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Review article

Clean-label alternatives for food preservation: An emerging trend

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ABSTRACT

Consumer demand for natural or ’clean-label’ food ingredients has risen over the past 50 years and continues growing. Consumers have become more aware of their health and, therefore, insist on transparency in the list of ingredients. Preservatives are the most crucial food additives, ensuring food safety and security. Despite tremendous technological advancements, food preservation remains a significant challenge worldwide, primarily because most are synthetic and non-biodegradable. As a result, the food industry is placing more value on microbiota and other natural sources for bio-preservation, leading to the substitution of conventional processing and chemical preservatives with natural alternatives to ensure ’clean-label.’ General Standard for Food Additives (GSFA) includes some of these ’clean-label’ options in its list of additives. However, they are very rarely capable of replacing a synthetic preservative on a ’one-for-one’ basis, putting pressure on researchers to decipher newer, cleaner, and more economical alternatives. Academic and scientific research has led to the discovery of several plant, animal, and microbial metabolites that may function as effective bio-preservatives. However, most have not yet been put in the market or are under trial.

Hence, the present review aims to summarise such relevant and potential metabolites with bio-preservative properties comprehensively. This article will help readers comprehend recent innovations in the ’clean-label’ era, provide informed choices to consumers, and improve the business of regulatory approvals.

1. Introduction

Consumers have become more aware of what they eat, where it comes from, and how the ingredients in food affect their healthy lives. They actively seek products with natural claims and consciously check the ingredient lists of the food products. For instance, a noticeable rise in the number of consumers, from 3 % to 78 %, who consider the ingredient list an essential item was reported in Europe between 2011 and 2013 by Sweetman [1]. Globally, consumers will likely move toward ’less processed foods’ that contain easy-to-understand constituents. Thus, consumer awareness has forced the food industry to explore natural ingredients and return to the traditional approach of food processing. Accordingly, this aspiration led to the ’clean-label’ trend [2].

Historically, the first "clean-label" application movement began to take shape in the UK some 20 years ago. It was one of the five main food market trends listed by a London-based market research firm, Mintel [3]. The term ’clean-label’ has a vague definition. However, it can be related to concepts and ideas like being natural, simple, less processed, and free from unexpected allergens [4]. The

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term "less processed" explains the food products that contain fewer synthetic ingredients and have undergone the least chemical/biophysical treatment. Edwards [5] described 'clean-label' most comprehensively as *being produced free of chemical additives, having easy-to-understand ingredient lists and being produced by the use of traditional techniques with limited processing.* Traditional and current 'clean-label' food preservation approaches are somewhat very similar. In the past, organic substances such as plant parts, salt, and turmeric were applied directly as bio-preservatives in various food applications. However, in modern "clean-label" methods, bio-preservatives made from less-processed plant materials, like phytochemicals and microbial metabolic products (Fig. 1), are used.

Among the different additives in food products, preservatives play a crucial role in preventing the proliferation of contaminating microorganisms. The food market is replete with a plethora of artificial food preservatives. For instance, acetic acid (International Numbering System; INS 260), ammonium salts of phosphatidic acid (INS 442), butylated hydroxyanisole (INS 320), potassium sorbate (INS 202), and sodium fumarates (INS 365) are some of the synthetic preservatives considered safe by the Food and Agriculture Organization/World Health Organization (FAO/WHO) for use in various food items. Economical, devoid of off-flavours, having antimicrobial activity over a wide pH range, and readily soluble are some significant properties of synthetic preservatives that have made them acquire a specific place in food applications. However, excessive use of synthetic preservatives concomitantly has various hazardous effects on human health, such as allergic reactions, cancerous growth, and potential cytotoxicity [6]. Efforts have been made to substitute synthetic preservatives with safer and Generally Recognised as Safe (GRAS) natural/clean-label preservatives to avoid such problems and meet consumers' inclinations. Several organic compounds have been reported to possess bio-preserving properties.

However, not all natural/clean-label compounds are safe to use, necessitating critical scrutiny and testing before declaring them safe. For instance, the *E. coli* strain Nissle 1917 was generally considered safe and beneficial and has been used as a probiotic to treat various intestinal diseases. However, since 2006, it has been known that this strain produces a genotoxin named colibactin, a potent DNA alkylator that plays a pivotal role in colorectal cancer development and a safety issues that can not be ignored in the interests of human health [7]. Therefore, the "clean-label" bio-preservative must not contain any virulence, antibiotic selection markers, or potent toxins that could cause diseases in humans or bacteria that are resistant to drugs.

The food industry is actively interested in developing more economical, organoleptic, and organic formulations. However, intensive testing, retesting, and analysis are required to switch from synthetic to completely natural/clean-label confidently. The biggest challenges companies face today are shorter shelf-life and the requirement of a larger dose of natural ingredients to meet efficiency at least par with synthetic additives. In addition, sensory and processing factors, regulatory aspects, and application methods are other issues that require constant vigilance of formulators while replacing artificial ingredients with 'clean-label.' Enzymes/proteins as preservatives, in particular, provide other unique challenges as their activities are affected by pH, temperature, other enzyme activity, secretion, and moisture level [8]. Overcoming these challenges would lead to the acceptance of natural ingredients for food preservation to a much greater extent.

Considering the growing penchant for natural/clean-label ingredients, we have comprehensively reviewed the most relevant scientific literature, news articles, and blog articles published over the last two decades. The authors' primary motivation for writing this review is to offer a comprehensive foundation for the topic, which is now developing into a fascinating study area. Authors have

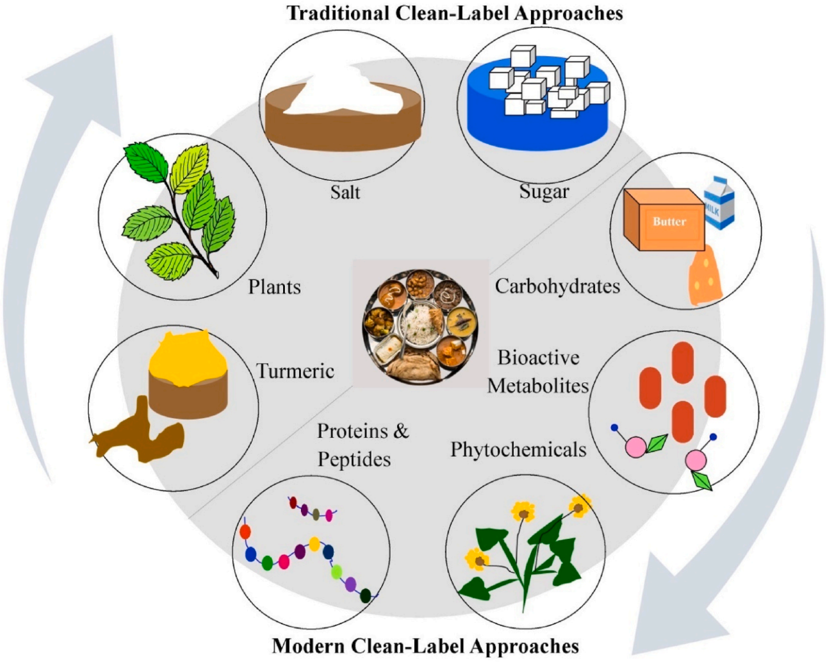

Fig. 1. A diagrammatic representation of traditional and modern clean-label approaches for food preservation.

also attempted to draw attention to the discrepancy in responsibility between approved rules and other "clean-label" preservatives. In this review, we provide a detailed account of various ’clean-label’ preservatives that are prevalent in the market or recommended by academic research. In addition, we have outlined perpetual bio-preservative sources like microorganisms, plants, and animals. Next, we studied the Codex General Standard for Food Additives [9] and identified ’clean-label’ preservatives in the existing list of international food standards. The authors also suggest an approach to overcome the gaps in the present guidelines and scope for future research. This study may help practitioners worldwide to appreciate the ’clean-label’ concept and define or implement regulatory parameters more rationally. Furthermore, this study may motivate policymakers to redefine the scale of food standards and classify preservatives into synthetics and ’clean-label’ formats.

2. Methodology

The authors adopted a proper road map for building this review using PRISMA (www.prisma-statement.org). The road map included a) background and new concepts of clean-label or natural preservatives; b) source, variety, and usage of clean-label or natural preservatives; and c) potential new applications, challenges, and future perspectives of clean-label food preservatives. The subject of the review is new and consumer perception-oriented. Therefore, in addition to referring to international and national journals, books, and book chapters, the authors consulted the websites of various food institutes and industries in the food sector, relevant country-specific regulatory guidelines and GSFA guidelines. In its most complete form, the current article is a mixed research project that combines insights, qualitative and quantitative findings from the literature.

The authors declare the use of licensed language editing tools to structure and draft this article. The "Authors Contribution" section mentions the roles of the individual authors. We conducted a comprehensive literature review and found no previous research addressing this topic, making our article a new and original addition to the field.

3. ’Clean-label’ food additives: promising bio-preservative candidates

Based on insights gleaned from the published literature, microorganisms, plants, and animals have been reported as significant sources of natural/clean-label preservatives in the form of their metabolic products, such as carbohydrates (polysaccharides), proteins/peptides and other metabolites (Fig. 2). Based on reviews of peer-reviewed literature and data from a variety of sources, it has been determined that plants produce the most bio-preservative metabolites, followed by microorganisms and animals. Different sources of ’clean-label’ preservatives have been elaborated on in individual sections as follows.

3.1. Microorganisms-derived preservatives

Microorganisms can be employed as a rich source of preservatives. Microbial sources have been reported to produce polysaccharides and proteins or peptides as their metabolic products, pivotal in combating pathogenic microorganisms’ proliferation. Whole cultures of microbial sources like lactic acid bacteria (LAB) can also be used directly as food preservatives. LABs have potential as food bio-preservatives because of their ability to produce antimicrobial peptides [10]. Besides, using LAB in food products is also considered a valuable addition due to its innumerable health-stimulating properties. Vegetable products such as tsukemono (Japanese preserved vegetables usually glazed in salt, brine, or a bed of rice bran), kimchi (Chinese cabbage and vegetable preparation), and sauerkraut (fermented cabbage) are preserved using LAB culture. The preparation method for these traditional oriental fermented

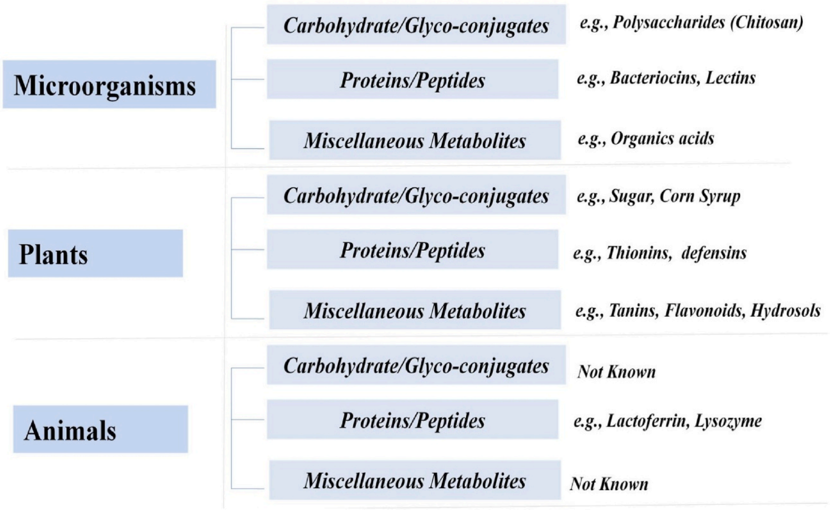

Fig. 2. An overview of different ‘clean-label’ food preservatives categories discussed in the article.

vegetable products comprises air-drying the vegetables and then exposing them to ambient temperature to allow microbial growth. After that, the vegetables are sealed in an anaerobic environment, and salt, spices, and other seasonings are added as additives. Fermented soybeans, for example, natto (Japan) and tempe (Indonesia), are a few other examples of products preserved using fermenting fungi or bacteria [9]. The bio-preservative properties of different metabolites of microorganisms have been discussed as follows.

3.1.1. Carbohydrate/Glycoconjugates

Some microorganisms are rich sources of carbohydrates, especially polysaccharides. *Aureobasidium* spp., *Azotobacter* spp., *Acetobacter* spp., *Leuconostoc* spp., and *Pichia* spp. are some examples of polysaccharide-producing microorganisms [11]. Microbial polysaccharides have been extensively used for numerous food applications despite the high cost associated with their production and purification. Microbial polysaccharides' exceptional technical and functional superiorities encourage industries to employ them as salient ingredients in various food items. Film forming, gelling, thickening, binding, and emulsifying are essential industrial applications of microbial polysaccharides. In addition, microbial polysaccharides can also play a key role as bio-preservatives. For instance, polysaccharides from microbial sources such as *Hansenula* sp., *Pichia* sp., and *Pachysolen* sp. have been reported to exhibit resistance against microbial attack and hence display the ability to be employed as natural/clean-label preservatives [11]. Mushroom chitosan is another example in this category that has been reported to show antimicrobial activity [12]. Three models have been designed to explain the bacteriocidal and bacteriostatic properties. The first and most acceptable model proposed an interaction between positively charged chitosan molecules and negatively charged microbial cell membranes. The second model suggested chitosan binding to microbial DNA, through which chitosan penetrated the microbial nuclei and further inhibited mRNA and protein synthesis. The third model proposed chelation of metals, suppression of spore components, and binding to nutrients essential for microbial growth [13]. However, instead of these proposed models, microbial sensitivity to chitosan is still debatable. Some researchers reported that Gram-positive bacteria such as *L. monocytogenes*, *B. cereus,* and *S. cereus* are more susceptible to chitosan [14]. At the same time, some authors strongly opposed it and demonstrated that hydrophilicity in Gram-negative bacteria is higher than that in Gram-positive bacteria and that they are, hence, more susceptible to the antimicrobial activity of chitosan [15]. The polysaccharide preparation from *Ganoderma lucidum* mushroom is also active against Gram-positive and Gram-negative bacteria [16]. Chitosan prepared from *Agaricus bisporus* displayed bioactivity against certain Gram-positive and Gram-negative bacterial colonies, namely *Salmonella* Typhimurium, *B. cereus*, *S. aureus*, *P. aeruoginosa,* and *E. coli* [17]. For its bioactivity against Gram-positive and Gram-negative bacteria, chitosan has strong potential as a 'clean-label' preservative.

Pullulan is another significant polysaccharide (produced by a yeast-like fungus, *Aureobasidium pullulans*) used by the food industry for various applications. General Standard for Food Additives (GSFA) has also enlisted it as a safe food additive for different foods such as fermented vegetables (catalogue number 04.2.2.7), flours (catalogue number 06.2.1), fresh pasta and noodles (catalogue number 06.4.1), and frozen egg products (catalogue number 10.2.2). This recognition highlights the potential of carbohydrate-derived ingredients as safe food bio-preservatives. However, food formulators require more research to support and utilise microbial polysaccharides as preservatives. Microorganisms are easy to grow and generally gives high product yield. These beneficial features of using microorganisms would help make cheaper, cleaner, and more effective preservatives to meet rising consumer demands.

3.1.2. Proteins/peptides

Proteins (enzymes) are large, complex, natural molecules catalysing varied biochemical reactions. Individually or synergistically, they catalyse specific reactions only to yield a particular product. Peptides are smaller strings of amino acids and possess potential for various pharmaceutical and food applications. Due to their natural origin and targeted biochemical activity, proteins/peptides are gaining significant market penetration as 'clean-label' preservatives. However, apparent factors can affect their bioactivity in food products. For instance, ingredients such as proteases, lipids, humectants, sugars, starches, metal ions, and matrices may interfere with the interaction between proteins and their target pathogens, hampering their bioactivity. It has also been suggested that proteases present in food sometimes digest antimicrobial peptides, which further influences their antimicrobial activity [18,19]. Likewise, proteins/peptides are very heat-labile and can lose structural integrity at elevated temperatures. Therefore, study on the effect of different factors or food ingredients on proteins/peptides should be characterized before selecting them for various food applications.

Bacteriocins are one of the best examples of peptide-based food preservatives. Bacteriocins have been discovered from Gram-negative bacteria such as *E. coli* (microcin, colicin) [20], *Pseudomonas aeruginosa* (Tailocins) [21] and also Gram-positive bacteria such as *Lactococcus lactis* [22], *Enterococcus faecium* [23], and *Pediococcus acidilactici* [24]. Bacteriocins are, by definition, ribosomally synthesised, small cationic molecules of prokaryotic origin having an approximate length of 30–60 amino acids. Bacteriocins are typically amphiphilic helical peptides secreted extracellularly by bacteria and possess antimicrobial properties. Several bacteriocins display significant properties such as broad spectrum (even transphyllum; e.g., pentocinMQ1, salivaricin B, nisin, subtilosin, etc.), stability, molecular amenability, diversity and low cytotoxicity [25]. However, a substantial number of bacteriocins exhibit narrow antimicrobial spectrum which is specific to their phylogeny or origin and hence are useful in preserving the essential microflora homeostasis of the food product [25]. Microorganisms are arguably the richest source of beneficial secondary metabolites, including antimicrobials like bacteriocins. In fact, several bacteriocins from microorganisms have been tested in the laboratory for their bio-preserving properties. Nisin and pediocin are the two leading examples of commercially available bacteriocins. Further, nisin is an FDA-approved and most widely accepted natural/clean-label preservative in food. Nisin is marketed under the name Nisaplin® [26], and its EU food additive number is E234 [24]. Nisin was first detected in fermented milk in 1928 [27]. Later, in 1953, England marketed it commercially as an antimicrobial agent [28]. Subsequently in 1969, FAO/WHO approved it as a safe food additive. In 1988, the FDA also approved the use of nisin and established it as a GRAS antimicrobial agent under 21 Code of Federal Regulations

(CFR) 184.1538 for cooked meat and poultry products [29]. The European Food Safety Authority (EFSA) Panel on Food Additives, Flavourings, Processing Aids, and Materials addressed the issue of antimicrobial resistance in 2006. It issued an opinion on the safe use of nisin as a food additive. The panel concluded that an Acceptable Daily Intake (ADI) of 0.13 mg/kg body weight per day, formerly standardised by the Scientific Committee on Foods, shall remain valid. Later, Dupont Nutrition and Biosciences requested the Health and Food Safety Directorate General for a) modifications in surroundings for the use of nisin, b) re-evaluation of safety and ADI, and c) modification of the specifications. Then, in 2013, the FAO/WHO Joint Expert Committee on Food Additives, at its 77th meeting, regulated ADI 0–2.0 mg/kg body weight per day based on a 13-week sub-chronic toxicity rat feeding study for nisin [30,31]. Nisin displays dual activity against spore-forming bacteria by a) restricting the outgrowth of spores and b) killing bacteria in their vegetative state. The principal target of nisin in a vegetative cell is its cytoplasmic membrane. 2, 3-didehydro amino acid residues in nisin act against germination by interacting with their membrane sulfhydryl groups. Nisin has also been reported to interact with lipid-II, a docking molecule (a membrane-bound precursor for cell wall synthesis) [32,33]. Recently, nisin has also been found to be active against *Mycobacterium paratuberculosis.* Nisin was observed to introduce holes in *M. paratuberculosis,* causing a 'bulging' phenotype in treated cells [34]. In another recent study, nisin was also proven to display antibacterial action against vancomycin-resistant enterococci (VRE). Nisin could be an effective supplementary agent to conventional antibiotics in managing VRE-linked infections [35]. Nisin, in combination with other biomolecules such as essential oils [36], lactates [37], lysozyme [38], and listeriophages [39], has also been reported to produce more elevated antimicrobial effect. For example, nisin, combined with curvaticin 13 (source: *L. curvatus* SB13), induced a high inhibitory effect on resistant cells of *L. monocytogenes* compared to the individual action of bacteriocin [40].

Pediocin is another crucial example of bacteriocin. Among various pediocins, pediocin AcH 1 was the first to be studied in detail and characterised [41]. Kerry Bioscience, Carrigaline, Ireland, markets pediocin PA-1 (ALTA® 2351) in the form of powder fermentates, while DuPont markets it in the form of freeze-dried cultures (CHOOZITTM FLAV 43) for commercial use in meat products [42] and sliced ham [43] (Santiago-Silva et al., 2009). However, pure bioactive pediocin is still not available on the market. Food technologists worldwide are trying to obtain a purified form of pediocin for food applications. Recently, Bédard et al. [44] reported the synthesis and characterisation of whole pediocin PA-1 and its novel analogues. These analogues were observed as potent inhibitors of *L. monocytogenes* and *Clostridium perfringens*, which manifests the potential of bacteriocins as natural/clean-label preservatives.

Given continual problems with foodborne pathogens, such as *L. monocytogenes*, coupled with concerns about the effects of preservatives on human health, there is a pressing need to research new and potential 'clean-label' preservatives. In this regard, glycocins (glycoactive bacteriocins) are the most recent discovery with notable antimicrobial activity, a unique mechanism of action, and potential 'clean-label' applications. Glycocin F [45], sublancin [46], thurandacin [47], bacillin [48], geocillicin [49], and enterocin 96 [50] are some of the first discovered examples of glycocins. The biological activity of glycocins depends on the presence of a post-translational modification, namely glycosylation. Attempts have been made to exploit the substrate affinities of glycosyltransferases (GTs), which will further help to construct variants of bacteriocins (glycosylated) with better traits and biological activity. For instance, Naegeli et al. [51] developed a sensitive assay to *in vitro* quantify glycopeptide formation by *Actinobacillus pleuropneumoniae* NGT and its substrate specificities. On the contrary, Sánchez-Rodríguez et al. [52] employed a network-based approach to identify different substrate classes of GTs. They inferred substrate relations for at least 20 GTs. Genome mining strategies, viz., BAGEL [53], RiPP-PRISM, RiPPMiner, RODEO (rapid ORF description and evaluation online), and Artemis of post-translationally modified peptides [53], are also current advancements in this arena to detect putative biosynthetic gene clusters (PBGCs) of glycocins. These PBGCs may aid in constructing recombinants and laboratory evolution of neoglycocins.

The indiscriminate use of antibiotics has led to the rise of multidrug-resistant microorganisms. Besides, these chemical-based antibiotics are non-biodegradable and tend to persist in the food chain for extended periods. This persistence of antibiotics has resulted in antibiotic pollution, which further has become a threat to human and animal health. Therefore, bacteriocins can be an eco-friendly, sustainable antibiotic substitute [54]. Various advantageous features of bacteriocins over antibiotics have been summarised in Table 1. Bacteriocins can offer several advantages in human and veterinary medicine, including a) being safe for consumption, b) being wholly digested in the gastrointestinal tract, c) more potent than conventional antibiotics, and d) being resistant to thermal treatments like pasteurisation and sterilisation. However, this application of bacteriocins still requires further research and

Table 1
Comparison of different benefits of bacteriocins over antibiotics.

Features	Bacteriocins	Antibiotics
Bioengineering	Possible	Lesser recommended
Biodegradability	High (due to natural existence)	Very low
Cytotoxicity	Very low	Low/High
Diversity	>800 units	~150 units
Dysbiosis	Low	Generated by broad host-range
Production		
Fermentation	Possible	Possible
Chemical synthesis	Possible for Class II	Risky
Spectrum	Some bacteriocins display broad (Nisin, Pentocin MQ1), while some display narrow (Sakacin, thuricidin) antimicrobial spectrum	Usually broad
Transmission in food chain	Low	High

understanding to establish their authenticity for medical applications.

3.1.3. *Miscellaneous metabolites with bio-preservative properties*

Microorganisms are rich sources of a plethora of metabolites. Amongst them, organic acids are imperative products of microbial metabolism, carrying one or more carboxylic groups in their molecule. Organic acids exhibit exemplary antimicrobial and anti-oxidative properties and have been granted a GRAS status [55–57]. Recently, the United States Department of Agriculture's (USDA) food safety has ratified the application of 5 % organic acids and final levels not exceeding the permitted levels, viz., 0.25 % sodium acetate and 5 % lactic acid [58,59]. Organic acids are generally more effective than inorganic acids, so they have been comprehensively used for food [60] and medical applications [61]. These acids are usually available in calcium, sodium or potassium salts to reduce odour volatility and expedite manufacturing [62]. Microbial sources such as *Lactococcus lactis* [63], *Aspergillus tamari* [64], *Clostridium ljungdahlii* [65], and *Rhizopus oryzae* [66] are familiar sources of organic acids, lactic acids, ascorbic acid, formic acid and fumaric acid, respectively which plays a significant role as bio-preservative. Due to the lipophilic nature of their undissociated form, organic acids alter proton and anionic concentrations in the cytoplasm to cross the cell membrane of pathogenic microorganisms. Consequently, it negatively affects purine bases and essential enzyme functionality, causing a decline in microbial viability [67].

Organic acids also dwindle internal pH of the cell, while they are not chemiosmotic. In a recent study, the effects of organic acids like formic acid, acetic acid, and fumaric acid on *Campylobacter* spp. have been studied. An *in vitro* synergistic combination effect of organic acids was observed against *Campylobacter* spp., which displays their promising bio-preservative property [68]. Kim and Rhee [69] also reported the synergistic effect of organic acids against *E. coli* and indicated a higher reduction rate in the bacterial population compared to individual treatment. However, extensive research on concentration optimisation, combinations of acids and interactions with pathogenic bacteria is necessary to maintain statutory guidelines for their safe use as bio-preservatives [70]. Besides, factors like the effect of their structure on cellular osmolarity and metabolism [71] and variation in their action on different strains [72] are also of peculiar interest in exploring the candidature of organic acids as bio-preservatives.

Lectins are other important metabolites that display significant antimicrobial activity. These proteins are abundant in nature and have been isolated from microorganisms, plants and animals. Lectins are natural carbohydrate-binding proteins that interact with carbohydrates on microbial surfaces and hence advance host-pathogen communications and host defence mechanisms [73]. Cells possessing complex carbohydrates on their surface carry specific binding sites for the lectins of other cells. Lectins control at least one characteristic and reversible binding to complex carbohydrates. The carbohydrate-binding property of lectins mediates interactions with pathogens, immunological defence mechanisms, inhibition of microbial cell adhesion and migration, and obstruction of pathogenic infections [74]. Cynovirin-N from *Nostoc ellipsosporum* [75], microvirin from *Microcystis aeruginosa* [76], and fungal lectin from the mushroom *Sparassis latifolia* [77] are some examples of microbial lectins that have shown acceptable biological activity against certain bacterial and viral species. Hence, it demonstrates their potential as 'clean-label' preservatives.

3.2. *Plant-derived preservatives*

Amongst various natural sources, plants are the perpetual choice as bio-preservatives. Earlier history also implicates their use in the treatment of various diseases. More than 20,000 plant species are used for various medical applications and are prospective reservoirs for deciphering novel drugs. Plant metabolites, known as phytochemicals, are an abundant source of their antimicrobial properties [78]. Phytochemicals are also responsible for colouring and protecting plants against various pests, pathogens, herbivores, and premature spoilage. Plants produce primary metabolites such as proteins, peptides, and carbohydrates for growth and metabolism, with some having bio-preservative properties. Secondary plant metabolites exhibit more versatile biological properties, including antibacterial, antifungal, and anti-inflammatory properties.

3.2.1. *Carbohydrates/Glycoconjugates*

Plant-based carbohydrates are widely recognised for their essential function as an energy source and component for storage. They are essential signalling molecules as well. Therefore, whereas most plant carbohydrates do not exhibit direct antibacterial properties, they can activate genes involved in defence [79]. Carbohydrates are organic compounds that impart various functional attributes to food. Carbohydrates exist in different degrees of polymerisation (DP) and glycosidic bond arrangements. The variation in their chemical structure brings different functional roles in plants. Carbohydrates like oligosaccharides with low DP (2–10) elicit a more rapid response than those with higher DP (25–40) [80]. Interestingly, β-1,3 glucans with high DP were more active against the tobacco mosaic virus than those with low DP. Despite their role as signalling molecules or elicitors, insufficient literature on their bio-preservative properties is available. Table sugar, or sucrose from plants, is the most extensively studied carbohydrate. Carbohydrates (sugars) serve as a bio-preservative by preventing microbial growth if used in a sufficient amount. Sugar is a traditional bio-preservative used to protect food from microbial attack and to preserve the colour, flavour, and texture of food products. Corn syrup is another perfect example of a plant-based carbohydrate additive that is used as a preservative and also imparts other applications in food, like a glossy appearance in ice cream, thickness in jams and jellies, sweetness in gums and starches [81]. Plant chitosan has antifungal properties [82]. However, more research and collaborative contributions of food technologists worldwide are necessary to divulge plant carbohydrates' bio-preservative or elicitor properties.

3.2.2. *Proteins/peptides*

Around 50 % of medicinal products are derived from plant components [83]. As a part of their defence mechanism, plants produce a variety of toxic effluents, like antimicrobial peptides and cell-penetrating peptides. Antimicrobial peptides kill pathogens by membrane permeabilization or interacting with phospholipids, while cell-penetrating peptides introduce diverse harmful molecules into cells in the absence of certain receptors [84]. Plant antimicrobial proteins can be isolated from roots, stems, leaves and flowers. Most plant antimicrobial proteins act by forming membrane pores, thereby causing ion and metabolite outflow, depolarisation, disruption in the respiratory process, and, subsequently, cell death [85]. Thionins are the first plant extract proteins reported to kill plant pathogens [86]. Thionins have also been found to be active against various bacterial, fungal and yeast strains [84]. The word thionin stands for two distinct groups of plant peptides, i.e., α/β-thionins and γ-thionins. The latter group, i.e., γ-thionins, shares remarkable similarities with other plant antimicrobial proteins, viz., defensins. α-hordothionins, β-hordothionins, crambin, purothionin and viscotoxin. Plant defensins are other important examples of antimicrobial peptides. The first plant defensins have been isolated from *Triticum aestivum* and *Hordeum vulgare*. They are small, basic, cysteine-rich and positively charged peptides. They have been reported to have biological activities against bacteria, fungus, proteinase and insect amylase inhibitors [84]. An authenticated model for the mode of plant defensins has not yet been proposed. However, defensins are believed to employ glycosylceramides as receptors to enter the fungal cell membrane. In response, the repulsion of defensins into the fungal cell membrane concatenates ion efflux, membrane disruption and destabilisation [87]. Various other plant antimicrobial peptides/proteins like lipid transfer proteins [88], pseudothionin [89], maltose binding proteins [90], fabatin [91], potato proteins [92], corn proteins [93], Zein [94], cyclotides [95], hevein-like proteins [84], Knottin-type peptides [96], and 2S1 albumin proteins [97] are persuasive examples of antimicrobials.

Cell-penetrating peptides also show excellent capability as antimicrobials. They assist in the transportation of cargo molecules (protein, peptide, polysaccharide or nucleic acid) into the live cell through their cell membrane [98]. Cell-penetrating peptides can efficiently penetrate the cell without causing noteworthy damage to the cell membrane [84,99]. Despite their effective antimicrobial properties, very scarce data is available on plant-penetrating peptides. This can be inflicted to indefinite use of antibiotics and other synthetic preservatives.

Lectins are other significant proteins from plants that have been reported to be fatal to pathogenic microorganisms. Plant lectins intercede antimicrobial activity by eliciting host immune responses, which further trigger the release of cytokines, consequently activating the defence mechanism and enhancing the macrophage-associated phagocytic activity during microbial infections. In Gram-positive and Gram-negative cells, lectins interact with N-acetylglucosamine, N-acetylmuramic acid and tetrapeptides linked to N-acetylmuramic acid [100]. While in fungal cells, it interacts with chitin and glucans in the cell wall. On interaction with chitin, lectins impair their synthesis and deposition on the cell wall, resulting in stunted hyphal development and spore germination [101]. Lectins from plants such as *Euphorbia helioscopia* [102], *Moringa oleifera* [103], and *Phthirusa pyrifolia* [104] have shown activity against various Gram-positive and Gram-negative bacteria, which demonstrates their candidature as potent natural/clean-label bio--preservatives. A well-oriented and directional approach in this field would enable us to explore more phytochemicals with bio-preservative properties and use them as an alternative to synthetic additives. This trend would satisfy consumer demand for natural/clean-label ingredients and be a first step towards adopting cleaner technology.

3.2.3. *Other metabolites with bio-preservative property*

Plant secondary metabolites, namely terpenoids, quinones, alkaloids, thiols and polyphenols, which give plants odour, pigmentation, and a specific flavour [105,106], have also been reported to exhibit bioactivity against pathogenic microorganisms such as *L. monocytogenes*, *B. cereus*, *Salmonella* spp., and *Campylobacter* sp [107]. For instance, terpenes and terpenoids (multicyclic structures) of essential oils derived from plants have received immense attention as bio-preservatives due to their antibacterial, antifungal, and antiviral properties [108]. Terpenoids like citral in camphor, menthol in *Salvia divinorum,* and cannabinoids in *Cannabis* are other plant secondary metabolites with bio-preservative properties [109]. Other important secondary metabolites of plants having noteworthy antibacterial activity are phenolic chemicals. Of the various phenolic compounds, carvacrol and thymol are known to have potent antibacterial activity [110]. These hydrophobic compounds limit the release of lipopolysaccharides from the outer membrane of bacteria. They also disturb the bacterial cytoplasmic membrane's structural and functional integrity by disrupting their lipid bilayer. Carvacrol, in particular, binds to the fatty acid chain and causes a destabilisation of the membrane structure, which further concatenates an increase in fluidity and permeability [111] and the release of intracellular components [112]. Some authors have reported decreased ATP production [113] and bacterial motility [110] with carvacrol. Curcumin from *Curcuma longa* is another significant phenolic pigment with antimicrobial activity against innumerable pathogenic bacteria. Even Codex Alimentarius, GSFA [9], has listed it as one of the safe food additives and defined its maximum permissible content (mg/kg) for various food categories such as flavoured milk beverages (catalogue number 01.1.4), chewing gum (catalogue number 05.2), soups and broths (catalogue number 12.5).

Alkaloids are other important phytochemicals or secondary metabolites enriched with medicinal properties. Morphine, cineline, brucine, emetine and strychnine are alkaloids with therapeutic value. An alkaloid, hasubananlactum, extracted from *Stephania glabra,* is bioactive against *Streptococcus mutans*, *Microsporeum gypseum*, and *S. aureus* [114]. Tannins in unripened fruits, green tea and red wine are also significant phytochemicals loaded with health-stimulating properties. Tannins cause the activation of phagocytic cells, enhance the immune system, and retard bacterial cell growth in the intestine [115]. Glucosinolates, i.e., glucoiberin, sinigrin, glucoerocin, and glucoiberverine, on the other hand, manifest antibacterial, antifungal, cancer-fighting, antioxidant and anti-inflammatory properties [109]. It has been found that these phytochemicals are very effective against specific fungal and bacterial pathogens.

Phytochemicals, due to their natural origin, bio-degradability and non-persistence in the food chain or ecosystem, unlike antibiotics, can be potent alternatives to synthetic additives. Phytochemicals from classes like phenols, alkaloids, coumarins and terpenes manifest proficiency in combating drug-resistant strains. Several phytochemicals have also been proven effective against molecular determinants such as membrane proteins, biofilms, bacterial cell communications and efflux pumps for achieving drug resistance [116]. Gull et al. [117] successfully tested four different extracts of *Lawsonia inermis* against Gram-positive and Gram-negative clinical isolates. Interestingly, not a single extract preparation showed any sign of toxidrome. Table 2 summarises such miscellaneous phytochemicals with bio-preserving potential.

Hydrosols can be another natural/'clean-label' food preservative in the plant category. Hydrosols are hydrophilic aromatic substances and by-products of hydro-distillation of aromatic plants [152]. Historically, hydrosols have been mainly used in traditional

Table 2
Antimicrobial spectrum of different extracts of plants.

Plant Name	Extract/Components	Antimicrobial Spectrum	Reference/s
Acalypha indica	Leaf extract	Antibacterial	[118]
Allium sativum	Solvent and water extracts	Antibacterial activity	[119]
Blumea eriantha	Alcoholic extract nanoparticles	Antibacterial	[120]
Callistemon viminalis	Methanolic flower extract	*Pseudomonas* spp.	[121]
Centella asiatica	Phenolic compounds and flavonoids	*B. cereus, E. coli, A. niger, C. albicans*	[122]
Cinnamomum javanicum	Solvent extracts of freeze-dried leaf and stem powder	*L. monocytogenes*	[123]
Citrus limon	Solvent and water extracts	Antibacterial activity	[119]
Eleagnus angustifolia	Ethanol extract	*Proteus mirabilis, Candida albicans, Enterococcus faecalis, E. coli, S. aureus,*	[124]
Eucalyptus microtheca	Alcoholic and aqueous extracts	*Penicillium digitatum, A. niger*	[125]
Fomitopsis lilacinogilva	Fruit extract	*B. cereus*	[126]
Ginja cherry	Stem extract	*Listeria innocua, S. aureus, S. enteridis*	[127]
Grape	Grape seed ethanolic extract	*L. monocytogenes, S. aureus, S. enterica*	[128]
Hibiscus sabdariffa	Water and ethanolic extract	*B. cereus, S. aureus, E. coli, P. aeruginosa*	[129]
Himanthalia elongata	Methanolic extract from plant	*P.* aeruginosa, *E. faecalis, L. monocytogenes*	[130]
Hippophae rhamnoides	Crude extracts of pomace, seeds and leaves	*L. monocytogenes, B.cereus, E. coli*	[131]
Hop plant	Bet acids	*L. monocytogenes*	[132]
Hylocereus polyrhizus	Fruit peel solvent extracts	*B. cereus, S. aureus, L. monocytogene*	[133]
Jatropha cutcas	Flavanoids, alkaloids, cardiac glycosides	*Kleibsella pneumonia, E. coli, A. niger, Penicillium notatum*	[134]
Lawsonia inermis	Methanolic leaf extract	*Pseudomonas* spp.	[121]
Mentha piperita	Plant extract	*S. aureus, E. coli*	[135]
Mentha × piperita	Menthol, menthone, limonene, germacrene	*P. aeruginosa, S. aureus*	[136]
Mentha pulegium	Menthone, isomenthone, cis-isopulegone	*E. coli, Salmonella typhimurium, S. aureus, P. aeruginosa, L. monocytogenes, B. cereus, A. niger, Aspergillus flavus*	[137]
Olea europaea	Leaves ethanol extract	*Bacillus cereus, S. enteridis, E. coli*	[138]
Origanum vulgare	Ethanolic extract	*Bacillus* sp. and *S. aureus*	[139]
Pimpinella anisum	Plant extract	*S. aureus, E. coli*	[135]
Pimpinella brachycarpa	Ethanolic extract	*S. aureus* and *B. subtilis*	[140]
Punica granatum	Ethanolic extract of pomegranate peel	*L. monocytogenes, S. aureus, S. enterica*	[128]
Prunus cerasus	Polyphenolic extracts of leaves	Antimicrobial activity	[141]
Psidium guajava	Methanolic bark extract	*Pseudomonas* spp.	[121]
Ribes nigrum	Polyphenolic extracts of leaves	Antimicrobial activity	[141]
Rosmarinus officinalis	Water and ethanolic extract	*B. cereus, S. aureus, E. coli*	[129]
Salvia officinalis	Leaves ethanol extract	*S. aureus, E. coli, Salmonella enteridis*	[138]
Scutellaria baicalensis	Ethanolic root extract	*L. monocytogenes, S. aureus, S. enterica*	[142]
Selaginella bryopteris	Plant extract nanoparticles	*S. aureus, E. coli, Aspergillus niger*	[143]
Syzygium aromaticum	Ethanolic extract	*B. cereus, S. aureus, Escherichia coli, P. aeruginosa, Salmonella typhi*	[144]
Tamarindus indica	Aqueous-ethanolic extract	*S. aureus, B. subtilis, L. monocytogenes*	[145]
Taraxacum officinale	Phenolic compounds	*S. aureus, B. cereus*	[146]
Tasmannia lanceolata	Solvent extracts of plant	*E. coli, S. aureus, Schizosaccharomyces pombe*	[147]
Terminalia ferdinandiana	Methanolic leaf extract	*Shewanella* spp.	[148]
Thymus vulgaris	Ethanolic extract	*S. aureus, P. aeruginosa*	[144]
Vaccinium corymbosum	Ethanolic extract of blueberries	*L. monocytogenes, Salmonella enteritidis*	[149]
Vaccinium sp.	Isorhamnetin-3-glucoside, phloridzin, hydroxybenzoic acid, epicatechin pelargonidin, chlorogenic acid	*S. aureus, E. coli*	[150]
Vaccinium sp.	Cranberry juice and extract	*L. monocytogenes, P. aeruginosa, S. aureus and E. coli*	[151]

medicines and refreshing drinks in various Mediterranean, Euro-Siberian, and South African countries. As by-products of distilleries, they can be a compelling and economical choice for various industrial applications. Hydrolates, for instance, are one of the finest flavouring agents in cosmetics, foods, perfumery and aromatherapy. Hydrosols are also natural bioactive compounds that have many health-benefiting properties, such as being an antioxidant [153], a bio-preservative [154], low toxicity [155], and an insecticide [155]. Their antagonistic property can be attributed to their complex chemical makeup, which inhibits microbial cell factories, biochemical pathways, cell membranes, and cell wall integrity. The Institute of Food Technologists also identified hydrosols such as vinegar-based preservatives as 'declaration-friendly preservatives' [156]. Under the *Hydrolon* range, European companies have already started using vinegar as a potential food preservative. They have cited many benefits of the ingredient, such as antagonising bacterial growth, retaining the colour of meat products, and not affecting the product's sensory properties [157]. There is a growing desire among researchers to find new hydrosols that have bioactivity. Recently, hydrosol of *Citrus aurantium* (sour orange) flower, rich in limonene, linalool, linalyl acetate and α-terpineol, was tested for its antimicrobial activity using a disc diffusion assay. Hydrosol was effective against *L. monocytogenes*, *E. coli*, *S. aureus,* and even against amoxicillin-resistant *B. cereus* [158]. In another study, hydrosol extracted from *Citrus aurantium* flower was found active against *Salmonella typhi*, *Micrococcus luteus*, *S. aureus*, *B. subtilis,* and *Enterobacter aerogenes* [159]. Hydrosols of orange blossom and rose water have also proven effective in controlling the growth of various pathogenic and food spoilage microorganisms [160]. Khan et al. [161] tested hydrosols (rich in carvacrol, thymol and terpinen-4-ol) from *Origanum vulgare* against various Gram-positive and Gram-negative strains and reported potent bioactivity of the same against tested strains. Hydrosols are a highly anticipated clean technology; however, this area still requires more thorough research to explore their applications in food bio-preservation.

3.3. *Animal-derived preservatives*

Among the different metabolites of animals, several protein hydrolysates are known to have antimicrobial activity against various microbial strains [19,162]. Protein hydrolysates interact with specific receptors to enable antibacterial, antifungal, antiviral, immunomodulatory, and antiproliferative applications [19]. For example, porcine blood hydrolysates have been reported to limit microbial proliferation in pork emulsions [163]. Other protein hydrolysates, such as casein hydrolysate [164], β-lactoglobulin, α-lactalbumin,

Table 3

'Clean label' permitted preservatives, according to General Standard for Food Additives (GSFA, Codex Stan 192–1995).

Preservative Name	Permissible Food Category	Food Catalogue Number	Permitted Maximum Value	Year Adopted	Reference
Curcumin (INS 100)	Flavoured fluid milk drinks	01.1.4	150 mg/kg	2017	Codex Alimentarius Codex Stan 192-1995
	Confectionary	05.2	300 mg/kg	2019	
	Chewing gum	05.3	300 mg/kg	2019	
	Decorations, toppings and sweet sauces	05.4	500 mg/kg	2019	
	Pre-cooked pastas and noodles	06.4.3	500 mg/kg	2019	
	Soups and broths	12.5	50 mg/kg	2015	
Grape skin extract (INS 163)	Flavoured fluid milk drinks	01.1.4	100 mg/kg	2017	
	Edible ices, including sherbet and sorbet	03.0	1000 mg/kg	2011	
	Cocoa-based spreads, including filling	05.1.3	200 mg/kg	2016	
	Soft candy	05.2.2	1700 mg/kg	2017	
	Processed meat, poultry	08.2	5000 mg/kg	2014	
Lysozyme (1105)	Ripened cheese	01.6.2	GMP	2019	
	Cider and perry	14.2.2	500 mg/kg	2004	
	Grape wines	14.2.3	500 mg/kg	2004	
Nisin[a] (INS 234)	Flavoured fluid milk drinks	01.1.4	12.5 mg/kg	2017	
	Ripened cheese	01.6.2	12.5 mg/kg	2019	
	Processed cheese	01.6.4	12.5 mg/kg	2018	
	Dairy-based desserts	01.7	12.5 mg/kg	2016	
	Fine bakery wares	07.2	6.25 mg/kg	2016	Codex Alimentarius Codex Stan 192-1995
	Edible casings	08.4	7 mg/kg	2015	
	Ready to eat soups and broths	12.5.1	5 mg/kg	2018	
Pullulan (INS 1204)	Fermented vegetable	04.2.2.7	GMP	2014	
	Flours	06.2.1	GMP	2014	
	Frozen battered fish and fish products	09.2.2	GMP	2017	
	Other sugar and syrups	11.4	GMP	2015	
	Coffee and coffee substitutes	14.1.5	GMP	2015	

GMP: Good manufacturing practice; INS: International Numbering System.

**Lactococcus lactis*, a microbial source for Nisin is also directly used as an alternative to Nisin in some marketed products as bio-protective culture (Befresh™ AC).

[a] GSFA recommended Nisin (processed and pure) as a 'clean label' preservative, however in market its alternatives like fermented sugar and vinegar clean-label (Proteria™ CV and Proteria™ AL) are also available.

serum albumin, immunoglobulins [165], and ovalbumin [166], are convincing examples of bioactive proteins with antimicrobial activity.

Another important example of an animal-based protein-based preservative with significant bioactive potential is whey protein isolates (WPI). WPIs are frequently found in various packaged foods, such as edible films. WPI-based films are transparent, odourless, and tasteless. In addition, they act as selective barriers to moisture, gas, solutes, lipids and aromas. WPI-based coatings are found to be effective against pathogenic bacteria and are also valuable for controlling the release of various antimicrobials [167]. However, WPI-based films themselves are not antimicrobial but can serve as carriers for different antimicrobial agents with an approach to widening the shelf life and safety of food products [168]. Recently, the antimicrobial activity of whey protein-ε-polylysine complexes against *E. coli* has been reported [169]. Whey protein in donkey milk is another rich source of antimicrobials and a fitting example of WPI. The antimicrobial activity of donkey milk can be attributed to minor whey proteins such as lactoferrin (Lf), immunoglobulins (Igs), lysozyme (Lyz), and lactoperoxidase [170]. In addition, lysozyme in donkey milk exhibits a synergistic effect with lactoferrin and some fatty acids, namely linoleic, lauric and oleic acids [171]. Lactoferrin interacts with the lipopolysaccharide of bacterial strains to induce disruption of their outer membrane, subsequently enhancing their susceptibility to lysozyme, which further results in cell death [172,173]. GSFA and Joint Expert Committee on Food Additives (JECFA) have also listed lysozyme and lactoperoxidase as safe preservatives in various food items. Foods like cheese, bread and wine have been preserved mainly through the use of the antimicrobial properties of lysozyme and lactoperoxidase. Although some milk protein isolates are considered 'clean label' preservatives, consumers allergic to milk and other milk constituents should take special precautions before consuming them.

Some animal lectins have also shown antimicrobial properties. C-type lectins (CTLs) in animals recognise and bind to glycans, subsequently activating host immune responses [174]. For instance, CTLs from *Litopenaeus vannamei* [175] and *Cynoglossus semilaevis* [176] displayed bioactivity against several viral and bacterial species, which highlights the potent candidature of animal-derived proteins as clean-label food bio-preservatives.

Codex General Standards for Food Additives has enlisted various 'clean-label' approaches. Based on their ADI and other relevant safety criteria listed under INS, some of the natural/clean-label preservatives discussed above have already been evaluated by JECFA for use in foods per the provisions of International Food Standards. Different food preservatives assessed and approved by the GSFA are summarised in Table 3. The use of these preservatives in various food products is technologically proven and complies with GSFA [9].

Table 4
'Clean-label' preservatives marketed as substitute to chemical additives.

Chemical Preservative (E Number)	Clean Label Alternatives	Marketed Product	Applications	Spectrum/Functionalities	Reference
Ascorbic acid (E300-304/INS 300)	Acerola extract	Guardox™ AE	Butter & cheese Fish & shellfish products, potato-based products	Avert browning & sustain sensorial characteristics Avert inodorous of unsaturated fatty acids Avert browning & discoloration	[177]
	Citrus-Lemon extract	Antibraun™	Fruits & vegetables	Avert browning	
	Fermented sugar	Fixolor™ AT	Juices	Avert browning, sustain sensorial characteristics & discoloration	
BHA (E320/INS 320)	Bamboo leaf extract	Guardox™ BL	Baked products	Retards oxidative rancidity	
Calcium propionate (E282/INS 282)	Cultured corn sugar	Proteria® CP	Baked products	Avert mold growth	
Citric acid (E330/INS 330)	Citrus fiber Citrus fiber	White Fiber™	Cooked meat	Elevates moisture retention and ionic strength	
Natamycin (E235/INS 235)		Antipack™	Dried sausage	Avert yeast & mold growth	
	Citrus extracts & fermented sugar	Antimix™ CC	Refrigerated goods		
	Lactobacillus sp.	Befresh™ LL	Fresh cheese		
	Lactobacillus paracasei, *L. freundenreichi*	Befresh™ AL	Yogurt		
Nitrite/Nitrate (E249-250/251–252)	Acerola extract and vinegar	Fixolor™ AL	Cured meat	Avert botulism toxin and enhances pink color	[177]
	Cultured sugar and vinegar	Proteria™ AL		Avert botulism toxin	
Potassium sorbate (E202/INS 202)	Cultured sugarcane juice	Fixolor™ AT	Soft & fruit drinks	Anti-Alicyclobacillus	
	Lactobacillus sp.	Befresh™ LL	Cheese	Avert yeast & mold growth	
	Mushroom chitosan	Chitoly™ AB	Grape wine	Avert yeast growth	
	Fermented sugar	Proteria™ CP	Baked products	Avert mold growth	
Sodium benzoate (E211/INS 211)	Citrus extracts	Planteria™ CF	Fruit juices	Avert yeast & mold growth	
	Citrus extracts & fermented sugar	Antimix™ CC	Jams, pickles & salad		
	Mushroom extracts	Mushria™	Carbonated drinks		
Sodium diacetate (E262/INS 262)	Cultured corn sugar	Proteria™ CP	Baked products	Avert mold growth	

BHA: Beta hydroxyl acid; E: European number; INS: International Numbering System. (Source: https://www.handary.com/category/aboutus/?id=10073).
(Source: https://www.handary.com/category/aboutus/?id=10073)

The 'clean-label' preservatives already present on the market as substitutes for synthetic preservatives are outlined in Table 4. The global 'clean-label' ingredient market is slated to grow at a compound annual growth rate (CAGR) of 6.75 % in the forecast period from 2021 to 2026. Currently, North America is the largest market for the production and use of 'clean-label' ingredients, but Asia Pacific is the fastest-growing market due to increasing living standards [178]. Globally growing demand for clean-label ingredients and approaches is hard to ignore. This further imposes immense pressure on food technologists worldwide to explore more natural preservatives and clean technology for their processing.

4. Industrial 'clean-label' products

At the industrial level, tremendous efforts have been made to develop formulations enriched with natural products as food preservatives. However, during processing several food industries encountered and overcome many technical challenges like variation in physical and chemical properties, odour, palatability, efficiency and storage. For example, green tea, rich in catechins (flavan-3-ol, a part of the chemical family of flavonoids) and other flavonoids, is water-soluble but not oil-soluble. Therefore, to develop an oil-based product with bio-preservative properties, one must overcome the solubility problem. Accordingly, Dupont Nutrition and Biosciences, experts in developing natural products, has developed an oil-soluble green tea extract that can be used for oil-based functionalities. The GUARDIAN® range of rosemary, acerola, and green tea extracts is their prideful discovery in this range.

Carbohydrate fermentate-based formulations are also one of the fastest-growing 'clean-label' products. Powdered preservatives, like most carbohydrates, offer more flexibility in food applications. However, because they are heavy in calories, many health-conscious people are reluctant to incorporate items with carbohydrate-based preservatives into their diets, especially those trying to lose a few extra pounds. Despite this, there is a growing global market for functional carbohydrates, also classified as good carbohydrates, due to their various advantageous features like low glycemic index, non-cariogenic properties, and slow digestion in the body. Their global market is expanding and is projected to grow at a CAGR of 6.1 % from 2019 to 2026 [179]. Due to their various inherent health-stimulating properties, food industries are encouraged to use carbohydrates in their formulations and are in a race to develop different carbohydrate-based preservatives. One example is 'Verdad Powder F80′, a carbohydrate-based product from a Dutch food and biochemical company. The primary ingredients of Verdad Powder F80 are fermented sugar and vinegar, and the product is sold with a 'clean-label' tag. This formulation is active against the foodborne pathogen *Listeria* and thereby extends the shelf life of the food product up to 40 days [180].

On this line, Cargill markets a range of 'native starches'. Native starches have been part of the food industry for decades. However, because of their degradation at elevated temperatures and in an acidic environment, formulators have been forced to switch to processed (chemical or enzymatic) food starches. Modified food starches are currently one of the largest artificial-sounding ingredient categories. So, efforts have been made to create food starches using corn, wheat, cassava, rice, and tapioca, with which consumers are familiar. Although there is no one-to-one substitution of modified food starch, a single native starch may not enhance food products' mouthfeel, stability, and texture. The food sector is now developing blended formulations to address this issue. DuPont Nutrition and Biosciences is involved in developing blended 'clean-label' carbohydrate-based preservatives. BioViaCL600, a blend of dextrose and vinegar, is their proud product in this category. This product is active against *Listeria* and has a shelf life of up to 40 days for a range of meat, poultry, and ready-to-eat products [156]. At the industrial level, efforts have also been made to develop some 'clean-label' tagged milk-based preservatives, such as non-fat dry milk and whey products. MicroGARD is one of the FDA-approved milk-based labels by DuPont Nutrition and Biosciences [181].

Various products derived from milk, sugar or wheat flour have been developed under this brand (Tables 5 and 6). These products are claimed to be effective against common food spoilage microorganisms.

Additionally, they reported to enhance the sensory qualities of food products. MicroGard®100 is a highly bioprotective agent that consists of fermentates from dairy cultures. In addition, it contains various natural metabolites that prevent microbial contamination of food when combined with the controlling physicochemical factors such as temperature, pH, and other formulation adjustments. It has been found effective against Gram-positive (*Listeria, Staphylococcus*) and Gram-negative bacteria (*E. coli, Salmonella*). Its field of application includes fresh pasta, spreads, fresh soups, and sauces. MicroGARD®400 is another non-fat dry milk fermentate inhibiting microbial growth [182]. It is an effective inhibitor of Gram-negative bacteria such as *Pseudomonas*, *Yersinia,* and *Salmonella* [181], as well as yeasts and moulds. In light of the above findings, natural compounds appear to hold great promise as 'clean-label' preservatives. Specific progressive inputs, like a study on the effect of different combinations and concentrations of 'clean-label' products

Table 5
Cultured/fermented dextrose/wheat starch fermentates marketed by DupontTM Nutrition and Biosciences.

Product	Spectrum	Applications	Reference
MicroGARD® 200 (Organic)	Gram-negative bacteria, yeast and mold	Pasta, side dishes, sauces	[26]
MicroGARD® 210	Gram-negative bacteria, yeast and mold	Pasta, sauces, high protein bars, nut bars, fruit bars, nutrition bars	
MicroGARD® 520 (Organic)	Gram-positive bacteria, spores, *Listeria*	Soups, dressings	
MicroGARD® CS1-50 (Organic)	Gram-positive bacteria, spores, *Listeria*	Sauces, soups, non-dairy products	
MicroGARD® 730 (Organic)	Broad spectrum	Cooked meat, poultry products, marinated and raw meat	
MicroGARD® 740	Broad spectrum	Cooked meat, poultry products, cured meat marinated and raw meat	
Wheat Starch Fermentates			
MicroGARD® 910F	Mold	Bread	[26]

Table 6
Milk fermentates marketed by Dupont<SUP>™ Nutrition and Biosciences.

Product	Spectrum	Applications	Reference
MicroGARD® 100 (Organic)	Gram-negative bacteria, yeast and mold	Smoothies, cheese, yogurt, sour cream	[26]
MicroGARD® 400	Broad	Flavoured milks, dairy spreads, cheese blends	
MicroGARD® 430	Broad	Cheese	
MicroGARD® CM1-50	*L. monocytogenes*, gram-positive bacteria, spores	Sauces, dressings, soups, puddings, dairy based meals and dips	

on human health and authentic clinical research data, would encourage their use as bio-preservatives. Besides, policymakers must use more legitimate guidelines to reduce misapprehension in their daily intake concentration and promote healthy living consumption.

5. Major challenges

During the past decade, significant advancements have been made in bio-preservatives. Nonetheless, some limitations and information gaps still need to be filled. Improving the technological characteristics of bio-based preservatives to make them efficient alternatives to artificial additives, faces several challenges. It is important to note that commercial 'clean-label' bio-preservatives are scarce, presumably because natural/organic compounds are easily affected by physical and chemical factors and varied food processing technologies. Furthermore, certain inherent counter chemicals produced by microbial cultures are a limitation in substituting synthetic preservatives completely with bio-based alternatives. Other important considerations include the effects on health and other safety-related matters. For example, there should be a standard procedure to incorporate safety studies before designating any microbial culture or organic compound as 'clean-label'.

Another main challenge is the high cost of product recovery. It is reported that even after scaling up, some products have a shallow titer value, which makes the adoption of bio-based technology even more difficult [183]. In this case, where the final product's titer value is meagre, immobilisation technologies like nanomaterials and organosilicon compounds can enhance the recyclability of the compound [184]. The challenges also encompass the need for solutions to produce and introduce plant-based bio-preservatives into the market successfully. However, toxicological issues related to bioactive compounds, such as alkaloids, are a concern. For instance, the toxicity evaluation of traditional Chinese medicines, including hepatotoxicity, nephrotoxicity, and cardiotoxicity, has been the subject of extensive metabolomic research [185]. Potential toxicological implications of other phytochemicals and plant parts with bio-preservative properties such as carvacrol, thymol, linalool, and limonene [186] and fruiting body [187] highlights the need for extensive research on their clinical effects and toxicity before releasing any natural/clean-label products.

The impact of bio-based preservatives on the organoleptic characteristics of food is another crucial aspect that needs deeper investigation. Generally, before marketing any product, its organoleptic properties are characterised. For instance, in a study, the organoleptic quality of a liquid food formula made from snail, tempeh, and moringa leaves was assessed by trained panellists. Most panellists liked the liquid food formula and demonstrated the importance of organoleptic acceptability in developing bio-preservatives [188].

The use of bio-protective cultures as an alternative to chemical preservatives or as a complementary tool to avoid or delay fungal spoilage of dairy products has been proposed to meet the growing consumer demand for naturally preserved food products [189]. The use of bio-based preservatives and technologies, such as fermentation, has also been recognised as an efficient technique for improving nutrient bioavailability and other functional properties of food products, which indirectly relate to the organoleptic characteristics of food [190]. Adding different types of bio-preservatives, such as bacteriocins, essential oils, and vinegar, can be another promising method to extend the shelf life of food products. Still, it requires further research and development and stringent guidelines to optimise effectiveness [191].

6. Future prospects

Notwithstanding the difficulties previously mentioned, the absence of a standard definition, and the different regulatory limitations on "clean-label" components, this movement is expanding quickly and is here to stay. The grocery market is already tuned to 'clean-label' to meet consumer's demand for organic products. In the search for 'clean-label' food preservatives, a lot of research and development has occurred in screening new natural substances with appreciable bio-preservative properties. The industry has introduced new formulations with 'clean-label' ingredients in food markets. Plant sources are the major contributors to bio-preservatives, followed by microbial and animal sources. With a future approach in mind, bioactive enzymes may be the most promising candidate as a direct edible additive in food. They can also be incorporated into edible food packaging, increasing their usefulness in various food applications. Another helpful approach is to develop different LAB variants. LABs are part of the human intestinal microflora. Therefore, combining their genetic constitution with other beneficial antimicrobial peptides/proteins will impart more health-stimulating properties. Glycosylated bacteriocins can be another potent 'clean-label' approach for food preservation. They target wide-spectrum foodborne pathogens, and hence, research is escalated worldwide to decipher newer novel bacteriocins like nisin with bio-preservative property. Phytochemicals/Nutraceutical industry is a fast-growing sector that has gained attention as perpetual choice for bio-preservatives. Nutraceuticals can be regarded as harnessing nature's gift with a futuristic approach. Nutraceutical industry can be the key to treat various food spoilage problems. They can be used in their native form or formulated with other valuable phytochemicals as a natural solution to various food tribulations.

The present article is a comprehensive compilation of organic compounds already in use or having potential as 'clean-label' bio-preservatives. This article provides a detailed explanation of current knowledge and future directions for this field of study. This review may facilitate regulatory bodies to update guidelines for better segregating synthetics and 'clean-label' products. Such segregation and tagging shall provide informed choices to the consumers and improve the business of regulatory approvals.

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Data availability

Data included in article/referenced in article.

CRediT authorship contribution statement

Kanika Chauhan: Writing – review & editing, Writing – original draft, Methodology. **Alka Rao:** Resources, Funding acquisition, Conceptualization.

Declaration of competing 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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