Research, Society and Development, v. 10, n. 9, e26710917906, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i9.17906

# Evaluation of the quality of commercial plant drugs with antidiabetic indications

## Avaliação da qualidade de drogas vegetais comerciais com indicação antidiabética

## Evaluación de la calidad de medicamentos vegetales comerciales con indicación antidiabética

Received: 07/05/2021 | Reviewed: 07/13/2021 | Accept: 07/17/2021 | Published: 07/25/2021

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**Abstract**
The use of medicinal plants for the treatment of diseases is an old practice and is widely used. However, many products are still marketed without the necessary quality. This study aimed to evaluate the organoleptic characteristics, presence of foreign material, packaging and labeling of plant drugs marketed for the control of diabetes. Comercial samples of cavalinha, jambolão and pata-de-vaca sold in two municipalities in southeastern Brazil were acquired. The analyses of the packaging and labels were performed based on Resolutions of the Collegiate Board of Directors of the Brazilian National Health Surveillance Agency (RDC No. 26/2014 and RDC No. 66/2014). The Brazilian Pharmacopoeia VI was used to guide the preparation of a sensory evaluation questionnaire and analysis of foreign material. None of the samples complied with the packaging requirements. Approximately 69% of the samples failed the sensory analysis. Regarding the analysis for the presence of foreign material, only sample J1 of jambolão was within the 2% w/w limit, as established in the Brazilian Pharmacopoeia. Based on simple and primary quality control analyses, it is concluded that the analyzed plant drugs are not in accordance with Brazilian legislation, putting the health of consumers of these teas at risk.
**Keywords:** *Syzygium cumini; Bauhinia forficate; Equisetum arvense;* Health legislation; Medicinal plants.

**Resumo**
O uso de plantas medicinais no tratamento de doenças é uma prática antiga e amplamente utilizada. Porém, muitos produtos ainda são comercializados sem a qualidade necessária. O objetivo deste estudo foi avaliar as características organolépticas, a presença de material estranho, embalagem e rotulagem de drogas vegetais comercializadas para o controle da diabetes. Foram adquiridas amostras comerciais de "cavalinha", "jambolão" e "pata-de-vaca" comercializadas em dois municípios do sudeste brasileiro. As análises das embalagens e rótulos foram realizadas com base nas Resoluções de Diretoria Colegiada da Agência Nacional de Vigilância Sanitária (RDC nº 26/2014 e RDC nº 66/2014). A Farmacopéia Brasileira VI foi utilizada para orientação da elaboração de questionário de avaliação sensorial e análise de material estranho. Nenhuma das amostras apresentou conformidade com as especificações técnicas exigidas para as embalagens. Cerca de 69% das amostras foram reprovadas na análise sensorial. Com relação à análise de pureza por presença de material estranho, apenas a amostra J1 de "jambolão" ficou dentro do limite de 2% p/p estabelecido na Farmacopéia Brasileira VI. A partir de análises simples e primárias de controle de qualidade, conclui-se que as drogas vegetais analisadas estão em desacordo com a legislação brasileira, o que coloca em risco a saúde dos consumidores destes chás.
**Palavras-chave:** *Syzygium cumini; Bauhinia forficate; Equisetum arvense;* Legislação sanitaria; Plantas medicinais.

**Resumen**
El uso de plantas medicinales para tratar enfermedades es una práctica antigua. Sin embargo, todavía se comercializan muchos productos sin la calidad necesaria. El objetivo fue evaluar las características organolépticas, la presencia de material extraño, el envasado y etiquetado de los medicamentos vegetales comercializados para el control de la diabetes. Se vendieron muestras comerciales de "cavalinha", "jambolão" y "pata-de-vaca" en dos municipios del

sureste de Brasil. Los análisis de los envases y etiquetas se realizaron en base a las Resoluciones del Consejo Colegiado de la Agencia Nacional de Vigilancia Sanitaria (RDC No. 26/2014 y RDC No. 66/2014). Se utilizó la Farmacopea Brasileña VI para orientar la elaboración de un cuestionario de evaluación sensorial y análisis de material extraño. Ninguna de las muestras cumplió con las especificaciones técnicas requeridas para el empaque. Aproximadamente el 69% de las muestras fallaron en el análisis sensorial. En cuanto al análisis de presencia de material extraño, solo la muestra J1 de "jambolão" estuvo dentro del límite de 2% p / p recomendado. A partir de análisis simples y primarios de control de calidad, se concluye que los medicamentos vegetales analizados están en desacuerdo con la legislación brasileña, poniendo en riesgo la salud de los consumidores.
**Palabras clave:** *Syzygium cumini; Bauhinia forficate; Equisetum arvense*; Legislación sanitaria; Plantas medicinales.

## 1. Introduction

The use of medicinal plants and herbal preparations is a practice that originates from the early days of medicine and is based on knowledge accumulated across generations, which for centuries formed the basis for the treatment of numerous diseases (Brasil, 2006). Medicinal plant preparations are usually administered in the form of teas prepared as infusions or decoctions. The part of the plant most commonly used by different populations are the leaves (Barbosa et al., 2017; Santos & Vilanova, 2017).

In recent years, there has been an increase in demand for medicinal plants and natural products in general (Melo, Amorim & Albuquerque, 2007). In Brazil, guidelines were developed for the development of actions aimed at the safe and rational use of medicinal plants and herbal medicines through the National Policy on Medicinal Plants and Herbal Medicines and the National Policy on Integrative and Complementary Practices of the Unified Health System (SUS) (Brasil, 2006). In February 2009, the Ministry of Health created the Brazilian National List of Medicinal Plants of Interest to the SUS (RENISUS), a list containing medicinal plants of popular use that should be prioritized in preclinical and clinical studies because they have the potential to generate products of interest to the SUS. In 2010, Ordinance no. 886 of the Ministry of Health established the Living Pharmacy ('Farmácia Viva'), allowing the production, preparation and dispensing of magistral and officinal preparations of medicinal plants and herbal medicines within the SUS (Brasil, 2010).

This increase in demand for plants and plant products has occurred because they are often considered healthier, are less toxic and have fewer side effects and/or adverse effects than synthetic products (Arulselvan et al., 2014). However, unwanted effects related to the use of herbal medicines have been frequent, which may be a consequence of the low quality of the products available on the market (World Health Organization [WHO], 2007); this low quality is related to contamination, substitution and adulteration, as well as the incorrect identification of the species, a lack of standardization and use without guidance (Arnous, Santos & Beinner, 2005).

A survey conducted from 1999 to 2009 on the reports of adverse events of the use of medicinal plants and their derivatives was performed by Balbino & Dias (2010) using data from the National Pharmacovigilance System. In that study, one-third of the reports were related to the use of medicinal plants or their derivatives not registered with the Brazilian Health Surveillance Agency (ANVISA), an agency that aims to promote the protection of the health of the Brazilian population.

According to Brazilian legislation, all processes involving medicinal plant products, from production to sale, are regulated by ANVISA, and such products can be classified as pharmaceutical or food products (Gomes, Elpo & Negrelle 2014). The Resolution of the Collegiate Board of Directors - RDC No. 26/2014 is the current standard for the registration of herbal medicines and the registration or notification of traditional herbal products for pharmaceutical purposes. According to this standardization, registration is an instrument through which the Ministry of Health regulates processes that may be related to the efficacy, safety and quality of products for their sale or consumption, while notification is communication to ANVISA about the intention to manufacture, import and/or sell traditional herbal products (THPs).

RDC No. 13/2013 defines a THP as the product obtained from active plant raw materials, whose safety is based on

traditional use, characterized by reproducibility and constancy of its quality. RDC No. 26/2014 (art. 22) establishes that the safety and effectiveness of THPs must be proven for a minimum period of 30 years, or simplified registration, which should be proven by their presence on the list of simplified registration THPs (Normative Instruction - NI no. 2, of May 13, 2014) or their presence in monographs of traditionally used herbal medicines of the European Community (EMA).

According to RDC No. 26/2014, the THP category includes medicinal teas, referring to plant drugs used for medicinal purposes, prepared in water by the consumer (Brasil, 2014a). Art. 38 of RDC No. 26/2014 allows notification as a THP only for plant drugs listed in the latest edition of the Brazilian Pharmacopoeia that have defined quality control protocols. Therefore, the other THPs should be registered. On the other hand, art.2 of RDC No. 26/2014 mentions art. 22 of Decree 8077 of 2013, which waives registration for medicinal plants in the form of plant drug. Thus, several plant drugs with medicinal purposes are marketed without registration and without notification to ANVISA.

Many plant drugs are marketed in Brazil due to their traditional use to treat diseases. However, even though they have been used for many years, there are still a small number of monographs of medicinal plants in the latest edition of the Brazilian Pharmacopoeia (Brasil, 2019), and in many cases, there are no data that prove the safety and efficacy of these products. Despite the recommendation of the World Health Organization to adopt procedures to ensure the quality of medicinal plants (Who, 2011), quality control for several plant species with medicinal properties marketed in Brazil is still very limited.

Diabetes mellitus (DM) is a chronic disease characterized by elevated blood glucose (hyperglycemia) resulting from impaired secretion and/or action of the hormone insulin, which is produced in the pancreas by β cells (American Diabetes Association, 2005). It is estimated that in Brazil, there are more than 13 million people with the disease, which represents approximately 6.9% of the population (Sociedade Brasileira de Diabetes [SBD], 2017). The use of antidiabetic teas is a common practice among diabetic patients (Siqueira et al., 2017). However, the quality of plant drugs found in the market is something that has concerned health professionals due to the lack of rigor in terms of ensuring product safety and guidelines for the consumer (Leal-Costa, Teodoro, Barbieri, Santos & Souza, 2018).

In this context, the present study aimed to evaluate the quality of the antidiabetic plant drugs *Syzygium cumini* (L.) Skeels (Myrtaceae), *Bauhinia forficata* Link (Fabaceae), and *Equisetum arvense* (L.) (Equisetaceae), which are listed in the RENISUS, through primary quality control trials.

## 2. Methodology

### 2.1 Plant material

Commercial samples of plant drugs declared to be cavalinha, jambolão and pata-de-vaca were acquired in pharmacies and natural product stores in the municipalities of Lavras (Minas Gerais - MG) and Ribeirão Preto (São Paulo - SP), Brazil. The samples were acquired based on availability at the time, making sure to acquire samples from different suppliers for each plant (Table 1).

### 2.2 Analysis of packaging

The packages and labels of the plant drugs cavalinha, jambolão and cow's hoof were analyzed to assess compliance with the requirements of RDC No. 26/2014, as modified by RDC No. 66/2014, where the plant drugs cavalinha, jambolão and pata-de-vaca are classified (Brasil, 2014a; Brasil, 2014b).

**Table 1 -** List of commercial samples evaluated and municipalities where they were acquired.

| **Common name** ***Scientific name*** | **Origin** | **Code** | **Part of the plant** | **Presentation** | **Weight (g)** |
|---|---|---|---|---|---|
| Cavalinha | Ribeirão Preto- SP | C1 | Aerial parts | packaged | 30 |
| *Equisetum arvense* | Lavras - MG | C2 | | bulk | 22 |
| | Lavras - MG | C3 | | packaged | 50 |
| | Lavras - MG | C4 | | packaged | 50 |
| Jambolão | Ribeirão Preto - SP | J1 | Leaves | packaged | 30 |
| *Syzygium cumini* | Lavras - MG | J2 | | bulk | 20 |
| | Lavras - MG | J3 | | packaged | 50 |
| Pata-de-vaca | Ribeirão Preto - SP | P1 | Leaves | packaged | 30 |
| *Bauhinia forficata* | Lavras - MG | C2 | | bulk | 22 |
| | Lavras - MG | C3 | | packaged | 50 |
| | Lavras - MG | C4 | | packaged | 50 |
| | Lavras - MG | C5 | | bulk | 20 |
| | Lavras - MG | C6 | | packaged | 20 |

Source: Authors.

### 2.3 Sensory analysis

The evaluation of the organoleptic characteristics was performed based on the method suggested by the Brazilian Pharmacopoeia, 6th edition (Brazil, 2019). Based on the parameters described in the Pharmacopoeia, a questionnaire containing 14 questions was prepared. These questions were related to the evaluation of organoleptic characteristics, such as shape, size, color, surface, texture, fracture, appearance of the cut surface, consistency and odor, in addition to a question about acceptance by the evaluator of each sample analyzed. After general instructions were provided, the questionnaire was applied to a group of 10 evaluators who had knowledge in the field. For the evaluation, approximately 3.0 g of plant material from the samples was taken from plant material free of foreign material. The samples were placed in Petri dishes on white bond paper. The evaluation was performed in daylight using a ruler and magnifying glass. The evaluation was performed by comparing obtained samples with authentic samples collected during the collection of medicinal plants for the Medicinal Plant Garden of the Federal University of Lavras (UFLA). The reference samples were processed, and their voucher specimens were deposited in the PAMG Herbarium of the Agricultural Research Company of Minas Gerais (EPAMIG) under registration numbers PAMG 58402 for cavalinha (*Equisetum arvense* L.), PAMG 58579 for jambolão (*Syzygium cumini* (L.) Skeels) and PAMG 58395 for cow's hoof (*Bauhinia forficata* Link).

### 2.4 Determination of foreign material

The presence of foreign material was analyzed following the methodology of the Brazilian Pharmacopoeia, 6th edition (Brazil, 2019). The entire content of the acquired samples (Table 1) was spread in thin layers on a smooth surface tray, and foreign materials were separated manually, first with the naked eye and then with the aid of a manual magnifying glass. The term “other structures” was used for damaged parts or unidentified materials.

## 3. Results and Discussion

### 3.1 Analysis of packaging

None of the samples had secondary packaging; therefore, all information was analyzed in the primary packaging. In general, protection against light was present for approximately 15% of the samples, while protection against moisture was found for approximately 84.6% of the samples. A safety seal was found for 61.5% of the samples.

The percentages of the samples that complied with the requirements of RDC No 26/2014 are shown in Table 2. Regarding the relevant product information, no sample included the commercial name, but all had the common name of the species; only 53.8% identified plant drugs by their scientific names (Table 2).

Regarding the technical-pharmaceutical information, no package provided guidance on individual doses and route of administration or contained individual dispensers. Likewise, information on warnings, restrictions of prolonged use or contraindications were absent from 100% of the samples. There was also no information on use for the elderly, and only 15.4% had information on use for children and pregnant women (Table 2). None of the commercial samples were accompanied by a technical leaflet, as required by RDC No. 26/2014. For 15.4% of the samples, the packages did not provide recommendations for seeking guidance from a health professional if symptoms persisted. The same percentage was observed for the mention of the pharmaceutical form, including incorrect mention of the term ‘dry extract’. The method of preparation, such as infusion or decoction, was mentioned on 46.15% of the packages. Only 7.7% had some information on how to preserve the product and only 15.4% failed to declare the expiration date for the product.

Regarding commercial information, less than 50% of the samples contained information about the name and address of the company that registered the product and the customer support contact number. Approximately 85% of the samples did not provide the name and address of the person responsible for the packaging or the name of the technical manager.

Regarding the legal aspects, no product was registered by the Ministry of Health, and no product was mentioned as being a 'traditional herbal medicine'. Last, less than 50% were reported to ANVISA (Table 2).

**3.2 Sensory analysis**

The sensory tests focused on visual, odor and texture analyses. The results of the pata-de-vaca samples are shown in Table 3. Authentic samples of pata-de-vacas have green to gray-brown leathery leaves. There was no standardization of the pata-de-vaca drugs regarding fragmentation. Samples P1, P3, P4 and P6 were classified as fragmented, P2 was classified as whole, and P5 was classified as crushed. Only sample P2 showed fragments with a standardized size of approximately 3 to 5 cm. Sensory analysis of samples of cavalinha and jambolão also showed many differences between commercial samples of the same plant and in relation to the reference sample of each one (not shown).

**Table 2 –** Percentage of samples analyzed whose packaging information met the requirements of DRC No. 26/2014.

| Requirements | Percentage of compliance (%) |
|---|---|
| Commercial name | 0 |
| Popular name | 100 |
| Botanical name | 53.8 |
| Company name or logo | 61.5 |
| Individual dose of the drug | 0 |
| Administration route | 0 |
| Pharmaceutical form | 15.4 |
| Recommendation to seek health professionals | 15.4 |
| Restriction of use by age group | 7.7 |
| Restriction of use for pregnant women | 7.7 |
| Warning phrases | 0 |
| Restriction on prolonged use | 0 |
| Contraindications | 0 |
| Preservation and storage instructions | 7.7 |
| Name and address of the company that registered the product | 46.2 |
| Name and address of the person responsible for packaging | 15.4 |
| Technical manager | 15.4 |
| National Registry of Legal Entities (CNPJ) | 61.5 |
| Customer support contact number | 46. 2 |
| Drug batch | 53.8 |
| Expiration date | 84.6 |
| Notification to ANVISA | 46.2 |
| Date of manufacture | 61.5 |
| Phrase: Traditional herbal medicine | 0 |
| Acronym “MS” and registration number with the Ministry of Health | 0 |

Source: Authors.

All commercial pata-de-vaca samples showed color different from the standard, and samples P2, P4 and P5 had spotted, discolored or darkened parts. The absence of a characteristic odor was observed for sample P4. Most of the samples had a weak odor compared with the odor of the authentic sample (Table 3). For the cavalinha samples, 50% were classified as crushed, 46% had shoots between 1 and 2 cm, and 80 to 100% of the evaluators classified the color as different from the reference sample. Samples C1 and C3 had darkened parts, while samples C2 and C4 had spotted, discolored or darkened parts. Regarding odor, the samples were classified as weak to moderate intensity. The cavalinha samples indicated a woody odor, except for sample C4, which exhibited a rancid odor.

Fragments predominated in jambolão samples, which were therefore not standardized. Samples of jambolão showed fragments ranging from 1 to 5 cm. All samples indicated a color different from the reference sample, the worst of which was sample J3, which had spots with darkened and discolored parts.

**Table 3 -** Qualitative parameters and percentage of predominant occurrences in the sensory analysis of commercial pata-de-vaca samples.

| Organoleptic characteristic | Parameter compared to the reference sample | Pata-de-vaca sample [1] | | | | | |
|---|---|---|---|---|---|---|---|
| | | **P1** | **P2** | **P3** | **P4** | **P5** | **P6** |
| Size | Predominant fragmentation | Fragmented | Whole | Fragmented | Fragmented | Crushed | Fragmented |
| | Standardized fragmentation | No | Yes | No | No | No | No |
| | Size of fragments | 2 to 3 cm | 3 to 5 cm | 4 to 5 cm | 2 to 3 cm | 2 to 3 cm | 2 to 3 cm |
| Color | Color | Different | Different | Different | Different | Different | Different |
| | Tone | Lighter | Darker | Darker | Darker | Darker | Darker |
| Odor | Odor intensity | Weak | Moderate | Weak | Odorless to weak | Weak | Weak to moderate |
| | Aromatic characteristic | Woody | Woody | Woody | Woody | Woody | Woody |

1- P1, P2, P3, P4, P5 and P6 are commercial samples. Source: Authors.

### 3.3 Determination of foreign material

Foreign materials of plant origin are listed in Table 4. Sample C1 had the lowest percentage of impurities (1.4%). Samples C2 and J3 stood out among samples of the same species because they contained more impurities (30.9% and 58%, respectively).

Stems, twigs and/or branches were observed in all samples. Samples C1, C3 and C4 showed reproductive structures (strobiles). In all of the cavalinha samples, in sample J1 and in samples P2, P3 and P5, leaves of other plant species were observed (Figure 1). Some damaged stems were found and removed from the cavalinha samples.

The pata-de-vaca samples showed a diversity of plant structures considered foreign materials and had the highest percentage of impurities (7.4% to 81%) compared to samples from other species, with P4 being the most impure.

Soil particles, such as dirt and sand, were found in samples C2, C3, C4, P1, P2, P3 and P5. Insects or parts of insects were found in samples C1, C4, P1 and P6 (Figure 1). Several structures were also found, such as feathers in P1 and parts of a cocoon in P5.

**Table 4 -** Results of the evaluation of the percentage of impurities and the types of foreign material found in commercial samples of cavalinha, jambolão and pata-de-vaca.

| | | Foreign material | | | |
|---|---|---|---|---|---|
| **Sample[1:]** | **Impurities (%)** | **Twigs and/or branches** | **Other structures** | **Insects** | **Soil residue** |
| C1 | 1.4% | + | - | + | - |
| C2 | 30.9% | + | + | - | + |
| C3 | 3.3% | - | + | - | + |
| C4 | 2.2% | + | + | + | + |
| J1 | 5.7% | + | + | - | - |
| J2 | 3.6% | + | - | - | - |
| J3 | 58% | + | - | - | - |
| P1 | 7.9% | + | + | + | + |
| P2 | 7.4% | + | + | - | + |
| P3 | 38.3% | + | + | - | + |
| P4 | 81% | + | + | - | - |
| P5 | 1.4% | + | + | - | + |
| P6 | 30.9% | + | + | + | - |

1- C: cavalinha; J: jambolão; P: pata-de-vaca; 1, 2, 3, 4, 5 and 6 are the commercial samples; "+" and "-" represent the presence or absence of the listed foreign material, respectively. Source: Authors.

**Figure 1 -** Commercial samples (left) and foreign materials (right) found in some samples of cavalinha, jambolão and cow's hoof.


C1 and C2: cavalinha; J1 and J2: jambolão; P2 and P3: pata-de-vaca. Insects or parts of insects in C1; leaves of other plant species in C2; stems, twigs and/or branches in J1, J2, P2 and P3; decomposition and/or microbial contamination in P3. Source: Authors.

## 4. Discussion

There is a wide variety of plant drugs sold in Brazil to assist in the treatment of diabetes, regardless of studies and procedures that prove quality, safety and therapeutic efficacy. Despite the advances obtained with the creation of the National Policy on Medicinal Plants and Herbal Medicine (Brasil, 2006), the National Policy on Integrative and Complementary Practices of the Unified Health System (SUS) (Brasil, 2006), RENISUS (Brasil, 2009) and Living Pharmacy (Brasil, 2010), these policy proposals were not accompanied by incentives for the research and development of quality products.

Even today, most products sold in Brazil have no guarantee as to their efficacy, safety and quality (MELO et al., 2007). A direct consequence of the low quality of products available in the market is the increase in the number of adverse effects related to the use of medicinal plants observed in recent years (Ekar & Kreft, 2019; Alonso-Castro et al., 2017).

The plant drugs used in this study, i.e., cavalinha, jambolão and pata-de-vaca, were easily found in establishments selling natural products. These species are listed in RENISUS and are indicated for the treatment of diabetes. According to RDC No. 26/2014, a traditional herbal product must provide proof of safe and effective use for at least 30 years (Brasil, 2014b). The use of pata-de-vaca, *Bauhinia forficata* (Link), as a treatment for diabetes has been described since the early

twentieth century (Miyake; Akisue & Akisue, 1986; Juliane, 1929). It is a species native to Brazil and one of the most commonly used in folk medicine (Mariángel et al., 2019); (Souza et al., 2018); (Franco et al., 2020). Jambolão, *Syzygium cumini* (L.) Skeels, is the species of this genus most used in folk medicine. Originally from India and naturalized in Brazil, there have been studies reporting its medicinal properties since 1986 (Nair & Santhakumari, 1986); (ELHAWARY et al., 2020). The species cavalinha, *Equisetum arvense* (L.), is the only one described in a pharmacopoeia (European Medicines Agency [EMA], 2016). It is widely used in Europe, mainly due to its two diuretic properties. Although many studies confirm the potential of these species in the treatment of diabetes in animal models and in vitro studies, there are few clinical studies confirming their hypoglycemic effect (Sidana et al., 2017; Mariángel, 2019; Hegedűs et al., 2020).

According to the World Health Organization (WHO), quality control has a direct impact on the safety and efficacy of plant products, and good agricultural and collection practices are the first step towards quality assurance, together with good manufacturing practices. Therefore, the development of appropriate methodologies is necessary to monitor and ensure the safety, efficacy and quality of medicinal plant products. For this purpose, the WHO has developed guidelines on good agricultural and collection practices, providing a detailed description of techniques and measures for the cultivation, collection, recording and documentation of data and information necessary for the production of medicinal plants, control of raw materials, processing and storage. Based on these guidelines, it is important that each country implement a quality assurance system that encompasses all the processes necessary for quality control (WHO, 2003, 2007).

According to RDC 26/2014, in art. 52, packaging must ensure the protection of the product against contamination and the effects of light and moisture and have a seal or safety seal that ensures the inviolability of the product. The results obtained in this study showed that there was no standardization in the type of packaging, some of which were sold without any protection from light, and that there was also no such warning on the label, corroborating previous data from the literature. In a packaging analysis study by Santos, Oliveira, Mota & Silva (2018), the lack of protection against light was observed for 100% of the evaluated labels; this lack of protection from light may compromise the freshness, taste, aroma and original characteristics of the metabolites. The lack of guidance leads to improper storage and can lead to loss of therapeutic activity.

Another aggravating factor is the lack of a seal on the packages. A seal disallows the packaged product from coming into contact with the external environment, protecting against moisture and contamination. Unsealed packages and bulk purchases were more subject to these factors because the products were exposed in plastic containers that were often opened and handled by vendors, in addition to being directly exposed to light. Another relevant piece of information that was absent on some packages was the botanical name of the species. Most of the packages without the botanical name were purchased in bulk, sold only by their popular name and delivered in packaging without any identification. Some sealed packages had the botanical name spelled incorrectly, while others mentioned only the genus. The purchase of plant drugs based on the genus alone may compromise the desired therapeutic efficacy because some species belonging to the same genus do not have the same biological activity. For example, genera such as *Bauhinia* have approximately 300 species (Bonilha et al., 2015), known by the same popular name in Brazil (‘pata-de-vaca’) but with variations in chemical composition (Ferreres et al., 2012). As the chemical composition of species can vary, the lack of specification is a risk to consumer health.

Information about the manufacturer was absent on all packages, making it difficult to identify the companies responsible for cultivation and processing. The lot information was also absent on the packages. This hinders product traceability and knowledge of the production process (Santos, Oliveira, Mota & Silva, 2018). According to Colet, Molin, Cavinatto, Baiotto and Oliveira (2015), the absence of information regarding a technical manager is worrying, as it means that there is no professional responsible for process evaluations, compromising the quality of commercialized products.

Nutritional labeling was present on some packages. It is likely that these products follow DRC No. 360/2003 guidelines, which provide for the technical regulation of packaged foods (Brazil, 2000, 2003, 2010b). This factor suggests that

some products are being marketed in the food category, despite being consumed for therapeutic purposes. After consulting the CNPJ reported on the packaging, it was observed that the products were sold by food companies. This was also confirmed by the notification to ANVISA present on some packages; the products were classified in the food category and are, therefore, exempt from registration according to Annex I of RDC No. 23/2000. Additionally, in RDC No. 27/2010, tea, spices and plant products are exempt from registration.

These factors may be reinforced by the fact that *Equisetum arvense*, *Syzygium cumini* and *Bauhinia forficata* are not included in the latest edition of the Brazilian Pharmacopoeia (Brasil, 2019) or on the list of herbal medicines with simplified registration or on the list of THPs with simplified registration according to NI No. 2, May 13 2014 (Brazil, 2014c). However, the three species evaluated have medicinal uses and, therefore, are not included on the list of species considered to be teas (Brasil, 2005, 2010b, 2010c). Thus, considering the provisions of RDC No. 26/2014, which are currently in force, plant drugs are THPs and should be registered. In addition, the species are included on the RENISUS list and are therefore species of health interest, with wide popular use to treat diseases.

Gomes, Elpo & Negrelle (2007) suggest that due to the greater ease of registering food products, species considered medicinal are sold in this category of products, possibly because the legislation allows species not included on the list to be marketed as teas. However, notably, according to this legislation, none of these species should have therapeutic or drug claims on the label (Brasil, 2005, 2010a, 2010b).

RDC 26/2014, modified by RDC 66/2014, establishes the need to include an information leaflet in the packaging of THPs. The information leaflet is intended to inform the consumer about the composition and use of the product (Brasil, 2014). Identification as a traditional herbal product, information on the presentations and composition, route of administration, warnings, claim of use registered with ANVISA, guidance on use, storage and possible adverse effects are information that should be present in the package leaflet. However, none of the acquired samples had such leaflets. The absence of an information leaflet was observed in a similar study, in which plant drugs acquired from pharmacies and drugstores of a municipality in southern Brazil were evaluated (Colet, Molin, Cavinatto, Baiotto & Oliveira, 2015).

According to Santos, Oliveira, Mota and Silva (2018), the lack of information and warnings on marketed products demonstrates disregard and a lack of respect for consumers, reinforcing the mentality that natural products do not cause any harm and promoting the incorrect use of products and health risks. Misconceptions regarding the part of the plant used and the form of preparation may result in therapeutic inefficacy and increase the risk of toxicity (Colet, Molin, Cavinatto, Baiotto & Oliveira, 2015).

The evaluation of organoleptic characteristics is included in the latest Brazilian Pharmacopoeia (Brazil, 2019) and WHO recommendations (Who, 2011) as a procedure to be performed in the evaluation of the quality of plant drugs. However, the most recent edition of the Brazilian Pharmacopoeia (Brazil, 2019) did not include organoleptic characteristics in the monographs of medicinal plants. In addition to subjectivity, another limiting factor in the use of organoleptic characteristics as a quality criterion is the lack of official reference documents for most medicinal species available on the market. The results in the literature show that there is large color variation between the reference samples and the samples analyzed due to numerous factors involving the supply chain for medicinal plants (Alvarenga et al. 2017; Amaral, Coutinho, Ribeiro & Oliveira, 2003). Darkened and spotted parts may be related to the processing and drying method, indicating a lack of standardization. A description of the specific odor of the evaluated plants was not found in the literature. The flavor was not evaluated for safety reasons. Furthermore, properties such as odor and taste may be characteristics of and associated with therapeutic effects (Medeiros; Pinto & Nascimento, 2015), and changes in these characteristics are indicative of changes in the chemical composition, justifying the relevance of this analysis for some species.

Regarding foreign materials, only cavalinha sample C1 had a value less than 2% w/w, within the limits required by the Pharmacopeia (6th edition) for plant drugs. Twigs and/or branches were present in all pata-de-vaca and jambolão samples, a finding that may be related to the fact that they are tree species. The presence of different plant parts of the same species or other species may compromise therapeutic efficacy and cause significant toxic effects because these foreign materials may have different chemical compositions (Silva; Silva & Michelin, 2013). The presence of reproductive structures may impair the efficacy of cavalinha, as only sterile stems of the plant are considered to have the desired chemical constituents (Pallag et al., 2016). These results are similar to those reported by other studies that also observed a large amount of foreign materials present in plant drugs sold in different locations (Engel, Ferreira, Cechinel-Filho & Meyre-Silva, 2008; Silva, Silva & Michelin, 2013; Silva, Cordier, Santos, Vita & Maia, 2015; Silva, Ribeiro & Ribeiro, 2017). The presence of soil particles is indicative of the lack of care during collection and processing and increases the possibility of spreading microorganisms. Foreign materials may also interfere with the measurement of the recommended dose, resulting in no effect due to the administration of an insufficient amount of plant drug. Therefore, the presence of foreign materials or impurities drastically compromises the quality of plant drugs, exposing the consumer to serious health risks.

Even if the available species have proven therapeutic effects, this alone does not guarantee safe use. Safety in use is associated with the quality of the final product, which depends directly on the cultivation, processing, packaging and availability of information on safe and rational use (Colet, Molin, Cavinatto, Baiotto & Oliveira, 2015). In this sense, instructing users, producers and workers of the regulatory sector regarding the legislation related to plant products with therapeutic purposes is extremely important for public health (Lima & Gomes, 2014).

## 5. Conclusion

The results showed that commercial samples of cavalinha, jambolão and pata-de-vaca, plant species indicated to treat diabetes, did not meet the recommended quality criteria. In fact, there is a large gap between what is regulated by ANVISA and the plant drugs that are commercially available. The products do not meet the minimum quality specifications required for THPs, compromising quality and bringing risks to the health of the consumer. Inadequate packaging, absence of important information for the consumer and disagreement with primary parameters indicate the need for more rigorous compliance with the regulations governing the marketing of these products. The implementation of quality control strategies in the entire supply chain for medicinal plants and strict surveillance are urgent and necessary to ensure the safe and effective use of medicinal plant drugs.

## Acknowledgments

The authors thank the National Council for Scientific and Technological Development (CNPq), the Minas Gerais Research Foundation (FAPEMIG) and the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES) for financial support and scholarships.

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