Advanced nano-drug delivery systems utilizing natural product-based innovations

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Abstract---Background: Natural products have historically played a crucial role in human health, spanning from early uses to modern medicine. Despite their extensive pharmacological potential, clinical applications are often limited by issues such as poor solubility and rapid metabolism. Aim: To explore the use of advanced nano-drug delivery systems to enhance the efficacy of natural products by overcoming their limitations and improving therapeutic outcomes. Methods: This review examines various nano-drug delivery systems that integrate natural products. It discusses advancements in nano-carriers, including liposomes, micelles, and self-assembled structures, focusing on their ability to improve drug solubility, stability, and targeted delivery. Results: Significant progress has been made in developing nano-carriers for natural products, including terpenoids, flavonoids, polyphenols, and alkaloids. Innovations such as targeting warheads and self-assembled systems have shown improved drug delivery and therapeutic efficacy in preclinical studies. Conclusion: Nano-drug delivery systems utilizing natural products offer promising solutions to overcome traditional limitations, enhancing drug bioavailability and targeted delivery. This advancement holds potential for revolutionizing the treatment of complex diseases and improving clinical outcomes.

Keywords---Nano-drug delivery, natural products, targeting warheads, self-assembly, drug solubility, therapeutic efficacy.

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Introduction

Throughout human history, natural products have been fundamental for sustaining life. They have been utilized in various applications, from early practices like paper-making to contemporary uses in fragrance and spice production, and more recently, in disease prevention and treatment (1, 2). With ongoing progress in separation technologies and pharmacological evaluation methods, an increasing array of bioactive compounds from natural sources has been discovered. The extensive structural diversity of these compounds, coupled with their diverse biological activities on various tissues and molecular targets, renders them invaluable in clinical settings, particularly for treating complex conditions such as cancer and cardiovascular diseases (3, 4).

Despite their potential, the clinical efficacy of natural products has often been underwhelming, leading many pharmaceutical companies to hesitate in their development (5–7). Challenges such as poor solubility, limited biological distribution, and rapid metabolic clearance frequently result in suboptimal plasma concentrations of these compounds. Additionally, drugs with high molecular weight and low lipophilicity struggle with permeability and absorption across biological membranes, resulting in inefficient drug transport and short half-lives. Addressing these issues through novel drug delivery methods remains a critical area of research (8, 9). Efforts to enhance the efficacy of natural products are essential for the development of innovative drugs with fewer side effects (10).

Nanotechnology has emerged as a pivotal tool in bridging biological and physical sciences. Nano-drug delivery systems, in particular, have attracted significant interest from the pharmaceutical industry (7, 11, 12). Nano-carriers facilitate drug delivery by encapsulating or attaching therapeutic agents and targeting specific tissues or organs through controlled release (9, 13). Unlike larger materials, nano-sized drugs can move more freely within the human body, enhancing their therapeutic potential (14–19). Despite the broad promise of nanotechnology, the application of nanoparticle-based delivery systems still faces limitations. These systems not only improve the residence time of drugs in the body but also offer advantages such as rapid extravasation and reduced macrophage phagocytosis. Nanostructures can also effectively co-load both hydrophilic and hydrophobic substances. Approved first-generation nano-drug delivery systems, including liposomes and micelles with inorganic nanoparticles (e.g., gold nanoparticles), highlight the advancements in drug delivery, imaging, and therapeutic functions (20, 21). Methods like thin film hydration, high-pressure homogenization, nanoprecipitation, and self-assembly allow for the incorporation of natural products into nano-carriers, representing significant strides in optimizing treatment outcomes through controlled drug release, enhanced solubility, improved targeting, and increased stability (22). Overall, nanotechnology offers substantial support for advancing natural products and modernizing their application.

Nano-Drug Delivery Systems and Natural Products

The integration of nanotechnology with natural products represents a rapidly evolving field with considerable potential. Utilizing nanocarriers for drug delivery

has emerged as a promising method to efficiently transport therapeutic agents to targeted locations within organs, tissues, or cells (6). The synergy between natural products and nanotechnology is particularly advantageous, as nanotechnology enables the encapsulation or attachment of one or more natural products within nano-drug delivery systems. These systems can significantly enhance the bioavailability, targeting precision, and controlled release characteristics of natural products. This advancement addresses many limitations associated with the clinical application of natural products, thereby amplifying their pharmacological benefits and contributing substantially to clinical practice.

Natural Product-Based Nano-Drug Delivery Systems with Targeting Warheads Mechanisms and Advantages

We are witnessing a new era in personalized healthcare where drugs are tailored to individual patient needs and delivered specifically to diseased cells. This area of research is gaining considerable attention (23). Nano-drug delivery systems, developed through advanced nanotechnology, have garnered significant interest for their ability to improve the bioavailability of insoluble drugs. Researchers often enhance these systems by incorporating targeting warheads, which facilitate selective delivery of therapeutic agents to pathological cells via receptor-mediated endocytosis (24, 25). Various reaction mechanisms, such as nucleophilic addition, nucleophilic substitution, and addition-elimination, are employed to attach these warheads, with nucleophilic addition and addition-elimination being the most commonly used (26). These mechanisms enable selective drug delivery, exemplified by aromatic electrophilic substitution targeting specific amino acids like tyrosine and tryptophan (26).

Targeted drug delivery systems offer several advantages over non-targeted ones. They provide the ability to deliver therapeutic drugs specifically to desired organs or tissues, minimizing non-specific uptake and toxicity to healthy cells (27). Furthermore, drugs that exhibit limited efficacy when administered in non-targeted forms at the maximum tolerated dose (MTD) can achieve improved outcomes when coupled with effective targeting warheads (27). For instance, nano-conjugates of polyethylene glycol or methoxy polyethylene glycol, modified with the targeting peptide T7 and linked to podophyllotoxin (PPT) (Pep-SS-NPs), demonstrate a significant increase in MTD (5.3 times) compared to free PPT (28). Additionally, targeting warheads can be linked to diagnostic agents, such as imaging agents, to detect overexpression of target receptors in pathological cells (29). Successful developments include folate-linked radiopharmaceutical imaging agents like 99mTc and 68Ga, which are used to identify tumors with high folate receptor expression necessary for effective drug delivery (30–33). Currently, extensive research is focused on synthesizing and studying warheads that specifically bind to receptors in both in vitro and in vivo settings. Integrins (α2β3, αvβ3, and α5β1) and aminopeptidase N (CD13) are common targets in tumor neovascular systems, recognized by cyclic RGD peptide and linear NGR peptide derivatives, respectively (34). Another prevalent example involves targeting the folate receptor on breast cancer cells, where folate-drug conjugates are synthesized and grafted onto nano-carriers to enhance internalization by cancer cells (35). This section provides a comprehensive overview of advancements in nano-drug delivery systems with targeting warheads.

Natural Products Delivered by Nano-Drug Delivery Systems with Targeting Warheads
Terpenoids

Terpenoids are extensively utilized across various industries, including medicine and food, and are composed of multiple C5H8 units (36). During the late 1990s, substantial research focused on the separation, purification, and structural analysis of terpenoids, leading to a deeper understanding of their medicinal potential. Terpenoids exhibit a range of pharmacological activities, such as anti-tumor, anti-inflammatory, antimicrobial, and antiviral effects, as well as applications in treating cardiovascular diseases (37–41). This section reviews the development of nano-drug delivery systems for notable terpenoid products, specifically triptolide and ginsenoside, to establish a foundation for further research.

Triptolide (TP), predominantly derived from *Tripterygium wilfordii* Hook.f., is a promising candidate for the next generation of anticancer drugs. It is a highly oxidized diterpenoid trioxide with analgesic, anti-inflammatory, and immunomodulatory properties. Several derivatives of triptolide are currently under clinical investigation (22, 42, 43). Advances in drug delivery technologies have been employed to address the clinical challenges associated with TP. For instance, one study (44) developed galactosylated chitosan-triptolide nanoparticles (GC-TP-NPs) to enhance targeted delivery to hepatocellular carcinoma. These nanoparticles demonstrated sustained release and were internalized by cells via the asialoglycoprotein receptor (ASGPR). In vivo studies showed significant accumulation of GC-TP-NPs in liver tumors, reduced systemic toxicity, and minimized male reproductive toxicity compared to free drug administration. The specific attachment of the galactose moiety to liver cancer cell receptors facilitated targeted drug delivery, highlighting the advantages of nano-drug delivery systems with targeting warheads. Another study by Huang et al. (45) developed Pluronic F127/P123 nanoparticles (TP-FPNPs) with folate as a targeting agent and incorporated TP. The TP-FPNPs demonstrated enhanced kidney targeting, prolonged in vivo residence, and improved cellular uptake, offering significantly better therapeutic effects for renal ischemia/reperfusion injury (IRI) compared to TP alone. The folate moiety facilitated cellular uptake via folate receptors on renal tubular cells, leading to controlled drug release and effective treatment of renal IRI, illustrating the potential of folate-functionalized drug-loaded nanoparticles for hydrophobic drug delivery in renal diseases.

Ginsenosides, also referred to as triterpenoid saponins, are primarily found in the dried root of ginseng and possess chemical and biological properties akin to glucocorticoids, indicating substantial therapeutic potential. However, their clinical application is hindered by poor solubility and bioavailability (46, 47). To overcome these limitations, various nano-drug delivery systems have been developed to enhance the pharmacological efficacy of ginsenosides (48). For example, Zhang et al. (49) utilized the A54 peptide to construct micelles loaded with ginsenoside compound K (CK) for liver targeting. The micelles were based on deoxycholic acid-O-carboxymethyl chitosan. Compared to CK alone, the polymer micelles significantly improved the anti-proliferative effect against liver cancer cell lines, demonstrating superior anti-cancer properties. The A54 peptide, specific to

liver cancer cells, enabled the micellar system to target and bind to liver cancer cell receptors, enhancing cellular uptake and extending CK's residence time in the bloodstream, thereby improving its bioavailability.

Flavonoids

Flavonoids possess a C15 backbone structure featuring two phenyl rings (C6-C3-C6). These compounds are recognized for their extensive therapeutic applications, including the ability to mitigate aging processes in various life systems and organs. They are also known for their preventive effects against cardiovascular diseases, Alzheimer's disease, and breast cancer (50–52). Given their therapeutic potential, substantial efforts have been made to enhance their solubility, improve gastrointestinal absorption, and reduce metabolic clearance. Moreover, flavonoids can interact with other dietary components, potentially leading to complexation or precipitation, which can degrade the compounds through microbial action, thereby affecting their stability and bioavailability. To address these challenges, researchers have focused on developing nano-carrier systems to specifically target and deliver flavonoid compounds. This approach has significantly improved the pharmacokinetics and pharmacodynamics of these drugs by altering their free forms (53, 54). Haroon Khan et al. (55) extensively reviewed the enhanced bioavailability and safety implications of flavonoid nano-drugs, while Paola Aiello and colleagues (56) evaluated in vivo studies of dietary flavonoid nanoparticles with anticancer properties. This section highlights recent advancements in nano-drug delivery systems for flavonoid compounds, focusing on gambogic acid and baicalin.

Gambogic Acid (GA) is an emerging flavonoid-based anticancer agent known for its potent tumor activity against various cancers, including colon, pancreatic, and breast cancers (57–60). However, its clinical application is constrained by limited solubility, short action duration, dose-dependent toxicity, and injection site discomfort (61, 62). To enhance bioavailability and clinical efficacy, numerous GA nano-formulations have been developed. One study (63) involved the modification of redox-sensitive chitosan nanoparticles (NPs) with hyaluronic acid (HA) to create HA-coated redox-sensitive chitosan NPs (HA(HECS-ss-OA)/GA) for targeted intracellular delivery of GA. These nanoparticles demonstrated excellent drug loading and, through in vivo and in vitro studies, showed superior anti-tumor efficacy compared to non-sensitive controls and HA-uncoated counterparts. The hyaluronic acid modification facilitated targeted delivery by binding to CD44 receptors on cancer cells, significantly improving drug safety and highlighting the potential of nano-drug delivery systems utilizing natural products as targeting agents.

Baicalin (BAI), extracted from the roots and stems of *Scutellaria baicalensis*, exhibits significant anticancer activity, particularly against breast and ovarian cancer cells (64–66). Researchers (67) developed folate-conjugated bovine serum albumin nanoparticles (FA-BSANPs/BAI) to enhance the delivery and tumor-targeting of BAI using the desolvation-crosslinking method. This folate-modified albumin system prolonged BAI's in vivo residence time and improved its tumor-targeting capability. By leveraging the elevated levels of folate receptors on breast cancer cells, this approach facilitated targeted drug delivery and significantly

enhanced therapeutic efficacy. Additionally, a research team (68) optimized a nano-carrier for neuroprotective agents using RVG29 peptide-modified polyethylene glycol-polylactic acid-co-glycolic acid nanoparticles. This carrier improved drug stability and continuous release, enhancing the effectiveness of neuroprotective agents delivered from the nasal route to the brain. The RVG29 peptide, derived from rabies virus glycoprotein, enabled brain-targeted drug delivery via receptor-mediated endocytosis, thereby enhancing BAI delivery to the brain and improving treatment outcomes for ischemic brain injury.

Polyphenols

Polyphenols are recognized for their potent antioxidant and anti-inflammatory properties, making them valuable for the clinical management of chronic diseases (69). These compounds, found in various vascular plants, are characterized by numerous hydroxyl groups on their aromatic rings (70). Despite their considerable therapeutic potential, polyphenols often suffer from structural instability when exposed to alkaline conditions, light, and heat, primarily due to their multiple hydroxyl groups. Additionally, their low solubility limits gastrointestinal absorption and bioavailability, thereby constraining their pharmaceutical and functional food applications (76). To address these challenges, nano-drug delivery systems have been developed to mitigate issues such as precipitation, rapid degradation, and elimination of polyphenolic compounds. Recent advancements in nano-carrier systems have successfully enhanced the stability and bioavailability of polyphenols (77, 78). This section reviews recent progress in nano-drug delivery systems for two polyphenolic compounds, resveratrol and curcumin, providing a theoretical foundation for future research in this area.

Resveratrol (RES), a natural polyphenol antioxidant with a trans-3,4',5-trihydroxystilbene structure, is found in plants like grapes, mulberries, peanuts, and rhubarb roots. RES is crucial for protecting blood vessels and DNA from oxidative damage, making it important for preventing and treating chronic inflammatory diseases. However, its limited physicochemical properties restrict its application as a standalone medication (79). Strategies such as encapsulation and controlled release using various carriers have emerged to improve RES's bioavailability (80). Jhaveri et al. (81) utilized transferrin-modified polyethylene glycol liposomes (Tf-RES-L) for RES delivery. These functionalized liposomes significantly increased glioblastoma multiforme cell apoptosis by activating the caspase 3/7 pathway, leveraging transferrin receptors upregulated in GBMs for targeted delivery. The functionalized liposomes exhibited uniform size distribution, increased stability, and enhanced cancer cell specificity, demonstrating the efficacy of nano-drug delivery systems with targeting warheads.

Curcumin (Cur), derived from the rhizome of *Curcuma longa*, is known for its antioxidant, wound-healing, and anticancer properties (82, 83). However, its application is limited by low bioavailability, high hydrophobicity, and light-induced degradation. One approach to overcome these issues involves encapsulating curcumin within biodegradable and biocompatible nanoparticles. Feng et al. (84) developed a CD44-targeted drug delivery system by conjugating

hyaluronic acid to propylene glycol-based ethosomes (HA-ES). The HA gel network on the surface of HA-ES reduced curcumin leakage and release, enhancing targeted delivery to inflamed psoriatic skin with high CD44 expression. This localized drug delivery system ensures drug stability and safety in non-target tissues, offering potential for enhanced drug accumulation in inflamed skin areas and other applications.

Alkaloids

Alkaloids are small nitrogenous organic compounds derived from amino acids and isolated from plants. They are categorized into various groups based on their chemical core structures, such as isoquinoline, quinoline, indole, and pyridine alkaloids (85). Numerous studies, both in vivo and clinical, have demonstrated the diverse pharmacological properties of alkaloids, including anticancer, antiviral, and anti-inflammatory effects (86–88). Despite their significant therapeutic potential, alkaloids often face challenges related to poor pharmacokinetics, incompatibility in biological media, and aggregation, which can hinder cellular uptake and limit clinical applications (89, 90). Contemporary research focuses on advancing nano-drug delivery systems with unique physical and chemical properties to protect encapsulated drugs from degradation, enhance permeability, and offer retention benefits (91, 92). This section highlights recent research on nano-drug delivery systems for alkaloids, using paclitaxel as a representative example.

Paclitaxel (PTX), a natural compound extracted from the bark of *Taxus brevifolia*, is renowned for its potent anti-tumor effects, particularly in treating ovarian and uterine cancers (93, 94). However, its clinical use is impeded by poor solubility, instability, tendency to precipitate, and toxicity (95, 96). To address these limitations, researchers (97) developed Tn-Lipo-PTX, a PEGylated paclitaxel nano-liposome with ASGPR targeting capabilities for hepatocellular carcinoma treatment. The use of a configurationally defined N-acetylgalactosamine as a targeting warhead enhanced paclitaxel's cytotoxicity toward liver cancer cells. This study underscores the effectiveness of nano-carriers with warhead modifications for delivering lipophilic drugs. Additionally, human H-chain ferritin (HFtn) has been explored for drug delivery due to its solubility, biodegradability, and uniform size distribution (98–101). Ma et al. (102) demonstrated that functionalizing the N-terminus of HFtn with the C-terminal cyclic peptide tLyP-1 enabled targeted paclitaxel delivery, greatly improving its ability to inhibit cancer cells and highlighting the potential of protein-functionalized targeting peptides for delivering hydrophobic drugs to tumor tissues.

Self-Assembled Nano-Drug Delivery Systems

Self-Assembly Process
- Definition: Self-assembly involves spontaneous formation of stable structures from fundamental units like molecules or nano-materials, driven by non-covalent interactions (e.g., hydrogen bonding, van der Waals forces, π–π stacking, electrostatic interactions).
- Forms: Results in structures such as micelles, liposomes, or helical belts.

- History: Early work by Ghadiri (1993) and Zhang on peptide nanotubes and ionizable peptides [103].

Strategies for Self-Assembly
- Top-Down: Creating nanostructures from larger structures.
- Bottom-Up: Using basic components and molecular recognition to build nanostructures.

Drug Self-Delivery Systems (DSDS)
- Concept: DSDSs use self-assembled drugs as both carriers and medications, enhancing drug encapsulation, loading capacity, and minimizing degradation.
- Advantages: Improved biocompatibility, stability, and safety by avoiding additional nano-catalysts.

Examples of Natural Product-Based Self-Assembled Systems

1. **Ursolic Acid (UA)**
   - Properties: Pentacyclic triterpenoid with anticancer effects.
   - System: Self-assembled carrier-free nano-drug system that improves solubility and tumor targeting.
   - Mechanism: Self-assembly driven by hydrophobic interactions and hydrogen bonding.

2. **Rhein (Rhe)**
   - Properties: Anthraquinone with potential in medical imaging and neurodegenerative disease treatment.
   - System: Controlled-release hydrogel made through self-assembly using π–π stacking and hydrogen bonds.
   - Applications: Alleviates inflammation, wound healing, and improved pharmacological effectiveness.

3. **Paclitaxel (PTX) and Ursolic Acid (UA)**
   - System: Self-assembled into a double-layered vesicle structure with high drug loading capacity.
   - Outcome: Synergistic effect with significant tumor inhibition and excellent therapeutic activity.

4. **Berberine (Ber) and Rhein (Rhe)**
   - System: Self-assembled nano-carrier enhancing antibacterial activity.
   - Result: Increased inhibition of Staphylococcus aureus compared to free drugs.

5. **Tannic Acid and Berberine**
   - System: Supramolecular self-assembly with drug conjugate HA for targeted delivery.
   - Effects: Enhanced drug uptake and anti-inflammatory effects in acute colitis.

Summary

The development of self-assembled nano-drug delivery systems using natural products shows promise in improving drug solubility, targeting, and therapeutic efficacy while addressing issues of stability and bioavailability. These advancements offer potential solutions to clinical challenges and highlight the innovative approaches being explored in drug delivery systems [103].

Self-Assembled Nano-Drug Delivery Systems

Peptide-Based Systems
- Characteristics: Peptides are bioactive compounds with excellent biocompatibility, biodegradability, and chemical versatility. They self-assemble into nanostructures under specific conditions (e.g., pH, ionic strength, light).
- Advantages: Customizable molecular design, effective functional regulation, peptide-specific biomolecular recognition.
- **Applications:**
    - Curcumin Delivery: Amphiphilic peptide R7L10 forms complexes with plasmid DNA to enhance solubility and cellular uptake of curcumin in acute lung injury models.
    - Hydrogels: Peptide-based hydrogels encapsulate drugs and respond to physiological conditions. Examples include FER-8 for PTX delivery and RADA16-I/RVDV16-I hydrogels for emodin delivery, showing improved stability and efficacy [103].
- Studies: Wang et al. reviewed design methodologies for peptide nano-drug delivery systems; Sis and Webber discussed design basics; Hsieh and Liaw proposed size and length control for nanotubes.

Metal-Coordinated Polyphenols
- Concept: Natural polyphenols can coordinate with metals to form metal-polyphenol nanonetworks (MPNs). These structures can improve drug solubility and stability.
- Applications:
    - Shikonin Delivery: Fe(III)-shikonin MPNs (FSSNs) enhance solubility and reduce toxicity. They trigger tumor cell apoptosis and necroptosis.
    - Curcumin and ICG: Curcumin-based MPNs (ICG @Cur-Gd NPs) with Gd3+ improve therapeutic efficacy and reduce biotoxicity through laser treatment.
    - Flavonoids: Flavonoid-based films (e.g., Myricetin, Quercetin) formed by Fe(III) coordination exhibit free radical scavenging activity and reusable surface coatings.
- Studies: Feng et al. developed FSSNs for tumor therapy; Wen et al. created curcumin-based MPNs for enhanced therapeutic efficacy; Bertleff-Zieschang et al. assembled flavonoid films for antioxidant applications [103].

Conclusion

The advancement of nano-drug delivery systems leveraging natural products represents a significant leap in pharmaceutical innovation. This approach addresses critical limitations faced by traditional natural products, such as poor solubility, limited bioavailability, and rapid metabolic clearance. By employing nanotechnology, researchers have successfully enhanced the delivery, targeting, and efficacy of various therapeutic agents derived from natural sources. Key innovations include the use of nano-carriers for improved solubility and targeted delivery, incorporating targeting warheads to enhance specificity, and utilizing

self-assembled nano-systems for controlled release and stability. Notable examples include the development of triptolide and ginsenoside-loaded nanoparticles, flavonoid-based nano-formulations, and self-assembled systems for polyphenols and alkaloids. These advancements demonstrate the potential for natural products to be used more effectively in clinical settings, offering improved therapeutic outcomes and reduced side effects. Overall, the integration of natural products with nano-drug delivery systems promises to revolutionize treatment modalities, particularly for complex diseases such as cancer and cardiovascular conditions. The ongoing research and development in this field are likely to yield further improvements in drug efficacy and patient outcomes, reinforcing the value of combining natural compounds with cutting-edge nanotechnology.

References

1. Khan IA, Smillie T. Implementing a "Quality by Design" Approach to Assure the Safety and Integrity of Botanical Dietary Supplements. *J Nat Prod*. 2012;75(9):1665–1673. doi:10.1021/np300434j
2. Mehta P, Shah R, Lohidasan S, Mahadik KR. Pharmacokinetic profile of phytoconstituent(s) isolated from medicinal plants-A comprehensive review. *J Tradit Complement Med*. 2015;5(4):207–227. doi:10.1016/j.jtcme.2014.11.041
3. Rodrigues T, Reker D, Schneider P, Schneider G. Counting on natural products for drug design. *Nat Chem*. 2016;8(6):531–541. doi:10.1038/nchem.2479
4. Vanti G. Recent strategies in nanodelivery systems for natural products: a review. *Environ Chem Lett*. 2021;19(6):4311–4326. doi:10.1007/s10311-021-01276-x
5. Beutler JA. Natural Products as a Foundation for Drug Discovery. *Curr Protoc Pharmacol*. 2009;46:9.11.1–9.11.21. doi:10.1002/0471141755.ph0911s46
6. Watkins R, Wu L, Zhang C, Davis RM, Xu B. Natural product-based nanomedicine: recent advances and issues. *Int J Nanomed*. 2015;10:6055–6074. doi:10.2147/IJN.S92162
7. Patra JK, Das G, Fraceto LF, et al. Nano based drug delivery systems: recent developments and future prospects. *J Nanobiotechnol*. 2018;16(1):71. doi:10.1186/s12951-018-0392-8
8. Martinho N, Damgé C, Reis CP. Recent Advances in Drug Delivery Systems. *J Biomater Nanobiotechnol*. 2011;02(05):510–526. doi:10.4236/jbnb.2011.225062
9. Jahangirian H, Lemraski EG, Webster TJ, Rafiee-Moghaddam R, Abdollahi Y. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. *Int J Nanomed*. 2017;12:2957–2978. doi:10.2147/IJN.S127683
10. Bonifácio BV, Silva PB, Ramos MADS, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: a review. *Int J Nanomed*. 2014;9:1–15. doi:10.2147/IJN.S52634
11. Liu Z, Tabakman S, Welsher K, Dai H. Carbon Nanotubes in Biology and Medicine: in vitro and in vivo Detection, Imaging and Drug Delivery. *Nano Res*. 2009;2(2):85–120. doi:10.1007/s12274-009-9009-8

12. Razzacki SZ, Thwar PK, Yang M, Ugaz VM, Burns MA. Integrated microsystems for controlled drug delivery. *Adv Drug Deliv Rev.* 2004;56(2):185–198. doi:10.1016/j.addr.2003.08.012

13. Lam PL, Wong WY, Bian Z, Chui CH, Gambari R. Recent advances in green nanoparticulate systems for drug delivery: efficient delivery and safety concern. *Nanomed.* 2017;12(4):357–385. doi:10.2217/nnm-2016-0305

14. Rudramurthy GR, Swamy MK, Sinniah UR, Ghasemzadeh A. Nanoparticles: alternatives Against Drug-Resistant Pathogenic Microbes. *Mol.* 2016;21(7):836.

15. Saka R, Chella N. Nanotechnology for delivery of natural therapeutic substances: a review. *Environ Chem Lett.* 2021;19(2):1097–1106. doi:10.1007/s10311-020-01103-9

16. Jain H, Chella N. Methods to improve the solubility of therapeutical natural products: a review. *Environ Chem Lett.* 2021;19(1):111–121. doi:10.1007/s10311-020-01082-x

17. Paroha S, Dewangan RP, Dubey RD, Sahoo PK. Conventional and nanomaterial-based techniques to increase the bioavailability of therapeutic natural products: a review. *Environ Chem Lett.* 2020;18(6):1767–1778. doi:10.1007/s10311-020-01038-1

18. Ita KB. Prodrugs for transdermal drug delivery – trends and challenges. *J Drug Target.* 2016;24(8):671–678. doi:10.3109/1061186X.2016.1154562

19. Fang JY, Leu YL. Prodrug strategy for enhancing drug delivery via skin. *Curr Drug Discov Technol.* 2006;3(3):211–224. doi:10.2174/157016306780136772

20. Shi X, Sun K, Baker JR. Spontaneous Formation of Functionalized Dendrimer-Stabilized Gold Nanoparticles. *J Phys Chem C Nanomater Interfaces.* 2009;112(22):8251–8258. doi:10.1021/jp801293a

21. Park SH, Oh SG, Mun JY, Han SS. Loading of gold nanoparticles inside the DPPC bilayers of liposome and their effects on membrane fluidities. *Colloids Surf B Biointerfaces.* 2006;48(2):112–118. doi:10.1016/j.colsurfb.2006.01.006

22. Qiao L, Han M, Gao S, et al. Research progress on nanotechnology for delivery of active ingredients from traditional Chinese medicines. *J Mater Chem B.* 2020;8(30):6333–6351. doi:10.1039/D0TB01260B

23. Ashley EA. Towards precision medicine. *Nat Rev Genet.* 2016;17(9):507–522. doi:10.1038/nrg.2016.86

24. Muro S. Challenges in design and characterization of ligand-targeted drug delivery systems. *J Control Release off J Control Release Soc.* 2012;164(2):125–137. doi:10.1016/j.jconrel.2012.05.052

25. Srinivasarao M, Galliford CV, Low PS. Principles in the design of ligand-targeted cancer therapeutics and imaging agents. *Nat Rev Drug Discov.* 2015;14(3):203–219. doi:10.1038/nrd4519

26. Péczka N, Orgován Z, Ábrányi-Balogh P, Keserű GM. Electrophilic warheads in covalent drug discovery: an overview. *Expert Opin Drug Discov.* 2022;17(4):413–422. doi:10.1080/17460441.2022.2034783

27. Srinivasarao M, Low PS. Ligand-Targeted Drug Delivery. *Chem Rev.* 2017;117(19):12133–12164. doi:10.1021/acs.chemrev.7b00013

28. Li Y, Chen M, Yao B, et al. Transferrin receptor-targeted redox/pH-sensitive podophyllotoxin prodrug micelles for multidrug-resistant breast cancer therapy. *J Mater Chem B.* 2019;7(38):5814–5824. doi:10.1039/C9TB00651F

29. Van Heertum RL, Scarimbolo R, Ford R, Berdougo E, O'Neal M. Companion diagnostics and molecular imaging-enhanced approaches for oncology clinical trials. *Drug Des Devel Ther*. 2015;9:5215–5223. doi:10.2147/DDDT.S87561

30. Maurer AH, Elsinga P, Fanti S, Nguyen B, Oyen WJG, Weber WA. Imaging the folate receptor on cancer cells with 99mTc-etarfolatide: properties, clinical use, and future potential of folate receptor imaging. *J Nucl Med off Publ Soc Nucl Med*. 2014;55(5):701–704.

31. Farkas R, Siwowska K, Ametamey SM, Schibli R, van der Meulen NP, Müller C. 64Cu- and 68Ga-Based PET Imaging of Folate Receptor-Positive Tumors: development and Evaluation of an Albumin-Binding NODAGA−Folate. *Mol Pharm*. 2016;13(6):1979–1987. doi:10.1021/acs.molpharmaceut.6b00143

32. Fani M, Tamma ML, Nicolas GP, et al. In Vivo Imaging of Folate Receptor Positive Tumor Xenografts Using Novel 68Ga-NODAGA-Folate Conjugates. *Mol Pharm*. 2012;9(5):1136–1145. doi:10.1021/mp200418f

33. Müller C, Schibli R. Folic Acid Conjugates for Nuclear Imaging of Folate Receptor–Positive Cancer. *J Nucl Med off Publ Soc Nucl Med*. 2011;52(1):1–4.

34. Jin SE, Jin HE, Hong SS. Targeted delivery system of nanobiomaterials in anticancer therapy: from cells to clinics. *BioMed Res Int*. 2014;2014:814208. doi:10.1155/2014/814208

35. Scaranti M, Cojocaru E, Banerjee S, Banerji U. Exploiting the folate receptor α in oncology. *Nat Rev Clin Oncol*. 2020;17(6):349–359. doi:10.1038/s41571-020-0339-5

36. Li-chao SUN, Shu-ying LI, Feng-zhong W, Feng-jiao XIN. Research Progresses in the Synthetic Biology of Terpenoids. *Biotechnol Bull*. 2017;33(1):64.

37. Lage H, Duarte N, Coburger C, Hilgeroth A, Ferreira MJU. Antitumor activity of terpenoids against classical and atypical multidrug resistant cancer cells. *Phytomedicine*. 2010;17(6):441–448. doi:10.1016/j.phymed.2009.07.009

38. Ge J, Liu Z, Zhong Z, et al. Natural terpenoids with anti-inflammatory activities: potential leads for anti-inflammatory drug discovery. *Bioorg Chem*. 2022;124:105817. doi:10.1016/j.bioorg.2022.105817

39. Yamaguchi T. Antibacterial effect of the combination of terpenoids. *Arch Microbiol*. 2022;204(8):520. doi:10.1007/s00203-022-03142-y

40. Lin LT, Chung CY, Hsu WC, et al. Saikosaponin b2 is a Naturally Occurring Terpenoid That Efficiently Inhibits Hepatitis C Virus Entry. *J Hepatol*. 2015;62(3):541–548. doi:10.1016/j.jhep.2014.10.040

41. Abdul Ghani MA, Ugusman A, Latip J, Zainalabidin S. Role of Terpenophenolics in Modulating Inflammation and Apoptosis in Cardiovascular Diseases: a Review. *Int J Mol Sci*. 2023;24(6):5339. doi:10.3390/ijms24065339

42. Gao J, Zhang Y, Liu X, Wu X, Huang L, Gao W. Triptolide: pharmacological spectrum, biosynthesis, chemical synthesis and derivatives. *Theranostics*. 2021;11(15):7199–7221. doi:10.7150/thno.57745

43. Xu H, Liu B. Triptolide-targeted delivery methods. *Eur J Med Chem*. 2019;164:342–351. doi:10.1016/j.ejmech.2018.12.058

44. Zhang YQ, Shen Y, Liao MM, et al. Galactosylated chitosan triptolide nanoparticles for overcoming hepatocellular carcinoma: enhanced

therapeutic efficacy, low toxicity, and validated network regulatory mechanisms. *Nanomedicine.* 2019;15(1):86–97.

45. Huang C, Zeng T, Li J, et al. Folate Receptor-Mediated Renal-Targeting Nanoplatform for the Specific Delivery of Triptolide to Treat Renal Ischemia/Reperfusion Injury. *ACS Biomater Sci Eng.* 2019;5(6):2877–2886. doi:10.1021/acsbiomaterials.9b00119

46. Qian T, Cai Z, Wong RNS, Mak NK, Jiang ZH. In vivo rat metabolism and pharmacokinetic studies of ginsenoside Rg3. *J Chromatogr B.* 2005;816(1):223–232. doi:10.1016/j.jchromb.2004.11.036

47. Xu QF, Fang XL, Chen DF. Pharmacokinetics and bioavailability of ginsenoside Rb1 and Rg1 from Panax notoginseng in rats. *J Ethnopharmacol.* 2003;84(2):187–192. doi:10.1016/S0378-8741(02)00317-3

48. Kim H, Lee JH, Kim JE, et al. Micro-/nano-sized delivery systems of ginsenosides for improved systemic bioavailability. *J Ginseng Res.* 2018;42(3):361–369. doi:10.1016/j.jgr.2017.12.003

49. Zhang J, Jiang Y, Li Y, et al. Micelles modified with a chitosan-derived homing peptide for targeted intracellular delivery of ginsenoside compound K to liver cancer cells. *Carbohydr Polym.* 2020;230:115576. doi:10.1016/j.carbpol.2019.115576

50. Winkel-Shirley B. Flavonoid biosynthesis. A colorful model for genetics, biochemistry, cell biology, and biotechnology. *Plant Physiol.* 2001;126(2):485–493. doi:10.1104/pp.126.2.485

51. Selvakumar P, Badgeley A, Murphy P, et al. Flavonoids and Other Polyphenols Act as Epigenetic Modifiers in Breast Cancer. *Nutrients.* 2020;12(3):761. doi:10.3390/nu12030761

52. Fernandes I, Pérez-Gregorio R, Soares S, Mateus N, De Freitas V. Wine Flavonoids in Health and Disease Prevention. *Mol.* 2017;22(2):292.

53. Amawi H, Ashby CR, Tiwari AK. Cancer chemoprevention through dietary flavonoids: what's limiting? *Chin J Cancer.* 2017;36(1):50. doi:10.1186/s40880-017-0217-4

54. Gao S, Hu M. Bioavailability challenges associated with development of anti-cancer phenolics. *Mini Rev Med Chem.* 2010;10(6):550–567. doi:10.2174/138955710791384081

55. Khan H, Ullah H, Martorell M, et al. Flavonoids nanoparticles in cancer: treatment, prevention and clinical prospects. *Semin Cancer Biol.* 2021;69:200–211. doi:10.1016/j.semcancer.2019.07.023

56. Aiello P, Consalvi S, Poce G, et al. Dietary flavonoids: nano delivery and nanoparticles for cancer therapy. *Semin Cancer Biol.* 2021;69:150–165. doi:10.1016/j.semcancer.2019.08.029

57. Zhou Z, Ma J. Gambogic acid suppresses colon cancer cell activity in vitro. *Exp Ther Med.* 2019;18(4):2917–2923. doi:10.3892/etm.2019.7912

58. Lin D, Lin X, He T, Xie G. Gambogic Acid Inhibits the Progression of Gastric Cancer via circRNA_ASAP2/miR-33a-5p/CDK7 Axis. *Cancer Manag Res.* 2020;12:9221–9233. doi:10.2147/CMAR.S269768

59. Wang H, Zhao Z, Lei S, et al. Gambogic acid induces autophagy and combines synergistically with chloroquine to suppress pancreatic cancer by increasing the accumulation of reactive oxygen species. *Cancer Cell Int.* 2019;19:7. doi:10.1186/s12935-018-0705-x

60. Wang Y, Liang X, Tong R, et al. Gambogic Acid-Loaded Polymeric Micelles for Improved Therapeutic Effect in Breast Cancer. *J Biomed Nanotechnol.* 2018;14(10):1695–1704. doi:10.1166/jbn.2018.2626

61. Li M, Su F, Zhu M, et al. Research Progress in the Field of Gambogic Acid and Its Derivatives as Antineoplastic Drugs. *Mol.* 2022;27(9):2937.

62. Wang X, Chen W. Gambogic acid is a novel anti-cancer agent that inhibits cell proliferation, angiogenesis and metastasis. *Anticancer Agents Med Chem.* 2012;12(8):994–1000. doi:10.2174/187152012802650066

63. Xu W, Wang H, Dong L, et al. Hyaluronic acid-decorated redox-sensitive chitosan micelles for tumor-specific intracellular delivery of gambogic acid. *Int J Nanomed.* 2019;14:4649–4666. doi:10.2147/IJN.S201110

64. Peng Y, Zhao FZ, Guo CS, et al. Effects and Mechanism of Baicalin on Apoptosis of Cervical Cancer HeLa Cells In-vitro. *Iran J Pharm Res IJPR.* 2015;14(1):251–261.

65. Mei ZQ, Wang S, Zhang H, et al. The combination of baicalin and baicalein enhances apoptosis via the ERK/p38 MAPK pathway in human breast cancer cells. *Acta Pharmacol Sin.* 2009;30(12):1648–1658. doi:10.1038/aps.2009.166

66. Gao C, Zhou Y, Li H, et al. Antitumor effects of baicalin on ovarian cancer cells through induction of cell apoptosis and inhibition of cell migration in vitro. *Mol Med Rep.* 2017;16(6):8729–8734. doi:10.3892/mmr.2017.7757

67. Meng F, Liu F, Lan M, et al. Preparation and evaluation of folate-modified albumin baicalin-loaded nanoparticles for the targeted treatment of breast cancer. *J Drug Deliv Sci Technol.* 2021;65:102603. doi:10.1016/j.jddst.2021.102603

68. Li X, Li S, Ma C, Li T, Yang L. Preparation of baicalin-loaded ligand-modified nanoparticles for nose-to-brain delivery for neuroprotection in cerebral ischemia. *Drug Deliv.* 2022;29(1):1282–1298. doi:10.1080/10717544.2022.2064564

69. Zhang Z, Qiu C, Li X, et al. Advances in research on interactions between polyphenols and biology-based nano-delivery systems and their applications in improving the bioavailability of polyphenols. *Trends Food Sci Technol.* 2021;116:492–500. doi:10.1016/j.tifs.2021.08.009

70. Kostić AŽ, Milinčić DD, Gašić UM, et al. Polyphenolic profile and antioxidant properties of bee-collected pollen from sunflower (Helianthus annuus L.) plant. *LWT.* 2019;112:108244.

71. Scalbert A, Johnson IT, Saltmarsh M. Polyphenols: antioxidants and beyond. *Am J Clin Nutr.* 2005;81(1):215S–217S. doi:10.1093/ajcn/81.1.215S

72. Davatgaran-Taghipour Y, Masoomzadeh S, Farzaei MH, et al. Polyphenol nanoformulations for cancer therapy: experimental evidence and clinical perspective. *Int J Nanomed.* 2017;12:2689–2702. doi:10.2147/IJN.S131973

73. Ignat I, Radu DG, Volf I, Pag AI, Popa VI. Antioxidant and antibacterial activities of some natural polyphenol. *Cellulose Chem Technol.* 2013;47(5–6):387–399.

74. Yahfoufi N, Alsadi N, Jambi M, Matar C. The Immunomodulatory and Anti-Inflammatory Role of Polyphenols. *Nutrients.* 2018;10(11):1618. doi:10.3390/nu10111618

1030

75. Zhao C, Wan X, Zhou S, Cao H. Natural Polyphenols: a Potential Therapeutic Approach to Hypoglycemia. *eFood.* 2020;1(2):107–118. doi:10.2991/efood.k.200302.001

76. Kumar Vivekanandhan D, Ranjan Prasad Verma P, Kumar Singh S. Emerging Technologies for Improving Bioavailability of Polyphenols. *Curr Nutr Food Sci.* 2016;12(1):12–22. doi:10.2174/1573401311666151015213704

77. Han Y, Zhou J, Hu Y, et al. Polyphenol-Based Nanoparticles for Intracellular Protein Delivery via Competing Supramolecular Interactions. *ACS Nano.* 2020;14(10):12972–12981. doi:10.1021/acsnano.0c04197

78. Neethirajan S, Jayas DS. Nanotechnology for the Food and Bioprocessing Industries. *Food Bioprocess Technol.* 2011;4(1):39–47. doi:10.1007/s11947-010-0328-2

79. Gowd V, Kanika JC, et al. Resveratrol and resveratrol nano-delivery systems in the treatment of inflammatory bowel disease. *J Nutr Biochem.* 2022;109:109101. doi:10.1016/j.jnutbio.2022.109101

80. Liang M, Guo M, Saw PE, Yao Y. Fully Natural Lecithin Encapsulated Nano-Resveratrol for Anti-Cancer Therapy. *Int J Nanomed.* 2022;17:2069–2078. doi:10.2147/IJN.S362418

81. Jhaveri A, Deshpande P, Pattni B, Torchilin V. Transferrin-targeted, resveratrol-loaded liposomes for the treatment of glioblastoma. *J Control Release.* 2018;277:89–101. doi:10.1016/j.jconrel.2018.03.006

82. Naksuriya O, Okonogi S. Comparison and combination effects on antioxidant power of curcumin with gallic acid, ascorbic acid, and xanthone. *Drug Discov Ther.* 2015;9(2):136–141. doi:10.5582/ddt.2015.01013

83. Vallianou NG, Evangelopoulos A, Schizas N, Kazazis C. Potential anticancer properties and mechanisms of action of curcumin. *Anticancer Res.* 2015;35(2):645–651.

84. Zhang Y, Xia Q, Li Y, et al. CD44 Assists the Topical Anti-Psoriatic Efficacy of Curcumin-Loaded Hyaluronan-Modified Ethosomes: a New Strategy for Clustering Drug in Inflammatory Skin. *Theranostics.* 2019;9(1):48. doi:10.7150/thno.29715

85. Yan Y, Li X, Zhang C, Lv L, Gao B, Li M. Research Progress on Antibacterial Activities and Mechanisms of Natural Alkaloids: a Review. *Antibiot Basel Switz.* 2021;10(3):318.

86. Qing ZX, Huang JL, Yang XY, et al. Anticancer and Reversing Multidrug Resistance Activities of Natural Isoquinoline Alkaloids and their Structure-activity Relationship. *Curr Med Chem.* 2018;25(38):5088–5114. doi:10.2174/0929867324666170920125135

87. Gorpenchenko TY, Grigorchuk VP, Bulgakov DV, Tchernoded GK, Bulgakov VP. Tempo-Spatial Pattern of Stepharine Accumulation in Stephania Glabra Morphogenic Tissues. *Int J Mol Sci.* 2019;20(4):808. doi:10.3390/ijms20040808

88. Souza CRM, Bezerra WP, Souto JT. Marine Alkaloids with Anti-Inflammatory Activity: current Knowledge and Future Perspectives. *Mar Drugs.* 2020;18(3):147. doi:10.3390/md18030147

89. Ma X, Zhou J, Zhang CX, et al. Modulation of drug-resistant membrane and apoptosis proteins of breast cancer stem cells by targeting berberine

liposomes. *Biomaterials.* 2013;34(18):4452–4465. doi:10.1016/j.biomaterials.2013.02.066

90. Majidzadeh H, Araj-Khodaei M, Ghaffari M, Torbati M, Ezzati Nazhad Dolatabadi J, Hamblin MR. Nano-based delivery systems for berberine: a modern anti-cancer herbal medicine. *Colloids Surf B Biointerfaces.* 2020;194:111188. doi:10.1016/j.colsurfb.2020.111188

91. Bregoli L, Movia D, Gavigan-Imedio JD, Lysaght J, Reynolds J, Prina-Mello A. Nanomedicine applied to translational oncology: a future perspective on cancer treatment. *Nanomedicine.* 2016;12(1):81–103. doi:10.1016/j.nano.2015.08.006

92. Jacob J, Haponiuk JT, Thomas S, Gopi S. Biopolymer based nanomaterials in drug delivery systems: a review. *Mater Today Chem.* 2018;9:43–55. doi:10.1016/j.mtchem.2018.05.002

93. Ingle SG, Pai RV, Monpara JD, Vavia PR. Liposils: an effective strategy for stabilizing Paclitaxel loaded liposomes by surface coating with silica. *Eur J Pharm Sci off J Eur Fed Pharm Sci.* 2018;122:51–63.

94. Wang F, Porter M, Konstantopoulos A, Zhang P, Cui H. Preclinical development of drug delivery systems for paclitaxel-based cancer chemotherapy. *J Control Release off J Control Release Soc.* 2017;267:100–118. doi:10.1016/j.jconrel.2017.09.026

95. Geisler JP, Linnemeier GC, Thomas AJ, Manahan KJ. Extreme drug resistance is common after prior exposure to paclitaxel. *Gynecol Oncol.* 2007;106(3):538–540. doi:10.1016/j.ygyno.2007.05.002

96. Ganta S, Amiji M. Coadministration of Paclitaxel and curcumin in nanoemulsion formulations to overcome multidrug resistance in tumor cells. *Mol Pharm.* 2009;6(3):928–939. doi:10.1021/mp800240j

97. Li T, Yu P, Chen Y, et al. N-acetylgalactosamine-decorated nanoliposomes for targeted delivery of paclitaxel to hepatocellular carcinoma. *Eur J Med Chem.* 2021;222:113605. doi:10.1016/j.ejmech.2021.113605

98. Khoshnejad M, Parhiz H, Shuvaev VV, Dmochowski IJ, Muzykantov VR. Ferritin-based drug delivery systems: hybrid nanocarriers for vascular immunotargeting. *J Control Release off J Control Release Soc.* 2018;282:13–24. doi:10.1016/j.jconrel.2018.02.042

99. Liang M, Fan K, Zhou M, et al. H-ferritin-nanocaged doxorubicin nanoparticles specifically target and kill tumors with a single-dose injection. *Proc Natl Acad Sci U S A.* 2014;111(41):14900–14905. doi:10.1073/pnas.1407808111

100. Fan K, Jia X, Zhou M, et al. Ferritin Nanocarrier Traverses the Blood Brain Barrier and Kills Glioma. *ACS Nano.* 2018;12(5):4105–4115. doi:10.1021/acsnano.7b06969

101. Pandolfi L, Bellini M, Vanna R, et al. H-Ferritin Enriches the Curcumin Uptake and Improves the Therapeutic Efficacy in Triple Negative Breast Cancer Cells. *Biomacromolecules.* 2017;18(10):3318–3330. doi:10.1021/acs.biomac.7b00974

102. Ma Y, Li R, Dong Y, et al. tLyP-1 Peptide Functionalized Human H Chain Ferritin for Targeted Delivery of Paclitaxel. *Int J Nanomed.* 2021;16:789. doi:10.2147/IJN.S289005

103. Lv, Y., Li, W., Liao, W., Jiang, H., Liu, Y., Cao, J., ... & Feng, Y. (2024). Nano-drug delivery systems based on natural products. *International Journal of Nanomedicine*, 541-569.

أنظمة توصيل الأدوية النانوية المتقدمة باستخدام ابتكارات قائمة على المنتجات الطبيعية

الملخص:

الخلفية: لعبت المنتجات الطبيعية تاريخيًا دورًا حاسمًا في صحة الإنسان، بدءًا من الاستخدامات المبكرة إلى الطب الحديث. على الرغم من إمكاناتها الدوائية الواسعة، غالبًا ما تكون التطبيقات السريرية محدودة بسبب مشكلات مثل ضعف الذوبان وسرعة الأيض.

الهدف: استكشاف استخدام أنظمة توصيل الأدوية النانوية المتقدمة لتعزيز فعالية المنتجات الطبيعية من خلال التغلب على محدودياتها وتحسين النتائج العلاجية.

الطرق: تستعرض هذه المراجعة الأنظمة المختلفة لتوصيل الأدوية النانوية التي تدمج المنتجات الطبيعية. وتناقش التقدمات في الناقلات النانوية، بما في ذلك الليبوسومات، والميكيلات، والهياكل ذات التجميع الذاتي، مع التركيز على قدرتها على تحسين ذوبان الأدوية واستقرارها وتوصيلها المستهدف.

النتائج: تم إحراز تقدم كبير في تطوير ناقلات نانوية للمنتجات الطبيعية، بما في ذلك التربينات، والفلافونويد، البوليفينولات، والقلويدات. وقد أظهرت الابتكارات مثل الرؤوس المستهدفة والأنظمة ذات التجميع الذاتي تحسينًا في توصيل الأدوية وفعاليتها العلاجية في الدراسات قبل السريرية.

الاستنتاج: تقدم أنظمة توصيل الأدوية النانوية التي تستخدم المنتجات الطبيعية حلولاً واعدة للتغلب على القيود التقليدية، مما يعزز توافر الأدوية الحيوي والتوصيل المستهدف. هذا التقدم يحمل إمكانات كبيرة في تحويل علاج الأمراض المعقدة وتحسين النتائج السريرية.

الكلمات الرئيسية: توصيل الأدوية النانوية، المنتجات الطبيعية، الرؤوس المستهدفة، التجميع الذاتي، ذوبان الأدوية، الفعالية العلاجية