

NANOTECHNOLOGY IN MEDICINAL PLANT RESEARCH: ENHANCING BIOAVAILABILITY AND EFFICACY

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Abstract

When it comes to boosting the therapeutic potential of phytochemicals, the incorporation of nanotechnology into research on medicinal plants offers a significant step with regard to improvement. The therapeutic use of plant-derived compounds is frequently restricted due to their low bioavailability, instability, and quick metabolism. This is despite the fact that plant-derived compounds have been shown to have pharmacological advantages. Nanotechnology provides novel solutions by means of nanoformulations, which include nanoparticles, liposomes, nanoemulsions, and nanocapsules. These nanoformulations enhance the solubility, targeted distribution, and prolonged release of herbal medications. The utilisation of these nanocarriers results in the enhancement of the absorption of active phytoconstituents at the cellular level, the reduction of needed doses, and the minimisation of degradation, hence maximising therapeutic efficacy while simultaneously minimising adverse effects. By overcoming the limits of traditional herbal medicine and offering a framework for the creation of innovative natural therapies that are more successful, this burgeoning field of multidisciplinary study has the potential to revolutionise herbal medicine. The purpose of this abstract is to bring attention to the potential and development that nanotechnology has made in terms of optimising the bioavailability and effectiveness of medicinal plants for sophisticated applications in the healthcare industry.

Keywords: Medicinal Plant, Nanotechnology, Bioavailability

Introduction

Since the beginning of time, medicinal plants have been an essential component of both traditional and contemporary medical practices. They provide a wealth of bioactive substances that are utilised in the treatment and prevention of a wide range of illnesses. Alkaloids, flavonoids, terpenoids, and polyphenols are examples of phytochemicals that display a wide variety of pharmacological actions. These activities include antioxidant, anti-inflammatory, antibacterial, anticancer, and immunomodulatory properties. Many plant-based chemicals, despite the fact that they have the potential to be used in therapeutic applications,

have not yet reached their full clinical potential. Their low bioavailability, which is frequently related to factors such as low solubility in water, fast breakdown in the gastrointestinal system, metabolic instability, and poor permeability across biological membranes, constitutes a considerable obstacle. Over the course of the past few years, nanotechnology has emerged as a potent instrument that can overcome these limits. When we talk about nanotechnology, we are referring to the process of designing, developing, and applying materials and technologies that have dimensions on the nanometre scale, which are generally between one and one hundred nanometres. When used to the realm of medicinal plant research, it enables the encapsulation, protection, and controlled release of phytoconstituents, which dramatically improves the pharmacokinetic and pharmacodynamic characteristics of the phytoconstituents. Nanoformulations, which include polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, liposomes, dendrimers, and nanogels, have demonstrated a significant amount of success in enhancing the solubility, stability, and bio-distribution of substances that are derived from plants. These nanocarriers lower the frequency of dose and minimise systemic toxicity, which makes herbal therapies more effective and patient-friendly. They achieve this by promoting targeted and sustained drug delivery which in turn reduces the frequency of dosing. The confluence of nanotechnology and phytomedicine provides a fresh platform for multidisciplinary research that may be used to solve issues that have been present for a long time in the field of natural product medication development. The research that has been conducted in this field has shown that delivery systems that are based on nanotechnology not only improve the bioavailability of plant extracts that are poorly soluble, but they also enhance the therapeutic actions of these extracts, making them more effective against complex diseases such as cancer, neurodegenerative disorders, and infectious diseases. This introduction lays the groundwork for a more in-depth investigation into the ways in which nanotechnology is reshaping the landscape of herbal medicine. The primary focus of this investigation will be on the optimisation of the bioavailability and effectiveness of medicinal plant extracts through the utilisation of novel nano-delivery systems.

The increased interest in plant-based treatments throughout the world, which is being driven by a need for safer and more natural alternatives to synthetic pharmaceuticals, has heightened the need for enhanced delivery systems that can maximise the potential of herbal medicines. Conventional administration methods, which include powders, capsules, and decoctions, frequently have problems with inconsistency in absorption, variations in the amounts of active ingredients, and difficulties in ensuring patient compliance. Not only do these limitations reduce the effectiveness of therapeutic interventions, but they also make it more difficult to incorporate herbal medicines into conventional healthcare environments. The development of delivery systems that are extremely effective, repeatable, and able to pass through biological barriers is made possible by nanotechnology, which provides a comprehensive solution to the problem. For example, it is well known that lipid-based nanoparticles, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), have the capacity to enhance the oral bioavailability of lipophilic phytochemicals including curcumin, quercetin, and resveratrol. In a similar manner, nanocarriers that are based on polymers can be developed to give controlled release profiles, expanding the duration of the drug's activity while simultaneously decreasing the number of times it needs to be administered. Not only do these technologies improve therapeutic index, but they also offer up new pathways for site-specific medication targeting. This is particularly useful in the treatment of neurological diseases and cancer, two areas in which conventional methods frequently fail to meet expectations. In addition, the nanoscale size of these carriers makes it possible for improvements in cellular absorption by endocytosis as well as greater permeability across epithelial barriers that are very tight. This characteristic is very important when it comes to transporting herbal medicines to difficult locations, such as the blood-brain barrier or intracellular compartments. It is

possible to further improve specificity by functionalising nanoparticles with targeted ligands, such as antibodies or peptides. This will reduce the impacts of off-target interactions and increase the effectiveness of the treatment. This topic has been further extended by recent breakthroughs in green nanotechnology, which have placed an emphasis on environmentally friendly synthesis processes that make use of plant extracts themselves as reducing and stabilising agents in the production of nanoparticle applications. This not only adheres to the ideals of sustainability, but it also provides a synergistic therapeutic effect when usage of plant-based nanoparticles is combined with the use of other herbal actives. Several obstacles still need to be overcome, despite the potential. There are a number of significant difficulties that need to be solved in order to promote the widespread acceptance of nano-herbal formulations. Some of these concerns include regulatory uncertainty, the possible toxicity of nanomaterials, high production costs, and little clinical evidence. Despite this, the future of nanotechnology in the field of medical plant research is bright. There is now research being conducted with the goals of refining nanoparticle design, enhancing safety profiles, and verifying efficacy via preclinical and clinical investigations. Taking this into consideration, the current research investigates the significant part that nanotechnology plays in improving the bioavailability and effectiveness of chemicals that are produced from medicinal plants. In this study, a number of different nanocarrier systems, their modes of action, the benefits that they impart, and the limits that need to be solved in order to successfully translate these systems into clinical applications are investigated. The findings of this investigation highlight how the combination of nanotechnology and phytomedicine has the potential to revolutionise natural medication therapy, which will ultimately contribute to the development of contemporary integrative clinical practices.

Nanoformulations of Medicinal Plant

Nano ultrafine technology and drug nanocarriers are the two types of techniques that are often utilised in the process of developing nanoformulations of active pharmaceutical compounds found in medicinal plants. Using nano ultrafine technology, such as the recrystallisation and pulverisation methods (for example, ball milling and airflow pulverisation), traditional Chinese medicines that are not suitable for industrial extraction processes, such as those that contain mineral or poisonous substances, as well as those that contain active ingredients that are easily destroyed, are finely ground. The expansion of the surface area of drug particles results in the generation of a large number of active components, which in turn imparts a wealth of chemical and physical qualities and characteristics. This technique, which represents the first technology for nano-traditional Chinese medicine, involves the processing and crushing of traditional Chinese medicine particles down to the nanometre level. The ultrafine technology is inherited and developed by nanocarrier encapsulation of pharmaceuticals, which enables changes in the distribution of medications, adjustment of release rate, and augmentation of bioavailability for drugs that are insoluble. Achieving passive targeting is accomplished by nanodrug carriers through the enhancement of permeability and retention effects. On the other hand, active targeting is accomplished by ligands linked to the surface of nanodrug carriers, which transport medications to specified cells or organs. Nanoparticles and drug nanocarriers are the two primary types of nano-dosage forms that are found in medicinal plants that contain active pharmacological substances. While drug nanocarriers demonstrate a varied range of dosage forms, including liposomes, nanoparticles, nanoemulsions, and colloidal polymers, nanoparticles of the active pharmacological compounds found in medicinal plants include nanosuspensions, nanoeutectics, and other forms that are considered to be related. In recent years, there have been significant advancements in the research and development of nanocarriers. These advancements have led to significant progress, which includes the

further modification of carrier surfaces and the incorporation of surface-active agents such as transferrin, folate, low-density lipoprotein, peptides, lectins, and epidermal growth factor. Drug targeting, bioavailability, and solubility are all significantly improved as a result of these changes. In addition, there have been reports of the development of innovative nano-based preparations of Chinese medicines. These preparations include eutectics, inorganic carriers, phospholipid complexes, and suspension gels. The enhancement of targeting, bioavailability, and solubility is becoming an increasingly important emphasis in the process of developing nano-dosage forms for active pharmacological compounds found in medicinal plants.

Nanoliposomes

As nanoscale bilayer lipid vesicles, nanoliposomes are generally between 20 and 200 nanometres in size and are predominantly made up of phospholipids and lipids. Their size normally ranges from 20 to 200 nanometres. It is also possible for them to include other molecules, such as carbohydrates, proteins, and sterols. Because of their bilayer structure, which is composed of lipid and aqueous components, nanoliposomes are able to encapsulate both hydrophilic and hydrophobic molecules separately or concurrently during the process of vesicle production, as seen in Figure 1. On the other hand, hydrophobic molecules are incorporated into the lipid bilayer membrane or vesicle, whilst hydrophilic compounds are contained inside the watery areas, including the central core. Compounds that are enclosed within nanoliposomes have the potential to be progressively released by double-layer diffusion or vesicle breakdown, which can be triggered by changes in the temperature, osmotic pressure, ionic strength, or pH. Nanoliposomes that enter the cell by receptor-mediated endocytosis or other endocytic routes initially enter the early endosomal vesicles. This is the first step in the process. It is possible for the structure and characteristics of nanoliposomes to undergo modifications as a result of the acidic environment that exists within endosomes. As an instance, certain pH-sensitive liposomes have the potential to release medications when exposed to the acidic environment of the stomach. The subsequent step involves the fusion of endosomes with lysosomes, as well as the transfer of nanoliposomes and the medicines that are encased inside them into lysosomes. It is possible for hydrolases to destroy pharmaceuticals within lysosomes. Certain nanoliposomes are built in such a way that they are able to resist being degraded by lysosomes. This allows for the release of medications within cells. Once some nanoliposomes have entered cells through caveolin-dependent endocytosis, they initially enter the subcellular compartments of the non-lysosomes and then gradually diffuse into the cytoplasm. Additionally, they may infiltrate organelles such as the Golgi apparatus and the endoplasmic reticulum. In these organelles, nanoliposomes and the drugs that they contain may be involved in certain physiological processes that occur within the cell. Alternatively, they may be secreted outside the cell through the transport mechanism of organelles in order to achieve cross-cellular transport of drugs or their effects in particular organelles. As will be explored in further detail in Section 2, nanoliposomes that are loaded with hydrophobic substances, such as phenolic compounds, considerably improve both their solubility and their bioavailability characteristics. Furthermore, the unique bilayer and biofilm structure of nanoliposomes is able to imitate the behaviour of actual cell membranes. This is because nanoliposomes closely resemble natural cell membranes. Because of this feature, tailored medication delivery into the cells is made possible, which dramatically reduces the amount of harm that is done to human tissues. Indisputable evidence suggests that nanoliposomes are both dependable and adaptable drug delivery platforms. In addition, the targeting-triggered release and stability features of these compounds

affect the pharmacokinetics and biological distribution of the medication, which holds significant potential for the treatment of tumours.

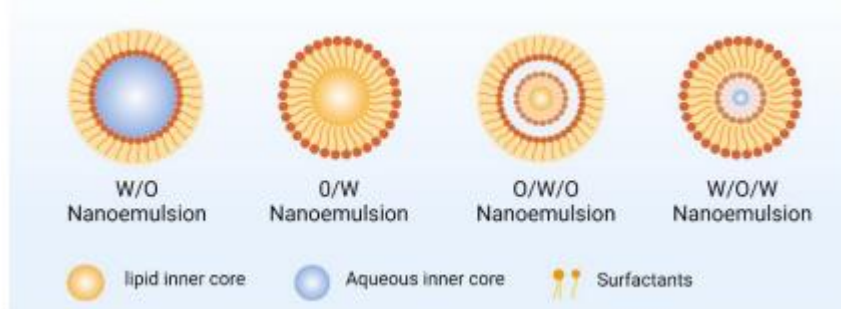


Figure 1. Different types of nanoliposomes.

Nanoemulsion

Nanoemulsions are the most effective drug delivery carriers because they provide excellent encapsulation and transport capabilities for medications that are either poorly soluble or lipophilic. This protects the pharmaceuticals from the effects of hydrolytic enzymes, the pH of the gastrointestinal tract, and other environmental variables. Following the nanoemulsion's introduction into the body, it is then carried via the circulatory system. Particle size, surface characteristics, and the capacity to attach to plasma proteins are some of the factors that influence its stability and the amount of time it takes for it to circulate in the blood. Smaller particle sizes and appropriate surface changes might lessen the likelihood of being recognised and eliminated by cells of the immune system, such as macrophages, which could result in an extension of the amount of time that the substance is present in the blood circulation. It is possible to enhance nanoemulsions in particular organs or tissues by employing either passive or active targeting techniques. For the purpose of passive targeting, the high permeability and retention effect (EPR effect) of the tumour tissues and other locations is utilised. This effect makes it simpler for nanoemulsions to aggregate at these sites. To achieve more accurate drug delivery, active targeting includes attaching particular antibodies, ligands, or molecules to the surface of the nanoemulsion. This allows the nanoemulsion to selectively recognise and bind to receptors on target tissues or cells, hence facilitating more targeted drug administration. For the most part, these isotropic systems are either completely transparent or somewhat transparent, and their particle sizes range from 20 to 500 nanometres. In order to accomplish dispersion, the medicine is spread uniformly throughout the nanodroplets. At the same time, equilibrium and stability are preserved by means of the interfacial layer of emulsifiers and co-emulsifiers, which guarantees both thermodynamic and kinetic stability. Nanoemulsions are characterised by their tiny droplet sizes and their capacity to solubilise pharmaceuticals that are hydrophobic and weakly soluble. This results in an increase in the drug's solubility and bioavailability when administered. The first step in the process of drug release from nanoemulsions is for the drug to go from the oil phase into the surfactant layer, and then it moves into the aqueous phase. In the process of diffusion from the oil, the dissolved medicine comes into contact with the water that is all around it, which dramatically increases the surface area of the drug.

As seen in Figure 3, nanoemulsions may be broken down into many different categories: oil-in-water, water-in-oil, oil-in-oil, water-in-water bicontinuous emulsions, and nanoemulsions. The oil droplets that make up an oil-in-water emulsion are distributed throughout the continuous aqueous phase of the emulsion. During

the formation of a water-in-oil emulsion, water droplets are distributed throughout an oil phase that is continuous. The production of water-in-oil nanoemulsions is accomplished using a two-step high-energy approach. This process involves the first emulsification of oil in the water phase, which is then followed by re-emulsification into the oil phase. The nanoemulsions in question are made up of a multi-chamber system, in which water-in-oil emulsions are disseminated as droplets inside an exterior aqueous phase. Nanogels that enclose internal oil droplets inside a hydrogel matrix are created using water-in-oil nanoemulsions as templates instead of nanogels themselves. When using the dual-continuous nanoemulsion system, droplets of both water and oil are distributed throughout the system without interruption.

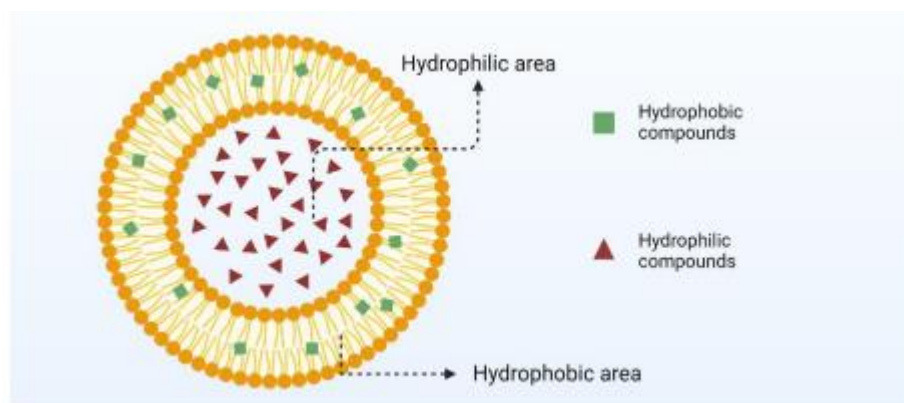


Figure 2. Structure of nanoemulsion.

Nano Micelles

Typically, nano micelles are self-assembled nanoscale colloidal dispersions that range in size from 10 to 100 nm. They are distinguished by hydrophobic cores and hydrophilic shells, which enables them to boost the solubility and stability of hydrophobic medicines. This process, which is driven by thermodynamics, takes place above a concentration threshold that is set by the copolymer. This threshold is referred to as the critical micelle concentration. Because of this structural trait, micelles are better shielded from identification by the monocyte–macrophage system, which results in a prolonged blood circulation. This is seen in Figure 3. across a process known as passive diffusion, nano micelles are able to enter the interstitial space and travel across the spaces that exist between vascular endothelial cells. The effectiveness of passive transport is affected by a number of factors, including particle size, surface qualities, and the balance between hydrophilic and hydrophobic properties. For instance, nano micelles that have smaller particle sizes and a moderate level of surface hydrophilicity are more likely to penetrate tissues through the intercellular space of the vascular endothelial cells. Transferrin, folate, low-density lipoprotein, peptides, lectins, and epidermal growth factor are some examples of chemicals that may be used to modify the exterior hydrophilic corona. Additionally, the polymer structure of the corona can give additional modification sites, which can help promote active targeting. In addition to being composed of polymer and surfactant micelles, nano micelles can take on a variety of morphologies, including spherical, tubular, reverse micelle, and bottle brush forms. These morphologies are determined by the hydrophobicity, hydrophilicity, and solvent conditions of the samples. They improve the cellular absorption of carrier micelles and provide an alternate internalisation channel via endosomes. This is an essential feature in disease, where the efficiency of medication therapy is influenced by drug efflux mechanisms that are associated to multidrug resistance. A extended mean residence time in the circulation, better bioavailability, accurate drug distribution to target tissues, and

perhaps lowered dose to attenuate nonspecific organ toxicity are some of the important pharmacokinetic benefits that are brought about as a result of these advantages.

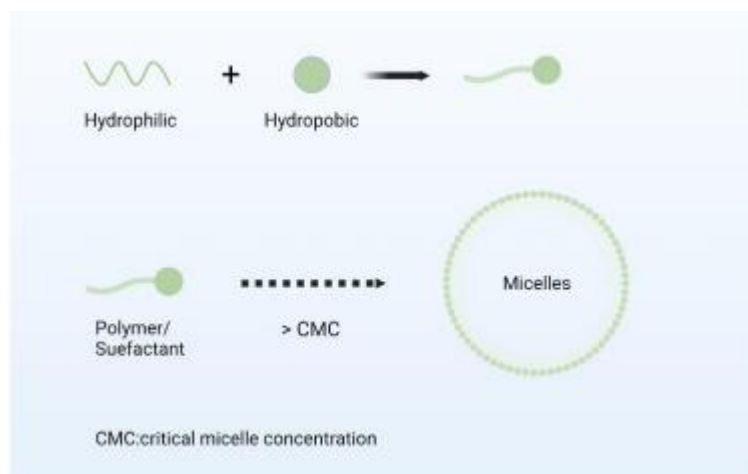


Figure 3. Formation mode of nano micelles.

Limitations of Conventional Herbal Medicine

It is common for traditional formulations of medicinal plants to have issues such as limited permeability, low water solubility, instability during storage, and degradation in the gastrointestinal tract. According to Patel et al. (2012), the majority of plant-derived bioactive compounds, including curcumin, quercetin, and resveratrol, have high pharmacological potential *in vitro*; but, because to their low bioavailability, they are unable to deliver the effects that are desired *in vivo*. Because of these constraints, the development of innovative delivery methods is required in order to improve the therapeutic value of these substances.

Role of Nanotechnology in Enhancing Bioavailability

In addition to enhancing the solubility and stability of phytochemicals, nanocarriers also increase their biodistribution. For example, curcumin-loaded polymeric nanoparticles have been shown to have improved solubility and greater cellular absorption, which ultimately results in improved anti-inflammatory and anticancer benefits (Mohanty et al., 2010). According to Li et al. (2013), quercetin-loaded liposomes have demonstrated enhanced antioxidant activity as well as prolonged release patterns.

Types of Nanocarriers Used in Phytomedicine

Various nanocarriers have been explored for the delivery of plant-based compounds:

- Liposomes: Phospholipid-based vesicles that encapsulate both hydrophilic and lipophilic compounds. They enhance drug absorption and reduce toxicity (Singh et al., 2017).
- Solid Lipid Nanoparticles (SLNs): These improve the controlled release and stability of phytochemicals like artemisinin and catechins (Mehnert & Mäder, 2012).
- Nanoemulsions: Known for their small droplet size and large surface area, they improve the solubility and absorption of poorly water-soluble herbal extracts such as neem and tulsi (Pardeike et al., 2009).

- Dendrimers: These offer precise molecular structure and high payload capacity, used for the targeted delivery of plant alkaloids and polyphenols (Patri et al., 2005).

Therapeutic Applications of Nanoformulated Herbal Compounds

Cancer: Nano-encapsulated paclitaxel from *Taxus brevifolia* has demonstrated improved antitumor activity and reduced systemic toxicity (Mukherjee et al., 2009).

Neurodegenerative Diseases: *Bacopa monnieri*-loaded nanoparticles have shown promise in improving cognitive function in Alzheimer's models (Kumar et al., 2016).

Antimicrobial Activity: Green-synthesized silver nanoparticles using plant extracts such as *Azadirachta indica* and *Ocimum sanctum* exhibit broad-spectrum antimicrobial properties (Rai et al., 2012).

Green Synthesis of Nanoparticles Using Plants

Utilising plant extracts for the purpose of green synthesis of metallic nanoparticles is a strategy that is both cost-effective and environmentally benign. These nanoparticles, which are supported by plants, are not only stable but also biocompatible and offer intrinsic therapeutic characteristics. It has been demonstrated by Mittal et al. (2014) that phytochemicals perform the functions of reducing and capping agents, which ultimately results in the creation of functionalised nanoparticles that exhibit increased bioactivity.

Conclusion

Increasing the therapeutic potential of phytochemicals is a huge step forward, and the use of nanotechnology into research on medicinal plants offers a substantial and important achievement. Traditional herbal medications, despite the fact that they contain a high concentration of bioactive chemicals, frequently have drawbacks such as low solubility, instability, poor absorption, and insufficient targeting inside the human body. Nanotechnology provides a solution to these issues by making it possible to design enhanced drug delivery systems. These systems include nanoparticles, liposomes, nanoemulsions, and dendrimers. These systems increase solubility, protect sensitive chemicals from degradation, and enable prolonged, controlled, and targeted release. Not only can these nanoformulations improve the pharmacokinetic and pharmacodynamic features of plant-based medications, but they also lower the doses that are necessary, minimise the adverse effects, and increase patient compliance. Cancer, microbial infections, inflammatory illnesses, and neurological problems are only some of the ailments that might potentially benefit from their application in the treatment of a broad variety of health issues. In addition, the green synthesis of nanoparticles through the use of plant extracts is in line with environmentally benign and sustainable scientific methods, successfully bridging the gap between traditional knowledge and contemporary technology. Although the potential is enormous, there are a number of obstacles that need to be overcome before nano-herbal formulations may be used in a safe and broad manner. These obstacles include large-scale production, regulatory difficulties, long-term toxicity studies, and cost-effectiveness. Herbal medicine, on the other hand, is likely to be transformed into therapeutic solutions that are more dependable, effective, and scientifically verified if research and development in this field continue to be conducted across

disciplinary lines. In conclusion, nanotechnology prepares the way for a new era of phytomedicine, one that is more precise, more potent, and ready to make a huge influence on healthcare all across the world.

References

- [1] Li, H., Zhao, X., Ma, Y., Zhai, G., & Li, L. (2013). Enhanced bioavailability and anticancer efficacy of quercetin-loaded liposomes in lung cancer. *International Journal of Pharmaceutics*, 455(1-2), 251–258.
- [2] Mehnert, W., & Mäder, K. (2012). Solid lipid nanoparticles: Production, characterization and applications. *Advanced Drug Delivery Reviews*, 64, 83–101.
- [3] Mohanty, C., Das, M., & Sahoo, S. K. (2010). Emerging role of nanocarriers to increase the solubility and bioavailability of curcumin. *Expert Opinion on Drug Delivery*, 7(6), 599–612.
- [4] Mukherjee, B., Bhattacharya, S., & Maitra, A. (2009). Enhanced antitumor efficacy and reduced toxicity of paclitaxel-loaded nanoparticles in breast cancer models. *Cancer Letters*, 273(1), 172–180.
- [5] Pardeike, J., Hommoss, A., & Müller, R. H. (2009). Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *International Journal of Pharmaceutics*, 366(1-2), 170–184.
- [6] Patel, K., & Patel, D. K. (2012). Challenges and opportunities in phytomedicine: Enhancing bioavailability through nanotechnology. *Journal of Acute Disease*, 1(1), 1–6.
- [7] Rai, M., Yadav, A., & Gade, A. (2012). Silver nanoparticles as a new generation of antimicrobials. *Biotechnology Advances*, 27(1), 76–83.
- [8] Singh, D., Rawat, A., Semalty, M., & Semalty, A. (2017). Quercetin-phospholipid complex: An amorphous pharmaceutical system in herbal drug delivery. *Drug Development and Industrial Pharmacy*, 43(7), 1175–1183.
- [9] Wang, K.L.; Chen, Q.; Shao, Y.Y.; Yin, S.S.; Liu, C.Y.; Liu, Y.M.; Wang, R.; Wang, T.; Qiu, Y.L.; Yu, H.Y. Anticancer activities of TCM and their active components against tumor metastasis. *Biomed. Pharmacother.* 2021, 133, 111044.
- [10] WHO. Selection and Use of Essential Medicines: Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2019 (including the 21st WHO Model List of Essential Medicines and the 7th WHO Model List of Essential Medicines for Children). In *Selection and Use of Essential Medicines: Report of the WHO Expert Committee on Selection and Use of Essential Medicines*; WHO: Geneva, Switzerland, 2019.
- [11] Tripathy, V.; Basak, B.B.; Varghese, T.S.; Saha, A. Residues and contaminants in medicinal herbs—A review. *Phytochem. Lett.* 2015, 14, 67–78.
- [12] Theodoridis, S.; Drakou, E.G.; Hickler, T.; Thines, M.; Nogues-Bravo, D. Evaluating natural medicinal resources and their exposure to global change. *Lancet Planet. Health* 2023, 7, E155–E163.
- [13] Vaou, N.; Stavropoulou, E.; Voidarou, C.; Tsigalou, C.; Bezirtzoglou, E. Towards Advances in Medicinal Plant Antimicrobial Activity: A Review Study on Challenges and Future Perspectives. *Microorganisms* 2021, 9, 2041.
- [14] Fan, P.H.; Wu, L.W.; Wang, Q.; Wang, Y.; Luo, H.M.; Song, J.Y.; Yang, M.H.; Yao, H.; Chen, S.L. Physiological and molecular mechanisms of medicinal plants in response to cadmium stress: Current status and future perspective. *J. Hazard. Mater.* 2023, 450, 131008.