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Review

Anthocyanin Delivery Systems: A Critical Review of Recent Research Findings

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Abstract: Anthocyanins (ACNs) are polyphenolic, water-soluble pigments, and phytochemicals, which in recent years, have garnered the interest of consumers, researchers, and industries for their various potential preventative and/or therapeutic health benefits and applications in the food industry. ACN-based processed foods have emerged as functional foods with significant therapeutic potential against various health conditions. However, their wider application in food and pharmaceutical formulations is hindered by their inherent instability under different environmental conditions, such as pH, light, and temperature, rendering them non-functional due to loss of biological activity. The current review focuses on the frequently used bio-based encapsulation materials for ACN-based delivery systems and their formulation techniques. Various bio-based materials including pectin, gums, pectin, proteins, lipids, phospholipids, and their conjugates are being widely used for targeted delivery and controlled release of bioactive compounds and drugs. The incorporation of advanced technologies seems to be promising in the context of extraction, encapsulation, and storage of ACNs. However, more comprehensive studies are required for the application of encapsulated ACNs in various food products, and improvements in their stability under different processing conditions.

Keywords: anthocyanins; delivery systems; stability; encapsulation; functional foods

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1. Introduction

Anthocyanins (ACNs) are an important class of over 700 polyphenolic, water-soluble natural pigments within the flavonoid family, and characterize various colors, including red, purple, and blue, in a wide range of vegetables, fruits, flowers, and seeds [1,2]. ACNs have demonstrated significant bioactive attributes, and health-promoting benefits, such as antioxidant, anticarcinogenic, anti-inflammatory, cardioprotective, and anti-neurodegenerative properties, as well as preventative effects against diabetes and ocular diseases, and improvement of vision health [3]. Furthermore, the ACNs isolated from various fruit berries have exhibited the potential to boost cognitive brain function and prevent age-related oxidative damage [4]. These natural pigments also exhibit good potential for various food-related applications. However, a major limitation regarding the use of ACNs for such applications is their degradation owing to sensitivity to various process-associated factors, such as temperature, light, pH, oxygen, co-pigmentation, enzymes, ascorbic acid, and sulfites [5].

The structure of ACNs generally comprises a single glucoside unit, although various ACNs contain multiple glucoside unit attachments in their structure (Figure 1), occurring

as simple sugars, or oligosaccharide side chains, in a characteristic tricyclic (C6-C3-C6) skeleton pattern, and, therefore, can be termed anthocyanidin glycosides [6]. The polar hydroxyl group [OH] present in ACNs facilitates the ACN molecules to form hydrogen bonds with water molecules [7]. The type of color imparted by an ACN, and its intensity is dictated by the number of OH and methoxyl (O-CH_3) groups present in the ACN structure, whereby a greater number of OH groups characterize a bluish shade, while more O-CH3 groups impart reddish hues [8]. All higher plants have ACNs in their various tissues, and the most widespread, naturally occurring ACNs are based on six aglycones: cyanidin (50%), pelargonidin (12%), petunidin (7%), delphinidin (12%), peonidin (12%), and malvidin (7%), differing only in terms of B-ring substitution patterns (Figure 1) [9].

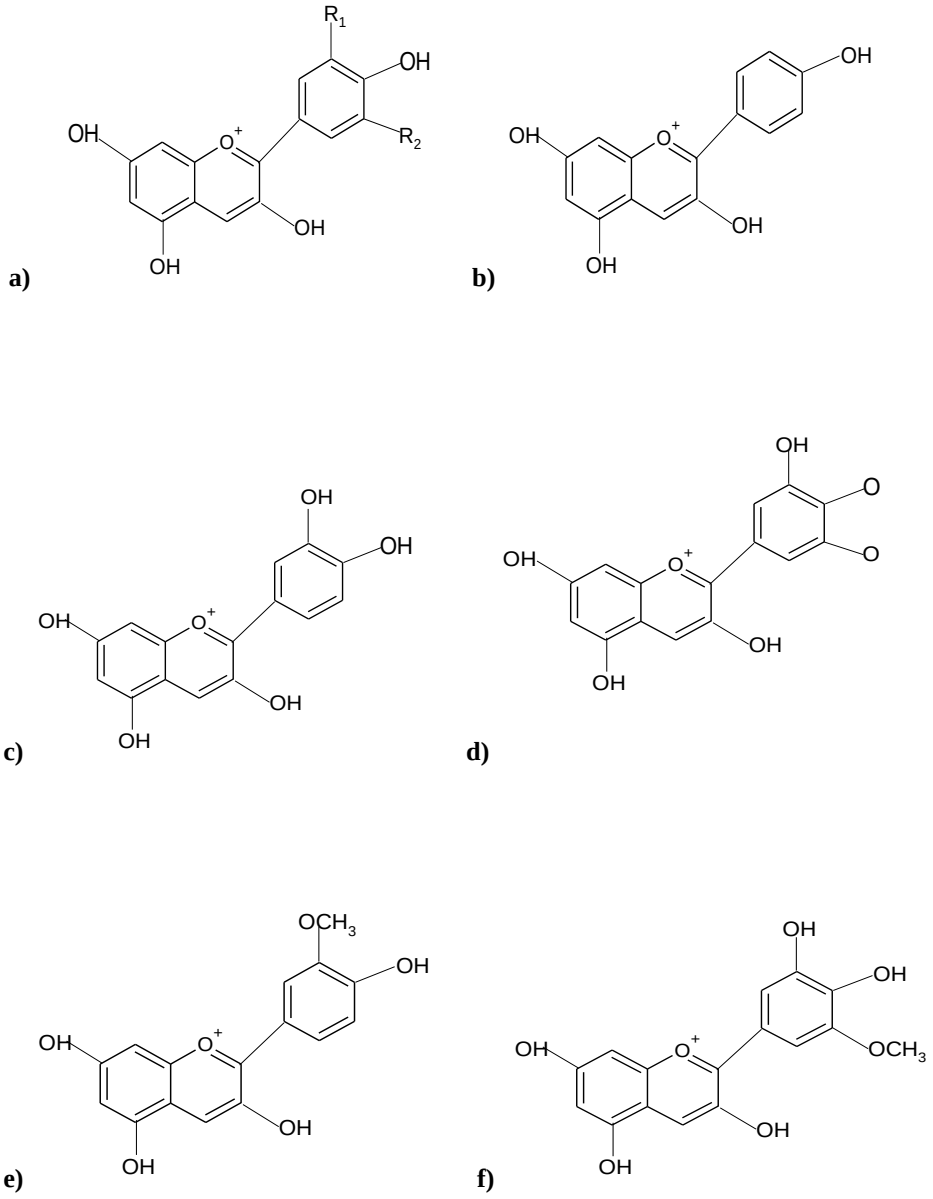

Figure 1. Chemical structures of predominant ACNs pigments present in various plants; (**a**) Basic structure of an ACN; (**b**) Pelargonidin; (**c**) Cyanidin; (**d**) Delphinidin; (**e**) Peonidin; (**f**) Petunidin.

ACNs present in fruits, although highly sensitive to chemical and enzymatic degradation reactions, are highly reactive molecules, with significant chemoprotective activity against various diseases, such as diabetes, obesity, and some cancers [5]. This enhanced chemical reactivity can be attributed to the presence of the specific pyrilium nucleus [C-ring]

in their structure [10]. Primary factors that affect the stability of ACNs include copigments, temperature, light, oxygen, pH, enzymes, metal ions, solvents, intramolecular, and intermolecular associations, other reactive compounds, as well as the type, and structure of the ACN pigment [11]. These factors, therefore, are key considerations in terms of applications involving ACNs in the food and pharmaceutical industries.

ACNs are being utilized as natural, water-soluble, Codex Alimentarius-approved food colorants (E163), and dyes for a diverse range of food and beverage products [12,13]. Encapsulated ACNs are also used as fortificants in cereal products (cookies, wafers, biscuits, and tortillas), juices, beverages, and milk products [14,15]. ACNs encapsulated in gelatin/CH electrosprayed microparticles could be used in formulating functional liquid and nutraceutical foods [16]. Additionally, ACNs are regarded as nutraceutical ingredients of considerable therapeutic potential for the development of advanced nutraceuticals and functional foods [4,17]. Furthermore, ACNs have also found applications in the cosmetics and pharmaceutical industries, for instance, for the development of health supplements [18,19]. As mentioned already, though the potential of applications is significant, the stability issues associated with ACNs limit their utilization in processing applications [20].

The limitation of ACNs in terms of food applications is directly related to their bioavailability; as they undergo extensive presystemic degradation, and hence, are poorly absorbed [21]. The bioavailability of ACNs is reportedly very low, with recoveries of <1% of the ingested dose of ACNs [22]. Albeit higher recoveries have been reported as well in some in vitro studies, reaching values of 12.4% [23,24]. ACNs are usually assimilated from the stomach and small intestine, although, a considerable proportion can reach the large intestine, where these ACNs are subjected to extensive catabolism, resulting in the formation of various metabolites, for instance, phenolic and propionic acids [22]. ACNs in their glycoside forms have demonstrated superior stability under low pH (1.5–4) conditions in the stomach, allowing for their absorption in the small intestine as intact molecules [25]. ACN aglycones, upon reaching intestinal epithelia, undergo metabolism before entering portal circulation, in two distinct phases, phase I metabolism (oxidation, reduction, and hydrolysis reactions), and phase II metabolism (conjugation reactions) [22].

Moreover, in the intestine, ACNs undergo sulfation, methylation, and glucuronidation under the influence of sulfotransferase, catechol-O-methyltransferase, and uridine-5′-diphospho-glucuronosyltransferase enzymes [26]. Alternatively, ACNs aglycones may undergo degradation and fragmentation induced by the action of deglycosylation enzymes produced by the colonic microbiota, resulting in the formation of aglycones that undergo further ring-opening, leading to the production of various aldehydes, and benzoic acids, such as vanillic, gallic, protocatechuic, and syringic acids [27]. Consequently, the proportion of phenolic acids increases, while that of ingested ACNs decreases, as they progress further along the gastrointestinal (GI) tract. The low in vivo bioavailability of ACNs can be attributed to their low permeability, low water solubility, inadequate gastric residence time, and high sensitivity to the GI environment, where they undergo substantial pH-dependent transformations [28]. Therefore, only a small portion of the consumed ACNs is recovered in plasma/urine, and <0.1% is excreted in the intact form [29]. This calls for the development of methods aimed at reducing the degradation of ingested ACNs, and therefore, enhancing their bioavailability [30].

ACNs can be stabilized by embedding them in nanocarrier systems to produce microcapsules, acylating their reactive groups, or forming copigments with other macromolecules [31]. A significant number of research studies have recorded the encapsulation of ACNs using different techniques and encapsulating materials [30,32–37]. Encapsulation technology is focused on the entrapment of bioactive compounds and the formation of one stable form, either in a solid or liquid state, which can significantly enhance ACN stability, bioaccessibility, and bioavailability [38]. One of the most commonly used encapsulation materials for ACNs, among others such as chitosan and Gum Arabic, are cyclodextrins (CDs), whereby the apolar guest molecules (for instance, amphiphilic ACN aglycones) can be trapped within the torus-shaped apolar cavity of CDs through electrostatic interactions,

hydrogen bonds, and van der Waals forces (utilizing techniques such as molecular inclusion or host-guest complexation) [39]. CDs owing to their hydrophobic interior, and hydrophilic exterior, allow them to form complexes with a wide range of organic components, thereby also permitting the selectivity of the organic compounds to be encapsulated, which can be attributed to the adaptable nature of the hydrophobic cavity of CDs, as well as its size [40]. Encapsulating bioactives such as ACNs in CDs offers significant advantages, including enhanced solubility, improved permeability across intestinal membranes, as well as improved bioavailability of the encapsulated materials [39].

However, a comprehensive review was needed to obtain a greater understanding of the advanced methods and formulations used for the stabilization of ACNs. The current review comprehensively reviewed all available advanced literature that depicts ACN encapsulation by way of different delivery systems and methods for their stability and subsequent applications and focuses on the frequently used bio-based encapsulation materials for ACN-based delivery systems.

1.1. Methodology

The keywords used to research and collect the literature for this critical review included: "anthocyanins", "delivery systems", "stability", "bioavailability", and "encapsulation", either individually, or in a combination thereof. Databases searched included PubMed, ScienceDirect, Google Scholar, Scopus, and Web of Science. The publication period beginning from 2001 was chosen as a starting point, with the recency of research as the prime focus for the inclusion of the majority of the studies. Close to 250 journal articles satisfied the criteria, and after review, 187 were shortlisted for inclusion in this review.

1.2. ACN Interactions with Wall Materials

Encapsulation technologies for ACNs are aimed at maintaining their stability under different pH conditions, as well as heat and light exposure. ACN interactions with encapsulated wall materials usually result from electrostatic interactions or hydrogen bonding. Liposomes (1% (*w*/*w*) soy lecithin) loaded with grape seed extract were formed by the electrostatic interaction of polyphenols with the phospholipid bilayer by using high-pressure homogenization (22,500 psi) [41]. Hydrogen bonding was observed in encapsulated flours prepared from sweet potatoes [purple-fleshed] spray-dried with different concentrations of maltodextrin and ascorbic acid, resulting not only in smoother flour granules but also higher total ACNs content, and improved antioxidant capacity as compared to non-encapsulated flours [42]. A similar phenomenon was observed between strawberry ACNs [negatively charged] and protonated amino groups of chitosan (CH) nanoparticles with an encapsulation efficiency of 58.09% with the 36.47% of ACNs (300–600 nm particle size) [43]. Other interactions were observed, such as hydrophobic interactions between β-lactoglobulin (β-Lg) and malvidin-3-O-glucoside, forming a complex that enhances the thermal stability, oxidative stability, and photostability of ACNs [44]. These interactions act as the main driving forces for the encapsulation of grape seed ACNs in chitin microspheres [45]. Pasukamonseta, Kwonb, and Adisakwattana [46] observed that microencapsulation of ternatin ACNs isolated from the floral extract of *Clitoria ternatea* (CT) with alginate and calcium chloride ($CaCl_2$) improved the stability, as well as the biological activity of ACNs in this case, although, the Fourier-transform infrared spectroscopy (FTIR) assay revealed no interaction between CT ACNs and alginate.

2. Bio-Based Materials Used for the Stabilization of ACNs

2.1. Pectin

Pectin (PC), a polysaccharide polymer, is a viable solution for the stabilization of ACNs by way of the formation of non-covalent complexes [47]. ACN metal chelate complexes solubilized in PC prevented the precipitation of ACNs in aqueous environments, making them a potential candidate for beverage-related applications [48]. The most probable mechanisms responsible for ACN-PC binding appear to be ionic interactions between

positively-charged ACN flavylium cations and free pectic carboxyl groups, and ACNs aromatic stacking on bound ACNs [49]. The binding exhibits an increasing trend, as pH becomes more acidic, given that flavylium cation is more dominant and prevalent in the pH range of 1–3, with the converse increase in pH values causing a decrease in the concentration of flavylium cations [50]. This trend can be seen in Figure 2, where the effect of pH on the color stability of ACNs can be observed. PCs isolated from sugar beet, apple, and citrus improved the stability characteristics of ACN extracts from blackcurrant, and strawberry, making them suitable for food and beverage applications [50].

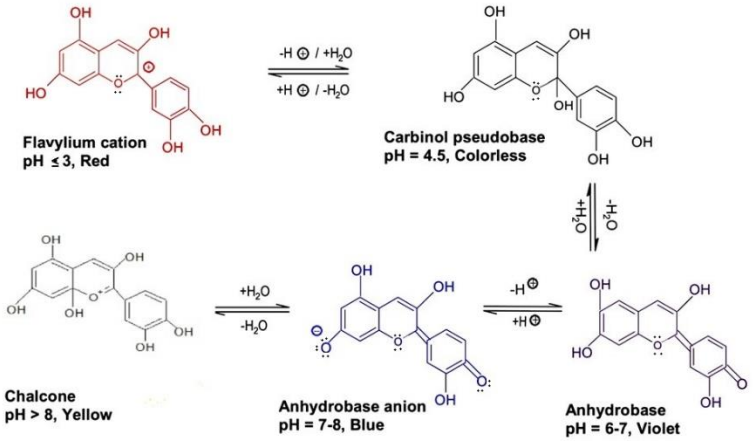

Figure 2. A pictorial description of the pH effect on ACN color stability; changes in ACN color pigments due to the chemical alteration in nitrogenous compounds under various pH conditions.

Similarly, blueberry PC (chelator-soluble) enhanced the stability attributes of malvidin-3-glucoside (M3G), blueberry extract, and cyanidin-3-glucoside (C3G) during in vitro GI digestion simulation studies [51]. ACNs with improved bioavailability influence the gut microbiota composition and increase the number of beneficial bacteria, lower inflammation, and alter the glycemic response, and other physiological responses [52].

2.2. Proteins

The interaction of ACNs with protein can improve the overall stability of the ACN-protein complex, as well as its functional, and nutritional properties [53]. ACNs and proteins combine owing to the inherent sensitivity of ACNs to alkaline oxidation, in turn yielding quinones [54], which tend to form strong and fairly stable C-N or C-S covalent bonds by way of the nucleophilic addition of mercaptan and amino groups on the protein side chains [55]. Given that the bioavailability of ACNs in the human body is markedly low [9], combining ACNs with proteins can significantly improve the stability of these compounds, as well as enhance their absorption rates [30].

ACNs from sour cherry (*Prunus cerasus* L.) peel were encapsulated with whey protein isolates (WPI) and acacia gums, with an encapsulation efficiency of 70.30 ± 2.20%, and the in vitro digestibility analyses indicated that WPIs protected ACNs against gastric digestion, thereby facilitating their release in the small intestine [56].

2.3. Lipids

Encapsulation of ACNs in emulsion droplets is a viable solution for enhancing their stability, and bioavailability. Studies have reported the encapsulation of ACNs in various types of emulsions, predominantly water-in-oil-in-water (W/O/W) emulsions [57]. The W/O/W emulsions have different internal and external values of pH, which may slow down pH-induced color changes in the encapsulated ACNs [58]. Phospholipids including lecithin isolated from the soybean, eggs, lecithin, and marine sources, as well as milk phospholipids, also form a major component of the liposome delivery systems [59].

The presence of cholesterol along with phospholipids has also proven significant for the stabilization of ACNs [60].

2.4. Biopolymer Complexes

Natural biopolymeric complexes, in particular, polysaccharides and protein matrices being utilized for the encapsulation of ACNs [61]. The presence of electrostatic interaction-induced supramolecular structures within these macromolecules, their non-hazardous nature, and their generally recognized as safe (GRAS) status render them highly versatile vehicles for encapsulating and delivering ACNs in food-associated applications [62]. Copigmentation intensifies and stabilizes the color of ACNs by protecting the flavylium cation of these pigments from nucleophilic attack [63].

The biopolymers widely reported to be suitable for the copigmentation of ACNs include PC, dextran sulfate, guar gum, gum arabic, and whey proteins [62]. For instance, in a study, gum arabic (0.05–5.0%) significantly improved the color stability of purple carrot ACNs when used for commercial beverage applications, with the highest stability levels occurring at intermediate gum arabic concentrations (1.5%) [64].

3. ACN Delivery Systems

Different types of colloidal particles can be used as viable delivery systems for ACNs (Figures 3 and 4), including, nanostructured lipid carriers (NLCs), solid-lipid nanoparticles (SLNs), liposomes, emulsions, and others [65]. In encapsulation, highly sensitive constituents are enclosed within a wall material before delivering inside a system and could be formed by nanoencapsulation (<1 µm) or microencapsulation (1–1000 µm) depending upon the particle size [66]. This significantly improves the stability, water solubility, and bioavailability of bioactive compounds [67] and prevents the enzymatic and chemical degradation of ACNs [68]. However, conventional microencapsulation has not proven effective in the context of stability studies for ACNs, primarily because of their bigger particle size and low encapsulation efficiency [69].

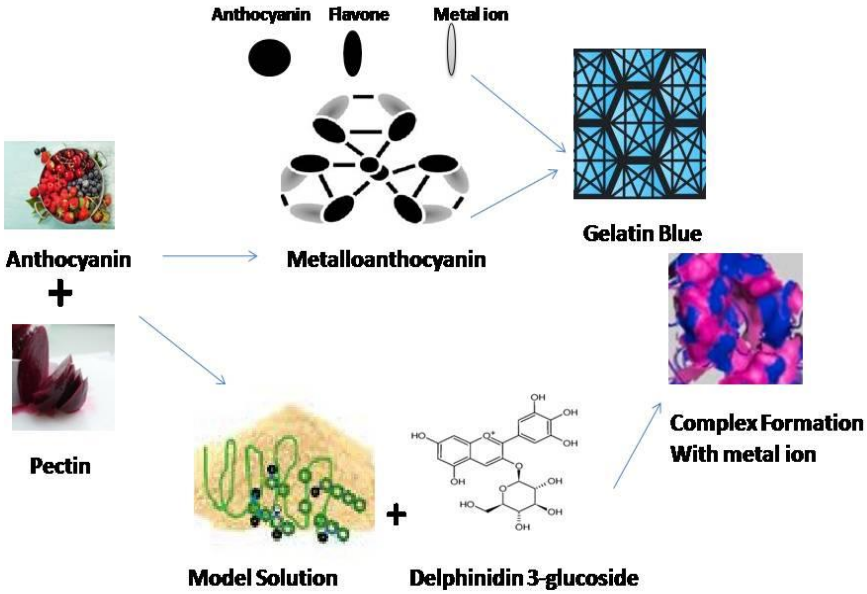

Figure 3. Pictorial representation showing the interaction of polysaccharide-based wall material (pectin) with the ACNs color pigments as encapsulating agents to increase the stability of ACNs.

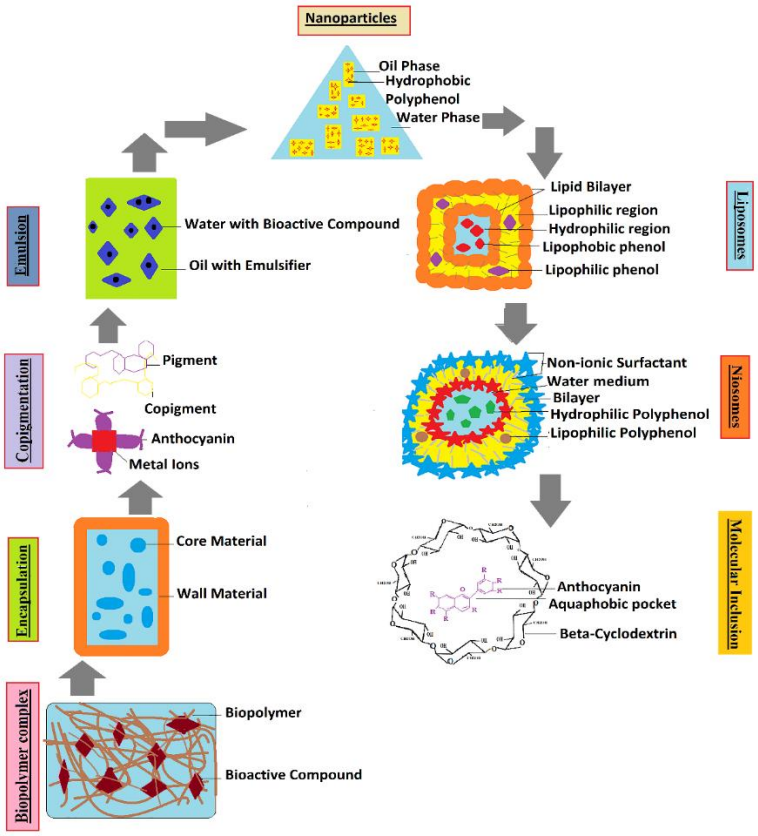

Figure 4. Formulation of different conventional and advanced delivery systems used for encapsulation of ACN pigments in different biopolymer complexes (carbohydrates, protein, lipids), and wall materials.

Different formulation and storage techniques related to encapsulation are summarized in Table 1. Protein-based delivery systems are frequently used in microencapsulation owing to various favorable attributes, such as cost-effectiveness, porous structure, surface-active nature, and ability to self-assemble, bind water molecules, and form stable, biodegradable hydrogels [70].

Table 1. Methods for encapsulation of anthocyanin using different material and their outcomes.

Method	Source	Encapsulation Material	Study Outcome	Reference
Spray drying	Grape juice	Maltodextrin, whey proteins, soybean	120 days of ACNs stability at 35 °C using soybean with maltodextrin (10% degradation)	[71]
	Pomegranate powder	Gum arabic and modified starch	Higher ACNs retention (60%)	[72]
	Jussara	Starch, inulin, and Maltodextrin	ACNs color maintained together with light stability at 50 °C for 38 days	[73]
	Barberry	Gum arabica, Maltodextrin, and gelatin	Microencapsulation efficiency of 92.8% was achieved during the study	[74]
	Grape pomace	Maltodextrins	11 days' half-life stability of encapsulated ACNs into apple pure matrix at 35 °C	[75]

Table 1. *Cont.*

Method	Source	Encapsulation Material	Study Outcome	Reference
	Jussara	Gum arabica, modified starch, whey proteins, or Soy protein isolate	The use of the two polysaccharides with either one of the proteins resulted in high encapsulation efficiency and ACNs retention	[76]
	Purple sweet potato	MC grafted with cinnamic acid	Maltodextrins with cinnamic acid improved ACNs stability over 30 days' storage time in comparison to maltodextrin or free ACNs	[77]
	Blueberry	Whey proteins	Encapsulated blueberry ACNs were more stable than blueberry extract	[78]
	Purple maize	Modified, normal, and waxy maize starches	Acetylated starches had superior encapsulating power for ACNs	[79]
	Black raspberry juice	Maltodextrin, fenugreek gum, and microcrystalline cellulose	Gum and cellulose increased the overall properties of the powders and ACN concentration	[80]
	Roselle extract	Maltodextrin, pectin, gelatin, Carboxy methyl cellulose, whey proteins, carrageenan, and Gum arabica	Pectin showed better retention and release, throughout the storage period	[81]
	Blueberry	Maltodextrin and Gum arabica	The use of an ultrasonic nozzle better protected the blueberry bioactive than the conventional nozzle and had similar results for AA and total ACN contents	[82,83]
	Jussara pulp	Gelatin, Gum arabica, maltodextrin	Optimization study pointed to 165 °C and 5% of carrier material as the best for ACNs retention. At 40 °C and 75% of relative humidity, ACNs half-life was 14 days when coated with GA	[84]
	Saffron anthocyanin	β-glucan and β-cyclodextrin	Higher concentrations of ACNs were protected from adverse stomach conditions by encapsulation	[85]
	Roselle extract	β-cyclodextrin, soy protein isolate, gelatin	Increased the thermal stability and encapsulation efficiency by 99% using the composite wall materials of purified roselle extract	[86]
Freeze-drying	Raspberry	Gum arabica and Soy proteins	Increased retention of ACNs by 36%	[30]
	Milk-Blackberry pulp	Maltodextrin and modified starch	High anthocyanin content and increased antioxidant capacity	[87]
	Sour cherry	Soy proteins and whey proteins	SP showed higher encapsulation efficiency and higher anthocyanin content	[88]
	Grape extract	Acacia gum and whey proteins	Improved encapsulation efficiency of ACN	[89]
	Wine grape pomace	Gum arabica and Maltodextrin	Samples had 91% encapsulation efficiency	[90]

Table 1. *Cont.*

Method	Source	Encapsulation Material	Study Outcome	Reference
	Saffron petal	Cress seed gum, Gum arabica, Maltodextrin	Cress seed gum had the same results for ACNs stability as other conventional wall materials however, lower color constancy	[91]
	Cherry juice	Maltodextrin and Gum arabica	ACN retention was 90%, in comparison to liquid juice (11%)	[92]
Electrospraying	Black carrot extract	Gelatin and chitosan	Faster release in the acetic acid medium with greater encapsulation efficiency	[16]
Ultrasonication	Anthocyanin	Lecithin	Sustained release and high stability of anthocyanin	[93]
Electrospinning	Sour cherry extract	Lactalbumin and gelatin	Increased bioaccessibility and stability of ACNs	[94]
Copigmentation	Blueberry	Chondroitin sulfate and kappa carrageenan	Effective protection against degradation at low pH	[95]
	Anthocyanin	Guar gum	High encapsulation efficiency and high kinetic stability	[57]
	Blueberry and Elderberry	Chondroitin and chitosan	Improved chemical stability and stable color of anthocyanin	[96]
	ACNs extract	Gum arabica	GA coating increased color stability and half-life of ACNs at high temperatures	[97]
	Bilberry	Dextran sulfate	During storage in dark conditions at 4 °C, ACN content decreased by 12% as compared to extract (35%)	[98]
Supercritical CO_2	Bilberry	Soy lecithin	Higher stability and encapsulation efficiency	[99]
Microwave	Roselle and Red Cabbage	Maltodextrin	Encapsulated ACNs were able to improve margarine stability against phase separation and oxidation	[100]
Extrusion	Haskap berries	Calcium-alginate	The increased residence time of microparticle gels in the stomach suggests a more controlled release of ACNs	[101,102]
	Clitoria ternatea petal flower extract	Alginate and calcium chloride	Thermal stability with inhibition of carbohydrate and lipid digestion	[26]
Evaporation	Cyanidin-3-glycoside extract	*N*-trimethyl chitosan-coated liposomes	Coating ACNs increase the antioxidant activity in rat's cornea, with higher transepithelial transport	[103]
Gelation	Jussara extract	Alginate, chitosan, whey proteins, gelatin	Alginate hydrogel beads and chitosan showed greater antioxidant capacity [higher protection] as compared to WP and gelatin	[104]
	Black rice	Maltodextrin, Gum arabica, whey proteins	Whey protein isolates exhibited a greater release of anthocyanin in GIT with enhanced antioxidant activity	[105]
	Mulberry	Alginate and chitosan beads	High ACN encapsulation efficiency	[106]

Table 1. *Cont.*

Method	Source	Encapsulation Material	Study Outcome	Reference
	Purple rice bran	Pectin, zein, and whey proteins	Pectin-WP and Pectin-zein-WP capsules have the potential of slowly releasing delivery systems for ACNs	[107]
	Blueberry	Chitosan/cellulose Chitosan/sodium tripolyphosphate	Cellulose nanocrystals had better ACN recovery and stability at pH 7 than sodium tripolyphosphate	[108]
Sol-gel technique	Black carrot	Silica (drug delivery system)	Nanoparticles with ACNs were able to inhibit 87.9% of neuroblastoma cells	[109]
Coacervation	Black rice	Gelatin-acacia gum and chitosan- Carboxymethylcellulose	Microcapsules can be applied for incorporating ACNs into nutraceuticals for controlled release	[110]
	Blueberry	Chitosan	Chitosan was able to stabilize ACNs after simulated GI fluid assay and storage	[111]
	Purple sweet potato	Konjac glucomannan	Extra chitosan oligosaccharides coat was needed to stabilize microspheres against stomach conditions and to release ACNs in the small intestine [in vitro]	[112]
Inclusion Complexes	Bignay and duhat extract	β-cyclodextrin	Increased encapsulation efficiency and possess enzyme inhibitory properties	[113]
Yeast mediated encapsulation	Chokeberry ACNs	*Saccharomyces cerevisiae* [yeast]	Yeast turned the ACNs efficiency around by 55%	[114]

These hydrogels, therefore, are not only suitable for encapsulating ACNs, ensuring stability, and controlled release, but also offer opportunities to be used for many food industry applications, such as thickeners (sauces, soups), texturizers (confections), and flavors (slow-release) [115]. Nanoencapsulated complexes comprising CH hydrochloride, carboxymethyl CH, and β-Lg incorporated with ACN extracts also improved their bioavailability and stability [116]. Another novel technique for encapsulation of ACN-rich extracts is by using niosomes, which have emerged as a suitable delivery system for ACNs, owing to the low toxicity and high biocompatibility attributes of these liposomal formulations [117]. Molecular inclusion complexes are another approach to stabilize ACNs, whereby ACNs have been coupled with β-cyclodextrins (β-CDs), resulting in slower GI stabilization, as well as protecting the ACNs from polymerization and hydration reactions [118]. This complexation with CDs increased thermal stability and reduced the degradation of ACNs, thereby protecting them in the difficult GI environment. Furthermore, the utilization of CDs as encapsulation materials for bioactive compounds may lead to enhanced solubility, greater permeability through intestinal membranes, as well as greater bioavailability of the encapsulated compounds [119].

3.1. Nanoparticles

In a study [120], ACN extracts encapsulated in β-Lg nanoparticles exhibited greater antioxidant activity and enhanced retention at various pH ranges: pH 6.8 (mouth), pH 6.9 (simulated gastric), and pH 2 (simulated intestinal), as compared to unencapsulated ACNs. Nanocarriers formulated using CH-PC complexes provided adequate protection against degradation by gastric juice and therefore, facilitated the release of ACNs in the small intestine [121]. Nanocomposites containing amphiphilic peptide C6M1 significantly improved the stability of ACNs against increased pH, elevated temperatures, and metallic ions [120].

Similarly, zein-ACN nanoparticles have been found to exhibit greater encapsulation efficiency and scavenging activity as compared to ACN extracts without nanocrystallization [122]. SLNs made up of solid lipid shells [high melting lipid matrix], also have a better encapsulation efficiency, slow rate of degradation, superior stability, and low cost of production, as compared to nanoemulsions (NEs) [123]. ACNs from red cabbage encapsulated in SLNs prepared by way of diluting the water-in-oil [W/O] microemulsions (MEs) containing ACNs in the aqueous phase exhibited greater stability under GI conditions, as compared to unencapsulated ACNs [69]. However, encapsulating ACNs in SLNs might be challenging owing to their tendency to partition into the aqueous phase during preparation procedures [124].

3.2. Liposomes

Liposomes have demonstrated the potential to protect and stabilize ACNs, ensuring their prolonged presence in the systemic circulation, and therefore, enhanced cellular uptake in the human body [125]. Nanoliposomes, resulting from particle size reduction of conventional liposomes using ultrasound, membrane extrusion, or high-pressure homogenization, in particular, has emerged as an excellent delivery system for ACNs, owing to their amphipathic, non-immunogenic, and non-toxic characteristics, biodegradability, and biocompatibility [69].

3.3. Emulsions

Multiple emulsions, or more colloquially, double emulsions, such as W/O/W emulsions, are garnering increasing interest in the context of encapsulation, enhanced retention, and improved protection of ACNs [126]. Huang and Zhou [127] encapsulated ACNs from black rice extract in a W/O/W emulsion, evaluated the changes in ACN concentration, and release attributes of the multiple emulsion by way of an in vitro simulated digestion study. The study reported a high microencapsulation efficiency of 99.45 $\pm$ 0.24%, and that the multiple emulsion-maintained encapsulations even after 2 h of exposure to gastric juice, thereby preventing the release of ACNs in the stomach environment [127].

Likewise, owning a large droplet surface area, and a reduction in particle size have made NEs a proven solution for increasing the functionality of ACNs contained within [128]. Furthermore, NEs provide greater stability against droplet aggregation and gravitational separation owing to their high surface-to-volume ratio, an attribute of critical significance from the perspective of shelf-life enhancement of various food and beverage industry products [129].

3.4. Biopolymer Particles

Biopolymer particles comprise a dense framework, including supramolecular structures formed through electrostatic interactions, which can be used to encapsulate and deliver ACNs in the human body [11]. The properties of the carrier type, or wall material, as well as the various interactions between the polymer system, and bioactive ensure that the release of the core components is initiated at a specific time and location within the human GI system [45].

Among the carrier agents, the most commonly used biopolymers for ACNs encapsulation in recent years include maltodextrins (19.56%), gums (15.22%), milk proteins (13.04%), starches, and their derivatives (>9.78%) [130]. Alginate, the polysaccharide isolated from various brown seaweeds, forms gels [through ionotropic gelation] in the presence of cations (Ca^{2+}, Ba^{2+}, Zn^{2+}) as crosslinkers, making these gels favorable options as delivery systems [131]. Natural polymers, when compared to their synthetic analogs, are highly biocompatible and biodegradable, and can be used for the entrapment of both hydrophilic and hydrophobic drugs [132]. A coacervated complex of CH and PC was used to encapsulate ACNs, with the subsequent in vitro analysis revealing that the bioaccessibility percentage of the coacervated ACNs formulation was markedly higher when compared to both the crude ACNs extract and the purified ACNs crystals [133].

More recently, dietary fibers have gained prominence as biocompatible, biodegradable, relatively less toxic, and cost-effective colon-targeted delivery systems for various natural polyphenols with therapeutic potential [134]. The various advantages imparted by these polymers include maintenance of the structural integrity of delivery systems, thereby shielding polyphenols from the harsh environmental conditions in the GI tract, facilitating the colonic microbe-mediated polyphenol biotransformation, strengthening dietary fiber-polyphenol interlinkages, improved colon-associated mucoadhesion, and resultant enhanced payload delivery, and synergistic prebiotic effects [135,136] reported that hydrogels prepared using glucomannan and xanthan gums isolated from konjac [*Amorphophallus konjac*] for encapsulation of ACNs offered superior protection against pH variations in the GI tract.

3.5. Copigmentation

Copigmentation stabilizes ACNs by way of the formation of a non-covalent molecular complex with a colorless organic or inorganic compound [63]. The 'sandwich' complex that results, therefore, renders greater protection to the flavylium chromophore against the water molecule-induced nucleophilic substitution, thereby preventing the degradation of ACNs to colorless chalcone and hemiketal forms [137]. PC-induced copigmentation of European bilberry (*Vaccinium myrtillus*) ACN extracts extended stability to both ACNs and the resulting multiple emulsions [62]. Furthermore, ACNs copigmented with PC or chondroitin sulfate (CS) (negative charge) combine with CH (positive charge), manifesting in the formation of polyelectrolyte complexes [PECs] that can be utilized as delivery systems and have been shown to enhance the biological function of ACNs [138]. The summary of the delivery system used for the ACNs-coloring pigment is presented in Table 2.

Table 2. Summary of the methods involved in the stability of the ACNs-coloring pigments.

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Blanching	Blanching helps to balance the substitution of the B-ring and the corresponding susceptibility to oxidation. Blanching can help to restore the color of malvidin and peonidin-based ACNs	The total ACNs concentration did not significantly affect by blanching. The overall proportion of polymeric color was found to be increased by 8% by blanching	Glycosylation during the blanching affects thermal stability. Pentosides are found less stable than hexoses in blanched chokeberries	It can ensure the thermal stability of ACNs in blueberries [*Vaccinium corymbosum*]. A total of 11% of ACNs concentration increased compared to juices from blanched fruits to non-blanched fruits, particularly berries	[139]
High-Pressure Processing (HPP)	HPP tends to promote minor changes in the ACNs content of fruits under ambient temperatures.	The increased pressure during HPP treatment leads to condensation reactions.	High temperature (>70 °C) during HPP can decrease the thermal stability at high pressure.	Application of moderate temperatures (45 °C) during HPP treatment results in increases in total ACNs concentration (about 9%) in blueberry juice and fruits.	[140,141]

Table 2. *Cont.*

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Copigmentation with coloring compounds	ACNs can be stabilized using intramolecular, intermolecular and self-association, co-pigmentation techniques. Vertical stacking and copigmentation lead to enhancement of the overall color intensity of ACNs	Flavonoids, phenolic acids, alkaloids, amino acids, purines, and polysaccharides are molecules used for the ACNs stabilization using copigmentation	Major factors affecting ACNs stability are type, the concentration of both ACNs and copigments, temperature, pH, and solvent type. pH is the most promising factor affecting the ACNs stability	With the pyruvate, ACNs tend to form pyranoanthocyanins and enhance the pH stability of the ACNs color	[142]
Copigmentation with flavonoids	ACNs can be stabilized by copigmenting with colorless flavonoids of plant cells	At low pH (<3), during in vitro analysis, ACNs tend to be redder and more stable, whereas colorless in a weakly acidic [pH 3–6] environment	At high pH (>6) the ACNs become unstable. The increased pH reduces the ACNs stability and promotes degradation	Purple sweet potato extract (PSPE) can be stabilized by changing the pH under 37 °C and its use can be increased to develop as healthy foods and drinks rich in ACNs at low pH	[143,144]
Copigmentation with metal ions	ACNs are composed of o-dihydroxy groups in their B-ring that can be stabilized by conjugating with various metal ions chelates. The promising metal ions are Mg^{2+}, K, Fe^{3+}, Al^{3+}, Cu^{2+}, Sn^{2+} and Mo^{2+}, which on conjugation with ACNs develop blue color	Co-pigmentation of ACNs with metal ions also reduced the metal ion toxicity	The interaction between o-di-hydroxyl ACNs and metal ions occurs under pH 5	In black carrots, orange juice, and red wines, ACNs were stabilized by forming the pyranoanthocyanins with metal ions. The blue color in cabbage is stabilized by the interaction between ACNs and Mo	[5,145–149]
Copigmentation with a methoxy group	The hydroxyl and methoxyl groups availability also promotes ACNs under neutral pH	The copigmentation of ACNs with the methoxy group causes acylation that improves the ACNs stability	in a neutral environment, ACNs stabilized by increasing the methylation in the B ring	Monoglycosides and di-glycoside compounds showed more tendency o of stabilization by avoiding the degradation of unstable intermediates into phenols of aldehydes	[150]
Copigmentation with whey protein	The fruits-derived ACNs including grape, purple corn, or black carrot can be stabilized by adding the preheated or native whey protein (WP) solutions in the dark at 4 °C for 4 weeks.	Copigmentation of ACNs with WP showed good stability	The preheating of WP before ACNs copigmentation produced more heat-stable and less UV-light stable compounds	The preheating of WP tends to protect ACNs from degradation. ACNs and WP combined pigments improve the performance of commercially available ACNs-based food colorants	[151]

Table 2. *Cont.*

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Copigmentation with carbohydrates	The non-polar interactions of polysaccharides [carbohydrates] cause the ACNs stability	Pectins and other carbohydrates inhibit the precipitation of the ACNs metal chelates, thus improving the color stability of the ACNs	Copigmentation of ACNs with the carbohydrates is the pH-dependent reaction, most of the fruit pectin exhibits good stability under pH 5	Guar gum, xanthan gum, pectin, alginate, gum arabic, chitosan, and modified starches exhibited good ACNs stability under controlled conditions	[11]
Nanoemulsion contained ACNs	Nanoemulsions containing the ACNs-rich mangosteen peel extract (MPE-NE) produced the self-nano emulsifying drug delivery system by stabilizing the ACNs	The nanoemulsion of ACNs had higher diffusion (97%) within 8 h in an in vitro analysis	Major factors affecting the nanoemulsions are particle size, zeta potential, and drug loading technique. In the nanoemulsion the droplet particle size, the ZP, and the drug loading were 20 nm, −12.40 mV, and 125 mg/5 mL, respectively	Nanoemulsion with MPE can increase penetration of predominant α-mangostin through the stratum corneum and can physically stabilize the ACNs for three months	[152]
Mangosteen extract-based nanoemulsion	ACNs were stabilized by forming nanoemulsion with ethyl acetate mangosteen extract using a high-speed homogenization	Nanoemulsion used to stabilize ACNs for 28 days without phase separation	Promising factors affecting the nanoemulsions were particle size, ZP, and drug loading technique.	The 28 days stabilized mangosteen nanoemulsion can be used for topical application	[153]
Red Cabbage ACNs-based nanoemulsions	Red cabbage ACNs were stabilized by being incorporated into solid lipid nanoparticles (SLNs) through W/O microemulsion. Red cabbage ACNs used as aqueous phase against the lipid phase consisted of palmitic acid and span 85 (surfactant) and egg lecithin	The red cabbage ACNs emulsion was stabilized at pH 3.0 (gastric fluid) at a low temperature of <25 °C	Major factors affecting the nanoemulsions are particle size, ZP, and phase selected for the ACNs incorporation and temperature [60 °C]	ACNs from red cabbage can be stabilized using nanoemulsions at 25 °C and pH 3. It is the most convenient lab scale technique used to stabilize the ACNs	[154]

Table 2. *Cont.*

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Nanoliposomes	ACNs can be stabilized by layer-by-layer coating with biopolymers, forming the nanoliposomes can be stabilized.	ACN-based nanoliposomes tend to increase the adsorption, stability, and bioavailability of ACNs. These liposomes are considered nontoxic and nonimmunogenic	The considering factors affecting the ACN-based nanoliposomes stability are heterogeneous size distribution, low encapsulation efficiency, high energy cost, and the presence of solvent/surfactant residue	ACN-based nanoliposomes can be prepared by thin-film hydration, ethanol injection, reverse phase evaporation	[155,156]
Nanoliposomes to encapsulate ACNs based extracts	To enhance the ACNs stability, *Hibiscus sabdariffa Linn* extract nanoliposomes formed using lecithin and cholesterol with an efficiency of 55%	The DPPH radical scavenging activity was increased from 11% to 64% of ACNs extract-based liposomes at 20–50 mg/mL	Factors affecting the stability of the ACN-based liposomes are particle size, increasing storage time, and a rise in temperature from 4 °C [206.2 nm] to 60 °C (157.5 nm)	During storage, about 35–40% of ACNs were found incorporated in nanoliposomes at 37 °C after 8 h and increase gradually to 45% after 24 hrs	[157]
Encapsulation of ACNs by multilamellar liposomes formation	*Hibiscus sabdariffa* ACNs can be stabilized by incorporating them into polysaccharide-based coatings particularly chitosan and pectin by forming in multilamellar liposomes using the layer-by-layer technique	The multilayered liposomes of *Hibiscus sabdariffa* provided the highest stability over 30 days and proved an effective carrier system for ACNs	Factors affecting the multilamellar liposome stability are the material used for the liposome, number of coatings, extract concentration, coating percentage, surface coverage, particle size	The inclusion of HS extract into multilamellar liposomes did not significantly change in particle size and storage stability of coated ACNs compared to uncoated ACNs	[158]
Lecithins Liposomes to encapsulate ACNs	Elderberry ACNs extract was stabilized using lecithins by forming nanoliposomes with a thin lipid film hydration technique.	Plant-based lecithin found a great potential to stabilize the ACNs coloring compounds.	The stability of ACN-based lecithin liposomes can be best improved at 4 °C in dark storage with a decrease in particle size to 166 nm	Soya lecithin liposome promoted the highest stability for the ACNs of blueberry extract, with low PDI (0.49), ZP −36.4 mV, and small particle size around 205 nm]	[159]

Table 2. *Cont.*

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Spray Drying	By spray drying, ACNs are atomized through a high-pressure nozzle followed by evaporation (150–220 °C) of the solvent to get the sprayed drops. Lastly, a cyclone is used to separate and recover the powdered product from the air.	This method is found quick, easy to adapt, cost-effective, and simple to scale up, with high encapsulation efficiency, and good storage stability.	Crucial parameters involved were the choice of suitable wall material for microencapsulation. Availability of the limited compounds that have low viscosity, solubility, film-forming capacity, and emulsifying properties.	Most used compounds are polysaccharides for spray-drying encapsulation of ACNs and polyphenolic compounds.	[5]
Freeze Drying	ACNs can be stabilized by freezing mechanism includes sublimation, desorption, and finally the storage of the resulting dry material	The simplest process takes place in the absence of air and at a low temperature, and, obtained compounds get resistant to oxidation	Impart high costs due to the use of vacuum technology. A long period for dehydration about 20 hrs. is required.	ACNs present in the black bran rice powders can be stabilized by this method	[5,160]
Green Solvent Extraction	ACNs stabilized during extraction from mulberry by using the green extraction solvent based on β-cyclodextrin and hydroxypropyl-β-cyclodextrin (β-CD)	β-cyclodextrin enhances ACNs stability by producing the fewer safety concerns	Optimal extraction can be obtained using β-cyclodextrin at 20 oC for 44.95 min at the concentration of 45 g L^{-1}.	This method helps to improve the ACNs stability during extraction and also improves the thermal stability	[161]
Formation of inclusion complex of β-CD	ACNs and their combinations were encapsulated in β-CD	ACNs stabilized by forming the inclusion complexes with β-CD	The molar ratio at 1:1 was maintained during the inclusion complex to attain the high encapsulation efficiency	Inclusion complexes help to increase the thermal and storage stability of the ACNs without changing the beneficial properties of these phenolic compounds	[162]
Pressurized Liquid Extraction (PLE) technique	During the extraction, the solvent used must be in a liquid state at more than the boiling point but less than its critical limit	PLE is an efficient, eco-friendly, and emerging technology to perform efficient ACNs extractions under high temperatures and pressure	The optimum conditions used for the PLE to extract black beans ACNs were ethanol: citric acid solution (30:70 *v/v*), with a flow rate of 4 mL min^{-1} under the temperature of 60 °C	The commercially acceptable technique used for the efficient extraction of ACNs from black beans	[163]

Table 2. *Cont.*

Methods Involved in the ACNs Stability	The Mechanism Involved in the Stability of ACNs	Advantages	Factors Affecting the Efficiency of Stability	Food Applications	References
Supercritical carbon dioxide (SC-CO_2) extraction	Red ACNs pigments from roselle calyces were extracted using the SC-CO_2. The total ACNS production was reported 1197 mg/ 100 g roselle calyces	SC-CO_2 is considered an efficient extraction technique with low degradation rates of ACNs	Three process control variables that affected the ACNs stability during SC-CO_2 extraction are pressure, temperature, and co-solvent ration [ethanol: water]	Maintaining the optimum conditions 27 MPa, 58 °C temperature, and 8.86% co-solvent ratio, maximum ACNs from roselle crystals can be extracted with a lower degradation rate and 2-fold higher yield than the conventional methods	[164]

4. Comparison of Formulation Techniques

Several research studies have explored ACN-based delivery systems and their potential applications in the food industry. The variations observed in the properties of the ACN-based delivery systems can be attributed to the choice of wall material and preparation techniques, making ACNs highly versatile additives for food and non-food applications. Despite their potential for industrial applications, ACN-based delivery systems suffer from certain drawbacks, restricting their application. The primary limiting factor in this regard is the inherent instability of ACNs which has remained a major concern in terms of their use in the processing of different food products. More recent research has indicated that ACNs exhibited optimal stability and functionality at low storage temperatures and pH values under 5 [125,165].

The stabilization of ACNs can be achieved by, among other things, various microencapsulation techniques, which can be categorized into chemical, physical, and physicochemical methods. Spray drying has become a promising method for the encapsulation of ANCs, as it is rapid, produces a high yield of encapsulated ACNs, and is easy to scale up if process parameters are optimized [166]. During surface drying, the optimization of process parameters including time and temperature is critical, as it may manifest in the production of unstable, non-uniform, or degraded ACNs, ultimately culminating in the loss of yield [167].

Freeze-drying is also regarded as an effective technique for the stabilization of the ACNs, provided that low temperature and pressure are maintained, as variations in temperature and pressure render ACNs more prone to oxidation, and therefore, instability [168]. However, long processing times, energy expenditure, instability, susceptibility to oxidation, and high process costs are major drawbacks of freeze-drying [167].

The use of electrohydrodynamic (EHD) processes including electrospinning and electrospraying (EHD atomization) has demonstrated multiple advantages over other encapsulation techniques in the context of encapsulation of food ingredients, such as low-cost (one-step production process), operation under mild conditions, the possibility of use of the majority of food-grade materials, high encapsulation efficiencies, and the feasibility of tailoring the size and morphology of the resulting encapsulated structures by altering the processing conditions [169]. One of the major considerations regarding this technique is the negative effect of high voltage on the quality of bioactives such as ACNs and biopolymer materials [170]. However, the research encompassing the effect of high voltage on the release rate of the ACNs is insufficient [171]. Further research into EHD processes, therefore, can improve the outcomes for encapsulated ACNs, and their application in food fortification and food packaging operations.

Inclusion complexes are considered an important chemical approach to encapsulate the ACNs (guest compound) in cavity-bearing host molecules by way of hydrophobic

interactions, hydrogen bonding, or van der Waals forces [167]. The technique has proven effective to stabilize the ACNs by preventing polymerization, oxidation, and thermal degradation. CDs, and in particular, β-CDs, have proven particularly effective with regard to the formation of inclusion complexes, and therefore, wider applications for the stabilization of food-based bioactive components. However, β-CDs exhibit very low solubility in water (1.85 g/100 mL), attributable to hydrogen bonding in their structures, and results in increased viscosity at high concentrations, as well as precipitation at very high concentrations [172]. Pickering emulsions have also proven effective for encapsulation of the ACNs, in particular, in combination with gliadin and soy proteins [173]. Pickering emulsions, as active delivery systems, are highly suitable for the encapsulation of bioactives and functional food ingredients, owing to their process stability, biosafety, bioaccessibility, biocompatibility, and controlled release attributes [174].

Likewise, liposomes have emerged as an advanced bio-based delivery system for the encapsulation of ACNs and offer advantages similar to Pickering emulsions. However, due to the presence of unsaturated fatty acids in their structure, oxidation of the liposome membranes remains a significant constraint [167]. The exclusion of oxygen has also been explored as a potential strategy for imparting greater stability to ACNs during processing operations and storage [175].

Biopolymeric nanoparticles (BPNs), essentially, the nanoparticles constructed from various natural polymers commonly distributed in a wide range of biological species, for instance, polysaccharides (starch, alginate, chitosan, pullulan, heparin, and hyaluronic acid), proteins (gelatin, collagen, albumin, zein, and β-casein), and protein-mimicking polypeptides (PMPs) (particularly cationic polypeptides, e.g., polyornithine, and polylysine) [176,177], are another emerging delivery system of increasing interest owing to their favorable characteristics such as good biodegradability, and biocompatibility, design simplicity, safety, and environmental-friendliness for various applications [178]. Owing to their ease of functionalization, and small size, BPNs can be utilized as a universal drug delivery system [179], with the potential of loading high concentrations of a drug substance, and protecting it against the human body's internal environment, thereby aiding in the maintenance of its bioactivity [180]. BPNs may also help in overcoming problems associated with the chemical stability, and solubility of phenolic compounds, such as ACNs, as studies have indicated that ACNs loaded into self-assembled BPNs exhibited superior thermal stability under processing conditions (90 °C) [181,182], and therefore, present as a valuable avenue of future research as delivery systems for applications involving ACNs.

Besides conventional techniques used for ACN extraction, different solvent-assisted extraction techniques are also considered effective for ACN extraction, and their subsequent use in foods and pharmaceuticals. The solvent-based extraction techniques, although offering superior operational ease, are marred by the generation of high solvent waste and their time-intensive nature. Irradiation-based ACN extraction techniques including ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), ultrasound-assisted enzymatic extraction (UAEE), and ultrasound-assisted deep eutectic solvent extraction (UA-DES-E) have also yielded a significant amount of ACNs with greater stability and reduced toxicity. However, the maintenance and equipment costs for these when compared to solvent and irradiation based ACN extraction techniques remain relatively higher [183]. Moreover, numerous factors associated with the stability of ACNs including oxygen, temperature, pH, the presence of metallic ions, and co-pigments also affect the choice of an extraction technique [184].

5. Conclusions, and Future Trends

The current review mainly focuses on the bio-based materials used for the encapsulation of ACNs, food-grade delivery systems, and food applications. Various bio-based materials including pectin, gums, PC, proteins, lipids, phospholipids, and their conjugates are being widely used for targeted delivery and controlled release of bioactive compounds and drugs. Currently, carbohydrate-based encapsulation materials are more common as

compared to those involving lipids and proteins. Future research should be aimed at optimizing the parameters for protein- and lipid-based encapsulation systems for wider acceptability. The stability and release attributes associated with various delivery systems are dependent on multiple process parameters, such as time, temperature, pressure, post-process treatments, and viscosity. Given that sufficient data related to these process parameters is lacking, more future studies focused on these aspects are required to enhance the stability and application potential of the encapsulated materials. Additionally, the selection of the microencapsulation process is primarily related to the thermosensitivity and solubility of the ACNs. It is important to consider while using any encapsulation technique whether there is a need for any post-encapsulation treatments. The incorporation of advanced technologies seems to be promising in the context of extraction, encapsulation, and storage of ACNs. However, more comprehensive studies are required for the application of encapsulated ACNs in various food products, and improvements in their stability under different processing conditions. Owing to their health claims, encapsulated ACNs can be used in food fortification, food packaging, and the production of functional foods.

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Abbreviations

ACNs	Anthocyanins
OH	Hydroxyl group
O-CH_3	Methoxyl
ADME	Absorption, metabolism, distribution, and excretion
EFSA	European Food Safety Authority
CH	Chitosan
C3G	Cyanidin-3-glucoside
WPI	Whey Protein Isolate
CDs	Cyclodextrin
SLNs	Solid Lipid Nanoparticles
W/O/W	Water-in-Oil-in-Water
NLCs	Nanostructured Lipid Carriers
β-CD	β-cyclodextrins
EHD	Electrohydrodynamic
CS	Chondroitin sulfate
BPNs	Biopolymeric nanoparticles
PMPs	Protein-mimicking polypeptides

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