International Journal of Pharmaceutical and Clinical Research

ISSN Print: 2664-7591
ISSN Online: 2664-7605
Impact Factor: RJIF 5.2
IJAN 2024; 6(1): 134-139
www.pharmaceuticaljournal.in
Received: 16-03-2024
Accepted: 21-04-2024

All author's name and affilation given after the references

Corresponding Author:
Edvande Xavier dos Santos Filho
[1] Academic Institute of Health and Biological Sciences, State University of Goiás - UEG, Itumbiara, Goiás, Brazil
[2] Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Herbal medicines physicochemical and microbiological analysis from a private compounding pharmacy at São Luís de Montes Belos, Goiás, Brazil

Luiz Cláudio Kehdi Guimarães, Bruna Barros de Queiroz e Oliveira, Matheus Mendes Naves, Luís Fellipe Ribeiro Vasconcelos, Fernanda Oliveira da Costa Caetano, Paulo Ricardo Pinheiro de Oliveira, Maraisa Arantes Miranda Henriques, Dhiego Gomes Filemon Bernardes, Matheus Lemos de Resende, Enzo Gabriel de Lima, Salatiel Nogueira Figueira, Veruska de Faria Patrocínio Moreira, Vitória Fernandes da Silva and Edvande Xavier dos Santos Filho

DOI: https://doi.org/10.33545/26647591.2024.v6.i1b.90

Abstract
Medicinal plants may be susceptible to a variety of contaminants throughout production chain. Indiscriminate use and production failures can expose the end consumer to harmful effects. Therefore, this study evaluated the physicochemical and microbiological quality of dry extract samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Melissa officinalis* Linn. and *Passiflora incarnata* Linn. obtained from October to December 2023 at a private compounding pharmacy in the city of São Luís de Montes Belos, Goiás, Brazil, as mandated by current legislation. All samples were authentic and corresponded to the phytotherapeutics under consideration. They exhibited a fine, homogeneous powder appearance with a distinctive color and odor. The moisture content, particle size, pH, and density fell within the pharmacopeia reference values. No bacterial or fungal contamination was observed. Results also revealed the unequivocal presence of flavonoids and tannins in all samples. Saponins were not detected only in the *Passiflora incarnata* Linn. extract. Finally, the *Equisetum arvense* Linn. sample exhibited very low water solubility. Findings demonstrate the adequate quality of the herbal samples used by the private compounding pharmacy, as all parameters conformed to the established pharmacopeial reference values.

Keywords: Quality control, herbal medicines, private compounding pharmacy, São Luís de Montes Belos, Goiás, Brazil

Introduction
Brazil exhibits a remarkable diversity of plant species, many of which have significant therapeutic potential. The richness of Brazilian flora is attributed to the various biomes that constitute its territory [1]. In this country, which holds immense potential for medicinal plants, traditional knowledge complements scientific research, enhancing the practices of managing and utilizing these resources [2].

The herbal medicine refers to a product that uses medicinal plants or their derivatives as raw materials, excluding those that contain isolated active substances [3]. Furthermore, phytotherapy, recognized as one of the Integrative and Complementary Practices (PIC) in the Brazilian Unified Health System (SUS), encompasses the use of medicinal plants in various pharmaceutical forms, including herbal medicines. Among the plant species with significant therapeutic activity and widely used by the Brazilian population are *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn [4].

Curcuma longa Linn., commonly known as turmeric, curcuma and/or açafrão-da-terra, belongs to the Zingiberaceae family. It is widely recognized and used in traditional medicine and culinary practices across various cultures. In phytotherapy, turmeric is valued for its anti-inflammatory, antioxidant, and antimicrobial properties, and is frequently applied to treat conditions such as arthritis, digestive issues, and skin diseases. Additionally, its main active compound, curcumin, has been the subject of numerous scientific studies due to its therapeutic potential in various pathologies, including chronic diseases and cancer [5]. *Cymbopogon citratus* (DC.) Stapf, commonly known as lemongrass, capim-cidreira and/or erva-cidreira, is a perennial herbaceous plant from the Poaceae family. Widely cultivated in different tropical and subtropical regions, lemongrass is valued for its digestive, sedative, and antimicrobial properties, often used to alleviate gastrointestinal disorders, combat insomnia, and reduce fever. Additionally, due to its citrusy aroma, it is extensively used in culinary practices as a seasoning in diverse types of cuisine, imparting refreshing flavor and aroma [6].

Equisetum arvense Linn., known as horsetail or cavalinha, and *Ginkgo biloba* Linn., commonly referred to as ginkgo or nogueira-do-japão, are notable plants belonging to distinct families in botanical taxonomy. While horsetail belongs to the Equisetaceae family, ginkgo is part of the Ginkgoaceae family. Both plants have traditionally been valued for their medicinal properties and various uses [7]. Horsetail is recognized for its diuretic and astringent properties, often used in herbal medicine to promote urinary system health and wound healing [8]. Yet ginkgo is appreciated for its neuroprotective and vasodilatory properties, being used to enhance memory, increase blood circulation, and treat cognitive disorders such as dementia [9].

Melissa officinalis Linn., commonly known as lemon balm or erva-cidreira, belongs to the Lamiaceae family and is valued for its calming and sedative properties, being used in the treatment of sleep disorders, anxiety, and nervous tension [10]. *Passiflora incarnata* Linn., often referred to as passionflower or maracujá, is part of the Passifloraceae family and is appreciated for its relaxing and anxiolytic properties, often used to reduce stress, promote sleep, and alleviate symptoms of anxiety [11, 12].

Medicinal plants may be subject to a variety of contaminants throughout their production chain [13]. Regardless the plant materials source, which may be wild or cultivated, there are vulnerabilities to microbiological contamination [14]. Microorganisms identified in plant samples may be pathogenic, or sample microbiological load may exceed limits established by legislation, emphasizing the importance of rigorous raw material quality control, especially after harvesting and during processing [15]. Brazilian legislation stipulates that herbal products must undergo physical, chemical, and microbiological quality tests as specified in pharmacopoeias recognized by the Brazilian Health Regulatory Agency (ANVISA) [16].

Considering the above, this study presented the physicochemical and microbiological quality characteristics of the vegetable raw materials of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn. and *Passiflora incarnata* Linn., developed at a private Compounding Pharmacy in the city of São Luís de Montes Belos, Goiás, Brazil. Additionally, this study was able to contribute to the improvement of practices adopted during the quality control testing of dried medicinal plant extracts.

Methodology

This qualitative laboratorial research analyzed dry extracts samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. obtained from October to December 2023 at a private Compounding Pharmacy (Latitude: 16.51963°S; Longitude: 50.36949°W) in the city of São Luís de Montes Belos, Goiás, Brazil. Experiments were performed in the Laboratories of Pharmacotechnics and Pharmaceutical Technology at the University Center Brasília de Goiás. Tests were performed in triplicate and all analyses and drugs reference standards were accomplished as recommended by Brazilian Pharmacopoeia 6th [16] and the Brazilian Society of Pharmacognosy (2020) [17].

Physicochemical evaluation

The conducted assays included the analysis of visual appearance, color, odor, moisture content, particle size distribution, pH determination, density, and solubility. Additionally, investigations were carried out to detect the presence of flavonoids, tannins, and saponins.

Microbiological evaluation

For the microbiological analyses, one gram of the dry extract from each sample was added to 9 mL of saline solution and subjected to serial dilutions at ratios of 1:10, 1:100, 1:1,000, 1:10,000, and 1:100,000 to assess the presence of molds and yeasts, total microorganisms, *Salmonella* spp., and *Shigella* spp.

Each dilution was inoculated in triplicate onto Petri dishes containing the culture media Potato Dextrose Agar (PDA/Himedia) for the detection of molds and yeasts; Plate Count Agar (PCA/Himedia) for the quantification of total microorganisms; and *Salmonella Shigella* Agar (SS/Acumedia) for the detection of *Salmonella* spp. and *Shigella* spp. Plates were incubated at 37°C for 24 to 48 hours.

Statistical analysis

Statistical analyses were conducted using the Windows version of GraphPad Prism 5.01 software. Grouped data analysis was performed using one-way ANOVA, followed by Bonferroni post-hoc tests, with significance set at $p < 0.05$.

Results and Discussion

Regarding extracts quality, the presence of technical-scientific information on the labels and leaflets, as well as the authenticity and purity of the products, was verified. It was observed that all samples were authentic and corresponded to the phytotherapeutics in question. However, they did not provide complete technical information on the packaging of the final products, such as the chemical constituents of each sample.

The organoleptic attributes of the dry extracts samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. exhibited a fine, homogeneous powder appearance with distinctive color and odor (Table 1).

Table 1: Organoleptic characteristics of the dry extracts from samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn.

Sample	Parameters		
	Aspect	**Color**	**Odor**
Curcuma longa Linn.	Fine, homogeneous powder	Orange-yellow	Characteristic
Cymbopogon citratus (DC.) Stapf	Fine, homogeneous powder	Light brown	Characteristic
Equisetum arvense Linn.	Fine, homogeneous powder	Greenish	Characteristic
Melissa officinalis Linn.	Fine, homogeneous powder	Light brown	Characteristic
Passiflora incarnata Linn.	Fine, homogeneous powder	Dark brown	Characteristic

Authors who conducted similar studies found organoleptic characteristics equivalent to those of the present study [18, 19], with an observation for data described by de Melo *et al.* (2007) [20], where variations of color ranging from light to dark brown were observed for *Cymbopogon citratus* (DC.) Stapf.

Samples results for moisture, particle size, and pH are described in Table 2. It is known that a percentage of moisture within the maximum allowed parameter acts as a factor in reducing or inhibiting microbial growth, promoting plant raw material microbiological stability [21]. In the samples of the analyzed phytotherapeutics, all results were within the parameters established by the Brazilian Pharmacopoeia 6th [16]. Interestingly, similar studies describe divergent results. Garbin *et al.* (2013) [22] evaluated the quality of 25 samples of plant species distributed to the population in the interior of the state of Paraná through a Basic Health Unit and found that none passed the microbiological quality control, moisture content, and other parameters. Similarly, studies conducted by Gonçalves *et al.* (2015) [23] failed samples marketed in pharmaceutical establishments in São Luís, Maranhão, Brazil.

Table 2: Moisture, particle size, and pH of the dry extracts from samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. one-way ANOVA, $p< 0.05$

Sample	Moisture (%)		Particle size		pH (10% aqueous solution)	
	Specification	**Result**	**Specification**	**Result**	**Reference**	**Result**
Curcuma longa Linn.	Maximum 5	2.10*	Minimum 90	91	-	5.49
Cymbopogon citratus (DC.) Stapf	Maximum 5	3	Minimum 90	91	4.0 to 7.0	5.87
Equisetum arvense Linn.	Maximum 5	2.2	-	93	4.0 to 6.0	5.93
Melissa officinalis Linn.	Maximum 5	1.7	Minimum 95	98	4.5 to 6.5	5.75
Passiflora incarnata Linn.	Maximum 6	3.5	Minimum 90	98	5.0 to 6.0	5.41
Reference values: Brazilian Pharmacopoeia 6th						
*Value provided by the manufacturer						
Granulometry: mesh ≤ 80/hole 180 µm						

A caracterização granulométrica dos materiais vegetais constitui um parâmetro crucial para determinar sua biodisponibilidade, pois essa análise define a área superficial disponível para interação com o solvente, indicando a taxa de dissolução. Dessa forma, partículas menores possuem uma área superficial maior, resultando em uma dissolução mais eficiente. No que tange à distribuição granulométrica, os extratos vegetais analisados demonstraram um tamanho médio de partículas conforme os parâmetros previstos, confirmando os valores fornecidos pelos fabricantes.

Plant materials granulometric characterization is a crucial parameter for determining their bioavailability, as this analysis defines the surface area available for solvent interaction, indicating the dissolution rate. Thus, smaller particles have a larger surface area, resulting in more efficient dissolution [24]. Regarding granulometric distribution, the analyzed plant extracts exhibited an average particle size within the expected parameters, confirming the values provided by the manufacturers. pH is a parameter that directly influences microorganisms' growth, as most bacterial species are neutrophiles, thriving in a pH range of 6.0 to 8.0 [25]. In this study, pH values obtained in a 10% aqueous solution are not conducive to microbiological contamination, as all samples exhibited a slightly acidic character, consistent with the values indicated by the product manufacturers. Brazilian researchers found related results, especially for *Equisetum arvense* Linn [19].

Table 3: Density and solubility analyzes of the dry extracts from samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. one-way ANOVA, $p< 0.05$.

Sample	Density (g/mL)		Solubility** (%)	
	Reference	**Result**	**Reference**	**Result**
Curcuma longa Linn.	0.340*	0.415	partially soluble*	partially soluble
Cymbopogon citratus (DC.) Stapf	0.300-0.600	0.384	soluble	very soluble
Equisetum arvense Linn.	0.350-0.900	0.475	practically insoluble*	practically insoluble
Melissa officinalis Linn.	0.200-0.500	0.23	partially soluble*	partially soluble
Passiflora incarnata Linn.	0.400-0.800	0.487	partially soluble*	partially soluble
Reference values: Brazilian Pharmacopoeia 6th				
*Value provided by the manufacturer				
**Solvent used: water				

Raw materials density determination can be performed by filling a predetermined volume with a known mass. This analysis is essential for selecting the appropriate capsule size for compounding, as well as for determining the necessary amount of active ingredient and excipients to be used, revealing the particle size of the sample components. Thus, determining the density of a raw material helps prevent errors in active ingredient concentration and reduces the likelihood of financial losses due to raw material waste [26]. In this study, the results are consistent with density analyses reported in other scientific works [19].

Water solubility is an essential parameter for evaluating the absorption of orally administered medications. Absorption is directly related to bioavailability, which can be defined as the relationship between the amount of the compound and the rate at which it reaches the site of action [26]. Regarding the solubility of the dry extracts evaluated in this study, *Cymbopogon citratus* (DC.) Stapf was classified as very soluble; while the extracts of *Curcuma longa* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. exhibited partial solubility; and the dry extract of *Equisetum arvense* Linn. was found to be partially insoluble.

In the plant kingdom, secondary metabolites form a group of unique molecules that play a crucial role in mediating the complex interaction between plants and their environment. These compounds, endowed with remarkable pharmacological activity, stand out as promising allies in the relentless pursuit of promoting and maintaining human health. Among the main examples are flavonoids, saponins, and tannins [27, 28]. With the aim of thoroughly characterizing the chemical constituents of the studied plant species, specific tests were conducted to detect the presence of flavonoids, saponins, and tannins in the obtained dry extracts. The results, compiled in Table 4, revealed the unequivocal presence of flavonoids in all samples. These compounds, extensively described in the scientific literature, present a wide range of beneficial effects on health, including anti-inflammatory, antiallergic, vasoprotective, antiulcerogenic, and antiviral properties [29].

Table 4: Presence of flavonoids, saponins and tannins in the dry extracts from samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Ginkgo biloba* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn.

Sample	Constituents			
	Flavonoids	Saponins	Tannins	
			Hydrolyzable	Condensates
Curcuma longa Linn.	Positive	Positive	Positive	Negative
Cymbopogon citratus (DC.) Stapf	Positive	Positive	Positive	Negative
Equisetum arvense Linn.	Positive	Positive	Negative	Positive
Melissa officinalis Linn.	Positive	Positive	Positive	Negative
Passiflora incarnata Linn.	Positive	Negative	Positive	Negative
Reference values: Brazilian Pharmacopoeia 6th				

Regarding the search for saponins, results demonstrated the presence of these compounds in the extracts of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn, and *Melissa officinalis* Linn. Saponins, in turn, boast a remarkable pharmacological profile, with hypocholesterolemic, anti-inflammatory, antihelminthic, and antiviral properties, paving the way for the development of new therapeutic strategies derived from these medicinal plants [30-32]. Finally, the investigation of tannins revealed the presence of this metabolite in all analyzed samples. These compounds have a wide application in the treatment of various dysfunctions, such as diarrhea, hypertension, rheumatism, hemorrhages, and wounds, due to their bactericidal, fungicidal, antiviral, and antitumor properties [33-35]. The presence of microbiological contaminants exceeding the limits established by current health regulations poses a significant threat to consumer health. Various microorganisms, including *Salmonella sp*. and *Shigella sp*., harbor pathogenic potential, causing transient or severe illnesses. Moreover, these pathogens can interfere with plant metabolism, altering the chemical properties of bioactive compounds, leading to reduced pharmacological efficacy or even toxin formation [36]. To ensure the safety and quality of botanical extracts, a comprehensive microbiological evaluation was conducted. The analysis revealed that all samples exhibited total bacterial counts below 10 UFC/g, with no detection of *Salmonella* sp. and/or *Shigella* sp. These results demonstrate that extracts comply with the standards established by the Brazilian Pharmacopoeia 6th [16], confirming the absence of pathogenic microorganisms and microbiological products quality.

In addition to bacterial investigation, fungal contamination was also evaluated. Results indicated that all samples presented fungal counts below 10^3 UFC/g, strictly adhering to the parameters set forth by current legislation [16]. It is noteworthy that contradictory findings were reported in studies by Beltrame *et al.* (2009) [37] and Montes *et al.* (2017) [38], who identified the presence of total bacteria and fungi in samples of *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., and *Melissa officinalis* Linn. This discrepancy could be attributed to factors such as distinct analytical methodologies, plant cultivation and storage conditions, and even genetic variability among plant species. This investigation findings conclusively demonstrate the good microbiological quality of the analyzed botanical extracts, confirming that products were free from pathogenic microorganisms and meet safety standards. The absence of microbiological contamination, coupled with proven pharmacological activity, position products as safe and effective alternative for treating various ailments.

Conclusion

Since strict quality control in compounding pharmacies is crucial for guaranteeing the safety of the end consumer, dry extract samples of *Curcuma longa* Linn., *Cymbopogon citratus* (DC.) Stapf, *Equisetum arvense* Linn., *Melissa officinalis* Linn., and *Passiflora incarnata* Linn. exhibited appropriate physicochemical and microbiological parameters that fell within the established pharmacopeial reference values. Results demonstrate the decent quality of the herbal samples used in the private compounding pharmacy under consideration.

Acknowledgement: Authors acknowledge material support provided by the University Center Brasília de Goiás.

Declaration of interest statement

Authors declare no conflicts of interest that could have impacted the design, execution, or reporting of this research.

References

1. de Matos RC, Bitencourt AFA, de Oliveira ADM, Prado VR, Machado RR, Scopel M. Evidence for the efficacy of anti-inflammatory plants used in Brazilian traditional medicine with ethnopharmacological relevance. Journal of Ethnopharmacology. 2024;329:118137.
2. Noguera NH, Noguera DCLH, Machado APDF, Reguengo LM, Nascimento RPD. Emerging berries from the Brazilian Amazon and Atlantic Forest biomes: new sources of bioactive compounds with potential health benefits. Food & Function; c2024. DOI: 10.1039/d4fo00182f.
3. Jarema M. Herbal drug treatment. Neuro Enocrinology Letters. 2008;29(1):93-104.
4. Brasil. Ministério da Saúde. Práticas integrativas e complementares: plantas medicinais e fitoterapia na Atenção Básica. Departamento de Atenção Básica. – Brasília: Ministério da Saúde; c2012. p. 156.
5. Fuloria S, Mehta J, Chandel A, Sekar M, Rani NNIM, Begum MY, *et al*. A Comprehensive Review on the Therapeutic Potential of *Curcuma longa* Linn. in Relation to its Major Active Constituent Curcumin. Frontiers in Pharmacology. 2022;13:820806.
6. Ekpenyong CE, Akpan E, Nyoh A. Ethnopharmacology, phytochemistry, and biological activities of *Cymbopogon citratus* (DC.) Stapf extracts. Chinese Journal of Natural Medicines. 2015;13(5):321-337.
7. Dragos D, Gilca M, Gaman L, Vlad A, Iosif L, Stoian I, Lupescu O. Phytomedicine in Joint Disorders. Nutrients. 201716;9(1):70.
8. Boeing T, Tafarelo Moreno KG, Gasparotto Junior A, Mota da Silva L, de Souza P. Phytochemistry and Pharmacology of the Genus *Equisetum* (Equisetaceae): A Narrative Review of the Species with Therapeutic Potential for Kidney Diseases. Evidence-based Complementary and Alternative Medicine. 2021;2021:6658434.
9. Eisvand F, Razavi BM, Hosseinzadeh H. The effects of *Ginkgo biloba* on metabolic syndrome: A review. Phytotherapy Research. 2020;34(8):1798-1811.
10. Petrisor G, Motelica L, Craciun LN, Oprea OC, Ficai D, Ficai A, *et al*. *Melissa officinalis*: Composition, Pharmacological Effects and Derived Release Systems-A Review. International Journal of Molecular Sciences. 2022;23(7):3591.
11. Miroddi M, Calapai G, Navarra M, Minciullo PL, Gangemi S. *Passiflora incarnata* L.: ethnopharmacology, clinical application, safety and evaluation of clinical trials. Journal of Ethnopharmacology. 2013;150(3):791-804.
12. Kim M, Lim HS, Lee HH, Kim TH. Role Identification of *Passiflora Incarnata* Linnaeus: A Mini Review. Journal of Menopausal Medicine. 2017;23(3):156-159.
13. Kosalec I, Cvek J, Tomić S. Contaminants of medicinal herbs and herbal products. Archives of Industrial Hygiene and Toxicology. 2009;60(4):485-501.
14. Sen T, Samanta SK. Medicinal plants, human health and biodiversity: a broad review. Advances in Biochemical Engineering/Biotechnology. 2015;147:59-110.
15. Ałtyn I, Twarużek M. Mycotoxin Contamination Concerns of Herbs and Medicinal Plants. Toxins (Basel). 2020;12(3):182.
16. Brazilian Pharmacopoeia. 6th edition, ANVISA, Brasília; c2024.
17. Sociedade Brasileira de Farmacognosia – SBFgnosia; c2020.
18. de Melo JG, Santos AG, de Amorim EL, do Nascimento SC, de Albuquerque UP. Medicinal plants used as antitumor agents in Brazil: An ethnobotanical approach. Evidence-based Complementary and Alternative Medicine. 2011;2011:365359.
19. Meotti FL, da Silva ACP, Gumy MP, Duarte AF, Carneiro VPP, Benedetti VP, *et al*. Physical, chemical and microbiological evaluation of herbal drugs used in a municipal pharmacy of manipulation. Research, Society and Development. 2021;10(8):e45710817557.
20. de Melo JG, Martins JDGR, Amorim ELC, Albuquerque UP. Qualidade de produtos a base de plantas medicinais comercializados no Brasil: Castanha-da-índia (*Aesculus hippocastanum* L.), capim-limão (*Cymbopogon citratus* (DC.) Stapf) e centela (*Centella asiatica* (L.) Urban). Acta Botanica Brasilica. 2007;21(1):27-36.
21. Oliveira OW, Petrovick PR. Secagem por aspersão (*spray drying*) de extratos vegetais: bases e aplicações. Revista Brasileira De Farmacognosia. 2010;20(4):641-650.
22. Garbin L, Tiuman TS, Krüger RL. Avaliação da Qualidade de Plantas Medicinais Distribuídas por uma Unidade de Saúde de um Município do Interior do Paraná. Revista Ciências Exatas e Naturais. 2013;15(1):77-93.
23. Gonçalves AH, Pereira AS, Santos GRS, Guimarães LGL. Atividade fungitóxica *in vitro* dos óleos essenciais de *Lippia sidoides* Cham., *Cymbopogon citratus* (D.C.) Stapf. e de seus constituintes majoritários no controle de *Rhizoctonia solani* e *Sclerotium rolfsii*. Revista Brasileira de Plantas Medicinais. 2015;17(4):1007-1015.
24. Garg V, Dhar VJ, Sharma A, Dutt R. Facts about standardization of herbal medicine: A review. Zhong Xi Yi Jie He Xue Bao. 2012;10(10):1077-1083.
25. Coelho RR, Oliveira RC, Drozdowicz A. Effect of pH on growth and respiration of microorganisms isolated from acid soil. Annals of Microbiology (Rio J). 1979;24:55-69.
26. Costa AS, da Silva DDM, de Jesus LC, Luiz LC, Batista RT, Bell MJV, *et al*. The importance of the choice of excipients in drug manipulation. Brazilian Journal of Health Review. 2021;4(4):16659-16670.
27. Zaynab M, Fatima M, Abbas S, Sharif Y, Umair M, Zafar MH, *et al*. Role of secondary metabolites in plant defense against pathogens. Microbial Pathogenesis. 2018;124:198-202.
28. Erb M, Kliebenstein DJ. Plant Secondary Metabolites as Defenses, Regulators, and Primary Metabolites: The Blurred Functional Trichotomy. Plant Physiology. 2020;184(1):39-52.
29. Dias MC, Pinto DCGA, Silva AMS. Plant Flavonoids: Chemical Characteristics and Biological Activity. Molecules. 2021;26(17):5377.
30. Campbell JB, Peerbaye YA. Saponin. Research in Immunology. 1992;143(5):526-530.
31. Reichert CL, Salminen H, Weiss J. *Quillaja* Saponin Characteristics and Functional Properties. Annual

Review of Food Science and Technology. 2019;10:43-73.
32. Li YH, Zou M, Han Q, Deng LR, Weinshilboum RM. Therapeutic potential of triterpenoid saponin anemoside B4 from *Pulsatilla chinensis*. Pharmacological Research. 2020;160:105079.
33. Chung KT, Wong TY, Wei CI, Huang YW, Lin Y. Tannins and human health: A review. Critical Reviews in Food Science and Nutrition. 1998;38(6):421-64.
34. Pizzi A. Tannins: Prospectives and Actual Industrial Applications. Biomolecules. 2019;9(8):344.
35. Maugeri A, Lombardo GE, Cirmi S, Süntar I, Barreca D, Laganà G, *et al*. Pharmacology and toxicology of tannins. Archives of Toxicology. 2022;96(5):1257-1277.
36. Monagas M, Brendler T, Brinckmann J, Dentali S, Gafner S, Giancaspro G, *et al*. Understanding plant to extract ratios in botanical extracts. Frontiers in Pharmacology. 2022;13:981978.
37. Beltrame FL, Ferroni DC, Villanova Alves BR, Pereira AV, Esmerino LA. Avaliação da qualidade das amostras comerciais de *Baccharis trimera* L. (Carqueja) vendidas no Estado do Paraná. Acta Scientiarum. Health Sciences. 2009;31(1):37-43.
38. Montes RA, Souza ROLS, Moraes SR, Miranda MG, Friede R, Lima ALS, *et al*. Qualidade Microbiológica de Drogas Vegetais Utilizadas na Fitoterapia Popular. Revista ESPACIOS. 2017;38(11):12-18.

Luiz Cláudio Kehdi Guimarães
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Bruna Barros de Queiroz e Oliveira
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Matheus Mendes Naves
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Luís Fellipe Ribeiro Vasconcelos
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Fernanda Oliveira da Costa Caetano
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Paulo Ricardo Pinheiro de Oliveira
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Maraisa Arantes Miranda Henriques
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Dhiego Gomes Filemon Bernardes
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Matheus Lemos de Resende
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Enzo Gabriel de Lima
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Salatiel Nogueira Figueira
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Veruska de Faria Patrocínio Moreira
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Vitória Fernandes da Silva
Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil

Edvande Xavier dos Santos Filho
[1] Academic Institute of Health and Biological Sciences, State University of Goiás - UEG, Itumbiara, Goiás, Brazil
[2] Zarna Faculty of Medicine, Itumbiara, Goiás, Brazil