen receptor glycoprotein VI on human platelets [163]. Furthermore, it has a function in controlling the utilization of mitochondrial substrates and the metabolism of cellular fatty acids in the hearts of diabetic mice [164]. Han et al. synthesized honokiol nanocrystals with particle sizes of around 117 nm to improve its oral bioavailability and facilitate its dispersion in the cardiovascular and cerebrovascular systems [165]. In the study found that HK-NSps, when stabilized with PVP and BSA, significantly increased the maximum concentration and area under the curve of Honokiol coarse suspension after oral administration. This was due to improved solubility, adhesion, and lymphatic transport channels. HK-NSps also showed potential in managing cardio-cerebrovascular disorders [165].

5.4. Nanotechnology applications in herbal medicine for skin health

The utilization of nanotechnology in herbal medicine for skin applications has witnessed a notable increase, aiming to augment the effectiveness of therapies. Through the integration of nanocarriers, herbal medicines have the potential to surmount obstacles such as limited water solubility, reduced stability, and inadequate targeting capacity. Delivery technologies based on nanotechnology, such as lipids,

Table 4
Physicochemical properties of nanoparticles loaded with various phytochemicals for cardiovascular disease treatment.

Phytochemicals	Nanoformulation	Average Size (nm)	Reference
Tanshinone IIA	Tanshinone-loaded LPNs treated with triphenylphosphonium-D-α-tocopheryl polyethylene glycol 1000 succinate.	~140	[166]
	Nanoparticles of tanshinone IIA	100–200	[167]
	Discoidal + Spherical HDL	132–138	[168]
Tilianin	Tilianin loaded ROS-scavenging nano-micelles	~70	[169]
Quercetin	Quercetin Load PLGA	340–370	[170]
		90–240	[159]
	Pluronic contains resveratrol and quercetin.	~22	[171]
Puerarin	Puerarin-loaded PEG-PE micelles	~16	[172]
	Puerarin loading and triphenylphosphonium modification in micelles.	~17	[173]
	Puerarin-loaded RGD modified and PEGylated lipid nanoparticles	110	[174]
Resveratrol	Resveratrol-Loaded PLGA Nanoparticles	102.7	[175]
	Resveratrol and curcumin co-delivery in polymeric micellar form.	25	[176]
	Solid lipid nanoresveratrol	~271	[177]

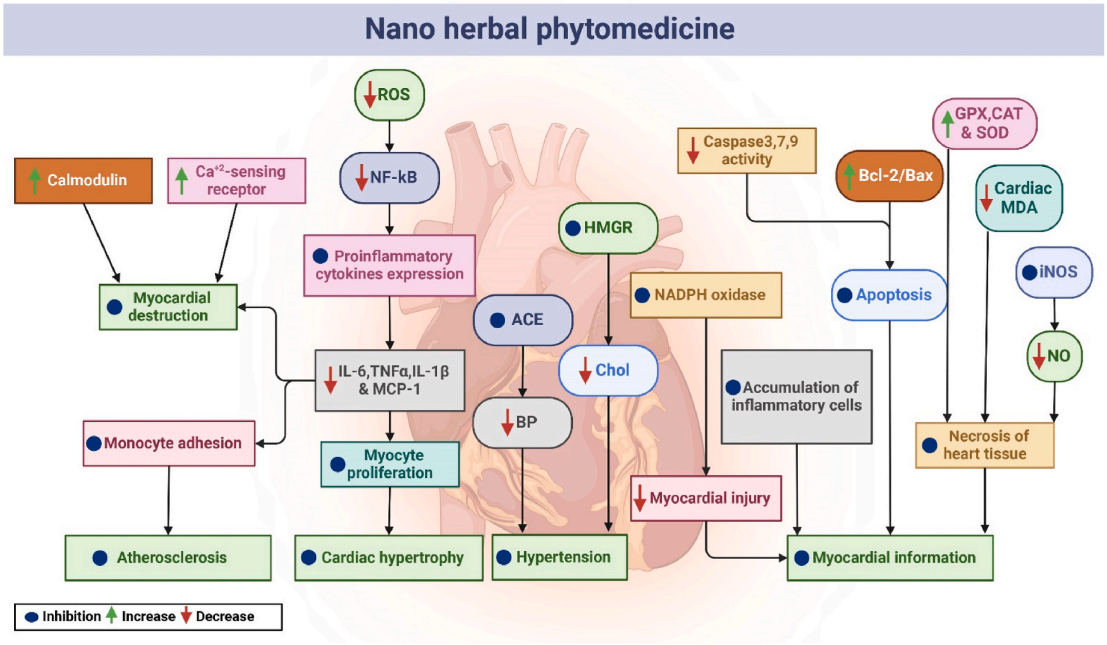

Fig. 13. The ways by which nano herbs phytomedicines exert their effects in CVDs
Abbreviations: (ROS) reactive oxygen species, (NF-κB) nuclear factor kappa B, (ACE) acetylcholinesterase, (HMGR) 3-hydroxy-3-methylglutaryl coenzyme A reductase, (BP) blood pressure, Cholesterol, (IL-6) interleukin 6, (IL-1β) denotes interleukin 1β, (TNF-α) signifies tumor necrosis factor-alpha, (MCP1) refers to monocyte chemotactic protein 1, (iNOS) denotes inducible nitric oxide synthase, (SOD) signifies superoxide dismutase, (GPX) glutathione peroxidase, (CAT) represents catalase, (NADPH) oxidase indicates nicotinamide adenine dinucleotide phosphate oxidase, (MDA) malondialdehyde.

polymers, or nanoemulsions, have demonstrated potential in enhancing the solubility, stability, bioavailability, and pharmacological efficacy of herbal products. The objective of this strategy is to enhance the efficacy of herbal remedies for dermatological diseases such as acne, dry skin, and photoaging [178]. The herbal capsule extracts have significant and highly adaptable effects on the skin, as depicted in Fig. 14.

5.4.1. Antioxidant and antiaging activities

The skin is the main barrier against air humidity, UV radiation, temperature, and toxic compounds [179]. The skin has many antioxidant defenses, such as superoxide dismutase and catalase, to fight free radicals and oxidative processes generated by external stressors [180]. However, intrinsic antioxidants may not be enough to resist excessive free radical production and cell oxidative damage [181]. Excessive free radicals damage DNA, proteins, and lipids, affecting skin structure and

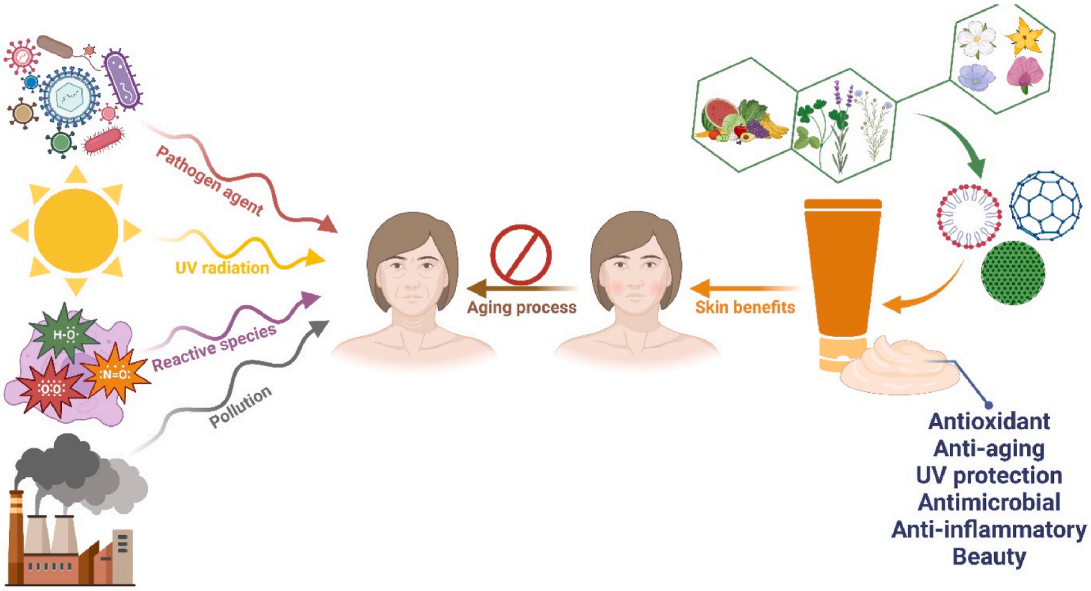

Fig. 14. Advantages of encapsulated phytochemicals derived from plant extracts for skin health.

function. The epidermal barrier is compromised, increasing transepidermal water loss (TEWL) and skin dryness. Free radical activation of matrix metalloproteinases (MMPs) produces hyaluronidase and elastase enzymes, which may accelerate aging. Aging skin loses strength and flexibility and develops wrinkles, sagging, and laxity. Nevertheless, transporting these substances in cosmetic goods presents drawbacks, including instability during manufacturing and storage, inadequate solubility, limited skin permeability, and skin bioavailability [182]. Due to these factors, encapsulation technology presents a potential resolution, as it effectively preserves stability and safeguards against degradation while ensuring safety and non-toxicity for application to the skin [183]. Furthermore, encapsulating natural antioxidants has enhanced their bioactivity and bioavailability [184]. However, only a few researchers have integrated bioactive elements derived from plant extracts into the final formulations of cosmetics. As stated before, plant extracts like C. annuum and B. excelsa were utilized as vitamin E sources [185]. Vitamin E functions as an antioxidant by preventing lipid peroxidation, thereby safeguarding the structural integrity of the cell membrane [186]. Furthermore, this vitamin is plentiful in the stratum corneum, the primary layer of the body's defense system. Tocopherol can hinder the activity of protein kinase C (PKC), resulting in a decrease in the expression of MMP-1 and, consequently, preventing the signals associated with skin ageing [187]. Yenilmez et al. evaluated a formulation that included vitamin E blended into chitosan microspheres in 10 female participants. Following one month of treatment, the formulation resulted in a significant increase in skin moisture (90%–120 % change in roughness) and elasticity (600–1000 per cent change in elasticity) while simultaneously reducing roughness (40 %–110 % change in roughness) [188]. Regarding its moisturizing and antiaging properties, Ijaz and Akhtar conducted a study to evaluate the efficacy of κ tocopherol when mixed into a nanostructured lipid carrier (NLC) gel. The study used a sample of 13 female volunteers. Following a 12-week trial period, the in vivo tests revealed that the formulation enhanced moisture levels by 80 % and caused skin stiffness, delaying aging [189]. The simultaneous administration of vitamin C and E exhibits a synergistic effect since vitamin C aids in preserving vitamin E in its active state [190]. In the previous part, we discussed a herbal extract that contains vitamins C and E. However, several herbal species, like ficus-indica, A. carambola, P. edulis and A. occidentale, O., have vitamin C in their composition. Rattanawiwatpong et al. assessed a 20 % w/w vitamin C and E serum and an encapsulated extract derived from Rubus idaeus leaf cell culture. An in vivo study was performed on a cohort of 50 human subjects with a mean age of 47. The findings exhibited improvements in skin texture, flakiness, and creases. After applying vitamin C for 2 and 4 months, the authors observed decreased melanin synthesis. However, treatment with vitamin E resulted in a reduction in hyperpigmentation signals [191]. Quercetin, a flavonoid found in M. oleifera, has been nanoencapsulated for potential skin applications due to its antioxidant properties [192]. Encapsulated Quercetin by NLC was used to create an efficacious and safe topical formulation. The stability and antioxidant capacity of quercetin was maintained in the formulation prepared by Pivetta et al. Permeability experiments have demonstrated that quercetin exhibits retention in the epidermis and dermis, enhancing the stratum corneum's hydration through its occlusive properties [193]. This phenomenon has been found to contribute to the delay of skin-aging signals.

5.4.2. UV radiation protection

Skin melanin absorbs UV radiation, the primary effective safeguard against damage [194]. Prolonged skin exposure to ultraviolet (UV) radiation generates significant free radicals. These free radicals initiate cellular structure and metabolism changes, leading to various skin illnesses. These disorders include erythema (sunburn), pigmentation (tanning), photoaging, and, in severe instances, skin cancer [195]. The research community faces difficulty in improving stability and penetration enhancers. The lipid nanoparticles containing resveratrol, vitamin E, and epigallocatechin gallate were created by Chen et al. [196]. The results of the photodegradation analysis conducted using UVA radiation revealed that resveratrol and vitamin E nanoparticles had significant efficacy in preventing degradation generated by UV radiation, with protection rates of approximately 40 % and 80 %, respectively [196]. The photoprotection capacity of α-tocopherol integrated into lipid nanoparticles was evaluated in a study conducted by Niculae et al. The scientists concluded that the inclusion of α-tocopherol enhances the photoprotective effects against UVA radiation by scavenging reactive oxygen species [197]. These chemicals can protect the skin against UV damage by scavenging reactive species [198]. The impact of lycopene, β-carotene, and lutein on UV-induced lipid peroxidation in human skin fibroblasts was assessed by Eichler et al. The utilization of liposomes as a medium for transporting carotenoids into human skin fibroblasts in a laboratory setting was documented. The study's findings indicated a reduction of around 40%–50 % in the production of thiobarbituric acid-reactive compounds following exposure to the formulation [199]. Additionally, it has been reported that the co-administration of β-carotene and β-tocopherol can mitigate erythema and decrease susceptibility to ultraviolet (UV) radiation [200]. Phenolic compounds possess chromophores inside their molecular structure, enabling them to effectively absorb ultraviolet (UV) light and provide protection against UV-induced skin damage [201]. Caffeic and ferulic acids have been found to protect the skin against UVB-induced erythema by inhibiting the lipid peroxidative chain reaction [202]. Katuwavila et al. assessed the permeation of caffeic acid into the epidermis by employing liposomal encapsulation as a carrier. The Franz diffusion cell assay findings proved that the encapsulation technique resulted in a 45 % increase in permeability after 7 h, demonstrating the effectiveness of photoprotection Katuwavila et al. [203]. Parisi et al. conducted a study where they enclosed ferulic acid within a mesoporous TiO2 matrix that did not contain surfactants. This encapsulation aimed to enhance the ferulic acid's stability and extend its antioxidant properties. The authors assessed the Sun Protection Factor (SPF), which reported a value of 14.7, which exceeded that of the formulation lacking ferulic acid [204]. Coumaric acid, a phenolic acid, can interfere with tyrosinase, an enzyme that plays a crucial role in melanogenesis [205]. Biswas et al. optimized the p-coumaric acid-phospholipid complex using RSM. The formulation's skin permeability and photoprotection efficiency were then assessed. Ex vivo Franz diffusion cell experiments showed that the formulation containing p-coumaric had six times the skin penetration of the placebo formulation. In vivo experiments assessed photoprotection against UVA and UVB radiations. In vitro, p-coumaric acid had UVA and UVB SPFs of 36 and 16, respectively. In the in vivo photoprotection experiment, p-coumaric acid increased glutathione peroxidase (GPx) activity and lowered GSH levels [206]. In addition, Quercetin can replace synthetic sunscreens despite its instability and penetration. Felippim et al. examined the photoprotective properties of nanoencapsulated quercetin formulations. The sensory features and skin hydration impact study included 60 female subjects. Using nanoencapsulated quercetin in the formulation improved skin hydration and reduced transepidermal water loss (TEWL), preserving stratum corneum water content. Ten participants were included in the study to calculate the sun protection factor (SPF). In vivo, the formulation and control had similar SPF values after irradiation [207].

5.4.3. Antimicrobial activity

Skin has one of the most extensive microbial colonization due to its dry, acidic, and nutrient-deficient surface. The skin covers most of the body and has a lower microbial population than other organs. Bacteria, fungi, and viruses dominate this microbiome [208]. According to recent studies, the most prevalent bacteria in chronic wounds include Staphylococcus, Pseudomonas, Escherichia coli, Proteus, and Enterococcus. These bacteria also cause severe tissue necrosis [209]. Noble metal nanoparticles, such as AgNPs, have been shown to kill Gram-positive and Gram-negative bacteria, fungi, protozoa, and viruses. These nanoparticles also inhibit biofilm development [210]. Topically applied

AgNPs regulate cytokines for optimal wound healing [211]. Aerva lanata is antimicrobial, anti-inflammatory, antidiabetic, and nephroprotective [209]. Rutin, quercetin, kaempferol, gallic acid, and ellagic acid are the main components responsible for these activities [209]. By reducing AgNO3 10:50 with the plant's aqueous extract, AgNPs were synthesized. In vitro produced 50 nm spherical nanoparticles showed remarkable structural stability in physiological fluids. Their ability to attach to MDR bacteria cell membranes shows that AgNP surface roughness affects antibacterial effectiveness against wound-associated bacteria [209]. Metal nanoparticles can be reduced and stabilized with plant extracts. The botanical green synthesis agent Artemisia haussknechtii leaf extract made zinc oxide nanoparticles (ZnO NPs) of 50–60 nm diameters. These nanoparticles were antimicrobial, antibiofilm, antiquorum sensing, and antimotility. Artemisia haussknechtii extract contains secondary metabolites such as thymol, linalool, α-terpineol, and myrcenol. When ZnO nanoparticles were made from this extract, they inhibited antibiotic-resistant Pseudomonas aeruginosa [212]. Gold nanoparticles (AuNPs) can penetrate biofilms and kill germs to fight microbial resistance. A nanoformulation ointment gel was made from Woodfordia fruticosa flower aqueous extract and biogenically synthesized gold nanoparticles (AuNPs). Quercetin-3-O-oxylopyranoside, myricetin-3-O-galloyl-d-galactopyranoside, and ellagic acid are in the extract. The nanoformulation gel enhanced wound healing by accelerating collagen aggregation and epithelial layer regeneration compared to 5 % povidone-iodine and a control group. In Wistar albino rats, the nanoformulation promoted wound healing and easily prevented scarring [213]. These studies demonstrate that nanotechnology and phytochemical characteristics can create novel antibacterial agents.

5.5. Nanotechnology in herbal medicine for viral diseases

Nanotechnology improves herbal bioactive chemical absorption, stability, and targeting for viral illness treatment. Green synthesis of herb-based nanoparticles is eco-friendly and less hazardous than chemical production. Nanocarrier systems boost the antiviral effects of plant-based extracts including neem, turmeric, and green tea in these nanoparticles. Silver nanoparticles made from herbal extracts reduce viral multiplication and boost immunity. Nanotechnology's precision in targeting viral infections is a major benefit. Liposomes, dendrimers, and polymeric nanocarriers manage active chemical release at infected areas, reducing systemic side effects. This method works well for drug-resistant virus strains where usual therapy fail. Nanoemulsions using herbal extracts protect sensitive chemicals from degradation and promote cellular absorption, improving antiviral bioavailability and activity. Nanotechnology in herbal medicine for viral infections is challenging despite its potential. Herbal input standardization is crucial due to plant source and extraction procedure diversity. Nanoparticle toxicity from long-term use needs further study. These sophisticated technologies are harder to integrate into mainstream antiviral medicines due to regulatory issues [214]. Nanotechnology may improve antiviral medications for HIV, herpes simplex, influenza, and hepatitis C viruses [215]. A recent research emphasises the potential of nanomaterials in the diagnosis and therapy of COVID-19, with the goal of enhancing comprehension and expediting advancements in this domain [216]. Nanotechnology has proven to be useful in multiple facets of treating COVID-19, encompassing diagnosis, prevention, treatment, medicines, and vaccinations [217]. Nanobiotechnology offers a promising approach to tackle the issues presented by COVID-19. The process entails the development of minuscule probes, vaccinations, and therapies that can be precisely adjusted to identify the virus, hinder its transmission, and provide medical care to people impacted. By adopting this approach, it can effectively mitigate the adverse consequences of antiviral medications and enable accurate administration of pharmaceuticals. Extensive scientific research has unequivocally established the antiviral effects of a multitude of plants. It is important to mention that specific plants have demonstrated potential in preventing the coronavirus family and the ACE2 enzyme, which might potentially help in inhibiting the novel coronavirus or be used as a form of symptomatic treatment [218]. The striking similarity in appearance and physical properties between SARS-CoV-2 and synthetic nanoparticles further confirms the effectiveness of nanoparticles as an intervention method. To perform specific functions, nanoparticles can be customised with different polymers and functional groups [219]. Furthermore, the chitosan nanoparticles containing catechin and epigallocatechin gallate (EGCG) exhibited enhanced intestinal absorption rates. Furthermore, scientists have utilized methanolic extracts derived from strawberries (*Fragaria ananassa* Duch.) and ginger (*Zingiber officinale*) to synthesize silver nanoparticles (AgNPs) for the purpose of investigating their ability to hinder the activity of SARS-CoV-2 [220]. In addition, the study utilized curcumin loaded (AuNPs) to specifically target and inhibit the growth of SARS-CoV-2 cells by inducing cell cycle arrest and death [221]. Curcumin has been discovered to suppress the action of SARS-CoV-2. By binding to the spike protein, it efficiently inhibits viral cell attachment and hinders the transmission of infection. Moreover, it exerts an influence on the RNA polymerase of the virus, which is an essential element for replication. Curcumin induces apoptosis in SARS-CoV-2-infected cells. This restricts the spread of viruses to adjacent cells. Moreover, liposomes containing resveratrol and gingerol, polymeric nanoparticles containing apigenin and EGCG, carbon nanotubes containing EGCG and ursolic acid, (AuNPs) containing quercetin and naringenin, and quantum dots containing berberine are also present. Targets many cellular processes, including as cell cycle arrest, apoptosis, and autophagy, to impede the development of cells infected with SARS-CoV-2. Demonstrates strong antiviral activity against SARS-CoV-2. It operates by binding to the spike protein of the virus, therefore inhibiting its capacity to adhere to and enter cells. Moreover, it hinders the operation of the virus's RNA polymerase, an essential enzyme for viral reproduction [222]. In addition, it can trigger apoptosis, or programmed cell death, in cells that have been infected with SARS-CoV-2. This helps in preventing the spread of the virus to others. Fig. 15 demonstrates the utilization of nanostructures to deliver phytochemicals from herbals for combating the COVID-19 virus.

5.6. Nanotechnology in herbal medicine for neurodegenerative diseases

Nanotechnology's utilization in herbal medicine for neurodegenerative illnesses exhibits considerable promise in the management of these conditions. Researchers have created nanoformulations of herbal extracts, such as curcumin, quercetin, resveratrol, and others, with the aim of improving medicine transport to the brain, increasing bioavailability, and minimizing negative effects [223]. Numerous studies have underscored the advantages of integrating nanotechnology with medicinal plants in order to advance the field of nano phytomedicine for neuro-therapeutics. These nanoformulated phytomedicines provide precise transport to the brain, are abundant in nature, and have little negative effects, making them highly valuable for treating neurodegenerative diseases [224]. Many herbal extracts, including curcumin, quercetin, resveratrol, piperine, *Ginkgo biloba*, and *Nigella sativa*, have been nanoformulated to increase medication distribution, bioavailability, and adverse effects [97]. The substance's nanoformulation may improve bioavailability and Alzheimer's disease treatment. In *vitro* research used curcumin-loaded lactoferrin nanoparticles to protect SKN-SH dopaminergic cells from rotenone-induced neurotoxicity. This model mimics Parkinson's symptoms. Additionally, curcumin's higher intracellular absorption, concentration, and retention boosted its neuroprotective effects [225]. Within a controlled laboratory environment, a modified form of curcumin combined with lipid and PEG molecules effectively decreased the aggregation of Aβ. Mourtas et al. discovered that liposomes derived from curcumin and liposomes containing anti-transferrin antibodies enhanced the penetration of medication in post-mortem samples of Alzheimer's disease [226]. Taylor et al. found

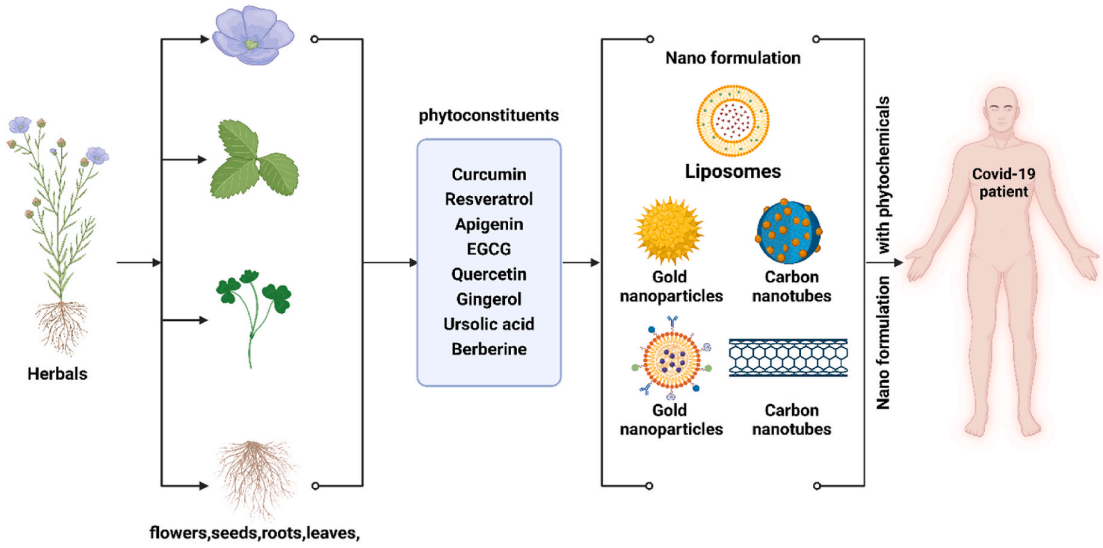

Fig. 15. Utilization of nanostructures to deliver phytochemicals from herbals for combating the COVID-19 virus.

that nanoliposomes with curcumin or curcumin derivatives can control or diminish Aβ oligomers or fibrils in lab settings [227]. these nanoliposomes showed significant affinity for Aβ peptides. In another in *vitro* study, apolipoprotein E3-mediated poly (butyl) cyanoacrylate nanoparticles (ApoE3-C-PBCA) enhanced Cur photostability and cellular absorption, prolonging drug release [228]. Mathew et al. found that Tet-1-conjugated PLGA-coated Cur NPs may treat Alzheimer's disease. This is because they reduce Aβ production, avoiding oxidation and free radical formation [229]. Moustas et al. found that nanoliposomes coated with curcumin strongly attracted Aβ1-42 fibril [230]. Zhao et al. found that conjugating curcumin with a zwitterionic polymer (carboxybetaine methacrylate)-NPs effectively inhibited Aβ42 fibril fibrillation compared to free curcumin [231]. In another study, Tiwari et al. found that curcumin-PLGA-NPs increased neuronal differentiation and cell proliferation genes in neural stem cells, causing neurogenesis. The utilization of curcumin-encapsulated solid lipid nanoparticles (CSLNs) resulted in enhanced HD in rats induced by 3-nitro propionic acid (3-NP) [232]. In the other hand various formulations of quercetin (QC), including nanocapsules, nanogels, liposomes, nanosuspensions, and microspheres, have been suggested in the literature. According to Ref. [233], QC-nanocapsulation has been identified as the most suitable form for QC. According to Kumar et al. the utilization of nanolipidic carriers (NLCs) loaded with QC resulted in enhanced bioavailability and distribution of QC to the brain, as well as an improvement in its antioxidant activity. The bioavailability and effectiveness of QC nanocrystals were found to be higher in PD-like rats compared to QC alone [234]. Ghaffari et al. observed a notable increase in antioxidant enzyme activity and total glutathione levels, along with a decrease in malondialdehyde levels, inside the hippocampus region [235]. According to Ghosh et al. the utilization of nanoencapsulated QC resulted in a notable enhancement of neuronal damage induced by ischemia reperfusion in vivo. This improvement is likely attributed to an increase in neuronal count and an elevation in antioxidant activity. QC-SLNs effectively mitigated aluminum-induced neurotoxicity in a laboratory setting [236]. Furthermore, the implementation of this approach resulted in significant enhancements in behavioral and memory capabilities within animal models of dementia and Alzheimer's disease [236]. A liposome structure consisting of ApoE-QC-RA-PA (QC and RA-loaded liposome with conjugated phosphatidic acid and grafted apolipoprotein E) was demonstrated to successfully traverse the blood-brain barrier (BBB) and mitigate the neurotoxic effects of amyloid-β1-42 in an Alzheimer's disease (AD) mouse. The lipid peroxidation level, acetylcholinesterase activity, and development of Aβ plaques were all reduced in the in *vivo* AD model using the same approach [237]. The degradation and death of cholinergic neurons in the hippocampus of animal models with Alzheimer's disease (AD) were found to be reduced by the lowering of oxidative stress following the nasal injection of QC liposomes [238]. A further investigation was conducted to develop and evaluate a nanoformulation of QC, namely nano-encapsulated QC, in a neuronal model of oxidative stress injury. In addition, resveratrol (RSV), also known as 3,5,40-trihydroxy-stilbene, is a naturally occurring flavonoid polyphenolic molecule belonging to the stilbene class of phytoalexins. The primary disadvantages of RSV include its rapid metabolism, limited water solubility, and low bioavailability [239]. According to Da Rocha Lindner et al. the neuroprotective capabilities of the medication against behavioral and neurochemical variation generated by 1-methyl-4--phenyl-1,2,3,6-tetrahydropyridine (MPTP) were enhanced in a mouse model of Parkinson's disease (PD) when RSV was loaded onto PS80-coated poly (lactide) nanoparticles [240]. The Aβ-triggered neuroinflammation was regulated in *vitro* by an optimized lipid-core nanoparticle loaded with RSV (RSV-LNC) [241]. In addition, Brozza et al. demonstrated that RSV-LNC effectively mitigated the deleterious impacts of amyloid-β1-42 in rats [242]. Finally, some researcher see have some problem or would be beneficial to include data on the cytotoxicity of these constructs on neuronal cells nanoformulations of some herbal extracts and compounds like coenzyme Q10, huperzine A, berberine, hesperidin, and others have demonstrated neuroprotective effects in Alzheimer's and Parkinson's disease models. Overall, the cytotoxicity of nanoherbals depends on the specific nanoparticle properties and the herbal compound being used. Careful design and evaluation of these nanoformulations is required to ensure their safety and efficacy for neurological applications [243,244].

5.7. Nanotechnology in herbal medicine for diabetes mellitus

The utilization of nanoformulations of herbal extracts in the context of herbal therapy for diabetes mellitus. Nanotechnology presents a hopeful option for enhancing the efficacy of herbal extracts by enabling precise transport to the intended location and enhancing their potency, all while minimizing toxicity and unpleasant reactions [7]. The utilization of nanotechnology in the development of herbal systems for diabetes treatment has been the subject of numerous studies. These studies have primarily concentrated on enhancing stability, improving drug delivery, and investigating the efficacy of different botanical

families such as Zingiberaceae, Asphodelaceae, Myrtaceae, Lamiaceae, and Ranunculaceae [245]. Despite the development of several treatment modalities and new therapeutic targets, herbal medicine remains the main diabetic treatment. Secondary metabolites from plants are a useful resource for mass nanoparticle production and are cost-effective and environmentally benign [246]. To progress pharmacy, nanoformulations must be characterized before preclinical and clinical studies. Thus, the nanoformulation outperformed commercially available medicines in anti-diabetic efficacy. The oral antidiabetic effectiveness of Tinospora Cordifolia phytochemicals was increased by lipid-based nanoemulsion [247]. Additionally, *Phaleria macrocarpa* leaf extract encapsulation had considerable antihyperglycemic effects [248]. PLGA nanoencapsulated *Syzygium jambolanum* [249] and *Gymnema sylvestre* [250] have been widely investigated and shown to be superior in various experimental conditions for anti-hyperglycemic activities. These findings apply to several diabetes medications. The lipid-based nanoformulation of *Talinum portulacifolium* (Forssk.) ethanolic extract showed significant antidiabetic effects in streptozotocin and high-fat diet-induced diabetic rats at 250 mg/kg body weight. Flavonoids and tannins in the extract caused the effect [251]. Green AgNP synthesis utilizing *Costus pictus* leaves. Stable (AgNPs) reduce toxicity and expense. It may treat diabetes better than other formulations [252]. Swarnalatha et al. examined how *Sphaeranthus amaranthoides* can produce silver nanoparticles (AgNPs) by inhibiting β-amylase and acarbose sugar in a diabetic animal model [253]. The main explanation is the presence of α-amylase inhibitors in the *S. amaranthoides* ethanolic extract. Biological processes have produced (AuNPs) from medicinal plants and extracts [254]. Extraction of *Mirabilis jalapa* flower extract [255] produced AuNPs with a 100 nm size and spherical shape. Body weight, serum blood glucose, lipid profile, transaminase activity, and renal dysfunction were improved in streptozotocin-induced diabetic rats after receiving a *Cassia fistula* stem bark nanoform. These effects were much stronger than with aqueous extracts [256]. Gold nanoparticles (AuNPs) synthesized from *Gymnema sylvestre* R. Br were tested for antidiabetic efficacy in wistar albino rats [257]. Huang et al. produced nanosized gold and silver from sun-dried *Cinnamom camphora* leaf at ambient temperatures [258]. Nanoparticles were also made from *Ocimum basilicum* leaf and flowers [259]. Copper nanoparticles (CuNPs) from *Dioscorea bulbifera* extract were antioxidant and antidiabetic [260]. This study was the first to demonstrate CuNPs' antidiabetic potential. This was due to their capacity to inhibit pig pancreatic β-amylase and crude murine pancreatic and intestinal amylase. This work also shows that biogenic may prevent free radical-induced diabetes mellitus (DM) and its complications [261]. The nanoformulation of stevioside from *Stevia rebaudiana* leaves is expected to have better antidiabetic effects and bioavailability than the pure medicine [262]. A nanoformulation of *Momordica charantia* with antidiabetic effects inhibited β-glucosidase and β-amylase enzymes in *vitro* [263]. In mice with type 2 diabetes mellitus (T2DM), encapsulated Chinese propolis, a herbal resinous material made from medicinal plant buds, significantly reduced fasting blood glucose levels compared to the diabetic control group [264]. Encapsulated propolis also reduced increased triglycerides in rats with type 2 diabetes mellitus (T2DM) by affecting insulin sensitivity and lipoprotein lipase activity. An assessment was conducted to examine the antidiabetic, antioxidant, and wound healing properties of nanoencapsulated Curcumin in male C57/B6 mice across various doses [265]. Venkatachalam et al. [266] conducted an assessment of the antidiabetic potential of a formulation containing propanoic acid, a bioactive component derived from *Cassia auriculata*, encapsulated by AuNPs. The diabetic treated rats exhibited reduced blood glucose, triglyceride, and cholesterol levels, as well as enhanced insulin levels at a concentration of 0.5 mg/kg body weight.

In their study, Lockman et al. [267] proposed that the toxicity and brain distribution profiles of nanoparticles (NPs) should take into account their surface charges. They further examined the impact of neutral and anionic NPs at low concentrations on the integrity of the blood-brain barrier. However, they found that higher levels of anionic and cationic NPs were found to be toxic. Cationic NPs have been found to induce blood coagulation and hemolysis, whereas anionic NPs have been reported to be non-toxic [268]. A recent analysis conducted by Costigan [269]. Fig. 16 illustrates the mode of action of nanodrugs. The mechanism by which therapeutic plants exert their effects.

6. Nanoherbals: innovations in food technology

The food sector benefits from the diverse applications of nanotechnology, which encompasses the incorporation of nanoherbal materials. The utilization of nanoparticles in the context of food processing, preservation, packaging, and safety enhancement encompasses the integration of herbal constituents. The utilization of nanoherbal materials in food items facilitates their multifunctionality as antioxidants, antimicrobials, and preservatives. Through the utilization of nanotechnology, the food sector has the potential to drive innovation and enhance the quality, safety, and shelf life of food products by including herbal components at the nanoscale.

6.1. Nanoherbals in food packaging and preservation

Nanoherbals in food packaging are a growing field that could improve food safety and preservation. specifically inorganic nanoparticles, has been studied to improve packaging materials' barrier properties, thermal stability, and functionality. This breakthrough could extend food shelf life and reduce waste. Although nanoherbals are not explicitly included in food packaging, the underlying concepts of nanotechnology in food packaging may improve food preservation and safety. Metal-based nanoparticles are often used as active agents with other antibacterial drugs and varied metal nanoparticles [270]. Nanoencapsulation can improve essential oils' physicochemical properties and health benefits in addition to stabilizing them during processing. Herbs and spices include renewable, biodegradable polyphenols, which are antioxidants and antimicrobial. These compounds are good for active food packaging [271]. Biopolymeric nanocarriers loaded with essential oils have antibacterial and antioxidant characteristics, making them a promising active food packaging option. This is because they inhibit microbe development in food [272]. The chicken meat was wrapped in a PLA sheet that contained bimetallic silver-copper (Ag-Cu) nanoparticles and cinnamon essential oil. The efficacy of composite films in packaging chicken samples was assessed against *Salmonella typhimurium*, *Campylobacter jejuni,* and *L. monocytogenes*. The antibacterial activity of the active packaging film containing Ag-Cu nanoparticles and 50 % CEO reached its peak after 21 days of storage in a refrigerator [273]. Buckwheat starch (BS) films with ZnO nanoparticles were highly antibacterial. The film for packaging fresh-cut mushrooms had *L. monocytogenes*-fighting activity at 3 % ZnO nanoparticles. After 6 days of storage, 0.86 log CFU/g decreased [273]. *E. coli* CFU growth was reduced by 96 % and 64.1 % using 50/50 TiO_2/ZnO nanoparticle-coated LDPE films. Films exposed to UV radiation alone and with fresh calf minced meat showed these decreases [274]. Using Montmorillonite clay and ginger extract as Ag nanoparticle mediators, the antibacterial polyvinyl alcohol-based nanocomposite had improved film properties. The in situ-formed film of nanocomposite clay and Ag nanoparticles showed antibacterial activity against *S. typhimurium* and *S. aureus*. *S. typhimurium* was significantly inhibited by the film [275]. Using composite antimicrobial films made of PLA/PEG/PCL/ZnO/CEO has been successful in packing scrambled eggs. These films have important antibacterial capabilities and may be preserved at 4 °C for 21 days, effectively fighting *S. aureus* and *E. coli*. Using eugenol, the active ingredient in clove oil, and ZnO together, the PLA/PEG/PCL/ZnO/CEO film completely suppressed E. coli [276]. The antibacterial effectiveness of nanocomposite poly (ethylene oxide) films, which have been modified with Ag nanoparticles and Acca sellowiana extracts, has been demonstrated against E. coli and S. aureus [277]. The research

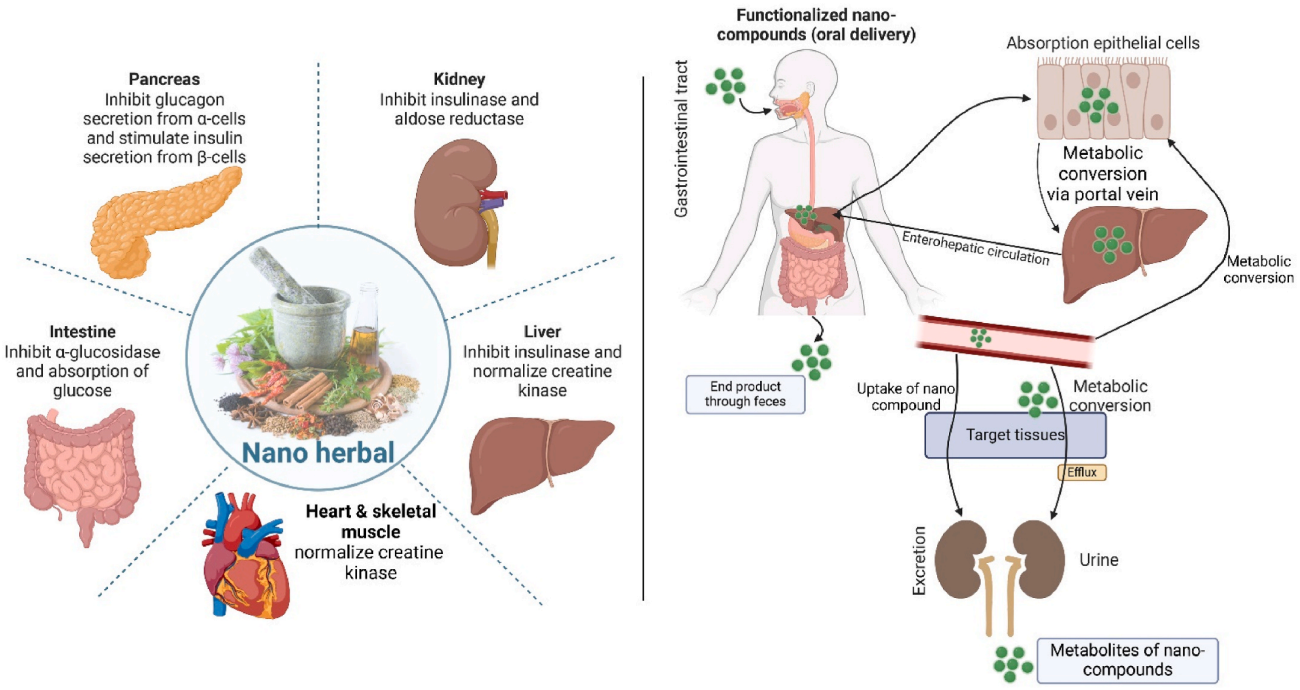

Fig. 16. (A) Nano herbals' mechanism of action (B) Nanodrugs' mechanism of action.

discovered that a chitosan-whey protein film, containing 2 % TiO_2 and Zataria multiflora essential oil, effectively suppressed the growth of Staph. aureus, E. coli, and Listeria. monocytogenes [278]. Clove bud essential oil was extracted and encapsulated in chitosan nanoparticles, which have antibacterial activities against *L. monocytogenes* and *S. aureus* [279]. The scientists incorporated clove essential oil (15–30 % (w/w)) and graphene oxide nanosheets (1 % (w/w)) into polylactic acid to produce nano packing films with antibacterial properties against Escherichia coli and Staphylococcus aureus. The optical and anti-UV properties of the film were influenced by the presence of graphene oxide nanosheets and essential oil [280]. Chitosan nanoparticles containing essential oils of cinnamomum, assai pulp, thyme, lemon, *Zataria multiflora*, tarragon) reduce food product oxidation and microbial growth [272]. Encapsulating essential oil derived from *Ziziphora clinopodioides* and *Rosmarinus officinalis* within sodium alginate (NaAlg) nanoparticles has the potential to significantly reduce bacterial growth and mitigate oxidative or sensory degradation in lamb patties over the storage period. The utilization of nanoparticles effectively mitigated the occurrence of patties' discoloration and unpleasant odor [281]. The successful extension of the shelf life of beef, together with its delayed release and antibacterial qualities, has been achieved through the encapsulation of chrysanthemum essential oil in chitosan. This has success rates for application in the field of food packaging [282]. involves the incorporation of essential oils derived from *Ocimum gratissimum* L. and *Ocimum basilicum* L. into PLA nanofibers. The present study aimed to assess the antifungal and anti-ocratoxigenic properties of PLA nanofibers incorporating essential oil against *A. niger*. Additionally, the study investigated the effects of these packaging materials on the physicochemical attributes, freshness, and shelf life of table grapes. Therefore, the developed active packaging shows potential and could be suitable for fruit applications. On the other hand foodborne microorganisms were suppressed by natural polymer and ZnO nanoparticles synergistically. Al-Nabulsi et al. [209] created a 0.0125 % ZnO nanoparticle-chitosan coating. The coating reduced *E. coli* O157:H7 count in white brined cheese by 2.5 CFU/g at 4 °C and 1.9 CFU/g at 10 °C. Multiple research studies

Have demonstrated the feasibility of integrating encapsulated herbs or spices into food packaging, edible film, or edible coating. As an example, the process of ionic gelation was employed to encapsulate cinnamon essential oil in nanoscale chitosan before its integration into a low-density polyethylene (LDPE) film. The study provided evidence that nanocapsules containing low-density polyethylene (LDPE) had significant antioxidant properties in safeguarding fresh pork from oxidation. Additionally, these nanocapsules displayed a strong antimicrobial activity against *Enterobacteriaceae* and *Pseudomonas* spp. [283]. The essential oil of *Paulownia tomentosa* flower and clove was nano-encapsulated using chitosan. The addition of nanoparticles to an edible coating effectively extended the shelf life of pork chops and pomegranate arils, mostly because of the antioxidant and anti-microbial properties of the essential oils [284]. In their study, Liu et al. [285] showed that the use of nanoemulsion coatings containing star anise essential oil, polylysine, and nisin had a favorable impact on the quality and shelf life of meat. Additionally, the coating significantly enhanced the sensory acceptability of the product. A separate investigation shown that the application of an edible coating composed of nanoliposome-encapsulated bay leaf extract, at a concentration of 1500 ppm, resulted in an extended duration of freshness for minced beef, approximately 16 days, when stored in a refrigerated environment [286]. The increased duration of product viability can be attributed to the antioxidant and antimicrobial properties of bay leaf extract, namely its effectiveness against *E. coli* and *S. aureus*. The usefulness of an edible covering composed of a nanoemulsion comprising chitosan and nutmeg oil to protect fresh strawberries from microbial growth, such as mold and yeast, was elucidated by Horison et al. [287]. This finding aligns with the results reported by Martinez et al. [288], who conducted a study involving the application of edible chitosan coating on strawberries infused with thyme essential oil. The application of chitosan-cinnamic acid nanogel for encapsulating *Mentha piperita* essential oils has been previously utilized for fruit coating. The study found that the edible coating, which contained nanocapsules at a concentration of 500 ppm, successfully suppressed the development of *A. flavus*. Additionally, it prevented water loss during storage, which is a

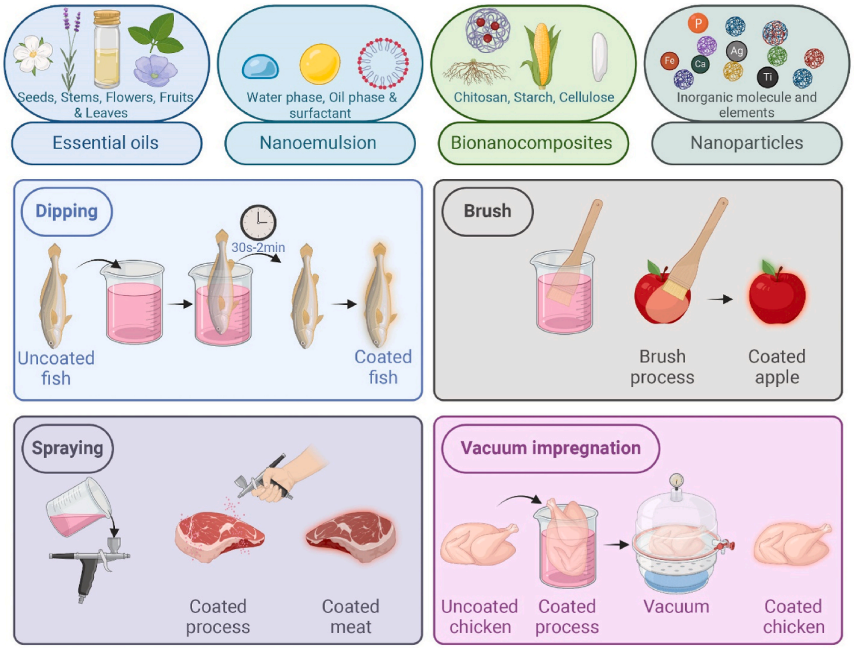

Fig. 17. Nanoherbal-based techniques for food preservation: Applications include essential oils, nanoemulsions, bionanocomposites, and nanoparticles using various coating methods such as dipping, brushing, spraying, and vacuum impregnation for enhanced preservation and quality maintenance of fish, fruits, meat, and poultry products.

typical function of edible coatings [289]. A separate study team demonstrated that the addition of zein-nanofiber and essential oils obtained from bay leaf and rosemary to edible coatings significantly inhibited the growth of *L. monocytogenes* and *S. aureus* in cheese slices. The presence of 1,8 cineole was found to be linked with the microbial activity [290]. Chitosan film containing *Garcinia atroviridis* extract effectively preserved mackerel fish. *Garcinia atroviridis* extract shown antimicrobial properties, namely against Pseudomonas aeruginosa, *B. subtilis*, and *S. aureus* [291]. The findings of Wai et al. [292] provide support for this outcome, as they utilized chitosan edible films containing musk lime extracts to preserve squids. The study group of Das et al. [293] stated that rice with an extended shelf life was achieved by adding chitosan nanobiopolymer that included coriander (*Coriandrum sativum*) essential oil. The nano biopolymer demonstrated both antifungal and antioxidant properties. In addition, Oregano (*Origanum vulgare*) essential oil nanocapsules were made in cheese using the phase inversion temperature method. Lee et al. [294] made rosemary-extracted nanoparticles. Nanoparticles with an average particle size of 212 nm were produced by ionic gelation of chitosan and β-poly glutamic acid. These nanoparticles inhibited *Bacillus subtilis* growth in ready-to-drink barley tea. Pinilla et al. showed that spice-extracted nanoparticles can inhibit microbe development in food goods, such as garlic. Garlic extract was liposome-encapsulated. Liposomes were then added to wheat bread. The report found that the liposome inhibited *Penicillium expansum*, *Aspergillus niger*, *Penicillium herquei*, *Fusarium graminearum*, and Aspergillus flavus growth. Thus, the baked product had a longer lifespan. A similar study found that garlic extract co-encapsulated in liposomes inhibited *L. monocytogenes*, *S. aureus*, *E. coli*, and *S. Enteritidis* in milk [295]. Jemma et al. [296] used herbal extract to extend milk preservation. The nanoemulsion with thyme essential oil inhibited *E. hirae* growth, according to the authors. Another study by Hadian et al. [297] used chitosan and benzoic acid to make a nanogel for rosemary leaf extract. *S. typhimurium* growth in beef cutlets was significantly reduced by nanogel with an average size of less than 100 nm at 0.5 mg/g. Thus, the product's shelf life was extended, but color values were affected. Encapsulating thyme essential oil in micro-sized particles required complex coacervation technique. The paper found that thyme essential oil inhibits cake germs and molds. Thus, the cake had a 30-day shelf life without preservatives [298]. Clove oil in liposomes inhibits E. coli and S. aureus. This is largely attributable to eugenol and eugenyl acetate in the oil. The antibacterial effect preserved tofu quality throughout storage [299]. The extensive research showing that encapsulated herb and spice extract suppresses microbial proliferation in diverse food products suggests that it could protect food quality and extend its shelf life. It can replace unhealthy synthetic preservatives. For meat products *Salmonella, Staphylococcus aureus*, *Clostridium jejuni*, *Escherichia coli* O157:H7, and *Listeria monocytogenes* are common meat contaminants [300]. Various investigations have demonstrated that antibacterial nanoemulsions derived from plants can effectively manage the growth of microorganisms in these commodities. Nanoemulsions have several applications such as enhancing meat and fish as supplements, dips, sprays, coatings, or films [301]. The addition of oregano oil nanoemulsions to chicken pate effectively inhibits the growth of *Staphylococcus aureus and Escherichia coli*, hence prolonging its shelf life [302]. Geraniol and linalool nanoemulsions exhibited bacteriostatic effects on *Escherichia coli K12, Listeria innocua, and Pseudomonas* lundensis in simulated meat settings [303]. Ghaderi-Ghahfarokhi et al. discovered that the application of chitosan/cinnamon oil nanoemulsions resulted in a decrease in the presence of *Streptococcus aureus, Enterobacteriaceae,* yeast, and mold in beef patties [304]. Abdou et al. discovered that nanoemulsions containing oil droplets coated with curcumin and pectin effectively suppressed the growth of psychrophilic bacteria, yeast, and mold in chilled chicken fillets [305]. Keykhosravy et al. discovered that nanoemulsions of essential oils from *Zataria multiflora* Boiss (ZEO) and *Bunium persicum Boiss* (BEO), along with chitosan, effectively suppressed the growth of microorganisms in refrigerated Turkey meat [306]. Fig. 17 illustrates four distinct methodologies in which essential oil serves as a foundational component for the production of nanoemulsions and films, while an edible coating is employed as a means of food preservation.

7. Nanotechnology in herbal medicine: challenges and future

Nanotechnology can enhance herbal medicine formulations by making them more soluble, absorbable, and more stable in bioactive ingredients. Liposomes, nanoemulsions, dendrimers, and polymeric nanoparticles control and direct herbal drug delivery to specific areas, improving therapeutic efficacy. These improvements in herbal medicine have also made the drugs more substantive by successfully passing away enzymatic degradation and first-pass metabolism [9]. Several problems hinder nanoparticle technology from being used in herbal medicine: non-standardized herbal plants and the non-existence of data on inter-species chemical diversity. Geography, seasonal growth, and the technology used in extraction affect what is made up of herbal extract bioactive components. Such variability restricts the repeatability of nanoherbal formulations. Nanoparticle toxicity is another factor. Nanocarriers can transport bioactive substances more efficiently. However, their small size and extended surface area may cause interaction with biological systems, resulting in bioaccumulation and long-term safety problems [7]. Economic and regulatory constraints are another factor that makes the situation difficult. Nanocarrier synthesis costs much money, which makes things even more expensive for these devices, and as a result, they become less useable in resource-deprived areas. There are no rigid regulations at present. Hence, nanoherbal mixtures are more difficult to authorize for pain treatment. Eliminating these hurdles means conducting very detailed safety assessments and specifying proper protocols. Improving biomaterials and eco-friendly nanocarriers is thus the most optimistic area for achieving success. Green nanoparticle synthesis based on the technique of plant extracts as reducing agents is environmentally benign and easily extensible. Experiments in nano-herbal formulation and optimization facilitated by AI and ML will likely make things faster. Integrating nanotechnology into herbal medicine demands worldwide regulatory norms and sound safety assessments. Nanotechnology could be the game changer for herbal medicine, but researchers, politicians, and industry stakeholders must come together and beat these obstacles.

8. Conclusions

The integration of nanotechnology with herbal medicine which is the solution to the shortcomings such as the low absorption, instability, and non-targeted delivery in traditional formulation. Nanoherbal systems such as liposomes, nanocapsules, and nanoemulsions offer the therapeutic efficacy and bioavailability of herbal compounds that is due to the fact that they are delivering target sites that are very precise and stable. These innovations are demonstrating the potential in areas such as cancer treatment where they utilize the EPR valve which opens the microcirculation to allow the drugs to get the tumors and in dermatology, they improve the stability and releasing properties of the drugs. Furthermore, nanoherbal formulations in the food industry provide more potent delivery of bioactive compounds that not only have nutritional but also functional benefits. Although there have been some developments, challenges remain regarding safety and the understanding of the long-term effects of nanoherbal formations. This research is to be relative to the concerns raised regarding the interactions of the nanoherbal formulations with the biological systems and the environmental implications they may have. To sum up, nanoherbal technologies are a new era in healthcare and nutrition exposing the potential of a safer and more effective therapeutic and nutritional future. Nevertheless, the requisite to continue probing in order to fully utilize them in a responsible manner.

CRediT authorship contribution statement

Farhang H. Awlqadr: Writing – review & editing, Data curation. **Kithar Rasheed Majeed:** Formal analysis, Data curation. **Ammar B. Altemimi:** Formal analysis, Data curation. **Arkan Mohammed Hassan:** Formal analysis, Data curation. **Syamand Ahmed Qadir:** Methodology, Investigation. **Mohammed N. Saeed:** Writing – review & editing, Supervision, Conceptualization. **Aryan Mahmood Faraj:** Methodology, Formal analysis. **Tablo H. Salih:** Software, Investigation. **Alaa Jabbar Abd Al-Manhel:** Formal analysis, Data curation. **Mazin A.A. Najm:** Methodology, Formal analysis. **Efstathia Tsakali:** Writing – review & editing, Visualization, Funding acquisition. **Jan F.M. Van Impe:** Software, Investigation. **Ahmed A. Abd El-Maksoud:** Writing – review & editing, Software. **Tarek Gamal Abedelmaksoud:** Writing – original draft, Data curation, Software, Methodology.

Informed consent statement

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Declaration of competing interest

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Data availability

Data will be made available on request.

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