JPPIPA 12(5) (2026)

Jurnal Penelitian Pendidikan IPA

http://jppipa.unram.ac.id/index.php/jppipa/index

Microparticle of Phenolic Compound and its Herbal Extracts: Fabrication, Characterization, and Therapeutic Application

Aisia Nurul Jasmine[1,2], Finna Setiawan[2,3], Kartini[2,4], Veerakiet Boonkanokwong[5], Aditya Trias Pradana[4*]

[1] Master of Pharmacy Program, Faculty of Pharmacy, Universitas Surabaya, Surabaya, 60293, East Java, Indonesia.
[2] Center of Excellence for Food Products and Health Supplements for Degenerative Conditions, Universitas Surabaya, Surabaya, 60293, East Java, Indonesia.
[3] Department of Drug Discovery and Development, Faculty of Pharmacy, Universitas Surabaya, Surabaya, 60293, East Java, Indonesia.
[4] Department of Pharmaceutical Manufacturing, Faculty of Pharmacy, University of Surabaya, Surabaya, 60293, East Java, Indonesia.
[5] Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, 10330, Bangkok, Thailand.

Received: March 13, 2026
Revised: April 02, 2026
Accepted: May 25, 2026
Published: May 31, 2026

Corresponding Author:
Aditya Trias Pradana
aditya_trias@staff.ubaya.ac.id

DOI: 10.29303/jppipa.v12i5.14810

Abstract: Phenolic compounds in herbal extracts exhibit broad therapeutic potential (antioxidant, anti-inflammatory, antidiabetic, antimicrobial, neuroprotective), yet are hindered by instability, poor solubility, and low bioavailability—critical limitations restricting their use in pharmaceutical and functional food products. This review aims to evaluate the fabrication techniques, characterization methods, and therapeutic applications of phenolic microparticles to address these research gapsA systematic approach was employed through searches on Google Scholar and ScienceDirect, applying inclusion criteria for original full-text studies reporting fabrication techniques, polymers, characterizations, or biological activities. Dominant techniques included spray drying, freeze drying, emulsification/coacervation, and ionic gelation, with primary wall materials comprising maltodextrin, chitosan, pectin, and PLGA. Characterization encompassed FTIR, SEM, DSC/TGA, particle size analysis, encapsulation efficiency (>70%), and release profiles in SGF/SIF media. Results demonstrate that microencapsulation enhances storage stability, gastrointestinal resilience, and bioavailability of phenolic compounds from diverse sources (bauhinia, moringa, citrus), while preserving antioxidant and antidiabetic activities. This review contributes to standardized formulation development for herbal pharmaceuticals and functional foods, although randomized clinical trials remain necessary to validate clinical benefits.

Keywords: Antioxidant activity; Bioavailability; Chlorogenic acid; Phenolic compounds; Quercetin

Introduction

Phenolic compounds are a class of secondary metabolites abundant in plants, recognized for their beneficial biological activities in promoting human health. These compounds exhibit antioxidant, anti-inflammatory, antimicrobial, and neuroprotective properties, supporting the development of nature-based therapies for degenerative diseases and infections (Bińkowska et al., 2024). The phytochemical potential of plants thus forms a cornerstone of modern pharmaceutical research aimed at herbal drug innovation.

The chemical structure of phenolic compounds, characterized by one or more hydroxyl (-OH) groups attached to an aromatic ring, underpins their biological activity (Bińkowska et al., 2024). Representative compounds such as gallic acid, catechin, quercetin, chlorogenic acid, and rutin have demonstrated efficacy. For instance, chlorogenic acid and rutin from Camellia sinensis protect cells against oxidative stress, DNA

How to Cite:
Jasmine, A. N., Setiawan, F., Kartini, Boonkanokwong, V., & Pradana, A. T. (2026). Microparticle of Phenolic Compound and its Herbal Extracts: Fabrication, Characterization, and Therapeutic Application. *Jurnal Penelitian Pendidikan IPA*, *12*(5), 143–158. https://doi.org/10.29303/jppipa.v12i5.14810

damage, and chronic inflammation (Singh et al., 2022), while Bauhinia ungulata exhibits significant antioxidant and antidiabetic activities (Remígio et al., 2024).

Despite these promising properties, the application of phenolic compounds in herbal medicines faces significant challenges due to poor physicochemical stability, limited solubility, and suboptimal bioavailability. The gastrointestinal environment, characterized by pH variations, enzymatic activity, and mucosal transport barriers, causes compound degradation before reaching therapeutic targets, thereby reducing treatment efficacy (Chu & Traverso, 2021). These limitations necessitate innovative drug delivery systems to protect active compounds, enhance solubility, and enable controlled release.

Various delivery systems, including polymeric nanoparticles, liposomes, nanoemulsions, and microparticles, have been developed to overcome these obstacles. Among these, microparticles (1–1,000 µm) offer distinct advantages by encapsulating bioactive compounds within polymer matrices, providing protection against degradation and facilitating controlled release under physiological conditions (Petrovic et al., 2023). This literature review aims to map the fabrication techniques, characterization methods, and therapeutic applications of phenolic-based microparticles and herbal extracts to advance herbal pharmaceutical development.

Method

Time and Location of the Research

This study was conducted from June to December 2025 at Universitas Surabaya. The research was carried out in the form of a literature review focusing on the application of microparticles in natural materials containing phenolic compounds.

Research Methods

Literature was searched using two scientific databases, namely Google Scholar and ScienceDirect. The search was conducted using a combination of keywords including therapeutic applications, herbal extract, encapsulation, characterization, microparticle, and phenolic acid. Boolean operators (AND, OR) were applied to broaden and refine the scope of relevant literature retrieval.

Research Stages

Article selection was carried out systematically in four stages following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework (Page et al., 2021): identification, screening, eligibility assessment, and final article selection (see Figure 1).

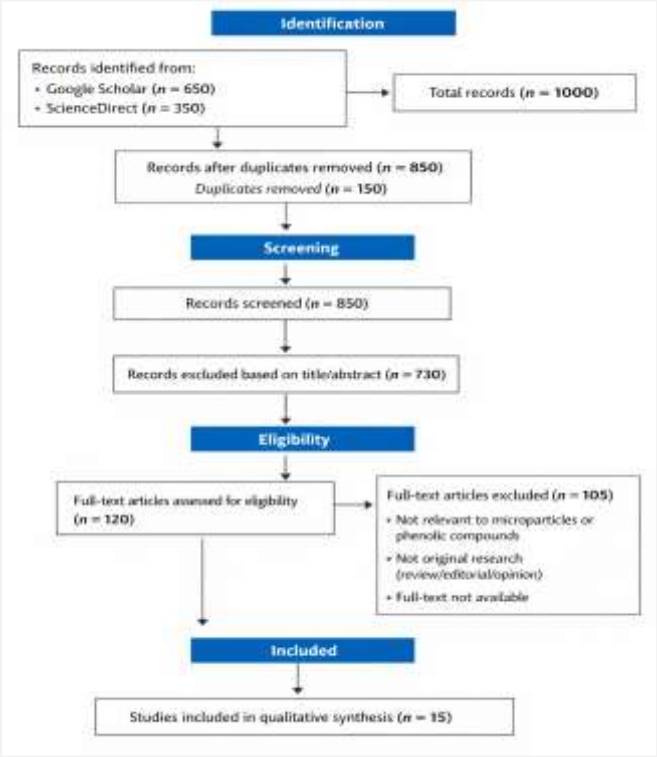

Figure 1. PRISMA diagram

Articles were included if they met all of the following criteria: written in Indonesian or English; constituted original research, whether in vitro, in vivo, or other relevant experimental studies; discussed microparticle applications in natural materials containing phenolic compounds derived from plants, fruits, vegetables, spices, or other natural products, with the aim of encapsulation, delivery, or enhancement of compound stability and bioactivity; and addressed at least one of the following aspects microparticle fabrication techniques, microparticle characterization, or biological activity testing of phenolic compounds. All included articles were required to be available in full-text form.

Articles were excluded if they were in the form of reviews, editorials, or scientific opinions, or if full-text versions were not available.

Data Analysis

Articles that met the inclusion criteria were qualitatively analyzed to evaluate microparticle fabrication techniques, types of polymers used, physicochemical characterization results, and the impact of formulations on the stability and biological activity of phenolic compounds.

Result and Discussion

Result

Phenols are plant secondary metabolites characterized by the presence of one or more hydroxyl (-OH) groups directly bound to an aromatic ring. These compounds belong to the polyphenol group and can be classified into two main categories based on their structure: derivatives of benzoic acid (such as gallic acid and vanillic acid) and derivatives of cinnamic acid (such as ferulic acid and p-coumaric acid). Phenolic compounds are distributed throughout various plant parts, including leaves, fruits, stems, and roots, playing an essential role in plant defense against environmental stress and pathogen attack, while also holding therapeutic potential for humans. They may exist in free form or conjugated with sugars and other organic acids (Dubey et al., 2022; Medina-Torres et al., 2019).

Phenolic compounds exhibit distinctive physicochemical properties, such as variable water solubility, pH sensitivity, and generally low thermal and photostability. Some phenolics, such as chlorogenic acid and rosmarinic acid, show good water solubility; however, in general, many phenolic compounds are unstable when exposed to heat, light, or extreme pH conditions. This instability may affect their biological effectiveness and safety in pharmaceutical and food applications. Furthermore, their phenolic structure allows them to act as antioxidants through proton donation and free radical stabilization. Therefore, formulation strategies such as microparticle-based delivery systems are required to enhance the stability and performance of phenolic compounds in various applications (Aldoghachi et al., 2021; Balasubramaniam et al., 2020).

The physicochemical properties of phenolic compounds also vary depending on their chemical structures, including crystal form, solubility, and stability under environmental conditions. One widely studied phenolic compound is quercetin, a flavonoid. Quercetin appears as a yellowish-gray crystalline powder with a melting point of approximately 313–316 °C. It is almost insoluble in water (about 0.001 mg/mL at 25 °C) but highly soluble in organic solvents such as ether and methanol (Frent et al., 2024). Its aromatic structure containing multiple hydroxyl groups enables it to act as a hydrogen and electron donor, thereby contributing to free radical stabilization and antioxidant activity (Wang et al., 2023). In addition to quercetin, chlorogenic acid and arbutin are also commonly found phenolic compounds in plants. Chlorogenic acid is known for its good water solubility and moderate stability under mild conditions, although it remains prone to degradation under heat and extreme pH. Arbutin, a glycosylated hydroquinone derivative, is water-soluble and widely applied in cosmetics and pharmaceuticals for its depigmenting activity.

Numerous plant species from the Ericaceae family are known to be rich in phenolic content. Examples include *Vaccinium myrtillus, V. corymbosum, V. vitis-idaea, Rhododendron luteum, R. ponticum, R. groenlandicum, Erica scoparia,* and *Calluna vulgaris*. The leaves of these plants contain major phenolics such as quercetin, chlorogenic acid, and arbutin (Stefănescu et al., 2019; Bińkowska et al., 2024). In blueberries (*Vaccinium* spp.), phenolic content is even higher in leaves than in fruits. Studies have shown a positive correlation between total phenolic content and antioxidant activity (Stefanescu et al., 2019).

Another well-known source of phenolic compounds is *Orthosiphon stamineus* (commonly known as Java tea or cat's whiskers), which has been traditionally used in various therapies. Pharmacologically, this plant exhibits a wide range of activities, including diuretic, hypouricemic, renoprotective, antioxidant, anti-inflammatory, hepatoprotective, gastroprotective, antihypertensive, antidiabetic, antihyperlipidemic, antimicrobial, and anorectic effects (Frent et al., 2024). Its phenolic constituents, such as sinensetin, eupatorin, and rosmarinic acid, are believed to contribute significantly to these therapeutic properties.

Phenolic compounds also exhibit a wide range of biological activities, including antioxidant, anti-inflammatory, antimicrobial, anticancer, and neuroprotective effects. These activities are largely associated with their ability to scavenge free radicals and inhibit pro-inflammatory enzymes. For instance, a study by Soliman et al. (2022) demonstrated that a combination of spinach and broccoli leaf extracts, both rich in phenolics, provided protective effects against neuroinflammation induced by $AlCl_3$ exposure. These compounds also contribute to the upregulation of endogenous antioxidant enzyme expression (Soliman et al., 2022; De Rodríguez et al., 2019).

Many Indonesian native plants are rich in phenolic compounds. Examples include *Melissa officinalis, Mentha* spp., *Origanum vulgare, Perilla frutescens, Lavandula angustifolia, Salvia officinalis, Satureja* spp., and *Plectranthus scutellarioides* (known locally as daun miana). Other plants such as jati belanda (*Guazuma ulmifolia*), saga (*Abrus precatorius*), binahong (*Anredera cordifolia*), and kenitu (*Chrysophyllum cainito*) have been reported to contain significant levels of flavonoids and phenolic acids with potential antioxidant and antiproliferative properties (Khojasteh et al., 2020).

Miana (*Coleus artropurpureus L.* Benth) is another natural antioxidant source capable of neutralizing free radicals due to its content of flavonoids, saponins, tannins, and alkaloids (Muadifah et al., 2023). Several

studies have reported the extraction of miana leaves using maceration with 96% ethanol, which revealed the presence of flavonoids, steroids, tannins, saponins, and anthocyanins. This plant is also widely used in Indonesian traditional medicine (Khotimah et al., 2018).

The determination of phenolic content is carried out using various analytical methods, such as spectrophotometry with the Folin-Ciocalteu reagent, high-performance liquid chromatography (HPLC), and total phenolic quantification assays. Some studies have employed quercetin, chlorogenic acid, and rutin as major markers in analysis. Research by Remigio et al. (2024) highlighted that HPLC was able to detect isoquercitrin, rutin, and p-coumaric acid as dominant components in Bauhinia ungulata extracts (Remigio et al., 2024).

Several phenolic compounds, such as gallic acid as shown in Figure 2, ferulic acid, and epigallocatechin gallate (EGCG), demonstrate a close relationship between their chemical structure particularly the position and number of hydroxyl (-OH) groups and specific pharmacological activities, such as antioxidant capacity. For example, EGCG found in green tea is highly effective as an antioxidant due to the ability of its hydroxyl groups to donate electrons and neutralize free radicals. Meanwhile, ferulic acid (Figure 3) shows potential in wound healing and antidiabetic activity. A study by Kamaruddin et al. (2017) reported that EGCG microparticles improved the stability of the compound by protecting it from oxidative and thermal degradation, while also enhancing its biological activity compared to its free form (Kamaruddin et al., 2017; Noudoost et al., 2015).

Figure 2. Gallic acid structure

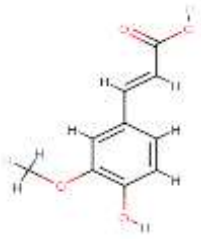

Figure 3. Ferulic acid structure

Limitations of phenolic compounds include low bioaccessibility and bioavailability due to instability during processing, storage, and digestion, entanglement in food matrices, and inhibition of intestinal absorption, so that in vivo activity is often not as high as predicted from in vitro tests. The large number of hydroxyl groups increases antioxidant activity, but also decreases membrane permeation and triggers strong interactions with proteins (e.g., salivary protein precipitation), which causes astringency and potentially reduces bioavailability. Polyphenols can act as pro-oxidants at high concentrations or in the presence of transition metals through autoxidation and the formation of reactive species such as H2O2, so the biological context and dosage determine the benefits versus risks. Chemically, some polyphenols, such as EGCG, are very sensitive to pH, light, heat, oxygen, and metal ions, which trigger epimerization, hydrolysis, and polymerization, resulting in decreased biological potency in neutral-alkaline environments. From a pharmacokinetic perspective, phase II conjugation (glucuronidation, sulfatation, methylation) and microbiota metabolism dominate, so the main circulating form is often a metabolite, for example EGCG-4″-sulfate, whose activity may differ from that of the aglycone (Secretan et al., 2021).

Discussion

Microparticles are drug or active compound delivery systems in the form of small particles ranging from 1 to 1,000 μm in size. This technology serves to protect active compounds from degradation caused by environmental factors such as heat, light, and oxygen, while simultaneously improving their bioavailability. In the context of phenolic compounds, microparticulation aims to encapsulate these compounds within a polymer matrix or colloidal system, thereby extending their shelf life, enabling controlled release, and directing their distribution more specifically within the body. The formation of microparticles typically involves several key steps, such as the creation of emulsions in which the active compound and protective polymer are dissolved or suspended in a given phase to produce oil-in-water or water-in-oil systems, followed by drying techniques such as spray drying or freeze drying to obtain solid particles. Another approach, coacervation, allows phase separation so that polymers selectively precipitate around the active compound, forming a protective layer. Through these mechanisms, phenolic compounds can be physically or chemically entrapped within a polymer matrix, thus being better protected against chemical and physical degradation both during storage and after administration (Trifković et al., 2016; Medina-Torres et al., 2019).

The microcrystallization approach is also applied to enhance the performance of phenolic compounds. Microcrystals are solid forms of bioactive compounds

crystallized in a controlled manner at the micrometer scale. Based on their characteristics, microcrystals can be categorized into: monolithic microcrystals, in which the entire particle consists of pure active compound; composite microcrystals, which combine phenolic compounds with polymers or other excipients to improve stability; and coated microcrystals, where phenolic crystals are covered with polymers or lipids to provide controlled release and protection against degradation. Microcrystals have been shown to improve solubility, dissolution rate, and bioavailability of phenolics, which naturally often exhibit low solubility. For example, microcrystallization of quercetin using the antisolvent precipitation technique achieved more than a tenfold increase in solubility compared to its conventional form, directly enhancing both its antioxidant activity and oral bioavailability (Sheng et al., 2019).

Several modern technologies can be applied in the fabrication of phenolic microparticles or microcrystals, including spray drying, freeze drying, ionic gelation, emulsification, as well as advanced methods such as microfluidics and multilayer coating. Among these, spray drying is the most commonly used because it is efficient and suitable for thermolabile compounds such as phenolics, while freeze drying is often selected when preserving the structural stability of the compound is crucial (da Silva Júnior et al., 2023; Ozkan et al., 2024).

Phenolic compounds are known to suffer from poor stability when exposed to temperature, light, oxidation, and variable pH conditions. Moreover, they often undergo degradation during storage or in the gastrointestinal tract before reaching their therapeutic target. Microparticulation addresses these challenges by creating protective systems that improve stability, slow release, and enhance absorption of active compounds, thereby optimizing their pharmacological effectiveness (González et al., 2018; Shaygannia et al., 2021). Furthermore, microparticle technology has been shown to enhance the effectiveness of phenolic compounds through controlled release, maintaining more stable plasma concentrations and prolonging biological activity. Microparticles also facilitate targeted delivery to specific regions of the gastrointestinal tract, reduce degradation in the stomach, and ultimately improve oral bioavailability (Ballesteros et al., 2017).

Several studies support these findings. For instance, the microencapsulation of green tea polyphenols by spray drying resulted in improved oxidative stability and higher bioavailability in in vivo models. Another study showed that microparticles formulated from pomegranate extract polyphenols enhanced antioxidant activity in a simulated gastrointestinal system and prolonged the release time of active compounds (Azarpazhooh et al., 2018). Thus, microparticulation not only protects phenolic compounds from degradation but also significantly enhances their pharmacological effectiveness by improving bioavailability, ensuring more consistent biological activity, and maximizing their therapeutic potential.

Various studies have applied microparticle fabrication techniques to phenolic compounds. For example, phenolic extracts from ciriguela fruit peel (*Spondias purpurea*) containing rutin, epicatechin gallate, chlorogenic acid, and quercetin have been successfully encapsulated into microparticles using spray drying and freeze drying methods. The results demonstrated high encapsulation efficiency of up to 98.8%, along with improved physicochemical properties and enhanced compound stability during storage (da Silva Júnior et al., 2023). In addition, multilayer microparticle systems for sequential release of phenolic compounds have also been developed, providing effective protection during the gastrointestinal phase and improving bioavailability (Ozkan et al., 2024). Several modern technologies can be employed for the fabrication of phenolic microparticles, including spray drying, freeze drying, ionic gelation, emulsification, as well as advanced approaches such as microfluidics and multilayer coating. Among these, spray drying is the most frequently used due to its efficiency and suitability for thermolabile compounds such as phenolics; meanwhile, freeze drying is often chosen when maintaining the structural stability of the compounds is essential (da Silva Júnior et al., 2023; Ozkan et al., 2024).

The microcrystallization approach has also been utilized to enhance the performance of phenolic compounds. Microcrystals are solid forms of bioactive compounds with micrometer-scale dimensions, crystallized in a controlled manner. Based on their characteristics, microcrystals can be classified into three types: monolithic microcrystals, in which the entire particle consists of pure crystals of the active compound; composite microcrystals, which combine phenolic compounds with polymers or other excipients to improve stability; and coated microcrystals, where phenolic crystals are coated with polymeric or lipid materials to provide controlled release and protection against degradation. The use of microcrystals has been shown to improve solubility, dissolution rate, and bioavailability of phenolics, which are often naturally poorly soluble. For instance, the microcrystallization of quercetin using the antisolvent precipitation technique resulted in more than a tenfold increase in solubility compared with its conventional form, directly enhancing its antioxidant activity and oral bioavailability (Sheng et al., 2019).

Several modern technologies are available for the fabrication of phenolic microparticles and microcrystals, including spray drying, freeze drying, ionic gelation,

emulsification, as well as advanced methods such as microfluidics and multilayer coating. Of these, spray drying remains the most widely employed due to its efficiency and applicability for thermolabile phenolics, while freeze drying is often selected when preservation of the compound's structural stability is of utmost importance (da Silva Júnior et al., 2023; Ozkan et al., 2024).

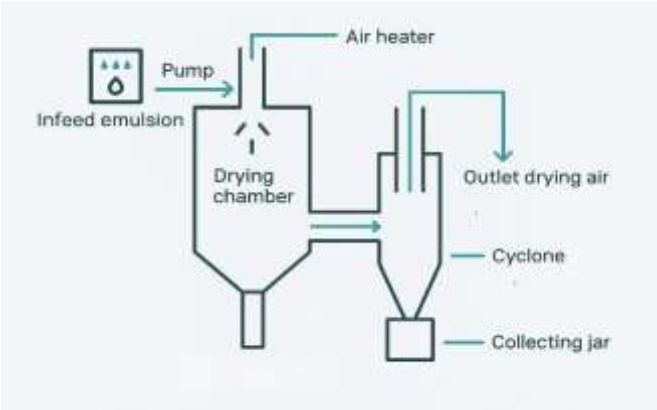

Figure 4. Spray drying

Spray drying is the most common and widely used technique for the microencapsulation of phenolics. The process involves atomizing a solution or suspension of the active compound and polymer into a high-temperature drying chamber, producing dry particles in a short period of time as shown in Figure 4. This technique is favored for its high efficiency, scalability, and ability to generate uniform and stable particles. The use of maltodextrin, gum arabic, and chitosan as coating polymers in spray drying has been shown to enhance encapsulation efficiency and antioxidant stability (Dadi et al., 2020; Zanoni et al., 2019). The advantages of this method include high process efficiency, industrial scalability, and the production of homogeneous, stable particles with improved shelf life (Kandasamy, 2022; Grgić et al., 2020). However, spray drying also presents limitations, such as potential thermal degradation of heat-sensitive compounds and restrictions in the choice of coating materials, which must be water-soluble and may limit formulation flexibility (Grgić et al., 2020).

Examples of studies demonstrating the effective application of spray drying to phenolics include *Bauhinia ungulata* var. *obtusifolia*. Remígio et al. (2024) successfully formulated microparticles containing rutin, chlorogenic acid, p-coumaric acid, and isoquercitrin using a combination of maltodextrin, pectin, CMC, and β-cyclodextrin. The study reported uniform particle size, high encapsulation efficiency, and preserved antioxidant and antidiabetic activity. Similarly, Remígio et al. (2024) compared five types of coating materials for phenolic spray-drying formulations, revealing differences in encapsulation efficiency and microstructural characteristics. Another example comes from *Echinacea purpurea*, where extracts rich in chicoric and caftaric acids were spray-dried with maltodextrin; characterization showed well-structured morphology, satisfactory encapsulation efficiency, and preserved antioxidant and immunostimulant activity (Dubey et al., 2022).

Freeze drying (lyophilization) is another technique used for microencapsulation, particularly for heat-sensitive compounds. The process involves freezing the solution, followed by water removal through sublimation under low pressure. Freeze drying produces highly porous particles and allows for better retention of phenolic compounds, although it requires longer processing times and higher production costs. This technique has also been applied with complex polymer combinations such as plant proteins and natural mucilage (Fredes et al., 2018; Mar et al., 2020).

Emulsification is employed for phenolic compounds that are oil-soluble or poorly soluble in water. This method involves forming oil-in-water (O/W) or water-in-oil (W/O) emulsions, stabilized with surfactants and coating polymers. Once a stable emulsion is achieved, drying or gelation is applied to produce solid particles. For example, tea and citrus peel extracts have been successfully encapsulated using double emulsion and complex coacervation methods, which improved the stability of active compounds (Massounga et al., 2018; Tuyet et al., 2018).

Ionic gelation exploits electrostatic interactions between charged polymers, such as positively charged chitosan, and counterions like TPP (tripolyphosphate), to form microparticle gels under mild temperature conditions. This technique is particularly suitable for phenolic compounds prone to degradation by heat or organic solvents. Chitosan nanoparticles produced through this method have been shown to enhance wound healing effectiveness and improve the stability of ferulic acid (Balasubramaniam et al., 2020; Dubey et al., 2022).

A wide range of natural and synthetic polymers have been employed in the microencapsulation of phenolic compounds (Table 1), while the physicochemical characteristics of the polymers are shown in Table 2. Maltodextrin is the most commonly applied polymer due to its neutral nature, high water solubility, low cost, and compatibility with various phenolic compounds. It also has the ability to form an amorphous matrix that protects phenolics from degradation caused by oxidation, light, and extreme pH conditions during storage (Remígio et al., 2024). In addition, gum arabic and pectin, both hydrophilic natural polymers, are frequently used because they provide a stable protective coating, enhance encapsulation efficiency, and possess good emulsifying

properties. Gum arabic, in particular, is often combined with maltodextrin in spray-drying techniques to produce microparticles with more uniform physical characteristics and higher solubility (Remígio et al., 2024).

Table 1. Polymer Applications for Phenol Microparticles

Polymer	Main role in phenolic microparticles	Technique
Maltodextrin	Neutral, water-soluble, inexpensive; forms amorphous protective matrix (anti-oxidation, light, extreme pH)	Spray drying; often combined
Gum arabic	Hydrophilic polysaccharide; good emulsifier; stable protective coating	Spray drying (often with maltodextrin)
Pectin	Hydrophilic polysaccharide; forms protective layer, ↑EE	Gelation/coacervation; multicomponent blends
Chitosan	Cationic biopolymer; bioadhesive, biocompatible; gastric protection; ↑intestinal absorption (opens tight junctions)	Coacervation/gelation; modifications (quaternized, carboxymethylated)
β-cyclodextrin	Inclusion complex: hydrophobic cavity traps phenolics, hydrophilic exterior; ↑solubility/stability/bioaccessibility	Inclusion complexation; can be combined with other polymers
Zein (corn protein)	Hydrophobic; self-assembly/electrospinning; suitable for lipophilic phenolics	Self-assembly; electrospinning; blends with polysaccharides
Whey protein (WPI/WPC)	Thermal gelation; emulsification; non-covalent interactions with polyphenols	O/W emulsion; pH adjustment, stirring speed, emulsifier control
Alginate	Anionic polysaccharide; Ca^{2+} ionotropic gel; gastric protection and intestinal release	Ionic gelation (Ca^{2+}); spray drying/multicomponent gelation
Enteric cellulose derivatives (HPMCP/HPMCAS/CAP/CAT)	pH-responsive coating; gastric protection; intestinal release	Enteric coating; diffusion through gel/layer dissolution
PLGA (biodegradable polyester)	Medium–long-term release; oxidative protection; targeting potential	Emulsion–solvent evaporation; blends with hydrophilic polymers
Grape seed extract	↑stability, solubility, ease of formulation into functional products	Spray drying with food-grade polymers

Table 2. Polymer Types and Physicochemical Characteristics

Polymer	Charge	Hydrophilicity	Solubility and pH	Source
Maltodextrin	Neutral	Hydrophilic	Water-soluble	(Kandasamy & Naveen, 2022)
Gum arabic	Weak anionic	Hydrophilic	Water-soluble	(Al-Hamayda et al., 2023)
Pectin	Anionic	Hydrophilic	Water-soluble; forms gel with Ca^{2+} (LM) or acid/sugar (HM)	(Ishwarya et al., 2021)
Chitosan	Cationic	Hydrophilic (in acid); less soluble in neutral	Soluble at acidic pH; insoluble at neutral–basic pH	(Ways et al., 2018)
β-Cyclodextrin	Neutral	Hydrophilic exterior, hydrophobic cavity	Water-soluble	(Liu et al., 2020)
Zein	Neutral–slightly anionic	Hydrophobic	Insoluble in water; soluble in ethanol	(Kasaai, 2018)
Whey protein (WPI/WPC)	Amphoteric (isoelectric point ~5.2)	Hydrophilic	Soluble near neutral pH; gels upon heating	(Khalesi et al., 2023)
Alginate	Anionic	Hydrophilic	Soluble as Na salt; gels with Ca^{2+}	(Abka-Khajouei et al., 2022)
Enteric cellulose derivatives (HPMCP/HPMCAS/CAP/CAT)	Anionic (ionized at high pH)	Hydrophilic	Soluble at ~pH 5.5–6.8	(Wathoni et al., 2020)
PLGA	Neutral	Hydrophobic	Insoluble in water; degrades via hydrolysis	(Guo et al., 2023)

Chitosan polymer has also attracted wide attention in the development of phenolic microparticles. Chitosan is a cationic biopolymer obtained from chitin deacetylation, well known for its bioadhesive,

biocompatible, and biodegradable properties. Its cationic character enables strong electrostatic interactions with the negatively charged components of the mucus and epithelial surfaces, thereby enhancing drug retention and intestinal absorption. Furthermore, chitosan and its derivatives have been shown to open tight junctions in the intestinal epithelium, facilitating paracellular transport and improving bioavailability (Ways et al., 2018). Chitosan can also be chemically modified into derivatives such as quaternized chitosan (trimethyl chitosan) or carboxymethyl chitosan, which provide improved solubility at physiological pH a key limitation of unmodified chitosan (Ways et al., 2018).

β-cyclodextrin is widely applied in phenolic microencapsulation because of its unique ability to form inclusion complexes. Its cyclic structure with a hydrophobic cavity can entrap relatively hydrophobic phenolic molecules, while its hydrophilic outer surface allows solubility in water. This improves the solubility, stability, and bioaccessibility of phenolics in biological systems. The use of polymer combinations often provides synergistic effects for instance, maltodextrin combined with gum arabic or with chitosan has been shown to enhance encapsulation efficiency, promote sustained release, and improve antioxidant activity following in vitro digestion simulation (Remígio et al., 2024; Remígio et al., 2024).

Zein (corn protein) is a hydrophobic polymer commonly employed to encapsulate relatively hydrophobic phenolics due to its ability to form stable particles through self-assembly or electrospinning, and it is often blended with polysaccharides to fine-tune release behavior. In electrospinning studies, zein–dextran fibers loaded with curcumin demonstrated that the zein fraction modulated hydrophobicity and release rate; zein contents of 15–30% altered flexibility, tensile strength, and optimized controlled release, underscoring the importance of protein–polysaccharide ratios in shaping release profiles. Recent reviews also highlight the design of multicomponent zein-based carriers for lipophilic actives, which improve stability during food processing and gastrointestinal transit, while enabling gradient structures for controlled release (Shu et al., 2025).

Whey proteins (WPI/WPC) are widely used as wall materials because of their thermal gelation, emulsifying capacity, and noncovalent interactions with polyphenols, although particle physicochemical properties must be optimized to avoid sensory drawbacks. Encapsulation of blueberry extract in whey protein matrices with initial sizes of 0.5–2.5 mm. Adjusting stirring speed and adding emulsifiers reduced particle size to ~70 μm, though low pH and extract ratio influenced spherical capsule formation due to altered protein–polyphenol electrostatic interactions. Whey protein–medium-chain triglyceride emulsions stabilized with gum arabic further demonstrated how gum arabic and $CaCl_2$ addition influenced size distribution, zeta potential, and improved encapsulation efficiency and resveratrol fluorescence at the oil–water interface (Pchelkina et al., 2022).

Alginate is an anionic polysaccharide that forms ionotropic gels with Ca^{2+}, making it suitable for protecting phenolics sensitive to gastric acidity and for targeted release in the intestine. It is often combined with proteins or other polysaccharides to enhance particle mechanical strength. In food applications, polysaccharide-based systems such as alginate have been reported to improve polyphenol stability during storage and processing, with good encapsulation efficiency when combined with spray drying or multicomponent ionic gelation. Recent reviews also emphasize that encapsulation within anionic hydrogel matrices helps preserve phenolic antioxidant activity during simulated digestion, especially when paired with film-forming polymers (Siddiqui et al., 2024).

Enteric cellulose derivatives such as hydroxypropyl methylcellulose phthalate (HPMCP), hydroxypropyl methylcellulose acetate succinate (HPMCAS), cellulose acetate phthalate (CAP), and cellulose acetate trimellitate (CAT) are widely used for pH-responsive release and gastric protection, which is particularly relevant for acid-sensitive phenolics. These materials form insoluble coatings at gastric pH and dissolve at intestinal pH, releasing the active compound either by diffusion through a viscous gel layer or after dissolution of the enteric coat. CAP, one of the earliest solutions, remains effective to this day. Studies have shown that CAP coating of microspheres prolongs release and improves colon targeting compared to uncoated formulations, demonstrating a principle that can be translated to polyphenols intended for colonic delivery (Martínez et al., 2025).

PLGA (poly(lactic-co-glycolic acid)) and other biodegradable polyesters are employed when medium- to long-term controlled release, oxidative protection, and targeted delivery are desired, although cost and food regulatory considerations remain important. Reviews on bioactive encapsulation for specific diets highlight that food-grade synthetic polymers and green systems yield promising results in stabilizing polyphenols during processing while enhancing antioxidant activity and controlled release profiles, opening opportunities for functional formulations with predictable release kinetics. Furthermore, combining PLGA with hydrophilic polymers can adjust matrix hydration and diffusion, thereby modulating phenolic release and bioaccessibility during digestion (Ran et al., 2024).

Additional studies underscore the role of polymers as carriers for phenolics in actual food applications and model matrices. Grape seed phenolic extract spray-dried into food polymers demonstrated improved stability, solubility, and ease of formulation into functional products, showing that polymer carrier design can maximize retention of bioactive properties throughout shelf life. Overall, recent literature emphasizes the importance of selecting or combining polymers such as hydrophobic proteins (zein), ionotropic gelling polysaccharides (alginate), enteric celluloses (HPMCP/HPMCAS/CAP), and lipid-based systems (liposomes) to achieve desired encapsulation efficiency, stability, and bioaccessibility of phenolics (Salem et al., 2024).

Fourier Transform Infrared Spectroscopy (FTIR) is a technique used to evaluate chemical or physical interactions between phenolic compounds and the polymers forming microparticles. Shifts in the characteristic absorption peaks of functional groups (e.g., OH, C=O, C–O–C) indicate the formation of hydrogen bonds, ionic bonds, or intermolecular interactions during the encapsulation process. Studies by Kamaruddin et al. (2017) and Dubey et al. (2022) confirmed that FTIR successfully demonstrated the formation of stable complexes between catechins or flavonoids and polymers such as PVP or soy protein isolate, which are critical to ensuring the integrity of active compounds within microparticle matrices (Kamaruddin et al., 2017; Dubey et al., 2022).

Scanning Electron Microscopy (SEM) is the principal method used to examine microparticle morphology, surface features, and coarse particle size. Smooth surface structures and regular spherical shapes are generally desirable for oral applications, as they enhance dissolution and stability. For example, microparticles prepared from *Vaccinium* spp. and Echinacea purpurea extracts displayed spherical shapes with uniform surfaces, reflecting optimized spray drying conditions and stable polymer formulations (Dubey et al., 2022; Stefanescu et al., 2022).

Differential Scanning Calorimetry (DSC) is employed to determine the thermal properties of microparticles, including melting point, glass transition temperature (Tg), and thermal degradation. Changes in thermal profiles after microencapsulation may indicate successful complex formation or structural transformation of the active compounds. For instance, Remígio et al. (2024) demonstrated that β-cyclodextrin combined with maltodextrin enhanced the thermal stability of phenolic compounds within microparticles, as evidenced by shifts in Tg and the disappearance of endothermic peaks observed in the free compounds (Remígio et al., 2024).

X-Ray Diffraction (XRD) provides insight into the crystallinity or amorphous nature of the resulting microparticles. Amorphous microparticles typically dissolve more readily and display better bioavailability than crystalline forms. Several studies have reported that encapsulating phenolics with maltodextrin or pectin transforms the crystalline structure of active compounds into an amorphous state, as observed by Fredes et al. (2018) in strawberry extract formulations and by Remígio et al. (2024) in Bauhinia microparticles (Fredes et al., 2018; Remígio et al., 2024).

Particle size and distribution are critical parameters in microparticle evaluation, as they influence release rate, stability, and absorption pathways in the body. Microparticles smaller than 10 µm generally demonstrate good suspension stability and rapid dissolution. For example, Peanparkdee et al. (2021) and Fernández-Luqueño et al. (2021) reported that phenolic microparticles from purple rice bran and Opuntia atropes, respectively, exhibited small (micro- to nano-scale) sizes with narrow distributions, contributing to high encapsulation efficiency and enhanced antioxidant activity (Peanparkdee et al., 2021; Fernández-Luqueño et al., 2021).

Encapsulation efficiency (EE) reflects the proportion of active compounds successfully retained within microparticles. High EE values indicate optimized techniques and coating materials. The stability of actives within microparticles is also assessed by measuring phenolic content and changes during storage. Many studies report EE values above 70%, such as green tea leaf extract (Zokti et al., 2016) and Moringa oleifera extract (González et al., 2018), indicating successful formulations in preserving active compounds (Zokti et al. 2016; González et al., 2018).

Release profiling of actives from microparticles is typically conducted in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) to assess the extent of controlled release. Sustained release is critical for prolonging pharmacological action and improving therapeutic effectiveness. Studies by Zokti et al. (2016) and Aldoghachi et al. (2021) showed that microparticles formulated with combinations of chitosan, gum arabic, and maltodextrin delayed release in the stomach and gradually released compounds in the intestine, thereby enhancing phenolic bioaccessibility (Zokti et al., 2016; Aldoghachi et al., 2021).

Biological activity of phenolics is preserved and in some cases enhanced through microencapsulation, particularly antioxidant, antidiabetic, and immunomodulatory functions. Encapsulation protects compounds from degradation caused by oxidation, light, and temperature, which often occur in their free forms. For example, microparticles from *Vaccinium* spp. leaf extract containing chlorogenic acid demonstrated

improved bioaccessibility and free radical scavenging after microencapsulation with maltodextrin and glucose (Stefănescu et al., 2022). Similarly, Bauhinia microparticles produced by spray drying showed more stable antioxidant and antidiabetic activities (Remígio et al., 2024; Remígio et al., 2024).

Comparative studies between free and microencapsulated phenolics often reveal superior bioactivity retention of the microparticle forms during storage and gastrointestinal passage. Dubey et al. (2022) reported that the analgesic activity of *Adenanthera pavonina* (saga) leaf extract significantly increased after microencapsulation, with high EE and uniform particle distribution. Likewise, Tülek et al. (2020) observed that the antioxidant activity of lemon balm extract remained high after microencapsulation, while its free form showed a decline in stability during storage (Dubey et al., 2022; Tülek et al., 2020). Several studies on Indonesian herbal plants also demonstrate that microencapsulation enhances the biological activity of phenolic-rich extracts. For example, *Guazuma ulmifolia* (jati Belanda) leaves, rich in flavonoids, displayed high antioxidant activity after spray drying with maltodextrin as the coating polymer (Morais et al., 2016).

Microencapsulation also plays a crucial role in improving bioavailability. Microparticles of Opuntia atropes containing isorhamnetin and p-coumaric acid exhibited high EE and nanoscale particle size, which correlated with enhanced bioavailability and antioxidant activity (Fernández-Luqueño et al., 2021). Similarly, formulations incorporating pectin and β-cyclodextrin as wall materials in Bauhinia extract improved active compound stability and enabled controlled release, supporting their use in antidiabetic and antioxidant therapies (Remígio et al., 2024).

The clinical potential of phenolic microparticles continues to develop, although most current research remains in vitro or preclinical. Yousefi et al. (2021) reported that encapsulating compounds such as fisetin and hesperidin from grape pomace and bilberry improved oral bioavailability, though clinical outcomes varied depending on the compound and formulation. Ozkan et al. (2024) also emphasized that while preclinical data are promising for anti-inflammatory, antiallergic, and cardioprotective applications, more randomized clinical trials are still needed to validate the therapeutic benefits of phenolic microparticles in humans (Yousefi et al., 2021; Ozkan et al., 2024).

Numerous studies as mentioned in Table 3 have explored spray drying techniques for encapsulating phenolic compounds from various plant sources, aiming to improve stability, encapsulation efficiency, and pharmacological activity retention. Findings show that the choice of wall polymers such as maltodextrin, gum arabic, β-cyclodextrin, pectin, and CMC significantly influences particle morphology, active compound retention, and antioxidant or therapeutic activity (Macías et al., 2020; Pattnaik et al., 2021). For clarity and comparison, Table 1 provides a summary of spray-drying-based microencapsulation strategies for phenolics, including plant sources, dominant phenolic compounds, wall polymers, characterization techniques, and observed pharmacological activities.

Table 3. Research Article Data Extraction

Plant Source	Phenolic Compounds	Research Method	Polymer Type	Characterization Techniques	Pharmacological Activity	Reference (Year)
Bauhinia ungulata L. var. *obtusifolia*	Chlorogenic acid, p-coumaric acid, rutin, isoquercitrin	Spray drying	Maltodextrin, pectin, CMC, β-cyclodextrin	Particle size, SEM, DSC, TGA, FTIR, HPLC, TPC, TFC, Encapsulation efficiency	Antioxidant, antidiabetic	Remígio et al. (2024)
Bauhinia ungulata L. var. *obtusifolia*	Chlorogenic acid, rutin, isoquercitrin, p-coumaric acid	Spray drying	Maltodextrin, β-cyclodextrin, pectin, CMC	Particle size, SEM, XRD, FTIR, HPLC, Encapsulation efficiency	Antioxidant, antidiabetic	Remigio et al. (2024)
Green tea (*Camellia sinensis*)	Catechins (EGCG)	Spray drying	Chitosan, alginate	Particle size, zeta potential, in vitro release, behavioral tests, biomarkers	Neuroprotective, enhanced bioavailability, controlled release	Mohammad baghban et al. (2024)
Olive leaf extract (*Olea europaea*)	Oleuropein, hydroxytyrosol, verbascoside	Freeze drying	Maltodextrin, trehalose	HPLC (oleuropein, hydroxytyrosol, verbascoside), DSC/Tg, SEM, RSM, TEAC/ABTS, EE oleuropein	Antioxidant	(González-Ortega et al. (2020)
Grape seed extract (Vitis vinifera)	Gallic acid, catechin, epicatechin, gallocatechin,	Freeze drying	Whey protein concentrate (WPC), maltodextrin, gum arabic	EE, DPPH, particle size (PSA), SEM, in vitro release (SGF/SIF)	Antioxidant	Martinović et al. (2024)

Plant Source	Phenolic Compounds	Research Method	Polymer Type	Characterization Techniques	Pharmacological Activity	Reference (Year)
	epigallocatechin, epicatechin-3-O-gallate, procyanidin B1/B2					
Vaccinium spp. leaves	Chlorogenic acid, catechin	Spray drying	Maltodextrin, glucose	Particle size, viscosity, SEM, HPLC, efficiency, simulated GI release profile	Antioxidant	Stefănescu et al. (2022)
Red grape juice (Vitis vinifera)	Anthocyanins expressed as cyanidin-3-glucoside equivalents (C3G)	Freeze drying	Whey protein isolate + chitosan	EE of anthocyanins, anthocyanin composition (C3G eq.)	Antioxidant	Mihalcea et al. (2020)
Echinacea purpurea aerial parts	Chicoric acid, caftaric acid	Spray drying	Maltodextrin	SEM, FTIR, encapsulation efficiency, particle morphology	Antioxidant, immunostimulant	Dubey et al. (2022)
Hibiscus sabdariffa (roselle)	Anthocyanins	Freeze drying	Maltodextrin, gum arabic, and blends with inulin/konjac glucomannan	EE of anthocyanins, antioxidant activity (FRAP/CUPRAC), powder physical properties	Antioxidant	Nguyen et al. (2022)
Hibiscus sabdariffa (roselle)	Anthocyanins	Freeze drying	Maltodextrin, gum arabic	Moisture content, color, solubility, sensory/physicochemical properties, carrier comparison	Antioxidant	Nguyen et al. (2022)
Olive leaf polyphenol-rich extract	Oleuropein, hydroxytyrosol	Freeze drying	Polymeric micelle	Size/ζ-potential, EE, stability, in vitro release, intestinal permeability	Antioxidant	Nanomateri al. (2023)
Ciriguela peel extract (*Spondias purpurea*)	Rutin, epicatechin gallate, chlorogenic acid, quercetin	Freeze drying	Maltodextrin, gum arabic	HPLC/DAD phenolic profile, EE, morphology (SEM), TPC stability	Antioxidant	Bergonzi et al. (2023)
Grape seeds (*Vitis vinifera*)	Proanthocyanidins	Spray drying	Maltodextrin, gum arabic	Morphology, solubility, storage stability, antioxidant activity	Antioxidant	Salem et al. (2024)
Plectranthus barbatus	Rosmarinic acid	Spray drying	Maltodextrin	Particle size, SEM, FTIR, TPC, encapsulation efficiency, DPPH	Antioxidant	Aldoghachi et al. (2021)
Hop extract (Humulus lupulus)	Alpha-acids	Freeze drying	Maltodextrin, gum arabic	Alpha-acid content, polyphenol EE, physicochemical/techno-functional properties, stability	Antioxidant	Tatasciore et al. (2023)

Conclusion

This review aimed to comprehensively map the fabrication techniques, characterization methods, and therapeutic applications of phenolic-based microparticles derived from herbal sources. The findings confirm that microencapsulation consistently addresses the core limitations of phenolic compounds poor stability, limited solubility, and suboptimal bioavailability through scalable methods including spray drying, freeze drying, emulsification, and ionic gelation, as well as emerging approaches such as microcrystallization and multilayer architectures. Unlike previous reviews that tend to focus on a single technique or compound class, this review integrates across fabrication strategies, wall-material selection, and multi-endpoint characterization, offering a broader translational framework for both food and pharmaceutical applications. Nevertheless, the current body of evidence has notable limitations. The majority of studies remain in vitro or preclinical, methodological protocols vary considerably across studies, and direct clinical data validating the therapeutic benefits of phenolic microparticles in humans are still scarce. These gaps restrict the generalizability of the findings and underscore the need for standardized evaluation frameworks and well-designed randomized clinical trials. From a practical standpoint, the evidence

positions phenolic microparticles as a viable platform for developing functional food ingredients and pharmaceutical dosage forms with improved shelf life, gastrointestinal resilience, and targeted release. Future efforts should prioritize scale-up validation, in vitro and in vivo correlation, and clinical translation to fully realize this potential. Ultimately, microencapsulation represents a scientifically grounded strategy to bridge the intrinsic instability of phenolic compounds with the demands of reliable, effective delivery in real-world applications.

Acknowledgments
This research was supported by the RIIM LPDP Grant and BRIN, grant numbers No. 104/IV/KS/10/2024 and No. 129/LPPM-01/PKS/X/2024. We thank the Universitas Surabaya, Indonesia, and the National Research and Innovation Agency, Indonesia.

Author Contributions
Conceptualization, K., A.T.P., and F.S.; methodology, A.N.J.; validation, A.T.P., F.S., and K.; formal analysis, A.N.J.; investigation, A.N.J.; resources, K.; data curation, A.N.J.; writing-original draft preparation, A.N.J.; writing-review and editing, A.T.P., F.S., K., and V.B.; visualization, A.N.J.; supervision, K. and V.B.; project administration, A.N.J.; funding acquisition, K. All authors have read and agreed to the published version of the manuscript.

Funding
This research was funded by University of Surabaya.

Conflicts of Interest
The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

Abka-khajouei, R., Tounsi, L., Shahabi, N., Patel, A. K., Abdelkafi, S., & Michaud, P. (2022). Structures, Properties and Applications of Alginates. *Marine Drugs*, *20*(6), 364. https://doi.org/10.3390/md20060364

Al-Hamayda, A., Abu-Jdayil, B., Ayyash, M., & Tannous, J. (2023). Advances in microencapsulation techniques using Arabic gum: A comprehensive review. *Industrial Crops and Products*, *205*, 117556. https://doi.org/10.1016/j.indcrop.2023.117556

Aldoghachi, F. E. H., Noor Al-Mousawi, U. M., & Shari, F. H. (2021). Antioxidant Activity of Rosmarinic Acid Extracted and Purified from Mentha piperita. *Archives of Razi Institute*, *76*(5), 1279–1287. https://doi.org/10.22092/ari.2021.356072.1770

Azarpazhooh, E., Sharayei, P., Zomorodi, S., & Ramaswamy, H. S. (2019). Physicochemical and Phytochemical Characterization and Storage Stability of Freeze-dried Encapsulated Pomegranate Peel Anthocyanin and In Vitro Evaluation of Its Antioxidant Activity. *Food and Bioprocess Technology*, *12*(2), 199–210. https://doi.org/10.1007/s11947-018-2195-1

Balasubramaniam, M. P., Murugan, P., Chenthamara, D., Ramakrishnan, S. G., Salim, A., Lin, F.-H., Robert, B., & Subramaniam, S. (2020). Synthesis of chitosan-ferulic acid conjugated poly(vinyl alcohol) polymer film for an improved wound healing. *Materials Today Communications*, *25*, 101510. https://doi.org/10.1016/j.mtcomm.2020.101510

Ballesteros, L. F., Ramirez, M. J., Orrego, C. E., Teixeira, J. A., & Mussatto, S. I. (2017). Encapsulation of antioxidant phenolic compounds extracted from spent coffee grounds by freeze-drying and spray-drying using different coating materials. *Food Chemistry*, *237*, 623–631. https://doi.org/10.1016/j.foodchem.2017.05.142

Barbu, V., Enachi, E., Andronoiu, D. G., Râpeanu, G., Stoica, M., Dumitraşcu, L., Stănciuc, N., & Mihalcea, L. (2020). Microencapsulation of Red Grape Juice by Freeze Drying and Application in Jelly Formulation. *Food Technology and Biotechnology*, *58*(1), 20–28. https://doi.org/10.17113/ftb.58.01.20.6429

Bergonzi, M. C., De Stefani, C., Vasarri, M., Ivanova Stojcheva, E., Ramos-Pineda, A. M., Baldi, F., Bilia, A. R., & Degl'Innocenti, D. (2023). Encapsulation of Olive Leaf Polyphenol-Rich Extract in Polymeric Micelles to Improve Its Intestinal Permeability. *Nanomaterials*, *13*(24), 3147. https://doi.org/10.3390/nano13243147

Bińkowska, W., Szpicer, A., Stelmasiak, A., Wojtasik-Kalinowska, I., & Półtorak, A. (2024). Microencapsulation of Polyphenols and Their Application in Food Technology. *Applied Sciences*, *14*(24), 11954. https://doi.org/10.3390/app142411954

Chu, J. N., & Traverso, G. (2022). Foundations of gastrointestinal-based drug delivery and future developments. *Nature Reviews Gastroenterology and Hepatology*, *19*(4), 219–238. https://doi.org/10.1038/s41575-021-00539-w

Cid-Ortega, S., & Guerrero-Beltran, J. A. (2022). Lyophilized Powder of Hibiscus sabdariffa (Roselle) Extracts using Gum Arabic and Maltodextrin as Carrier Agents. *Journal of Food Research*, *11*(2), 1. https://doi.org/10.5539/jfr.v11n2p1

da Silva Júnior, M. E., Araújo, M. V. R. L., Martins, A. C. S., dos Santos Lima, M., da Silva, F. L. H., Converti, A., & Maciel, M. I. S. (2023). Microencapsulation by

spray-drying and freeze-drying of extract of phenolic compounds obtained from ciriguela peel. *Scientific Reports*, *13*(1), 41598–023–40390–4. https://doi.org/10.1038/s41598-023-40390-4

Dadi, D. W., Emire, S. A., Hagos, A. D., & Eun, J.-B. (2020). Physical and Functional Properties, Digestibility, and Storage Stability of Spray- and Freeze-Dried Microencapsulated Bioactive Products from Moringa stenopetala Leaves Extract. *Industrial Crops and Products*, *156*, 112891. https://doi.org/10.1016/j.indcrop.2020.112891

de Rodríguez, D. J., Puente-Romero, G. N., Díaz-Jiménez, L., Rodríguez-García, R., Ramírez-Rodríguez, H., Villarreal-Quintanilla, J. A., Flores-López, M. L., Carrillo-Lomelí, D. A., & Genisheva, Z. A. (2019). In vitro gastrointestinal digestion of microencapsulated extracts of Flourensia cernua, F. microphylla, and F. retinophylla. *Industrial Crops and Products*, *138*, 111444. https://doi.org/10.1016/j.indcrop.2019.06.007

Dubey, S. K., Parab, S., Achalla, V. P. K., Narwaria, A., Sharma, S., Jaswanth Gowda, B. H., & Kesharwani, P. (2022). Microparticulate and nanotechnology mediated drug delivery system for the delivery of herbal extracts. *Journal of Biomaterials Science, Polymer Edition*, *33*(12), 1531–1554. https://doi.org/10.1080/09205063.2022.2065408

Fernández-Luqueño, F., Medina-Pérez, G., Pérez-Soto, E., Espino-Manzano, S., Peralta-Adauto, L., Pérez-Ríos, S., & Campos-Montiel, R. (2021). Bioactive Compounds of Opuntia spp. Acid Fruits: Micro and Nano-Emulsified Extracts and Applications in Nutraceutical Foods. *Molecules*, *26*(21), 6429. https://doi.org/10.3390/molecules26216429

Fredes, C., Becerra, C., Parada, J., & Robert, P. (2018). The Microencapsulation of Maqui (Aristotelia chilensis (Mol.) Stuntz) Juice by Spray-Drying and Freeze-Drying Produces Powders with Similar Anthocyanin Stability and Bioaccessibility. *Molecules*, *23*(5), 1227. https://doi.org/10.3390/molecules23051227

Frenţ, O.-D., Stefan, L., Morgovan, C. M., Duteanu, N., Dejeu, I. L., Marian, E., Vicaş, L., & Manole, F. (2024). A Systematic Review: Quercetin—Secondary Metabolite of the Flavonol Class, with Multiple Health Benefits and Low Bioavailability. *International Journal of Molecular Sciences*, *25*(22), 12091. https://doi.org/10.3390/ijms252212091

Girma, B., Gure, A., & Wedajo, F. (2020). Influence of Altitude on Caffeine, 5-Caffeoylquinic Acid, and Nicotinic Acid Contents of Arabica Coffee Varieties. *Journal of Chemistry*, *2020*, 1–7. https://doi.org/10.1155/2020/3904761

González-Ortega, R., Faieta, M., Di Mattia, C. D., Valbonetti, L., & Pittia, P. (2020). Microencapsulation of olive leaf extract by freeze-drying: Effect of carrier composition on process efficiency and technological properties of the powders. *Journal of Food Engineering*, *285*, 110089. https://doi.org/10.1016/j.jfoodeng.2020.110089

González, E., Gómez-Caravaca, A. M., Giménez, B., Cebrián, R., Maqueda, M., Martínez-Férez, A., Segura-Carretero, A., & Robert, P. (2019). Evolution of the phenolic compounds profile of olive leaf extract encapsulated by spray-drying during in vitro gastrointestinal digestion. *Food Chemistry*, *279*, 40–48. https://doi.org/10.1016/j.foodchem.2018.11.127

Grgić, J., Šelo, G., Planinić, M., Tišma, M., & Bucić-Kojić, A. (2020). Role of the Encapsulation in Bioavailability of Phenolic Compounds. *Antioxidants*, *9*(10), 923. https://doi.org/10.3390/antiox9100923

Guo, X., Zuo, X., Zhou, Z., Gu, Y., Zheng, H., Wang, X., Wang, G., Xu, C., & Wang, F. (2023). PLGA-Based Micro/Nanoparticles: An Overview of Their Applications in Respiratory Diseases. *International Journal of Molecular Sciences*, *24*(5), 4333. https://doi.org/10.3390/ijms24054333

Ishwarya S., P., R., S., & Nisha, P. (2022). Advances and prospects in the food applications of pectin hydrogels. *Critical Reviews in Food Science and Nutrition*, *62*(16), 4393–4417. https://doi.org/10.1080/10408398.2021.1875394

Kamaruddin, Edikresnha, D., Sriyanti, I., Munir, M. M., & Khairurrijal. (2017). Synthesis of Polyvinylpyrrolidone (PVP)-Green Tea Extract Composite Nanostructures using Electrohydrodynamic Spraying Technique. *IOP Conference Series: Materials Science and Engineering*, *202*, 012043. https://doi.org/10.1088/1757-899X/202/1/012043

Kandasamy, S., & Naveen, R. (2022). A review on the encapsulation of bioactive components using spray-drying and freeze-drying techniques. *Journal of Food Process Engineering*, *45*(8). https://doi.org/10.1111/jfpe.14059

Kasaai, M. R. (2018). Zein and zein -based nano-materials for food and nutrition applications: A review. *Trends in Food Science & Technology*, *79*, 184–197. https://doi.org/10.1016/j.tifs.2018.07.015

Khalesi, H., Zhao, Y., Sun, C., Lu, W., Cao, Y., Zhang, Y., Kadkhodaee, R., & Fang, Y. (2024). Influence of amyloid fibril length and ionic strength on WPI-based fiber-hydrogel composites: Microstructural, rheological and water holding properties. *Food Hydrocolloids*, *148*, 109499. https://doi.org/10.1016/j.foodhyd.2023.109499

Khojasteh, A., Mirjalili, M. H., Alcalde, M. A., Cusido, R. M., Eibl, R., & Palazon, J. (2020). Powerful Plant

Antioxidants: A New Biosustainable Approach to the Production of Rosmarinic Acid. *Antioxidants*, *9*(12), 1273. https://doi.org/10.3390/antiox9121273

Khotimah, H., Agustina, R., & Ardana, M. (2018). Pengaruh Lama Penyimpanan Terhadap Aktivitas Antioksidan Ekstrak Daun Miana (Coleus atropurpureus L. Benth). *Proceeding of Mulawarman Pharmaceuticals Conferences*, *8*, 1–7. https://doi.org/10.25026/mpc.v8i1.295

Liu, Y., Chen, Y., Gao, X., Fu, J., & Hu, L. (2022). Application of cyclodextrin in food industry. *Critical Reviews in Food Science and Nutrition*, *62*(10), 2627–2640. https://doi.org/10.1080/10408398.2020.1856035

Macías-Cortés, E., Gallegos-Infante, J. A., Rocha-Guzmán, N. E., Moreno-Jiménez, M. R., Medina-Torres, L., & González-Laredo, R. F. (2019). Microencapsulation of phenolic compounds: Technologies and novel polymers. *Revista Mexicana de Ingeniería Química*, *19*(2), 491–521. https://doi.org/10.24275/rmiq/Alim642

Mar, J. M., Silva, L. S., Rabelo, M. da S., Muniz, M. P., Nunomura, S. M., Correa, R. F., Kinupp, V. F., Campelo, P. H., Bezerra, J. de A., & Sanches, E. A. (2020). Encapsulation of Amazonian Blueberry juices: Evaluation of bioactive compounds and stability. *LWT*, *124*, 109152. https://doi.org/10.1016/j.lwt.2020.109152

Martínez, E., Gamboa, J., Finkielstein, C. V, Cañas, A. I., Osorio, M. A., Vélez, Y., Llinas, N., & Castro, C. I. (2025). Oral dosage forms for drug delivery to the colon: an existing gap between research and commercial applications. *Journal of Materials Science: Materials in Medicine*, *36*(1), 24. https://doi.org/10.1007/s10856-025-06868-5

Martinović, J., Ambrus, R., Planinić, M., Šelo, G., Klarić, A.-M., Perković, G., & Bucić-Kojić, A. (2024). Microencapsulation of Grape Pomace Extracts with Alginate-Based Coatings by Freeze-Drying: Release Kinetics and In Vitro Bioaccessibility Assessment of Phenolic Compounds. *Gels*, *10*(6), 353. https://doi.org/10.3390/gels10060353

Massounga Bora, A. F., Ma, S., Li, X., & Liu, L. (2018). Application of microencapsulation for the safe delivery of green tea polyphenols in food systems: Review and recent advances. *Food Research International*, *105*, 241–249. https://doi.org/10.1016/j.foodres.2017.11.047

Medina-Torres, L., Núñez-Ramírez, D. M., Calderas, F., González-Laredo, R. F., Minjares-Fuentes, R., Valadez-García, M. A., Bernad-Bernad, M. J., & Manero, O. (2019). Microencapsulation of gallic acid by spray drying with aloe vera mucilage (aloe barbadensis miller) as wall material. *Industrial Crops and Products*, *138*, 111461. https://doi.org/10.1016/j.indcrop.2019.06.024

Mohammadbaghban, E., Taravati, A., Najafzadehvarzi, H., Khaleghzadeh-Ahangar, H., & Tohidi, F. (2024). Oral administration of encapsulated catechin in chitosan-alginate nanoparticles improves cognitive function and neurodegeneration in an aluminum chloride-induced rat model of Alzheimer's disease. *Physiological Reports*, *12*(13), 16095. https://doi.org/10.14814/phy2.16095

Morais, S. M., Calixto-Júnior, J. T., Ribeiro, L. M., Sousa, H. A., Silva, A. A. S., Figueiredo, F. G., Matias, E. F. F., Boligon, A. A., Athayde, M. L., Morais-Braga, M. F. B., & Coutinho, H. D. M. (2017). Phenolic composition and antioxidant, anticholinesterase and antibiotic-modulating antifungal activities of Guazuma ulmifolia Lam. (Malvaceae) ethanol extract. *South African Journal of Botany*, *110*, 251–257. https://doi.org/10.1016/j.sajb.2016.08.003

Muadifah, A., Isma, E. A., & Putri, A. E. (2022). Analisis Mutu Aktivitas Antioksidan Fraksi Daun Miana (Coleus artropurpureus L. Benth) Terhadap Masa Simpan Permen Jelly. *Stikes Karya Putra Bangsa*, *19*, 2003–2005. Retrieved from http://repository.stikes-kartrasa.ac.id/133/

Nguyen, Q.-D., Dang, T.-T., Nguyen, T.-V.-L., Nguyen, T.-T.-D., & Nguyen, N.-N. (2022). Microencapsulation of roselle (Hibiscus sabdariffa L.) anthocyanins: Effects of different carriers on selected physicochemical properties and antioxidant activities of spray-dried and freeze-dried powder. *International Journal of Food Properties*, *25*(1), 359–374. https://doi.org/10.1080/10942912.2022.2044846

Ozkan, G., Ceyhan, T., Çatalkaya, G., Rajan, L., Ullah, H., Daglia, M., & Capanoglu, E. (2024). Encapsulated phenolic compounds: clinical efficacy of a novel delivery method. *Phytochemistry Reviews*, *23*(3), 781–819. https://doi.org/10.1007/s11101-023-09909-5

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*, *372*, *n71*, n71. https://doi.org/10.1136/bmj.n71

Pattnaik, M., Pandey, P., Martin, G. J. O., Mishra, H. N., & Ashokkumar, M. (2021). Innovative Technologies for Extraction and Microencapsulation of Bioactives from Plant-Based Food Waste and Their Applications in Functional

Food Development. *Foods*, *10*(2), 279. https://doi.org/10.3390/foods10020279

Pchelkina, V., Chernukha, I., Nikitina, M., & Ilin, N. (2023). Pig adipose tissue of two different breeds and locations: morphology and Raman studies. *Foods and Raw Materials*, 1–9. https://doi.org/10.21603/2308-4057-2023-1-547

Peanparkdee, M., Borompichaichartkul, C., & Iwamoto, S. (2021). Bioaccessibility and antioxidant activity of phenolic acids, flavonoids, and anthocyanins of encapsulated Thai rice bran extracts during in vitro gastrointestinal digestion. *Food Chemistry*, *361*, 130161. https://doi.org/10.1016/j.foodchem.2021.130161

Petrovic, S. M., & Barbinta-Patrascu, M.-E. (2023). Organic and Biogenic Nanocarriers as Bio-Friendly Systems for Bioactive Compounds' Delivery: State-of-the Art and Challenges. *Materials*, *16*(24), 7550. https://doi.org/10.3390/ma16247550

Ran, Y., Li, F., Xu, Z., Zeng, K., & Ming, J. (2024). Recent advances in dietary polyphenols (DPs): antioxidant activities, nutrient interactions, delivery systems, and potential applications. *Food & Function*, *15*(20), 10213–10232. https://doi.org/10.1039/D4FO02111H

Remígio, M. S. do N., Greco, T., Silva Júnior, J. O. C., Converti, A., Ribeiro-Costa, R. M., Rossi, A., & Barbosa, W. L. R. (2024). Spray-Drying Microencapsulation of Bauhinia ungulata L. var. obtusifolia Aqueous Extract Containing Phenolic Compounds: A Comparative Study Using Different Wall Materials. *Pharmaceutics*, *16*(4), 488. https://doi.org/10.3390/pharmaceutics16040488

Salem, Y., Sunoqrot, S., Rajha, H. N., Abusulieh, S., Afif, C., Francis, H., Touma, J. A., Louka, N., & Maroun, R. G. (2024). Grape seed phenolic extracts encapsulation in polymeric nanoparticles: Characterization and in vitro evaluation against skin melanoma. *Journal of Drug Delivery Science and Technology*, *100*, 106094. https://doi.org/10.1016/j.jddst.2024.106094

Secretan, P.-H., Thirion, O., Sadou Yayé, H., Damy, T., Astier, A., Paul, M., & Do, B. (2021). Simple Approach to Enhance Green Tea Epigallocatechin Gallate Stability in Aqueous Solutions and Bioavailability: Experimental and Theoretical Characterizations. *Pharmaceuticals*, *14*(12), 1242. https://doi.org/10.3390/ph14121242

Shaygannia, S., Eshaghi, M. R., Fazel, M., & Hashemiravan, M. (2021). The Effect of Microencapsulation of Phenolic Compounds from Lemon Waste by Persian and Basil Seed Gums on the Chemical and Microbiological Properties of Mayonnaise. *Preventive Nutrition and Food Science*, *26*(1), 82–91. https://doi.org/10.3746/pnf.2021.26.1.82

Sheng, F., Chow, P. S., Hu, J., Cheng, S., Guo, L., & Dong, Y. (2020). Preparation of quercetin nanorod/microcrystalline cellulose formulation via fluid bed coating crystallization for dissolution enhancement. *International Journal of Pharmaceutics*, *576*, 118983. https://doi.org/10.1016/j.ijpharm.2019.118983

Shu, D., Liu, Y., Xu, J., & Yuan, Y. (2025). Carrier design based on zein: From the perspectives of multi-molecule encapsulation, probiotic encapsulation, and application standards. *Current Research in Food Science*, *11*, 101145. https://doi.org/10.1016/j.crfs.2025.101145

Siddiqui, S. A., Singh, P., Utama, D. T., Samatra, M. Y., Ahmad, A., & Wani, S. A. (2024). RETRACTED: Encapsulation of bioactive compounds in foods for diabetics - sources, encapsulation technologies, market trends and future perspectives – A systematic review. *Food and Bioproducts Processing*, *147*, 277–303. https://doi.org/10.1016/j.fbp.2024.07.007

Singh, A. K., Singla, R. K., & Pandey, A. K. (2023). Chlorogenic Acid: A Dietary Phenolic Acid with Promising Pharmacotherapeutic Potential. *Current Medicinal Chemistry*, *30*(34), 3905–3926. https://doi.org/10.2174/0929867329666220816154634

Soliman, T. N., Mohammed, D. M., El-Messery, T. M., Elaaser, M., Zaky, A. A., Eun, J.-B., Shim, J.-H., & El-Said, M. M. (2022). Microencapsulation of Plant Phenolic Extracts Using Complex Coacervation Incorporated in Ultrafiltered Cheese Against AlCl3-Induced Neuroinflammation in Rats. *Frontiers in Nutrition*, *9*, 929977. https://doi.org/10.3389/fnut.2022.929977

Ştefănescu, B. E., Nemes, S.-A., Teleky, B.-E., Călinoiu, L. F., Mitrea, L., Martău, G. A., Szabo, K., Mihai, M., Vodnar, D. C., & Crişan, G. (2022). Microencapsulation and Bioaccessibility of Phenolic Compounds of Vaccinium Leaf Extracts. *Antioxidants*, *11*(4), 674. https://doi.org/10.3390/antiox11040674

Ştefănescu, B. E., Szabo, K., Mocan, A., & Crişan, G. (2019). Phenolic Compounds from Five Ericaceae Species Leaves and Their Related Bioavailability and Health Benefits. *Molecules*, *24*(11), 2046. https://doi.org/10.3390/molecules24112046

Tatasciore, S., Santarelli, V., Neri, L., González Ortega, R., Faieta, M., Di Mattia, C. D., Di Michele, A., & Pittia, P. (2023). Freeze-Drying Microencapsulation of Hop Extract: Effect of Carrier Composition on Physical, Techno-Functional, and Stability Properties. *Antioxidants*, *12*(2), 442. https://doi.org/10.3390/antiox12020442

Tran, T. T. A., & Nguyen, H. V. H. (2018). Effects of spray-drying temperatures and carriers on physical and antioxidant properties of lemongrass leaf extract powder. *Beverages*, *4*(4), 84. https://doi.org/10.3390/beverages4040084

Trifković, K., Đorđević, V., Balanč, B., Kalušević, A., Lević, S., Bugarski, B., & Nedović, V. (2016). Novel approaches in nanoencapsulation of aromas and flavors. In *Encapsulations* (pp. 363–419). Elsevier. https://doi.org/10.1016/B978-0-12-804307-3.00009-0

Tülek, Z., Alaşalvar, H., Başyiğit, B., Berktas, S., Salum, P., Erbay, Z., Telci, I., & Çam, M. (2021). Extraction optimization and microencapsulation of phenolic antioxidant compounds from lemon balm (Melissa officinalis L.): Instant soluble tea production. *Journal of Food Processing and Preservation*, *45*(1). https://doi.org/10.1111/jfpp.14995

Wang, J., Zhang, X., Li, S., Zhang, T., Sui, W., Zhang, M., Yang, S., & Chen, H. (2024). Physical properties, phenolic profile and antioxidant capacity of Java tea (Clerodendranthus spicatus) stems as affected by steam explosion treatment. *Food Chemistry*, *440*, 138190. https://doi.org/10.1016/j.foodchem.2023.138190

Wathoni, N., Nguyen, A. N., Rusdin, A., Umar, A. K., Mohammed, A. F. A., Motoyama, K., Joni, I. M., & Muchtaridi, M. (2020). Enteric-Coated Strategies in Colorectal Cancer Nanoparticle Drug Delivery System. *Drug Design, Development and Therapy*, *Volume 14*, 4387–4405. https://doi.org/10.2147/DDDT.S273612

Ways, T. M., Lau, W., & Khutoryanskiy, V. (2018). Chitosan and Its Derivatives for Application in Mucoadhesive Drug Delivery Systems. *Polymers*, *10*(3), 267. https://doi.org/10.3390/polym10030267

Yadav, K., Bajaj, R. K., Mandal, S., & Mann, B. (2020). Encapsulation of grape seed extract phenolics using whey protein concentrate, maltodextrin and gum arabica blends. *Journal of Food Science and Technology*, *57*(2), 426–434. https://doi.org/10.1007/s13197-019-04070-4

Yousefi, M., Shadnoush, M., Sohrabvandi, S., Khorshidian, N., Amir, M., & Mortazavian. (2021). Encapsulation Systems for Delivery of Flavonoids: A Review. *Biointerface Research in Applied Chemistry*, *11*(6), 13934–13951. https://doi.org/10.33263/BRIAC116.1393413951

Zanoni, F., Primiterra, M., Angeli, N., & Zoccatelli, G. (2020). Microencapsulation by spray-drying of polyphenols extracted from red chicory and red cabbage: Effects on stability and color properties. *Food Chemistry*, *307*, 125535. https://doi.org/10.1016/j.foodchem.2019.125535

Zokti, J., Sham Baharin, B., Mohammed, A., & Abas, F. (2016). Green Tea Leaves Extract: Microencapsulation, Physicochemical and Storage Stability Study. *Molecules*, *21*(8), 940. https://doi.org/10.3390/molecules21080940