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Turmeric products: Evaluation of curcumin and trace elements

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ABSTRACT

Turmeric (*Curcuma longa* L.) is valued for its coloring properties, flavor enhancement, functionality, as well as antioxidant and anti-inflammatory effects, which help prevent various diseases. This study aimed to evaluate the levels of curcumin and trace elements (Cr, Co, Ni, As, Mo, Cd, Sb, Ba, Hg, and Pb) in 30 samples of turmeric capsules. The quantification of curcumin was performed by spectrophotometry, with results ranging from 0.03 g/100 g to 37.6 g/100 g. The concentration of trace elements was determined by ICP-MS after acid digestion of the samples. Except for the elements Sb and Hg, which showed levels below the quantification limits (0.002 and 0.008 mg/kg, respectively), the results were: Cr (<0.008–0.083 mg/kg), Co (<0.003–0.78 mg/kg), Ni (<0.008–1.61 mg/kg), As (<0.003–0.083 mg/kg), Mo (<0.008–1.21 mg/kg), Cd (<0.002–0.076 mg/kg), Ba (<0.008–23.48 mg/kg), and Pb (<0.008–0.619 mg/kg). The interaction between curcumin and the trace elements was complex, with no direct relationship found between them. The estimated daily intake (EDI) of curcumin varied from 0.004 to 2.684 mg/kg of body weight, with 13 samples below 10 % of the acceptable daily intake (ADI), 12 samples between 10 % and 50 % of the ADI, and three samples above 50 %. For trace elements, Co showed the highest contribution, corresponding to 2.72 % of the health-based guidance value established by EFSA. A careful approach in marketing turmeric-based products is fundamental to ensure their quality, efficacy, and safety for consumers.

1. Introduction

Recent studies have shown the impact of consumers' demand for foods with functional benefits, such as stress reduction, immune system strengthening, and promotion of healthy aging (Mintel, 2020; Zuo et al., 2023). *Curcuma longa* L. (turmeric), a plant species native to Southeast Asia, stands out for its functional appeal and health-promoting properties. Primarily cultivated for its rhizome, turmeric is commonly used in powdered form to season and color foods (Araújo & Leon, 2001).

Curcuma longa L. has been used in Traditional Chinese Medicine (TCM) due to its health benefits. According to the US Food and Drug Administration (FDA) (2022), turmeric is a botanical compound classified as a dietary supplement, i.e., intended to supplement the diet. The extract of turmeric rhizomes has been authorized for use in food supplements in Brazil, with a daily consumption recommendation, for those over 19 years old, in the range of 80 to 130 mg (Brasil, 2021a), while the turmeric capsule is classified as a herbal medicine according to RDC 463/2021 (Brasil, 2021b).

The pharmacological properties of turmeric have been widely studied, such as anti-inflammatory, antioxidant, anticancer, and neuroprotective activities (Chainani-Wu, 2003; Jiang et al., 2007; Lantz et al., 2005), which have been associated with curcumin, its main curcuminoid (Martins et al., 2023). Curcumin acts as a metal chelating agent, capable of forming complexes with toxic elements such as copper (Cu), chromium (Cr), arsenic (As), mercury (Hg), lead (Pb), and cadmium (Cd). This action helps protect the body against oxidative stress, which is associated with impaired metabolism and cellular malfunction (Kotha & Luthria, 2019).

Curcumin can be used as a food additive and consists of a yellow-orange powder with at least 90 % of coloring material, comprising curcumin or diferuloylmethane, as well as demethoxycurcumin and bis demethoxycurcumin. In Brazil, curcumin is currently authorized by the

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Brazilian Health Regulatory Agency (ANVISA) as a colour food additive in 71 food categories. The use of curcumin in butter is allowed with no specified limit to achieve the desired effect, as long as it preserves the identity of the product (*quantum satis*). In the other categories, its use is restricted to limits ranging from 10 mg/kg (vegetable creams and margarine) to 530 mg/kg (dairy products) (Brasil, 2007; Brasil, 2023). According to the Joint FAO/WHO Expert Committee on Food Additives – JECFA (JECFA, 2004) and the European Food Safety Authority – EFSA (EFSA, 2010a), curcumin has an Acceptable Daily Intake (ADI) of 0–3 mg/kg body weight (JECFA, 2004, Ganiger et al., 2007).

The quality and safety of turmeric-based products depend on several factors throughout the production chain, including high levels of toxic elements in the soil contamination by pesticides, as well as adulteration during the manufacturing process (Xu et al., 2019). As observed for many plant species, various factors can affect the composition of turmeric rhizomes, such as soil type, fertilization, irrigation intensity, stage of rhizome development, and quality of agricultural management (Pereira & Stringheta, 1998; Zuo et al., 2023). In addition to natural variations, turmeric-based products face the challenge of intentional modifications. Controlling these changes is complex due to the lengthy supply chain, the ease of adulteration in powdered products, and the lack of effective methods to detect such adulterations (Khodabakhshian et al., 2021). Adulteration not only causes financial losses but can also expose consumers to toxic compounds, leading to serious health impacts (Forsyth et al., 2018).

The study by Boscariol et al. (2022) evaluated the quality of seven turmeric samples sold in pharmacies and health food stores in Sorocaba, São Paulo, Brazil. The analysis included the determination of Cd, Pb, Hg, Co, As, V, and Ni using X-ray fluorescence with energy dispersion (EDXRF), as well as measuring curcumin concentration by ultra-violet–visible (UV–Vis) spectroscopy. The results revealed variable levels of both metals and curcumin in the samples (Brazilian Pharmacopoeia), with these variations being associated with inadequate quality of the raw materials, underscoring the need for improved quality control. No studies were found that addressed trace elements, curcumin content, or the form of presentation and labeling on curcumin capsules.

Given this context, this study aimed to conduct a comprehensive assessment of the labeling and presentation of samples, curcumin levels and the presence of 10 trace elements (Cr, Co, Ni, As, Mo, Cd, Sb, Ba, Hg, and Pb) in 30 turmeric capsules marketed in Brazil. An exposure assessment and risk characterization, as well as an analysis of the descriptions provided by manufacturers and sellers, were also carried out.

2. Materials and methods

2.1. Reagents and materials

Reagents of analytical grade or higher were used: water purified by reverse osmosis (Gehaka, São Paulo, Brazil), concentrated nitric acid (HNO_3) purified by sub-boiling distillation (Distillacid-Berghof, Eningen, Germany), hydrogen peroxide (H_2O_2) 30 % and ethyl alcohol (Merck, Darmstadt, Germany). The argon and helium gases (Air Liquide, Campinas, Brazil) were used for the ICP-MS analysis.

2.2. Sampling

Thirty samples of turmeric capsules were purchased in the e-commerce, through 20 websites which referenced the presence of turmeric. The information on the labels enabled the samples to be classified into 4 categories: FIT=phytotherapeutic product, TCM=Traditional Chinese Medicine product, NIN=product with novel ingredient, and SUP=food supplement. The samples were stored at room temperature and the internal contents of the capsules (n = 4/sample) were homogenized using a mortar before analysis. The sample identification and the information contained on the label are described in Table 1. A discussion on the labeling and presentation of the samples was conducted to understand

Table 1
Composition of turmeric capsules.

Classification	Sample	Type of capsule	Recommended dose (g/day)	List of ingredients (label)
TCM	C1	Hard	0.55	Turmeric powder (*Curcuma longa* L) and piperine dry extract (*Piper nigrum* L.). Capsule: titanium dioxide and gelatin
	C4	Hard	1.5	Curcuma longa, anti-caking agents: microcrystalline cellulose and tricalcium phosphate, lubricant: magnesium silicate. Capsule: gelatin, humectant glycerin, and purified water
	C6	Hard	NA	Turmeric rhizome powder (*Curcumae longae* rhizoma). Capsule: gelatin
	C8	Hard	1.5	Turmeric (*Curcuma longa*), black pepper (*Piper nigrum*) and corn starch. Capsule: gelatin, humectant glycerin, and red colorant
	C15	Hard	2.0	*Curcuma longa* L, microcrystalline cellulose and starch stabilizer, silicon dioxide anti-caking agent. Capsule: cellulose, chlorophyll, and drinking water
	C16	Hard	NA	Turmeric powder
FIT	C2	Hard	1.0	*Curcuma longa*. Capsule: gelatin, humectant glycerin
	C21	Hard	3.03	*Curcuma longa* – Turmeric and piperine
SUP	C3	Hard	0.55	Turmeric (*Curcuma longa L*) powder. Capsules: gelatin and titanium dioxide
	C5	Hard	1.8	Turmeric (*Curcuma longa*). Capsule: coating agent hydroxypropyl methylcellulose
	C7	Hard	1.95	Turmeric, L-ascorbic acid, and black pepper. Capsule: gelatin and purified water
	C9	Hard	2.0	Turmeric with black pepper
	C10	Hard	1.0	*Curcuma longa* and black pepper aroma. Capsule: gelatin and deionized water
	C11	Hard	1.5	Turmeric (*Curcuma longa*), black pepper (*Piper nigrum*) and corn starch. Capsule: gelatin, humectant glycerin
	C12	Hard	1.0	Concentrated stabilized turmeric,

(*continued on next page*)

Table 1 (*continued*)

Classification	Sample	Type of capsule	Recommended dose (g/day)	List of ingredients (label)
				black pepper, and sufficient quantity of excipient. Capsule: Hydride (cellulose capsule), microcrystalline cellulose, magnesium stearate (vegetable source) and silicon dioxide
	C13	Hard	1.41	Adjuvant: dehydrated turmeric powder, black pepper powder, vitamin C, vitamin D3, vitamin E, selenium, and zinc. Capsule: gelling agent gelatin, vehicle water
	C14	Hard	3.9	*Curcuma longa* rhizome extract, black pepper (*Piper nigrum* L.). Capsule: gelatin and humectant glycerin
	C17	Hard	1.5	Turmeric powder. Capsule: gelatin and humectant glycerin
	C18	Hard	2.4	Turmeric rhizome extract, microcrystalline cellulose and starch stabilizer, and silicon dioxide anti-caking agent. Capsule: cellulose, inorganic colorant chlorophyll, titanium dioxide, and drinking water
	C19	Soft	0.5	Medium-chain triglycerides (vehicle), *Curcuma longa* rhizome extract, selenium-enriched yeast (selenium), DL-alpha tocopherol acetate (vitamin E), and methylcobalamin (vitamin B12). Capsule: gelatin, purified water, and humectant glycerin
	C20	Hard	1.0	Turmeric. Capsule: vegetarian gelatin and purified water
	C22	Hard	2.0	100 % Turmeric
	C24	Hard	1.0	Curcuma longa rhizome extract (Curcumin), corn starch, and INS170i stabilizer. Capsule: gelatin and humectant glycerin
	C25	Hard	1.2	Turmeric (*Curcuma longa*) powder. Capsule: gelatin and humectant glycerin
	C26	Hard	1.0	Turmeric powder, pepper powder. Excipient: starch. Anti-caking agent: silicon dioxide. Capsule: hypromellose
	C27	Tablets	2.0	*Curcuma longa*, black pepper, magnesium stearate, anti-caking agent: silicon dioxide
	C28	Tablets	2.8	Turmeric powder. Carrier: maltodextrin. Lubricant: magnesium stearate; anti-caking agent: silicon dioxide
	C29	Soft	1.0	Medium-chain triglycerides, turmeric rhizome extract, and sunflower lecithin emulsifier. Capsule: gelatin, purified water, humectant glycerin, and colorants – turmeric and annatto
	C30	Hard	1.0	*Curcuma longa* and black pepper flavoring. Capsule: gelatin and deionized water
NIN	C23	Hard	1.0	Turmeric powder and anti-caking agent talc. Capsule: gelatin.

FIT=phytotherapeutic product; **TCM**=Traditional Chinese Medicine product; **NIN**=product with novel ingredient; **SUP**=food supplement; **NA**=Not available.

how these products are presented to consumers.

Due to the unavailability of certified reference materials to validate the analytical method and compare results, a sample of turmeric *in natura* was purchased in Campinas-SP and spiked experiments were performed at three different levels (0.005, 0.025, and 0.050 mg/kg).

2.3. Determination of curcumin content

The analysis of curcumin was conducted as described by the curcumin monograph (JECFA, 2003) and by the Adolfo Lutz Institute (IAL, 2008). For that, 0.1 g of the sample was weighed and dissolved in analytical-grade ethyl alcohol in a 200 mL volumetric flask. Then, 10 mL of the solution was transferred to a 100 mL volumetric flask and the volume was made up of ethyl alcohol. Absorbance measurements were carried out at 425 nm using a UV–Vis spectrophotometer (Agilent Technologies, Mulgrave, Australia) and 1 cm cuvettes. The analyses were performed in duplicate and analytical blanks were prepared with analytical grade ethyl alcohol.

The curcumin content was calculated according to the relationship:

$$Curcumincontent(g/100g) = \frac{A*200*100}{10*M*1607}$$

where: A=absorbance at 425 nm; M=sample weight (g); ε (molar absorptivity) = 1607 L/mol.cm (IAL, 2008).

2.4. Determination of trace elements

For the determination of trace elements (Cr, Co, Ni, As, Mo, Cd, Sb, Ba, Hg, and Pb), the acid digestion method in a digester block (Tecnal, Piracicaba, Brazil) was used, as proposed by Rebellato et al. (2020). An aliquot of 0.25 g of the sample was weighed into a glass tube and 4 mL of nitric acid was added. The mixture was heated in a digester block for 2 h at 100 °C. After cooling, 2 mL of hydrogen peroxide (30 %) was added and the tube was heated again for 2 h at 100 °C. After cooling, the contents were transferred to a graduated tube and the volume was made up to 20 mL with ultrapure water and filtered (PTFE, 0.45 μm) for analysis by ICP-MS. The tests were carried out in triplicate, including analytical blanks to guarantee the accuracy of the results.

The trace elements were quantified using ICP-MS (iCAP RQ, Thermo Scientific, Bremen, Alemanha), under optimal conditions: Power = 1500 W; Ar flow rate = 14.0 L/min; Auxiliary Ar = 0.80 L/min; He flow rate = 5.00 mL/min; Micromist nebulizer flow rate = 0.98 L/min; Dwell time = 0.3 s and 0.02 s (IS=internal standard); Isotopes ^{53}Cr, ^{59}Co, ^{60}Ni, ^{75}As, ^{97}Mo, ^{111}Cd, ^{123}Sb, ^{137}Ba, ^{20}2Hg, ^{208}Pb, ^{45}Sc (IS), ^{72}Ge (IS), ^{103}Rh (IS), ^{115}In (IS), ^{209}Bi (IS), ^{195}Pt. The analytical curves ranged from 0.0001 to 1.0 mg/L.

2.4.1. Analytical quality control

The analytical control was evaluated by the figures of merit: limit of detection (LOD), limit of quantification (LOQ), accuracy, and precision, according to INMETRO (2020) and AOAC (2016). LOD and LOQ were calculated as LOD=3* s* f and LOQ=5* s* f; where s = standard deviation of the concentration of 10 blank experiments and f = dilution factor (80x). The results are shown in Table 2.

The LODs and LOQs ranged from 0.0004 to 0.008 mg/kg and were considered adequate for all elements. Accuracy was assessed by recovery tests at three fortification levels (0.005, 0.025, and 0.050 mg/kg) and recovery values ranged from 66 % (As) to 108 % (Ba). Precision was assessed by analyzing the turmeric sample *in natura* (n = 7) and the coefficient of variation ranged from 1.0 % (Pb) to 2.9 % (Ba). All results were in accordance with the guidelines of INMETRO (2020) and AOAC (2016).

2.5. Exposure assessment and risk characterization

Due to the recognition of the medicinal properties of turmeric and its use in culinary ("homology of medicine and food"), the exposure assessment and risk characterization were used to evaluate the safety of the samples (Kunnumakkara et al, 2016; Hewlings & Kalman 2017).

The Estimated Daily Intake (EDI) of curcumin and trace elements from the consumption of the samples was determined using the equation: EDI (mg/kg body weight) = (C×D) / P; where: C=concentration of curcumin or trace element in the sample (mg/g); D=recommended daily intake (g), P=body weight (bw) of the adult individual (70 kg). The risk characterization was evaluated by comparing the EDI with the safety parameters of curcumin and trace elements.

2.6. Statistical analysis

The results for trace elements were presented as mean $\bar{x} \pm$ standard deviation (SD) and subjected to F-test, one-way analysis of variance (ANOVA), with a 95 % confidence level. All analyses were performed using the software Statistic 7.0 (StatSoft, Tulsa, EUA) and the multivariate analysis was conducted by Pirouette 3.11 (Infometrix, Woodinville, EUA).

3. Results and discussion

3.1. Labeling and presentation of samples

As shown in Table 1**,** the most common form of presentation of the samples was the hard capsule (86.6 %), followed by soft capsules (2.7 %) and tablets (2.7 %). Concerning the composition, 30 % of the samples (C2, C3, C5, C6, C16, C17, C20, C22, and C25) contained turmeric exclusively. Around 43 % of the samples included pepper (C1, C7, C8, C9, C10, C11, C12, C13, C14, C21, C26, C27, and C30), while 27 % (C4, C15, C18, C19, C23, C24, C28, and C29) contained ingredients other than pepper. The addition of pepper, or piperine, to these products, is a strategy to improve the bioavailability of curcumin, which in turn is characterized by rapid metabolism and accelerated systemic elimination (Anand et al., 2007; Shoba et al.,1998; Martins et al., 2023).

Regarding consumption recommendations, two samples did not display this information on their labels. Studies involving the consumer population can help identify the motivations for consumption and assess whether the doses of curcumin consumed are adequate for the expected benefits and the dosages recommended in the literature.

In Brazil, there are few studies evaluating turmeric-based products on the market, concerning their nutritional, chemical, biological, and/or regulatory compliance aspects. To understand the characteristics that are most associated with turmeric consumption, an analysis of the descriptions found on the websites from which the samples were purchased was conducted. The data was compiled into a word cloud (Fig. 1).

From the description of the samples, 113 different terms were listed, and the most relevant were "anti-inflammatory" (22 occurrences), "antioxidant" (19 occurrences), "cholesterol" (11 occurrences), and "liver" (10 occurrences). The websites selling four samples (C16, C18, C25, and C29) mentioned no benefits associated with turmeric consumption. In Brazil, both Traditional Chinese Medicine (TCM) products and supplements (SUP) are not authorized to make therapeutic or health claims (Brasil, 2014; Brasil, 2018; Brasil, 2021a). As reported by Molin et al. (2019), claims often result from spontaneous strategies adopted by retailers, and the lack of regulation in the marketing of these products often leads to inappropriate content. This practice can expose consumers

Table 2
Results of the limit of detection (LOD), the limit of quantification (LOQ), accuracy (experimental values, and recovery, n = 3), and precision (coefficient of variation, CV%; n = 7) for the trace elements.

Element	LOD (mg/kg)	LOQ (mg/kg)	Accuracy						Precision (CV, %)
			Level 1 (0.005 mg/kg)		Level 2 (0.025 mg/kg)		Level 3 (0.050 mg/kg)		
			mg/kg	%	mg/kg	%	mg/kg	%	
Cr	0.0024	0.0080	0.0047	94	0.0251	100	0.0516	103	2.2
Co	0.0008	0.0032	0.0045	90	0.0226	90	0.0452	90	1.8
Ni	0.0024	0.0080	0.0042	85	0.0220	88	0.0448	90	2.1
As	0.0008	0.0032	0.0034	68	0.0166	66	0.0328	66	1.7
Mo	0.0024	0.0080	0.0041	82	0.0235	94	0.0477	95	1.1
Cd	0.0004	0.0016	0.0035	70	0.0172	69	0.0339	68	1.6
Sb	0.0008	0.0032	0.0034	68	0.0179	71	0.0360	72	1.9
Ba	0.0024	0.0080	0.0054	108	0.0206	82	0.0397	79	2.9
Hg	0.0016	0.0080	0.0033	67	0.0180	72	0.0359	72	1.4
Pb	0.0024	0.0080	0.0043	86	0.0220	88	0.0442	88	1.0

LOD=Limit of detection; **LOQ**=Limit of quantification; **CV**=coefficient of variation, n = 7.

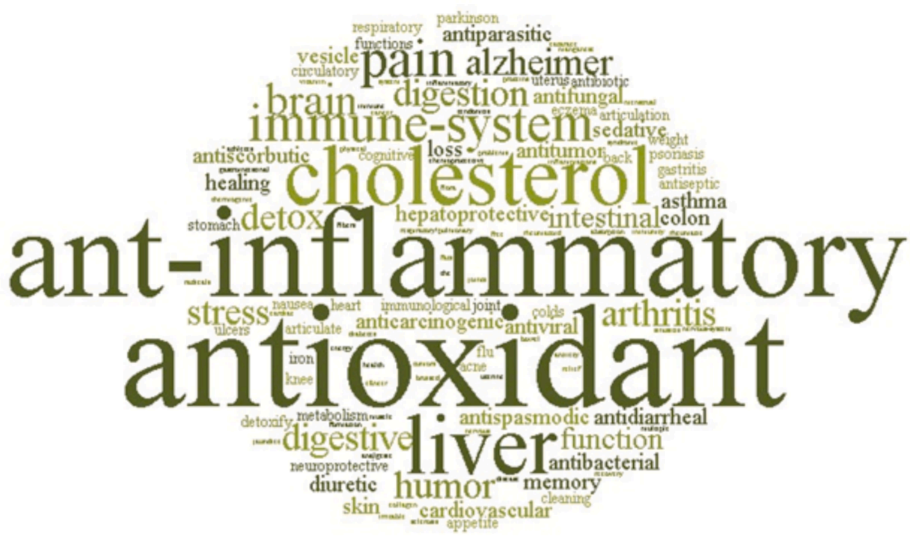

Fig. 1. Terms used in the description of turmeric products on websites.

to misleading information, negatively impacting their purchasing experience.

3.2. Curcumin content

The curcumin contents of the capsules are shown in Table 3. The curcumin content ranged from 0.030 g/100 g in sample C10 to 37.6 g/100 g in sample C19, with an average of 3.52 g/100 g and a median of 1.48 g/100 g. These results indicate an asymmetric distribution, with a concentration of values in the lower range, result in agreement with the study by Boscariol et al. (2022). According to Govindarajan & Stahl (1980), around 1 to 6 % of the rhizome's composition corresponds to curcuminoids. Of the 30 samples evaluated, 47 % (n = 16) had a content within this range and the soft capsules (C19 and C29) had a curcumin content of more than 6 %, probably due to the form in which they were marketed (liquid) or the use of turmeric extract in their formulation. Nine SUP samples (C10, C14, C17, C18, C20, C26, C27, C28, and C30) and three TCM samples (C4, C15, and C16), corresponding to 40 % of the total samples, had an average curcumin content of less than 1 %, which may be associated with the presence of other ingredients in the formulation. Samples with curcumin levels lower than 0.39 % (C16, C17, and C20 containing 0.16 ± 0.01, 0.39 ± 0.01, and 0.214 ± 0.001 g/100 g, respectively), with only the turmeric declared in their list of ingredients (Table 1), suggest incomplete description of the constituents on the labels.

Table 3
Curcumin contents (x ± SD g/100 g) of the samples, estimated exposure, and contribution to the Acceptable Daily Intake (ADI).

Sample		Curcumin content (g/100 g)	Estimated exposure (mg/kg bw)	Contribution to the ADI (%)
TCM	**C1**	5.04 ± 0.05	0.396	13.2
	C4	0.41 ± 0.01	0.088	2.9
	C6	2.26 ± 0.03	NA	NA
	C8	1.48 ± 0.01	0.316	10.5
	C15	0.134 ± 0.001	0.038	1.3
	C16	0.16 ± 0.01	NA	NA
FIT	**C2**	1.48 ± 0.03	0.212	7.1
	C21	1.08 ± 0.01	0.466	15.5
SUP	**C3**	4.94 ± 0.13	0.388	12.9
	C5	3.26 ± 0.02	0.837	27.9
	C7	5.62 ± 0.05	1.566	52.2
	C9	1.52 ± 0.06	0.434	14.5
	C10	0.030 ± 0.002	0.004	0.1
	C11	2.59 ± 0.18	0.555	18.5
	C12	2.37 ± 0.03	0.339	11.3
	C13	1.22 ± 0.01	0.247	8.2
	C14	0.91 ± 0.02	0.509	17.0
	C17	0.39 ± 0.01	0.084	2.8
	C18	0.083 ± 0.001	0.028	0.9
	C19	37.6 ± 3.8	2.684	89.5
	C20	0.214 ± 0.001	0.031	1.0
	C22	3.48 ± 0.03	0.995	33.2
	C24	1.84 ± 0.02	0.263	8.8
	C25	3.90 ± 0.01	0.668	22.3
	C26	0.041 ± 0.003	0.006	0.2
	C27	0.071 ± 0.001	0.020	0.7
	C28	0.328 ± 0.002	0.131	4.4
	C29	17.6 ± 0.2	2.512	83.7
	C30	0.128 ± 0.002	0.018	0.6
NIN	**C23**	5.49 ± 0.11	0.784	26.1

FIT=phytotherapeutic product; **TCM**=Traditional Chinese Medicine product; **NIN**=product with novel ingredient; **SUP**=food supplement; **NA**=Not available.

According to the manufacturers' recommendations (Table 1), the estimated daily intake (EDI) of curcumin varied from 0.004 to 2.684 mg/kg bw. Compared to the ADI, which provides an estimate of the amount of a substance considered safe for daily and continuous consumption, the exposure in 13 scenarios was less than 10 % of the ADI; in 12 scenarios, it ranged between 10 and 50 % of the ADI while in three scenarios it exceeded 50 % of the ADI. Therefore, it is clear that the consumption of these product categories significantly contributes to the intake of curcumin, thus requiring an integrated assessment of the exposure to the substance used as a food additive and as a seasoning as well. This assessment is necessary to determine the exposure to the compound and to establish regulatory measures to ensure the consumers' safety.

3.3. Trace elements

The levels of the inorganic elements present in the turmeric sample *in natura* and the turmeric capsules are shown in Table 4, except for the elements Sb and Hg, which showed results below the LOQs (0.002 and 0.008 mg/kg, respectively).

As can be seen in Table 4, the concentrations of the inorganic elements varied among the samples, with significant differences ($p < 0.05$) observed by One-way ANOVA and Tukey's test. The results can be due to the different brands of the samples analyzed, variations in the capsule formulations, and differences in the origin of the raw materials (Filipiak-

Table 4
Concentration of trace elements ($\bar{x} \pm$ SD mg/kg) of the samples.

Sample		Cr	Co	Ni	As	Mo	Cd	Ba	Pb
		$\bar{x} \pm$ SD mg/kg							
In Natura		0.056 ± 0.004	0.010 ± 0.002	0.061 ± 0.003	<LOQ	0.031 ± 0.004	<LOQ	1.84 ± 0.25	0.054 ± 0.008
TCM	**C1**	0.10 ± 0.01	0.018 ± 0.002	0.10 ± 0.02	<LOQ	0.160 ± 0.004	<LOQ	1.52 ± 0.16	0.030 ± 0.003
	C4	0.37 ± 0.03	0.39 ± 0.03	0.54 ± 0.04	<LOQ	0.01 ± 0.002	<LOQ	3.98 ± 0.21	0.023 ± 0.001
	C6	0.09 ± 0.02	0.022 ± 0.001	0.13 ± 0.01	<LOQ	0.15 ± 0.03	<LOQ	0.56 ± 0.05	<LOQ
	C8	0.30 ± 0.04	0.15 ± 0.02	0.25 ± 0.04	<LOQ	0.12 ± 0.01	0.013 ± 0.001	12.49 ± 0.35	0.21 ± 0.02
	C15	0.20 ± 0.01	0.05 ± 0.01	0.16 ± 0.01	<LOQ	0.031 ± 0.002	<LOQ	4.04 ± 0.22	0.55 ± 0.08
	C16	0.86 ± 0.09	0.111 ± 0.004	0.40 ± 0.05	0.06 ± 0.01	0.04 ± 0.01	<LOQ	2.35 ± 0.06	<LOQ
FIT	**C2**	0.14 ± 0.04	<LOQ	0.023 ± 0.005	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
	C21	1.27 ± 0.13	0.15 ± 0.02	0.43 ± 0.02	0.04 ± 0.01	0.05 ± 0.01	0.020 ± 0.001	18.49 ± 0.40	0.44 ± 0.04
SUP	**C3**	0.15 ± 0.03	0.033 ± 0.002	0.05 ± 0.01	<LOQ	0.20 ± 0.01	<LOQ	3.31 ± 0.26	0.04 ± 0.01
	C5	0.57 ± 0.07	0.34 ± 0.02	0.64 ± 0.01	0.03 ± 0.01	0.10 ± 0.01	<LOQ	5.16 ± 0.17	0.191 ± 0.003
	C7	0.16 ± 0.01	0.109 ± 0.005	0.26 ± 0.01	<LOQ	0.057 ± 0.004	<LOQ	9.63 ± 0.48	0.08 ± 0.01
	C9	0.06 ± 0.01	<LOQ	0.05 ± 0.01	<LOQ	0.06 ± 0.01	<LOQ	0.54 ± 0.09	<LOQ
	C10	0.14 ± 0.01	0.17 ± 0.01	0.26 ± 0.01	<LOQ	0.021 ± 0.004	<LOQ	2.66 ± 0.17	0.05 ± 0.01
	C11	1.10 ± 0.05	0.12 ± 0.01	0.73 ± 0.03	0.08 ± 0.01	0.049 ± 0.003	<LOQ	4.08 ± 0.13	0.16 ± 0.03
	C12	0.38 ± 0.04	0.31 ± 0.03	0.23 ± 0.03	<LOQ	0.65 ± 0.01	<LOQ	14.46 ± 0.23	0.16 ± 0.02
	C13	0.33 ± 0.06	0.082 ± 0.005	0.17 ± 0.03	0.027 ± 0.001	1.21 ± 0.08	<LOQ	11.79 ± 0.72	0.32 ± 0.03
	C14	1.73 ± 0.16	0.78 ± 0.08	1.61 ± 0.09	0.031 ± 0.003	0.13 ± 0.02	0.034 ± 0.003	8.94 ± 0.31	0.62 ± 0.10
	C17	1.00 ± 0.09	0.26 ± 0.02	0.55 ± 0.06	0.02 ± 0.01	0.021 ± 0.001	<LOQ	11.62 ± 0.55	0.07 ± 0.01
	C18	0.17 ± 0.02	0.044 ± 0.002	0.11 ± 0.02	<LOQ	0.26 ± 0.01	<LOQ	4.46 ± 0.07	<LOQ
	C19	0.81 ± 0.07	0.275 ± 0.004	0.438 ± 0.001	<LOQ	0.27 ± 0.01	0.02 ± 0.002	23.48 ± 0.47	0.11 ± 0.01
	C20	0.33 ± 0.03	0.59 ± 0.05	0.134 ± 0.002	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
	C22	<LOQ	0.029 ± 0.002	0.06 ± 0.01	<LOQ	<LOQ	<LOQ	0.37 ± 0.06	0.13 ± 0.01
	C24	<LOQ	0.022 ± 0.001	1.39 ± 0.05	<LOQ	<LOQ	<LOQ	0.82 ± 0.20	0.08 ± 0.02
	C25	0.85 ± 0.10	0.205 ± 0.002	0.55 ± 0.01	<LOQ	0.65 ± 0.02	<LOQ	17.45 ± 0.77	0.15 ± 0.02
	C26	0.13 ± 0.01	0.125 ± 0.002	0.38 ± 0.03	<LOQ	0.017 ± 0.001	<LOQ	4.06 ± 0.19	0.16 ± 0.03
	C27	0.23 ± 0.03	0.21 ± 0.03	0.31 ± 0.02	<LOQ	0.31 ± 0.02	0.026 ± 0.003	10.38 ± 0.65	0.24 ± 0.01
	C28	0.53 ± 0.08	0.19 ± 0.01	0.40 ± 0.02	<LOQ	0.222 ± 0.005	<LOQ	22.09 ± 0.75	0.56 ± 0.04
	C29	0.48 ± 0.09	0.29 ± 0.02	0.39 ± 0.04	<LOQ	0.32 ± 0.04	<LOQ	22.63 ± 1.24	0.29 ± 0.05
	C30	0.34 ± 0.03	0.012 ± 0.001	0.28 ± 0.02	<LOQ	0.013 ± 0.004	<LOQ	0.80 ± 0.11	0.13 ± 0.02
NIN	**C23**	0.47 ± 0.02	0.30 ± 0.02	0.87 ± 0.02	0.083 ± 0.002	0.21 ± 0.01	0.076 ± 0.004	9.99 ± 0.25	0.41 ± 0.06

FIT=phytotherapeutic product; **TCM**=Traditional Chinese Medicine product; **NIN**=product with novel ingredient; **SUP**=food supplement. **LOQ**=0.008 (Cr, Ni, Mo, Ba, Pb); 0.003 (Co, As) and 0.002 (Cd) mg/kg.

Szok et al., 2015; Benutić et al., 2022).

The presence of the trace elements Cr, Co, Ni, and Mo in the turmeric *in natura* and turmeric capsules may be due to the essential role of these elements for plants (Filipiak-Szok et al., 2015). The levels of As and Cd were below the LOQ for turmeric *in natura* and for most of the capsules. However, exceptions were observed for As in eight samples (C5, C11, C13, C14, C17, C16, C21, and C23) and Cd in six samples (C14, C19, C27, C8, C21, and C23), corresponding to the products from four different categories presented in Table 1. These results corroborate the findings of Filipiak-Szok et al. (2015), who reported similar levels of Pb, Cd, As, and Sb in two turmeric samples.

For inorganic contaminants, Brazilian legislation does not establish maximum tolerated limits (MTLs) for turmeric or rhizomes (Brasil, 2022). MTLs are established for the roots and tubers category, which includes total As (0.20 mg/kg), Cd (0.10 mg/kg), and Pb (0.10 mg/kg). These last two limits are also covered by European Regulation 2023/915 (EU, 2023) for the same category. The European regulation also sets maximum Pb levels of 0.80 and 1.50 mg/kg for turmeric *in natura* and rhizomes, respectively (EU, 2023).

Regarding the concentrations of the elements As, Cd, and Pb, which have MTLs according to the legislation in force in Brazil (Brasil, 2022), all samples were below the maximum values established for As and Cd in roots and tubers. For Pb, the levels were above the MTL (0.10 mg/kg) in 10 SUP samples (C5, C11, C12, C13, C14, C25, C26, C27, C28, and C29), two TCM samples (C8 and C15), one FIT sample (C21), in addition to the sample classified as NIN (C23) and the sample *in natura*. However, when considering the limit set by the European Union for turmeric *in natura* (0.80 mg/kg), all samples showed levels below this limit.

Some samples presented higher Pb concentration when compared to the elements As and Cd. This result may be due to an inherent characteristic of the plant (*Curcuma longa*) or the soil in which it is grown. Zuo et al. (2023) have compiled the results about heavy metals in Traditional Chinese Medicine (TCM) products over the last 10 years and reported that although the proportion of samples exceeding the limits for Pb, Cd, As, and Hg was generally low, contamination in certain TCM, such as the presence of Cd in turmeric, cannot be overlooked. There are also differences in the levels of heavy metal contamination in TCM from different cultivation regions. High Pb levels may be due to the improper use of lead chromate ($PbCrO_4$) to enhance the color of turmeric. Forsyth et al. (2018) and Gleason et al. (2014) found high Pb levels in blood samples from Asian individuals and turmeric samples consumed by those individuals. Lead exposure can cause behavioral problems, learning deficits, anemia, miscarriage, and premature birth (Wani, Aram & Usmani, 2015).

Hierarchical clustering analysis (HCA) was used to explore the similarity in the trace element composition among turmeric capsules. The results were arranged in a 30x8 matrix, where the rows represent the samples and the columns represent the trace elements. Data were normalized and the analysis was conducted using Euclidean distance. In this technique, samples that show greater similarity in their trace element composition ($s = 0.494$) are positioned closer to each other on the dendrogram (Fig. 2).

Fig. 2 allowed the samples to be classified into three distinct groups (Groups A, B, and C), as follows:

– Group A (Samples C01, C02, C03, C06, C07, C09, C10, C15, C18, C22, C24, C26, and C30), characterized by the lowest concentrations of the trace elements As, Cd, Cr, Co, Mo, and Ba;

– Group B (Samples C11 and C16), characterized by high concentrations of As and Cr;

– Group C (Samples C04, C05, C08, C12, C17, C19, C21, C25, C27, C28, and C29), containing a high Ba concentration. The samples classified as supplements predominated in this group.

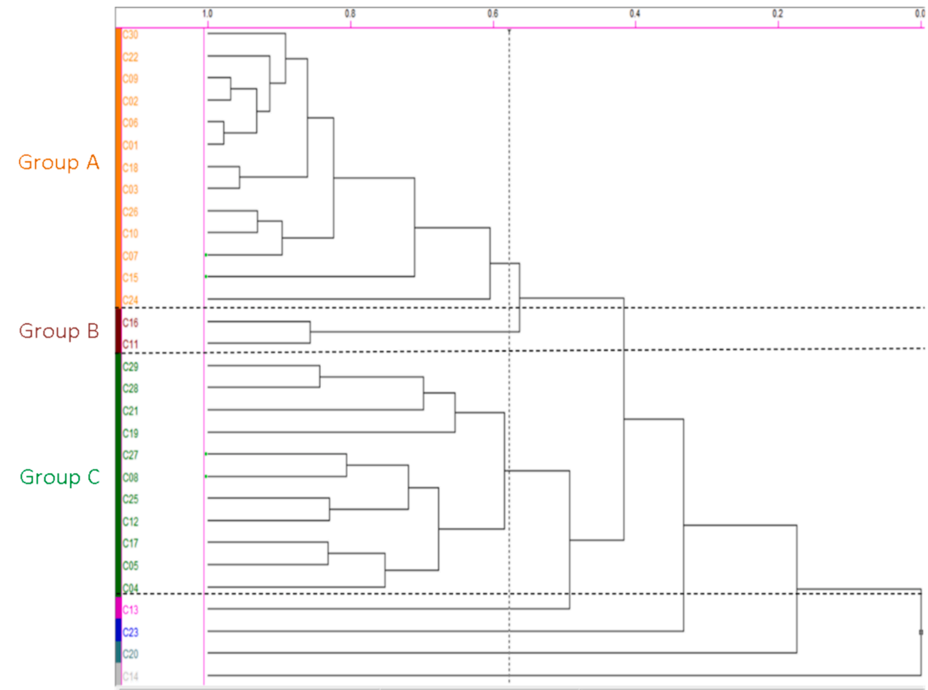

Fig. 2. Hierarchical cluster analysis (HCA) of turmeric samples.

Four samples did not cluster with the others (C13, C14, C20, and C23), presenting different trace element compositions. Sample C13 (SUP), a supplement enriched with vitamins and minerals, showed high Mo levels with 1.21 mg/kg. Sample C14 (SUP), a supplement combining turmeric and pepper, exhibited higher Cr, Co, Ni, and Pb levels, with values of 1.73, 0.78, 1.61, and 0.62 mg/kg, respectively. Sample C20 (SUP), a supplement containing only turmeric, exhibited high Co levels with 0.59 mg/kg. Finally, sample C23 (NIN), composed solely of turmeric, had quantifiable levels of As and Cd with concentrations of 0.083 and 0.076 mg/kg, respectively.

Table 5
Estimated daily intake (EDI) of trace elements by consuming the dose of turmeric capsules recommended by the manufacturers, considering an adult weighing 70 kg.

Sample		**EDI (µg/kg bw)**							
		Cr	**Co**	**Ni**	**As**	**Mo**	**Cd**	**Ba**	**Pb**
In Natura		–	–	–	–	–	–	–	–
TCM	**C1**	0.0008	0.0001	0.0008	ND	0.0013	ND	0.012	0.0002
	C4	0.0079	0.0084	0.0116	ND	0.0002	ND	0.085	0.0005
	C6	–	–	–	–	–	–	–	–
	C8	0.0064	0.0032	0.0054	ND	0.0026	0.0003	0.268	0.0045
	C15	0.0057	0.0014	0.0046	ND	0.0009	ND	0.115	0.0157
—	**C16**	–	–	–	–	–	–	–	–
FIT	**C2**	0.0020	ND	0.0003	ND	ND	ND	ND	ND
	C21	0.0550	0.0065	0.0186	0.0017	0.0022	0.0009	0.800	0.0190
SUP	**C3**	0.0012	0.0003	0.0004	ND	0.0016	ND	0.026	0.0003
	C5	0.0147	0.0087	0.0165	0.0008	0.0026	ND	0.133	0.0049
	C7	0.0045	0.0030	0.0072	ND	0.0016	ND	0.268	0.0022
	C9	0.0017	ND	0.0014	ND	0.0017	ND	0.015	ND
	C10	0.0020	0.0024	0.0037	ND	0.0003	ND	0.038	0.0007
	C11	0.0236	0.0026	0.0156	0.0017	0.0011	ND	0.087	0.0034
	C12	0.0054	0.0044	0.0033	ND	0.0093	ND	0.207	0.0023
	C13	0.0066	0.0017	0.0034	0.0005	0.0244	ND	0.237	0.0064
	C14	0.0964	0.0435	0.0897	0.0017	0.0072	0.0019	0.498	0.0345
	C17	0.0214	0.0056	0.0118	0.0004	0.0005	ND	0.249	0.0015
	C18	0.0058	0.0015	0.0038	ND	0.0089	ND	0.153	ND
	C19	0.0058	0.0020	0.0031	ND	0.0019	0.0001	0.168	0.0008
	C20	0.0047	0.0084	0.0019	ND	ND	ND	ND	ND
	C22	ND	0.0008	0.0017	ND	ND	ND	0.011	0.0037
	C24	ND	0.0003	0.0199	ND	ND	ND	0.012	0.0011
	C25	0.0146	0.0035	0.0094	ND	0.0111	ND	0.299	0.0026
	C26	0.0019	0.0018	0.0054	ND	0.0002	ND	0.058	0.0023
	C27	0.0066	0.0060	0.0089	ND	0.0089	0.0007	0.297	0.0069
	C28	0.0212	0.0076	0.0160	ND	0.0089	ND	0.884	0.0224
	C29	0.0069	0.0041	0.0056	ND	0.0046	ND	0.323	0.0041
	C30	0.0049	0.0002	0.0040	ND	0.0002	ND	0.011	0.0019
NIN	**C23**	0.0067	0.0043	0.0124	0.0012	0.0030	0.0011	0.143	0.0059

FIT=phytotherapeutic product; **TCM**=Traditional Chinese Medicine product; **NIN**=product with novel ingredient; **SUP**=food supplement; **ND**=Not Determined.

3.3.1. Exposure assessment

The EDI of trace elements is shown in Table 5, which considers the daily portion of turmeric capsules recommended by the manufacturers (Table 1) and a standard weight of 70 kg for adults.

To characterize the risk associated with the exposure to trace elements, similarly to the work of Fioravanti et al. (2023), the EDI values were compared to the health-based guidance values available in the literature: Benchmark Dose Lower Limit (BMDL) for inorganic As (3.0 μg/kg bw day) and Pb (15 μg/kg bw day); Provisional Tolerable Monthly Intake (PTMI) for Cd (25 μg/kg bw month); Tolerable Daily Intake (TDI) for Cr III (300 μg/kg bw day), Ni (13 μg/kg bw day) and Ba (200 μg/kg bw day); Upper Intake Level (UL) for Mo (600 μg day) and health-based guidance value for Co (1.6 μg/kg bw day) for threshold effects (EFSA, 2010b, 2012a,b, 2013, 2020, 2021, 2022; FAO/WHO, 2011, 2022). Table 6 shows the most significant contributions identified in the risk characterization associated with exposure to the trace elements studied, calculated according to item 2.5.

In general, the daily intake values were low, ranging from 0.0002 to 0.096 μg/kg bw for the trace elements As, Cd, Co, Cr, Ni, and Pb in the samples where these elements were quantifiable. For Mo and Ba, the daily intake varied between 0.013 and 1.71 μg/kg bw and 0.011 and 0.88 μg/kg bw, respectively. The results in Table 6 show that the health-based guidance values were higher than the EDI observed in the exposure assessment. The greater contributions were identified for the samples classified as supplements, with emphasis on the estimated values for Co and Ni in sample C14, corresponding to 2.72 % of the health-based guidance value for threshold effects and 0.69 % of the TDI, respectively.

4. Conclusion

The results of this study revealed a wide variation in the levels of curcumin and trace elements, notably concerning Pb levels above 0.1 mg/kg and low concentrations of curcumin (<0.39 g/100 g). The interactions between curcumin and the trace elements are complex, with no direct relationship between these compounds.

The comparative analysis of curcumin exposure showed that most scenarios fall below 50 % of the ADI, suggesting a moderate impact from the consumption of these products. Concerning the trace elements, the greater contribution in the risk characterization was observed for Co, which corresponded to approximately 3 % of the health-based guidance value established by EFSA for threshold effects. A comprehensive evaluation of the consumption of turmeric capsules is recommended to ensure quality, safety, and efficacy for consumers.

CRediT authorship contribution statement

Maria Isabel Andrekowisk Fioravanti: Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Fernanda Peixoto Pizano:** Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ana Paula Rebellato:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation. **Raquel Fernanda Milani:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation. **Marcelo Antonio Morgano:** Writing – review & editing, Supervision, Resources, Conceptualization. **Adriana Pavesi Arisseto Bragotto:** Writing – review & editing, Resources, 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.

Table 6
Risk characterization associated with exposure to trace elements through the consumption of the recommended dose of turmeric capsules by manufacturers, considering a 70 kg adult.

Trace element	Health-based guidance value (HBGV)		Major contributions
Cr	TDI	Cr III, 300 μg/kg bw (EFSA, 2014)	C14 = 0.032 % (SUP) C21 = 0.018 % (FIT)
Co	HBVG for threshold effects	1.6 μg/kg bw (EFSA, 2012b)	C14 = 2.72 % (SUP) C5 = 0.55 % (SUP)
Ni	TDI	13 μg/kg bw (EFSA, 2020)	C14 = 0.69 % (SUP) C24 = 0.15 % (SUP)
As	$BMDL_{0.5}$	i-As, 3.0 μg/kg bw (FAO/WHO, 2011)	C14 = 0.058 % (SUP) C11 = 0.057 % (SUP)
Mo	UL	600 μg (EFSA, 2013)	C13 = 0.28 % (SUP) C25 = 0.13 % (SUP)
Cd	PTMI	25 μg/kg bw (FAO/WHO, 2022)	C14 = 0.23 % (SUP) C23 = 0.13 % (NIN)
Ba	TDI	200 μg/kg bw (EFSA, 2022)	C21 = 0.44 % (SUP) C21 = 0.40 % (FIT)
Pb	$BMDL_{01}$	15 μg/kg bw (EFSA, 2010)	C14 = 0.23 % (SUP) C28 = 0.15 % (NIN)

BMDL=Benchmark Dose Lower Limit; **PTMI**=Provisional Tolerable Monthly Intake; **TDI**=Tolerable Daily Intake; **UL**=Upper Intake Level.

Data availability

Data will be made available on request.

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References

Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: Problems and promises. *Molecular Pharmaceutics, 4*(6), 807–818. https://doi.org/10.1021/mp700113r

Aoac. (2016). *International, Official Methods of Analysis of AOAC International*. Guidelines for standard method performance requirements (Appendix F): AOAC International, Gaithersburg.

Araújo, C. A. C., & Leon, L. L. (2001). Biological activities of Curcuma longa L. *Memorias Do Instituto Oswaldo Cruz, 96*(5), 723–728. https://doi.org/10.1590/S0074-02762001000500026

Benutić, A., Marciuš, B., Nemet, I., & Rončević, S. (2022). Chemometric classification and discrimination of herbal dietary supplements based on ICP-MS elemental profiling. *Journal of Food Composition and Analysis, 114*(July). https://doi.org/10.1016/j.jfca.2022.104794

Boscariol, R., Paulino, T. H., Oliveira, J. M., Jr., Balcão, V. M., & Vila, M. M. D. C. (2022). Characterization of commercially available turmeric for use in pharmaceutical products and food supplements. *Journal of the Brazilian Chemical Society, 33*(12), 1392–1401. https://doi.org/10.21577/0103-5053.20220073

Brasil (2021a). *Instrução Normativa - IN n° 102, de 15 de outubro de 2021*. Altera a Instrução Normativa n° 28, de 26 de julho de 2018, que estabelece as listas de constituintes, de limites de uso, de alegações e de rotulagem complementar dos suplementos alimentares. Available online: https://antigo.anvisa.gov.br/documents/10181/6254004/IN_102_2021_.pdf/855785e7-43cc-438b-aa6a-7893e26afdd2. Accessed on April 4th. 2024.

Brasil, (2007). *Instrução Normativa n° 28, de 12 de junho de 2007*. Aprova o Regulamento Técnico para fixação de identidade e qualidade de composto lácteo. Available online: https://sistemasweb.agricultura.gov.br/sislegis/action/detalhaAto.do?method=consultarLegislacaoFederal. Accessed on April 4th. 2024.

Brasil, (2014). *Resolução da Diretoria Colegiada - RDC n° 21, de 25 de abril de 2014*. Dispõe Sobre a fabricação e comercialização de produtos da Medicina Tradicional Chinesa (MTC). Available online: https://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2014/rdc0021_25_04_2014.pdf. Accessed on April 4th. 2024.

Brasil, (2018). *Instrução Normativa - IN n° 28, de 26 de julho de 2018*. Estabelece as listas de constituintes, de limites de uso, de alegações e de rotulagem complementar dos suplementos alimentares. Available online: https://antigo.anvisa.gov.br/documents/10181/3898888/IN_28_2018_COMP.pdf/db9c7460-ae66-4f78-8576-dfd019bc9fa1. Accessed on April 4th. 2024.

Brasil, (2021b). *Resolução da Diretoria Colegiada - RDC n° 463/22*. Dispõe Sobre a aprovação do Formulário de Fitoterápicos da Farmacopeia Brasileira, 2ª edição. Available online: https://antigo.anvisa.gov.br/documents/10181/4311647/RDC_463_2021_.pdf/6fa88ab7-b38f-437a-9f7e-b6c74ce17d7e#:~:text=Disp%C3%B5e%20sobre%20a%20aprova%C3%A7%C3%A3o%20do,de%201999%2C%20e%20ao%20art. Accessed on April 4th. 2024.

Brasil, (2022). *Instrução Normativa - IN n° 160, de 1 de julho de 2022*. Limites máximos Tolerados (LMT) de Contaminantes em Alimentos. Available online: https://antigo.anvisa.gov.br/documents/10181/2718376/IN_160_2022_.pdf. Accessed on April 4th. 2024.

Brasil, (2023). *Resolução da Diretoria Colegiada n° 778, de 1 de março de 2023*. Dispõe sobre os princípios gerais, as funções tecnológicas e as condições de uso de aditivos alimentares e coadjuvantes de tecnologia em alimentos. Available online: https://antigo.anvisa.gov.br/documents/10181/6561857/%281%29RDC_778_2023_COMP.pdf/7d7e07dc-a9fa-4631-90bc-d6e8584d5ade. Accessed on April 4th. 2024.

Chainani-Wu, N. (2003). Safety and Anti-Inflammatory Activity of Curcumin: A Component of Tumeric (Curcuma longa). *The Journal of Alternative and Complementary Medicine, 9*(1), 173–203. https://doi.org/10.1089/107555303321223035

EFSA, 2010a. Scientific Opinion on the re-evaluation of curcumin (E 100) as a food additive. *EFSA Journal*, v. 8, n. 9, p 1679-1724, 2010. Available online: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1679. Accessed on April 4th. 2024.

Efsa. (2010b). Panel on contaminants in the food chain (CONTAM); scientific opinion on lead in food. *EFSA Journal., 8*(4), 1570. https://doi.org/10.2903/j.efsa.2010.1570

Efsa. (2012a). Cadmium dietary exposure in the European population. *EFSA Journal., 10*(1), 37. https://doi.org/10.2903/j.efsa.2012.2551

Efsa. (2012b). Panel on additives and products or substances used in animal feed (FEEDAP); scientific opinion on safety and efficacy of cobalt compounds (E3) as feed additives for all animal species: Cobaltous acetate tetrahydrate, basic cobaltous carbonate monohydrate and cobaltous sulphate heptahydrate, based on a dossier submitted by TREAC EEIG. *EFSA Journal., 10*(7), 2791. https://doi.org/10.2903/j.efsa.2012.2791

EFSA, 2013. Panel (EFSA panel on dietetic products, nutrition and allergies), 2013. Scientific opinion on dietary reference values for molybdenum, 35 *EFSA Journal*. 11 (8), 3333. doi: 10.2903/j.efsa.2013.3333.

Efsa. (2014). Panel (EFSA Panel on Contaminants in the Food Chain - CONTAM), 2014. *Scientific Opinion on the risks to public health related to the presence of chromium in food and drinking water, EFSA Journal., 12*(3), 3595. https://doi.org/10.2903/j.efsa.2014.3595

Efsa. (2020). Scientific opinion on the update of the risk assessment of nickel in food and drinking water. *EFSA Journal., 18*(11), 101. https://doi.org/10.2903/j.efsa.2020.6268

Efsa. (2021). Scientific report on the chronic dietary exposure to inorganic arsenic. *EFSA Journal., 19*(1), 6380. https://doi.org/10.2903/j.efsa.2021.6380

Efsa. (2022). Risk assessment of rare earth elements, antimony, barium, boron, lithium, tellurium, thallium and vanadium in teas, 12. *EFSA Journal., 20*(S1), e200410.

EU, 2023. *Commission Regulation (EU) 2023/915, of 25 April 2023*. On maximum levels for certain contaminants in food and repealing Regulation (EC) No 1881/2006 (Text with EEA relevance). Available online: https://faolex.fao.org/docs/pdf/eur217510.pdf. Accessed on April 4th. 2024.

FAO/WHO, 2011. Evaluation of certain food additives and contaminants: seventy-third report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Tech. Rep. Ser. 960, 227. Available online: https://iris.who.int/bitstream/handle/10665/44515/WHO_TRS_960_eng.pdf. Accessed on April 4th. 2024.

FAO/WHO, 2022. Codex Committee on Contaminants in Foods: working document for information and use in discussions related to contaminants. CF/15 INF/01. CODEX Alimentarius Commission, 15 th sess(Aprill). Available online: https://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-735-15%252FINFDOC%252FCF15_INF01x.pdf. Accessed on April 4th. 2024.

FDA, 2022. US Food and Drug Administration. Understanding Dietary Supplements. Available at: https://www.fda.gov/media/158337/download. Accessed on April 4th. 2024.

Filipiak-Szok, A., Kurzawa, M., & Szłyk, E. (2015). Determination of toxic metals by ICP-MS in Asiatic and European medicinal plants and dietary supplements. *Journal of Trace Elements in Medicine and Biology, 30*, 54–58. https://doi.org/10.1016/j.jtemb.2014.10.008

Fioravanti, M. I. A., Rebellato, A. P., Milani, R. F., Morgano, M. A., & Bragotto, A. P. A. (2023). Toxic inorganic elements in plant-based beverages: Total concentration, dietary exposure and bioaccessibility. *J. Food Compos. Anal., 123*, Article 105565. https://doi.org/10.1016/j.jfca.2023.105565

Forsyth, J. E., Saiful Islam, M., Parvez, S. M., Raqib, R., Sajjadur Rahman, M., Marie Muehe, E., Fendorf, S., & Luby, S. P. (2018). Prevalence of elevated blood lead levels among pregnant women and sources of lead exposure in rural Bangladesh: A case control study. *Environmental Research, 166*(April), 1–9. https://doi.org/10.1016/j.envres.2018.04.019

Ganiger, S., Malleshappa, H. N., Krishnappa, H., Rajashekhar, G., Ramakrishna Rao, V., & Sullivan, F. (2007). A two generation reproductive toxicity study with curcumin, turmeric yellow. *Wistar rats. Food and Chemical Toxicology, 45*(1), 64–69. https://doi.org/10.1016/j.fct.2006.07.016

Gleason, K., Shine, J. P., Shobnam, N., Rokoff, L. B., Suchanda, H. S., Ibne Hasan, M. O. S., Mostofa, G., Amarasiriwardena, C., Quamruzzaman, Q., Rahman, M., Kile, M. L., Bellinger, D. C., Christiani, D. C., Wright, R. O., & Mazumdar, M. (2014). Contaminated Turmeric Is a Potential Source of Lead Exposure for Children in Rural Bangladesh. *Journal of Environmental and Public Health, 2014*, 3–8. https://doi.org/10.1155/2014/730636

Govindarajan, V. S. & Stahl, W. H. (1980). Turmeric—chemistry, technology, and quality. In *C R C Critical Reviews in Food Science and Nutrition* (Vol. 12, Issue 3). doi: 10.1080/10408398009527278.

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A Review of Its Effects on Human Health. *Foods*. Oct 22;6(10):92. doi: 10.3390/foods6100092.

IAL, 2008. Métodos físico-químicos para análise de alimentos. Coordenadores Odair Zenebon, Neus Sadocco Pascuet e Paulo Tiglea. 4. ed. São Paulo: Instituto Adolfo Lutz, 2008, 1020 p. Available at: http://www.ial.sp.gov.br/resources/editorinplace/ial/2016_{31}9/analisedealimentosial_2008.pdf. Accessed on April 4th. 2024.

INMETRO, 2020. The national institute of metrology, standardization and industrial quality, DOQ-CGCRE-008. Revision 09. Available at: https://app.sogi.com.br/Manager/texto/arquivo/exibir/arquivo?eyJ0eXAiOiJKV1QiLCJhbGciOiJIUzI1NiJ9AFFIjAvMTM4ODM3NS9TR19SZXF1aXNpdG9fTGVnYWxfVGV4dG8vMC8wL0RPUS1DZ2NyZS04XzA5LnBkZi8wLzAiAFFBcMYdNmecpDn0m0Dj4vzJmvMJZMAYtW6mtkIlj0C7fk. Accessed on April 4th. 2024.

JECFA, 2003. Joint FAO/WHO Expert Committee on Food Additives. 61st JECFA - Chemical and Technical Assessment (CTA), Curcumin. Available at: https://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/61/Curcumin.pdf. Accessed on April 4th. 2024.

JECFA, 2004. *Joint FAO/WHO Expert Committee on Food Additives*. Evaluation of certain food additives and contaminants: sixty-first report of the Joint FAO/WHO Expert Committee on Food Additives, 2004. Available at: https://iris.who.int/handle/10665/42849. Accessed on April 4th. 2024.

Jiang, J., Wang, W., Sun, Y. J., Hu, M., Li, F., & Zhu, D. Y. (2007). Neuroprotective effect of curcumin on focal cerebral ischemic rats by preventing blood-brain barrier damage. *European Journal of Pharmacology, 561*(1–3), 54–62. https://doi.org/10.1016/j.ejphar.2006.12.028

Khodabakhshian, R., Bayati, M. R., & Emadi, B. (2021). An evaluation of IR spectroscopy for authentication of adulterated turmeric powder using pattern recognition. *Food Chemistry, 364*(February), Article 130406. https://doi.org/10.1016/j.foodchem.2021.130406

Kotha, R. R., & Luthria, D. L. (2019). Curcumin: Biological, Pharmaceutical, Nutraceutical, and Analytical Aspects. *Molecules, 24*(16), 2930. https://doi.org/10.3390/molecules24162930

Kunnumakkara, A. B., Bordoloi, D., Padmavathi, G., Monisha, J., Roy, N. K., Prasad, S., & Aggarwal, B. B. (2016). Curcumin, The Golden Nutraceutical: Multitargeting for Multiple Chronic Diseases. *British Journal of Pharmacology*. https://doi.org/10.1111/bph.13621

Lantz, R. C., Chen, G. J., Solyom, A. M., Jolad, S. D., & Timmermann, B. N. (2005). The effect of turmeric extracts on inflammatory mediator production. *Phytomedicine, 12*(6–7), 445–452. https://doi.org/10.1016/j.phymed.2003.12.011

Martins, A. S. P., Alves, M. C., Araújo, O. R. P., Camatari, F. O. S., Goulart, M. O. F., & Moura, F. A. (2023). Curcumin in inflammatory bowel diseases: Cellular targets and molecular mechanisms. *Biocell, 47*, 2547–2566. https://doi.org/10.32604/biocell.2023.043253

MINTEL, 2020. Food and nutrition claims: Incl impact of COVID-19. Available at: reports.mintel.com. Accessed on April 4th. 2024.

Molin, T. R. D., Leal, G. C., Müller, L. S., Muratt, D. T., Marcon, G. Z., de Carvalho, L. M., & Viana, C. (2019). Regulatory framework for dietary supplements and the public health challenge. *Revista de Saude Publica, 53*, 1–12. https://doi.org/10.11606/S1518-8787.2019053001263

Pereira, A. S., & Stringehta, P. C. (1998). Considerações sobre a cultura e processamento do açafrão. *Horticultura Brasileira, 16*(2), 102–105.

Rebellato, A. P., Orlando, E. A., Thedoropoulos, V. C. T., Greiner, R., & Pallone, J. A. L. (2020). Effect of phytase treatment of sorghum flour, an alternative for gluten free foods and bioaccessibility of essential minerals. *Journal of Food Science and Technology, 57*(9), 3474–3481. https://doi.org/10.1007/s13197-020-04382-w

Shoba, G., Joy, D., Joseph, T., Majeed, M., Rajendran, R., & Srinivas, P. S. S. R. (1998). Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Medica, 64*(4), 353–356. https://doi.org/10.1055/s-2006-957450

Wani, A. L., Ara, A., & Usmani, J. A. (2015). Lead toxicity: A review. *Interdisciplinary Toxicology, 8*(2), 55–64. https://doi.org/10.1515/intox-2015-0009

Xu, M., Huang, B., Gao, F., Zhai, C., Yang, Y., Li, L., Wang, W., & Shi, L. (2019). Assesment of adulterated traditional Chinese medicines in China: 2003–2017. *Frontiers in Pharmacology, 10*(November), 1–8. https://doi.org/10.3389/fphar.2019.01446

Zuo, T. T., Li, Y. L., Wang, Y., Guo, Y. S., Shen, M. R., Yu, J. D., Li, J., Jin, H. Y., Wei, F., & Ma, S. C. (2023). Distribution, speciation, bioavailability, risk assessment, and limit standards of heavy metals in Chinese herbal medicines. *Pharmacological Research - Modern Chinese Medicine, 6*(31). https://doi.org/10.1016/j.prmcm.2023.100218