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Edible clay minerals and related layered materials for loading and delivery of food bioactives: interaction mechanisms, applications, and safety—A mixed systematic–narrative review

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Systematic Review

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Abstract

Edible clay minerals are emerging as promising food-grade carriers for the stabilization and delivery of sensitive bioactive compounds, including polyphenols, vitamins, peptides, and essential oils. This systematic review with mechanistic narrative synthesis examines how clay architecture (lamellar smectites, tubular halloysite, fibrous clays, and synthetic discoidal clays), layer charge, and surface chemistry govern adsorption, ion exchange, intercalation, and confinement mechanisms associated with encapsulation performance and controlled release under processing and gastrointestinal-relevant conditions. The evidence synthesis followed PRISMA guidelines and included 56 studies, complemented by bibliometric analysis and mechanistic interpretation based on spectroscopy, diffraction techniques, and computational approaches, including molecular dynamics (MD) and density functional theory (DFT). Distinct structure–function relationships were identified among clay families: smectites favor cooperative adsorption and interlayer intercalation; halloysite nanotubes promote lumen confinement and co-loading; laponite supports colloidal assembly with biopolymers; and layered double hydroxides (LDH) enable anion exchange and pH-responsive release. Practical relevance was further demonstrated through applications in yogurt, clarified juices, hydrogels, aerogels, and active packaging films. Across the reviewed studies, encapsulation efficiencies generally ranged from approximately 37% to 99.7%, while loading capacities varied from tens to hundreds of mg/g depending on the bioactive compound, clay charge characteristics (CEC/AEC), and loading strategy. Four main incorporation routes were consistently identified—batch adsorption, vacuum-assisted loading, sequential assembly, and site titration—each influencing the balance among electrostatic interactions, hydrogen bonding, and dispersion forces. Finally, current regulatory and food-safety considerations are discussed, and key research priorities are proposed regarding long-term biosafety, bioaccessibility/bioavailability, migration assessment, and industrial scale-up with purity control.

1. Introduction

The growing demand for functional foods and nutraceuticals has positioned therapeutic bioactive compounds as fundamental elements for health promotion and disease prevention. Bioactive components—such as antioxidants, polyphenols, vitamins, bioactive peptides, and alkaloids [1, 2]—serve dual purposes: they offer technological applications as natural colorants and antimicrobials [2–5], and they promote nutritional security by reducing the risk of cancer, cardiovascular, and neurodegenerative diseases [4, 6–8]. However, the direct application of these bioactive compounds is often limited by their high susceptibility to degradation under adverse processing conditions and within the gastrointestinal tract, as well as their low solubility and bioavailability. To overcome these challenges, recent comprehensive reviews highlight the use of nanoencapsulation and the development of nanoscale delivery systems (nanocarriers) as highly promising technological strategies in the food industry. These nanotechnological approaches not only protect fragile functional ingredients but also ensure their controlled release, enhance their stability, and significantly improve their intestinal absorption and overall bioactivity [9–11].

Natural additives can be optimized using an integrative approach based on the co-adsorption of bioactive compounds and drugs, promoting synergistic nutritional–pharmacological effects [12–14]. However, the intrinsic instability of bioactives when exposed to oxygen, light, and temperature remains a significant challenge during processing and storage [11–13]. Furthermore, their sensitivity to extreme pH levels and gastrointestinal enzymatic activity severely limits their bioavailability and nutraceutical efficacy [15, 16]. This challenge has driven the development of advanced delivery systems designed to protect the functional integrity of these compounds until they reach their targeted site of action [15].

Among these solutions, natural, synthetic, and modified clays provide a highly promising platform for the stabilization and controlled release of bioactives. Through physical adsorption, specific chemical interactions, and the formation of nanocomposites, clays can effectively encapsulate extracts and bioactives, even enhancing their synergistic effects alongside medications [2, 17, 18]. Montmorillonite, bentonite, halloysite, and other abundant aluminosilicate minerals have emerged as multifunctional materials of immense interest in food science due to their unique physicochemical properties, high adsorption capacity, and excellent biocompatibility [19]. Their lamellar and fibrous structures allow for tailored chemical and physical modifications to suit specific applications [1, 20], enabling the stabilization of bioactives at the nanoscale [6, 21].

Current applications of clays in food systems span liquid, solid, and semi-solid matrices—including beverages, dairy products, and nutraceutical formulations—where their incorporation significantly improves product functionality and shelf life [5, 22, 23]. Despite these advances, critical knowledge gaps remain. There is an urgent need for more extensive *in vitro* and *in vivo* trials to guarantee their safety and efficacy upon oral administration, as well as a need to develop multicomponent systems that fully exploit the synergies between clays and bioactives [24–26].

This article systematically reviews the advances and trends in utilizing clays for the stabilization of bioactive compounds. It examines adsorption mechanisms, stabilization strategies, innovative applications in food and nutraceuticals, and key technological gaps. By integrating a bibliometric analysis with an in-depth technical evaluation of clay-bioactive systems, this review provides a quantitative and critical basis to assess the state of the art and guide future research in this interdisciplinary field where food science and health converge.

2. Methods

This review followed the PRISMA reporting guideline for systematic reviews and meta-analyses [27], with a mixed systematic–narrative design tailored to materials/food science evidence. A PRISMA flow diagram summarises identification, screening, eligibility, and inclusion (**Fig. 1**). No automation tools were used at any stage.

2.1. Protocol and registration

No formal protocol was registered a priori (e.g., PROSPERO/OSF), given the scope spanning analytical in vitro studies, food-matrix trials, and materials science papers where PROSPERO does not accept protocols. The review questions, eligibility criteria, data items, and synthesis plan were specified before screening and are reported below, consistent with PRISMA 2020 guidance.

2.2. Eligibility criteria (PICOS framing adapted)

- Population/Context: Edible systems and oral nutraceutical contexts (food matrices, beverages, powders/capsules, edible coatings) where clay minerals are part of the formulation.

- Intervention/Exposure: Natural or modified clays (e.g., montmorillonite/bentonite, halloysite, kaolin, sepiolite, palygorskite/attapulgite, laponite®, layered double hydroxides, aminoclays) used as stabilisers/adsorbents/carriers of bioactives.

- Comparators: Not mandatory (single-arm physico-chemical or functional assessments eligible).

- Outcomes: Encapsulation/adsorption/loading (EE, LC, q_{max}), stability/retention under processing or storage, release kinetics, antioxidant/antimicrobial/functional readouts, interactions/characterisation, techno-functional performance in food matrices, biocompatibility/safety indicators.

- Study design & document type: Peer-reviewed original articles (English/Spanish); experimental in vitro, in-matrix food tests, preclinical pharmacotechnical studies.

- Exclusions: Packaging-only studies without ingestion relevance, environmental remediation studies, veterinary or cosmetic applications, patents, conference abstracts, purely theoretical models without experimental validation, and records without accessible full text. Packaging-focused studies addressing migration, exposure, or regulatory considerations were excluded from the PRISMA corpus but were considered narratively in the safety and regulatory discussion where relevant.

2.3. Information source

Scopus, Web of Science Core Collection, and PubMed/MEDLINE were searched. No restrictions on publication date or status were applied at the search stage. The most recent search was conducted on 13 September 2025. Reference lists of included records were scanned to identify additional studies.

2.4 Search strategy

A comprehensive strategy combined controlled vocabulary and free-text terms relating to clay minerals, bioactive compounds, stabilisation/encapsulation mechanisms, and edible contexts. The primary databases searched were Scopus, Web of Science (WoS) Core Collection, and PubMed. The core conceptual string was:

(clay OR montmorillonite OR bentonite OR halloysite OR sepiolite OR palygorskite OR kaolinite OR laponite OR "layered double hydroxide" OR LDH OR aminoclay) AND (polyphenol OR antioxidant* OR anthocyanin* OR vitamin* OR peptide* OR nutraceutical* OR "essential oil*" OR curcumin OR flavonoid*) AND (stabilis* OR encapsulat* OR adsorb* OR "controlled release" OR intercalat*) AND (food* OR edible OR supplement* OR "oral formulation*" OR beverage* OR yogurt OR juice) NOT (packag* OR wastewater OR "soil remediation" OR cosmetic* OR veterinary)*

The final yield of 56 included studies reflects a highly specific focus strictly on internal edible matrices and oral delivery systems, effectively filtering out the vast, peripheral literature associated with food packaging films and environmental remediation. To ensure full reproducibility, the exact database-specific search strings (including field tags such as Scopus TITLE-ABS-KEY, WoS TS=, and PubMed Title/Abstract) are detailed in Supplementary Table S1. Furthermore, the reference library exports used during screening are provided as Online Resource 1 (RIS) and Online Resource 2 (BibTeX, .BIB).

2.5 Selection process

All records retrieved from each database were exported and consolidated into a single spreadsheet, where manual de-duplication was performed by matching titles, authors, journal, year, and DOI; no machine learning or automation was used. Titles/abstracts were manually screened against the eligibility criteria. Full-text assessment was then undertaken for potentially eligible items. Any uncertainties were resolved by discussion within the author team; escalation to the senior author occurred as needed. For clarity, the bibliometric mapping and the metadata synthesis were performed exclusively on the final set of 56 records included after PRISMA screening. Additional references cited throughout the manuscript serve background, mechanistic, or regulatory context and are not part of the quantitative/bibliometric dataset.

2.6. Reporting bias and small-study effects

Given the non-clinical nature and diversity of study designs, funnel plots and formal small-study bias tests were not performed. Potential reporting biases were addressed qualitatively by triangulating outcomes across material and bioactive classes and by discussing selective reporting concerns in the limitations.

2.7. Certainty (confidence) of the evidence

GRADE was not applied, as the corpus largely comprises in vitro/materials studies and food matrix experiments without clinical endpoints. Overall confidence is discussed narratively, emphasizing indirectness to human health outcomes and variability in protocols, in line with PRISMA recommendations for non-clinical syntheses.

2.8 Bibliometric mapping

Keyword co-occurrence networks and overlay visualisations were generated with VOSviewer (VOSviewer version 1.6.20) to contextualise thematic structure and temporal trends; these analyses complement, but do not replace, the systematic synthesis.

3. Results and discussion

3.1. Bibliometric analysis

3.1.1. Prisma flow

The identification and screening process followed a coherent and traceable sequence across databases (Fig. 1). A total of 247 records were retrieved (Scopus: 17; Web of Science: 142; PubMed: 88). After manual screening of titles and abstracts, 182 records were excluded. Full texts of 65 reports were assessed, and nine duplicates were removed, resulting in 56 studies included in the qualitative synthesis and bibliometric analysis. No automation tools were used, and all reports were accessible. The PRISMA flow demonstrates methodological rigor, with clear manual exclusions and consistent record tracking (247 − 182 = 65; 65 − 9 = 56). However, no trial registries or grey literature were included, potentially limiting coverage. Additionally, deduplication prior to screening was not performed, increasing workload, and exclusion reasons were broadly categorized. Overall, the process yielded a curated set of 56 studies while indicating areas for improved transparency.

3.1.2. Keyword co-occurrence mapping

The VOSviewer maps provide insight into the thematic structure and temporal evolution of research on clay-based stabilization of bioactive compounds in edible systems. In the cluster visualization (Fig. 2A), montmorillonite and halloysite act as central nodes, connecting antioxidant-related terms (e.g., polyphenols, anthocyanins), application concepts (controlled release, stability, gelation), and material categories (laponite®, aminoclay, nanomaterials). Their prominence reflects the dominance of smectite and tubular aluminosilicates, likely due to their well-established loading capacity and compatibility with food-grade biopolymers. The linkage through controlled release and gelation highlights the relevance of clay–biopolymer composites for modulating release kinetics and protecting bioactives. The overlay visualization (Fig. 2B) reveals a temporal shift. Established topics (montmorillonite, halloysite, antioxidants) appear in earlier periods, while newer terms such as curcumin, aminoclay, nanomaterials, and laponite®/gelation indicate recent research trends. This suggests a transition from conventional antioxidant stabilization toward advanced systems targeting lipophilic compounds, functionalized clays, and engineered nanocomposites for improved solubility and sustained release. The presence of layered double hydroxides and generic nanomaterials indicates the emergence of alternative or complementary inorganic platforms in edible delivery systems.

Figure 3 summarizes the main descriptors of the 56 studies included in this review, providing an overview of clay-based systems in edible and nutraceutical applications. The material distribution is dominated by montmorillonite, halloysite, bentonite, and laponite®, which together represent nearly 70% of the studies (Fig. 3A). This reflects a preference for well-characterized, commercially available clays, while fibrous clays remain underexplored, highlighting a research gap. The similar proportion of native and modified clays (Fig. 3B) indicates two parallel research directions: assessing intrinsic clay–bioactive interactions and enhancing performance through surface functionalization. This balance suggests a mature field where natural materials coexist with increasingly relevant engineered systems. Bioactive compounds show high diversity, with the “Other” category predominating (39.3%), followed by anthocyanins, curcumin, and vitamins (Fig. 3C). Although antioxidants remain central, the low representation of essential oils, proteins, and pharmaceutical ingredients (~ 16% combined) points to challenges in stabilizing structurally complex or sensitive molecules. Geographically, contributions are concentrated in China, Italy, Brazil, and Iran (Fig. 3D), likely reflecting resource availability and strong materials science research. This may also explain the emphasis on physicochemical studies over toxicological or clinical evaluations. The increasing publication trend, with peaks in 2019, 2022, and 2025 (Fig. 3E), highlights growing interest driven by advances in encapsulation and demand for functional ingredients. This pattern suggests a transition toward consolidation, with both diversification and specialization in materials and bioactives.

Figure 4 reveals affinity patterns between clay types and bioactive compounds, showing how structural and chemical properties determine their suitability. Some clays exhibit highly specific interactions: mica and related silicates/oxides are associated with anthocyanins and flavonoids, while sepiolite and palygorskite (attapulgite) are linked to drugs and essential oils, suggesting selectivity toward aromatic or hydrophobic molecules. In contrast, halloysite, montmorillonite, and bentonite display broader versatility, interacting with multiple bioactive classes due to their high surface area and ion-exchange capacity; halloysite’s tubular structure further enables binding of both hydrophilic and hydrophobic compounds. Laponite® shows moderate versatility, mainly associated with anthocyanins, curcumin, and vitamins, while layered double hydroxides preferentially interact with vitamins and anionic molecules, consistent with their positively charged layers. Kaolin and aminoclays exhibit more limited interactions, indicating the need for modification to expand functionality. Overall, the heatmap highlights the importance of matching clay properties with bioactive characteristics and underscores the limited exploration of proteins, peptides, and complex polyphenols as opportunities for future research.

Overall, the bibliometric analysis reveals a field in consolidation, characterized by the dominance of certain materials, the diversification of bioactive compounds, and the emergence of new functionalization and controlled release strategies. These patterns not only reflect research trends but also highlight that clay selection is closely linked to its structural, chemical, and interaction properties with bioactives. In this context, it becomes necessary to further explore, from a more mechanistic and scientific perspective, the different types of clays and their specific behavior in food systems.

3.2. Types of Clays Used in Food Systems

3.2.1. Lamellar Clays

Lamellar clays comprise layered silicates with 2:1 or 1:1 tetrahedral–octahedral arrangements, including montmorillonite, bentonite, kaolinite, and layered double hydroxides (LDHs) (Fig. 5; Table 1) [28–33]. Their functionality is mainly governed by ion-exchange capacity and interlayer accessibility, which determine adsorption and intercalation behavior toward bioactive compounds [29, 34, 35]. Smectites such as montmorillonite favor electrostatic adsorption and pH-responsive release of ionizable molecules due to their high cation exchange capacity, whereas kaolinite behaves as a more inert and structurally stable support [28, 31, 32]. In contrast, LDHs possess positively charged layers that promote anion exchange and acid-triggered release [30, 33, 36]. Across these systems, electrostatic interactions, hydrogen bonding, and van der Waals forces dominate stabilization mechanisms, as reported for nisin adsorption onto montmorillonite through frustrated intercalation [28, 31, 35].

3.2.2. Tubular Clays

Halloysite nanotubes are the main representatives of tubular clays and consist of rolled 1:1 aluminosilicate layers forming hollow non-expanding nanotubes (Fig. 5; Table 1) [24, 37]. Their functionality derives primarily from dual-charge behavior, with negatively charged external siloxane surfaces and positively charged aluminol-rich lumens, enabling selective adsorption and co-encapsulation of compounds with different polarities [24, 38]. In contrast to lamellar smectites, halloysite mainly stabilizes bioactives through lumen confinement, hydrogen bonding, coordination interactions, and electrostatic forces, which contribute to protection against environmental degradation and controlled release behavior [24].

3.2.3. Fibrous Clays

Fibrous clays such as sepiolite and palygorskite exhibit inverted 2:1 phyllosilicate structures with channel-like nanofibrous morphologies (Fig. 5; Table 1) [39, 40]. Their performance is more strongly associated with porosity, channel architecture, and silanol-rich surfaces than with exchange capacity alone, enabling adsorption and molecular sieving of low-molecular-weight compounds [40, 41]. Hydrogen bonding, coordination interactions, and size-exclusion effects are the dominant stabilization mechanisms, supporting the dispersion and solubilization of poorly soluble bioactives for oral delivery applications [40, 42].

3.2.4. Discoidal Clays

Laponite® is a synthetic hectorite-like nanoclay characterized by discoidal nanoplatelets with negatively charged faces and positively charged edges (Fig. 5; Table 1) [43, 44]. Its uniform charge distribution and high surface area favor exfoliation in aqueous media and strong interactions with biopolymers, proteins, and polysaccharides [43–45]. Ion exchange, cation bridging, and non-covalent interactions promote gel formation, colloidal stabilization, and sustained release behavior in edible nanocomposite systems [43].

The structural and functional diversity of natural clays highlights that their performance in food systems is determined not only by their morphology and exchange capacity, but also by the nature of their surfaces and their interaction mechanisms with bioactive compounds. However, these intrinsic properties may become limiting when facing challenges such as low affinity for hydrophobic compounds, restricted loading capacity, or lack of selectivity. In this context, the need to modify and functionalize clays arises to optimize their physicochemical properties and expand their range of applications, leading to the development of advanced hybrid materials, which are addressed in the following section.

Table 1
Structural, surface, and functional characteristics of major clay families used in edible delivery systems.

Clay family	Representative clays	Structural organization / morphology	Surface charge behavior	CEC/AEC (cmol(+)/kg)	Dominant interaction mechanisms	Main functional advantages in edible systems	Represe bioactive applicati
Lamellar clays	Montmorillonite (MMT), bentonite, kaolinite, layered double hydroxides (LDHs)	Layered silicates formed by stacked tetrahedral silica and octahedral sheets in 2:1 or 1:1 arrangements; expandable interlayer domains (except kaolinite)	Mostly negatively charged (MMT/bentonite/kaolinite); LDHs possess positively charged layers balanced by hydrated interlayer anions	MMT: ~82; Kaolinite: ~5.7; LDH (AEC): ~250	Electrostatic adsorption, ion exchange, intercalation, hydrogen bonding, van der Waals interactions	High loading capacity, interlayer expansion, pH-responsive release, chemical/mechanical stabilization of sensitive compounds	Polypher peptides vitamins, ionizable bioactive adsorpti frustrate intercala
Tubular clays	Halloysite nanotubes (HNTs)	Hollow non-expanding nanotubes formed by scrolling of 1:1 aluminosilicate layers; external diameter 40–70 nm; lumen 10–40 nm	Dual charge distribution: negatively charged siloxane outer surface and positively charged aluminol lumen	~ 7.4	Lumen confinement, hydrogen bonding, electrostatic interactions, coordination interactions, dispersion forces	Selective adsorption, co-encapsulation of hydrophilic/hydrophobic compounds, protection against environmental degradation, controlled release	Polypher phenolic essentia multifun nutraceu systems
Fibrous clays	Sepiolite, palygorskite (attapulgite)	2:1 phyllosilicates with inverted fibrous/channel-like structures; nanofiber or nanorod morphology with longitudinal channels	Predominantly silanol-rich external surfaces; functionality governed more by porosity than charge	Palygorskite: ~1.2; Sepiolite: ~39.9	Hydrogen bonding, coordination interactions, molecular sieving, size-exclusion effects	High surface area and porosity, adsorption of low-molar-mass compounds, enhanced dispersion and solubilization of poorly soluble molecules	Essentia hydropho compou delivery s
Discoidal clays	Laponite®	Synthetic hectorite-like discoidal nanoplatelets; diameter 25–30 nm; thickness ~ 1 nm; exfoliates in aqueous media	Negatively charged faces and positively charged edges	~ 63.3	Ion exchange, cation/water bridging, non-covalent interactions with macromolecules	Gel formation, colloidal stabilization, reinforcement of polymer matrices, sustained release behavior	Curcumi proteins, polysacc hydrogel beverage systems

3.2.5. Modified clays

Natural clays are frequently modified to overcome limitations such as low porosity and limited affinity for organic phases, thereby improving adsorption, compatibility, and controlled release performance [32, 53]. Acid activation using mineral acids (e.g., HCl, H_2SO_4, H_3PO_4) removes impurities and structural cations, increasing surface area, porosity, acidity, and interlayer accessibility in materials such as bentonite and smectites [32, 47, 56]. Organic functionalization with surfactants or phospholipids enhances hydrophobicity and compatibility with polymeric matrices by expanding interlayer spacing and tuning surface interactions [28, 46, 57, 58]. Advanced hybrid systems such as aminoclays further provide high surface area and positive surface charge, enabling immobilization of biomacromolecules [59]. In tubular systems, halloysite nanotubes act as nanocontainers for encapsulation and sustained release due to their hollow lumen structure and dual charge distribution, which also enables selective functionalization and pH-responsive coatings [32, 39, 60–62].

From a food-grade standpoint, clay modification must be interpreted as a performance–compliance trade-off: while activation and functionalization can markedly improve adsorption, compatibility with organics, and controlled-release behavior, they may also introduce residual reagents, soluble ions, or low-molecular-weight organic modifiers that are irrelevant in non-food applications but critical for ingestion or food-contact safety [63]. Acid activation can remain compatible with food uses only when post-treatment washing/neutralisation is demonstrated and batch specifications confirm that residual acidity and extractable metals are controlled, since acid treatment can substantially alter clay chemistry, pH, and textural properties [63]. Organic modification with quaternary ammonium surfactants is a particularly important “edibility risk” case: these modifiers are used to increase organophilicity and polymer compatibility, but migration behavior must be assessed because the type of organic modifier can measurably influence overall migration into fatty simulants in polymer–organoclay food-packaging systems [64], and migration testing has been explicitly applied to surfactant-modified organoclays incorporated into starch-based films under food-packaging regulatory frameworks [65]. In this context, organomodification remains potentially food-compatible only when the modifier chemistry is controlled and migration results meet relevant limits, reinforcing that performance gains (e.g., intercalation/charge reversal and improved dispersion) must be balanced against exposure considerations [46, 65]. Polymer grafting and layer-by-layer biopolymer coatings can mitigate release of “free” modifiers through covalent attachment or food-compatible shells and enable controlled/pH-responsive release architectures, but food-grade suitability still depends on using compatible reagents and demonstrating low residual monomers/initiators/crosslinkers [39]. Finally, nanospecific risk assessment in food and food-contact contexts requires explicit characterization of small-particle fractions and particle-size distributions when relevant to

exposure, supporting the need to treat “food-grade modification” as a specification- and exposure-based claim rather than a purely performance-based one [66, 67].

Having established the structural, physicochemical, and functional foundations of both natural and modified clays, it is essential to examine how these properties translate into the effective incorporation of bioactive compounds. In this context, the performance of these systems depends not only on the type of clay, but also on the methodologies employed for loading, encapsulation, and characterization of the compounds.

3.2.6. Quantitative structure–function relationships

To strengthen mechanistic-to-design interpretation, this section summarises quantitative relationships between clay descriptors and encapsulation performance reported across the curated corpus [46, 68, 69]. In general, higher exchange capacity and accessible interlayer spacing promote ion-exchange and intercalation mechanisms, enhancing the uptake of ionisable compounds and increasing encapsulation efficiency or loading capacity [46, 68]. Similarly, zeta potential is closely associated with colloidal stability, dispersion behavior, and interaction strength in aqueous systems [69]. Accordingly, descriptor ranges by clay family are summarized in Section 3.2 and correlated with EE and LC values when reported. Studies lacking key descriptors are identified as reporting gaps, supporting the recommendation of minimum characterization parameters, including exchange capacity, zeta potential at defined pH/ionic strength, and XRD basal spacing for expandable layered clays [46, 68, 69].

3.3. Functional Compounds Studied for Stabilization with Clays

3.3.1. Loading and Encapsulation Methodologies

Batch Method

This technique is based on the principle of physicochemical equilibrium in a solid–liquid system, where a defined amount of adsorbent is brought into contact with a fixed volume of solution (Fig. 7A) [37]. The main mechanism involves mechanical agitation to maximize mass transfer and ensure homogeneous contact between solute molecules and the active sites of the clay, followed by phase separation through centrifugation or filtration [70]. This method is the most versatile and is particularly suitable for ionizable or polar compounds that depend on diffusion toward the external surface or interlayer space of the mineral, allowing the evaluation of critical parameters such as adsorption kinetics and equilibrium isotherms [37].

Vacuum Method

The physicochemical principle of this methodology is the displacement of gases through a pressure differential to facilitate liquid penetration into nanometric cavities [71]. The mechanism consists of subjecting the dry clay to vacuum cycles to remove trapped air within its structure, allowing that, upon restoring pressure or adding the solution, the liquid is forced by capillarity into confined spaces (Fig. 7B) [71]. This technique is specific to clays with tubular morphology and is most suitable for compounds requiring physical confinement and protection from the external environment, as it maximizes loading efficiency within the internal lumen of nanotubes [72].

Sequential Adsorption

This methodology operates under the principle of stepwise or multilayer functionalization, where the clay surface is modified in an ordered manner (Fig. 7C) [73]. The mechanism involves successive adsorption processes in which the binding of the first component may facilitate or act as an anchoring platform for the second, involving interactions ranging from dative and coordination bonds to electrostatic forces [30, 73]. It is the optimal strategy for the development of complex bionanocomposites and hybrid systems aimed at integrating multiple biological or chemical functions into a single inorganic carrier [73].

Titration

The principle of this technique is the quantitative and stoichiometric evaluation of reactive sites on the mineral surface [50]. The mechanism consists of the gradual addition of an agent with high affinity for exchange sites until complete saturation is reached, which is identified by a detectable physical change, such as the appearance of residual coloration or a variation in the absorbance of the supernatant (Fig. 7D) [50, 56]. This methodology is the most suitable for the analytical characterization of clays, allowing precise determination of cation exchange capacity (CEC) and specific surface area through the adsorption of probe molecules [56].

3.3.2. Stabilization Performance of Bioactive Compounds in Clay-Based Systems

Clay-based systems demonstrated broad applicability for stabilizing sensitive nutraceutical compounds under processing, storage, and gastrointestinal conditions. Across the reviewed studies, encapsulation efficiency (EE) ranged from ~ 40% to > 99%, depending on clay family, surface modification, and loading strategy (Table 2). Halloysite nanotubes and montmorillonite were the most frequently reported carriers, particularly for anthocyanins, phenolics, peptides, vitamins, and curcumin-based systems. Functional outcomes included sustained release, improved antioxidant retention, antimicrobial activity against foodborne pathogens, and enhanced antiproliferative performance in cancer-related models.

Layered and tubular clays showed distinct stabilization behaviors. Montmorillonite-based systems mainly relied on interlayer adsorption and electrostatic interactions, whereas halloysite systems favored lumen confinement and delayed release. Laponite® demonstrated strong performance in antioxidant pigment stabilization, including jambolan anthocyanins with DPPH inhibition values around 70% [29]. Bentonite-based systems also achieved relevant encapsulation efficiencies for phenolic compounds (~ 40.8% EE) [3]. In therapeutic-oriented applications, punicalagin–montmorillonite hybrids improved antiproliferative activity in HT-29 cells [19], while halloysite-based nanocomposites showed activity in breast cancer-related systems [23]. Table 2

summarizes the quantitative stabilization performance, loading capacities, interaction mechanisms, and representative applications reported for the main clay–bioactive systems.

Table 2
Adsorption and stabilization of bioactives in clays: loading capacities, mechanisms, and food applications.

Clay Type	Bioactive Compound	Main Bioactivity	Adsorption, Loading Capacity	Highli
Bentonite (Montmorillonite as main component)	Green propolis extract phenolic compounds	Antioxidant and antimicrobial targeted for natural additive applications	Adsorption Efficiency: ~40.8% of total phenolic compounds adsorbed.	• Biohy antiox • Max analyz • Phys mecha
Halloysite Nanotubes	Anthocyanins and phenolic acids from *Prunus spinosa* L. (blackthorn) extract.	Antioxidant and controlled release for functional foods	Loading Efficiency: ~9.4% w/w (Calculated with TGA and estimated volumetrically).EE: 61.85%	• Effec encap nanot • Appli incorp prolon
Laponite®	Anthocyanins (from jambolan fruit, *Syzygium cumini*)	Antioxidant activity (70% DPPH inhibition)	1.5 mg/g, max adsorption capacity at equilibrium	• Biohy theore absor • Phys mecha antiox • Appli photos
Laponite®	Anthocyanins extracted from eggplant (*Solanum melongena* L.) peel	Antioxidant and natural coloring properties	14.65 mg/g (Maximum adsorption capacity)	The re sensit food i
Montmorillonite	Anthocyanins extracted from jambolan (*Syzygium cumini*) fruit	Antioxidant, antimicrobial	212.04 mg/g (Maximum adsorption capacity)	• Deve biohyb monit real-ti • Mont adsor higher biohyb
Montmorillonite	Acerola juice anthocyanins (Cyanidin-3-O-rhamnoside and Pelargonidin-3-O-rhamnoside)	Antioxidant capacity	• 6% Mnt retained > 56% anthocyanins. • 4% Mnt retained 52% (most efficient combination). • Non-linear relation (2% Mnt retained only 14%).	• Adsc Interc excha • Food Clarifi applic
Montmorillonite	Punicalagin from pomegranate peel extract (and other hydrophilic phenolics like gallic acid and catechin)	Antiproliferative activity against cancer cell lines; enhanced cellular absorption, especially in HT-29 enterocytic cells	• For the extract/Montmorillonite complex, Punicalagin A and B content was 42 and 42.5 mg/g, respectively. • Optimal loading obtained with extract:Mt ratio of 5:1.	• Absc Interc • Impr compo • Impr bioava • Pote byproc peel e
Montmorillonite (NaCl treated)	Vitamin B6	Essential water-soluble vitamin; cofactor in enzymatic reactions.	285.71 mg/g at pH 6.5	Better encap releas 6.5.
Montmorillonite (CaCl2 treated)	Vitamin B6	Essential water-soluble vitamin; cofactor in enzymatic reactions.	312.5 mg/g at pH 6.5	Better encap releas 6.5.
Montmorillonite	Glutathione	Antioxidant; functions in detoxification and immune response.	38.57 ± 2.22%	• Absc Interc • Sligh of pha tests.

Clay Type	Bioactive Compound	Main Bioactivity	Adsorption, Loading Capacity	Highli
Montmorillonite (treated with polyvinylacetal diethylaminoacetate)	Glutathione	Antioxidant; functions in detoxification and immune response.	24.09 ± 0.70%	• Polyr stabili • Signi antiox • Grea impro • Impr
Montmorillonite	Nisin (NL = 1.50)	Antimicrobial activity against Gram-positive bacteria.	Nisin loading = 1.5 times the clay's ion exchange capacity.	• Coop mecha • Show agains
Montmorillonite	Nisin (NL = 3.00)	Antimicrobial activity against Gram-positive bacteria.	Nisin loading = 3 times the clay's ion exchange capacity.	• Show • Prefe nisin.
LDH Clay - Layered Double Hydroxides (Mg Al Azelate)	Polyphenols, Flavonoids, Anthocyanins (from Pomegranate Juice)	Antioxidant	~ 179.9 mg GAE/g clay	• High 180 m • Antic 48.8%
LDH Clay - Layered Double Hydroxides (Mg Al Hydroxide Chloride)	Polyphenols, Flavonoids, Anthocyanins (from Pomegranate Juice)	Antioxidant	~ 62.5 mg GAE/g clay	• High mg GA • Antic increa
LDH Clay - Zinc Chlorohydroxide	Polyphenols, Flavonoids, Anthocyanins (from Pomegranate Juice)	Antioxidant	~ 60.8 mg GAE/g clay	• High mg GA • Antic activit
Bentonite	Polyphenols, Flavonoids, Anthocyanins (from Pomegranate Juice)	Antioxidant	EE: ~11.45 mg GAE / g bentonite	• Mode capac • Phys and po
Palygorskite	Ginger essential oil	Antimicrobial (Preservation)	Oil loading rate was approximately 18.66%	• The produ therm antiba • Signi capac applic
Halloysite	Epigallocatechin Gallate	Antioxidant / Anti-inflammatory	Loading Efficiency: ~16.4%	• The produ Reacti scave • In in it prot cells f
Bentonite	L-Ascorbic Acid (Vitamin C)	Antioxidant capacity	Adsorption capacity (qe): ~450 mg L-ascorbic acid/g clay	• Impr LAA, s radiati • Mate toxico
Halloysite	Nisin	Antimicrobial against Listeria monocytogenes, Clostridium perfringens, Staphylococcus aureus.	Adsorption of 75% at 2.5 mg/mL	• Signi capac • Indic releas
Halloysite	Pediocin	Antimicrobial against Listeria monocytogenes and Clostridium perfringens.	Adsorption of 96.9% at 300 mg/mL	Better both B agar.
Laponite®	Curcumin	Potent anti-inflammatory, antioxidant and antimicrobial activity.	E.E: N.R. Mixed in dispersions with equal concentration 1:1	Demo releas curcu hydro laponi

Clay Type	Bioactive Compound	Main Bioactivity	Adsorption, Loading Capacity	Highli
Halloysite Nanotubes covalently bonded to Hectorite	Curcumin and Doxorubicin	Antiproliferative effect via P-Glycoprotein (P-gp) inhibition to improve Doxorubicin accumulation in breast cancer cells	Curcumin Loading: ~3% w/w	Synerg accum effecti chemo potent tumor
Laponite®	Curcumin	Antioxidant activity (ABTS and DPPH radical scavenging).	EE of 73.4% for the 0.5% laponite® nanocomposite loaded with 0.10% curcumin.	• Nanc releva antiox phase • Susta simula condit
Halloysite Nanotubes	Ascorbic Acid and natural dye extracts (Brazilwood, Blackberry, Beetroot)	Antioxidant activity (DPPH radical scavenging).	• Loading Capacity (LC) of ascorbic acid: 105.19 mg AA/g halloysite (10.52% w/w). • Extract content in final hybrid pigments: >40% w/w for all three extracts.	The pr antiox with ir due to
Natural Zeolite (87% clinoptilolite)	Caffeine	Stimulant, metabolism and cardiovascular function modifier.	• EE: 36.4% • Max equilibrium capacity (qmax): 0.42 mg/g.	Zeolite caffeir mecha interac hydrog chemi caffeir zeolite with ir mesop applic produ consu
Natural Zeolite (87% clinoptilolite)	D,L-α-tocopherol acetate (Vitamin E)	Antioxidant (prevents lipid peroxidation and cellular damage from oxidative stress).	• EE: 78% • Experimental max equilibrium capacity (qmax): 9.9 µg/mg	• Hete proces covera mecha hydrog • Optir encap 6.5-7.(applic produ consu
Alkalized Clinoptilolite (CLS-5, modified natural clinoptilolite)	Extract rich in catechin from Acacia catechu (Catechin)	Antioxidant	• EE: 32% • Max encapsulation capacity (EC): 0.98 µg/mg	• Enca involv betwe and cl • In vit gastri 88% e a sust withou Potent applic produ consu

EE: Encapsulation Efficiency; *: Value calculated from methodology data; MCF7, HT-29 and MRC-5: Cell types representing breast cancer (MCF7), colon cancer (HT-29), and normal fetal lung cells (MRC-5); qMax: Maximum adsorption/encapsulation .

3.4. Applications in Food and Agri-Food Systems

Modified clays have been incorporated into a wide range of food matrices, primarily for fortification, preservation, and active packaging purposes (Table 3), where performance under real conditions is critical. In the dairy industry, for example, the encapsulation of plant-derived antioxidants within clay nanoparticles has demonstrated outstanding performance. Yogurt fortification with halloysite nanotubes loaded with blackthorn (*Prunus spinosa* L.) extract significantly prolonged the release of polyphenols and phenolic acids, suggesting that dairy proteins play a relevant role in modulating release kinetics [22]. Similarly, bentonite has been used as a wine additive, achieving up to a 10% reduction in biogenic amines such as histamine, with direct implications for product quality and safety [82]. In the context of fresh food preservation, innovative porous matrices for active packaging have been developed. Aerogels composed of pullulan, gelatin, and polyvinyl alcohol, loaded with HNTs encapsulating thyme essential oil, have been applied as cushioning and active packaging materials for blueberries (*Vaccinium corymbosum* L.) [83]. This system effectively maintained fruit firmness, mass, and color, while significantly reducing Botrytis cinerea infestation and exhibiting high biocompatibility, with cell viabilities exceeding 94%. Clay applications also extend indirectly to the

food system through agriculture. Bentonite stabilized with sulfur and orange waste, used as an organo-mineral fertilizer in lettuce (*Lactuca sativa* L.) cultivation, significantly improved the nutraceutical quality of the crop by increasing secondary metabolite content, including flavonoids and vitamins C and E, as well as the concentration of essential cations such as potassium and magnesium [84].

Table 3
Clay-based delivery systems for bioactive compounds in food, agri-food, and nutraceutical-related applications.

Food Matrix	Bioactive Compound	Clay Type / Modification	Format	Key Outcome	Quan Metri
Yogurt	Anthocyanins, iridoids (loganic acid, cornuside)	Halloysite nanotubes	Yogurt fortification with encapsulated powder	Yogurt enrichment significantly prolonged the release of iridoids.	Encap 8.5 w Prolo of log and c yogur
Yogurt	Polyphenols (3-O-caffeoylquinic acid, cyanidins, peonidin)	Halloysite nanotubes or HNT–maltodextrin	Yogurt fortification with encapsulated powder	Addition to yogurt significantly prolonged the release of all polyphenolic compounds.	Encap efficie 37.62 yogur with H
Lettuce (*Lactuca sativa* L.)	Flavonoids, vitamins C and E, phenolic compounds	Bentonite (in SBO fertilizer)	Organic–mineral fertilizer (indirect application)	SBO fertilizer increased secondary metabolites (flavonoids, vitamins C and E) in lettuce.	SBO 2 K; SB increa and M
Blueberries (*Vaccinium corymbosum* L.)	Thyme essential oil	Halloysite nanotubes / PGP aerogel	Active packaging / cushioning material	The aerogel (12% TEO@HNTs–PGP) maintained firmness and reduced *Botrytis cinerea* infestation.	Cell v excee 94%, biocc
Porcine placenta extract (pPEs, food/feed additive)	Proteins, amino acids (glutamic acid, aspartic acid, leucine)	Bentonite (1% in alginate microspheres)	Microspheres (capsules) for oral administration	F2 formulation maintained protein stability for > 120 days at 25°C and showed controlled release.	Stabi 120 d of 99 partic 14.65
Wine	Biogenic amines (histamine)	Bentonite	Additive	Bentonite reduced histamine concentration.	Hista reduc 10%.

3.5. Nutraceutical Systems and Targeted Oral Delivery

Nutraceutical products require advanced delivery systems capable of protecting bioactive compounds against the harsh conditions of the gastrointestinal tract. In this context, clays combined with biopolymers have proven to be highly effective matrices for capsules, microspheres, hydrogels, and aerogels. A notable example is the encapsulation of porcine placenta extract into alginate microspheres containing 1% bentonite and a chitosan coating, achieving an encapsulation efficiency of 99.72% and an average particle size of 14.65 ± 0.08 µm [25]. These microspheres exhibited sustained release behavior and remarkable protein stability, retaining 75.9% of activity after 120 days of storage at 25°C. For the delivery of sensitive proteins, such as bovine serum albumin or insulin, layered double hydroxide-based multilayer nanocomposites, including aminoclay/chitosan-glycol/Eudragit (EGAC) systems, have demonstrated high conformational stability in simulated gastric and intestinal fluids, minimizing protein release at gastric pH [89]. The pH-sensitive nature of the Eudragit® S100 coating ensures that the main release occurs in the intestine, thereby promoting intestinal absorption. layered double hydroxides have also been successfully applied to the controlled delivery of vitamins, as exemplified by the ZnAl–VitB3 system, in which vitamin B3 is gradually released under acidic conditions, reaching 90% release within 60 minutes and thus helping to prevent dosage peaks [36]. In more complex therapeutic applications, such as the treatment of inflammatory bowel diseases, alginate microspheres containing modified HNTs and probiotics achieved survival rates exceeding 80% after exposure to simulated gastric fluid, indicating superior performance [90].

3.6. Safety, digestibility, and regulatory status

3.6.1. Edibility criteria and nanospecific requirements for food-contact exposure

The edibility and food compatibility of clay-based systems depend not only on their intrinsic biocompatibility, but also on authorised uses, purity specifications, contaminant control, and nanospecific physicochemical characteristics (Table 4). Current EFSA nano-risk assessment frameworks distinguish direct ingestion-oriented systems from food-contact materials, where exposure may occur indirectly through particle migration or transfer phenomena [91, 92]. Consequently, materials intended for edible or food-contact applications require case-specific evaluation of nanoparticle fractions, particle-size distribution, and migration behavior under realistic use conditions. Although several clay families possess a long history of food, pharmaceutical, or feed-related use, no EFSA halloysite-specific scientific opinion for food-contact applications was identified during the present review. Nevertheless, a limited number of studies have evaluated migration phenomena in HNT-containing films under food simulant conditions. For example, PVA/starch/glycerol films reinforced with HNTs were tested using hydrophilic, lipophilic, and acidic food simulants, showing composition-dependent migration of Al and Si species and overall migration values influenced by HNT loading and simulant polarity [93]. Additional studies have also assessed the stability of PLA/HNT nanocomposites in ethanolic food simulants [94]. However, migration data remain limited, heterogeneous, and insufficiently standardised for comprehensive risk assessment under realistic long-term food-contact conditions. Therefore, migration behavior and oral toxicokinetic evaluation continue to represent

important evidence gaps for the safe implementation of halloysite-based food-contact systems. In this context, food compatibility should be interpreted according to both regulatory acceptance and compliance with food-grade specifications, including purity, trace contaminant control, and nanospecific safety characterization (Table 4).

3.6.2. Biocompatibility, oral fate, and regulatory status of edible clays

Most edible clay systems exhibit favorable biocompatibility profiles, limited systemic absorption, and predominant gastrointestinal excretion after oral administration (Table 4) [35, 95]. Lamellar clays such as montmorillonite and bentonite possess the strongest regulatory background, including FDA/EFSA acceptance and long-standing pharmaceutical use as gastrointestinal protectants and excipients [96, 97]. Similarly, layered double hydroxides and aminoclays have demonstrated high compatibility as oral delivery platforms due to their controlled degradation behavior and efficient elimination pathways [98, 99]. Nevertheless, safety profiles remain material- and dose-dependent. Halloysite nanotubes, for example, exhibit low cytotoxicity and high in vitro biocompatibility [78], but some in vivo studies have reported potential aluminum accumulation and fibrotic responses following prolonged exposure [61]. In parallel, purity control, residual modifiers, and particle-size distribution remain critical variables influencing food-grade compatibility across both natural and synthetic clay systems (Table 4).

Table 4
Summary of food-compatibility, safety assessment, and regulatory status of nanoclays in oral and food systems.

Clay Material	Regulatory Status & Authorization	Main Safety Findings	Reported Toxicity or Risk Concerns	Purity & Contaminant Considerations	Particle-Size & Nanostructure	Main Conclusion on Edibility/Food Compatibility	Key Referen (Author, Year)
Montmorillonite (MMT) / Bentonite	**FDA/EFSA**: Accepted as safe food additives. **Pharmacopoeias**: Listed as pharmaceutical excipients and gastrointestinal drugs (e.g., Smecta®).	Mucoadhesive properties stabilize the intestinal mucus barrier. Short-term safety confirmed in human trials (NovaSil).	Predominantly excreted; minimal systemic absorption observed.	Natural origin requires monitoring for trace heavy metals and environmental impurities.	2:1 phyllosilicate; stacked lamellar platelets; particle size typically 1–2 μm.	**High**; robust history of use as oral therapeutic protectors.	[35]
Halloysite Nanotubes (HNTs)	**Traditional Medicine**: Main component of "Chishizhi," used for centuries for diarrhea and hemostasis.	Well-documented biocompatibility and low cytotoxicity across multiple cell lines.	Potential Al accumulation and fibrotic response in lungs reported in mice after 30-day oral dosing.	Natural 1:1 aluminosilicate; may contain trace metal impurities depending on deposit.	Tubular morphology; 0.2–2.0 μm length, 10–40 nm internal lumen.	**Edible**; requires dosage optimization to mitigate bioaccumulation risks.	[60, 61]
Layered Double Hydroxides (LDHs)	**Pharmacopoeias**: Listed in European and US pharmacopoeias as excipients and antacids.	High biocompatibility; inorganic supports pose no risk to human health.	Acid-triggered dissolution in the stomach releases metal cations (Mg, Zn, Al).	Primarily synthetic, allowing for high purity and tunable chemical composition.	Stacked brucite-like layers with high anion exchange capacity.	**Highly compatible**; pH-dependent degradation facilitates clearance.	[36, 100
Aminoclay (AC)	**Research Status**: Investigational organic-inorganic hybrid drug carrier.	Nontoxic and rapidly eliminated via urinary and hepatobiliary pathways.	Low risk of long-term tissue accumulation due to efficient clearance.	Functionalized with aminopropyl groups; requires monitoring for residual modifiers.	Layered Magnesium Phyllosilicate with positive surface charge.	**High biocompatibility**; suitable for oral protein and drug delivery.	[59, 101
Sepiolite / Palygorskite	**Animal Feed**: Accepted under feed regulations (e.g., Adsorbo®). Palygorskite used as an anti-diarrheal drug.	Sepiolite used historically in food processing (e.g., sugar juice decolorization).	Palygorskite can exhibit limited dispersion and biocompatibility in specific forms.	Natural fibrous minerals; purity depends on mining and refining processes.	Fibrous morphology; nanorods/nanoneedles with structural zeolite channels.	**Compatible**; historical use as processing aids supports food safety.	[53, 95]
Laponite® (LAP)	**Technical Grade**: Synthetic smectite used in consumer products.	Investigated for localized drug delivery with reported cytocompatibility.	Synthetic nature ensures consistent chemical composition and lack of contaminants.	Chemically pure: SiO_2, MgO, Li_2O, Na_2O.	Ultrathin nanodiscs (approx. 25–30 nm diameter, 1 nm thickness).	**Potentially edible**; synthetic purity offers advantages for safety standardization.	[43]

3.7. Modeling and Future Perspectives of Clay–Bioactive Interactions

Molecular dynamics (MD) simulations and density functional theory (DFT) calculations have improved the mechanistic understanding of clay–bioactive interactions relevant to food and nutraceutical delivery systems. These approaches enable atomistic-level evaluation of adsorption, intercalation, and release mechanisms in layered and tubular clays, particularly under gastrointestinal-relevant conditions. Current evidence indicates that electrostatic interactions,

hydrogen bonding, and hydration-mediated stabilization are the predominant mechanisms governing the retention and controlled release of food bioactives such as anthocyanins, curcumin, peptides, and vitamins [96, 97].

Computational and experimental studies demonstrate that pH, ionic strength, and surface modification strongly influence bioactive loading and release behavior. For example, layered double hydroxides exhibit acid-triggered decomposition and controlled anion release under gastric conditions, whereas modified montmorillonite systems can retain compounds at acidic pH and promote release in intestinal environments [31]. Similarly, halloysite nanotubes enable lumen-based encapsulation and delayed release through biopolymer coatings, improving the protection of sensitive compounds during gastrointestinal transit [39]. These findings support the use of computational modeling as a predictive tool for designing food-grade delivery systems with improved stability and bioaccessibility.

The intercalation and adsorption of compounds such as anthocyanins are strongly influenced by their chemical nature and the surrounding environment, including pH, medium polarity, and stabilizing agents, which dictate secondary interactions with clay surfaces and neighboring molecules. The predominant stabilization mechanisms involve electrostatic interactions, hydrogen bonding, van der Waals forces, and cation-bridging phenomena mediated by divalent ions such as Ca^{2+} and Mg^{2+} (Fig. 8) [102]. Anthocyanins mainly interact through hydroxyl-rich aromatic regions, whereas curcumin adsorption is additionally promoted by hydrophobic interactions and dispersion forces associated with its conjugated structure [103, 104].

Future research should prioritize standardized descriptor reporting (CEC/AEC, zeta potential, d-spacing, BET surface area, and particle-size distribution) to facilitate quantitative comparisons across studies. Additional priorities include validation in real food matrices at realistic doses, gastrointestinal bioaccessibility and bioavailability assessment, migration and exposure studies for food-contact systems, and scalable GMP-compatible purification and modification strategies. These aspects will be essential to translate clay-based bioactive delivery systems from laboratory research to industrial food and nutraceutical applications.

4. Conclusions

This mixed systematic–narrative review consolidates and interprets the state of the art on edible clay minerals as functional carriers for food-relevant bioactives, explicitly linking structure (lamellar/tubular/fibrous/discoidal), surface chemistry and ion-exchange, with loading, stability and release validated in food matrices and nutraceutical formats. Across 56 studies mapped and screened under PRISMA 2020, montmorillonite/bentonite, halloysite, laponite® and LDHs dominate the evidence base and enable reproducible gains in encapsulation efficiency, antioxidant retention, photostability and controlled delivery of polyphenols, vitamins, peptides and essential oils under edible or oral conditions.

Quantitative performance, in context. Multiple in-matrix applications substantiate functional benefits: halloysite- or clay-fortified yogurts prolong the release of plant phenolics; montmorillonite stabilizes anthocyanins in clarified juices; laponite® and montmorillonite sustain antioxidant activity and color performance; palygorskite/kaolin/zeolite hybrids enhance thermal stability and extend antimicrobial activity. Typical ranges observed in the curated corpus include EE from ~ 37% up to ~ 99.7%, q_{max} or loadings from the tens to hundreds of mg/g (e.g., anthocyanins, vitamins, punicalagin), and matrix-relevant stability gains (e.g., > 56% anthocyanin retention in acerola juice at specific MMT loadings). These outcomes align with electrostatic, hydrogen-bonding and dispersion/π–π mechanisms expected for layered silicates and tubular hosts, and with pH/ionic-strength responsiveness observed in LDHs and modified clays.

Mechanism-to-design rules. Integrating material typology (Sections 3.2–3.3), loading routes (Section 4.1) and modeling (Section 5.3), the review articulates practical design rules for edible delivery: (i) Lamellar smectites (MMT/bentonite) with moderate–high CEC favor intercalation/cooperative adsorption of ionizable molecules and peptides (e.g., nisin), yielding high payloads and pH-tuned release; (ii) Halloysite nanotubes provide lumen confinement + dual-charge surfaces for co-loading hydrophilic/hydrophobic actives, benefiting vacuum-assisted loading and polymer “end-sealing”; (iii) Laponite® nanoplatelets excel at colloidal assembly with biopolymers and pigment stabilization in beverages and gels; (iv) LDHs offer anion-exchange and acid-triggered release ideal for vitamins/anionic phenolics; and (v) Fibrous clays (palygorskite/sepiolite) leverage silanol-rich channels for volatile retention and antimicrobial EO delivery. Together, these rules connect charge density, interlayer space and hydrophobicity tuning to EE/ q_{max} and release kinetics in realistic foods.

Methods that matter. Four practical routes recur and should be selected by intended mechanism: batch adsorption for ionizable/polar solutes; vacuum-assisted loading for nanotubular confinement; sequential/layer-by-layer assembly to build multi-functional biointerfaces; and titrimetric site probing for CEC/site quantification and rational dosing. Method choice directly conditions the balance of electrostatics vs. H-bonding vs. dispersion, and therefore the observed EE, stability and release in matrix.

Safety and translation. Converging evidence and long-standing uses indicate that several natural clays (e.g., montmorillonite/bentonite) are compatible with the GRAS/EFSA context when purity and dose are controlled; nevertheless, dose–material–modification specificity remains essential, particularly for nanotubular aluminosilicates, where long-term/toxicokinetic evidence at food-realistic doses is still limited. Batch-to-batch purity, trace metals, particle size and surface modification must be specified and quality-controlled for nutraceutical/food uses.

What this review adds. Beyond cataloguing, the review unifies materials science with food/nutraceutical validation: it maps the literature (2015–2025) and distils mechanism-anchored design rules that explain why certain clay–bioactive–matrix triads outperform others; it links loading routes to interfacial mechanisms and matrix outcomes; and it frames safety/regulatory guardrails alongside industrialization constraints (purity, scale-up, GMP-compatible modification). The bibliometric signal also shows a transition from classic smectites/antioxidants to hybrid nanocomposites and lipophilic actives (e.g., curcumin) and aminated surfaces, consistent with a maturing field seeking functionality beyond mere adsorption.

The evidence is dominated by in vitro/materials studies and bench-scale food trials; human bioavailability and long-term safety remain underrepresented, and fibrous clays are comparatively underexplored despite their promising channel chemistry. Therefore, the following actions are recommended: (i) dose-ranging and matrix-specific safety and bioavailability studies for leading clay–bioactive pairs; (ii) standardized reporting of CEC/AEC, particle characteristics, and modification chemistry to enable meta-analysis; (iii) process-level studies addressing scale-up, purification, and cost, particularly for hybrid systems (biopolymer–clay aerogels/films); and (iv) model-driven optimization (MD/DFT combined with empirical release models) to tailor charge, pH, and ionic strength to targeted gastrointestinal release windows. These steps define a credible pathway from TRL 3–4 prototypes to TRL 6–8 under food-grade constraints. Properly selected and engineered, edible clays constitute versatile, scalable, and regulation-compatible platforms for stabilizing and delivering bioactive compounds in foods and nutraceuticals, with mechanism-backed improvements in stability and functionality already demonstrated in systems such as yogurts, clarified juices, hydrogels/aerogels, and active films. Further advances in safety assessment, standardization, and scale-up are expected to unlock their full translational potential as Nutraceuticals 4.0 carriers.

Declarations

Conflict of Interest

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

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Data Availability

The data that support the findings of this study are available within the article and its supplementary materials. Any additional data related to this systematic review are available from the corresponding author upon reasonable request. The list of the 56 PRISMA-included records used for the bibliometric analyses is provided in Online Resource 1 (RIS) and Online Resource 2 (BIB), distinct from additional narrative references cited for context.

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Figures

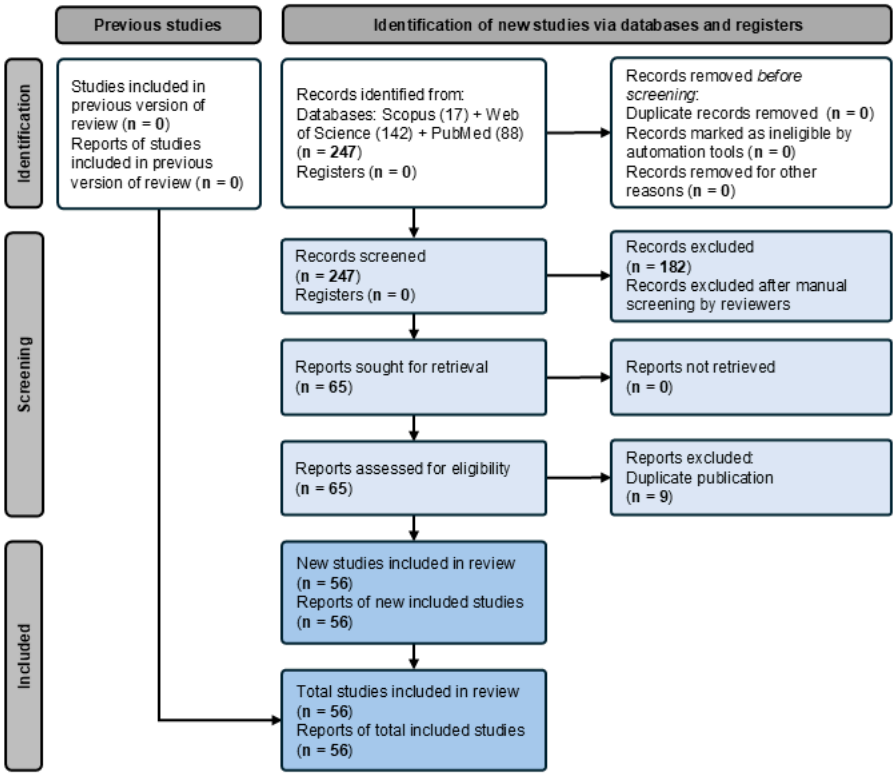


Figure 1

PRISMA 2020 Flow Diagram for Study Selection in the Systematic Review [27]

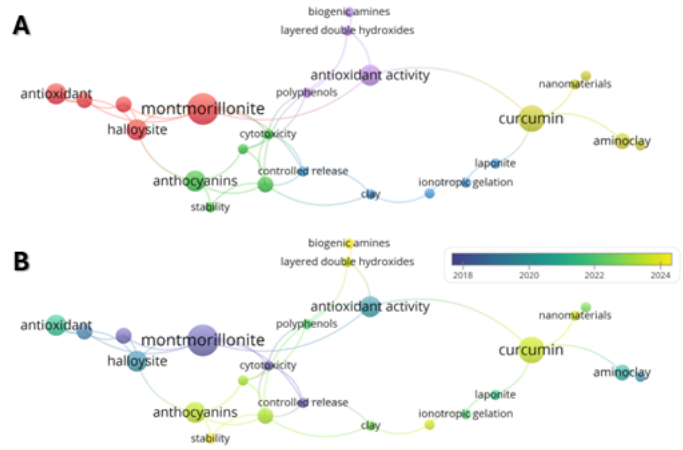


Figure 2

VOSviewer keyword co-occurrence network maps: (A) cluster visualization showing the thematic structure and (B) overlay visualization showing the temporal evolution of research on clay-based bioactive delivery systems.

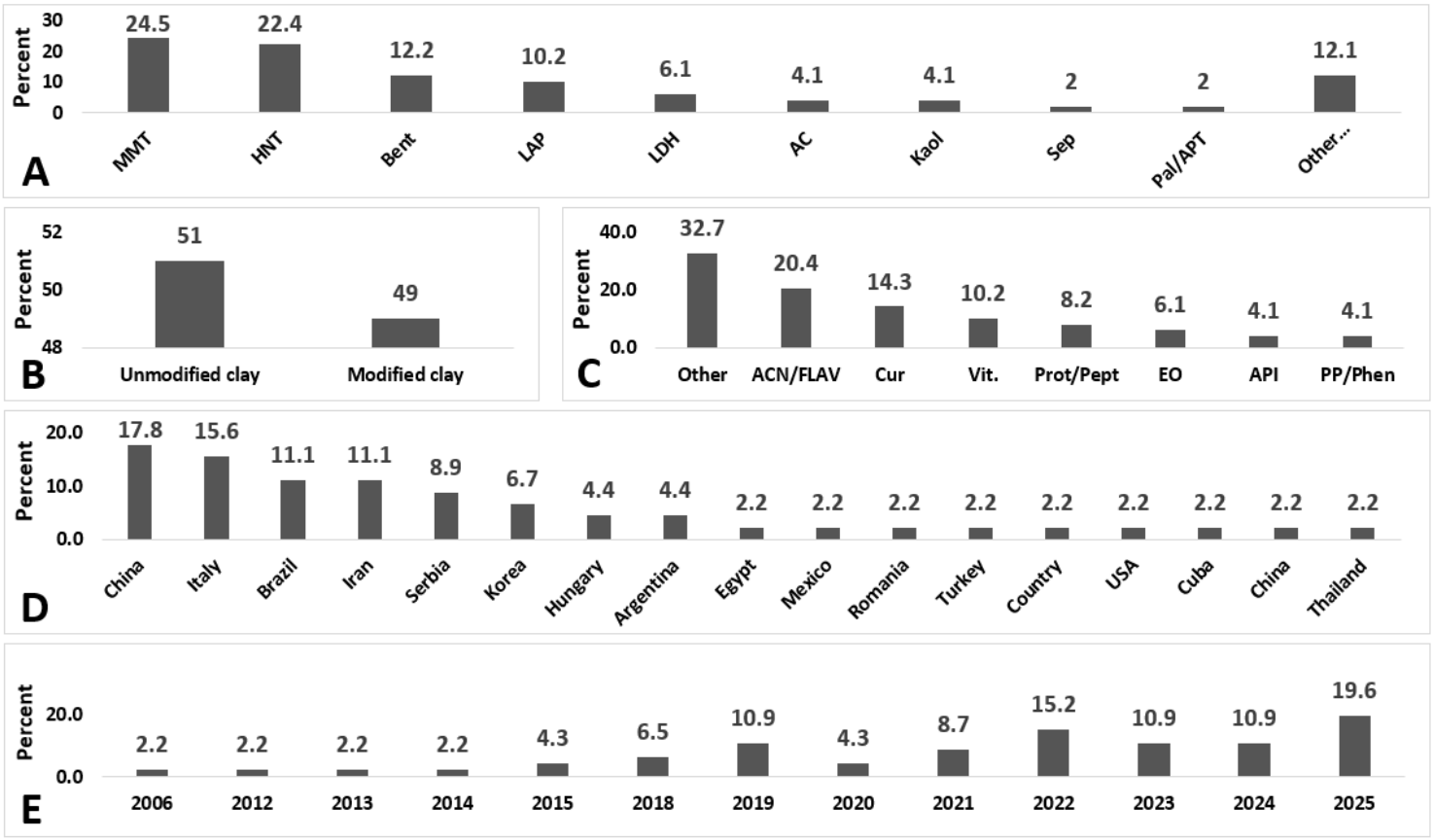


Figure 3

Meta-data overview of clay-based studies: clay-type distribution (A); modified vs unmodified clay (B); bioactive category distribution (C); primary country of publication (D); publication year trend (E). Abbreviations: MMT=Montmorillonite; HNT=Halloysite Nanotubes; Bent=Bentonite; LAP=Laponite®; LDH=Layered Double Hydroxide; AC=Aminoclay; Kaol=Kaolin/Kaolinite; Sep=Sepiolite; Pal/APT=Palygorskite/Attapulgite; ACN/FLAV=Anthocyanins/Flavonoids; Cur=Curcumin; Vit.=Vitamins; Prot/Pept=Proteins/Peptides; EO=Essential Oils; API=Active Pharmaceutical Ingredient (Drugs); PP/Phen=Polyphenols/Phenolics.

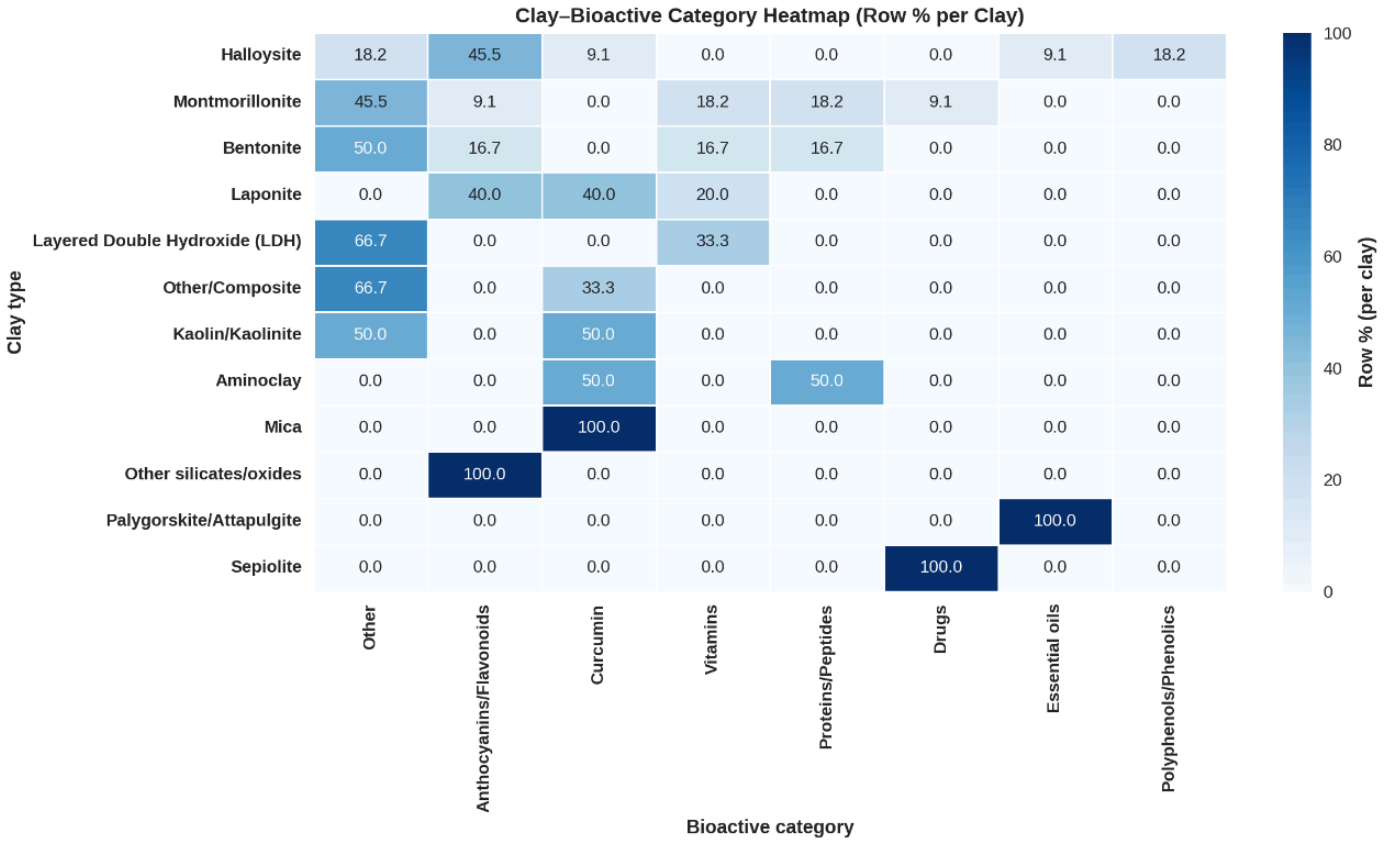


Figure 4

Clay–Bioactive Category Heatmap (Row % per Clay).

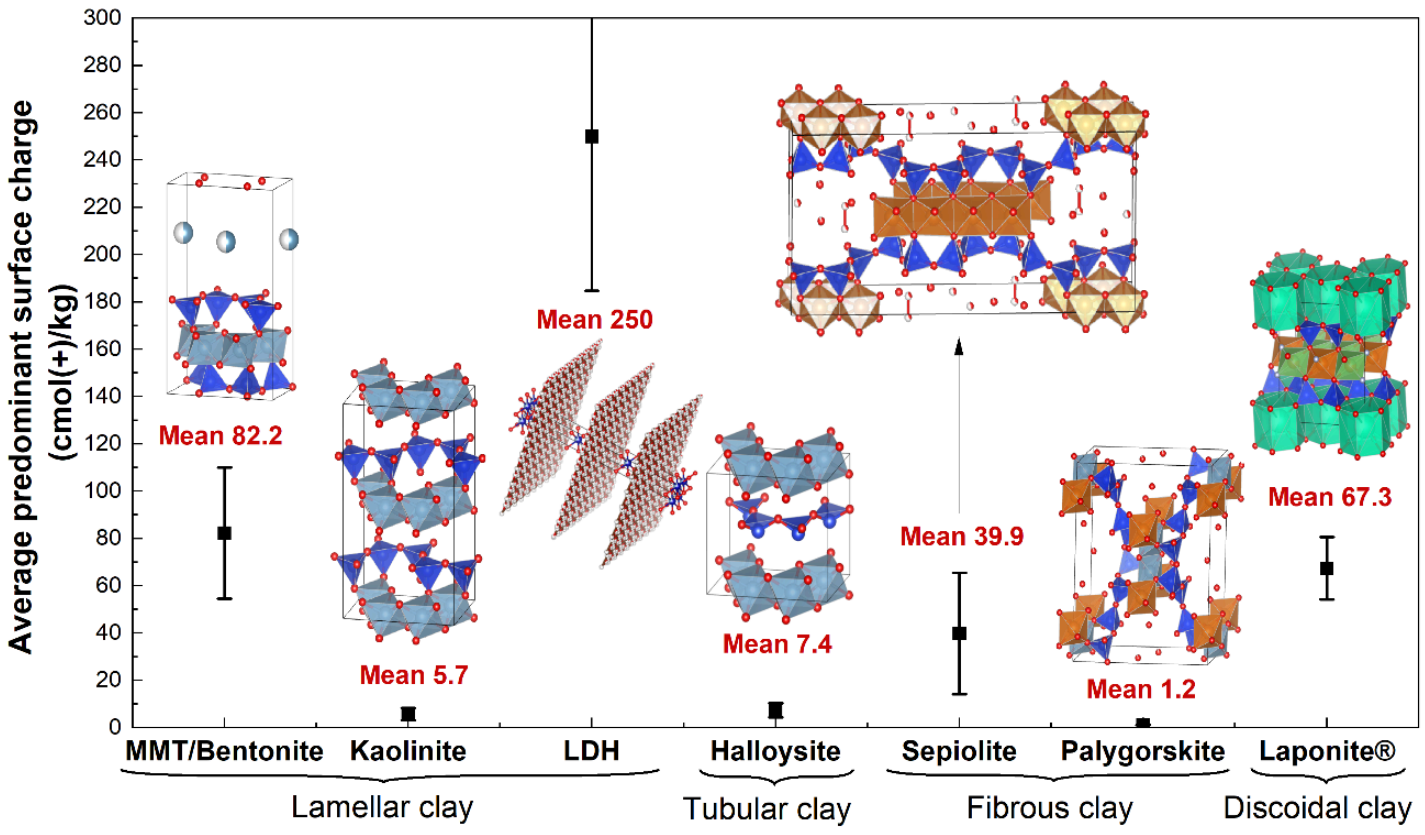


Figure 5

Average Predominant Surface Charge Across Clay Families with Representative 3D Structural Models Generated in VESTA v.3. The mean values and standard deviations were compiled and calculated from multiple literature sources [20,36,37,40–42,44–54].

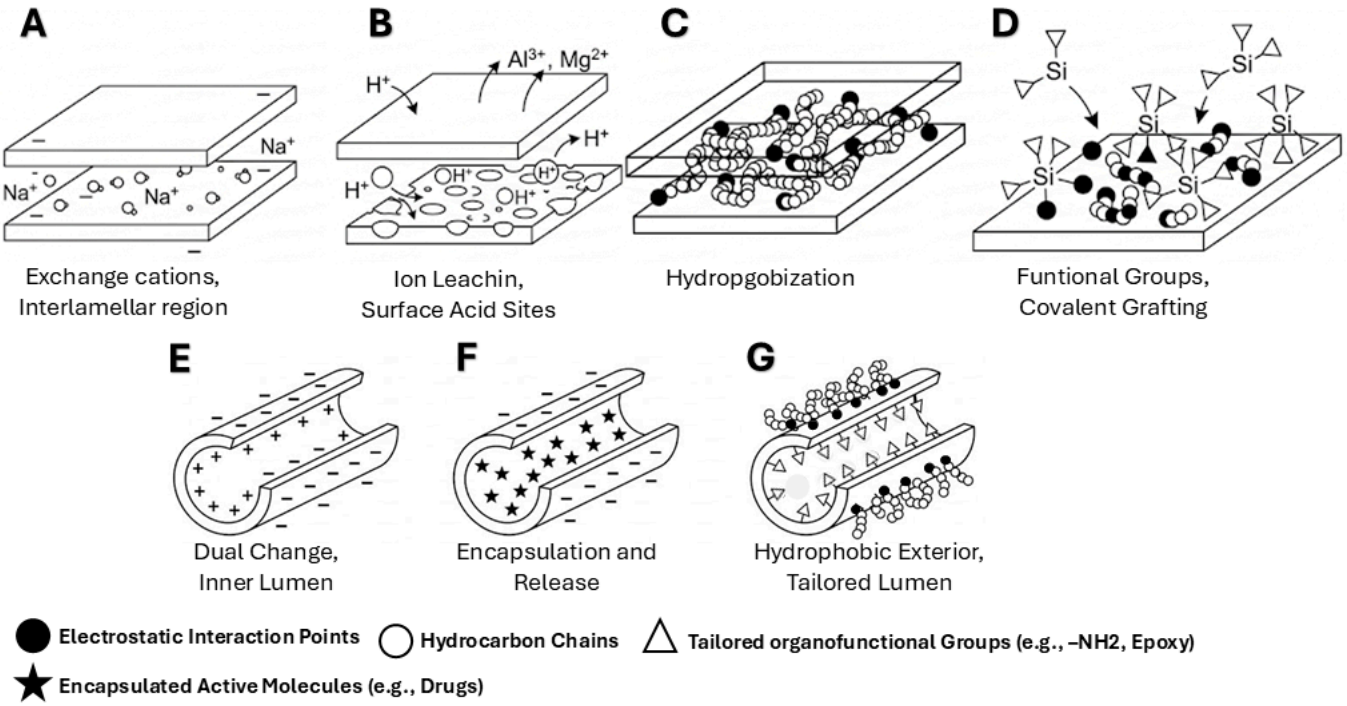


Figure 6

Schematic representation of pristine platelet clays (A), acid-modified (B), organomodified via hydrophobization (C), and with the addition of covalent functional groups (D); and pristine tubular clays showing their dual charge (E), with encapsulation of active compounds (F), and with selective functionalization (G).

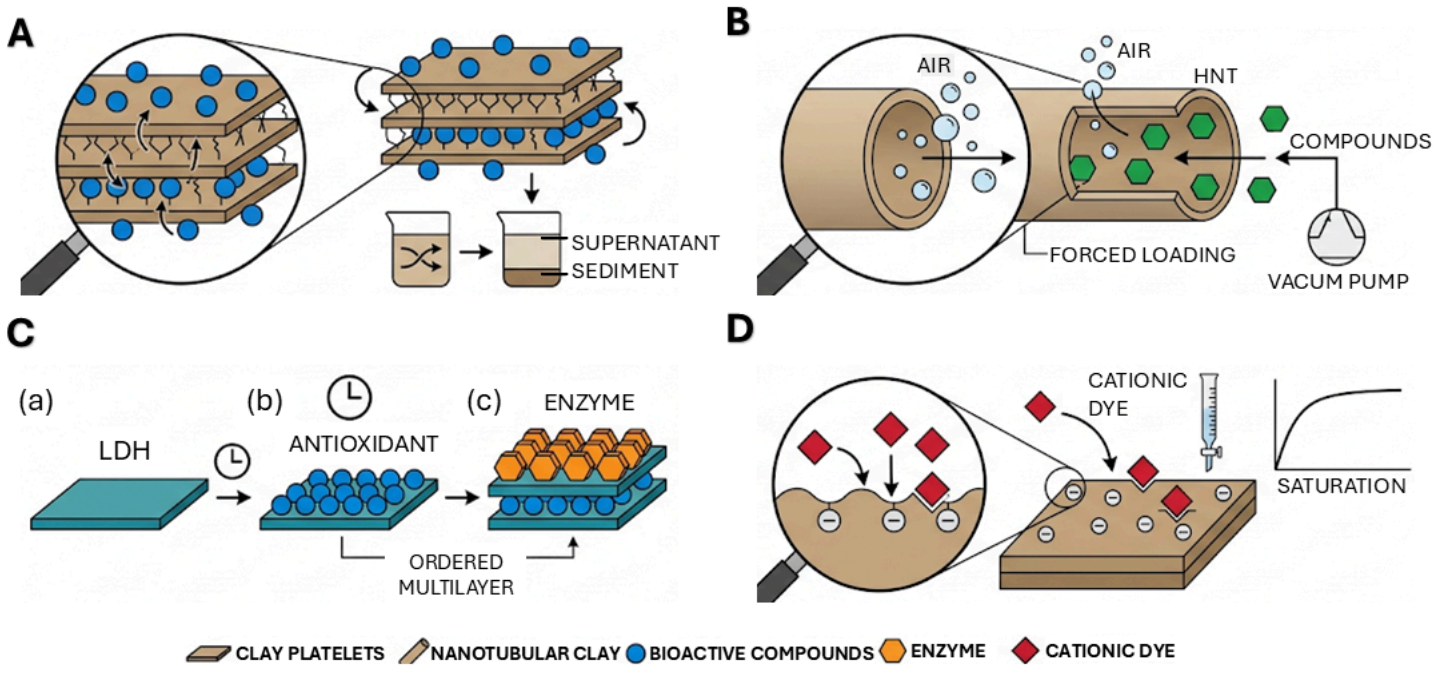


Figure 7

Key methods used to incorporate, assemble, and characterize bioactive compounds in clay-based materials: (A) a liquid-phase adsorption process in which molecules attach to clay platelets through agitation followed by phase separation [37]; (B) a vacuum-assisted loading scheme illustrating how compounds enter the lumen of nanotubular clays under negative pressure [22]; (C) a sequential layer-by-layer assembly method in which antioxidants and

enzymes are deposited in an ordered manner onto a surface, forming structured multilayers [74]; and (D) a titration procedure to measure cation-exchange capacity, represented by the progressive incorporation of a cationic dye until the active sites of the material become saturated [50,56].

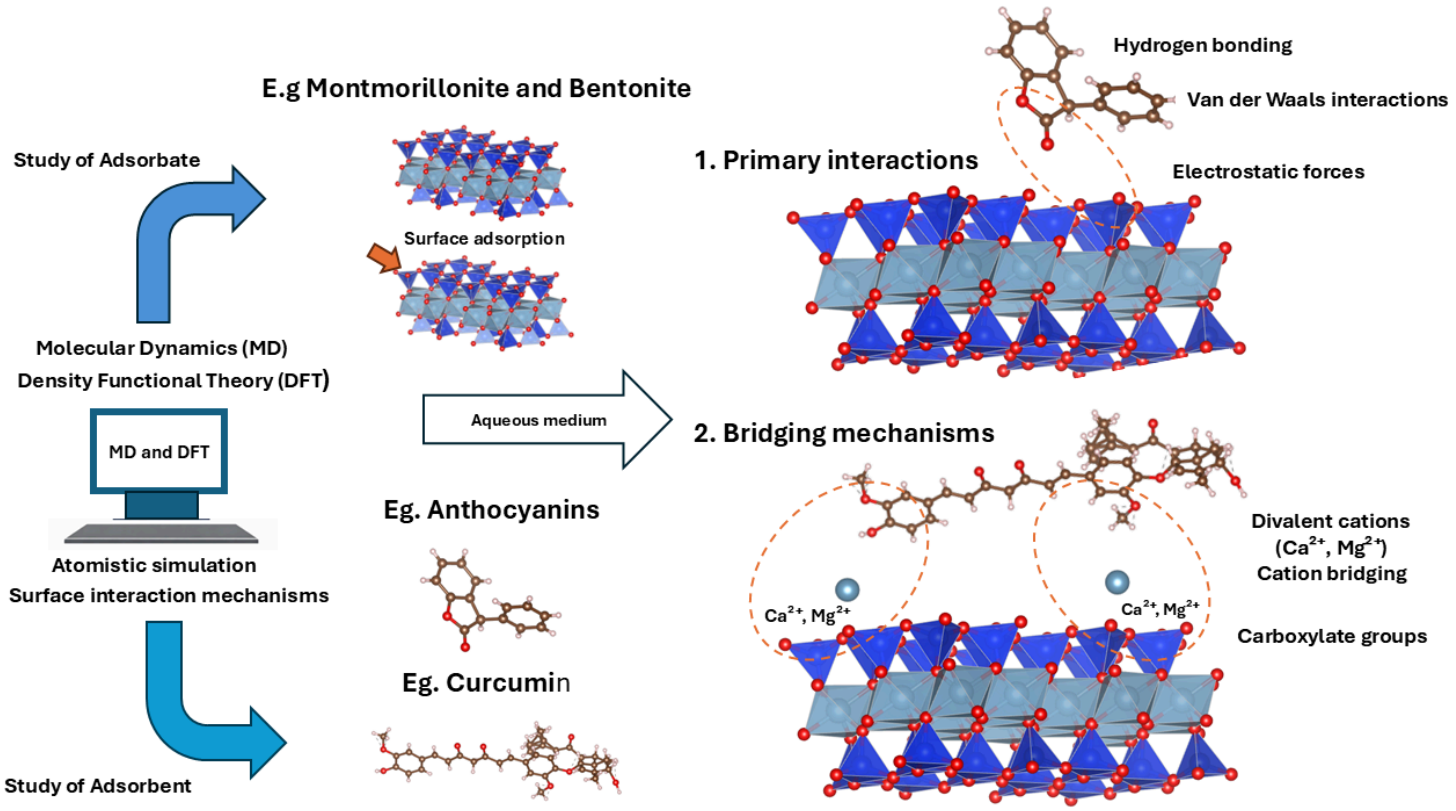


Figure 8

Possible adsorption mechanisms of anthocyanins or curcumin on the surface of materials such as montmorillonite and bentonite.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- OnlineSourse2.bib
- SupplementaryTableS1OnlineSourse3.docx
- OnlineSourse1.rar