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Review

Extraction and Purification of Catechins from Tea Leaves: An Overview of Methods, Advantages, and Disadvantages

Oana Cioanca [1], Ionut-Iulian Lungu [2,*], Ioana Mita-Baciu [3], Silvia Robu [4], Ana Flavia Burlec [5], Monica Hancianu [1] and Florina Crivoi [6]

[1] Department of Pharmacognosy, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania; oana.cioanca@umfiasi.ro (O.C.); monica.hancianu@umfiasi.ro (M.H.)
[2] Department of General and Inorganic Chemistry, Faculty of Pharmacy, "Grigore. T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania
[3] Department of Pharmacology, Faculty of Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania; ioana-alexandra.humulescu@umfiasi.ro
[4] Department of Pharmacognosy, Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, 35 Al. I. Cuza Street, 800216 Galati, Romania; silvia.robu@ugal.ro
[5] Department of Drug Analysis, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, 16 University Street, 700115 Iasi, Romania; ana-flavia.l.burlec@umfiasi.ro
[6] Department of Pharmaceutical Physics, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, 16 University Street, 700115 Iasi, Romania; florina.crivoi@umfiasi.ro
* Correspondence: ionut-iulian.lungu@umfiasi.ro; Tel.: +40-743308128

Abstract: This review study explores the complex methods involved in the extraction and purification of polyphenols, specifically catechins, prominent compounds that are bioactive and found in plant-based extracts and foods like tea. This study also addresses the challenges that may arise from the complex chemical structure of catechins and their inherent variability across botanical sources. Despite these shortcomings and obstacles, catechins and catechin derivatives present significant potential, particularly in healthcare but also in the food industry. Their enhanced antioxidant properties have been exhaustively investigated and associated with countless health benefits, making them promising agents with numerous applications, most notably in healthcare against chronic diseases. Furthermore, catechins have numerous applications across various industries, including food and beverage, cosmetics, agriculture, and materials science. This review is a compilation of the most notable and recent research found in the literature and emphasizes the importance of continued research and innovation in catechin separation, extraction, and utilization, which hold promise for advancing human health and technological progress across multiple domains.

Keywords: catechins; HPLC; extraction methods; purification; tea polyphenols

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1. Introduction

Catechins, a class of polyphenolic compounds predominantly found in tea, particularly green tea, have garnered substantial scientific interest in recent years owing to their diverse physiological effects and potential therapeutic applications [1]. These bioactive molecules, characterized by their antioxidant properties, are part of the flavonoid family and are present in various plant-based foods like cocoa, berries, and apples. Catechins' chemical structure, comprising two benzene rings linked by a dihydropyran heterocycle, enables them to scavenge free radicals and reactive oxygen species, thus mitigating oxidative stress and its associated health risks [2].

Catechins (Figure 1) are characterized by a flavan-3-ol framework featuring two aromatic rings linked by a three-carbon bridge. The fundamental catechin structure includes two phenolic hydroxyl groups positioned on adjacent carbon atoms, resulting in a catechol moiety—the origin of the term "catechin". The positioning of hydroxyl groups on the B-ring of the catechin molecule significantly influences its chemical and biological attributes [3].

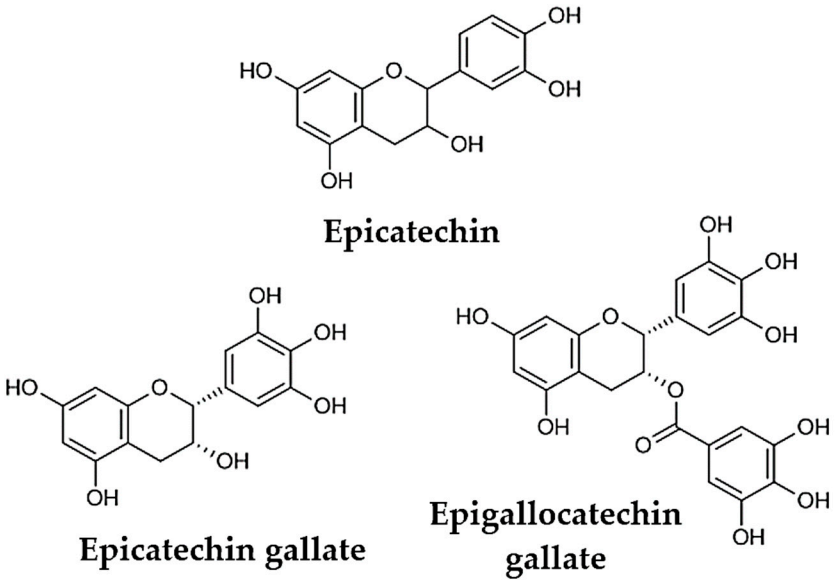

Figure 1. Catechins and their specific structures.

The importance of separating catechins from plant extracts cannot be overstated, particularly in scientific research and industrial applications. Catechins, a subclass of flavonoids, possess diverse bioactive properties and are widely recognized for their potential health benefits, ranging from antioxidant and anti-inflammatory effects to cardiovascular protection and cancer prevention. However, the efficacy of catechins hinges on their purity and concentration, which necessitates precise separation techniques [4].

Separating catechins from plant extracts is essential for several reasons. Firstly, it enables the isolation of individual compounds, allowing researchers to study their specific biological activities and mechanisms of action. By purifying catechins from complex mixtures, scientists can elucidate their pharmacological properties and explore their therapeutic potential in various disease models [5].

Separating catechins facilitates accurate quantification, which is essential for determining their concentration in plant materials and commercial products. High-quality analytical data are crucial for assessing the potency and consistency of catechin-rich supplements, ensuring their efficacy and safety for consumers. Additionally, precise quantification enables researchers to establish dose–response relationships and optimize therapeutic interventions in clinical studies [6].

The separation of catechins from plant extracts is indispensable for quality control and standardization in the food and beverage industry. Whether in green tea, cocoa, or dietary supplements, catechin content directly impacts the nutritional value and health claims of products. By employing validated separation methods, manufacturers can ensure the authenticity and potency of catechin-containing ingredients, meeting regulatory requirements and consumer expectations for natural antioxidants.

The importance of separating catechins from plant extracts lies in its fundamental role in scientific research, industrial production, and product quality assurance. By employing sophisticated separation techniques such as chromatography, researchers and manufacturers can unlock the full potential of catechins, harnessing their health-promoting properties for the benefit of human health and well-being [7,8].

By adhering to stringent regulatory standards for pharmaceutical use, purification processes ensure that catechin extracts meet exacting criteria for purity, safety, and efficacy. This regulatory adherence underscores the commitment of pharmaceutical firms to delivering products of the utmost quality and integrity [9,10].

Purified catechins serve as invaluable assets in drug development endeavors, offering promising starting points for the creation of novel drugs and formulations. The literature does not report any catechin-based or drugs derived from catechins and only highlights

the use of catechins in preventive care and as dietary supplements. Their diverse biological activities present opportunities for innovation in addressing a wide spectrum of diseases and health conditions.

In conclusion, the meticulous separation and purification of catechins for pharmaceutical purposes represent a cornerstone in the pursuit of safer, more effective, and reliable therapeutic interventions. This dedication to quality and innovation ultimately benefits patients and contributes to the advancement of healthcare practices on a broader scale.

2. Materials and Methods

A thorough exploration of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, was conducted to identify pertinent studies. The search utilized keywords such as "catechins", "flavonoids", "green tea", "health benefits", "isolation", and "separation". This search strategy aimed to encompass articles, reviews, and meta-analyses focusing on catechins' physiological effects, mechanisms of action, and therapeutic potential.

Studies meeting the following criteria were included: discussion of methods for catechins' isolation and purification. Only articles written in English and published in peer-reviewed journals were considered. Both preclinical and clinical studies were incorporated to provide a comprehensive overview. No limitations were set on the publication date to encompass a wide range of research findings. More than 250 articles were found; however, we selected only 128 that contained all the information for the present study. A two-stage screening process was implemented, where first articles were searched using programs like Google Scholar, PudMed, and ScienceDirect, analyzing their titles and abstracts to identify relevant data. After which, in the second stage, full-text analysis was conducted to ensure that they met all selection criteria.

Relevant data, including study design, participant characteristics, intervention details, outcomes measured, and key findings, were extracted from eligible studies. Data extraction was performed by multiple reviewers, and certain standards, such as clinical trials, relevancy, and novelty, were set in place to ensure consistency. These data were synthesized to offer an overview of catechins' physiological effects, therapeutic potential, and methods for their isolation and purification from plant extracts.

Descriptive analysis, both qualitative and quantitative, like meta-analysis, was employed to synthesize the findings of included studies, with a focus on studies about the extraction and separation of catechins from different plant extracts. Through qualitative synthesis, key themes and trends were identified. Where applicable, quantitative data were summarized using tables, figures, and narrative synthesis. The synthesized findings are presented to provide insights into the current understanding of catechins and to guide future research and clinical applications.

3. Results

The process of separating catechins from tea leaves using different methods (Table 1) is a captivating exploration of the intricate chemistry underlying this beloved beverage.

Catechins are well-known for their antioxidant properties and health benefits, making them a subject of interest for researchers and tea enthusiasts alike. Understanding how various solvents interact with tea leaves to extract these valuable compounds sheds light on the complexity of tea chemistry and its potential applications in health and wellness [11].

It is important to begin by acknowledging the composition of tea leaves, which contain a range of chemical compounds such as catechins, caffeine, tannins, and volatile oils, each with its own solubility characteristics. Catechins, being polyphenolic compounds, exhibit different levels of solubility in various solvents based on factors like polarity, temperature, and pH.

Table 1. The different techniques employed in catechin separation.

Technique	Description	Advantages	Disadvantages
HPLC (High-Performance Liquid Chromatography)	Separates catechins based on differences in polarity and interaction with stationary phase.	High resolution and sensitivity	Requires expensive equipment and consumables
		Wide range of column and solvent options	Time-consuming analysis
		Quantitative analysis capability	
TLC (Thin-Layer Chromatography)	Separates catechins on a thin layer of adsorbent material, often silica gel, based on polarity.	Simple, inexpensive setup	Lower resolution compared to HPLC
		Rapid screening of samples	Less quantitative compared to HPLC
		Visual detection of separated compounds	
SFE (Supercritical Fluid Extraction)	Extracts total catechins using supercritical fluids, typically CO_2, which offers tunable selectivity.	Selective extraction of target compounds	Requires specialized equipment and expertise
		Environmentally friendly process	High initial setup costs
		Can be combined with other separation techniques	Limited scalability

3.1. Solvent Systems for Multi-Stage Separations

One commonly utilized solvent for extracting catechins is water, particularly hot water, typically used in traditional tea brewing methods. The heat aids in breaking down the cell walls of tea leaves, facilitating the release of catechins into the water. However, the efficiency of extraction may vary depending on steeping duration and agitation, potentially resulting in the extraction of bitter-tasting compounds like tannins [12]. Figure 2 illustrates a general method used for the solvent-based extraction of catechins.

While water serves as the conventional solvent for extracting phenolics from tea, alternative non-polar green solvents like butanol, ethyl acetate, and ethanol have been noted for their efficacy in extracting polyphenols and decaffeinating [11].

Another solvent employed for catechin extraction is ethanol, known for its ability to dissolve a wide range of organic compounds including catechins. Immersing tea leaves in ethanol can lead to more efficient catechin extraction compared to water alone, particularly at higher ethanol concentrations. Nevertheless, ethanol extraction may also draw out undesirable compounds, such as caffeine, impacting the flavor of the final extract.

In a study, ethanol at a concentration of 95% (v/v) was deemed the optimal solvent for extracting polyphenols, while ethyl acetate was utilized to concentrate the catechins obtained from rapidly mechanically extracted tea leaf juice [13].

Decaffeination is an important part of separating catechins from green tea. The decaffeination process involves the use of four equal volumes of chloroform at 60 °C. Following this, an EGCG-rich aqueous fraction is acquired through the partitioning of the decaffeinated fraction with ethyl hexanoate and subsequent partitioning of the EGCG-rich aqueous fraction using propyl acetate. The solvent is then evaporated from the solution, leaving behind residues that are dissolved in water and freeze-dried to obtain the powdered form. This method is utilized for purifying EGCG from green tea, resulting in an approximate 80% purity of EGCG [14].

Moreover, organic solvents like acetone or methanol have been investigated for catechin extraction due to their higher solubility compared to water, potentially resulting

in extracts with elevated catechin concentrations. However, concerns about safety and environmental impact arise with the use of organic solvents, especially in food and beverage applications.

Additionally, supercritical fluid extraction (SFE) has emerged as a promising method for catechin extraction. In SFE, carbon dioxide is pressurized above its critical point to act as a solvent. Supercritical CO_2 possesses both gas-like and liquid-like properties, effectively penetrating tea leaves and dissolving catechins. SFE offers advantages such as higher selectivity, reduced solvent usage, and minimal environmental impact compared to traditional organic solvents [15].

Each solvent and extraction technique presents its own set of advantages and limitations, with the choice depending on factors like desired purity, efficiency, safety, and environmental concerns. Furthermore, catechin-rich solutions obtained from extraction can undergo further processing using methods such as chromatography or filtration to isolate and purify specific catechin compounds for various applications, including dietary supplements, functional foods, and pharmaceuticals [16].

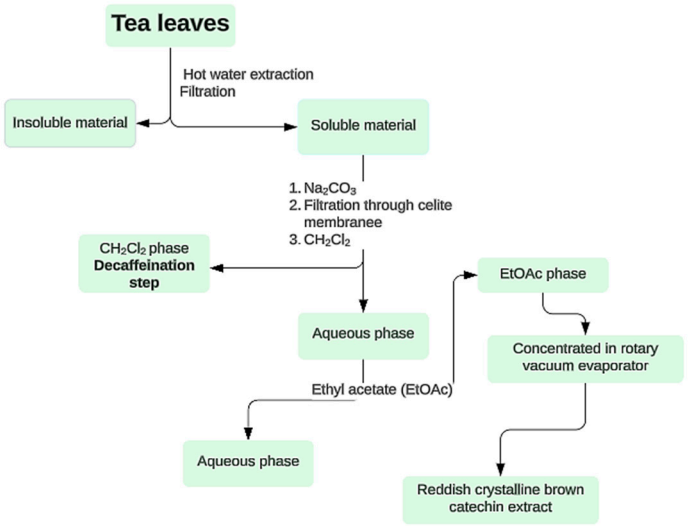

Figure 2. General method for extracting and separating catechins from tea leaves [17].

3.2. Complex Methods and Instrumentation for Separation

Tea contains a multitude of polyphenols with varying compositions. In addition to the usual major types, there are numerous trace and unidentified polyphenols in tea. Consequently, it is imperative to discuss analytical methods for tea polyphenol compounds based on specific analytical needs. The determination of tea polyphenols can be categorized into two groups based on different quantitative and qualitative requirements: total polyphenols and individual polyphenols in tea. As depicted in Figure 3, methods for analyzing total tea polyphenols encompass titration, spectrophotometry, near-infrared spectroscopy, electrochemical techniques, etc. Among these, spectrophotometry stands out as the most commonly utilized, often following international standard protocols.

Separating catechins from plant extracts provides numerous advantages in both research and industrial applications. Firstly, isolating catechins allows for a more focused investigation into their specific health benefits and mechanisms of action [18].

Analytical chemistry provides a diverse range of techniques for extracting and separating catechins, vital bioactive compounds found abundantly in various plant sources, particularly tea leaves. Among these methods are electrochemical analysis, infrared spectroscopy, titration, and spectrophotometry, each offering distinct advantages and limitations in catechin analysis.

Electrochemical analysis stands out for its remarkable sensitivity and selectivity, enabling precise quantification of catechins in complex matrices. Techniques like cyclic voltam-

metry and amperometry allow real-time monitoring of catechin oxidation or reduction processes, providing valuable insights into their electrochemical behavior. Nevertheless, challenges such as electrode fouling and interference from other compounds require careful method optimization [19,20].

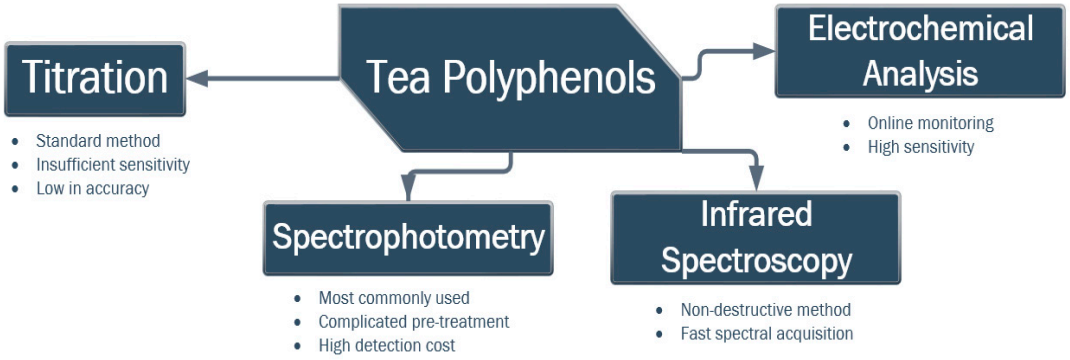

Figure 3. Different methods for analyzing tea polyphenols, their advantages and disadvantages.

Infrared spectroscopy offers a swift and non-destructive approach to catechin identification based on molecular vibrations. By measuring the absorption of infrared radiation, specific functional groups within catechins can be identified, facilitating qualitative analysis. Despite its usefulness in structural elucidation, infrared spectroscopy may lack the sensitivity required for quantification, especially in trace analysis scenarios.

Titration methods, particularly those involving complexation or oxidation-reduction reactions, provide robust quantitative determination of catechins. For instance, the Folin–Ciocalteu assay relies on the reduction of a chromogenic reagent by catechins, resulting in a colored product whose intensity correlates with catechin concentration. While titration techniques deliver reliable results and require minimal instrumentation, they require specially calibrated techniques and control over the equipment. This method is best used for quantitative analysis and may lack specificity in complex sample matrices [21].

Spectrophotometry, including UV-Vis and fluorescence spectroscopy, remains essential in catechin analysis due to its versatility and widespread availability. UV-Vis spectroscopy exploits the absorbance of light by catechins at specific wavelengths, enabling quantitative determination based on Beer–Lambert law principles. Fluorescence spectroscopy enhances sensitivity, particularly in trace analysis, by measuring catechin-induced fluorescence emission. However, challenges such as spectral interference from co-extracted compounds and the need for suitable calibration standards must be addressed during method development [22].

Separating and purifying catechins from plant matter and tea involves a range of methods aimed at efficiently isolating these bioactive compounds. One commonly used technique, because of its cost-effectiveness and simplicity, is solvent extraction, where the plant material or tea leaves are immersed in a suitable solvent that can form hydrogen bonds with catechins, such as ethanol or water, to dissolve them. Afterward, the solvent is evaporated, leaving a concentrated extract containing catechins, which can then undergo further purification steps [23,24].

The Folin–Ciocalteu colorimetric method, represented in Figure 4, is the most utilized approach for quantifying the total polyphenolic compounds found in plant species [25]. The current international standard method for determining total tea polyphenols employs the Folin–Ciocalteu reagent as the chromogenic agent. In this method, a 70% methanolic solution is employed to extract tea polyphenols from ground tea samples in a water bath at 70 °C [26,27].

The hydroxyl groups in the tea extracts are oxidized by the Folin–Ciocalteu reagent, resulting in a blue coloration of the extracts. Gallic acid serves as the calibration standard for quantifying tea polyphenols, with a maximum absorption wavelength of 765 nm [28].

While these methods demonstrate good acuity, they suffer from the drawback of requiring complex pretreatments and incurring high detection costs.

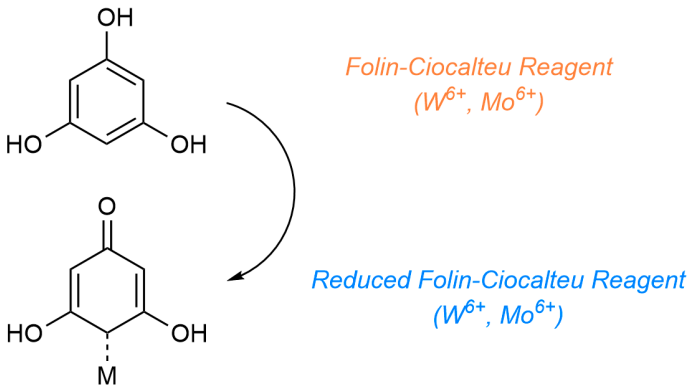

Figure 4. The mechanism of action of the Folin–Ciocalteu reagent.

Nevertheless, this method remains widely employed for determining total polyphenols in tea and is often utilized as a standard for verifying the accuracy of newly developed methods [29].

In addition to the aforementioned chromogenic reagents, there are alternative chromogenic agents for determining total tea polyphenols through visible spectrophotometry.

For instance, a group of researchers employed 18-MPC (18-molybdodiphosphate heteropoly complex) as a chromogenic reagent for determining total tea polyphenols in green tea, demonstrating superior selectivity compared to the Folin–Ciocalteu reagent [30,31].

Another method is chromatography, which includes various techniques such as column chromatography, thin-layer chromatography (TLC) (Figure 5), and high-performance liquid chromatography (HPLC) (Figure 6). These methods rely on the different affinities of catechins for the stationary and mobile phases, enabling the separation of catechins based on their molecular properties.

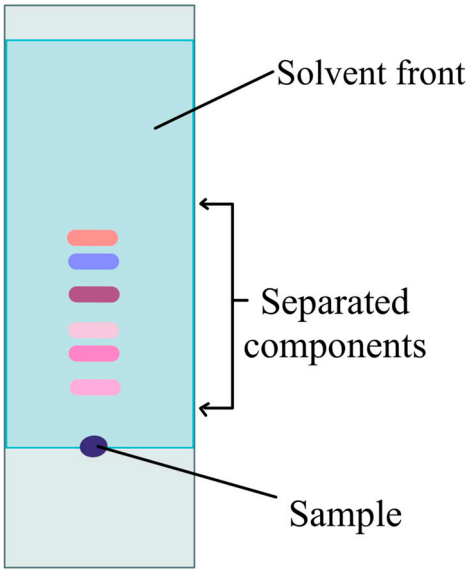

Figure 5. Simplified TLC method.

The experimental procedure initiates with the meticulous preparation of samples containing catechins extracted from botanical or tea sources or other catechin-rich materials [32].

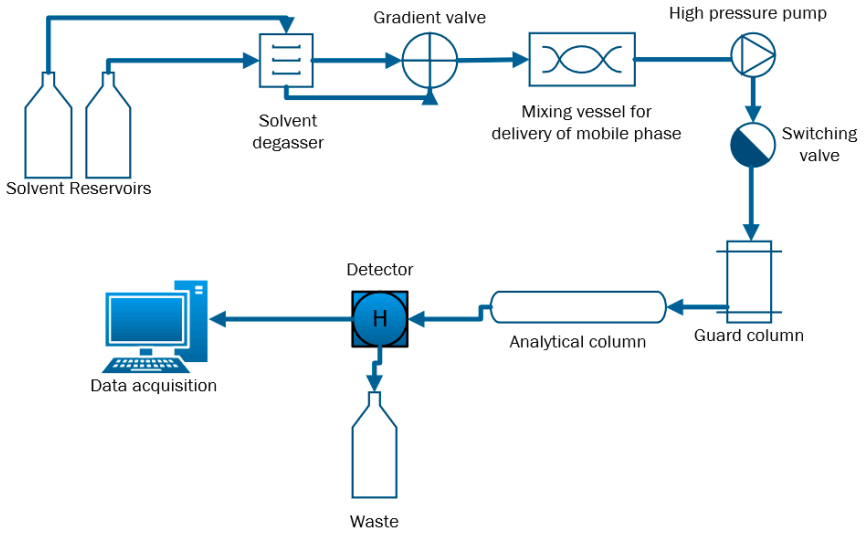

Figure 6. HPLC systematic overview and mechanism.

This process involves dissolving the samples in a carefully chosen solvent, such as methanol or ethanol, to achieve optimal concentration. Following this, a baseline is drawn near the lower edge of a TLC plate, primarily composed of silica gel, using a graphite pencil with precision. Minute volumes (typically ranging from 1 to 5 µL) of the prepared sample solution are then deposited onto the designated baseline using precise instrumentation like a microcapillary tube or glass pipette, ensuring thorough desiccation to prevent any smudging [33].

Subsequently, the TLC plate is placed in a development chamber containing a customized solvent system, typically consisting of blends of ethyl acetate, methanol, acetic acid, and water, such as ethyl acetate/methanol (9:1), methanol/water (9:1) or ethanol/water (7:3), and sealed to facilitate solvent migration via capillary action. Upon nearing the terminal extent of solvent migration, the TLC plate is carefully removed and dried. Post-drying, visualization is accomplished using an appropriate method, with UV light emission (254 nm or 365 nm) commonly utilized for catechin detection, resulting in distinguishable spots on the TLC plate [34].

Comparative analysis against established standards or reference compounds aids in identifying catechin constituents within the sample, with Rf (retention factor) values serving to refine identification if necessary. For quantitative analysis, individual spots are excised from the TLC plate and subjected to elution from the silica gel matrix using a carefully selected solvent. Following elution, analytical scrutiny, potentially employing advanced techniques like HPLC, enables meticulous quantification [35].

HPLC, renowned for its high resolution and sensitivity, is commonly utilized for precise quantification and purification of catechins from complex mixtures [36,37].

HPLC (Figure 6) is extensively utilized for the extraction and purification of catechins from plant extracts and tea due to its exceptional precision and adaptability. In the realm of catechin analysis, HPLC's capability to meticulously separate individual catechin compounds from complex mixtures with extraordinary resolution is unparalleled [38].

This high resolution proves particularly crucial when dealing with intricate matrices like plant extracts and tea, where numerous compounds may coexist [39]. Through meticulous adjustment of parameters such as the mobile phase composition, stationary phase type, and flow rate, HPLC enables the selective separation of catechins based on their distinct molecular properties, including size, polarity, and charge.

Consequently, researchers can accurately identify and quantify individual catechins present in the sample, facilitating comprehensive analyses of their concentration levels and distribution patterns [40].

HPLC with appropriate detection exhibits remarkable sensitivity, allowing for the detection and quantification of catechins even at extremely low concentrations. This attribute is essential for assessing catechins' pharmacokinetics and bioavailability in biological samples, as well as for detecting trace amounts of these bioactive compounds in plant extracts and tea [41].

By employing various detection methods, such as ultraviolet (UV) or fluorescence detection, HPLC enhances sensitivity and selectivity in catechin analysis [42,43]. UV detection, widely utilized due to its simplicity and broad applicability, provides robust detection of catechins based on their characteristic absorption spectra.

Conversely, fluorescence detection enhances sensitivity and specificity for specific catechins, enabling more refined analyses of complex samples. This combination of high sensitivity, resolution, and compatibility with diverse detection methods underscores HPLC's pivotal role in unraveling the intricacies of catechin chemistry and facilitating advancements in research and industry applications [44,45].

On the other hand, chromatography (Figure 7) emerges as the predominant method for both qualitative and quantitative analysis of individual polyphenols in tea. Different chromatography techniques (TLC, HPLC, GC) offer unique benefits and drawbacks. For example, while HPLC provides high resolution and versatility, it demands expensive equipment and expertise in comparison to TLC, which can be cost-effective but cannot offer a high degree of precision [46].

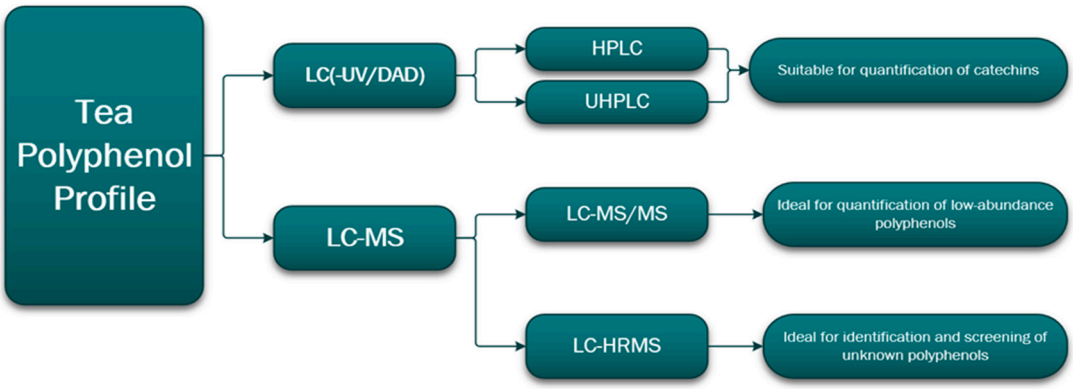

Figure 7. Different types of liquid chromatography configurations for separating tea polyphenols.

Nowadays, hyphenated techniques coupled with mass spectrometry (LC–MS/MS) remain the most-used methods for the identification of known and unknown compounds in vegetal material. Depending on the capacity of the system, the precision of the chemical identification allows researchers to explore both targeted and untargeted screening [47,48].

HPLC is effective for determining the prevalent tea polyphenols typically measured in mg/g units [49]. However, UV or DAD detectors face challenges in meeting the stringent sensitivity requirements for trace polyphenols in tea [50]. Mass spectrometry (MS) stands out for its suitability in analyzing trace polyphenols with low concentrations in intricate matrices due to its notable advantages in sensitivity, precision, and resolution.

LC–MS combines the separation capabilities of LC with the robust identification capabilities of MS, offering an effective approach for analyzing complex organic mixtures [51,52]. This method yields extensive information about complex mixtures, enabling qualitative and quantitative analysis of hundreds of components in a single analysis [53]. Numerous studies explore polyphenol analysis using LC–MS, with several reviews and book chapters dedicated to the subject.

In comparison to single-stage MS, MS/MS offers enhanced selectivity and sensitivity, simplifying complex and laborious sample preparations and emerging as the primary analytical technique [54]. Table 2 summarizes the notable applications of LC–MS in determining tea polyphenols over the past decade. UHPLC combined with MS (UHPLC–

MS/MS) emerges as the most prevalent technique for tea polyphenol analysis, facilitating effective separation, high-throughput processing, and highly sensitive analysis of tea polyphenols [55].

Table 2. Liquid chromatography methods for the separation and determination of investigated compounds.

Tea Types	Targets	Analytical Method	Mobile Phase (Solutions A and B)	Solid to Liquid Ratio (g/mL)	References
Fresh tea leaves	EC, EGC, ECG, and EGCG	UHPLC–ESI–MS/MS	A (0.1% formic acid); B (acetonitrile containing 0.1% formic acid)	1:100	[56]
Green tea	Methylselenocysteine, seelenomethionine, selenocysteine, catechin, epicatechin, EGCG	HILIC–MS/MS	A (methanol); B (8 mM ammonium acetate pH 7 (85/15, *v*/*v*))	1:50	[57]
Black tea	Apigenin/quercetin/kaempferol glycosides, theaflavins, theasinensin and galloylglucoses	HPLC–MS/MS	A (0.1% formic acid in water with 5% methanol); B (0.1% formic acid in methanol with 5% water)	1:60	[58]
White tea	4 flavoalkaloids	UHPLC–ESI–MS/MS	A (0.1% aqueous formic acid); B (0.1% formic acid acetonitrile)	1:40	[59]
Flower tea	10 phenolic acids and 10 flavonoid glycosides	UHPLC–ESI–MS/MS	A (0.1% aqueous formic acid); B (acetonitrile)	1:50	[60]

In the majority of research papers, the mobile phase utilized for analyzing catechins in green tea and dried tea leaves typically consists of water, acids such as trifluoroacetic acid, phosphoric acid, and acetic acid, along with either methanol or acetonitrile. For the column (double end-capped monomeric C18, high-purity silica, 3.0 mm × 150 mm, 5 µm particle size) and the mobile phase, a blend of eluent A (acetonitrile + 0.1% acetic acid) and B (0.1% acetic acid in water) was employed across various gradient elution systems. This strategic choice aimed to achieve two key objectives: reducing analysis time and enhancing the separation between the seven catechins, as well as gallic acid (GA) and caffeine (Caf). By leveraging these specific components and employing gradient elution techniques, researchers endeavored to optimize the efficiency and accuracy of catechin analysis in tea samples [61].

Mass spectrometry serves as an analytical technique for determining the mass-to-charge ratio (m/z), which provides data that are crucial for compound identification and quantification. The electrospray ionization source (ESI) stands out as the predominant ionization technology utilized. Typically, tea polyphenols in the ESI source are ionized in a negative ion mode, resulting in the generation of deprotonated molecular ions.

Notably, tea presents a highly intricate matrix containing significant quantities of alkaloids, polyphenols, and distinctive tea pigments like theaflavins and thearubigins [62]. Consequently, polyphenol targets may encounter interference from co-eluting compounds, leading to ionization suppression or enhancement within the electrospray ionization (ESI) source. This phenomenon is particularly pronounced in matrices of both dry tea and fresh leaves. Hence, purification is frequently necessary to extract and purify the targets during sample preparation for tea analysis via LC–MS [63].

Membrane filtration techniques like ultrafiltration and nanofiltration can be employed to separate catechins based on their molecular size and charge. These methods use semipermeable membranes to selectively retain catechins while allowing smaller molecules to pass through. Membrane filtration offers advantages such as scalability, minimal solvent usage,

and low energy consumption, making it suitable for large-scale catechin purification from plant extracts and tea [64,65].

Moreover, precipitation methods can isolate catechins from plant extracts and tea. Chemical agents like acids, bases, or salts are added to the extract to precipitate catechins, which can then be separated via filtration or centrifugation. Alternatively, protein precipitation methods such as trichloroacetic acid (TCA) precipitation can remove proteins and other impurities from the extract, leaving purified catechins [66].

Supercritical fluid extraction, Figure 8, is another technique used to extract and purify catechins. In SFE, carbon dioxide acts as a solvent under supercritical conditions (above the critical pressure of CO_2, which is 73.8 bar (7.38 MPa) at a critical temperature of 31.1 °C), facilitating efficient catechin extraction while avoiding thermal degradation. SFE offers advantages like selectivity, minimal solvent residue contamination, and environmental friendliness, making it appealing for catechin extraction and purification [67].

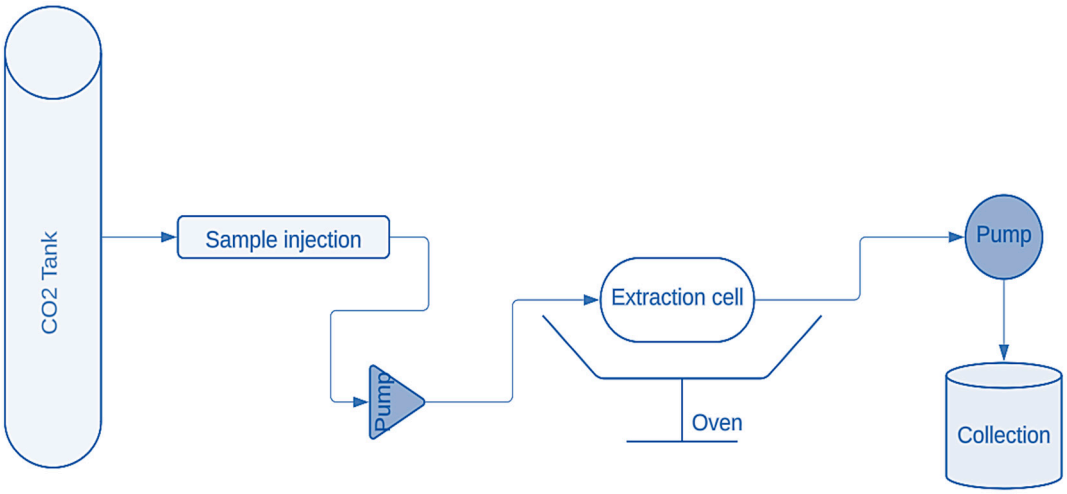

Figure 8. SFE catechin extraction and purification.

The process involves exposing the tea leaves to supercritical CO_2, which behaves both as a gas and a liquid under specific temperature and pressure conditions. In its supercritical state, CO_2 exhibits enhanced solvent properties, allowing it to penetrate the plant material and dissolve the target compounds, including catechins [68].

The advantages of superfluid extraction include its ability to selectively extract target compounds while leaving undesirable components behind, as well as its relatively mild extraction conditions, which help preserve the integrity of the extracted compounds. Additionally, CO_2 is considered safe, non-toxic, and environmentally friendly.

Researchers have explored the application of superfluid extraction for the extraction of catechins from tea leaves due to its efficiency and potential for high-purity extracts. Studies have demonstrated the effectiveness of SFE in extracting catechins, including epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC), from various types of tea leaves.

Supercritical fluid extraction presents an enticing alternative to conventional solvent extraction for extracting various bioactive compounds, including catechins. In a study conducted by Ruslan et al. (2018), the researchers employed a method using 5% (v/v) methanol as a modifier to the supercritical fluid to extract catechin from betel nuts. They achieved the highest concentrations of both extract (34.00 mg/g sample) and catechin (565.38 ppm) at conditions of 30 MPa, 70 °C, and 4 mL/min [69].

Garcia et al. (2006) conducted experiments utilizing superheated water at temperatures from 50 to 150 °C and high pressure (1500 psi) to keep the solvent in liquid state for the subcritical extraction of catechins from the by-product of winery processing, namely the wine pomace of Tempranillo grapes (*Vitis vinifera* L.). This approach yielded between

0.14 and 0.47 Mg/g dw. The method allows precise control over pressure and temperature, facilitating targeted extraction of specific catechins while minimizing co-extraction of undesirable compounds, thereby producing purer extracts with enhanced bioactivity. Operating at lower temperatures compared to conventional methods also prevents thermal degradation. However, addressing challenges related to cost, optimization complexity, and extraction yields is imperative for the broader adoption of this method [70].

Overall, superfluid extraction offers a promising approach for the extraction of catechins from tea leaves, providing high-quality extracts with potential applications in the food, pharmaceutical, and cosmetic industries.

Solid-phase extraction (SPE) can isolate and purify catechins from plant extracts and tea. In SPE, a solid sorbent material (silica-based or a metal–organic framework) with a specific affinity for catechins is packed into a column, and the extract is passed through under controlled conditions. Catechins selectively adsorb onto the sorbent material while other components are eluted, resulting in purified catechins [71].

Furthermore, preparative chromatography allows large-scale purification of catechins using chromatographic techniques. Preparative chromatography systems equipped with columns packed with the stationary phases enable the separation of catechins from complex mixtures with high purity and yield [72]. This method is particularly useful for industrial-scale production of purified catechins for various applications [73].

Enzymatic hydrolysis can also release catechins from glycoside forms present in plant extracts and tea. Enzymes like β-glucosidase are added to catalyze the hydrolysis of glycosidic bonds, liberating free catechins. This method enhances catechins' bioavailability by extracting them from complex structures like glycosides and polymers. Reducing the molecular weight of catechins makes them pass easier though the epithelium of the gastrointestinal tract, increasing absorption [74].

Lastly, combining multiple separation and purification techniques can achieve optimal results; for example, the sample can be firstly purified using SPE, removing contaminants, after which HPLC is used. These approaches leverage the strengths of each method to overcome limitations and attain higher purity and yield of catechins from plant extracts and tea [75]. By integrating techniques like solvent extraction, chromatography, membrane filtration, and enzymatic hydrolysis, researchers and manufacturers can tailor the purification process to meet specific requirements for catechin isolation and purification [76].

4. Discussion

Obtaining pure catechin compounds enables researchers to conduct controlled experiments, elucidating the effects of individual catechins on various physiological processes, such as antioxidant activity, anti-inflammatory properties, and anti-cancer effects. This targeted approach deepens our understanding of catechins' therapeutic potential and facilitates the development of more effective treatments for diseases ranging from cardiovascular disorders to neurodegenerative conditions [77].

Secondly, the isolation of catechins from plant extracts enhances their bioavailability and potency, leading to improved efficacy in therapeutic applications. Extracting and purifying catechins from plant sources eliminates unwanted compounds and impurities, thereby increasing the concentration of active ingredients in the final product. This purification process ensures that catechins reach their target tissues and exert their beneficial effects more efficiently [78,79].

Various techniques can be employed to separate catechins from plant extracts, including solvent extraction, chromatography (such as HPLC), and membrane filtration. These methods allow for the precise isolation and purification of catechins while minimizing degradation and preserving their bioactivity.

Additionally, advancements in technology, such as UHPLC, have led to the development of more efficient and cost-effective processes for catechin separation, paving the way for their widespread use in pharmaceuticals, nutraceuticals, and functional foods [80].

The anti-cancer potential of catechins, particularly EGCG, has been extensively investigated, with evidence suggesting their ability to inhibit cancer cell proliferation, induce apoptosis, and impede angiogenesis. Furthermore, catechins' metabolic effects, including enhanced fat oxidation and improved insulin sensitivity, hold promise in weight management and type 2 diabetes prevention and management [81].

Catechins' neuroprotective effects have also garnered attention, with research indicating their ability to protect neurons from oxidative stress and neurotoxicity, potentially mitigating the risk of neurodegenerative diseases like Alzheimer's and Parkinson's. Moreover, catechins may support cognitive function through their interactions with neurotransmitter systems and neuroplasticity mechanisms [82–84].

Catechins represent a class of bioactive compounds with diverse health-promoting properties, offering potential therapeutic avenues for various diseases. This review aims to comprehensively explore the physiological effects, mechanisms of action, and therapeutic potential of catechins, shedding light on their significance in promoting overall health and well-being [85]. Despite promising findings from preclinical studies, further research, particularly clinical trials, is needed to elucidate catechins' efficacy, optimal dosages, and long-term effects in human populations [86].

It is well known that catechins are widely dispersed among various plant-based foods and beverages. Green tea is an abundant dietary source of catechins, prominently featuring epigallocatechin gallate as the primary and biologically active catechin.

Other catechins present in green tea include epicatechin, epicatechin gallate, and epigallocatechin [87,88]. These catechins play different roles in shaping the flavor profile and health benefits of green teas [89]. However, it is crucial to recognize that the concentration of catechins in green tea may fluctuate depending on factors like tea variety, processing techniques, and brewing methods (temperature and extraction time are the most important factors).

Beyond green tea, catechins can also be found in other varieties of tea, albeit in diminished amounts [90,91]. Black tea and oolong tea harbor catechins, although their levels are reduced due to the fermentation or oxidation processes involved in their production. Nevertheless, these teas still confer some health benefits attributed to catechins, albeit to a lesser extent than green tea [92,93]. Recently, for more demanding users, tea manufacturers have brought on the market a variety of green and black tea blends to which flower petals, fruits, and other flavors, such as vanilla or bergamot, are added. Such mixtures are intended to increase the number of consumers, transforming the less aromatic infusions into an interesting experience.

Catechins are also prevalent in various other plant-based foods. Cocoa and dark chocolate, for instance, are noteworthy sources of catechins, including catechin and epicatechin, contributing to their antioxidant prowess. Additionally, fruits such as berries (e.g., strawberries, blueberries, raspberries) and apples contain catechins, albeit in smaller amounts compared to tea and cocoa. These foods offer a diverse assortment of flavonoids, including catechins, which contribute to their potential health benefits [94,95].

Prominent catechins in tea leaves encompass (-)-epicatechin, (-)-epigallocatechin, (-)-epicatechin gallate, and (-)-epigallocatechin gallate. These catechins differ chemically primarily due to variations in hydroxyl group arrangement and the presence of galloyl (gallate) groups [96].

EGCG, the principal and biologically active catechin in green tea, stands out due to a galloyl (gallate) ester moiety at the 3-position on the C-ring. This gallate ester confers robust antioxidant properties to EGCG, rendering it a key contributor to the health benefits associated with green tea consumption. Extensively researched, EGCG exhibits diverse biological activities, including antioxidant, anti-inflammatory, anti-cancer, and neuroprotective effects [97].

ECG, akin to EGCG, harbors a galloyl ester at the 3-position of the C-ring but lacks a hydroxyl group on the B-ring. This structural variance modulates its antioxidant activity and biological effects, albeit to a lesser extent compared to EGCG. ECG manifests

antioxidant, anti-inflammatory, and cardioprotective attributes, contributing to its potential health advantages.

EGC lacks a galloyl ester but features multiple hydroxyl groups on the B-ring. Despite displaying weaker antioxidant activity relative to EGCG and ECG, EGC still contributes to the overall antioxidant capacity of tea. EGC has been linked to various health benefits, including cardiovascular protection and potential anti-cancer effects.

EC, the simplest catechin lacking a galloyl ester or additional hydroxyl groups on the B-ring, exhibits comparatively lower antioxidant activity than its derivatives. Nevertheless, it remains a contributor to the overall antioxidant profile of tea and has been investigated for its potential health-promoting effects [98,99].

Beyond these major catechins, numerous derivatives with diverse chemical structures and biological activities exist. Catechin derivatives may arise from modifications such as glycosylation, acylation, or polymerization, yielding a plethora of compounds with varied properties [100,101].

For instance, epicatechin gallate and epigallocatechin gallate represent gallate ester-containing derivatives of catechins, markedly enhancing their antioxidant potency and biological activities compared to non-gallate counterparts.

Additionally, theaflavins and thearubigins emerge from catechin oxidation and polymerization during tea fermentation, contributing to the color, flavor, and health benefits of black tea.

Moreover, catechin glycosides, like epicatechin gallate-3-O-glucoside and epigallocatechin gallate-3-O-glucoside, are conjugated forms with glucose molecules. These glycosides exhibit altered solubility and bioavailability relative to their aglycone forms, potentially possessing unique biological activities [102,103].

The chemical distinctions among catechins and their derivatives, encompassing variations in hydroxyl group arrangement, gallate ester presence, and glycosylation status, are pivotal determinants of their antioxidant potency, bioavailability, and biological activities. Grasping these structural nuances is essential for comprehending the diverse health-promoting effects of catechins and exploring their potential therapeutic applications.

The tea plant (*Camellia sinensis*) is a dietary source rich in all types of catechins, most importantly containing epigallocatechin gallate, the most abundant and bioactive catechin. Epicatechin, epicatechin gallate, and epigallocatechin are present among the other catechins from the tea plant, although in varying concentrations influenced by diverse factors such as tea variety, processing techniques, and brewing methods. While green tea boasts higher catechin levels compared to other tea variants like black or oolong tea, the fermentation process involved in their production may lead to catechin degradation and loss of beneficial compounds [104].

Furthermore, some nuts, seeds, and legumes also contain catechins, albeit in lesser quantities compared to tea and specific fruits. For example, almonds, peanuts, and pecans contain catechins, bolstering their antioxidant capacity and potential health effects. Additionally, certain herbs and spices, such as cinnamon, thyme, and cloves, contain varying levels of catechins, expanding the spectrum of dietary sources of these bioactive compounds [105].

Numerous studies have unveiled a myriad of potential health benefits associated with catechins consumption, particularly in cardiovascular health enhancement. Catechins have been shown to ameliorate blood vessel function, reduce blood pressure, and lower cholesterol levels, collectively mitigating the risk of cardiovascular diseases. Additionally, catechins' anti-inflammatory properties render them beneficial in modulating immune responses and alleviating inflammatory conditions such as arthritis and inflammatory bowel disease [106].

Pharmaceutical enterprises devote significant resources to the isolation and refinement of catechins to ensure the consistent presence of active constituents in their products. This rigorous purification process not only guarantees precise dosing but also heightens the effectiveness of the final pharmaceutical formulations.

Through purification techniques, catechins undergo a transformation that enhances their bioavailability, rendering them more easily absorbed by the body. This heightened bioavailability translates to more dependable therapeutic effects, instilling confidence in the outcomes of treatment regimens [107].

Moreover, the purification of catechins plays a pivotal role in minimizing the likelihood of adverse reactions or side effects in patients. By meticulously eliminating impurities and contaminants, pharmaceutical firms prioritize the safety and well-being of individuals reliant on these products for their health needs.

Additionally, purified catechins demonstrate superior stability profiles, contributing to the prolonged shelf life of pharmaceutical preparations. This enhanced stability ensures that products maintain their potency and effectiveness over time, promoting sustainability in healthcare practices [108].

Furthermore, the concentration of active constituents achieved through separation and purification processes amplifies the pharmacological activity of catechins. This heightened activity holds promise for the development of pharmaceutical products delivering more potent and efficient therapeutic outcomes.

The customization capabilities inherent in purification processes empower pharmaceutical enterprises to isolate specific catechin compounds tailored to address diverse therapeutic requirements. This versatility facilitates the development of specialized formulations targeting various health conditions, catering to the unique needs of patients.

The extraction of catechins presents formidable challenges due to their intricate molecular structure and coexistence with other compounds in plant extracts and tea. A significant hurdle lies in the variability of catechin content among diverse plant species and tea varieties, as well as within different parts of the same plant [109]. This variability mandates precise extraction and purification techniques to ensure consistent and dependable results [110]. Catechins are prone to degradation during extraction processes, particularly when exposed to high temperatures or prolonged exposure to light and oxygen. Hence, maintaining optimal extraction conditions is paramount to preserve catechin integrity and ensure the accuracy of results obtained [111].

Despite these challenges, which can be partially resolved by optimizing solvent systems, pH, temperature, or combining different methods, the extraction and purification of catechins offer a myriad of advantages and hold immense promise across various fields; Table 3 offers data on the different factors that can have an influence in the separation and purification processes. Notably, their robust antioxidant activity stands out as a key advantage, extensively studied and proven to confer numerous health benefits [112,113]. Catechins boast potent free radical-scavenging properties, aiding in the reduction of oxidative stress and inflammation, thereby potentially mitigating the risk of chronic diseases such as cardiovascular diseases, cancer, and neurodegenerative disorders. Moreover, catechins exhibit the ability to modulate various cellular signaling pathways implicated in cell proliferation, apoptosis, and inflammation, underscoring their potential as therapeutic agents for addressing a broad spectrum of ailments [27].

Some concerns arose in the last recent years, referring to the use of catechins in concentrated forms (additional use of food supplements rich in catechins), which may cause liver problems if daily doses are at least 800 mg or more. However, EFSA studies confirmed that natural and dietary sources with catechins are safe and, in rational consumption, should not pose any health threats [28].

The isolated catechin compounds have found applications (Figure 9) beyond the realm of healthcare, permeating diverse sectors. In the food and beverage industry, catechins serve as natural antioxidants and preservatives, prolonging the shelf life of products and preventing lipid oxidation, thereby upholding product quality and freshness [114,115].

A primary benefit of catechin extraction lies in their potent antioxidant activity. These compounds display scavenging effects against harmful free radicals, implicated in oxidative stress and cellular damage. By neutralizing free radicals, catechins shield cells and

tissues from oxidative harm, thus lowering the risk of chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders.

Table 3. Factors influencing the separation and purification of catechins, highlighting their significance in optimizing processes for yield, purity, and quality.

Factor	Influence on Separation and Purification	Significance
Plant Source	The source plant's catechin content affects extraction yield and composition, e.g., green tea leaves, cocoa beans, berries, and apples.	Determines initial catechin concentration and composition, impacting overall process efficiency and product quality.
Extraction Methods	The chosen extraction technique affects catechin yield and purity, e.g., solvent extraction, SFE, steam distillation, and SPE.	Determines how catechins are extracted, influencing both the quantity and quality of the final product.
Solvent Selection	Choice of solvent impacts catechin extraction efficiency and purity, e.g., ethanol, methanol, water, ethyl acetate, acetone, and acetonitrile.	Solvents selectively extract catechins based on polarity, affecting the yield and purity of the extract.
Temperature	Temperature influences extraction kinetics and catechin stability. Temperatures ranging between 50 °C and 80 °C are high enough to dissolve the catechins but low enough not to degrade them.	Balances extraction rate and catechin preservation, requiring optimization for maximal yield and quality.
pH	pH affects catechin solubility and stability during extraction. An acidic pH between 3 and 5 is regarded as being optimal because, in this range, catechins tend to be more stable and soluble. An acidic environment also helps prevent the degradation of catechins.	Influences catechin solubility and integrity, requiring pH optimization for efficient extraction.
Extraction Time	Duration of extraction impacts catechin yield and quality. The extraction time is also dependent on the method used. High extraction temperature and pressure methods are fast (under 1 h) and can easily degrade the catechins, while milder conditions require more time for maximum efficiency.	Balances yield and degradation, necessitating optimal extraction times for maximal efficiency.
Particle Size	Finer particle size enhances surface area for extraction, increasing efficiency.	Increases contact between solvent and plant material, improving catechin extraction efficiency.
Presence of Co-Extractives	Other compounds in the plant may interfere with catechin extraction.	Co-extractives can affect extraction selectivity and purity of the final product.
Separation Technique	Various techniques isolate catechins from complex mixtures.	Essential for purifying catechins from complex matrices for analysis or application.
Column Material (for Chromatography)	Choice of column material influences separation efficiency. C18 columns are the most commonly used and widely available for catechin analysis using HPLC. Phenyl-based stationary phases, such as phenyl-hexyl, can also be used and are effective for separating catechins.	Impacts interactions between catechins and stationary phase, affecting separation quality.
Mobile Phase Composition (for Chromatography)	Mobile phase composition affects separation efficiency.	Alters catechin solubility and interactions, influencing separation quality.
Purification Method	Various methods purify catechins from impurities.	Essential for obtaining high-purity catechin products for various applications.
Stability	Catechin stability during processing impacts product quality.	Ensures preservation of catechin integrity throughout processing, preventing degradation.

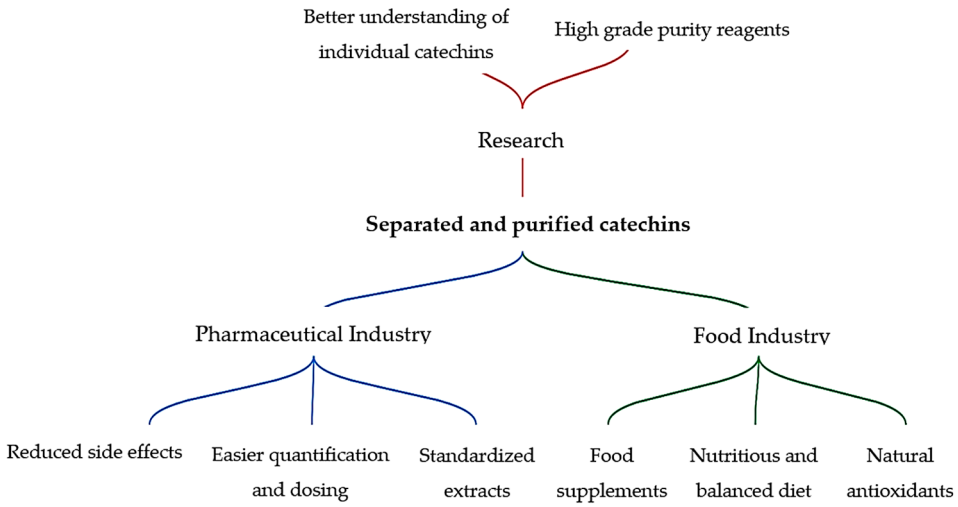

Figure 9. The multiple uses of purified catechins in diverse fields.

Furthermore, catechins have been extensively researched for their potential to promote cardiovascular health. Studies suggest that catechins may help reduce blood pressure, lower cholesterol levels, and enhance blood vessel function, thereby mitigating the risk of heart disease and stroke. Extracting catechins enables the formulation of dietary supplements or functional foods aimed at supporting heart health [116,117].

In the realm of skincare, catechins have garnered attention for their anti-inflammatory and anti-aging properties. These compounds safeguard the skin from UV-induced damage, inhibit collagen degradation, and enhance skin hydration and elasticity. Extracting catechins facilitates the development of skincare products such as creams, serums, and sunscreens, harnessing these beneficial effects to foster healthy and youthful-looking skin [118].

Catechins exhibit antimicrobial properties, making them valuable in combating bacterial and viral infections. Research indicates that catechins may inhibit the growth of various pathogens, including bacteria accountable for dental caries and respiratory infections. Extracted catechins could be integrated into oral care products, throat lozenges, or disinfectant solutions to help prevent infections and maintain oral and respiratory health [119].

In the pharmaceutical sector, catechin extraction enables the isolation and purification of these compounds for therapeutic applications. Catechins hold promise in various areas, including cancer prevention and treatment, weight management, and cognitive health. By extracting and purifying catechins, pharmaceutical companies can devise standardized formulations with precise dosages and consistent efficacy, ensuring optimal therapeutic outcomes for patients [120].

Additionally, catechins present potential applications in the food and beverage industry, where they can serve as natural food additives or preservatives owing to their antioxidant and antimicrobial properties. Extracting catechins from plant sources provides a sustainable and eco-friendly alternative to synthetic additives, contributing to the development of healthier and safer food products. In comparison to synthesized additives, extracted catechins have minimal to no side effects, most of the time are pure, and are agents with proven health benefits that humans consume every day.

They are also incorporated into functional foods (especially fortified meat preparations) and dietary supplements to augment their nutritional value and health-promoting attributes. In the realm of cosmetics and skincare, catechins are esteemed for their anti-aging and skin-protective effects, combatting oxidative stress and UV-induced damage to promote skin health and vitality [121,122].

Moreover, in the agricultural domain, catechins have piqued interest for their potential as natural pesticides and insecticides, offering eco-friendly alternatives to synthetic chemicals. Leveraging catechins' insecticidal and antimicrobial properties, researchers explore

their efficacy in controlling pests and pathogens in crops while minimizing environmental impact [123,124].

Catechins hold promise in materials science and nanotechnology; they are investigated for their role in developing bioactive coatings, films, and nanoparticles with applications in drug delivery, tissue engineering, and environmental remediation [125,126].

5. Conclusions

In conclusion, while the extraction and purification of catechins present formidable challenges due to their intricate molecular structure and variable content across plant sources, overcoming these hurdles offers substantial benefits and holds significant potential across various domains.

Our review has found that even though there are numerous methods for the extraction and separation of catechins, each one has its own unique advantages and disadvantages and has particular applications for niche interests and uses. For example, while solvent systems are easily accessible, they lack precision and might not be as effective in quantitative analysis. However, different methods can be used to enhance the purification of catechins, such as SFE, followed by HPLC. Our efforts have revealed that, for the efficient separation of catechins from other compounds or closely related polyphenols, not one method in particular but a combination of various methods, techniques, and equipment is the most ideal.

Catechins' robust antioxidant properties, extensively validated through scientific investigation, position them as promising candidates for therapeutic interventions against chronic diseases as well as promising dietary components for preventive care. The versatile applications of catechins extend beyond healthcare, spanning industries such as food and beverage, cosmetics, agriculture, and materials science. Their adaptability and diverse benefits underscore their crucial role in advancing human health and technological innovation.

This study is a general compilation of the data found in the present literature and approaches the field of catechin extraction and separation from a beginner level of understanding. For future research we plan to delve deeper into this subject with the goal of acquiring new data and information, possibly improving the current methods. Our research team foresees this as a field of current and future interest as more and more people become health-conscious and seek green and natural remedies.

Consequently, ongoing scholarly inquiry and innovative efforts in catechin research are poised to yield further insights and advancements, fostering expanded utilization and enhanced impact across multifaceted fields. Future prospects indicate the use of catechin in approved medications as well as the synthesis of different catechin derivatives.

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