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Article

Characterization of Commercially Available Turmeric for Use in Pharmaceutical Products and Food Supplements

Rodrigo Boscariol,[a] Thais H. Paulino,[a] José M. Oliveira Jr.,[a] Victor M. Balcão[,a,b] and Marta M. D. C. Vila*[,a]

[a]*Laboratório de Biofilmes e Bacteriófagos (PhageLab), Universidade de Sorocaba, 18023-000 Sorocaba-SP, Brazil*

[b]*Departamento de Biologia e Centro de Estudos do Ambiente e do Mar (CESAM), Universidade de Aveiro, Campus Universitário de Santiago, P-3810-193 Aveiro, Portugal*

We addressed some physicochemical and biological differences in commercial turmeric, acquired from both handling pharmacies and stores selling natural products for quality assessment. For this, it was determined the melting point, antioxidant activity by 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH), antimicrobial activity via the agar disk-diffusion assay, metallic contaminants by X-ray fluorescence with energy dispersion (EDXRF), spectral behaviors by Fourier transform infrared (FTIR) and ultraviolet-visible (UV-Vis) and determination of curcumin concentration by UV-Vis. The results obtained of the several commercial turmeric samples were not homogeneous, showing in fact significant differences regarding melting points, UV-Vis spectral scan profiles, and FTIR spectra, presenting toxic metals and quite low curcumin contents. This sheds light on the urge to implement adequate quality control in this type of raw material for human safe use of curcumin. Particularly, contamination with heavy metals, such as mercury, is a serious health problem, due to its high toxicity and accumulative power in the body.

Keywords: commercial turmeric, curcumin, physicochemical characterization, antimicrobial activity

Introduction

Curcumin is a compound derived from turmeric (*Curcuma longa* L.) (3 to 5%) that exhibits an extensive spectrum of biological activities.[1,2] *Curcuma longa* L. is a plant belonging to the Zingiberaceae family, cultivated normally in south and southeast tropical Asia.[3,4]

Curcumin, 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadien-3,5-dione, is a substance with low solubility in water being estimated to be 11 ng mL^{-1}.[5] Currently, the action of curcumin in several diseases has been re-evaluated based on the proof of its capacity anti-inflammatory, antioxidant, chemoprotective, tissue-protective, antibacterial, anti-fungal, antiviral, metabolism-regulating, immuno-modulating, antineoplastic and anti-depressant properties.[5-8] Thus, curcumin has been used in the treatment of arthritis, diabetes, psoriasis, gastrointestinal diseases, acute heart disease, anxiety, hyperlipidemia, liver disease, bacterial infections, inflammation, etc.[9-11] However, the major problems with curcumin is its poor bioavailability, probably due to poor absorption, rapid metabolism and rapid systemic elimination. Hence, efforts have been made to improve the bioavailability of curcumin and consequent bio-efficacy,[12] such as formulating nanoparticles, liposomes, micelles, solid dispersions, emulsions, and microspheres containing curcumin.[5,10]

This plant species is also used to produce the yellow color in food, cosmetic and in some drug preparations. Currently, interest in natural dyes, particularly for use in food, has grown due to consumer demand for healthier products, together with the evidence of the harmful effects of many artificial dyes.[13] The most commonly used natural dyes for obtained the yellow color is carotenoids (bixin, lutein and crocin), betalains (betaxanthins), flavonoids (carthamin), curcuminoids (curcumin) and riboflavins.[14]

Brazil has favorable climatic conditions for the cultivation of *C. longa*. However, it is necessary to establish more rigorous quality standards for the expansion of the market.[15] The quality of plant products may vary due

*e-mail: victor.balcao@prof.uniso.br; marta.vila@prof.uniso.br
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to different agricultural practices, climate change and manufacturing systems[15,16] causing significant variations in the amount of curcumin.[17] In addition, due to its many potential commercial applications, adulteration of curcumin with botanical additives and chemical substances has increased.[18] Medicinal plants are still important resources for health around the world. However, the main problem with herbal medicines is that they are prone to tampering and substitution. In this way, it is extremely important to establish quality parameters for each plant species and carry out inspections.[19]

In this perspective, it is of greatest importance to evaluate curcumin in commercially available turmeric samples for the production of pharmaceutical products and food supplements, because such large chemical variability will result in ineffective products or even in the potential for toxicity. This way, the objective of this research was to evaluate some physicochemical and biological parameters of different samples of curcumin, in order to verify if the products that are commercially available are safe for human consumption.

Experimental

Chemicals

The samples analyzed were constituted of dry commercial turmeric extracts and were acquired in the region of Sorocaba, SP (Brazil). Commercial turmeric powder was acquired from manipulation pharmacies (samples 1-5) and local establishments selling natural products (samples 6 and 7). Water was purified in a Master System All (model MS2000, Gehaka, São Paulo, Brazil). As standard it was used curcumin from Sigma-Aldrich (Ref. No. C1386, CAS No. 1386, St. Louis, MO, USA) with a purity of 98.0%. DPPH (2,2-diphenyl-1-picrylhydrazyl) (ref. Sigma D9132-1G) was purchased from Sigma-Aldrich (St. Louis MO, USA). High performance liquid chromatography (HPLC)-grade methanol (LiChrosolv®, CAS-No. 67-56-1) was purchased from Merck (Darmstadt, Germany). L-Ascorbic acid was purchased from Sigma-Aldrich (ref. Sigma A92902, CAS No. 50-81-7, St. Louis, MO, USA). TSB (trypticase soy broth) and TSA (trypticase soy agar) were purchased from Merck KGaA (Darmstadt, Germany).

Bacterial strains

Staphylococcus aureus strains CCCD-6538, CCCD-29213; CCCD-14458; CCCD-33591; and CCCD-43300, *Pseudomonas aeruginosa* CCCD-P004 and *Escherichia coli* CCCD-E003, from the Collection Culture Cefar Diagnóstica, were kindly donated by the Hospital of Clinics at Unicamp (Campinas, SP, Brazil).

Procedures

Melting point

The melting points of the commercial turmeric extracts and pure curcumin were obtained using a digitally micro-processed heating device from Gehaka (model PF 1500 FARMA, São Paulo, Brazil). The temperature increase occurred at rate of 1 °C min^{-1}. All the analytical procedures were done in triplicate.

Antioxidant activity by DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate)

The antioxidant activity was described by Brand-Williams *et al.*[20] with adaptations by Duarte-Almeida *et al.*[21]

To prepare the reagent DPPH, 4 mg of 2,2-diphenyl-1-picrilhhydrazyl was dissolved in 100 mL of ethanol. Curcumin samples were prepared in methanol at a concentration of 1.0 mg mL^{-1}, as positive control it was used L-ascorbic acid, as negative control it was used water and DPPH reagent, and ultrapure water was used as blank. For the assay, 500 µL of the curcumin solution (1.0 mg mL^{-1} in methanol) were added to 3.5 mL of DPPH reagent. The same procedure was followed for ascorbic acid (1.0 mg mL^{-1} in methanol). For the blank, 500 µL of ultrapure water were added to 3.5 mL of DPPH reagent. The samples were homogenized and kept in the dark for 25 min. Their absorbances were then read at the wavelength of 517 nm on a UV-Vis spectrophotometer from Agilent (model Cary 60 UV-Vis, Santa Clara, CA, USA). The antioxidant activity (AA) was calculated according to equation 1, where AA (%) is the percentage of antioxidant activity and Abs is the absorbance at the used wavelength.

$$AA(\%) = \{(Abs_{sample} - Abs_{blank})/(Abs_{ascorbic\ acid} - Abs_{blank})\} \times 100 \quad (1)$$

Antimicrobial activity via the agar disk-diffusion assay

The antimicrobial activity of the commercial turmeric and standard curcumin samples was determined via the agar disk-diffusion technique for susceptibility to antimicrobials, according to the Clinical and Laboratory Standards Institute.[22] The antimicrobial activity assays were carried out using *Staphylococcus aureus* strains (CCCD-6538, CCCD-29213, CCCD-14458, CCCD-33591, CCCD-43300); *Pseudomonas aeruginosa* (CCCD-P004) and *Escherichia coli* (CCCD-E003).

For revival of the bacterial strains, the lyophilized pellets were suspended in 50 mL TSB and incubated

at 37 °C during 24 h. Subsequently, bacterial cultures were homogenized and inoculated by spreading in Petri dishes with solidified TSA. Curcumin samples in ethanol (100 μg mL^{-1}) were impregnated in sterile filter paper discs (ca. 6.0 mm in diameter) and dried at 36 °C during 24 h to remove the solvent and produce ca. 90 μg curcumin *per* disc. The disks impregnated with curcumin were then applied over the inoculated TSA medium in the Petri plates, which were incubated at 37 °C during 24 h. The negative standard of inhibition was 30 μg tetracycline *per* sterile paper disk (Sensidisc DME, TET30, DME-Diagnósticos Microbiológicos Especializados, Araçatuba, SP, Brazil) whereas the positive standard of inhibition was a sterile paper disc impregnated with sterile saline solution (NaCl 0.9% m/m). Petri dishes were incubated at 37 ± 0.5 °C for 24 h. After this period, the presence of growth inhibition halos was observed.

Fourier transform infrared spectrophotometry (FTIR) analyses

2 mg of each sample was ground with 300 mg of KBr. This mixture was pressed in a Shimadzu brand hydraulic press (model SSP-10A, Kyoto, Japan) to obtain transparent discs. The infrared spectra were reading using a Fourier transform infrared spectrophotometer (FTIR) Shimadzu (model IR-Affinity-1, Shimadzu, Kyoto, Japan), in the wavenumber range from 4000 to 400 cm^{-1}, with a resolution of 2 cm^{-1}.

Metallic contaminants in the commercial turmeric samples by X-ray fluorescence with energy dispersion (EDXRF)

Metallic contaminants in the samples were determined in a compact EDXRF system by Malvern Panalytical (Santo Amaro, SP, Brazil), composed of a silicon detector (silicon drift diode) with an area of 25 mm^2 and thickness of 500 μm, protected by a beryllium window of 12.5 μm. The X-ray source used for excitation of the samples consisted of a miniature X-ray tube with an Ag anode (Amptek, Bedford MA, USA). The X-ray tube was set up to work at a voltage of 30 kV and current of 10 μA. The energy resolution of the detection system was ca. 125 eV, quoted as the full width at half maximum (FWHM) for Mn Kα 5.9 keV X-rays from a ^{55}Fe source. All measurements were carried out using atmospheric air, and the measuring time was set for 45 min for each sample. The Epsilon software (Malvern Panalytical, Santo Amaro, SP, Brazil) was used for signal control and data acquisition. The EDXRF system was calibrated with control samples. Tablets of approximately 5 mm high by 22 mm in diameter were produced using a spectrometric sample compaction press (PDCA-40, São Paulo, SP, Brazil) by applying a force of 15 tons.

UV-Vis spectra of curcumin samples

UV-Vis spectrophotometric scans (from 200 to 800 nm) of the commercial turmeric and standard curcumin samples in methanol (10 μg mL^{-1}) were carried out using quartz cuvettes in a UV-Vis spectrophotometer from Agilent (model Cary 60 UV-Vis, Santa Clara, CA, USA).[23,24] The determination of curcumin concentration in the commercial turmeric samples was based on the procedure described by Rapalli *et al.*[23] and Singh and Avupati.[24] Stock solutions of 100 μg mL^{-1} were prepared by dissolving 2.5 mg of each sample in 25 mL methanol. All solutions were sonicated during 15 min and filtered through Whatman filter paper No. 41. From the stock solutions, a concentration of 5 μg mL^{-1} was produced via dilution with methanol. Standard curcumin solutions (Sigma-Aldrich, Ref. No. C1386, CAS No. 1386, St. Louis, MO, USA) in methanol were produced in concentrations ranging from 1 to 15 μg mL^{-1} and used to obtain the calibration curve. All spectrophotometric measurements were performed at a wavelength of 421 nm.

Results and Discussion

The use of medicinal herbal products has increased over the past three decades by 80%.[25] Many people use herbal medicines in primary healthcare. Although therapies with medicinal herbal products have shown potential efficacy for the treatment of several diseases, many products from plant species are few and poorly controlled.[25] Adding to this, the growing demand for medicinal herbal products has transformed the large-scale manufacture of these products into a routine. Large scale production may result in longer storage times with concomitant possible product deterioration.[26] Hence, standardization of some parameters for the establishment of a consistent biological activity or simply to maintain the quality of production and manufacturing of herbal drugs is of utmost importance.[25] *Curcuma longa* L. is, worldwide, a plant of high medicinal and economic value. Although the key active ingredients have been studied extensively, the concerns remain about the quality of commercial extracts.[27]

Melting point

Physical characterization is a crucial factor for assessing the quality of crude drugs. Simple methods such as, for example, melting point, are useful in this regard. The results obtained for the melting point of the commercial turmeric and standard curcumin samples are displayed in Figure 1.

There was no difference observed between the values of the melting points between samples acquired in handling

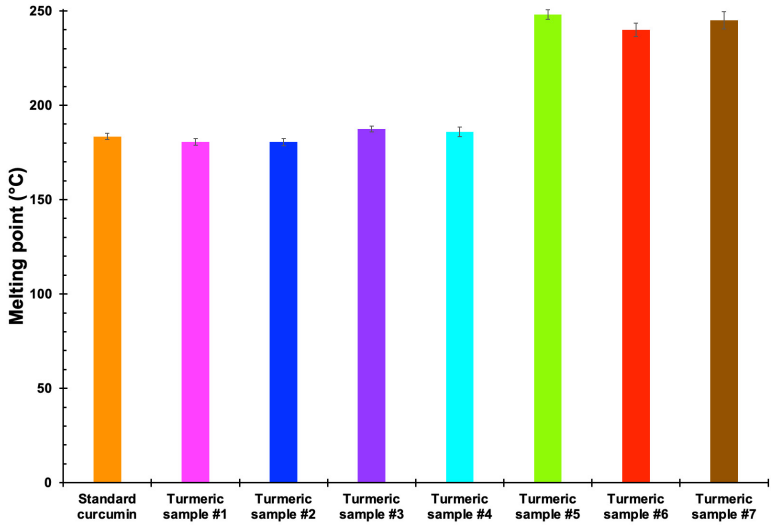

Figure 1. Average melting point of commercial turmeric and standard curcumin samples. All values represent the mean of three experiments, and the error bars represent the standard deviations.

pharmacies, when compared with the values of the melting point of the standard curcumin sample. However, in commercial turmeric samples acquired in establishments selling natural products, there was a significant difference in those values, indicating a possible contamination or adulteration of the product (Figure 1). The average value (n = 3) of the melting point obtained for the standard sample of curcumin (183.5 ± 1.7 °C) showed a value very close to the information provided by the manufacturer (viz. 183 °C). Bagchi *et al.*[28] reported a value of 180 °C, whereas Priyadarsini[29] reported a value of 183 °C for this physical parameter. These variations are expected since the melting point for pure chemicals or phytochemicals is constant, but crude drugs from animal or plant origin contain mixed chemicals, and that is why they are described with certain range of melting point.[30]

Antioxidant activity

Curcumin extracts have strong antioxidant activity and this way can be important in disease prevention and health preservation.[31] Thus, evaluating this characteristic can be a way of evaluating the quality of samples.

The antioxidant activity of the commercial turmeric and standard curcumin samples was carried out via the DPPH method. Among the *in vitro* methods the DPPH method is the most popular one due to its simplicity, speed, and low cost.[32] In this method, DPPH is a free radical that becomes stable after accepting an electron or hydrogen radical. The method is based on the discoloration of a solution composed of stable DPPH radicals (violet color) by the transfer of electrons from an antioxidant compound to a free radical, DPPH•, which, when reduced, loses its purple color.[21,33]

Table 1 displays the results obtained for the antioxidant activities of all commercial turmeric and standard curcumin samples assayed.

Table 1. Antioxidant activity (AA) of curcumin samples (n = 3). Pure curcumin (Sigma-Aldrich), curcumin 1 to 5 acquired in handling pharmacies, curcumin 6 and 7 acquired in natural products establishments

Sample	AA / %
Standard curcumin	93.11
Commercial turmeric sample 1	85.86
Commercial turmeric sample 2	84.03
Commercial turmeric sample 3	85.59
Commercial turmeric sample 4	84.18
Commercial turmeric sample 5	5.33
Commercial turmeric sample 6	22.23
Commercial turmeric sample 7	23.32

Determination of the antioxidant activity revealed that commercial turmeric samples 5, 6 and 7 exhibited a lower antioxidant capacity when compared to the remaining commercial turmeric samples, as displayed in Table 1. The low values of antioxidant activity of the samples obtained in bulk from establishments selling natural products (viz. 22.23 and 23.32%) can be explained in terms of a putative exposure to environmental conditions, favoring loss of antioxidant capacity. Curcumin is a substance with potent antioxidant activity, which has been demonstrated by several *in vitro* studies, suggesting that such antioxidant activity arises from either the hydroxyl group or the methylene group of the α-diketone (heptadiene-dione) portion of curcumin. The phenolic hydroxyl group is also

important for the antioxidant activity of curcumin.[12,34,35] In free radical reactions, the curcumin hydrogen most easily removable is that of the phenol-OH group, resulting in the formation of phenoxy radicals. These radicals are stabilized by resonance through a keto-enol structure that allows an almost perfect conjugation between the two aromatic rings containing the active antioxidant centers.[36,37]

Antimicrobial activity via the agar disk-diffusion assay

Verification of the antimicrobial activity of the commercial turmeric and standard curcumin samples was also carried out, since some studies[33,38] have reported antimicrobial activity in products obtained from turmeric.

Several *in vitro* laboratory methods can be used to evaluate the antimicrobial activity of plant extracts. Among the most common, the disk-diffusion was selected because is a well-known procedure and provides good qualitative results.[39]

Notwithstanding such reports on the antimicrobial activity of curcumin, no antimicrobial activity whatsoever was observed in the commercial turmeric and standard curcumin samples in the microorganisms tested, as can be observed by inspection of the results displayed in Figure 2. According to several authors,[11,37,40] the absence of antimicrobial activity of turmeric extracts may be associated with the hydrophobic characteristic of curcuminoids, which makes it difficult for them to permeate into the environment.

Fourier transform infrared spectrophotometry (FTIR) analysis

The employment of the FTIR aimed to identify the characteristic functional groups in curcumin samples and this way check for possible tampering or falsifications. According to Lestari and Indrayanto[36] and Dhakal *et al.*,[18] pure curcumin samples should exhibit peaks at 3511, 1630, 1601, 1510, 1429, 1278 and 1028 cm^{-1}. A long shallow peak at 3255 cm^{-1} and a sharp peak at 3507 cm^{-1} indicate

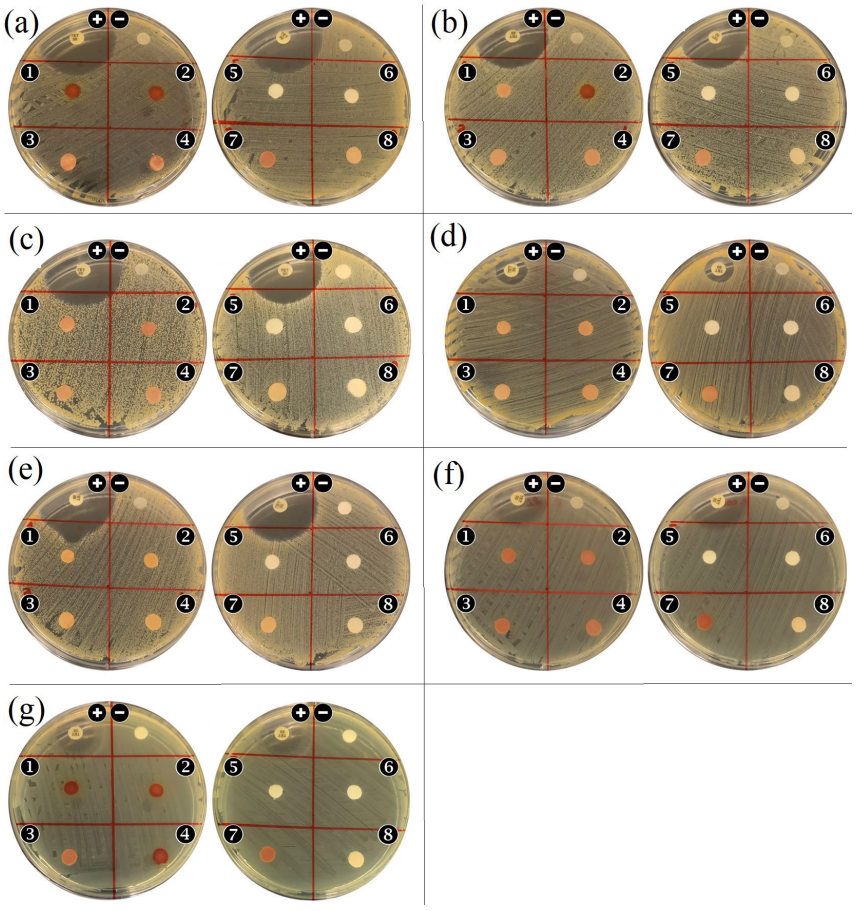

Figure 2. Results of the antimicrobial activity assays of both commercial turmeric and standard curcumin via the agar disk-diffusion methodology. (a) *Staphylococcus aureus* CCCD-6538; (b) *Staphylococcus aureus* CCCD-29213; (c) *Staphylococcus aureus* CCCD-14458; (d) *Staphylococcus aureus* CCCD-33591; (e) *Staphylococcus aureus* CCCD-43300; (f) *Escherichia coli* CCCD-E003; (g) *Pseudomonas aeruginosa* CCCD-P004; (+) positive control (disc with 30 µg tetracycline); (–) negative control (disc with saline solution (NaCl 0.9% m/m)). (1) Standard curcumin; (2-6) handling pharmacies; (7, 8) turmeric from establishments selling natural products.

the presence of the hydroxyl functional group (–OH). The peak detected at 1626 cm^{-1} has a predominantly mixed character regarding the double bond between carbons (C=C) and the carbonyl functional group (C=O), whereas a strong band at 1600 cm^{-1} is attributed to the vibrations of symmetrical stretching of the aromatic ring ($C–C_{ring}$). The peak at 1504 cm^{-1} is attributed to the carbonyl functional group (C=O), the peak attributed to enol (C–O) is displayed at 1273 cm^{-1}, the peak at 1026 cm^{-1} refers to the ether functional group (C–O–C), and the *cis*-CH vibration of the aromatic ring appears at 714 cm^{-1}.[3,36,41]

The peaks displayed in the standard curcumin spectrum at 466.77, 542.00, 574.79, 599.86, 713.66, 810.1, 856.39, 885.33, 962.48, 1028.06, 1116.78, 1151.50, 1182.36, 1205.51, 1232.51, 1280.73, 1313.52, 1427.32, 1508.33, 1600.92, 1627.92 and 3510.45 cm^{-1} (Figure 3a) could also be observed in samples 1, 2 and 3 (Figures 3b, 3c and 3d). For sample 3 (Figure 3d) variations in peak intensity were observed between 3000 and 3500 cm^{-1}, suggesting a stretching of the hydroxyl group (–OH) of primary alcohols.[3,33] The spectrum of sample 4 (Figure 3e) shows variations in peak intensity between 466 and 810 cm^{-1} and in the range of 3500 cm^{-1}. Observing the spectra of samples 5, 6 and 7 (Figures 3f, 3g, 3h) peaks are observed at 921.97, 1078.2, 1155.36, 1514.12, 1631.78 and 2927 cm^{-1}. Significant changes can be observed in both the intensity and range of the wavenumbers relative to the standard curcumin (Figure 3a), which can be attributed to different interactions between functional groups of curcumin; these observations also reinforce the evidence of either polymorphism or pseudo-polymorphism, or even adulterations in the products.[3]

The results obtained in the FTIR analyses performed to the standard curcumin and commercial turmeric samples are displayed in Figure 3 in the form of normalized spectra.

Metallic contaminants by X-ray fluorescence with energy dispersion (EDXRF)

The presence of metallic elements is common in all medicinal plants, since numerous agricultural, domestic, medical, industrial and technological applications have led to extensive distribution of heavy metals all over the environment.[39] Attempting to avoid damage to the health, there are tolerable limits of such metals in foodstuff. Monitoring of quality control and evaluation of medicines plants is an important aspect as in the production as well as in the distribution on the pharmaceutical market.[42] The Brazilian Pharmacopoeia (BF)[43] admits, for medicinal plants in general, up to 20 ppm of heavy metals, which cannot exceed the limits of 1 ppm of cadmium, 5.0 ppm of lead, 0.1 ppm of mercury and 5.0 ppm of arsenic. However, the BF indicates as methods of analysis of heavy metals only limit tests and atomic absorption. The X-ray fluorescence method has significant advantages over these two methods, such as the accuracy, minimal sample preparation and multi-element analysis.[44] However, studies using X-ray fluorescence in pharmaceutical products are scarce.

The EDXRF equipment utilized uses different energies to excite the sample and, for each excitation energy, only for some elements the concentrations are obtained. Hence, for detection of low elements, low excitation energies were used, whereas for detection of heavy metals higher

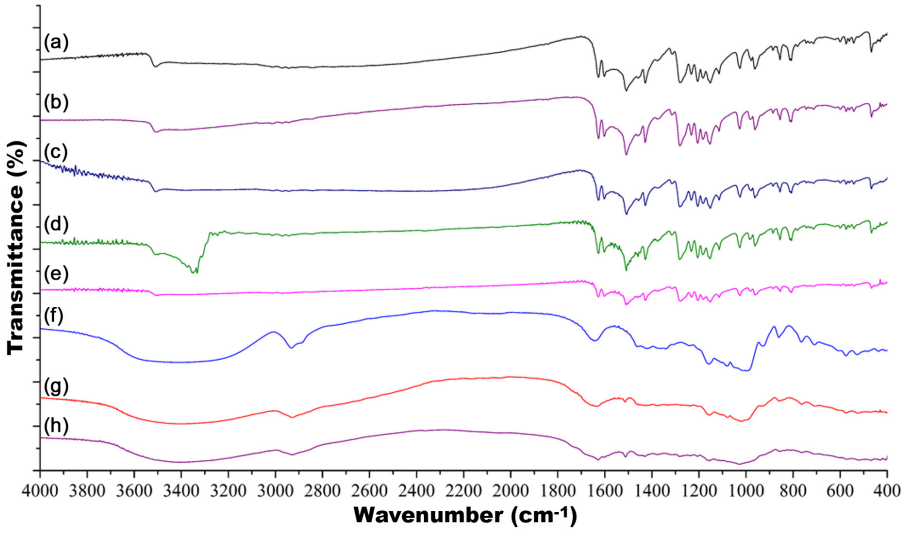

Figure 3. FTIR spectra of samples of pure curcumin and commercial turmeric. (a) Pure curcumin; (b) curcumin 1; (c) curcumin 2; (d) curcumin 3; (e) curcumin 4; (f) curcumin 5; (g) curcumin 6; (h) curcumin 7. Samples 2-6 were acquired in handling pharmacies, whereas samples 7 and 8 were acquired in establishments selling natural products.

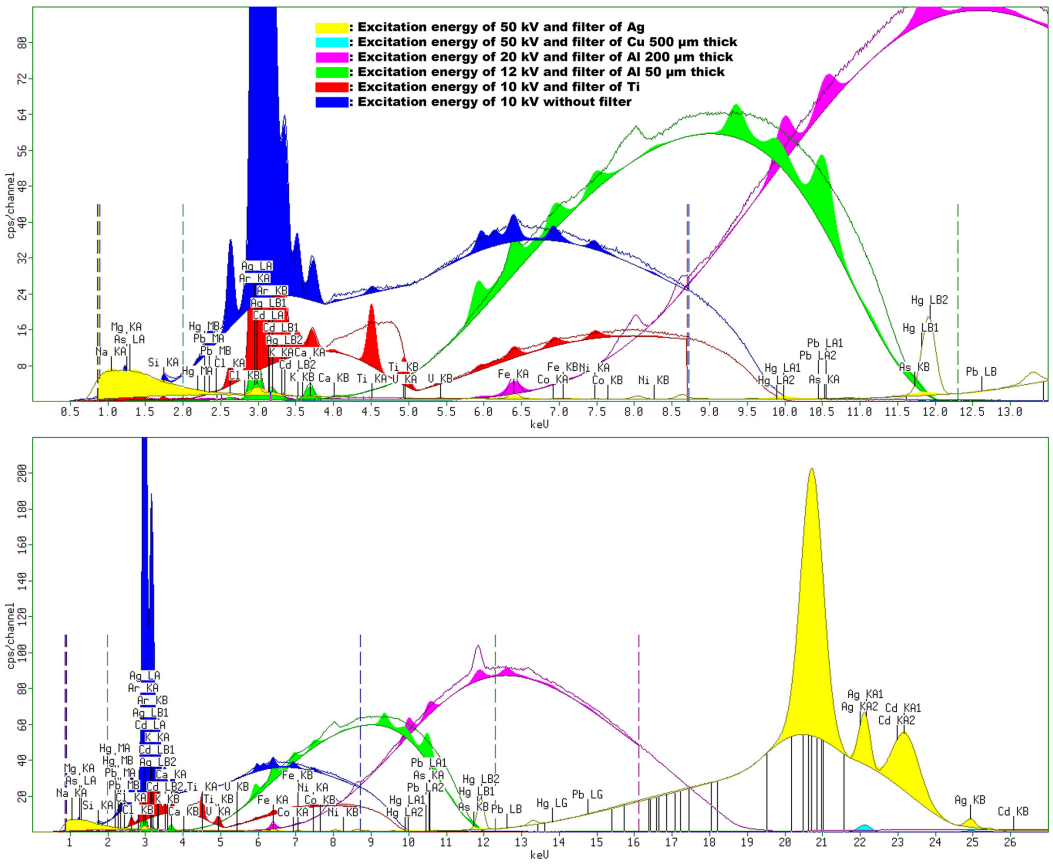

Figure 4. EDXRF spectrum of one of the turmeric samples (viz. curcumin sample 6), showing the different excitation energies used in the elemental detection.

excitation energies were used to hit the sample, allowing emission of elemental characteristic X-rays. Figure 4 displays the EDXRF spectrum of one of the turmeric samples (viz. curcumin sample 6), showing different excitation energies.

The average concentrations (and respective standard deviations) of cadmium (Cd), lead (Pb), mercury (Hg), cobalt (Co), arsenic (As), vanadium (V) and nickel (Ni) in standard curcumin and commercial turmeric samples are displayed in Figure 5.

The presence of these metallic contaminants was detected in all samples assayed (except for the standard curcumin). Seven samples indicated the presence of Hg and Cd; there was no detection of the presence of Pb, Co and V. Regarding Hg, with the exception of samples 6 and 7, all the other samples exhibited Hg above the acceptable level (≤ 0.1 ppm). Sample 4 showed the highest levels of Hg (21.33 ppm), Cd (2.45 ppm), As (1.06 ppm) and Ni (1.54 ppm).

Although metals such as copper (Cu), iron (Fe), manganese (Mn) and zinc (Zn) have physiological functions in the body, many of the metals encountered in the samples assayed have no benefits to the human physiology, such as Pb, Hg and Cd, and can even interfere with the functions

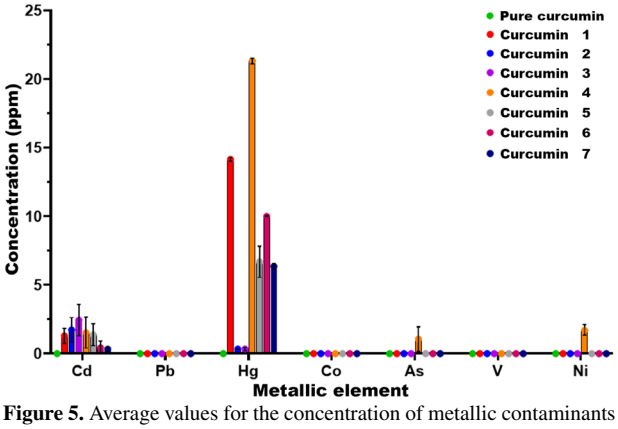

Figure 5. Average values for the concentration of metallic contaminants present in standard curcumin and commercial turmeric samples. Samples 1-5 were acquired in handling pharmacies, whereas samples 6 and 7 were acquired in establishments selling natural products. Values represent the mean of three determinations and error bars the standard deviations.

of various organs and systems in the body, such as the central nervous system, the hematopoietic system, the liver and kidneys.[40] Exposure to Hg compounds leads to toxic effects in the cardiovascular, pulmonary, urinary, gastrointestinal, neurological and skin systems, which might become fatal.[45] Environmental contamination and exposure to heavy metals, such as As, Cd, Pb and Hg, is a serious and growing global problem, being even more

serious in some developing countries, where the economy has been prioritized over environmental issues.[46,47] Air, soil and water, are known to be polluted by heavy metals.[40] Particularly, contamination of soils by Hg is often due to the addition of this heavy metal as part of fertilizers, lime, sludges, and manures and the most of the plants that uptake Hg tend to accumulate it on the roots.[48]

Based on the results obtained for the presence of metallic contaminants in the standard curcumin and commercial turmeric samples assayed, a greater control in relation to the determination of heavy metals in these products is of utmost importance if they are to be used in pharmaceutical and food applications. The consumption of plant materials or herbal drugs contaminated by heavy metals can lead to intoxication and consequent detrimental effects to the human health. Even when present at not so high concentrations, such heavy metals tend to accumulate in the body over time due to their non-biodegradable and persistent nature, which will eventually be detrimental to health.[49]

UV-Vis method for determination of the amount of curcumin and spectral behavior

UV-Vis spectroscopic method has been reported to be suitable to determine concentration of curcumin and offers simplicity, rapidity and reliability. In this sense, it was used to verify the spectral behavior as well as to determine the concentration of curcumin in the samples.[50]

The results obtained in the UV-Vis spectral scans performed to standard curcumin and commercial turmeric samples are displayed in Figure 6. The maximum absorption wavelength of curcumin in all samples assayed occurred at 421 nm. These results were similar to those reported by Sharma *et al.*[51] In another study by Singh and Avupati,[24] where the solvent used was ethyl acetate, the maximum absorption of curcumin occurred at 418 nm. Despite absorbing at the same wavelength of 421 nm, commercial turmeric samples 5, 6 and 7 exhibited much lower absorption intensity (Figure 6), which may indicate low levels of curcumin.

The spectrophotometric method used showed a good linear correlation, producing as calibration curve: $Abs_{421nm} = 0.1643 \times (\text{curcumin} / (\mu g\ mL^{-1})) - 0.00254$ (coefficient of determination $r^2 = 0.995$). As can be observed from inspection of the data displayed in Table 2, three of the commercial turmeric samples (viz. curcumin 5, 6 and 7) presented curcumin values well below the expected value, with these results corroborating the FTIR spectra (Figure 3) and the UV-Vis spectral scans (Figure 6).

Table 2. Curcumin content of the standard curcumin and commercial turmeric samples, as determined spectrophotometrically. Samples 1-5 were acquired in handling pharmacies, whereas samples 6 and 7 were acquired in establishments selling natural products

Sample	Sample amount assayed / ($\mu g\ mL^{-1}$)	Amount of curcumin found / ($\mu g\ mL^{-1}$)	Average amount of curcumin / (%, m/m)
Pure curcumin	5.000	4.964	99.28
Curcumin 1	5.000	4.797	95.94
Curcumin 2	5.000	4.771	95.42
Curcumin 3	5.000	4.065	81.30
Curcumin 4	5.000	3.848	76.96
Curcumin 5	5.000	0.925	18.50
Curcumin 6	5.000	1.316	26.32
Curcumin 7	5.000	1.414	28.28

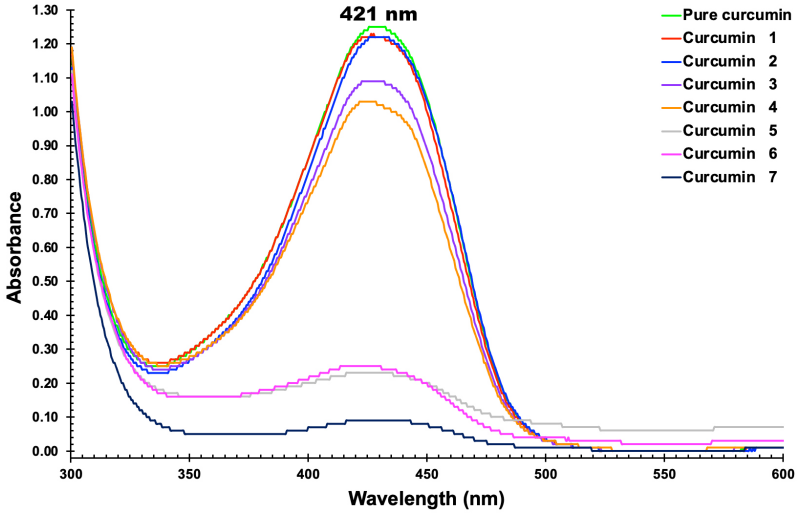

Figure 6. UV-Vis spectral scans of samples of standard curcumin and commercial turmeric samples. Samples 1-5 were acquired in handling pharmacies, whereas samples 6 and 7 were acquired in establishments selling natural products.

Commercially available saffron extracts possess three curcuminoids, 77% (m/m) of which are pure curcumin, 17% (m/m) are demethoxycurcumin and 3% (m/m) are bisdemethoxycurcumin.[5,10,24] Evidently, different species of turmeric may present different weight percentages of these curcuminoids.[11] However, for medicinal purposes, it is important to correctly identify the species, in order to ensure adequate levels of curcumin.

Samples 1 to 3 were purchased from a handling pharmacy and showed good levels of curcumin (Table 2). Sample 4 was also acquired in a handling pharmacy but, although showing a lower content in curcumin, it is still within the specifications encountered in the specialty literature where amounts of 77% (m/m) of curcumin in dry extracts are reported.[5,10,24] Regarding sample 5, despite having been acquired in a handling pharmacy, it presented curcumin values much lower than expected (Table 2). Samples 6 and 7, acquired in commercial establishments selling natural products, also presented concentrations of curcumin substantially lower in comparison to the other commercial turmeric samples (Table 2).

Conclusions

It can be concluded that the physicochemical characteristics of the several commercial turmeric samples were not homogeneous, showing in fact significant differences regarding melting points, UV-Vis spectral scan profiles and FTIR spectra, presenting toxic metals and quite low curcumin contents. The results obtained indicated that there is no adequate quality control in this type of raw material. The purchase of herbal products is a real challenge, as there is no homogeneity among commercial establishments with regard to the origin of the product, which can substantially impact negatively the performance of the commercialized products. Particularly, contamination with heavy metals, such as mercury, due to its high toxicity and accumulative power can cause serious health problems. In this way, there is a need for greater rigor in the quality control of these products, both in free trade products in stores specializing in herbs and spices, as well as in raw materials for handling pharmacies.

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Author Contributions

All authors read and agreed with the published version of the manuscript. Specifically, R.B. performed the experiments; T.H.P. analyzed the presence of metals by X-say fluorescence; J.M.O.Jr. and V.M.B. analyzed the data obtained; R.B., V.M.B. and M.M.D.C.V. wrote the text; M.M.D.C.V. and V.M.B. were responsible for the general supervision of the work.

References

1. Di Nardo, V.; Gianfaldoni, S.; Tchernev, G.; Wollina, U.; Barygina, V.; Lotti, J.; Daaboul, F.; Lotti, T.; *Maced. J. Med. Sci.* **2018**, *6*, 218. [Crossref]
2. Dutta, S.; Chawla, S.; Kumai, S.; *J. Rational Pharmacother. Res*. **2018**, *4*, 12.
3. Fugita, R. A.; Gálico, D. A.; Guerra, R.; Perpetuo, G.; Treu-Filho, O.; Galhiane, M. S.; Mendes, R. A.; Bannach, G.; *Braz. J. Therm. Anal.* **2012**, *1*, 19. [Link]
4. Guimarães, A. F.; Vinhas, A. C. A.; Gomes, A. F.; Souza, L. H.; Krepsky, P. B.; *Quim. Nova* **2020**, *43*, 909. [Crossref]
5. Stohs, S. J.; Ray, S. D.; Ji, J.; Bucci, L. R.; Preuss, H.; *Molecules* **2020**, *25*, 1397. [Crossref]
6. Noorafshan, A.; Ashkani-Esfahan, S.; *Curr. Pharm. Des.* **2013**, *19*, 2032. [Crossref]
7. Hussain, Z.; Thu, H. E.; Amjad, M. W.; Hussain, F.; Ahmed, T. A.; Khan, S.; *Mater. Sci. Eng*. **2017**, *77*, 1316. [Crossref]
8. Rendon, A.; Schäkel, K.; *Int. J. Mol. Sci*. **2019**, *20*, 1475. [Crossref]
9. Burapan, S.; Kim, M.; Paisooksantivatana, Y.; Eser, B. E.; Han, J.; *Foods* **2020**, *9*, 1219. [Crossref]
10. Hassanzadeh, K.; Bucarello, L.; Dragotto, J.; Mohammadi, A.; Corbo, M.; Feligioni, M.; *Int. J. Mol. Sci*. **2020**, *21*, 6619. [Crossref]
11. Khalid, S.; Rizwan, B.; Aslam, A.; Sharmeen, Z.; Zubair, R.; Arif, A.; Mahmood, S.; Fatima, M.; *Merit. Res. J. Food Sci. Technol.* **2020**, *5*, 32. [Crossref]
12. Gupta, S. C.; Patchva, S.; Koh, W.; Aggarwal, B. B.; *Clin. Exp. Pharmacol. Physiol*. **2012**, *39*, 283. [Crossref]
13. Imam, H.; Salam, N. E.; *Egypt. Dent. J.* **2018**, *64*, 3, 2241. [Crossref]
14. Luzardo-Ocampo, I.; Ramírez-Jiménez, A. K.; Yañez, J.; Mojica, L.; Luna-Vital, D. A.; *Foods* **2021**, *10*, 634. [Crossref]
15. Souza, C. R. A.; Glória, M. B. A.; *Braz. Arch. Biol. Technol.* **1998**, *41*, 1. [Crossref]
16. Hartanti, D.; Theeravi, J.; *J. Indonesia* **2018**, *15*, 257. [Crossref]
17. Li, S.; Yuan, W.; Deng, G.; Wang, P.; Yang, P.; Aggarwal, B. B.; *Pharm. Crops* **2011**, *2*, 28. [Crossref]
18. Dhakal, S.; Schmidt, W. F.; Kim, M.; Tang, X.; Peng, Y.; Chao, K.; *Foods* **2019**, *8*, 143. [Crossref]

19. Donga, S.; Moteriya, P.; Pande, J.; Chanda, S.; *J. Pharmacogn. Phytochem*. **2017**, *6*, 242. [Link]
20. Brand-Williams, W.; Cuvelier, M. E.; Berset, C.; *LWT-Food Sci. Technol.* **1995**, *28*, 25. [Crossref]
21. Duarte-Almeida, J. M.; Santos, R. J.; Genovesi, M. I.; Lajolo, F. M.; *Food Sci. Technol*. **2006**, *26*, 446. [Crossref]
22. Clinical and Laboratory Standards Institute (CLSI); *Performance Standards for Antimicrobial Susceptibility Testing: Twenty-First Informational Supplement, CLSI document M100-S21*; CSLI: Wayne, PA, 2018.
23. Rapalli, V. K.; Kaul, V.; Gorantla, S.; Waghule, T.; Dubey, S. K.; Pandey, M. M.; Singhvi, G.; *Spectrochim. Acta, Part A* **2020**, *224*, 117392. [Crossref]
24. Singh, A.; Avupati, V. R.; *J. Young Pharm*. **2017**, *9*, 491. [Crossref]
25. Ekor, M.; *Front. Pharmacol.* **2014**, *4*, Article 177. [Crossref]
26. Kumadoh, D.; Ofori-Kwakye, K.; *J. Crit. Rev.* **2017**, *4*, 1. [Crossref]
27. Chatzinasiou, L.; Booker, A.; MacLennan, E.; Mackonochie, M.; Heinrich, M.; *J. Herb. Med.* **2019**, *17-18*, 100281. [Crossref]
28. Bagchi, A.; Anusree, R.; Prosenjit, M.; Ali Tausif, M.; *Univers. J. Pharm.* **2015**, *4*, 48.
29. Priyadarsini, K. I.; *Molecules* **2014**, *19*, 20091. [Crossref]
30. Prakash, K. D.; Shivaji, G. S.; Rohidas, K. P.; Patel, V.; Bhalke, R.; *Int. J. Pharm. Drug Anal*. **2017**, *5*, 82. [Link]
31. Borra, S. K.; Gurumurthy, P.; Mahendra, J.; Jayamathi, K. M.; Cherian, C. N.; Chand, R.; *J. Med. Plants Res*. **2013**, *7*, 2680. [Crossref]
32. Torre, M. P.; Cavero, R. Y.; Calvo, M. I.; Vizmanos, J. L.; *Antioxidants* **2019**, *8*, 142. [Crossref]
33. Cerveira, M. M.; Vianna, H. S.; Ferrer, E. D. K.; Rosa, B. N.; Pereira, C. M. P.; Baldissera, M. D.; Lopes, L. Q. S.; Rech, V. C.; Giongo, J. L.; Vaucher, R. A.; *Biomed. Pharmacother*. **2021**, *133*, 111052. [Crossref]
34. Košťálováa, D.; Bezáková, L.; Račková, L.; Mošovská, S.; Šturdík, E.; *Acta Chim. Slov*. **2013**, *6*, 89. [Crossref]
35. Kocaadam, B.; Şanlier, N.; *Crit. Rev. Food Sci. Nutr*. **2017**, *57*, 2889. [Crossref]
36. Lestari, M. L. A. D.; Indrayanto, G. In *Profiles of Drug Substances, Excipients and Related Methodology*; Brittain, H., ed.; Academic Press: Cambridge, Massachusetts, USA, 2014, ch. 39. [Crossref] accessed in May 2022
37. Abrahams, S.; Haylett, W. L.; Johnson, G.; Carr, J. A.; Bardien, S.; *Neuroscience* **2019**, *406*, 1. [Crossref]
38. Moghadamtousi, S. Z.; Kadir, H. A.; Hassandarvish, P.; Tajik, H.; Abubakar, S.; Zandi, K.; *Biomed. Res. Int.* **2014**, *2014*, 186864. [Crossref]
39. Balouiri, M.; Sadiki, M.; Ibnsouda, S. K.; *J. Pharm. Anal.* **2016**, *6*, 71. [Crossref]
40. Amadi, C. N.; Offor, S. J.; Frazzoli, C.; Orisakwe, O. E.; *Environ. Sci. Pollut. Res*. **2019**, *26*, 18032. [Crossref]
41. Kolev, T. M.; Velcheva, E. A.; Stambolyska, B. A.; Spiteller, M.; *Int. J. Quantum Chem.* **2005**, *102*, 1069. [Crossref]
42. Lukačovičová, O.; *Acta Chim. Slov*. **2018**, *11*, 74. [Crossref]
43. *Farmacopeia Brasileira*, 6th ed.; Anvisa: Brasília, 2019.
44. Towett, E. K.; Shepherda, K. D.; Drake, B. L.; *Spectrometry* **2015**, *45*, 117. [Crossref]
45. Bhattacharya, S.; *Interdiscip. Toxicol*. **2018**, *11*, 247. [Crossref]
46. Wu, H.; *J. Heavy Metal Toxic. Dis*. **2016**, *1*, 1. [Link]
47. Mohajeri, M.; Rezaee, M.; Sahebkar, A.; *BioFactors* **2017**, *43*, 645. [Crossref]
48. Azevedo, R.; Rodriguez, E.; *J. Bot*. **2012**, Article ID 848614. [Crossref]
49. Ezeabara, C. A.; Ogochukwu, O.; Emeka, N.; Okeke, C. U.; Mbaekwe, E. I.; *Int. J. Trop. Dis. Health* **2014**, *4*, 1044. [Crossref]
50. Murti, Y. B.; Hartini, Y. S.; Hinrichs, W; L. J.; Frijlink, H. W.; Setyaningsih, D.; *J. Young Pharm*. **2019**, *11*, 26. [Crossref]
51. Sharma, K.; Agrawal, S. S.; Gupta, M.; *Int. J. Drug Dev. Res.* **2012**, *4*, 375. [Link]

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