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2D materials for nutraceutical delivery and smart packaging: multifunctional, sustainable, and responsive applications

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Materials in the form of two-dimensional (2D) structures have recently become a revolutionary platform in nutraceutical delivery and smart food packaging, solving the problem of poor solubility, stability, and bioavailability of bioactive compounds. Traditional delivery systems are not always effective in preventing the degradation of sensitive nutraceuticals like polyphenols, flavonoids, vitamins, and probiotics in response to light, heat, pH changes, or enzyme activity, which reduces their therapeutic potential. Similarly, conventional packaging materials offer little protection and no active food freshness monitoring, which leads to shorter shelf life and poor quality. The novelty of this review is the focus on the multifunctional potential of 2D materials in improving nutraceutical delivery and allowing smart, antimicrobial packaging with targeted, responsive, and sustainable applications. In contrast to the existing reviews that mainly focus on biomedical or pharmaceutical applications, this review summarizes nutraceutical-specific advances, critically evaluates various 2D materials, including graphene and graphene derivatives, MXenes, layered double hydroxides (LDHs), transition metal dichalcogenides (TMDs), and 2D metal–organic frameworks (MOFs), and points out regulatory, toxicological, and sustainability issues that are essential to real-world translation. Recent reports indicate that 2D materials can be used to efficiently encapsulate bioactives and enhance solubility, chemical stability, and controlled or stimuli-responsive release. In addition, these materials offer antimicrobial, antioxidant and sensing properties to packaging, allowing real-time monitoring and extended shelf life. Collectively, these features turn traditional delivery and packaging into smart, multifunctional platforms. Although these developments have been made, there are still challenges such as the possibility of biosafety issues, lack of standard procedures, regulatory frameworks, and challenges of scalable production. The future outlook focuses on the development of safe, biodegradable, and commercially viable 2D materials, along with standardized evaluation platforms, to provide sustainable, effective, and market-ready nutraceutical delivery and smart packaging solutions.

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1. Introduction

Two-dimensional (2D) materials are a class of nanostructures, characterized by atomic thickness and large lateral dimensions. During the last few years, scientists have become more interested in 2D materials because of their exceptional physicochemical properties, including high surface area, mechanical strength, tunable surface chemistry, changed surface properties and marked changes in electrical characteristics. As a result, such materials are expected to be useful in various biomedical and healthcare areas, mainly for delivering drugs, biosensing and developing smart packaging.

To begin with, Jayakumar *et al.*,[1] pointed out how 2D materials could help with drug delivery and packaging in the healthcare field. Afterwards, the world of research has expanded at a very fast pace. Zhang *et al.*[2] and Mei *et al.*[3] have thoroughly discussed the usage of 2D materials in targeted chemotherapy, gene delivery and immunotherapy. In the same way, Wang *et al.*,[4] studied employing 2D materials other than graphene as nanocarriers for cancer treatment and this points to a growing interest in a wider range of materials for biomedical applications. Even though 2D materials are well established in traditional medicine, people are starting to look at their possible uses in nutraceuticals which mix nutrients and drugs for health and illness prevention. Still, although there is a lot of literature about biomedical applications, specific studies on nutraceuticals are still few. At the same time, 2D materials are proving useful in the field of advanced packaging technologies. The team of Jafarzadeh *et al.*[5] noted that these substances can be applied to sustainable smart packaging, improving barrier properties and enabling real-time sensing of food quality and spoilage. Being able to protect and communicate easily makes 2D materials the best candidates for nutraceutical packaging in

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the future. In their reviews, Chimene *et al.*[6] and Kurapati *et al.*[7] discuss the potential applications of 2D nanomaterials beyond graphene, emphasizing the importance of their biocompatibility, usefulness in treating diseases, and potential applications in biosensors.

Nutraceuticals, such as bioactive compounds, like polyphenols, vitamins, carotenoids, and probiotics, have gained a lot of attention because of their potential in health promotion and disease prevention. However, the translation of these compounds into functional foods and supplements is often limited by intrinsic limitations. Most nutraceuticals have low aqueous solubility, chemical instability during storage or gastrointestinal transit, and low bioavailability, which severely limit their therapeutic potential.[8] At the same time, the packaging systems used to deliver and protect food products are largely passive, serving as inert barriers that provide little protection against microbial contamination, oxidation, or nutrient degradation. These issues point to a major bottleneck: despite the abundance and potential of nutraceuticals, the absence of effective delivery and protective systems remains a major obstacle to their full potential in real-life applications.[9]

To overcome these difficulties, different nanocarrier systems like liposomes, nanoemulsions, polymeric nanoparticles, and micelles have been investigated to deliver nutraceuticals. These systems are able to enhance solubility, protect compounds against degradation, and provide controlled release.[9] Likewise, active packaging with nanocomposites, natural antimicrobials, and biopolymer matrices have progressed beyond the traditional plastic-based methods.[10] In spite of these successes, there are still significant gaps. Most systems are unstable at physiological or food-processing conditions, have low loading capacity, and are subject to batch-to-batch variability. Moreover, their practical application in the nutraceutical and food industries is still limited by scalability, regulatory acceptance, and consumer safety issues.[11] Therefore, there is an immediate need to have alternative strategies that are not only superior in terms of functionality but also robust, scalable, and versatile.

In this regard, 2D materials have become attractive options because of their structural and physicochemical flexibility. In contrast to traditional nanocarriers, 2D materials offer ultra-high surface-to-volume ratios, surface chemistry that can be tailored, and multifunctional properties, including antimicrobial activity and environmental responsiveness. Graphene and its derivatives, MXenes, layered double hydroxides (LDHs), transition metal dichalcogenides (TMDs), and 2D metalorganic frameworks (MOFs) have already shown great promise in biomedical and environmental applications. In more recent years, novel types of materials, such as 2D oxides, tellurides, and silicates, have broadened the material space, with properties such as high catalytic activity, tunable conductivity, and biomineral compatibility. Such multifunctional characteristics render 2D materials not only to be a vehicle of nutraceutical encapsulation and delivery but also an active ingredient in smart, antimicrobial, and sustainable packaging. New 2D materials, such as oxides, tellurides, and silicates, are potential candidates to be applied in advanced applications. 2D tellurides (*e.g.*, WTe_2, $MoTe_2$) have tunable conductivity and topological insulation, which can be used to create stimuli-responsive nutraceutical delivery and smart packaging.[12] Silicates are abundant and scalable, with piezoelectricity, 2D magnetism, and catalytic activity, and thus are appropriate as active delivery and packaging systems. 2D oxides have nanoscale functionalities in catalysis, sensing, and sustainable energy.[13]

The combination of these low-dimensional properties with better synthesis and characterization methods suggests their potential in both current and emerging technologies. Although there are numerous reviews on 2D materials, they have been limited to biomedical, energy storage, or environmental applications, with little discussion of food and nutraceutical systems. To the best of our knowledge, this is the first review to thoroughly discuss the multifunctional potential of 2D materials in nutraceutical delivery and smart packaging. In particular, we discuss how these materials can improve bioactive stability and bioavailability, provide targeted and stimuli-responsive release, and add active functionalities to packaging systems, including antimicrobial protection and freshness sensing. By doing so, this review not only summarizes the existing developments but also highlights the existing gaps in terms of scalability, safety, regulatory frameworks, and consumer perception. We aim to present a prospective view of how 2D materials can revolutionize nutraceutical technologies by turning passive protection systems into intelligent, responsive, and sustainable platforms.

2. Types of 2D materials relevant to nutraceuticals

2.1 Graphene and graphene oxide

From the expanding collection of two-dimensional materials, graphene and graphene oxide (GO) make significant progress in the field of biomedical innovation. The reason they are important in nutraceutical delivery is due to a mix of structural versatility, chemical tunability, and biocompatibility, making them ideal candidates for next-generation functional systems.

Graphene, which is just one layer of carbon atoms arranged in a honeycomb shape, has an unusual surface area, tough material strength, excellent conductivity and flexibility. Still, because it is hydrophobic and chemical inert, which can limit its applicability in biological environments. Because of these problems, scientists have found that graphene oxide (GO) which is rich in oxygen-containing functional groups, is a better option for biomedical use. With these functional groups, they are water-soluble, can be easily mixed in water and are able to hold more drugs due to π–π stacking, hydrogen bonds and electrostatic interactions. According to Liu *et al.*,[14] both graphene and GO have great potential to carry drugs, since they can handle a large payload, release drugs at controlled times and be altered to achieve targeted effects. This conclusion has been supported by the following works by Priyadarsini *et al.*[15] and Byun[16] which again discussed the multiple biomedical applications of these materials, including gene delivery (Fig. 1) and photothermal therapy. Recent advancements include the development of stimuli-responsive nano-graphene carriers,

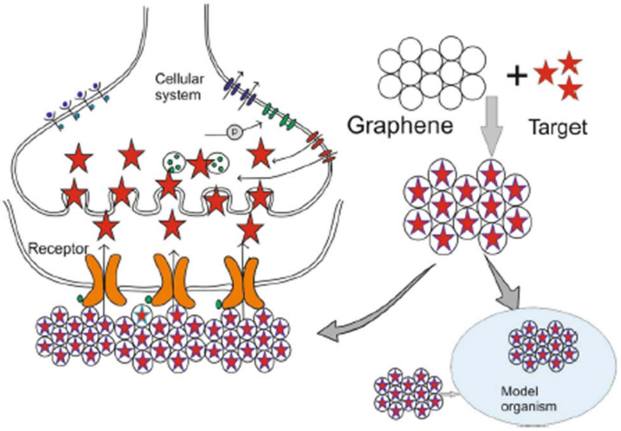

Fig. 1 Graphene as a carrier for target (gene or small molecular drug) delivery – graphene and its derivatives provide an ultrahigh surface area and abundant functional groups, which allow efficient loading of therapeutic agents. The figure is obtained from ref. 15 under a Creative Common (CC BY) License.

which can be triggered by pH, chemical interactions, thermal, photo, and magnetic induction for controlled drug release.

While much of the focus has been on pharmaceutical applications, the transition into nutraceutical delivery is both natural and promising. GO's wide surface and functionalizability allow it to efficiently load bioactive compounds such as polyphenols, flavonoids, curcuminoids and vitamins, all of which are hard to solubilize and absorb by the body. Jampílek[17] and Plachá[18] pointed out that GO might be useful in this area, mainly because its biodegradability and be modified to suit different applications. As well as focusing on delivery, GO and graphene derivatives are being studied for use in advanced and smart types of packaging. Following an example given by Plachá *et al.*,[18] these materials can confer antimicrobial protection, strengthen the packaging and add sensors to ensure the freshness of the food and nutraceuticals being stored is checked. Also, creating a complete physicochemical characterization of 2D carbon materials, in line with Albers *et al.*,[19] advances the possibility of translating laboratory graphene-based developments into common nutraceutical products.

Graphene and graphene oxide are central to 2D material research and may play a key role in future advances in nutrition delivery and advanced packaging. Their flexible structures, versatile surfaces, and consistent biomedical performance position them to provide innovative, effective, and eco-friendly solutions for today's healthcare needs.

Graphene and graphene oxide are applied in nutraceutical delivery and smart packaging because of their high surface area and strong interactions with bioactives such as vitamins and polyphenols. They are more chemically stable and easier to handle than MXenes but are less electrically conductive. Graphene is also more flexible than LDHs, providing antimicrobial and barrier properties. The limitations include the possibility of oxidative stress, residual synthesis agents, and bio persistence over time (Zhang *et al.*, Liu *et al.*).[14,20]

2.2 MXenes

Among the newer two-dimensional (2D) materials, MXenes have gained importance for their multifunctionality and excellence in biomedical, sensing, and therapeutic applications. In 2011, MXenes were found to be 2D transition metal carbides, nitrides or carbonitrides, typically derived from layered MAX phases through selective etching processes. They have a general formula of $M_{n+1}X_nT_x$, where M stands for a transition metal, X can be carbon or nitrogen and T includes possible surface groups (for instance, –OH, –F, –O), allowing these materials to be easily modified and made bioactive. What makes MXenes particularly attractive for nutraceutical delivery and packaging is their unique combination of hydrophilicity, high surface area, electrical conductivity, mechanical flexibility, and tunable surface chemistry. Being oxygen-free, MXenes are able to work with various biomolecules and easily pick up and store sensitive compounds such as antioxidants, polyphenols and micronutrients.

Lu *et al.*[21] and Huang *et al.*[22] proved that MXenes can be useful for drug delivery, killing bacteria, photothermal therapy and sensing biological substances. Although only a few studies look at MXenes in nutraceutical systems, their successful use in therapy, real-time biosensing and coating designs makes them suitable for use in nutraceutical products in the future. Antimicrobial effects from MXenes, discovered by Pogorielov[23] and Sagadevan,[24] suggest that special films made of MXene materials could be used in active packaging, protecting nutraceutical goods from harmful microbes and allowing them to maintain freshness and safety for more time. MXenes' usefulness in biosensing is shown by Rohaizad *et al.*,[25] so they can now be used in creating packaging that tracks the environmental conditions, spoilage and changes in nutrients constantly. Even though evaluating these factors is necessary, Szuplewska *et al.*,[26] as well as Sagadevan,[24] have demonstrated that MXenes can show helpful results, if they are carefully functionalized or embedded in composite systems. In addition, these features enable them to improve as safe and responsive carriers and materials for nutraceutical products.

Overall, MXenes are a major advancement in 2D materials, with adaptability and multifunctional properties that make them highly promising for nutraceutical formulation, preservation, and packaging.

MXenes, such as $Ti_3C_2T_x$, are potential nutraceutical delivery and smart packaging materials due to their high conductivity, hydrophilic surfaces, and antimicrobial properties. They are able to liberate bioactives in response to pH or redox changes and can be incorporated into films or coatings. MXenes conduct electricity better than graphene but are less stable in air or water. The challenges are that it may leach heavy metals, and it is hard to produce in large scale. Recent research demonstrates MXene-curcumin carriers and MXene-based food coatings.[27,28]

2.3 2D metal organic frameworks (MOFs)

2D metal–organic frameworks (2D MOFs) are standing out as an important group for both nutraceutical delivery and the development of smart packaging in the world of newer 2D materials.

Because their structure consists of metal ions or metal clusters bridged by organic ligands, the resulting 2D MOFs bring the best aspects of inorganic chemistry and organic chemistry, making them useful for unique porosity, high surface area, customized properties and several uses. Because 2D MOFs are so thin, they improve on the traits of 3D MOFs and show better transport, bioavailability and interfacial interaction potential, so they are very effective at delivering vitamins, polyphenols, probiotics and antioxidants. This structural thinness enhances guest–host interactions and enables precise control over molecule encapsulation and release, which is crucial in the nutraceutical field.

Kumar *et al.*[29] show that 2D MOFs have performed well in therapeutic delivery, tissue engineering, sensing and imaging in biology. Since they work well in certain systems, their utility in controlled release systems and high-capacity cargo loading makes the transition into nutraceutical delivery systems a natural progression. A comprehensive review by Zhao *et al.*[30] highlights that 2D MOF nanosheets perform multifunctionality such as carrying, stabilizing and covering sensitive substances. Flexible design of the framework allows them to be carefully adjusted so that nutraceuticals are released only in certain sections of the gastrointestinal tract. Besides, MOFs are made of modular components which enables scientists to design them to care for specific reactions with bioactives or stimuli from the environment, making them suitable for smart packaging. Imagine a food package that can conserve the food, monitor its freshness, and even release protective ingredients to prevent spoilage. MOF-based systems have made these ideas practical today.

Studies done by Lin *et al.*[31] and Chakraborty *et al.*[32] prove that people are working more on creating scalable 2D MOFs which is important for practical implementation in food and nutraceutical sectors. Although current research mainly deals with biomedical and catalysis, the versatile, sensitive and customizable properties of 2D MOFs could make them important in nutraceutical delivery as well as smart packaging technologies.

Moreover, two-dimensional metal–organic frameworks (MOFs) offer tunable pores to load bioactives in high amounts and can be functionalized to exhibit antimicrobial properties. They also have gas adsorption properties that can be used to monitor freshness in smart packaging. MOFs have a greater encapsulation capacity and gas-sensing performance than graphene derivatives compared to LDHs. Nevertheless, their stability in aqueous or humid conditions and possible metal ion leaching are issues of concern to practical applications. Recent studies of Kumar *et al.*,[29] and Angeli *et al.*,[33] show the encapsulation of probiotics in MOFs and antimicrobial packaging films, which indicates the potential of MOFs in nutraceutical and packaging applications.

2.4 Layered double hydroxides (LDHs)

Layered double hydroxides, sometimes called anionic clays, are an exceptional class of two-dimensional, lamellar nanomaterials that are valuable for encapsulation, stabilization and slow release of nutraceuticals. LDH structures are built from positively charged brucite type layers with exchangeable anions and water molecules in the spaces between the layers (Fig. 2). Because of their unique structure, LDHs have powerful anion exchanging abilities, a large surface area, adjustable properties and are biocompatible, so they are ideal for transporting bioactive compounds.

What differentiates LDHs is that they are able to hold negatively charged biomolecules inside their layers such as vitamins (for example, folic acid), phenolic compounds, probiotics and antioxidants. Not only does this help protect essential nutraceuticals from degraded by light, heat or any pH change, but it also leads to sustained and targeted release, which is best for better bioavailability and greater effectiveness. According to Nalawade *et al.*[35] and Bini *et al.*,[36] this is why LDHs can be quickly used to formulate and deliver nutraceuticals. Du *et al.*,[37] point out that LDHs can be easily adapted for various biomedical purposes because they are both biocompatible and biodegradable and can be modified to serve in oral dietary supplements, packaging bioactive materials and surface coatings. They are also responsive to changes in pH which allows them to release their cargo at the right sites in the gut and bring great changes to the nutraceutical sector. According to Richetta *et al.*,[38] the size of their interlamellar space can be precisely controlled, allowing LDHs to successfully bind many nutraceutical actives, from hydrophilic polyphenols to sensitive enzymes. Recent studies from Yan *et al.*[39] and Arrabito *et al.*[34] prove that LDH based nanocomposites can be used as synergistic delivery systems; combining LDHs with polymers or other nanomaterials to create hybrid platforms that are biostable, multifunctional, and responsive to biological cues.

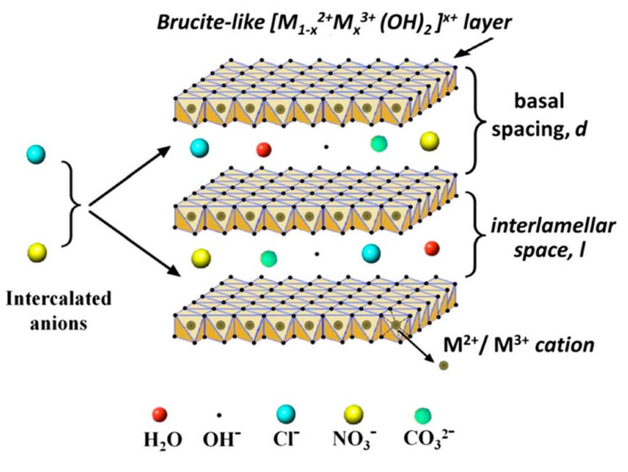

Fig. 2 Schematic structure of M^{2+}/M^{3+} layered double hydroxides (LDHs), showing the brucite-like layers with charge-balancing anions (Cl^-, NO_3^-, CO_3^{2-}) intercalated in the interlamellar space, together with water molecules and hydroxyl groups. This layered architecture provides high anion-exchange capacity and tunable interlayer spacing, enabling LDHs to act as versatile carriers for negatively charged nutraceuticals, antioxidants, and preservatives. The intercalation ability illustrated here underpins their role in controlled release and stabilization within food and packaging applications. The figure is obtained from ref. 34 under a Creative Common (CC BY) License.

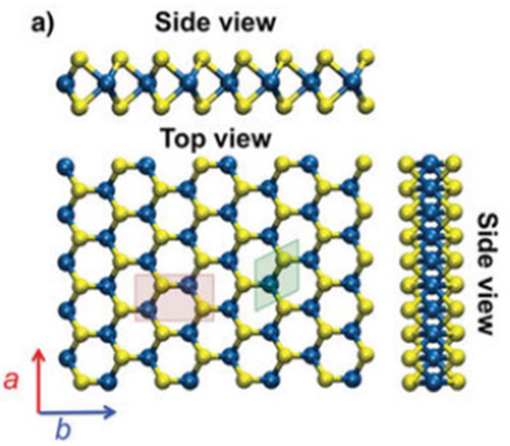

Fig. 3 Atomic structure of two-dimensional transition-metal dichalcogenides (TMDs) of the general formula MX_2, where M = Mo, W, or Ti. The schematic highlights the layered arrangement, in which a transition-metal atom sheet is sandwiched between two chalcogen atom layers, as well as the in-plane lattice vectors (a and b). This unique architecture imparts TMDs with tunable band gaps, high surface area, and strong light–matter interactions, making them promising candidates for applications such as antioxidant stabilization, photothermal antimicrobial packaging, and stimuli-responsive nutraceutical delivery. The figure is obtained from ref. 42 under a Creative Common (CC BY) License.

Even though the use of LDHs in food and nutraceuticals is under development, their strong proof of safety, low toxicity, ease of preparation and versatility mean they are already considered the next-generation carriers. If additional development occurs, LDHs could start being used widely, not only for encapsulation but also for intelligent nutraceutical packaging that helps in storage, monitors freshness and triggers release.

LDHs are safer and more biodegradable than MXenes but less versatile than graphene or MOFs, with slower release kinetics and limited multifunctionality. Chronic toxicity studies are limited. Mishra *et al.*[40] show that recent developments include vitamin C delivery systems based on LDH and protective packaging films with improved functionality (Yu *et al.*[41]), which can be applied in functional foods.

2.5 Transition metal dichalcogenides (TMDs)

As versatile next-generation biomedical and nutraceutical candidates, transition metal dichalcogenides (TMDs) are getting much attention. They have a general chemical formula of MX_2 (where M is a transition metal like Mo, W, or Ti and X is a chalcogen like S, Se, or Te) (Fig. 3). They are rapidly emerging as versatile candidates for next-generation biomedical and nutraceutical applications.

They are special for both therapeutic and diagnostic functions, because they have a thin texture, tunable band gaps, cover a high amount of surface and chemical modifications can be made. Among the most studied TMDs, molybdenum disulfide (MoS_2) and tungsten diselenide (WSe_2) have received significant attention because of their excellent biocompatibility, remarkable photothermal properties, and high drug-loading capacity.[43] As a result of these properties, TMDs can transfer bioactive substances and release them in response to pH, light or enzymes, which is very useful for nutraceuticals.

Such studies by Li *et al.*[44] and Anju *et al.*[45] explain how TMDs can be enhanced with polymers, specific molecules and modifications of their surface to ensure they are soluble, stable and compatible inside nutraceutical products. For instance, surface-modified MoS_2 nanosheets can securely release antioxidants, vitamins and polyphenols which can help in their better absorption and less impact in the gastrointestinal system. Recent work by Raghunathan *et al.*[46] indicate that the function of TMDs as highly sensitive biosensors, so they can successfully detect any spoilage signs, microbial contamination and environmental changes. For this reason, they might be applied in intelligent food packaging systems that protect nutraceutical foods while monitoring freshness and safety continuously.

Table 1 Key properties, advantages, limitations, and nutraceutical relevance of major 2D materials (graphene & graphene oxides, MXenes, LDHs, MOFs, and TMDs)

Material	Key properties	Advantages	Limitations/toxicological concerns	Nutraceutical relevance
Graphene & graphene oxides	High surface area, strong π–π interactions, antimicrobial, barrier properties	Effective encapsulation, stability improvement, antimicrobial activity	Potential oxidative stress, persistence, synthesis residues	Encapsulation of polyphenols, vitamins; antimicrobial food packaging
MXenes	High conductivity, hydrophilicity, tunable surface chemistry	Controlled release, sensing, antimicrobial coatings	Oxidation instability, limited long-term safety data	Stimuli-responsive delivery, intelligent packaging sensors
LDHs	Layered structure, ion-exchange capacity, biocompatible	Good loading of charged nutraceuticals, pH-responsive release	Limited stability in acidic conditions	Probiotic/vitamin delivery, pH-responsive food packaging
MOFs	High porosity, tunable pore size, catalytic properties	Large loading capacity, multifunctional delivery	Possible metal ion leaching, stability issues in moisture	Encapsulation of bioactives, oxygen scavenging in packaging
TMDs (e.g., MoS_2, WTe_2)	Unique optical/electronic properties, catalytic, sensing ability	Photothermal response, antioxidant functions	Limited toxicity data, synthesis scalability issues	Smart packaging sensors, antioxidant protection of bioactives

Besides, because of their photothermal and photodynamic properties, they are useful for theranostic applications in functional foods and supplements meant to benefit those recovering from cancer, also control inflammation or reduce oxidative stress. Before using them in nutraceutical products widely, concerns such as water solubility, their long-term effects and manufacturing scalability, should be handled. According to Agarwal *et al.*[47] and Kalantar-Zadeh *et al.*,[48] current advances in synthesis and functionalization are steadily overcoming these limitations. Overall, TMDs are a cutting-edge type of 2D materials with a lot of applications in encapsulating nutraceuticals, controlled drug delivery and smart packaging. Their ability to be customized for different environments demonstrates how well-suited they are for precise nutraceutical applications in the future.

TMDs are more effective in photothermal response than graphene but are less studied in food applications than MXenes and MOFs. Limitations are possible cytotoxicity, complicated and expensive synthesis, and a lack of *in vivo* studies. Recent reports demonstrate MoS_2 based antioxidant carriers (Li and Wong)[44] and TMD enabled antimicrobial packaging (Hu *et al.*),[49] which demonstrates their potential in smart, functional materials.

The following summary table highlights the key properties, advantages, limitations, and nutraceutical relevance of major 2D materials (graphene & graphene oxides, MXenes, LDHs, MOFs, and TMDs) (Table 1).

3. Key properties of 2D materials for nutraceutical applications

3.1 High surface area

What draws the most attention to two-dimensional (2D) materials is their outstanding surface area-to-volume ratio, making them useful in nutraceutical science. Due to their one-atom layer structure, the sheets provide maximum interaction with bioactive substances, target biomolecules and cellular membranes. It has been widely stated, in several studies (Jayakumar *et al.*,[1] Rohaizad *et al.*,[25] Chimene *et al.*[6]), that this high surface area is fundamental for the use of nanoparticles in bioencapsulation, targeted delivery and sensing. In the nutraceutical context, it allows the better loading of molecules such as polyphenols, flavonoids, vitamins and probiotics increases the carrying capacity of a nanocarrier. Also, it controls and sustains release profiles by spreading the molecules evenly over the surface, enabling fine-tuned nutrient delivery in response to environmental triggers such as pH and enzymes. Moreover, nutraceuticals that do not easily mix in water improve when placed on 2D materials and facilitate their stabilization in aqueous environments. For example, graphene oxide, MXenes and 2D metal–organic frameworks are used because they have a large surface that allows them to keep nutraceutical compounds secure from fast digestion and boost their presence in the body.

Furthermore, this concept is useful in other ways as well, apart from delivery. A 2D material's large surface area helps these devices detect very low levels of biomarkers that indicate risk or toxins in the environment which is important for making safe and shelf-stable nutraceutical packaging. All in all, what truly drives 2D materials' wide abilities in nutraceutical science is their high surface contact area. From encapsulation to detection, this property empowers next-generation formulations that are smarter, safer, and significantly more effective.

3.2 Functionalization strategies of 2D materials

A special aspect of two-dimensional (2D) materials is that they can have their functionalization ability in different ways to address various needs in different fields. Martínez-Hernández *et al.*[50] indicate that this capability transforms them from passive carriers into intelligent, multifunctional platforms that are ideally suited for nutraceutical delivery, sensing, and protection. Because they have a lot of surfaces and can easily change their chemistry, graphene derivatives, TMDs, MXenes and 2D MOFs make great platforms for adding various nutraceutical compounds. This includes vitamins, antioxidants, polyphenols, peptides and probiotics and natural biopolymers like chitosan, alginate or keratin for improved corporeal integration.

There are many important benefits of using functionalization in nutraceuticals. Functionalization enhances biocompatibility; using biopolymers or amino acids improves adhesion to tissues and lowers their harmful effects. Using functional ligands, they can be guided straight to the target tissues, such as the wall of the intestines or microbes in the gut. Apart from those, smart linkers help release bioactives in response to pH, enzymes or redox conditions which improve their bioavailability. Dispersion is also improved by functionalization *via* improving solubility and stability of hydrophobic nutraceutical compounds in aqueous systems. According to findings of Li *et al.*,[44] and Murugan *et al.*,[51] attaching functional molecules or targeting factors to TMDs and graphene has helped their use in medicine, giving a clear hint on how they might be used in nutraceuticals. Also, it is possible to design 2D MOFs and LDHs at the atomic scale to trap, protect and hold nutraceuticals, so they are safe from any changes during storage and digestion. Brill *et al.*[52] explain that functionalization changes both the surface features like hydrophilicity and charge and enables the nanosystem to transform from flat to 3D shapes, enabling multi-level loading and release strategies.

In essence, the functionalization potential of 2D materials is a gateway to precision nutraceuticals; systems that are smart, bioadaptive, and therapeutically efficient. With this property, 2D materials don't just carry bioactives, they actively engage with the biological environment to optimize health outcomes.

3.3 Biocompatibility and degradability

For nutraceuticals, safety and sustainability are just as critical as efficacy. That's why biocompatibility and degradability stand out as essential properties when considering 2D materials for use in nutraceutical formulations, delivery systems, or edible sensors. Chen *et al.*,[53] Martín *et al.*,[54] indicate that the remarkable compatibility in biological conditions (from stomach to the

Table 2 Summary of key 2D materials, their adsorption mechanisms, target compounds, and nutraceutical applications, highlighting their unique properties and relevant references supporting their roles in advanced nutraceutical delivery and packaging systems

2D material	Adsorption mechanism	Target compounds	Nutraceutical applications	Unique features	References
Graphene/graphene oxide (GO)	π–π stacking, hydrogen bonding *via* oxygen groups	Polyphenols, flavonoids, vitamins	Smart nutrient delivery, antioxidant stabilization, polyphenol enrichment	Large surface area, oxygen-rich surface, high affinity for aromatics	Oliveira *et al.*[58]
MoS_2/TMDCs	Electrostatic and van der Waals interactions	Nucleobases, enzymes, small biomolecules	Nutrient sensing, bioactive compound encapsulation	Tunable surfaces, high binding capacity	Vovusha *et al.*[59]
Boron nitride (BN) nanosheets	Hydrophobic–hydrophilic interaction, porous structure	Pharmaceuticals, vitamins	Oral delivery systems, gut-stable formulations	Stable in digestive pH, chemically inert	Goyal *et al.*;[60] Liu *et al.*[61]
MXenes	pH/redox-sensitive interactions, ion-exchange	Trace minerals, peptides, antioxidants	Controlled release, responsive nutrient delivery	Electrically conductive, high ion adsorption, surface tunable	VahidMohammadi *et al.*[62]

whole body) has been found in graphene, MoS_2, WS_2, BN and MXenes because of their thin and simple structure which makes it possible to change their surface molecules. Biocompatibility matters in nutraceuticals, because they should have non-toxic interactions. When they are functionalized right, 2D materials usually cause no harmful or irritating effects which are mainly advantageous for mucosal or oral delivery. Lobo *et al.*[55] have shown the materials like MoS_2 and h-BN are able to merge into biological systems without changing the function of the cells in which they are inserted as a result of biocompatibility of those materials. Several studies confirm that 2D materials can be ingested safely in small doses, especially when coated with natural biomolecules like polysaccharides, peptides, or lipids. What truly elevates 2D materials for nutraceutical use is their capacity to degrade naturally, either enzymatically, hydrolytically, or *via* oxidative processes. This "degradation-by-design" concept (Ma *et al.*[56]) ensures minimal accumulation in the body or the environment. Not only that but also it confirms the controlled release of nutraceuticals, as degradation can be tuned to digestive or cellular conditions. Degradability also important for safe clearance through renal or hepatic pathways. For instance, He *et al.*[57] indicate a gastric fluid solution can dissolve liquid phase exfoliated nanosheets while ensuring that the encapsulated bioactives are released in controlled amounts. Such behavior ensures efficient bioavailability and minimizes long-term residue which are crucial for daily nutraceutical supplements.

In summary, the biocompatible and degradable nature of 2D materials allows them to be used in clean-label nutraceuticals of the future. Biodegradable nanosheets for targeting the digestive system or absorbable sensors embedded in smart foods are materials which are safe, sustainable, and effective solutions for human health.

3.4 Adsorption properties

Adsorption is one of the outstanding features that two-dimensional (2D) materials possess. From graphene and MoS_2 to MXenes, boron nitride (BN), and 2D metal–organic frameworks (MOFs), these ultrathin sheets offer vast, accessible surface areas coupled with tunable surface chemistry, making them ideal platforms for capturing, concentrating, and delivering bioactive compounds. Table 2 below outlines the various adsorption mechanisms, targets, and nutraceutical applications of various 2D materials, supported by key literature references.

MXenes & MOFs offer new adsorptive capabilities and have the ability to trap and release minerals, trace elements, or nutraceutical actives according to changes in pH or redox cues. There are many things that make their adsorption such effective. The layers that are very thin expose more of the active sites. Also, can adjust the way a nutraceutical compound interacts with the specific nutraceutical molecule by adjusting surface chemistry. It has a high affinity for organics; the molecules can easily attach to antioxidants, peptides, and amino acids. Some biomolecules are separated into different groups by selection binding. These can be used in real world applications such as smart nutrient delivery, extraction of plant bioactives, and contaminant binding. In smart nutrient delivery, the adsorbed compounds can be released in response to gut conditions (pH, enzymes). Extracting plant bioactives especially useful in herbal and botanical nutraceuticals. Additionally, some 2D materials can adsorb toxins, heavy metals, or residual drugs during digestion or formulation, improving product safety.

Adsorption is not just a function; it's a superpower of 2D materials. Their ability to capture, hold, and release nutraceutical compounds on demand makes them invaluable in designing next-generation supplements, smart foods, and health-monitoring tools. These materials aren't just passive carriers; they're active participants in optimizing health outcomes.

4. Applications in nutraceutical delivery

The four synergistic advantages of 2D carriers include: (i) protection and encapsulation of bioactives against degradation by environmental factors (light, pH, oxygen, enzymes); (ii) controlled and targeted release, where payloads are delivered in a site-specific manner in response to biological or external stimuli; (iii) enhanced bioavailability, as 2D nanoscaffolds enhance the solubility, intestinal absorption, and cellular uptake of poorly soluble nutraceuticals such as curcumin and resveratrol. The combination of these properties demonstrates that 2D materials can revolutionize the delivery of nutraceuticals by turning it into smart, responsive, and efficient therapeutic systems (Fig. 4).

4.1 Encapsulation and protection of bioactives

The nutraceutical industry has placed a great reliance on encapsulation technologies since it enhances delivery, stability, and bioavailability of bioactive compounds. These technologies help overcome significant nutraceutical formulation challenges that include poor solubility, degradation during processing or storage and low gastrointestinal absorption.

Nanotechnology and microencapsulation are the two main wrestled strategies to boost the performance of nutraceuticals. Gul *et al.*[9] in their study observe that nanotechnology when used in conjunction with microencapsulation methods enhances the efficacy and bioavailability of bioactive compounds greatly. In the same manner, Leena *et al.*[63] highlight that nanoencapsulation does not only ensure that sensitive ingredients are not degraded in the environment but also promote enhanced absorption in the human body. This is supported by Augustin and Sanguansri[64] who showed how microencapsulation has the ability to stabilize nutraceuticals within food matrices to enhance their delivery and functionality in real-world food applications. Certain systems have been designed to customize delivery depending on the physicochemical character of the nutraceuticals. Aditya *et al.*[65] describe the importance of delivery systems developed to entrain hydrophilic bioactives with lipids, surfactants, and other materials to substantially enhance the stability of these compounds and their biological activity. Conversely, McClements[66] pays attention to nanoscale systems of lipophilic bioactives, which enhance dispersibility and solubility, and guarantee enhanced bioavailability of food-based delivery systems. The other important application of encapsulation technologies is

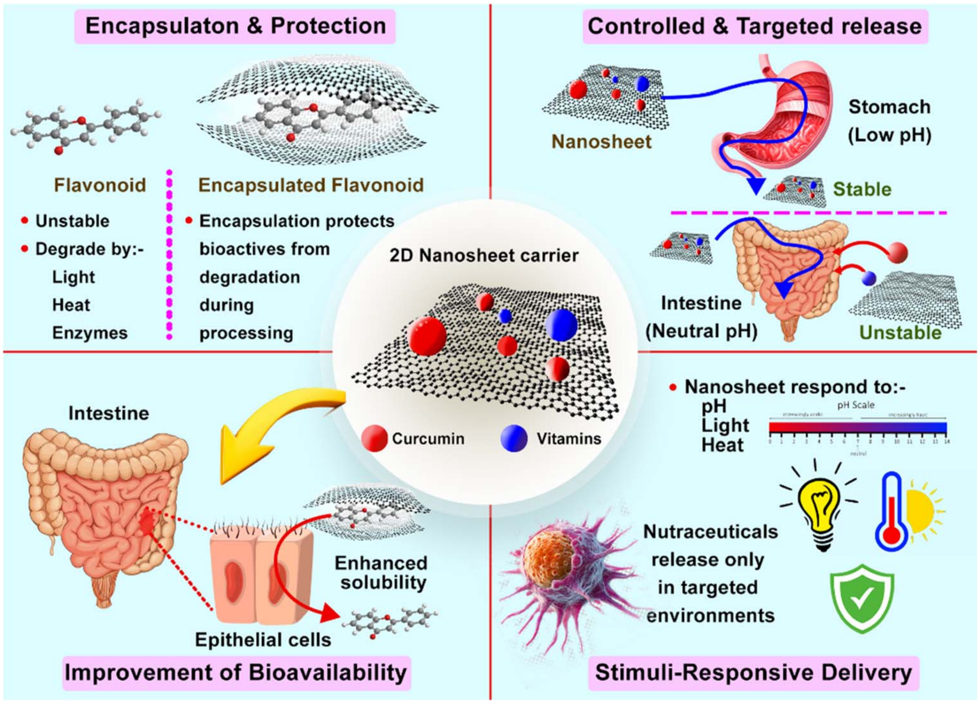

Fig. 4 Multifunctional uses of 2D materials in nutraceutical delivery (authors' work).

controlled release. Garti and McClements[67] extensively reviews many different methods of controlled release methods and encapsulation materials, including emulsions and liposomes, that are useful to bring about sustained or targeted release of bioactives in foods and pharmaceutical applications. To complement this, they present the wider encapsulation technologies and delivery systems, including the innovations which run between microspheres to complex coacervates, being specifically designed to target the food ingredients and nutraceutical applications.

Future directions, as by Xu *et al.*,[68] is emerging on more advanced approaches to encapsulation to enhance solubility, stability, and bioavailability. While this newer work is still gaining recognition, it reflects the ongoing innovation in the field. Overall, encapsulation plays a vital role in modern nutraceutical delivery by offering protection, controlled release, and enhanced functionality of bioactive ingredients. These systems ensure that nutraceuticals maintain their potency and deliver health benefits effectively when incorporated into food products or supplements.

4.2 Controlled and targeted release

Nanotechnology in the science of nutraceuticals and dietary supplements has brought in advanced functions to what has been the traditional delivery systems into something advanced and capable of ensuring increased therapeutic effects through a controlled and release-based delivery mechanism. This development is especially topical because nutraceuticals are characterized by poor solubility in waters, low gastrointestinal stability, and bioavailability, and quick breakdown. The latest studies stress the role of nanotechnology-based formulations that would increase the accuracy of the delivery of bioactives and reduce off target effects, as well as guarantee the maintenance of therapeutic levels. As an example, Gul *et al.*[9] indicated based on their studies that nanostructured carriers greatly improve bioavailability and efficacy of nutraceuticals since they increase the solubility, absorption and transport across biological barriers.

The microfluidic-assisted encapsulation has become one of the new methods in this area. Microfluidic systems also allow constructing uniform, monodisperse nanoparticles with the ability to encapsulate bioactives with a high yield, as shown by Liu *et al.*[69] The systems have the added benefits of controlling and stimulus responsive release profiles hence protecting sensitive compounds during digestion and releasing them in a particular physiological condition. Rizk and Aly[70] focus on the therapeutic applications of nutraceuticals (based on nanotechnology) in a variety of diseases and note that their efficacy is connected to the enhanced targeting and sustained release abilities. On the same note, Manocha *et al.*,[71] have highlighted the application of nanocarriers like solid lipid nanoparticles, nanoemulsions, and polymeric nanoparticles in breaking the bioavailability jigs.

One of the most attractive directions is the incorporation of 2D materials including graphene oxide and layered double hydroxides which have large surface areas and surface functionalities that can be adjusted as well as acting in response to environmental stimuli. These characteristics enable them to be ideal delivery vehicles in terms of site-specific utilization of nutraceuticals as has been mentioned by Christena *et al.*[72] The systems are able to be engineered based on when the system releases the payload upon signal change due to pH, temperature, or enzyme breakdown which reduces system exposure and increases therapeutics. Food-grade applications were greased by earlier preliminary studies of Garti and McClements,[67] which led to the controlled release systems. Upon this, Singh *et al.*[73] and Surve *et al.*[74] continued to explain how nanocarriers enhance stability, storage, and bioactivity of nutraceuticals, even at poor processing and storage practices.

A combination of these developments is a paradigm shift in the delivery of nutraceuticals, poised to result in the next generation of functional food products and therapeutic supplements with reduced rapidly by using a combination of precise spatiotemporal control, the frequency of dosing, and better health outcomes. The continuous merging of 2D materials promises to bring such systems to a brand new level of performance, flexibility and clinical relevance.

4.3 Improvement of bioavailability

The main pitfall with the oral administration of the nutraceuticals is their low aqueous solubility and unsatisfactory systemic bioavailability, which are especially evident in phytochemicals, *e.g.*, curcumin and resveratrol. These compounds have a strong biological activity, but they are limited by their poor physicochemical properties such as a low permeability, rapid degradation and ineffective absorption through gastrointestinal membranes. Nanotechnology foundations such as nanoemulsions, nanoliposomes, polymeric nanoparticles, and 2D nanomaterial-integrated carriers have proved to be revolutionary solutions in overcoming these challenges. The platforms also promoted the solubility, stability, and cellular uptake of nutraceuticals that are lipophilic by raising their interaction with the biological fluids and transport systems at their surface.

According to Mohanty *et al.*,[75] nanocarriers enhance both the aqueous solubility and bioavailability of curcumin by protecting it against degradation in environmental media and promoting the dispersion of curcumin in biological media. On the same note, Peng *et al.*[76] have shown that saponin-coated curcumin nanoparticles produced using the easy and convenient pH-driven loading procedure had increased solubility, bio accessibility, and gastrointestinal stability. Wang *et al.*[77] highlighted how nanotechnology influences the bioavailability and bioactivity of diet-based phytochemicals, with curcumin and resveratrol as key examples. These nano carriers function as solubilizing matrices whereby the compounds do not crystallize hence, they can be absorbed in greater capacity to the small intestine.

Furthermore, research articles by Manocha *et al.*[71] and Gul *et al.*[9] advocate the application of nanotechnology to meet bioavailability challenges by using physicochemical optimization, enhanced mucosal permeability, and regulated release activities. The nanostructured systems like the PLGA (poly(-lactic-*co*-glycolic acid)) nanoparticles, micelles, and nano-emulsions have proved repeatedly that they can extend circulation time and deliver targets in a specific delivery. A second-generation solution is 2D materials such as graphene oxide (GO), MXenes and layered double hydroxides (LDHs) which are ultra-thin, have a tunable surface chemistry and very large adsorption capacity. These characteristics make these compounds capable of encapsulation and stabilization of the poorly water-soluble bioactives. As nanoscaffolds or hybrid delivery matrices 2D materials may facilitate the generation of localized concentration gradients, which can facilitate passive and active transport across epithelial barriers. In addition, Ali *et al.*,[78] and Leena *et al.*,[63] support the argument that nano-encapsulation upsurges and expands the water dispersibility of nutraceutical constituents as well as the bioavailability of their functionality. Not only do these systems safeguard the payload against enzymatic degradation, but also allow controlled, stimulus-responsive release, which is especially advantageous in compound with narrow absorption windows.

The ultrathin and tunable nature of surfaces makes 2D materials possess an unprecedented opportunity to be able to recreate the biological membranes, a high loading demands, and site specific releases. Such incorporation into oral delivery systems provides an exciting potential avenue to adjust drug food interactions, extend intestinal transit times and improve the bioavailability of difficult nutraceuticals, such as curcumin.

4.4 pH responsive or stimuli responsive systems

The therapeutic encapsulation of nutraceuticals is transforming to active controlled delivery through stimuli responsive and site directed mechanisms. There has been a steadily increasing amount of research highlighting the emergence of pH-responsive and multi-stimuli-sensitive nanocarriers in surmounting restrictions of traditional nutraceutical bioavailability, stability and residence in the system. Stimuli-responsive delivery systems are designed in a way that they will react to an internal physiological stimuli (*e.g.* pH, temperature, enzymes, redox state) or external stimuli (*e.g.* light, magnetic field), in this way, they will be able to deliver a stimulation in a controlled way, also, with time control. Stimuli-responsive nanocarriers offer targeted nutraceutical delivery to tumor cells by exploiting the unique tumor microenvironment, such as acidic pH or elevated enzyme levels. These systems remain stable in normal tissues but undergo structural changes in response to tumor-specific stimuli, enabling localized, controlled release of bioactives that enhance therapeutic efficacy while minimizing off-target effects (Fig. 5).

These attributes play a very critical role in preparing to traverse the fluid-like gastrointestinal (GI) terrain and

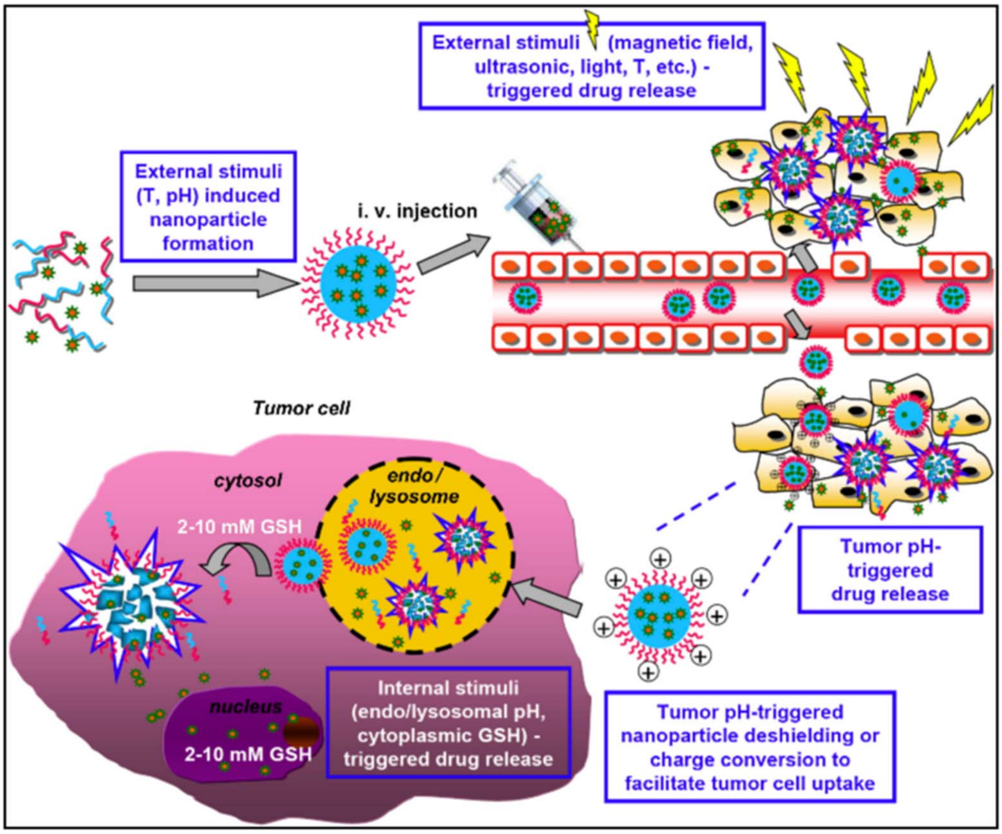

Fig. 5 Schematic of stimuli-responsive polymeric nanomicelles for targeted drug delivery. Micelles form in response to external pH or temperature changes, encapsulate drugs, and release them preferentially under acidic conditions and high redox potential, enhancing intracellular uptake and therapeutic efficacy in cancer cells. The figure is obtained from ref. 79 under a Creative Common (CC BY) License.

promoting specific discharge of delicate nutraceuticals. The GI tract proposes a natural pH gradient, acidic in the stomach (<~pH 1–3), and neutral-to-slightly basic in the intestines (=~pH 6–8). PH-sensitive delivery systems should be stable in the stomach but upon encountering the more neutral environment of the intestines, they should either dissemble or release their endowment as a guarantees of better absorption and degradation reduction.

According to a study by Zhu *et al.*,[80] the pH-sensitive nanocarriers have an advantage of a spatial–temporal payload release, therefore, they are also suitable in the development of nutraceutical formulation as an oral delivery. Such systems have also been incorporated in the development of smart delivery systems in curcumin, polyphenols and vitamins and their bioactivity maintained and bioavailability enhanced. Moreover, Yang *et al.*[81] surveyed a range of progressive oral platforms such as biodegradable polymers, microfluidics, and 3D-printed structures which are currently under functionalization using ph-sensitive, enzyme-degradable coatings to streamline delivery dynamics. New developments reveal that 2D materials, including boron nitride nanosheets, graphene oxide (GO) and transition metal dichalcogenides (TMDs), can become multi-responsive nanocarriers owing to their ultrathin structure, large aspect ratios and controllable surface chemistry.

Specifically, Cheng *et al.*[82] created a dual stimuli-responsive boron nitride nanosystem that could respond to changes in pH (as well as temperature) and had an enormous potential of up considered intelligent, triggered delivery of nutraceuticals in extreme conditions of the GI tract. These nanosheets also have independently controllable swelling, encapsulation, and release characteristics, making them suitable to regulated delivery of curcumin, resveratrol, and probiotics. On the same note, Zhang *et al.*[2] expanded the functional versatility of 2D materials in slow drug supramolecular delivery nanosystem as they responded to environmental stimuli and could be developed into oral and transdermal nutraceutical platforms. Furthermore, combination of 2D nanocarriers into microfluidic systems (Liu *et al.*)[14] can provide a sophisticated fabrication approach to the development of precision-engineered and responsive nutraceutical carrier platforms with defined release profiles. Due to the interventive action of delivery systems on bioavailability, stability, and therapeutic properties of bioactive food ingredients, bioavailability, stability, and therapeutic potential of bioactive food ingredients enhanced through stimuli-responsive delivery can be covered by Shishir *et al.*[83] and Ganta *et al.*[84] The systems are particularly helpful when:

- pH-dependent polyphenol and carotenoids.
- Thermo sensitive antioxidants and enzymes.
- Redox-sensitive peptides or phytocytes.

These intelligent systems are specifically designed in nanoemulsions, liposomes, nanoparticles made from polymers, and currently, even more with 2D material scaffolds with the expected rapid reaction time, surface functionalization, and synergistic loading capacity.

The combined power of the stimuli-responsive systems and 2D materials can bring unprecedented promise to the next generation nutraceutical carrier by endeavoring to be able to sense, adapt, and their response to a complex biological environment. The next step of discoveries will be functionalizing the ligands on the surface, multi-responsive release/multitasking, and intelligent packaging platforms, where 2D materials will not only transport the bioactives but will also read and respond to environmental clues as well as to biological markers.

5. Applications in nutraceutical packaging

2D materials such as graphene oxide, MXenes, LDHs, MOFs, and TMDs serve as multifunctional building blocks for next-generation packaging. Antimicrobial and antioxidant packaging incorporates 2D materials into edible or biodegradable films, enhancing barrier properties, inhibiting microbial growth, and protecting bioactives from oxidation, thereby extending shelf life. Smart packaging integrates 2D materials as sensing and responsive components, enabling real-time monitoring of food quality through detection of pH, oxygen, VOCs, or temperature, as well as controlled nutraceutical release. Together, these innovations shift packaging from passive protection towards active, intelligent, and sustainable systems, though scalability, safety, biodegradability, and consumer acceptance remain critical challenges (Fig. 6).

5.1 Antimicrobial and antioxidant packaging

New technology in the nutraceutical preservation industry has come to the fore in the form of antimicrobial and antioxidant packaging, which provides a two-fold benefit in shelf life extension and the promotion of product safety coupled with health promoting functionalities. According to Petkoska *et al.*,[85] active edible packaging systems should be used in such a way that the functional bioactive agents can be included in a consumable film to deliver nutraceuticals to the body, but also to provide protection of food matrices. A complete review of such active packaging technologies antimicrobial and antioxidant layers was practically given by Yildirim *et al.*[86] to control microbial growth and oxidative degradation of perishable products. Amongst the innovative achievements, the 2D materials such as MXenes have aroused significant interest, as they appear as good choices to ensure functional packaging of nutraceuticals due to their desirable barrier properties, thermal stability, and intrinsic antibacterial activity (Zhou *et al.*).[87] Sustainable alternatives to synthetic materials are biodegradable packaging that uses natural, and synthetics reviewed by Motelicia *et al.*[88] which may be mixed with nanostructures to increase efficacy. As evidenced by Topuz and Uyar,[89] electrospun nanofibers are especially beneficial in making packaging substances with the potential of increased antibacterial, antifungal, and antioxidant properties, as well as active and passive protective measures. Similarly, Suvarna *et al.*[90] pointed out the increasing importance of antimicrobial nanomaterials as functional natural preservatives in the food and nutraceutical sector. Even though the addition of nanomaterials and natural antimicrobials to packaging has enormous potential, Makwana *et al.*[91] warn of the importance of the toxicological assessment of

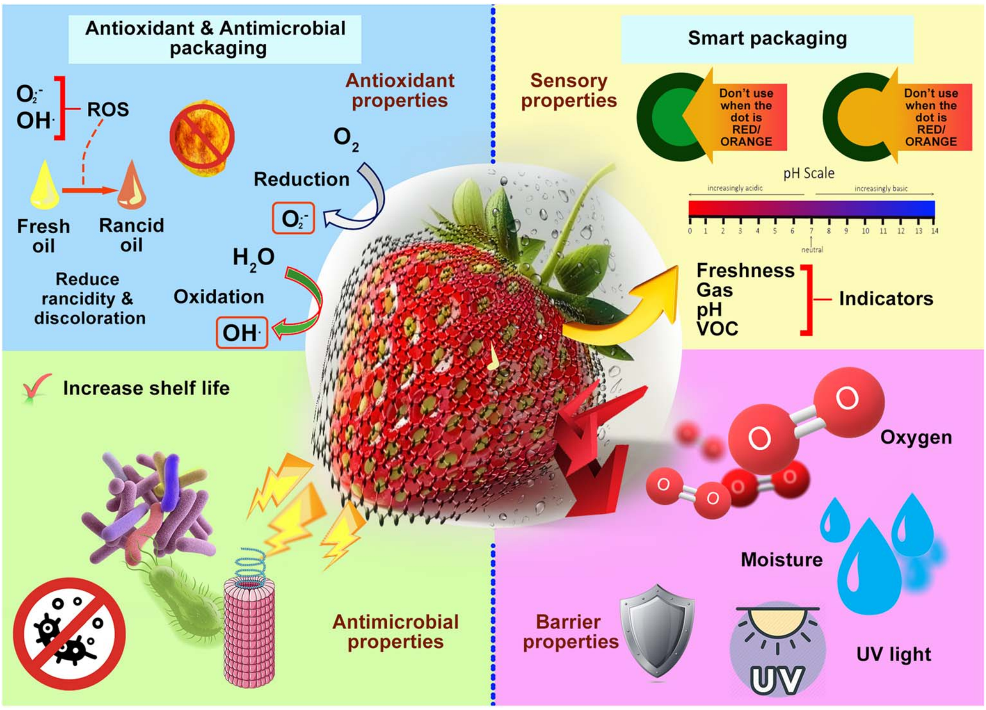

Fig. 6 Applications of 2D materials in nutraceutical packaging (authors' work).

these nanomaterials and natural antimicrobials to make it widely applicable as a packaging protective barrier. All these developments make the 2D materials the next generation building block in sustainable, smart, and biofunctional packaging structures meant to support the emerging needs of nutraceutical packaging protection and delivery.

5.2 Smart packaging

Smart packaging has created a transformational approach in the nutraceutical front that has solved the need to ensure increased safety of products, real time monitoring of quality, longer shelf life and greater consumer awareness. Considering the number of technological solutions, there is an emergent technology that is relatively new but with very high potential and that is an enhancement of the intelligent packaging system with the incorporation of 2D materials where packaging is no longer just a passive shield but an active agent in the maintenance of products and their monitoring. The 2D material including but not limited to graphene oxide, MXenes, boron nitride nanosheet, and transition metal dichalcogenide (TMD) exhibit remarkable physicochemical properties, such as high surface-to-volume area, adjustable electrical and optical behaviors, and strong mechanical strength. The characteristics qualify them as the preferred choice of inclusion in smart packaging platforms. Jafarzadeh *et al.*[5] note that 2D materials may be utilized in making intelligent food packaging by creating films that could detect changes in the environment like pH, temperature and humidity, among others, which are important predictors of product shelf time and spoilage. This pointed out the use of 2D materials in intelligent packaging platforms, both ensuring their protection, and their ability to detect when the environmental conditions have changed, allowing real-time quality control (Fig. 7).

MXenes have also been of the most interest being one of the most promising materials owing to excellent barrier properties, a high level of electrical conductivity, and thermal stability. According to the article of Zhou *et al.*,[87] MXenes can become multifunctional packaging material afforded to precious nutraceuticals, real-time analysis of their environment, and even active correction of internal microenvironments. These are highly suitable to a wide range of polymers, which make them easy to mix in flexible films, whilst the layered structure in these enhances the containing/stabilizing effect of the active compounds. The active use of sensing in smart packaging can be possible using 2D-based nanomaterials. Moustafa *et al.*[92] explain how smart packaging films using such constituents can be used as early warning designations, converting color or conductive when isometric with volatile substances or plunges in pH, to be able to show the deterioration of nutraceuticals or spoilage of carrier food materials. This contributes to improved food safety, reduces unnecessary waste, and empowers consumers to make informed decisions about product quality.

Working on active edible packaging, Petkoska *et al.*[85] outline the role of such systems in the ability to provide bioactive substances and trace their state in a timely manner. These edible films can be engineered using 2D materials as a vehicle of controlled and responsive release of nutraceuticals and increase their bioavailability and functional effects at the closely timed location of the consumption. These two functions are in tandem with the prevailing consumer demand concerning

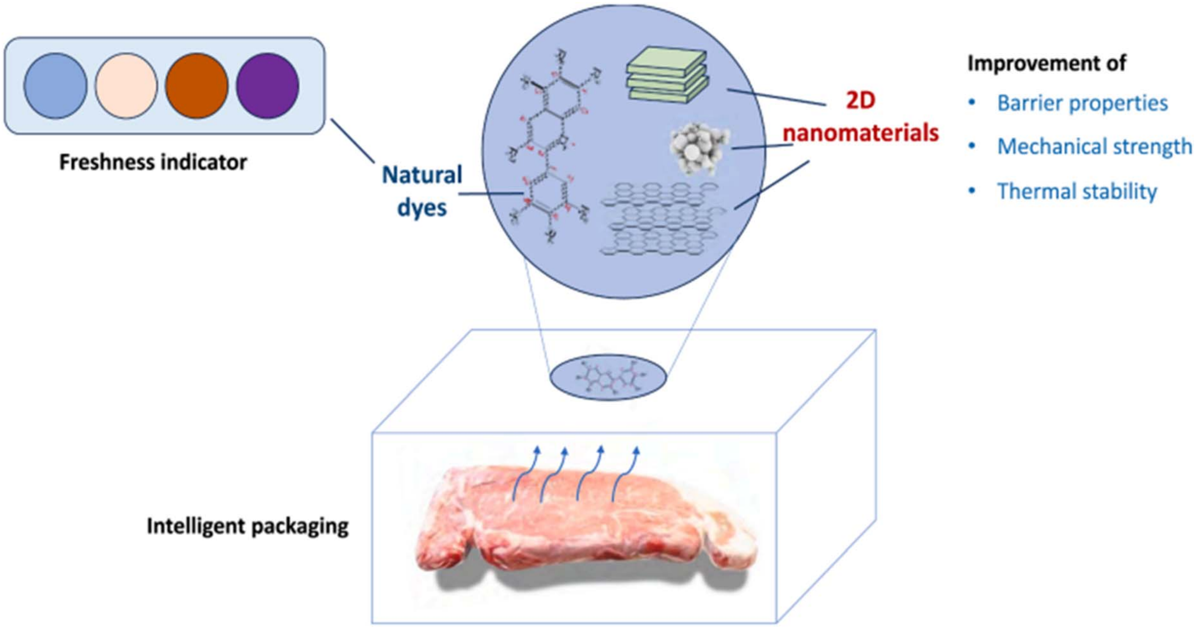

Fig. 7 Schematic overview of 2D materials in intelligent food packaging, highlighting their antimicrobial, antioxidant, barrier, and sensing functions for real-time freshness monitoring and active protection of food products. The figure is obtained from ref. 5 under a Creative Common (CC BY) License.

sustainability, clean labeling, and convenience. The formulation view implies that Christena *et al.*[72] and Ali *et al.*[78] point out that nanotechnology enhances the solvability, dispersion and absorption of poorly water-soluble nutraceuticals. The 2D nanostructures provide nanoencapsulation of bioactives to protect them against degradation during processing and storage as well as the directed release thus the maximum efficacy and no waste. It is of special importance to lipophilic preparations such as curcumin, omega-3 fatty acids, and carotenoids, whose bioavailability is hampered when using conventional delivery methods. Furthermore, Godínez-García *et al.*[93] remark that 2D engineered materials are also used to increase their use in smart packaging solutions designed specifically to be used in the agro and food sectors. The use of these contributes to the objectives of sustainability by way of minimizing food loss and enhancing the traceability of products enriched with nutraceuticals. Likewise, Sozer and Kokini[94] described the initial use of nanotechnology in food wrap, foreseeing the emergence of smart delivery procedures, which are now becoming more possible with the development of 2D material science. Moreover, the possibility of 2D material-derived nanocoatings to impart useful functionalities (such as antioxidant activity) that can retard the oxidative degradation of unstable nutrients including polyunsaturated fatty acids, vitamins, and phenolic compounds should also be mentioned. Coatings of this type may be sensitive to outside influences like light or heat or mechanical stress, to trigger release of protective chemicals or the change in permeability. This interplay of each other between packaging and content makes the nutraceutical active and bioavailable until the moment of intake.

The development of 2D materials into viable smart packaging prototypes has been on the rise in recent years. GO and its derivatives have been used in biodegradable films to detect freshness indicators like pH, ammonia, and volatile organic compounds (VOCs). According to Moustafa *et al.*,[92] GO-based films are capable of monitoring food quality in real-time without the need of specialized equipment, with visible colorimetric changes serving as indicators of spoilage. Similarly, nanocomposites based on layered double hydroxide (LDH) have been used as active layers in packaging films, not only to improve barrier properties, but also to release antimicrobial agents in a controlled manner, thereby extending the shelf life of perishable products such as dairy and meat. MXenes have also been found to be promising candidates because of their high conductivity and tunable surface chemistry. Jafarzadeh *et al.*[5] demonstrated that MXene-based films are capable of detecting exposure to oxygen, which can be used to detect spoilage or contamination early. Besides, edible films have been developed by incorporating biopolymers with GO and metal–organic frameworks (MOFs), which allow the delivery of nutraceuticals and monitoring of food quality simultaneously (Petkoska *et al.*).[85] These examples, though still in the pilot stage, show the multifunctional character of 2D materials in changing packaging as a passive protection to active monitoring systems.

Although there are encouraging findings, commercialization of 2D material-based packaging is still low. The significant problem is the expensive synthesis and processing, especially of high-purity graphene derivatives, MXenes, and MOFs. Food-grade production methods are still in development and are not as competitive as conventional polymers or even first-generation smart packaging technologies. The integration of nanosensors into films further complicates and increases the cost, which hinders industrial adoption (Sundaresan *et al.*).[95] Consumer acceptance is also a major obstacle safety, toxicity, and transparency issues are also a major factor in purchasing behavior. Consumer surveys indicate that people are not willing to purchase food that is packaged using nanotechnology-based materials unless they are informed of the functional benefits (Amin *et al.*).[96] Furthermore, as it was stressed in the previous studies by Biji *et al.*,[97] cultural and regional differences are also significant: not all consumer groups are equally willing to accept nanotechnology in food. Thus, clear regulatory policies, risk communication, and consumer education will be required to gain consumer trust and attain wider market penetration.

Another important factor in the design of smart packaging is sustainability. The combination of 2D materials with biodegradable polymers, including chitosan, starch, cellulose, or PLA, allows creating environmentally friendly methods. According to the studies by Petkoska *et al.*[87] and Salgado *et al.*,[98] these composites demonstrate better mechanical and antimicrobial properties and partial biodegradability. Nevertheless, the inherent non-biodegradability of most 2D materials is a cause of concern. The persistence of polyfluoroalkyl substances (PFAS) in the environment is demonstrated by PFAS-GO, which has ambiguous impacts on ecosystems (Moustafa *et al.*),[92] and MXenes have no defined biodegradation pathways, making disposal difficult. Recycling is also problematic, as nanomaterials cannot be easily separated out of polymer matrices, and thus reuse is not economically viable. Recent studies highlight the importance of green synthesis methods and functionalization, including coating nanomaterials with biodegradable layers, to minimize toxicity (Das *et al.*).[99] However, there are few comprehensive life-cycle assessments, and it is important to know the actual environmental impact of these materials before they are widely used.

The integration of 2D materials into smart packaging is a paradigm shift towards intelligent and sustainable food protection. However, three major gaps need to be filled: (i) scalable, low-cost, food-safe synthesis processes; (ii) robust regulatory and consumer acceptance systems; and (iii) the creation of biodegradable and recyclable nanocomposites. As Jafarzadeh *et al.*[5] and Sundaresan *et al.*[95] point out, pilot prototypes prove the technical feasibility, but the real-world translation will involve a trade-off between performance, affordability, and sustainability. As material science and policy continue to advance, 2D material-based smart packaging has a high potential to revolutionize food preservation, safety monitoring, and nutraceutical delivery in the next 10 years.

6. Current challenges and future perspectives

Among the 2D materials which have received growing attention as a functional drug and biomedical delivery platform, are graphene, MXenes, black phosphorus, and transition metal dichalcogenides (TMDs). They possess several physicochemical characteristics or feature that could be described as exceptional including high specific surface area, readily tunable surface chemistry, and responsive capabilities to stimuli, which provide them with an advantageous appeal within the context of emerging provisions of nutraceutical delivery and smart packaging applications. Though they have already demonstrated their effectiveness in the pharmaceutical sphere, these components are in their early stage of transition to nutraceutical systems as a bunch of specific challenges and research gaps are still present there.

According to the findings presented by Zhang *et al.*,[20] 2D materials have become an untapped beneficial area in terms of controlled drug release and release to the target destination. The systems can be further extrapolated to nutraceuticals, especially in compounds that are not readily soluble, are not stable in body or are quickly biodegradable. Nevertheless, as observed by Kurapati *et al.*,[7] Zhang *et al.*,[2] there are challenges to the safe and reproducible applications of these products in consumer-based products such as functional foods and dietary supplements, which include colloidal instability, batch-to-batch discrepancy, and lack of sufficient information on biocompatibility. Moreover, there is no real-time bio-interaction study with these technologies in the complex gastrointestinal environment, which makes adapting it to oral delivery of nutraceuticals even more difficult. Possible uses of 2D material in packaging have been considered in more detail over the recent years. Jafarzadeh *et al.*[5] note that 2D materials have been shifting to intelligent and responsive packaging, such as in monitoring temperatures, pH value, humidity, or oxidation degree. Although this novelty is crucial to the integrity of nutraceuticals throughout transportation and storage operations, the introduction of sensing parts and their combination with edible elements and their safety in different conditions (light, moisture, temperature) present substantial challenges to both engineers and legislators.

The key problem remains to be synthesis and standardization of 2D materials, as the point is emphasized in Naikoo *et al.*[100] There are variations in the number of layers, lateral dimensions of the layer, as well as the layered surface functional groups that directly influence their biological activity and safety, and thus these factors are hard to predict and control the performance of such layers in conditions of food use. They have no harmonized manufacturing protocols to permit production on a scale of relative replicability and affordability to restrict their commercial potentiality. Further, the majority of works, like those by Li *et al.*[101] and Khanam *et al.*,[102] are devoted to energy use for therapeutic effects, and direct assessment in food-grade materials or interactions with nutraceutical multi-component systems polyphenols, vitamins, or probiotics is rare.

With respect to regulatory and translational outlooks, the route towards 2D materials acceptance in nutraceutical systems is not well developed. Most 2D materials are not recognized by the FDA (Food and Drug Administration) or the EFSA (European Food Safety Authority) as suitable to contact or ingest in food and this is mainly because of the lack of any toxicological data and the challenges in determining their long-term compatibility with biology and mechanisms of degradation.

Although 2D materials have a lot of potential in nutraceutical delivery and smart packaging, there are still a number of challenges to overcome before they can be used on an industrial scale. The cost-effectiveness and scalability are also of concern, with the existing synthesis methods of materials such as graphene and TMDs being energy-intensive, chemically hazardous, or limited in yield, which is not suitable to large-scale production without further optimization. The large-scale synthesis of 2D nanosheets is a possibility with solid lithiation and exfoliation (Zhang *et al.*).[103] Sonication is a common technique, but more sophisticated exfoliation techniques, such as mechanical, hydrothermal, and electrochemical exfoliation, are being developed to offer greater scalability (Zheng and Lee).[104] Laser scribing, printing, and roll-to-roll processes are being developed as cost-effective manufacturing methods of 2D material-based energy storage devices (Mendoza-Sánchez and Gogotsi).[105] Nevertheless, there are still difficulties in regulating the size, thickness, and chemical stability of nanosheets. The environmental sustainability of 2D materials is also an issue, with most not being naturally biodegradable, difficult to recycle once incorporated into polymer matrices, and potentially releasing toxic ions or persisting in the environment. The materials can be used to address environmental challenges like water treatment, desalination, and gas separation (Shams *et al.* and Yadav *et al.*).[106,107] Nevertheless, as the production increases, it is important to consider their environmental effects and sustainability. Life cycle assessments indicate that the use of waste materials as precursors is not always the most sustainable option because of energy-intensive recycling processes (Munuera *et al.*).[108] To make sure that the implementation is safe, it is necessary to evaluate and reduce the risks that 2D materials may cause. Toxicity and environmental fate studies have been mainly conducted on graphene, although studies on other 2D materials are emerging. The riskiness of these materials is directly proportional to their structural parameters and physicochemical properties, which is why it is important to carefully design experiments in toxicological studies (Guiney *et al.*).[109]

Safety is also a major consideration, with *in vivo* toxicological studies indicating the potential accumulation, oxidative stress, and inflammatory effects of graphene, MXenes, and TMDs, whereas LDHs are relatively safe but have no long-term chronic exposure data. Studies have shown that the toxicity of 2D materials is strongly dependent on dose, cell type, exposure mode, and material-specific properties (Wu *et al.*).[110] Oxidative stress has been found to be a major factor in the toxicity of 2D materials, and reactive oxygen species are a major contributor (Maruthupandy *et al.*).[111] Although most 2D materials have low cytotoxicity and good biocompatibility, some studies have shown toxicity to stem cells and embryos (Wu *et al.*).[110] The stability and possible degradation of 2D materials are also factors to consider in toxicity assessment. Researchers underline the necessity of proactive and thorough toxicological research to guarantee the safe production and use of 2D materials (Korah *et al.*, Wang *et al.*).[112,113] To counter the euphoria that exists around these materials, future studies should aim at green and scalable synthesis, including hydrothermal and bio-inspired synthesis, which minimizes the use of toxic precursors. Life-cycle assessment (including recyclability and degradation behavior), and systematic *in vivo* toxicological studies to ensure safe, sustainable, and commercially viable applications. Moreover, the factors of environmental and human exposure modeling, the life cycle assessment, and gut sense of the consumer are still under-researched. By focusing on these directions, future research can harness the full potential of 2D materials to create intelligent, multifunctional, and environmentally responsible nutraceutical delivery and packaging systems.

Moving ahead, additional work is needed to achieve safe-by-design 2D materials, predictive bio interaction modeling, migration modeling and compatibility with common nutraceuticals, through encapsulation. The partnership of material scientists, toxicologists, food technologists, and regulatory agencies working across disciplines should be the key to gaining the maximum opportunity of 2D materials in nutraceutical packaging and delivery systems. The translation process involves more than scientific innovation, but advanced regulatory vision and consumer confidence as well.

7. Conclusion

Two-dimensional (2D) materials are no longer confined to laboratories exploring biomedical applications; they are now emerging as powerful tools to transform nutraceutical delivery and packaging. This review has highlighted how graphene derivatives, MXenes, layered double hydroxides (LDHs), metal–organic frameworks (MOFs), transition metal dichalcogenides (TMDs), and boron nitride nanosheets can overcome long-standing challenges of poor solubility, instability, and weak bioavailability of nutraceutical compounds, while also enabling smart, antimicrobial, and responsive packaging. The novel contribution of this review lies in emphasizing the multifunctional potential of 2D materials in enhancing nutraceutical delivery and enabling smart packaging with targeted, responsive, and sustainable applications. Unlike existing reviews that focus largely on biomedical or pharmaceutical contexts, we bring nutraceutical-specific challenges and opportunities to the forefront. Current studies are still dominated by *in vitro* demonstrations, with limited *in vivo* or clinical validation in food systems. Toxicological profiles, long-term biosafety, and consumer acceptance remain poorly understood. Moreover, the lack of standardized synthesis protocols leads to inconsistencies in performance and hinders regulatory approval. Looking ahead, several future directions are critical. The scalable and green synthesis of 2D materials must be prioritized to enable affordable and environmentally responsible applications. Also, safe-by-design strategies and predictive toxicology frameworks should be developed to address biosafety and regulatory approval. Moreover, consumer perception and acceptance of nanotechnology in food must be studied, as successful translation depends on public trust as much as on scientific progress. Finally, multidisciplinary collaboration between chemists, food scientists, toxicologists, and regulatory agencies will be essential to realize the full promise of 2D materials in nutraceutical science. While challenges remain, 2D materials hold the potential to redefine nutraceutical delivery and packaging into intelligent, safe, and sustainable platforms. With continued innovation and cross-sector collaboration, they may serve as the foundation for a new era of functional foods and health products tailored to the needs of modern consumers.

Author contributions

Dinithi Senanayake – literature search and drafted the initial manuscript. Imalka Munaweera – conceptualization, supervision, writing, review and editing the manuscript. All authors have given approval to the final version of the manuscript.

Conflicts of interest

The authors declare that there is no conflict of interest.

Data availability

No primary research results, software or code have been included, and no new data were generated or analyzed as part of this review.

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