



## A comprehensive review of nano-delivery system for tea polyphenols: Construction, applications, and challenges

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### ABSTRACT

Tea polyphenols (TPs) are important bioactive compounds in tea and have excellent physiological regulation functions. However, the extraction and purification of TPs are key technologies affecting their further application, and the chemical instability, poor bioavailability of TPs are major challenges for researchers. In the past decade, therefore, research and development of advanced carrier systems for the delivery of TPs has been greatly promoted to improve their poor stability and poor bioavailability. In this review, the properties and function of TPs are introduced, and the recent advances in the extraction and purification technologies are systematically summarized. Particularly, the intelligent delivery of TPs via novel nano-carriers is critically reviewed, and the application of TPs nano-delivery system in medical field and food industry is also described. Finally, the main limitations, current challenges and future perspectives are highlighted in order to provide research ideas for exploiting nano-delivery carriers and their application in TPs.

### 1. Introduction

Tea (*Camellia sinensis*) is a genus of Theaceae, and it is a product made of tea buds and leaves. Tea is recognized as a healthy drink in the world, which has the effect of refreshing and reducing blood pressure. Together with coffee and cocoa, it is considered to be one of the three major non-alcoholic beverages in the world (Z. W. Zhou et al., 2019b). China has a history of planting tea trees for thousands of years, and was the first country to discover tea trees, harvest tea leaves and drink tea. In recent years, a large number of plantings have been carried out in tropical and subtropical regions, and as far as our native regions are concerned, there are over 400 species of tea planted, and there are 14 tea genera. There are mainly six types of tea in China, namely green tea, black tea, oolong tea, yellow tea, white tea and dark tea (Tang et al., 2019). Tea contains mainly polysaccharides, polyphenols, chlorophyll, beta-carotene, multivitamins, caffeine, flavonoids, pyrroloquinoline quinone, protein and amino acids, but also contains calcium, iron, manganese, copper, magnesium and many other minerals Samanta (2020). Tea polyphenols (TPs) are the main components that determine the color, aroma, taste and efficacy of tea leaves, accounting for 20 %-30

% of the dry weight of tea leaves (Lorenzo & Munekata, 2016), is the most abundant class of soluble components in tea, and the most important substance for tea to exert its health benefits. TPs have strong antioxidant properties, and its main component, epigallocatechin gallate (EGCG), has about 100 times more reducing properties than L-ascorbic acid. In addition, TPs also have anti-tumor effects (Sur & Panda, 2017), anti-diabetic (Granja et al., 2017), anti-virus (Falcó et al., 2018), anti-radiation (Xie et al., 2020), anti-bacterial function (H. F. He, 2017), also can be used as an adsorbent, is widely used in food processing and other fields. With the growing trend of aging population, the public health consciousness and living standards of the society are improving in the background, more and more attention to the application of TPs in real life and its potential value, the development and utilization of TPs in functional products will be further highlighted.

The extraction, separation and purification techniques of TPs are key to the product development and application of TPs, but they are highly susceptible to oxidative degradation during their extraction and utilization due to the influence of external environment. Nano-carriers have the characteristics of targeted transport, biocompatibility, and degradability. The construction of a new nano-delivery system with high

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sensitivity and good accuracy based on nano-carriers can effectively improve the problems of poor stability and low bioavailability of TPs components (Fig. 1A). Therefore, in the preparation of TPs products, the in-depth study of nano-delivery system can promote the TPs industry to break through the development bottleneck, which has far-reaching significance.

This review presents a review on the rapid development of extraction, purification, analytical and detection techniques and nano-delivery systems of TPs this year. The composition, biological activity, purification techniques and analytical methods of TPs are reviewed, and the advantages and disadvantages of various methods are compared and analyzed, with emphasis on the latest research progress of nano-delivery carriers and their applications in the purification and analysis of TPs.

## 2. Composition and properties of tea polyphenols

### 2.1. Composition of tea polyphenols

According to their different structures, they are mainly divided into catechins, anthocyanins, flavonoids, and phenolic acids. Among them, the highest content of catechin is the main component, accounting for about 60 %-80 % of TPs, which mainly affects the taste and color of tea, and is a key compound for tea products to promote human health. Catechins mainly consist of several monomers such as (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), (-)-epigallocatechin gallate (EGCG), and so forth (Yan et al., 2020) (Fig. 2A). Recent studies have shown that the modification of catechins can produce a variety of catechin derivatives (such as theaflavin, thearubigin, thearubin,) with greater potency and wider applications (H. Zhang et al., 2017).

### 2.2. Properties of tea polyphenols

#### 2.2.1. Physical properties of tea polyphenols

Pure TPs is a white crystalline substance with no fixed shape. Taste bitter and astringent, good heat and acid resistance, perishable, slightly hygroscopic, easy to oxidation in the humid air and appear light yellow to brown. Under normal temperature and dry environmental conditions, TPs is green or light yellow powder, it has several phenolic hydroxyl groups in its molecular structure, so it has a strong hydrophilic, easily soluble in water, but also soluble in methanol, glacial acetic acid, ethyl acetate and other organic solvents, slightly soluble in grease, very difficult to dissolve in benzene, chloroform, petroleum ether and other substances (Saric et al., 2016) only to extract high purity TPs, but also to

detect the content of TPs. Since the phenolic hydroxyl groups in TPs can be oxidized with oxidants in reduction reactions, they are highly susceptible to redox reactions in the presence of polyphenol.

#### 2.2.2. Chemical properties of tea polyphenols

TPs ionization can produce  $H^+$ , making the solution acidic. The pH of the extract is 5.7, and it is more stable at pH 4–8. The phenolic hydroxyl groups of TPs can react with amino acids of proteins to precipitate them (Xiong et al., 2020). Complexation with a variety of metal ions (such as  $Fe^{3+}$  and  $K^+$ ) produces precipitates or complexes of different colors. Under strong oxidizing conditions, their phenolic hydroxyl groups are oxidized, leading to the opening and oxidative degradation of benzene and alkane rings. Due to this property, the use of potassium permanganate titration can be used to detect the content of TPs.

## 3. Extraction and purification of tea polyphenols

Biopolymers tea polyphenols all need to be extracted and purified from tea leaves for further application into tea polyphenols nano-delivery systems. Commonly used extraction methods include microwave extraction method, ultrasonic extraction method, solvent extraction method, resin adsorption extraction method and enzyme extraction method. In recent years, many researchers have explored the optimal process conditions for the extraction of TPs (Table 1).

### 3.1. Extraction of tea polyphenols

The microwave extraction method is to use the target molecules in the microwave field can occur high-frequency motion, through the dipole rotation and ion conduction two ways of internal and external simultaneous heating, prompting the cell rupture, thereby increasing the diffusion rate of TPs and other substances, so that they are quickly and efficiently extracted. The ultrasonic extraction method uses the mechanical crushing and cavitation effect of ultrasonic waves to generate shock waves and shear force, which causes cell fragmentation, increases the diffusion rate of TPs, and shortens the extraction time.

Solvent extraction method is divided into water extraction method and organic solvent extraction method, which is the most commonly used traditional polyphenol extraction method. Using the difference in solubility of TPs in different solvents, TPs are first extracted from tea leaves with water, ethanol and other organic solvents, then chloroform is used to remove impurities, separated by ethyl acetate, and finally ethyl acetate is recovered to obtain crude TPs. Different concentrations of extraction solvents thus affect the extraction rate and extraction

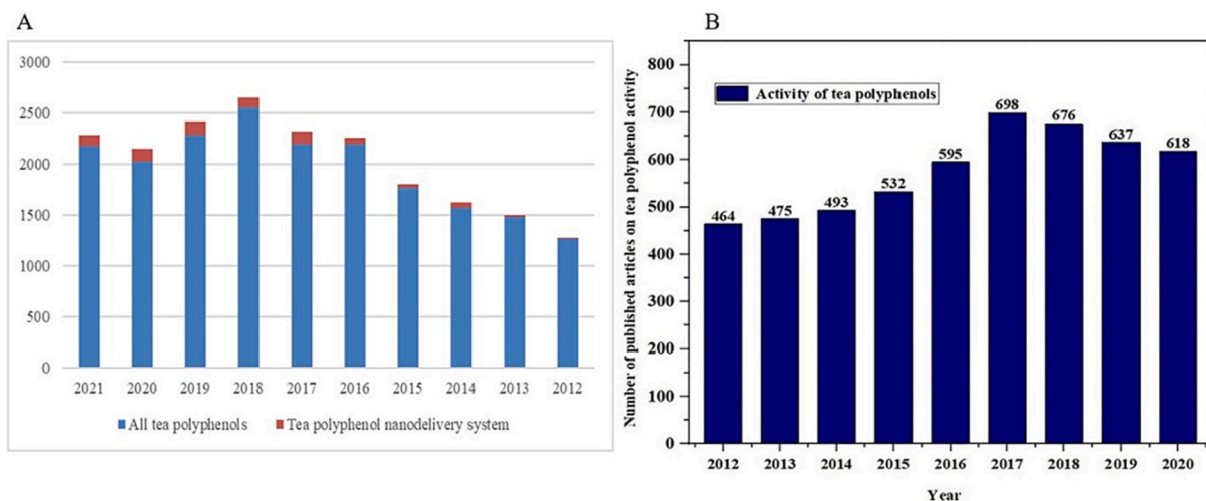


Fig. 1. (A) Trends in the number of articles on tea polyphenols and tea polyphenols nanodelivery systems from 2011 to 2021. (B) Graph of the number of published articles on tea polyphenols activity between 2012 and 2021 (data collected from the Web of Science).

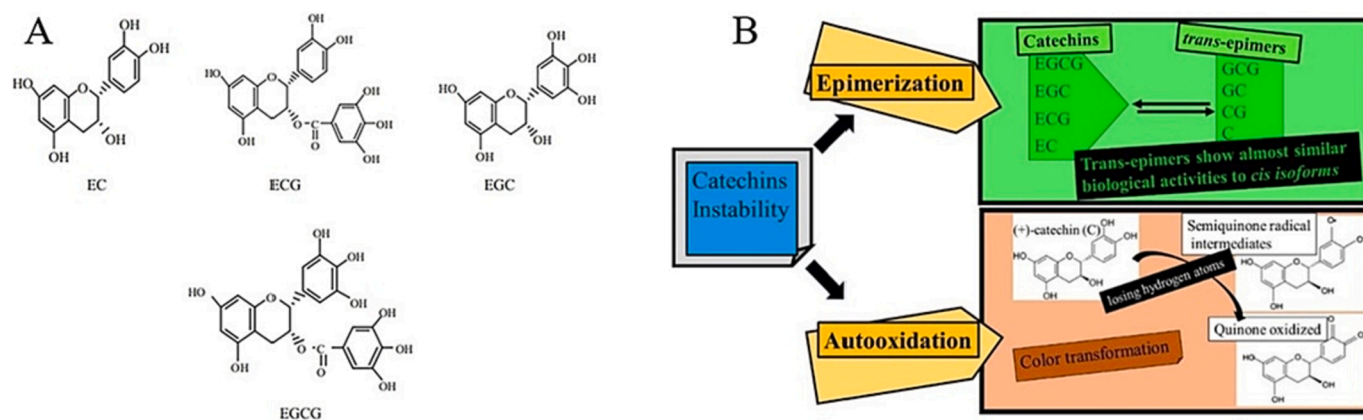


Fig. 2. (A) Structure diagram of main components of catechins (Puligundla et al. 2017). (B) Schematic diagram of the instability mechanism of catechins (A. Rashidinejad et al. 2021).

**Table 1**  
Application of tea polyphenols extraction methods.

Source	Extraction methods	Conditions	Identification/quantification methods	Major results	References
fresh green tea leaves	microwave extraction method	identifying temperature as the main influencing factor, using microwave heating to reach a system temperature of 65 °C, after 7.8 min, three extraction cycles and acetic acid (pH 4).	HPLC–UV	the extraction of EGCG and EGC was measured up to 95 %.	Ghasemzadeh-Mohammadi et al., 2017
green tea	microwave extraction method	the microwave intensity is 600 W, the microwave radiation time is 3 min, the number of microwave radiation is once, and the solid-to-liquid ratio is 1:20.	HPLC–UV	MAE is especially suitable for the extraction of tea polyphenols from green tea, among the four factors selected, the microwave irradiate time plays the largest role and the tea/water ratio plays the lowest role.	D. C. Li & Jiang, 2010
tea leaves	microwave extraction method	a kind of magnetic ionic liquid (C <sub>3</sub> MIMFeCl <sub>4</sub> ) was used as green medium for tea polyphenols, the solid–liquid ratio was 1:20, the microwave power was 200 W, and the extraction time was 7 min.	UV–Vis	the highest extraction efficiency of 0.8 mol/L C <sub>3</sub> MIMFeCl <sub>4</sub> could be obtained as 159.8 mg/g	Z. Guo et al., 2019
green tea	ultrasonic extraction method	the TPC value was 243 ± 7 mg, when the liquid-to-solid ratio was 36:1, the ultrasonic power was 461.5 W, and the ultrasonic time was 21 min.	HPLC	deep eutectic solvents (DESS) and ultrasound-assisted extraction method (UAE) is a good method for extracting antioxidant polyphenols from green tea with promising applications.	Luo et al., 2020
Pu'er tea	solvent extraction method	under four conditions of extraction temperature, extraction time, material-to-liquid ratio and different concentrations of ethanol aqueous solution.	HPLC	the highest extraction mass fraction of TPs was 13.86 % for aqueous ethanol solution, followed by distilled water at 9.67 % and anhydrous ethanol was the lowest at 5.49 %	Duan et al., 2013
green tea	Resin adsorption extraction method	followed by ultrafiltration with a CA-Ti composite ultrafiltration membrane, adsorption with PA resin.	HPLC	after adsorption on the resin and elution with mixed solvents, purified products containing more than 90 % TPs were obtained.	P. Li et al., 2005
green tea	Resin adsorption extraction method	–	HPLC	obtained EGCG products with 98 % concentration	Y. H. Gao et al., 2013
green tea	Enzyme extraction method	the optimum process parameters for enzymatic digestion were complex cellulase: pectinase: protease = 1:1:1, enzyme addition of 0.75 %, enzymatic digestion for 60 min at an enzymatic digestion temperature of 45 °C, tea to water ratio (m/v) of 1:12	HPLC	The average yield of the product was 26.23 %.	Geng et al., 2013

purity of TPs. It is better to choose glass containers for extraction and to prevent polyphenol hydrolysis, as well as rapid stirring. The resin adsorption extraction method uses resin to selectively adsorb TPs so that they can be separated from other components. According to different resin types, it can be divided into three methods, namely, gel column separation method, adsorption column separation method, an ion-exchange column separation method. The adsorbent is selected according to the quality requirement of the product, or different adsorbents can be mixed and used in columns according to the proportion. The resin adsorption method can be used together with new separation

techniques such as microfiltration, supercritical fluid extraction, and clarification techniques to improve the yield and purity of TPs. The enzyme extraction method utilizes the specificity and high efficiency of enzymes and selects the corresponding suitable enzymes to act on the plant cell wall components according to their composition to degrade them, thus separating the effective intracellular components. Enzyme extraction method is divided into two steps: enzymatic treatment and extraction of active ingredients. Enzyme extraction method mainly includes single enzyme digestion method and compound enzyme digestion method. The enzymes that can be used to extract TPs are cellulase,

pectinase, and papain. Selecting the right quantity of enzymes can soften the plant cell walls and promote the flow of active ingredients from the cells, thus extracting TPs gently and efficiently. If the enzymes are too much, they will complex with TPs and affect further extraction. The experimental conditions of this method are highly demanding, and the reaction conditions, substrate concentration, enzyme concentration, and other relevant factors need to be determined well.

### 3.2. Purification of tea polyphenols

Common purification methods include the resin adsorption method, membrane filtration method and ion precipitation method.

The resin adsorption method uses the different equilibrium partition coefficients of the components of the mixture in the stationary and mobile phases and uses macroporous adsorption resin, ion exchange resin, polyamide resin, etc. As adsorbents to selectively adsorb TPs to separate them from other components, and then elute them by eluent to obtain purified TPs. The key of this method is to select suitable fillers and eluents to obtain high purity TPs products.

Membrane filtration uses the concentration gradient or potential difference generated between the two sides of the membrane to further purify TPs by selectively permeating the membrane according to the difference in molecular weight, thus separating them from macromolecules such as proteins. The membrane filtration method includes microfiltration (Asad et al., 2021), ultrafiltration (Dan & Bird, 2010), nano-filtration (H. et al., 2021), reverse osmosis (Chong et al., 2021). The membrane filtration method does not cause damage to the TPs components, and the purified TPs have high biological activity. The process is simple, mild, safe, and non-polluting. However, the cost is high and the membrane is easily contaminated and its performance is reduced, so the application is limited at present.

TPs can be complexed with  $\text{Ca}^{2+}$ ,  $\text{Al}^{3+}$ , and other metal ions to form precipitates, and then dissolved with dilute sulfuric acid, can be replaced from the mixture, and then concentrated and dried to complete the purification of TPs. The extraction rate of TPs can reach 10–30 % and the purity can reach more than 96 % by ionic precipitation method (Cao et al., 2001). This method has low cost, a high extraction rate of TPs, and high purity and good color of the products obtained. However, TPs are easily oxidized during the preparation process, and the residual metal ions in the product can corrode the equipment and limit the process.

## 4. Construction of tea polyphenols nano-delivery system

In recent years, nanotechnology has been a rapidly developing field with high research intensity. With its advantages of small and controllable particle size, high specific surface area, high loading capacity, modification with functionalized surface, and high chemical and physical stability, it has been widely used in many fields such as chemical catalysis, gas storage, drug delivery, and chromatographic separation, and has made great progress. Some of its advantages provide the prerequisite for the construction of TPs nano-delivery systems, and high safety and excellent biocompatibility are important features of nano-carriers (Ahmadi et al., 2019). In order to improve the problems of poor stability and low bioavailability of TPs (Fig. 2B), and to achieve precise delivery of TPs by using nano-carriers as bioactive molecules while increasing the solubility as well as bioavailability of the complex, researchers embedded TPs and their components on the surface of nano-sorbent materials and used different modality strategies to develop and design efficient TPs nano-delivery systems.

The particle size applied to the TPs nano-carrier is usually between 1 and 200 nm to change the delivery of TPs with a stable nano-carrier structure to improve the solubility and chemical stability of TPs, while the TPs nano-delivery system has high thermal stability and mechanical properties, which makes TPs not affected by the external environment and enhances the antioxidant properties and antibacterial properties of TPs, making TPs in various fields with good application prospects.

Currently, common TPs nano-delivery systems include natural polymer nano-carriers, nano-liposomes, nano-emulsions, nano-particles, nano-capsules (Fig. 3A), which are mainly used for the nano-delivery of catechins in TPs. All systems have their own advantages and disadvantages (Table 2).

### 4.1. Natural polymer nano-carriers for the construction of tea polyphenols nano-delivery system

Natural polymer nano-carriers with good biocompatibility and biodegradability are regarded as ideal drug carriers and are an important research direction with great potential for development. At present, natural polymer nano-carriers commonly used for the preparation of TPs nano-delivery systems include proteins and polysaccharides.

Proteins are important molecular substances in living organisms composed of chains of amino acid units linked by complex and diverse structures, which are widely present in various organisms and play important functional properties. Proteins are excellent nano-carrier matrices, and their own existing three-dimensional spatial network structure is easy to load and encapsulate drugs, which can reversibly bind to EGCG, an important component of TPs, through hydrogen bonding and hydrophobic interactions, leading to structural and functional changes of proteins in the complex, thus affecting their emulsification and stability. Polysaccharides are monosaccharide polymers linked by glycosidic bonds, which are very widely available and also have a variety of physicochemical properties. Polysaccharides have many favorable properties at the same time, such as non-toxicity, low cost, hydrophilicity and availability of chemical modification reaction sites (Baldwin & Kiick, 2010; Freeman et al., 2015). The special biological bonding properties that allow them to adhere to biological tissues by hydrogen bonding, like proteins, can be used as a good carrier material for delivering substances such as TPs.

Currently, researchers have demonstrated that using protein as a carrier to encapsulate TPs. Wu (Wu et al., 2017) using the water-soluble protein  $\beta$ -lactoglobulin ( $\beta$ -LG), which complexes with EGCG to give EGCG a good anti-proliferative effect on some tumor cells, to encapsulate EGCG. Since EGCG has a greater affinity for heat-treated  $\beta$ -LG than for natural  $\beta$ -LG through hydrogen bonding and hydrophobic interactions with phenolic hydroxyl groups, the thermal modification of  $\beta$ -LG bound to EGCG, to form stable co-assembled nano-particles (E $\beta$ -NPs). The results showed the inhibitory effect of E $\beta$ -NPs on cell proliferation, the analysis of the induction of apoptosis of tumor cells by E $\beta$ -NPs compared with natural EGCG, and the elucidation of the anticancer effect and mechanism of action of this nano-formulation, and E $\beta$ -NPS can be used to enhance the chemopreventive effect of EGCG in functional foods.

Catechins are very sensitive to pH (alkaline) and high relative humidity (>65 %), which limits their application in food. Liu (Y. Liu et al., 2018) prepared a TPs nano-delivery system for breast cancer cell inhibition using chitosan nano-particles as TPs carriers loaded with epigallocatechin-3-O-gallate (EGCG), an important component of TPs, due to the excellent features of chitosan nano-particles such as good biocompatibility and biodegradability, and the ability to improve targeting, slow release of drugs, and enhanced drug absorption. The inhibition rate and biocompatibility were systematically characterized and comprehensively analyzed, and the results showed that the system improved the biocompatibility and stability of EGCG in vivo while avoiding the toxicity caused by high EGCG concentration, and the chitosan-EGCG nano-particles had an inhibitory effect on the growth of breast cancer cells, and the inhibition rate could reach 21.91 %.

The combination of polysaccharide and protein can also be used as a composite carrier of TPs. The interaction forces between the two biomolecules mainly include electrostatic interaction forces, covalent bonding, hydrogen bonding, ionic bonding, hydrophobic interaction forces and van der Waals forces. The two are combined by different forces, and then the synthesized complex surface is fine-tuned and self-

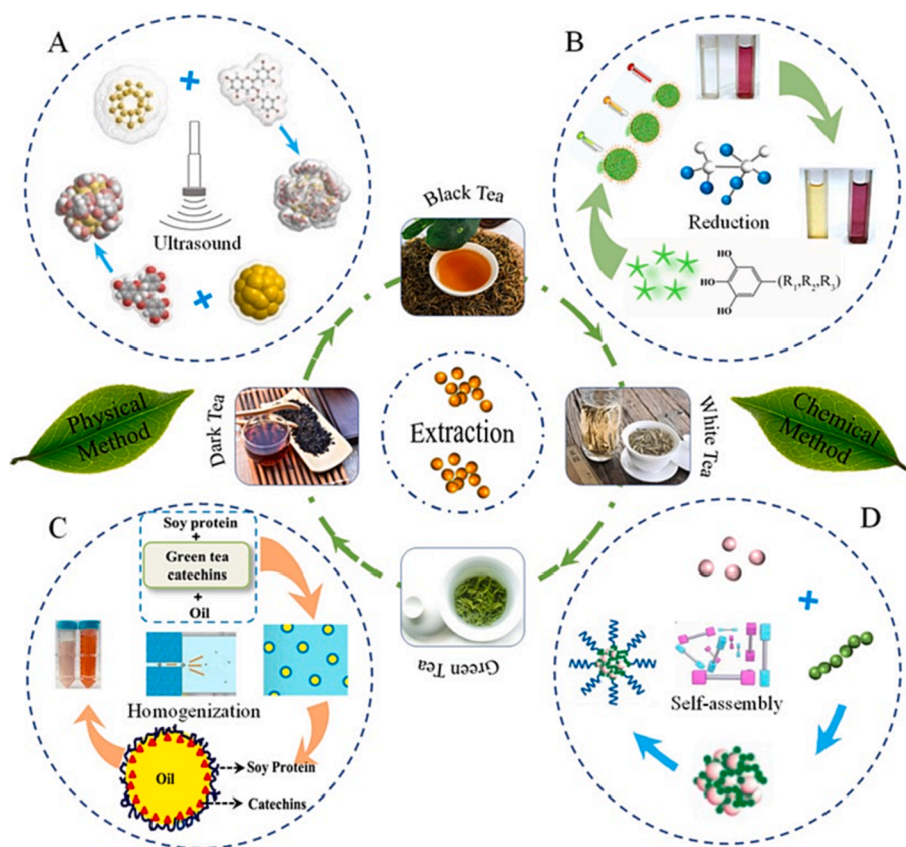


Fig. 3. (A) Schematic diagram of the structure of tea polyphenols nano-capsules shown by ultrasound (Hsieh et al., 2011). (B) Preparation process of Au nanoparticles of tea polyphenols (Qin et al., 2021). (C) Homogenization process of tea polyphenols nano-liposomes (Peng et al., 2018). (D) Self-assembly process of tea polyphenols nano-particles (Chung et al., 2014).

assembled to obtain polysaccharide-protein composite nano-carriers, which strengthen the interaction forces with the loaded TPs and make the composite structure with higher physicochemical properties and thermal stability, and not easy to be decomposed in the complex external environment in order to further improve the bioavailability of TPs.

Lin (Lin et al., 2015) using protein (lysozyme) and polysaccharide (pectin) gel properties, higher viscosity, plasticity and stronger water binding ability, the TPs delivery system was constructed based on the model of lysozyme and pectin. Lysozyme-pectin was prepared as nanoparticles by self-assembly, and the effects of different pH, protein and polysaccharide mass ratios, ionic strength and temperature on the lysozyme and pectin complexes were determined by measuring turbidity, zeta potential and microstructure simultaneously. The results showed that EGCG loaded with lysozyme and pectin nano-composite carriers had better stability and significantly slower degradation rate than free EGCG. Liang (Liang et al., 2017) prepared maize alcohol-soluble protein-coated chitosan nano-particles (CSNPS) as an EGCG encapsulation and delivery system with greater potential. This study systematically compared the effects of different reaction parameters on nano-composite carriers, such as the concentration of maize alcoholic protein, the concentration and encapsulation rate of EGCE, the molar mass ratio of maize alcoholic protein to chitosan, and by physicochemical and structural characterization. The results showed that electrostatic interactions and hydrogen bonding were the main forces of this nano-composite carrier, and the synthesized nano-composite carrier was spherical with smooth surface, and the corn alcohol soluble protein-chitosan coating significantly improved the controlled release performance and corresponding antioxidant activity of EGCG under 50 % and 95 % ethanol conditions, indicating that ZEIN/CSNPS is a novel thin film encapsulation material in food and medical applications.

#### 4.2. Tea polyphenols nano-liposome

Nano-liposome is a microscopic bimolecular delivery system composed of phospholipids and cholesterol in aqueous solution, which not only can wrap lipid bilayer and hydrophilic substances in the intermediate hydrophilic cavity and can control the delivery of hydrophilic and hydrophobic compounds, thus reducing the hazard of active substances in the environment, increasing the solubility of TPs, improving the utilization of TPs components, etc., but also can well control the release rate of TPs components, and compared with other nano-delivery systems, nano-liposome has the advantages of easy degradation, weaker immunity, lower toxicity and increased active compounds.

Nano-liposome have special physicochemical properties, so the loading properties of the material can be increased by adding surface functional groups. Istenic (Istenic et al., 2016) used a liposome precursor method in which EGCG was added directly to a mixture of lipids and ethanol, followed by the dropwise addition of a small amount of citric acid solution to the mixture to induce the formation of liposomes (Fig. 4A). EGCG was encapsulated in nano-liposomes, a delivery system that is more stable under acidic conditions, and subsequently the nano-liposomes were combined with alginate and chitosan particles, three nano-liposome encapsulation systems were prepared, namely, nano-liposomes, alginate nano-liposomes, and chitosan nano-liposomes for encapsulating EGCG. The experimental results showed that all three encapsulation systems had high encapsulation efficiency (>97 %) and slow release effect, and could mitigate the degradation of EGCG to make it have high stability performance, and EGCG-loaded nano-liposomes as well as alginate and chitosan particles containing EGCG nano-liposomes had the ability to stabilize EGCG. Ahmadi (Ahmadi et al., 2022) to improve the insolubility of white TPs and some special odors that limit

**Table 2**  
Comparison of advantages and disadvantages of tea polyphenols nano-delivery carriers.

Tea polyphenols nano-delivery system	Advantages	Disadvantages	References
Natural polymer nano-carriers for the construction of tea polyphenols nano-delivery system	It has advantages such as green, high efficiency, good sustainability, biocompatibility and biodegradability as bio-based nano-carrier. Due to its own three-dimensional spatial structure, it is easy to load and encapsulate medicines, and is less harmful to the application environment as a tea polyphenols delivery carrier, which is more widely used in the healthcare field.	The complex structure of natural polymer monomers usually requires suitable and efficient polymerization techniques.	Wu et al., 2017; L. Lin et al., 2015
Tea polyphenols nano-liposomes	It can be completely biodegraded with no residue and low toxicity, reducing the hazard of active substances in the environment and increasing the solubility of tea polyphenols.	There were some slight side effects and the encapsulation rate of tea polyphenols was not very homogeneous.	Istenic et al., 2016
Tea polyphenols nano-emulsions	The smaller particle size can improve the solubility of tea polyphenols nano-emulsions, reduce the enzymatic digestion of tea polyphenols in the body and make it easy to be absorbed. It has high thermal stability and high bioavailability.	This nano-carrier has poor mechanical strength and stability, and requires high fabrication cost and emulsification process.	Meng et al., 2019
Tea polyphenols nano-particles	This nano-carrier has a wide variety of synthetic templates, therefore its shape and particle size can be easily controlled in the synthesis.	The reactants and synthetic materials are organic substances, which are potentially dangerous. Metal nano-particles can cause cell membrane damage and disrupt the permeability of cell membranes during the application process.	Wang et al., 2018
Tea polyphenols nano-capsules	With larger cavities and higher surface area, the loading rate of tea polyphenols has a greater advantage compared with other carriers. The nano-carrier has excellent mechanical strength and durability, so it is not easy to be destroyed and decomposed during the application. Smaller size, easy to penetrate various cell	The complete shell structure and closed structure of nano-capsules cause high mass transfer resistance, so the application process of tea polyphenols nano-capsules is often accompanied by disadvantages such as incomplete release of active ingredients. Poor structural stability, low	Ho et al., 2017  Tian et al., 2021

**Table 2 (continued)**

Tea polyphenols nano-delivery system	Advantages	Disadvantages	References
Tea polyphenols hydrogel nano-delivery system	membranes of the human body, and easy to be engulfed by cells, so that the load of tea polyphenols in vivo utilization rate is high, the decomposition will not cause harm to the human body.	strength, poor toughness.	

the application of white TPs, researchers prepared TPs nano-liposomes to increase the bioavailability and stability of TPs, to protect them from degradation by internal and external factors and to retard chemical reactions. The extraction conditions of polyphenols in white tea were optimized, and the effects of liposomes on the encapsulation of white TPs were explored by optimizing different ratios of phospholipids and cholesterol as wall materials encapsulated in nano-liposomes, and the liposome particle characteristics, encapsulation efficiency, morphology, interaction and thermal properties were analyzed. The results showed that the encapsulation rate of white TPs by nano-liposomes was high and there was interaction between them, and the stability of white TPs was enhanced by nano-liposomes, so the application of nano-liposomes for loading white TPs has good prospects.

Nano-liposomes prepared using different preparation methods and different types of phospholipids have different encapsulation abilities for TPs. Gülseren (Gülseren et al. 2012) compared the functional properties of TPs nano-liposomes prepared from soybean phospholipids and milk phospholipids, and prepared spherical liposome dispersions by high-pressure homogenization to investigate their physical properties as well as the encapsulation ability of TPs. The results showed that the TPs nano-liposomes prepared using lactic acid phospholipids exhibited stronger encapsulation capacity (58 %) and physicochemical stability compared with soybean liposomes, which may be related to the higher phospholipid content of lactic acid phospholipids and the characteristic structure of spherical liposomes, which are less susceptible to environmental cleavage and exhibit efficient polyphenol delivery. Therefore, the nano-liposomes prepared from lactic acid phospholipids by high-pressure homogenization method can be widely used as carriers for TPs nano-delivery systems.

Lu (Lu et al., 2011) prepared TPs nano-liposomes by ultrasonic film dispersion method to prevent the decomposition of TPs due to their high sensitivity to oxygen and light, which reduces the stability of TPs and thus limits their application. The preparation method and process conditions of TPs nano-liposomes were optimized, in which the ratio of liposome composition phospholipid to cholesterol was 4:1, the ratio of loaded TPs to phospholipid was 0.125:1, PBS pH 6.62, and the average particle size of TPs was 160.4 nm. The encapsulation rate of TPs by nano-liposomes prepared by dispersion method using ultrasonic thin film method was 60.09 %, therefore, this method is an efficient method to prepare nano-liposomes, which has a greater advantage to increase the loading efficiency, oxidation performance, stability performance and prolong the storage time of TPs, and has a wide application prospect.

Zou (Zou et al., 2014) compared the effects of two TPs nano-liposome preparation methods on the encapsulation rate of TPs, for studying the stability and release characteristics of TPs in alkaline media, preparation of green TPs nano-liposomes (TPN) by combining injection of ethanol with dynamic high-pressure microfluidization (DHPM) under mild conditions. Purified TPN (40 mg/mL phospholipid) was extracted at a pressure of 120 MPa with one cycle. Compared with the original solution of TPs, its antioxidant properties and ability to scavenge free radicals

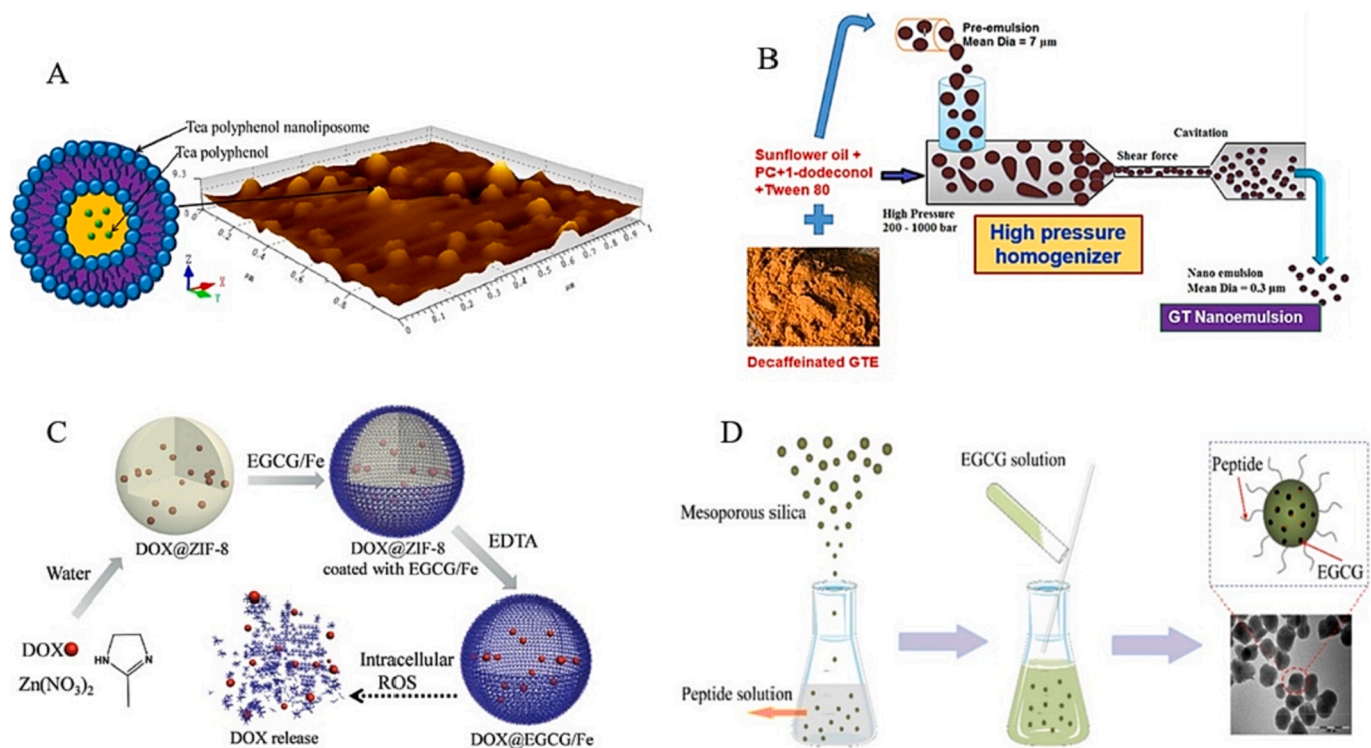


Fig. 4. (A) AFM micrograph of tea polyphenols nano-liposome (Zou et al., 2014). (B) Diagram of synthesis of nano-emulsion (Gadkari et al., 2017). (C) Diagram of synthesis of DOX@ZIF-8@EGCE (Wang et al., 2018). (D) The loading of EGCG into nanoparticle carriers functionalized with the hollow shell structure (Ding et al., 2015)

DPPH were not diminished, and TPN had good physicochemical properties with an encapsulation rate of 78.5 %, it was higher than the encapsulation rate of the nano-liposomes prepared using high-pressure homogenization method and ultrasonic film method, and had better stability and slow release performance under alkaline conditions, releasing only 29.8 % of TPs after 24 h. The system maintained the activity of TPs for a significantly longer time, which provided theoretical and practical guidance for the further application of TPs nano-liposomes.

Liposomes have the potential to become drug carriers due to their good entrapment ability, biocompatibility, and safety. Current experiments on parenteral liposome delivery are successful, but in practice, oral delivery of liposomes needs to be hindered by various barriers, such as instability in the gastrointestinal tract, difficulties in cross biofilm, and mass production (H. He et al., 2019). The development of oral liposomal delivery of drugs is still at a bottleneck due to the lack of understanding of gastrointestinal absorption mechanisms. Recently, several researchers are investigating improving oral drug delivery stability and liposome stability, and permeability by modulating the lipid bilayer and adding combinations of polymers or ligands. In conclusion, the practical application of nano-liposome delivery systems still faces great challenges.

#### 4.3. Tea polyphenols nano-emulsions

Nano-emulsions are transparent or translucent dispersions composed of the oil phase, water phase, surfactant, and co-surfactant (Fig. 3C), which not only improve the stability and bioavailability of active substances but also have sustained release and targeting effects (Dai et al., 2020).

Meng (Meng et al., 2019) to improve the instability of TPs and  $\beta$ -carotene, as well as their low bioavailability when taken orally, which limits their application, prepared TPs- $\beta$ -carotene water-in-oil (W/O) nano-emulsions consisting of TPs- $\beta$ -carotene (TP-BC) as the core oil

phase and TPs as the aqueous phase using a nano-emulsifier to stabilize the oil-water interface in the environment to mitigate the environmental adverse effects on TPs and  $\beta$ -carotene, can scavenge free radicals in food and prevent the oxidation of unsaturated fatty acids, while TPs can also act as an antioxidant to protect  $\beta$ -carotene from degradation, which can be of great help in developing functional nutritional supplements.

Gadkari (Gadkari et al., 2017) Researchers prepared green tea nano-emulsions using high pressure homogenization (HPH) technology with 1-dodecanol as the carrier material to improve the physicochemical stability of catechins and improve the release characteristics of TPs from green tea components for effective utilization of TPs (Fig. 4B). The results showed that the stability of the nano-emulsions varied under different environmental stresses (different pH, temperature, and salt concentration in the environment), and the high temperature short time heat treatment had less effect on the chemical composition changes, droplet diameter, and peritectic structure of the nano-emulsions compared to the low temperature long time heat treatment, and when the homogenization pressure was 60 MPa and four cycles and 1 %, (w/v) Tween 80 concentration, the emulsion particle size was the smallest and the encapsulation efficiency was the highest, 0.280 mm and 83.16 %, respectively. From FT-IR showed no chemical interaction between the carrier and the encapsulated catechins, and when the emulsion was released in vitro under gastrointestinal simulated conditions, the emulsion composition followed a trend of slow and continuous release of catechins, which provides an idea for the nutrition industry to expand the production and commercialization of catechin emulsions. Peng (Peng et al., 2018) prepared TPs nano-emulsions by emulsifying TPs with corn oil and polysorbate 80 using a high-pressure homogeneous emulsification method. The particle size of the prepared oil-in-water TP nano-emulsion droplets was 99.42 nm, and the stability of this nano-emulsion was good. In vitro simulated digestion experiments showed that by comparing rats fed with aqueous TPs solution with rats fed with TPs nano-emulsion, the maximum plasma concentrations of EGCG and EGC in vivo were significantly reduced, but the area of the plasma

concentration curve increased, indicating that the use of nano-emulsion delivery system was able to improve the absorption of EGCG in rats by controlled release of TPs, and the use of TPs nano-emulsion delivery systems has gained importance in the food and nutrition industry.

#### 4.4. Tea polyphenols nano-particles

Nano-particles are formed by the process of covalent and non-covalent assembly of monomers, which have large porosity, high specific surface area, low effective density and large internal cavities, and are widely used in drug delivery and energy storage (H. Zhang et al., 2017). Nano-particles are often prepared by the sacrificial template method, and the corresponding nano-particles are synthesized by the controlled deposition of particle monomers on the template surface (Fig. 3D), and their shape and diameter can be directly controlled during the synthesis process, so the synthesized carriers have functional specificity. Therefore, tea polyphenols nano-particles have a very wide application prospect as antioxidants. Chen (G. Chen et al., 2021) prepared tea polyphenols nano-particles based on nano-hollow nano-particles by increasing the inner surface and cavity volume, mainly using cationic polymers with metal ions self-assembled to form bowl-shaped structure of tea polyphenols nano-particles with strong free radical scavenging ability, anticancer activity, high adsorption to guest molecules and pH-dependent release properties. The novel bowl-shaped structure and its formation mechanism have the potential to stimulate other innovative methods for the preparation of nano-particles with specific structures, providing ideas for the study of tea polyphenols nano-carriers.

Metal nano-particles due to their unique properties have potential applications in catalysis, pharmaceuticals, however, metal nano-particles exist synthetic materials are toxic and disrupt cell membrane permeability, so their properties are improved by combining metal nano-particles with bio-based molecules, Begum (Begum et al., 2009) prepared tea polyphenols Au nano-particles and Ag nano-particles from black tea extract tea polyphenols (Fig. 3B), tea polyphenols by reducing metal ions subsequently form metal nano-particles with rapid synthesis and structural stability, which can improve the potential hazards of metal nano-particles in applications.

#### 4.5. Tea polyphenols nano-capsules

In recent years, nano-capsules have been playing an important role in exploring new drug and technology applications and drug delivery due to their renewable material content. The high biocompatibility, biodegradability and special physicochemical properties of polymeric materials, which can be completely degraded to carbon dioxide and water or some water-soluble molecular groups in vivo without causing toxicity to the organism, are widely used in biomedical fields by polymerizing to form polymeric nano-particles to encapsulate drugs. Common wall polymers include  $\beta$ -cyclodextrin, chitosan, and so on.

Ho (Ho et al., 2017) in order to improve the disadvantages of catechin, the main component of antioxidant TPs, which is slightly soluble in water and sensitive to oxygen, light and pH, catechin nano-capsule inclusion compounds were prepared by hybrid coating method, and catechin nano-capsules were prepared with catechin as the core material and  $\beta$ -cyclodextrin as the wall material to improve their application in food. The results showed that the specific morphology of the TPs nano-capsules depended on the structural arrangement of different polymer materials. Under the conditions of different environmental and physiological parameters, the  $\beta$ -cyclodextrin nano-capsules had strong stability in common food mechanisms due to the special structure of the encapsulated catechins, and the highest antioxidant retention in low concentration oil, sugar or protein models with significantly lower degradation rates. This suggests that encapsulation of catechins with  $\beta$ -cyclodextrin can be further applied to functional foods.

Wang (Wang et al., 2018) reactive oxygen species (ROS)-responsive

biodegradable nano-capsules were investigated for efficient delivery of EGCG by encapsulating green TPs (EGCG) in a metal-organic backbone ZIF-8 using a metal network as the basic framework (Fig. 4C). DOX-doped ZIF-8 nano-particles were synthesized by co-precipitation method to be suspended in aqueous solutions of EGCG and ferric chloride under mild conditions with the template ZIF-8 was coated with a layer of EGCG-Fe (III) complex, and when the template was removed a new DOX-encapsulated EGCG-Fe (III) nano-capsule (DOX@EGCG/Fe-NCs) with a diameter of 399 nm was obtained. The results showed that the prepared DOX@EGCG/Fe-NCs could be used to inhibit tumor cell growth and reduce ROS during the degradation process EGCG/Fe-NCs are expected to be efficient nano-carriers for cancer treatment because of their low toxicity, low side effects and good biocompatibility.

The main purpose of nano-capsule encapsulation of drugs is to protect the drug, increase its stability, prolong its life and enable controlled release of the drug, however, the different types of various wall materials and different encapsulation methods lead to different encapsulation efficiency and protection ability of the drug, therefore, when the preparation of TPs nano-capsules is carried out, suitable polymer materials should be selected according to the actual use of TPs.

#### 4.6. Tea polyphenols hydrogel nano-delivery system

Nanogel, whose main body is hydrogel, is a cross-linked hydrophilic polymer that can adsorb and store large amounts of delivered drugs while maintaining a three-dimensional mesh structure. The development of hydrogel from large gel, then to microgel, and finally to nanogel, the characteristic advantages are gradually shown, generally the particle size of nanogel is usually less than 200 nm, its size is smaller, when used for human delivery of drugs such as TPs, it is easy to be engulfed by cells, easy to penetrate various protective membranes of human body, such as brain membrane, so as to achieve brain drug delivery, and nanogel compared to other nano-delivery carriers it has the characteristics of high drug-carrying efficiency and does not cause harm to the release environment after decomposition.

Hu (Hu et al., 2020) developed a novel self-assembly of the food polysaccharide salicylic acid and N,N,N-trimethyl chitosan to form TPs nanogels, which effectively encapsulated green TPs into the nano-polysaccharide hydrogels and released them in a sustained mode. The results showed that electrostatic interaction was the driving force for the complexation process between the two polysaccharides and the ratio of the two polysaccharides had a significant effect on the swelling behavior and morphological characteristics of the hydrogel, and the nano-carrier with a maximum pore size of 55  $\mu$ m could reach a cumulative release of 94.5 % of TPs within 8 h. Biodegradation studies showed that this polysaccharide hydrogel carrier can be well degraded in the presence of lysozyme, with good biocompatibility, antibacterial activity and biological bonding activity, which is expected to be a promising system for the preparation of TPs hydrogels for food engineering applications.

Tian (Tian et al., 2021) in order to improve the stability and retention of TPs, hydrogel carriers encapsulating TPs were prepared to increase the bioavailability of TPs by slow release of TPs into the potential gel mixture. Different ratios of the composite hydrogels were compared and it was found that the slowest release was achieved when xanthan gum (XG)/lacustrine bean gum (LBG) was released at a ratio of 6:4. TPPs were encapsulated in water-in-oil (W/O) emulsions containing XG/LBG blends, and the effects of emulsifier concentration and XG/LBG blends (6:4) on the stability of W/O emulsions were investigated. The results showed that the concentrations of emulsifier and XG/LBG had a large effect on the appearance and stability of W/O emulsions. As the emulsifier concentration increased, the droplet size of the emulsion decreased, while the stability increased. TPPs were encapsulated in W/O emulsions containing XG/LBG mixtures and the retention of TPPs exceeded 70 % after storage at 25°C for 30 days.

Polymeric TPs nanohydrogels have a wide range of applications in biomedicine, tissue engineering and other fields due to their unique



structural characteristics and physicochemical properties.

## 5. Application of tea polyphenols

The production and sale of tea beverages and their functional active ingredients TPs have a history of more than ten years at home and abroad. Tea culture in China has a long history, and the rich tea resources provide a solid material basis for the wide application of TPs, which have been proven to have a variety of biological and pharmacological activities, TPs can be widely used in food preparation, pharmaceutical industry and functional health products and other fields, and are more widely used in life and industry. Based on the excellent biological activity and non-toxic, non-side effects of TPs, the nano-delivery carrier gives it excellent performance, improving the poor water solubility, low bioavailability, low in vivo absorption rate and low in vitro instability of TPs, and making it have the characteristics of targeted transport and controlled release of TPs, achieving the precise release of TPs, extending the aging period of TPs, and lifting the limitations of TPs in practical applications. The practical application of TPs is limited.

### 5.1. Biological activities of tea polyphenols

TPs are a kind of TPs are an ideal natural antioxidant to maintain the dynamic balance of free radicals by activating the intracellular antioxidant defense system (Fig. 1B), and their active phenolic hydroxyl groups can directly scavenge reactive oxygen radicals, prevent the proliferation and expansion of lipid radicals in the body, and inhibit lipid peroxidation due to the main chemical structure of TPs is 2-benzopyran derivatives, which contain o-phenol group can provide active hydrogen generation More stable phenolic radicals to scavenge ROS and free radicals ( $O_2^-$ ,  $-OH$ ), making the antioxidant properties of TPs much higher than those of other antioxidants (Rothenberg et al., 2018). In vivo experiments showed that TPs could increase serum catalase (CAT), glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) levels and decrease malondialdehyde (MDA) production in rats, and these findings revealed that TPs regulate the redox enzyme system and improve the antioxidant capacity of the body. Guo (Guo et al., 1996) compared the protective effects of four major catechin analogs against iron-induced lipid peroxidation in synaptosomes, with antioxidant efficiencies in the order of EGCG > ECG > EGC > EC. Other researchers (F. J. Lin et al., 2021) have found that black tea has great potential for antioxidant research as a functional ingredient or packaging material in foods. Its bioactive compounds (such as flavonoids, theaflavins, phenolic compounds and polysaccharides) possess strong antioxidant activity, increase the activity of antioxidant enzymes and modulate the Nrf2 pathway.

A multinational study on the pathological analysis of TPs has shown that tea consumption can reduce the incidence of cardiovascular diseases (Kobalka et al., 2015), and that TPs in green tea can convert blood pressure-related enzymatic activities, thus playing a role in unblocking blood flow and lowering blood pressure, helping to alleviate and prevent the effects of atherosclerosis on human health. played a key role in stabilizing blood pressure by improving the function of the body's blood vessels. Kuriyama (Kuriyama et al., 2006) study found that TPs can reduce the number of tumor formation, but also effectively block the synthesis of carcinogens such as nitrites in the body, with the effect of directly killing cancer cells and enhancing immunity, inhibiting the occurrence of various carcinogens. EGCG treatment lies in the activation of cell death signals and induction of apoptosis of cancer cells without affecting normal cells, thereby inhibiting cancer. TPs are antioxidant-based, induce detoxification system, have strong scavenging effect on reactive oxygen radicals, thus protecting DNA from oxidative damage and preventing tumorigenesis (Gao et al., 2022), with anti-tumor and anti-mutagenic effects, they also inhibit self-renewal, proliferation and survival of tumor initiating populations, thus limiting the carcinogenic process during cancer initiation and promotion, which is related to the

regulation of membrane tissue (Bimonte et al., 2020). TPs promote the hydrolysis of fatty acids and fats, reduce the accumulation of cholesterol and triglycerides, and also inhibit the activity of sucrase and amylase, reducing the digestion and absorption of carbohydrates by the body and blocking their conversion into fat, thus providing weight loss. In addition, TPs aim to improve the aging process in the brain and are considered epidemiologically controllable therapeutic agents that may play a role as neuroprotective agents in progressive neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease (Fernando et al., 2017; Weinreb et al., 2004).

TPs have antibacterial properties, which can improve immune performance by increasing the activity and quantity of immunoglobulins in the body and inducing changes in the activity of antibodies, An (An et al., 2004) found through experiments that green tea aqueous extract and its main functional factor, TPs, can inhibit the growth and reproduction of microorganisms such as *Staphylococcus* spp. and *Streptococcus* spp. 50 %-100 %, thus improving the immune performance of the human body. TPs also have good antiviral properties against a variety of viruses, such as common influenza virus, hepatitis B virus, Zhou (Z. D. Zhou et al., 2019a) experiments have shown that TPs can significantly inhibit endogenous dopamine (DA)-related toxicity, thereby protecting DA neurons, while TPs with more phenolic hydroxyl groups and a ring structure have stronger protective functions, and the evidence that phenolic hydroxyl groups can directly bind to DAQ further enhances the protective function of TPs.

TPs can prevent and control allergic reactions and inflammation caused by having allergic reactions. Chinese researchers found that black tea has the effect of preventing and treating asthma, and foreign researchers have also reported a lot on this property of TPs. Pajank (Pajank et al., 2006) found that TPs, the main active ingredient in the aqueous extract of green tea, has an inhibitory effect on proteases in vivo, thus playing a role in inhibiting inflammation and preventing allergic reactions. Chen (P. C. Chen et al., 2002) experimentally demonstrated that TPs can block the internal 1L-21 $\beta$  signaling pathway and keep the signaling factor secretion, thus preventing the inflammation caused by allergies.

TPs have a strong adsorption capacity for heavy metals at the same time, where catechol chelates metal ions and combines to form metal complexes to precipitate and affect the oxidation process, which can help reduce the toxicity of heavy metals in the body (Khan & Mukhtar, 2007). As a water-soluble substance, TPs also have cosmetic, pore-shrinking and anti-aging effects. In addition, TPs are known as "ultra-violet filters", interacting with target molecules to improve the resistance of DNA molecules to radiation and reduce the degree of radiation-induced cell transformation in vitro, thus providing protection. TPs have been used as the main ingredient to produce anti-radiation oral tablets with antioxidant effect, safe and convenient for astronauts to take to enhance immunity and improve the radiation of the human body from space effect (Khan et al., 2007).

### 5.2. Application of tea polyphenols delivery system

#### 5.2.1. Application of tea polyphenols nano-delivery system in healthcare field

TPs are widely used in healthcare applications because of their biological activity as antitumor drugs, cardiovascular health drugs, antiviral agents, etc. However, TPs have the disadvantages of low biological activity, short duration of anticancer effect and low utilization rate. In recent years, nanotechnology has been widely used in the field of health care, and nano-delivery carriers have the characteristics of small particle size, large specific surface area, strong adhesion, targeted transport and controlled release. The application of TPs nano-delivery system for cancer treatment provides a new solution to improve the bioavailability, anti-cancer activity and anti-cancer efficacy of TPs.

Chu (Chu et al., 2019) investigated a variety of natural compounds with potential applications for developing anticancer treatments, often

limited by instability and low tissue distribution. Among them, the combination of EGCG and curcumin (CU) could improve the efficacy and have a synergistic effect, and a targeted nano-particle delivery system consisting of hyaluronic acid, rockwool and polyethylene glycol-gelatin was used to deliver EGCG and CU in order to improve the synergistic effect of the combination of the two compounds in order to improve the limitation of uneven tumor distribution and to improve the synergistic effect of the two compounds. The effects and efficacy were observed in prostate cancer cells and in situ prostate tumor models, respectively. The results showed that the EGCG/CU nanocomplex was regulated by Ph and played a slow-release role to avoid the rapid release of teicoplanin, which was absorbed by more cells and had a better anti-cancer effect, and the synergistic effect of EGCG/CU nano-delivery system in tumor treatment was greatly improved, which has a greater potential for application in prostate cancer treatment. Ding (Ding et al., 2015) developed an extracted anticancer drug without side effects by exploiting the anticancer effect of EGCG, a major component of green tea, and by combining the colloidal mesoporous silica (CMS) with a mammary tumor-seeking cell-penetrating peptide, a drug delivery system loaded with EGCG, CMS@peptide@EGCG (Fig. 4D, Fig. 5A), was successfully prepared, and the in vivo treatment of the complex on cancerous mice showed that the mammary tumors were significantly smaller and the tumor suppression rate reached. The in vivo treatment of cancerous mice with this complex showed that the mammary tumors were significantly smaller and the tumor suppression rate reached 89.66 % without significant damage to other organs in the body, thus proving that EGCG is a highly effective anti-cancer drug without side effects.

Hong (Hong et al., 2014) prepared CS/PAA nano-particles for loading catechins, which enhanced the stability of catechin EGCG in the gastrointestinal tract and significantly enhanced the oral anti-

atherosclerotic effect in rabbits by reducing serum triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol levels (Fig. 5B). Zhang (J. Zhang et al., 2013) used EGCG/CS nano-liposomes, which significantly enhanced the stability of EGCG at pH 7.4, increased the sustained release of EGCG in macrophages and EGCG content, enhanced the anti-atherosclerotic activity of EGCG by reducing the cholesterol ester content in macrophages, and significantly inhibited the secretion of inflammatory factors.

The nanocarrier-encapsulated TPs have the ability to target transport to tumor cells and other cancerous cells for precise release of TPs, and in addition, it has been reported that this nano-delivery carrier for targeted transport of TPs can effectively improve the accumulation of TPs in cancerous cells, which is due to the fact that the nano-carrier can be internalized into cancerous cells through receptor-mediated endocytosis, avoiding higher load spillover phenomenon (Jiang et al., 2021).

Currently, TPs nano-delivery systems have been used for the production of various health drugs, such as weight loss drugs, cardiovascular health drugs, and drugs for the prevention of hyperlipidemia and hypertension.

### 5.2.2. Application of tea polyphenols nano-particle delivery system in food industry

The application of TPs in the food industry is limited by the sensitivity of TPs to temperature, light, pH, oxygen and other factors, due to the harsh environment of the gastrointestinal tract, the low permeability of the normal mode, only a small portion of ingested TPs are absorbed, in order to overcome these obstacles, the application of TPs nanotechnology in food industry (Feng et al., 2019). In the application in the food industry, the nanomaterials encapsulating TPs generally need to meet food grade requirements, and they are divided into two categories

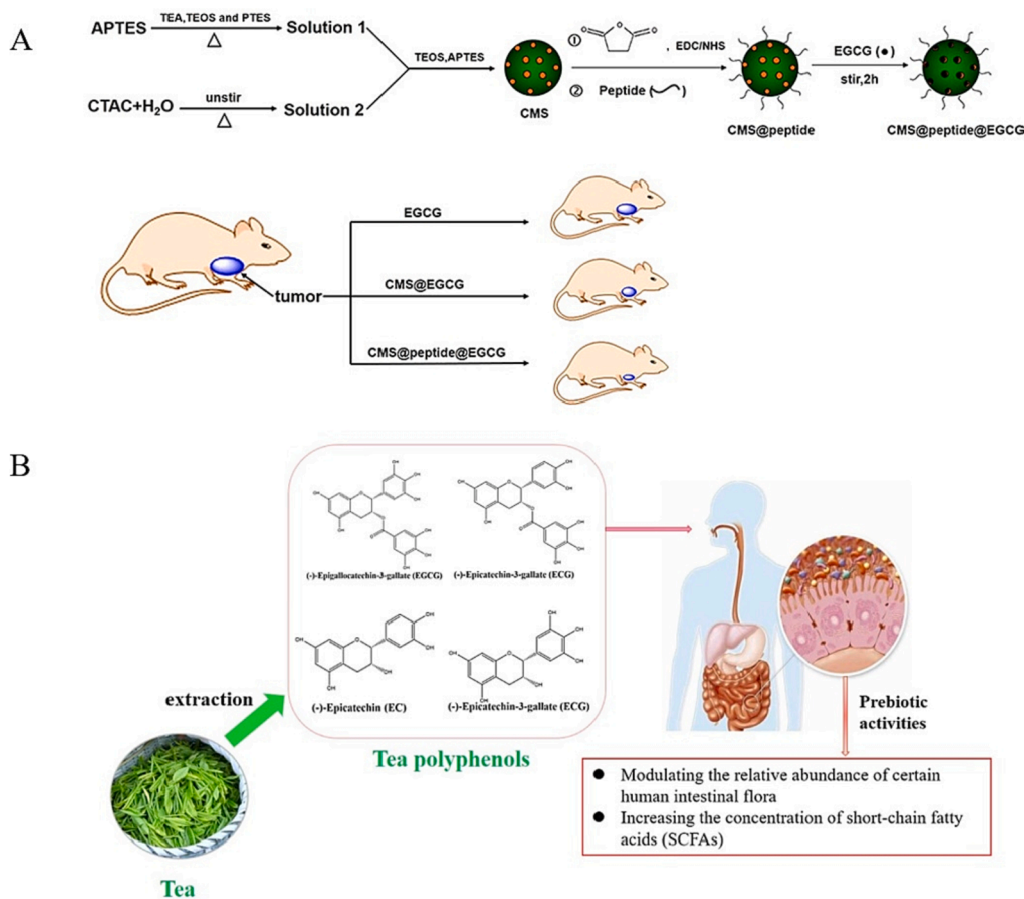


Fig. 5. (A) Schematic diagram of the synthesis and in vivo experiments of CMS@peptide@EGCG (Ding et al., 2015). (B) Tea polyphenols have shown potential health benefits in the gut (Yin et al. 2020).

according to their molecular weight, phospholipid nano-carriers for small molecules and polysaccharide protein polymer carriers for large molecules (Gómez-Mascaraque et al., 2017). TPs nano-delivery systems are not only used as antioxidants, deodorants, etc., but also used in making various dairy products, bakery products (Izza et al., 2022). To improve the biological activity of TPs, improve food quality, improve the bioavailability efficiency of TPs, stability of active compounds, in order to realize the functionalization of TPs food.

It (Rashidinejad et al., 2016) was shown that the main active substance of TPs, catechin, was combined with phospholipid-based nano-delivery carrier nano-liposomes to form TPs nano-liposomes, used liposome encapsulation technology to protect green tea antioxidants in full-fat cheese, and used nano-liposomes to encapsulate TPs to improve the nutritional value of cheese and increase the antioxidant capacity and total phenolic content of TPs. In vitro simulated gastrointestinal digestion experiments showed that TPs in full-fat cheese could still be extracted from the gastrointestinal tract after 6 h, indicating that TPs nano-liposomes could effectively protect TPs in tea cheese from degradation and deliver green TPs to the human body for action. In addition to cheese, TPs nano-delivery systems can also be added to other beverages. Feng (Feng et al., 2019) prepared low-methoxyl pectin-coated nano-liposomes encapsulating resveratrol and epigallocatechin and added them to orange juice. The low-methoxy pectin of the nano-liposomes could bridge with metal ions in orange juice to form a network gel, while the liposomes were negatively charged by being encapsulated by low valent oxygen pectin. Compared with other liposomes, the stability state of pectin nano-liposomes was superior, and the nano-liposomes maintained good stability after pasteurization with stronger antioxidant activity, while the composite nano-liposomes also maintained the best slow release efficiency. In recent years, researchers (Gómez-Mascaraque et al., 2017) have also added nano-liposomes encapsulated with other bioactive ingredients in baked goods such as cookies, bread, etc. The use of TPs nano-delivery systems to improve the stability of TPs and the nutritional value of cookies and other foods has important applications.

TPs nano-delivery system is not only used in the production of various dairy products, bakery products to enhance the biological activity of TPs, improve food quality, improve the bioavailability of TPs, the stability of active compounds, in order to achieve the functionalization of TPs food (Ma et al., 2021; Yang et al., 2021). And because of its antioxidant properties, non-toxic properties, etc, it is often used as an antioxidant, deodorant, added to the packaging polymer mechanism for food preservation, nanomaterials because of its high encapsulation rate and slow release properties so that the addition of TPs active food packaging has more potential applications (Forbes-Hernández & Wang, 2020; Shao et al., 2018). Liu (F. Liu et al., 2017) studied a TPs -chitosan nano-delivery system and wrapped a gelatin film in t TPs he outer layer, which improved the antioxidant capacity and aging period of the gelatin film, increased the denseness of the film, and also had strong free radical scavenging ability, which could delay the oxidation of soybean oil for more than 14 days. The gelatin/chitosan-chitosan 30 % composite membrane showed the longest delay in the release of TPs and the highest scavenging activity of  $80.50 \pm 4.67\%$  ( $p < 0.05$ ) for DPPH radicals after 14 d. Ma used starch nanofibers loaded with TPs and participated in the preparation of starch nanofibers to introduce antioxidant activity into the films, which improved the mechanical properties and hydrophobicity of the films. The antioxidant activity of the membrane gradually increased with the increase of TPs content.

## 6. Conclusion and outlook

In recent years, tea polyphenols have attracted much attention due to their important biological activities and medicinal values, and are widely used in major fields such as food and medicine. However, the complex composition of tea polyphenols themselves, the results obtained by different extraction and purification and analytical methods

vary greatly and with low precision, which affects the extraction purity and intrinsic quality of tea polyphenols. Meanwhile, the instability of tea polyphenols leads to their low in vivo absorption efficiency and low bioavailability, which greatly limits the application and development of tea polyphenols compounds. The effective combination of nanotechnology and tea polyphenols to prepare tea polyphenols nano-delivery system to improve the stability and bioavailability of tea polyphenols provides a material basis for the precise delivery of tea polyphenols and the application of tea polyphenols and their functional products.

This work reviews the physicochemical properties of tea polyphenols, briefly explains the extraction and purification methods of tea polyphenols, and focuses on the research progress of tea polyphenols nano-delivery systems and their applications in food industry and healthcare. Although the research on the delivery of tea polyphenols using nanotechnology has been very extensive, it faces great challenges in practical applications based on the instability of tea polyphenols and the safety of nano-carriers.

- (1) The human gastrointestinal tract has a complex transport and digestion mechanism, to realize the successful application of the tea polyphenols nano-delivery system to the field of oral drugs, researchers need to further study the absorption and metabolism mechanism of drugs in the intestinal tract and try to solve the stability problem of oral drugs in the gastrointestinal tract.
- (2) The tea polyphenols nano-delivery system has good prospects for development, but a large number of systematic clinical trials are needed to use it in the factory production of functional products.
- (3) More research is needed to better understand the interaction between these nano-carriers and tea polyphenols, and to continuously explore and optimize the preparation process of nano-carriers to accelerate the development of more economical, stable, highly available and slow-release nano-carriers.
- (4) At present, the application of tea polyphenols nano-delivery system in the market is mainly reflected in the food industry and health care, which should be combined with the functional properties of tea polyphenols to broaden its application scope and realize the efficient, stable, green and safe release and application of tea polyphenols.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

No data was used for the research described in the article.

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