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Spices and gastrointestinal health benefits: a state-of-the-art

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ABSTRACT

Spices represent the basis of traditional medicine through the Middle East to Eastern Mediterranean and Europe since antiquity. In Western countries, spices are frequently used to impart flavor, reduce the need for salt and fatty condiments, improve digestion, and enhance their antioxidant effects. Thus, their diet-health linkages have drawn the attention of consumers, the scientific community, and the food industry. Indeed, their bioactive components are of considerable significance, making spices promising components to be included in a personalized diet. Numerous studies have demonstrated the antioxidant, antimicrobial and gastro-protective properties of spices and their role in preventing many diseases has been dissected. This review presents an overviewof the most common spices highlighting their anti-inflammatory, prebiotic, and anti-tumoral properties. Human clinical trials, specifically randomized controlled trials, are necessary to describe and demonstrate their health benefits to define it as a functional food.

KEYWORDS

SPICES

ANTI-INFLAMMATION

PREBIOTIC

DIET

FUNCTIONAL FOOD

INTRODUCTION

Spices are an important part of human nutrition and have a place in all the world's cultures. Spices were among the most valuable food of trade in ancient and medieval times. Around 3500 BC, the ancient Egyptians used various spices to flavor food and cosmetics and embalmer their dead[1]. In 2000 BC, a precursor of curry was discovered in India, while Egyptian papyruses from 1555 BC highlighted the use of coriander, garlic, cumin, and thyme. The uses of spices spread through the Middle East to the Eastern Mediterranean and Europe. Nowadays, in Western countries, spices are well-known to impart flavor and reduce the need for salt and fatty condiments, improve digestion, and provide the organism with extra antioxidants that prevent the appearance of physiological and metabolic alterations. Recently, their diet-health linkages have drawn the attention of consumers, researchers, and the food industry. Indeed, their bioactive components are of considerable significance, making spices potential therapeutic benefits for health. Thus, most spices are characterized by antioxidant, antimicrobial, and gastro-protective properties, and the role diet plays in preventing and treating many illnesses has been dissected. In this review, efforts are made to highlight the anti-inflammatory, prebiotic, and anti-tumoral properties of the leading used spices in daily life.

Biological components of spices

Spices are composed of a wide range of biological components. Ginger contains several identified bioactive constituents, including gingerol and gingerol-like compounds and antioxidants such as beta-carotene, ascorbic acid, polyphenols, terpenoids, and alkaloids[2,3]. Piper contains terpenes, antioxidants, B vitamins, and alkaloids such as piperine and piperine-like compounds. It has been used medicinally for its anti-inflammatory, antiasthmatic, analgesic, antiepileptic, chemopreventative, and anthelminthic effects[4,5]. Black pepper biotransforms and increases the bioavailability of phytochemical substrates[6]. The main bioactive compounds in turmeric are curcuminoids, which contain curcumin, demethoxycurcumin, and bisdemethoxycurcumin[7,8]. Other turmeric constituents include diaryl heptanoids, turmerones, diarylpentanoids, phenylpropenes, monoterpenes, sesquiterpenes, diterpenes, triterpenoids, sterols, and various alkaloids[9]. Cilantro (*Coriandrum sativum* L.), a member of the Apiaceae family with nutritional and medicinal properties, contains mainly linalool but also geranyl acetate, caryophyllene, camphor, and p-cymene. Essential oil of seeds mainly contains linalool, whereas that of leaves contains decanal, decanol, cyclodecane, and dodecena[10]. Chemical analysis indicated clearly that linalool was the main component of coriander essential oil[11]. Clove represents one of the major vegetal sources of phenolic compounds such as flavonoids, hidroxibenzoic acids, hidroxicinamic acids and hidroxiphenyl propens. Eugenol is the main bioactive compound of clove[12,13]. Saffron is another medicinal plant rich in carotenoids and terpenes. The major products of saffron are crocins and crocetin (carotenoids) deriving from zeaxanthin, pirocrocin and safranal, which give it its taste and aroma, respectively[14]. Saffron and its major compounds representing by carotenoids (crocetin, crocin, picocrocrocin), vitamins (thiamine, riboflavin), minerals, terpenoids and other volatile compounds (ketones, aldehydes, esters, c13-nor isoprenoids, saturated hydrocarbons, acetic acid) have also powerful antioxidant and anti-inflammatory properties. Table 1 illustrates the main components of the most used spices and their potential biological effects on gastrointestinal tract.

Spices and anti-inflammatory effects

The inflammation is a protective response of the organism which appears during a microorganism invasion, an anti-hygiene exposure, or cellular damage, causing the progression of numerous diseases[22]. Ginger and its active compounds are anti-inflammatory, inhibiting the synthesis of prostaglandins and leukotrienes. Two recent meta-analyses showed that ginger supplementation has an inflammatory effect, reducing serum levels of C-reactive protein (CRP), tumor necrosis factor (TNF, interleukin (IL)-6, and prostaglandin E_2 (PGE2)[22-24]. The prominent ginger bioactive component is the 6-shogaol which gives all its anti-inflammatory properties to the substance. *In vivo* studies showed that the 6-shogaol inhibits leukocyte tissue infiltration and has a protective effect over the epithelial cells in the colon[25,26]. In a recent animal study conducted by Wang et al[27] evaluating the impact of oral ginger powder administration on aspirin-induced gastric damage in rats, it turns out that the added integration of ginger powder stopped the formation of lesions of the gastric mucosa as opposed to aspirin which caused the formation of ulcers. Thus, ginger powder and its compounds, like the 6-shogaol, show protective effects against gastric ulcers on top of remarkable anti-inflammatory properties[25].

Cinnamon essential oil (CEO) is a natural substance of plant origin that has always been used in food spices. Recent studies have also shown that cinnamaldehyde's containing in CEO has significant anti-inflammatory properties[29]. Interestingly, the CEO's anti-inflammatory effects could protect against inflammatory bowel disease (IBD)[29]. Indeed, the intake of the CEO reduced the colitis development in rats[28]. A more considerable diversity and abundance of the gut microbiota and a decreased abundance in *Helicobacter* and *Bacteroides* were shown[29].

Moreover, cinnamon contains polyphenols well-known to have significant anti-inflammatory effect[30]. In chili pepper, flavonoids, phenolic acids, carotenoids, and ascorbic acid also have anti-inflammatory properties such as the capsaicin, 6,7-dihydrocapsaicin, homo-capsaicin, homodihydrocapsain, nordihydrocapsaicin[31]. Moreover, pepper stalk, placenta, pericarp, and seed extracts are excellent sources of flavonoids such as luteolin and apigenin. These effective antioxidants may protect against various chronic diseases such as cancers, cardiovascular diseases, and type 2 diabetes. Moreover, compared to chili pepper fruits, chili pepper leaves have a higher beneficial effect on the anti-inflammatory spectrum[32].

Furthermore, the capsaicinoids that give spiciness to the chili pepper also have anti-inflammatory properties[31].

Turmeric has also shown an anti-inflammatory effect by inhibiting cyclo-oxygenase 2 (COX-2), prostaglandins, leukotrienes, and other inflammatory mediators[33]. Indeed, a recent controlled randomized study has demonstrated a reduction of the serum concentration of proinflammatory cytokines in fifty-nine patients with metabolic syndrome consuming 1 g of turmeric a day for eight weeks[34]. The anti-inflammatory effects are found mainly in essential oil due to the presence of bioactive compounds such as linalool and geranyl acetate.

Table 1. Main components of the most used spices and their potential biological effects on GI tract.

Spices	Main components	Potential biological effects on GI tract		
		Anti-inflammatory	Prebiotic	Anti-tumoral
Ginger[15]	• Volatile oil • Gingerol analogs • Diarylheptanoids • Phenyl-alkanoids • Sulfonates • Steroids • Monoterpenoid glycosides compounds	• Inhibition of the synthesis of prostaglandins and leukotrienes • Reduction of serum levels of CRP, TNF, IL-6, and PGE2	• *In vitro* inhibitory activity towards some inflammatory gut species	• Anti-tumor action through important mediators involved in cell processes • • High potential chemopreventive properties
Cinnamon[16]	• Essential oils • Cinnamaldehyde • Cinnamic acid • Cinnamate • Eugenol • Water-soluble polyphenols (catechin, epicatechin, procyanidin, quercetin, kaempferol, and polyphenolic polymers) • Flavonoids (proanthocyanidins and oligomers of cinnamtannins)	• Decrease of the levels of inflammatory cytokines, nitrite NO, PGE2, IL-6, IL-8, and TNF-α	• Promotion of the growth of gut bacteria such as Bifidobacterium spp. and Lactobacillus spp. • Inhibitory activity against *Ruminococcus spp.*	• Anti-tumor properties with a potent induction of apoptosis from induction of ROS
Chili pepper[17]	• Carotenoids: lutein, β-carotene, β-cryptoxanthin, zeaxanthin, violaxanthin, capsanthin, capsorubin; • Vitamins C and E • Phenolic compounds, such as flavonoids: quercetin, luteolin, and phenolic acids • Capsaicinoids	• Inhibition of pro-inflammatory cytokine production (Capsaicin)	• Increase of numbers of key gut microbial genera, such as *Bacteroides, Akkermansia*, *Prevotella*, *Lachnospiraceae* and *Ruminococcaceae* (Capsaicin) • Reduction of numbers of *Escherichia* (Capsaicin) • Increase in SCFAs especially butanoic acid	• Pro-apoptotic and anti-proliferative effect (Capsaicin)
Turmeric[18]	• Demethoxy curcumin and bisdemethoxycurcumin • Vitamins C and E • Several minerals, as well as B-group vitamins (i.e., B2, B6, and B9 vitamins) • Volatile oils • Resins	• Inhibition of cyclo-oxygenase 2 (COX-2), prostaglandins, leukotrienes, and other inflammatory mediators	• Enhance of the growth of beneficial *Bifidobacterium spp.* and *Lactobacillus spp.* while repressing the growth of several *Ruminococcus spp.*	• Inhibition of the proliferation, invasion, metastasis, and angiogenesis • Induction of apoptosis and autophagy, through miRNA and incRNA-mediated mechanisms

Table 1. Main components of the most used spices and their potential biological effects on GI tract. (continues)

Cilantro (Coriander)[19]	• Linalool • 1,8-cineole (eucalyptol). • Polypheeranyl acetate, caryophyllene, camphor, and p-cymenenols, • Flavonoids, phenolic acids, terpenes, vitamins, and many phytosterols • Gallic acid, thymol, and bornyl acetate	• Antioxidant activity due to the activity of polyphenols, vitamins, and sterol constituents of coriander		
Black pepper[20]	• Lignans • Alkaloids: piperine • Flavonoids • Polyphenols • Amides • Aromatic compounds	• Increase of the bioavailability of phytochemical substrates • Inhibition of the 5-lipoxygenase and COX-2 (piperine) • Inhibition of the levels of proinflammatory cytokines (piperine)	• Potential role in regulating intestinal microbiota by promoting the growth of beneficial bacteria on the one hand and suppressing pathogenic bacteria on the other	
Saffron[21]	• Carotenoids: crocetin, crocin, picocrocrocin • Vitamins: thiamine, riboflavin • Minerals • Terpenoids • Other volatile compounds: ketones, aldehydes, esters, c13-nor isoprenoids saturated hydrocarbons, acetic acid • Flavonoids: kaempferol, quercetin, epicatechin, anthocyanins • Phenolic acids 4-hydroxy benzoic acid, salicylic acid, gallic acid, vanillic acid, rosmarinic acid, chlorogenic acid • Hydrolyzable and condensed tannins	• Reduction of the levels of inflammatory cytokines (crocetin and crocin) • Improvement of the levels of glutathione and reduces lipid peroxidation (crocetin and crocin)		• Pro-apoptotic and anti-proliferative effect

Abbreviations: COX-2, Cyclooxygenase-2; CRP, C-reactive protein; GI, gastrointestinal tract; IL-6. Interleukin-6; PGE2, prostaglandin; ROS, reactive oxygen species; SCFA, short-chain fatty acids; TNF, tumor necrosis factor

For its anti-inflammatory activities, essential cilantro oil is suggested to treat chronic anti-inflammatory diseases. Indeed, recent studies have shown how integrating critical cilantro oil improves anti-inflammatory activity by 1%[35]. Various *in vivo* and *in vitro* studies of black pepper demonstrated that piperine had various anti-inflammatory activities[36]. Indeed, piperine can inhibit the 5-lipoxygenase and COX-2, two enzymes involved in the anti-inflammatory mediators' biosynthesis[36]. Piperine also appears able to inhibit the levels of proinflammatory cytokines[36].

Interestingly, a recent study has shown how piperine is effective against harmful ulcer effects. Therefore, the integration of piperine could be associated with better inflammatory protection[16]. A relevant spice is saffron, owing to the presence of crocin, a bioactive component. It has shown impressive anti-inflammatory properties and has been used to treat inflammatory diseases. In recent years, many studies have been conducted to analyze saffron compounds and their action on humans. Active saffron components seem able to reduce inflammatory cytokines[37]. The anti-inflammatory effect of crocin and crocetin has been studied on organs such as the stomach, intestines, liver, and kidneys. This saffron component improves the levels of glutathione and reduces lipid peroxidation. The saffron components were also revealed to be effective for inflammatory digestive disorders[38]. Numerous studies have demonstrated the beneficial effects of carotenoid crocin and crocetin over gastritis, peptic ulcer, irritable bowel syndrome, and IBD[38]. Crocin also has a gastroprotective impact on ethanol-induced gastric injuries[38].

Spices and prebiotic effects

The latest studies have shown relevant prebiotic benefits as effects of spices' consumption. Prebiotics are characterized as a group of non-digestible carbohydrates fermented by the intestinal microbiota. It selectively enhances the survival and growth of the restricted number of gut microbes, thus establishing a balanced colonial microflora[39]. It helps boost the immune function, improves colonic cohesion, reduces pathogenic microflora, down-regulation of allergic reactions, and stimulates lipid metabolism and mineral absorption[40,41]. Human microbiota studies have revealed the significant prebiotic potential of medicinal herbs – including ginger, black pepper, cinnamon, chili pepper, and curry leaves used in digestive health and disease via the microbial metabolism of herb-provided substrates, e.g., sugars, glycans, and amino acids[42]. The gut microbiota encodes the untold biotransformation potential of phytochemicals, exemplified by microbiota-dependent bioconversion of polyphenolic compounds that serve to increase their absorption and bioactivity, including anti-inflammatory compounds[43,44]. Both fibers and phytochemicals in medicinal herbs used as spices appear to promote beneficial microbes' growth and inhibit potentially inflammatory species' growth[45]. These spices likely interact with the gut microbiota to induce gastrointestinal and systemic effects[46]. Indeed, these spices contain constituents that have medicinal value, such as polyphenols, which are known to be metabolized by gut microbiota[42]. It is worthwhile to point out that black pepper possesses prebiotic-like effects by promoting the growth of beneficial bacteria on the one hand and suppressing pathogenic bacteria on the other, suggesting its potential role in regulating intestinal microbiota and the enhancement of gastrointestinal health[47]. The great interest in curcumin is due to its anti-carcinogenic effects potentially mediated by inducing apoptosis, inhibiting the cell cycle, and positive modulatory effects on the microbiome[48]. However, the impact of these herb constituents on gut microbiota and the microbial metabolism of these spices and their components remain incompletely understood. The spices of interest display both increases and specific inhibitory effects. Indeed, ginger exhibits in vitro antibacterial activity towards inflammatory gut species such as *Escherichia coli* and *Klebsiella pneumonia*[49]. Both ginger and turmeric enhance the growth of beneficial *Bifidobacterium spp*. and *Lactobacillus spp.* while repressing the growth of several *Ruminococcus spp*. derived from clinical samples[50].

Cinnamon also could promote the growth of gut bacteria such as *Bifidobacterium spp*. and *Lactobacillus spp.* with varying degrees[51]. Cinnamon has high inhibitory activity against *Ruminococcus spp.*, but minimal or no activity against selected strains of *Bacteroides, Finegoldia, E. coli, Salmonella, and Staphylococcus*. Cinnamaldehyde, a cinnamon's bioactive component, exhibited more potent in vitro antibacterial properties against five common foodborne pathogenic bacteria (*Bacillus cereus, Listeria monocytogenes, S. aureus, E. coli, and Salmonella anatum*) [51]. *Fusobacterium spp.* was also susceptible to cinnamon. Cinnamon exhibited modest activity against toxigenic *C. difficile* and a few strains of other *Clostridium*[51].

Regarding chili pepper, its health benefits, including an anti-inflammatory potential and protective effects against obesity, are often attributed to the response of the gut microbial community to capsaicin[52]. Studies concerning capsaicin (CAP), the bioactive compound in chili peppers, have shown it can have a beneficial effect *in vivo* when part of a regular diet. *In vivo* studies have shown that CAP can alter the gut microbial population

at the genus level in mice and humans. In both *in vivo* mouse studies, dietary CAP reduced weight gain and food intake. It increased the population numbers of key gut microbial genera, such as *Bacteroides, Akkermansia*, and *Prevotella*, while reducing the population numbers of *Escherichia* and *Sutterella*[53,54]. These changes in gut microbial composition are likely to account for many of the positive health changes associated with CAP treatment. Another *in vivo* study revealed a significant difference in gut microbial community diversity with dietary CAP, including an increase in *Lachnospiraceae* and *Ruminococcaceae*, species that produce short chain fatty acids (SCFAs), especially butanoic acid[55].
Conversely, a further *in vivo* mouse study found that CAP consumption decreased *Bacteroides* and *Parabacteroides*, though CAP was associated with increased SCFA production[56]. These changes in the bacterial population are reflected in changes in SCFA production and bile acid metabolism with dietary CAP[53,57]. It has been speculated that these SCFAs changes that occur due to shifts in the gut microbial community cause the positive health effects associated with CAP, including the promotion of glucose homeostasis. Due to the rising instances of obesity, diabetes, and irritable bowel disease, it is crucial to assess the effect of CAP on the gut microbiota for the possibility of its use as a preventative measure for the condition mentioned above.

Spices and anti-tumoral effects

Many studies on natural plant therapeutic agents have shown some species' anti-tumor effects. Turmeric is a polyphenol extracted from *Curcuma longa,* and *curcumin* is a type of polyphenol derived from the roots of turmeric plants. Curcumin has demonstrated therapeutic efficacy in the treatments against gastric cancer, liver cancer, and colorectal cancer (CRC)[58]. It is considered a spice with anti-tumor activity and inhibits proliferation, invasion, metastasis, and angiogenesis[58]. It also induces apoptosis and autophagy, making the body sensitive to radiotherapy and chemotherapy through miRNA and incRNA-mediated mechanisms[58]. Regarding inhibition of the invasion and metastasis of malignant cells, curcumin affects lung, colon, and cervical cancer[59]. Curcumin also has anti-tumor effects on A172 human glioblastoma cells through autophagy induction. It was observed that when A172 cells were treated with 10nm of curcumin for a specific time, the percentage of dead trypan blue-positive cells increased[60]. Therefore, studies have shown that this spice also has anti-tumor effects on cancer cells of pancreatic, prostate, and esophageal cancer (ESCC). However, one of the limitations in clinical use is its poor bioavailability in humans because curcumin is not easily soluble in water; thus, oral administration does not reach sufficient blood concentrations to obtain therapeutic efficacy. So that it was developed a preparation of curcumin disseminated with colloidal submicron particles, making it easily disperse in water called theracurmin, to improve its bioavailability. Highly bioavailable curcumin has shown anti-tumor effects on various types of ESCC cells and xenografted tumors[61].
Moreover, turmeric extract has effects on human ovarian cancer cells[62]. A study has shown that cell viability is reduced with the highest turmeric concentration[62].
Ginger and its phenolic derivatives also have anticancer action through the arrest of the cell cycle, induction of cancer cell death, misbalancing of redox homeostasis, inhibition of cell proliferation, angiogenesis, migration, and dissemination of cancer cells in different cancer types such as breast cancer, prostate cancer, ovarian cancer, colon cancer, hepatocellular carcinoma, gastric adenocarcinoma, non-small lung epithelium, melanoma, endometrial adenocarcinoma, cervical cancer, lung cancer, head and neck squamous carcinoma, pancreatic cancer[63]. Ginger derivates have high potential chemopreventive properties, and another advantage is that they do not cause side effects. On the other side, their biological applications are limited due to their hydrophobic nature, so it's necessary to use advanced extraction methods to improve their bioavailability[63].
Another medicinal plant with preventive activity against tumors is curry leaves. Indeed, attention has been paid to their varieties of phytochemical components: *Murraya koenigii (M. Koenigii)*, *Micromelum minutum (M. minutum)*, and *Clausena indica*[64]. Their constituents upregulate genes p53 with tumor suppressor activity and downregulate the genes responsible for tumor development[64]. Other compounds of these curry leaves activate apoptosis and the cyclooxygenase pathway[64].
An experimental study demonstrated that alkaloid extracts from *M. Koenigii* have cytotoxic activities in the breast cancer cell line MDA-MB-231 and inhibit inflammation and induce apoptosis in human colon cancer cells (HT-29) in vitro[65]. Another evidence is significant cytotoxic, anticancer, and apoptosis activities in prostate cancer shown by a carbazole alkaloid isolated from *M. koenigii* and *M. minutum*, and its analogs[66]. Potential nutraceutical chemopreventive agents from *M. minutum* leaves have effects on cervical cancer and liver cancer cell lines. In contrast, extracts from its roots have inhibitory effects against the KB cell line. An important alkaloid extract is girinimbine with apoptotic activity on A549 lung cancer cells and another one is Koenimbine isolated from *M. koenigii* studied to assess the efficacy of the inhibition of breast cancer cells

through apoptosis and it has an inhibitory activity of proliferation on prostate cancer cells[66]. Thus plants and their derivates have been shown to have effects against human cancer by stopping or slowing down multiple pathways of carcinogenesis. One of these is cloves, specifically a compound called beta (β)-caryophyllene (BCP), a sesquiterpene. This one is also responsible for the spiciness of black pepper.

Cinnamon is one of the most important herbal drugs traditionally applied to treat gastric diseases, including gastric cancer. An early study on water-soluble extracts of cinnamon showed that it increases the glutathione S-transferase (GST) activity in mice administered urethane, a carcinogenic substance, and prevents carcinogenesis. Cinnamaldehyde or its source *Cinnamomum cassia* powder is reportedly a potent inducer of apoptosis in human promyelocytic leukemia[67]. Studies on the properties of *Cinnamomum zeylanicum* and *Cinnamomum cassia* may imply anti-tumor properties. Cinnamaldehyde was a potent inducer of apoptosis in many studies; this results from induction of reactive oxygen species (ROS). 2-hydroxycinnamaldehyde and 2-benzoyloxycinnamaldehyde isolated from *C. cassia* inhibited in vitro growth of 29 kinds of human cancer cells and in vivo growth of SW-620 human tumor xenograft[68].

Capsaicin, in red peppers, has been demonstrated to induce apoptosis in colon adenocarcinoma, pancreatic cancer, hepatocellular carcinoma, prostate cancer, breast cancer, and many others[69]. The mechanism, not fully elucidated, involves intracellular calcium increase, ROS generation, disruption of mitochondrial membrane transition potential, and activation of transcription factors[69]. *Crocus sativus L* (saffron) and its active components have shown several beneficial pharmacological effects such as anticonvulsant, antidepressant, anti-inflammatory, anti-tumor, radical scavenger effects, learning, and memory-improving effects[70]. Saffron aqueous extract inhibits the progression of gastric cancer in rats[71]. Apoptosis is induced by *C. sativus* in different cancer types (e.g., colorectal, pancreatic, and bladder cancer). Stigmas of *C. sativus* contain crocin, anthocyanin, carotene, and lycopene. These constituents have anti-tumor effects by inhibiting cell growth[72].

PERSPECTIVES AND CONCLUSIONS

As reported above, spices and their specific components have multifunctional properties promoting human health, specifically on the gastrointestinal tract. In recent years, there has been an increased interest on the part of consumers, researchers, and the food industry in how food products can help maintain the health of the organism. At the same time, the role of diet in preventing and treating many illnesses has been demonstrated in various studies. The concept of “adequate nutrition,” representing the quantity and daily distribution of nutrients (carbohydrates, proteins, fats, vitamins, and minerals), is slowly being replaced by the concept of “optimal nutrition,” which also includes the potentiality of foods to promote health, and reduce the risk of developing diseases; hence the term functional food appears. Thus, spices could be used from a functional food point of view, although clear nutritional recommendations about spices are still lacking.

Indeed, although consumers express interest in functional foods such as spices that promote health, health claims related to spices are costly and require a lot of investment. Health claims are science-based and related to the health benefits of products that help consumers to prevent disease and improve their health through dietary decisions using nutritional information. But first, the benefits must be scientifically and widely proven. Specifications for spice health claims are still relatively unclear, and therefore industry could argue that there is a certain amount of inherited cultural knowledge and little scientific evidence. In this context, human clinical trials, specifically randomized controlled trials, are fundamental, and the value of these trials for the food industry is undeniable. Still, too often, nutrients are extracted from their context, following the same methodology used for drug testing. In any case, in many cultures, using spices to prevent or cure pathologies is essential and may serve as the basis for building scientific evidence supporting health benefits.

Conflict of Interest

The authors declare that they have no conflict of interest concerning this article.

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