

The Possibility of Interactions between Medicinal Herbs and Allopathic Medicines used by Patients Attended at Basic Care Units of the Brazilian Unified Health System

Oliveira SGD¹, Piva E^{2*} and Lund RG³

¹Laboratory of Microbiology, School of Dentistry, Federal University of Pelotas (UFPEL), Brazil

²Department of Restorative Dentistry, School of Dentistry, Federal University of Pelotas (UFPEL), Brazil

³Laboratory of Microbiology, School of Dentistry, Federal University of Pelotas (UFPEL), Brazil

Abstract

Background: The use of medicinal plants as an alternative healthcare is widespread in developing countries. This is due to several factors ranging from the belief of the absence of side effects to the difficulty of access to allopathic medicines. Seen it, it is of utmost importance the study of the use of these medicinal plants and its relationship with allopathic medicine and the public health system. The objective of this study was to identify the range of natural health products and conventional drug therapies used by patients assisted by basic care units of the Brazilian Unified Health System.

Methods: Five basic health units in the city of Pelotas were selected by a convenience sample and patients were interviewed about how they were treated, including their use of natural products. The questionnaires have closed and semi-closed questions. The questionnaires have questions about the use of medicinal plants and if their use was concomitant with allopathic medicines.

Results: Most sample-comprising patients at basic health units (94.6%) reported using herbal medicine as an alternative and complementary therapy, and 64% also admitted growing some type of plant with medicinal purposes in their homes for their own use. Furthermore, 55.2% of patients taking herbal medicine to treat their illnesses did without the concurrent use of synthetic chemical drugs. 43.84% of interviewed patients were using some allopathic medicine daily. The possibility of interactions between anticoagulants and 'boldo' was found in the literature as well as the 'lemon' with chloroquine and also between 'chamomile' and anticoagulants and analgesics.

Conclusions: It is important to educate the public about the adverse effects of concomitant use of herbal and allopathic as these problems occur in the absence of knowledge of users, who often self-medicate with herbs, and health professionals who do not have sufficient clarity on the correct concepts of herbal medicine.

Keywords: Phytotherapeutic drugs; Complementary medicine; Public health; Herb-drug interaction; Adverse effects.

Introduction

Herbal Medicine is a highly popular complementary or alternative mode of treatment with an annual turnover of US\$ 60 billion with a constantly growing market [1]. As one of the top 10 consumers of herbal medicines, Brazil is believed to have about 66% of its population using medicinal plants as the only alternative for the treatment of their diseases. Some factors that contribute towards the spread of this therapy are the natural origin of the drugs, the belief in their safe use and the alleged lack of side effects [2].

The World Health Organization (WHO) has noted that it is important to incorporate modern with traditional medicine to implement health systems and improve the population's health. Due to formally stimulated interest in medicinal herbs and traditional medicines, WHO has deemed it worthwhile to provide assistance to countries in their promotion of health programs which are better adapted to local socio-economic situations [3,4]. Several Brazilian states have already introduced the use of herbal medicines within the public health system [5-8]. According to the 2010 Brazilian Unified Health System's official data, herbal therapy made its way into the government health system of sixteen Brazilian states [9].

Authors suggest that one of the major factors contributing to the increasing popularity of herbs in developed countries and the sustained use in developing countries is the perception that herbal remedies are efficacious, and in some cases more so than physician-prescribed allopathic medicines. This favorable level of perceived efficacy would support continued use, and in a significant number of patients, concomitant use with conventional allopathic medicines. This scenario, of concomitant herb-drug use, raises the growing public

health concern of potentially harmful interactions [10].

It is known still that the indiscriminate use of medicinal plants and herbs is due to the lack of knowledge on their adverse effects. Almost one third of current users of herbal medicines do not know about the risk of herb-drug interactions [11]. A drug-herb interaction can be defined as pharmacologic or clinical response to the co-administration of a traditional drug or pharmaceutical preparation and a herbal product [12]. The idea that herbal medicines have no adverse effects is erroneous and ignores the obvious fact that certain herbs may change the distribution and effect of certain allopathic medicines, affect their metabolism and eliminate the good effects of the formulations [1,2,13]. Moreover, it is clear that there is an increased risk of adverse interactions between herbal and allopathic medicines than between herbal medicines and synthetic drugs, which is due to the diversity of pharmacologically active chemical constituents in the medicinal herbs. On the other hand, synthetic drugs have unique chemical identities [14].

***Corresponding author:** Evandro Piva, Department of Restorative Dentistry, School of Dentistry, Federal University of Pelotas (UFPEL), Brazil, Tel: 555332226690; Email: evpiva@gmail.com

Received February 14, 2015; **Accepted** February 27, 2015; **Published** March 01, 2015

Citation: Oliveira SGD, Piva E, Lund RG (2015) The Possibility of Interactions between Medicinal Herbs and Allopathic Medicines used by Patients Attended at Basic Care Units of the Brazilian Unified Health System. Nat Prod Chem Res 3: 171. doi:10.4172/2329-6836.1000171

Copyright: © 2015 Oliveira SGD, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Further aggravating the problems reported above studies report that most herbal users did concomitantly with allopathic medicines, without the knowledge of your doctor [10,15]. The prevalence of drug-herb interactions is extensive but unknown, signifying the negligence of the consumers in reporting adverse herb reaction or drug-herb interactions [16]. This practice can further consolidate the perception that this potentially dangerous practice is safe and encourage further concomitant use herb - drug uninformed ways [10]. There is an obvious importance of public awareness of the potential dangers of herb-drug combinations, as several studies show a relatively high incidence of adverse effects associated with this practice [10,17-19].

Due to the above issue, current investigation analyzes the main medicinal plants consumed by patients of the Brazilian Unified Health System in some basic health units of Pelotas RS Brazil, and verifies possible interactions between medicinal herbs and allopathic medicines.

Methodology

The municipality of Pelotas in the southern state of Rio Grande do Sul, Brazil, on the banks of the São Gonçalo Canal, at 31°46'19" S and 52°20'33" W, has an area of 1,921.80 square kilometers, at an altitude of 7 mts, featuring a typical humid subtropical climate. Pelotas has a population of 323,034 inhabitants, including 22,082 residents in the countryside. The municipality's economy consists of agribusiness and trade [20].

Half-structured and structured questionnaires were carried out during one year in five Basic Health Units (BHUs) in Pelotas, selected according to their importance, diversity of service and location in the municipality so that the covering of a more diverse population and an expansion of the investigation could be achieved. The questionnaire was performed by two students previously calibrated within the pilot project. A previous meeting was held to eliminate doubts with regard the questions of the questionnaire and possible responses. The questionnaire could be adjusted and uniformity between the interviewers could be obtained. Selection condition was that subjects were patients attended by the Brazilian Unified Health System. The project was approved by the Committee for Ethics in Research of the Faculty of Dentistry, Federal University of Pelotas (Resolution 083/2009). The patients were randomly chosen, asked whether they wanted to participate in the research and then interviewed while they were waiting for their respective health service. All interviews were conducted after the signing of the consent form.

The questionnaire aimed to report the socio-economical characteristics of the informants to link the use of medicinal plants with income, age and gender, for a comparison with other similar studies. It also investigated the botanical and ecological characteristics of plants used for medicinal purposes and their alleged therapies to identify possible drug interactions.

Information on each plant was registered, or rather, its name, section of the plant used, preparation and storage methods, season in which it was harvested, its alleged therapeutic purposes, information on herb administration (frequency, concomitant use with allopathic medicines, effects) and duration of the treatment.

Formal interviews and some occasional conversations with 333 people were performed. After the application of the questionnaires, data were tabulated and analyzed.

The use values (UVs) [21] for each plant were also collected. For this measurement, we used the formula $UVIS = (Uis)/nis$, where

Uis is the number of uses mentioned by the interviewee for the species, and nis is the number of interviews with the informant. The UVIS and Uis values were the same in our experiment, as only one interview was conducted with each interviewee. To calculate the value of use of each of the species, the UVs were used in the formula $UVs = UVIS/n$, where UVIS equals the value to an informant of using a particular plant species, and n is the total number of informants interviewed. Any interviewee could cite all species.

A descriptive statistical analysis was performed using the SPSS version 10.0 software package, and the Chi-square test was used. Significant differences were accepted at the $p < 0.05$ value.

In this article, a literature overview is provided of known or suspected interactions of the plants considered important by the population studied with conventional allopathic therapies.

Results

Most sample-comprising patients at basic health units (94.6%) reported using herbal medicine as an alternative and complementary therapy, and 64% also admitted growing some type of plant with medicinal purposes in their homes for their own use. Further, 55.2% of patients taking herbal medicine to treat their illnesses did so without the concurrent use of synthetic chemical drugs. In fact, 43.84% of interviewed patients were using some allopathic medicine daily, with a prevalence (46.6%) of hypertension drugs. A mere 3.42% of the sample revealed that they make use of allopathic medicines without the use of herbal medicine as a complementary treatment (Table 1).

Since the sample was predominantly (84%) female, "gender" had a significant role in the choice of herbal medicine as a form of therapy ($p = 0.008$). However, the option for the use of allopathic drugs was not correlated with the respondents' gender ($p = 1$).

Most interviewed patients were within the 41-50 year old (21.02%) age bracket, followed by the 21-30 year old (20.42%) age bracket. A breakdown in percentages for herbal use occurred at different ages ($p = 3.6$) in the case of treatment of signs and symptoms of the disease, or rather, there was a significant correlation between age and use of herbal medicines. The same factor was also observed for cases in which allopathic drugs were used ($p = 2.8$).

Most interviewed patients (64.3%) had an income between US\$ 269-537 although family income did not seem to be decisive in the decision to use herbal and allopathic medicines ($p = 2.3$).

Moreover, the patients interviewed were free to talk about which plants they used for the treatment of various diseases (Figures 1 and 2). Direct objective questions were used and the following results were obtained: 52.9% reported using herbs for pain relief; in fact, 27.1% cited the use of macela (*Achyrocline satureioides* Lam) for this purpose. Twelve percent reported the use of teas to treat diabetes, with 43.9% using the "insulin" (or princess) vine (*Cissus sicyoides* L) for this purpose. On the other hand, 34% reported the use of teas to treat

Allopathic Medicine	Herbal Medicine		Total
	Use	No use	
Use	141 96.58%	5 3.42%	146 100%
No use	174 93.05%	13 6.95%	187 100%
Total	315 94.59%	18 5.41%	333 100%

Table 1: Absolute and relative frequencies of use of herbal medicine associated with allopathic drugs.

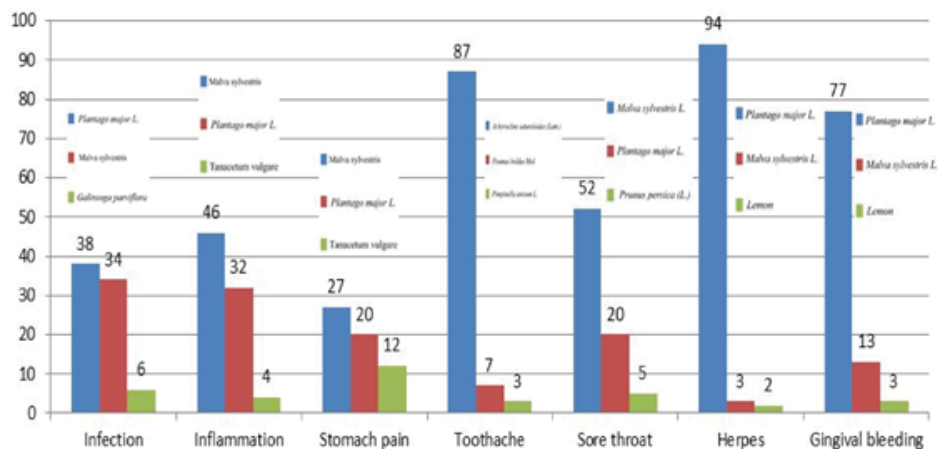


Figure 1: Use of various medicinal plants for different diseases.

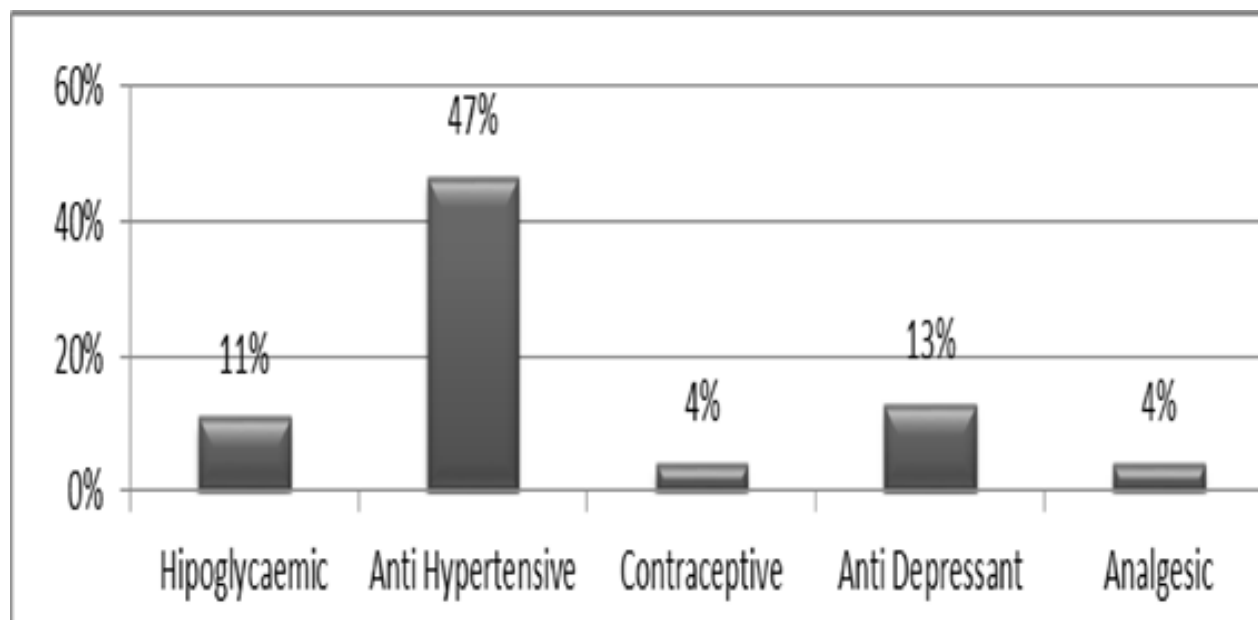


Figure 2: Diseases treated with allopathic medicine.

toothache: the common Malva (*Malva sylvestris L.*) was the plant used by 86.7% of interviewed patients. About 50% of patients used some herbal remedies to treat sore throat, with 51.6% using the ‘Tansagem’ (*Plantago spp, Plantago major*) for this purpose. The groundsell (*Baccharis genistelloides*) against obesity and overweight was cited by 25.3% of interviewed patients, whilst 22.5% reported the use of teas for the same purpose. About 20% of users treated thrush or herpes with the flower of the black elder (*Sambucus nigra L.*) (95%). Forty percent used plants to treat any type of inflammation and the common mallow (*Malva sylvestris L.*) was used by 46% of interviewed patients. Only 21.3% used herbal medicines to treat injuries and a type of aloe (*Aloe arborescens Mill*) was the most used (36.6%).

In current study 65 different plants were reported against different types of illnesses, of which the common mallow (*Malva sylvestris L.*) was the most cited (29.6%) specifically for dental pain (31.1%). Infection (55.3%) was the most frequent symptom reported which occasioned

the use of herbal plants and plantain (*Plantago spp, Plantago major*) was the most cited plant to treat this problem (37.3%).

In current study, the importance of each medicinal plant for the community under analysis was obtained by calculation, or rather, the higher the number of usages of the medicinal herb, the more important it is for the community. This fact was considered relevant for the review of the literature review on possible drug interactions, adverse reactions and contraindications. The ten plants considered important by the population studied are given below in the use value order:

1. Common mallow (*Malva sylvestris L.*)
2. Plantain (*Plantago spp.*)
3. Macela (*Achyrocline satuireioides*)
4. Boldo (*Peumus boldus*)
5. Black elder (*Sambucus nigra L.*)
6. Groundsell bush (*Baccharis genistelloides*)

7. Lemon balm (*Melissa officinalis*)
8. Tansy (*Tanacetum vulgare L.*)
9. Aniseed (*Pimpinella anisum*)
10. Camomile or chamomile (*Matricaria recutita L.*)

The ten above-mentioned plants were analyzed for their possible drug interactions or adverse effects found in the literature.

Discussion

Most respondents (94.6%) reported knowing and using medicinal plants for the treatment of various signs and symptoms of different diseases for themselves and their family. These data are consistent with other studies that demonstrate the widespread use of plants for medicinal purposes. Brasileiro *et al* [22] studied the population assisted by the Family Health Strategy in Governador Valadares MG Brazil, and found that 91.9% of the interviewed frequently used herbs to treat diseases, whereas only 8.1% did not. The indiscriminate use of medicinal plants is due to the fact that users are not aware of the adverse effects they may produce. Mahady *et al.* [23] reported that 65% of individuals claimed that herbal medicines were a safe therapy. The safety concept is highly misleading in the case of most plants used as medicinal since many have significant toxic side effects [24]. To make matters worse, they also registered that 70% of patients who used herbal medicine as treatment did not report the fact to their physicians or health professionals [15]. Consequently, no monitoring of drug interactions occurs since the concomitant use of two drugs is not acknowledged [25].

Current study showed that users reported that they have some medicinal plants at home (64%). The use of medicinal plants is facilitated when the patients grow the plants and probably use them fresh [22]. Another interesting information is that 55.2% of respondents exclusively use medicinal plants to treat their illnesses. It is a well-known fact that Brazil is one among the ten countries that most consume plants for medicinal purposes [26]. In addition to such a high demand, few studies characterize the exclusive use of medicinal plants by Brazilians. These individuals primarily endeavor to heal their illnesses and those of their families at home, without any medical supervision. If the symptoms do not disappear, they seek medical advice and take the prescribed synthetic drugs. This behavior is either due to drug prices or to the unavailability of the free medicine by the health care system [27].

Many patients interviewed (43.8%) claimed using allopathic medicines regularly. The costs of drugs have a similar pattern with spending on health care, or rather, the poorest people, with more morbidities and therefore requiring a greater need of drugs, tend to spend less. The restriction in the use of drugs among people with low purchasing power becomes evident when one notes that the weight of spending on household income is proportionally greater than that for people with higher incomes [28].

The most common pathology was arterial hypertension (46.6%) and agrees with the same trend found by Lima-Costa *et al.* [29] in a PNAD description among patients of the Brazilian National Health Care system. Only 3.42% of the sample made use of allopathic medicines without herbal medicine as complementary treatment. This result is very similar to research by Peng *et al.* [30] where about 43% of herbal medicines users also took synthetic drugs concomitantly; 52.2% only used herbal medicine against disorders; 1.5% used only allopathy; and 4% did not use any of the two forms of treatment. Unfortunately, there is a great lack of studies on the use of allopathic and herbal medicines in Brazil so that a greater importance to the issue could be provided.

Most of the interviewed in the sample were females (84%). The gender characteristic was highly significant in the use of herbal medicine as a form of therapy ($p=0.008$), since the option for the use of allopathic drugs was not correlated with the gender of the respondents ($p=1$). The predominance of females has already been reported in the literature. In fact, as a rule, women are responsible for the cultivation and preparation of medicinal plants. They are also responsible for the feeding and care of children or other family members when they become ill [8].

The age group of most respondents lay in the 41-50 years age bracket (21.02%), followed by the 21-30 years age one (20.42%). Again there was a breakdown of herbal use, at different ages, for the treatment of signs and symptoms of diseases with no significant correlation between a certain age and use of herbal medicines. Since there was no exclusion or inclusion of respondents by age, the respondents' age groups were very comprehensive (20 years above 60 years old). Other studies have reported that people over 30 years were more open to discuss the use of medicinal plants, while young people would prefer to use chemically synthesized drugs and showed various levels of disbelief in the healing power of medicinal plants [27]. Several authors have shown that the knowledge and use of medicinal plants is not only undergoing a gradual decline but any knowledge of medicinal plants is restricted to communities in rural areas [31-33]. Current data differed with regard to results of the less than 20-year-olds who featured 91% of supporters of herbal medicine. Percentage rose to 96% among people within the 20 - 30-year-old brackets.

Respondents (64.3%) had predominantly an income between 1 and 2 Brazilian minimum wages or US\$ 269-537. Some studies have linked the use of herbal medicines with high schooling levels and income in developing countries such as Brazil [34]. However, current study was restricted to users of the government health system who have lower income levels and schooling [34].

Respondents were free to mention the plants used for the treatment of diseases. Most reported using the plantain (*Plantago major*) in the treatment of infections, with a 38% preference, followed by the common mallow (*Malva sylvestris L.*) (34%) and by the potato weed (sometimes called gallant soldier) (*Galinsoga parviflora Cav.*) (6%). The common mallow (*Malva sylvestris L.*) was the favorite plant against inflammation (46%), gingival bleeding (77%) and toothache (87%). The macela (*Achyrocline satureioides*) was the most cited plant for the treatment of stomach pain (27%), followed by boldo (*Peumus boldus*) (20%) and aniseed (*Pimpinella anisum*) (12%). In the case of sore throat, the tansy (*Tanacetum vulgare L.*) was mentioned by 52%; the common mallow (*Malva sylvestris L.*) by 20% and lemon by 5%, in the users' preference. For the treatment of herpes the most mentioned plant was the black elder (*Sambucus nigra L.*) with 94%, followed by aniseed (*Pimpinella anisum L.*) with 2%.

The common mallow (*Malva sylvestris*) was one of the most cited plants in the study. In the literature, the mallow is mentioned as a drug against inflammation, fever, diseases of the bladder and throat and for general infections, ovarian infections, cystitis, genital cleansing, mouth wounds and wounds in general. It is also employed as a bronchodilator, expectorant, anti-tussive and anti-diarrheal medicine. The mallow is also highly recommended for acne and skincare and as an antiseptic, emollient and demulcent [35]. Due to these properties, the use of this plant in the prophylaxis and periodontal treatment of oral and pharyngeal irritation is widespread [36]. No type of harmful interaction with the common mallow has been found or documented in the literature. In fact, the National Health Surveillance Agency, through

its Resolution RDC 17 issued on February 24, 2000, confirms the effectiveness of *Malva sylvestris*, unaware of its toxicity [37].

'Tançagem' (*Plantago major*) was the most frequently cited medicinal herb by the interviewed in current study for the treatment of infections. There are reports in the literature on the use of this plant for the treatment of nasopharyngeal inflammation [38]. Other studies also report that 'tançagem' (*Plantago major*) is used in the treatment of several diseases such as skin diseases, infectious diseases, digestive, respiratory, reproduction, blood circulation problems, and the relief of pain and the reduction of fever against tumors [39]. Scanty information exists in the scientific literature on the plant's adverse effects and drug interactions. Several Internet sites report on its adverse effects and mention arrhythmia, heart arrest, allergic reactions and irritations.

The macela (*Achyrocline satureioides*) is the most commonly used drug against stomach pain and is commonly used in folk medicine as a tea to treat digestive problems and inflammation. Infusions of *A. satureioides* flowers are widely used in Brazilian folk medicine as a digestive, antispasmodic, anti-inflammatory and hypoglycemic agent for the treatment of gastrointestinal disorders and for the decrease of blood cholesterol levels. Although some previous studies are extant, the toxic effects of *A. satureioides* extracts are little known. In a study using hematological *Achyrocline satureioides* (Lam.) DC in mice, Martins *et al.* [40] detected macrocytosis, eosinopenia, neutropenia and lymphocytosis.

The boldo (*Peumus sp*) was the second most commonly cited herbal medicine to treat stomach pain, due to alkali boldine confirmed by many reports [41]. Boldine and boldo extracts are known for their hepatoprotective and choleric properties which stimulate the bile flow [42]. In addition to its beneficial activities on the gastrointestinal tract, boldine exerts anti-inflammatory and antipyretic responses. The boldine is an effective inhibitor of prostaglandin synthesis [43] responsible for pain transmission. The interaction between warfarin and boldo may be found in the literature. Warfarin is an antivitamin K (AVK) drug or oral anticoagulant and may interact with different anticoagulant actions of herbal medicines such as the boldo. In one case reported in the literature the boldo-warfarin interaction just increased the anticoagulant parameter in a 67 year old patient [44].

The black elder (*Sambucus nigra*), a plant cited by respondents in current research for the treatment of herpes simplex virus (HSV-1) commonly associated with facial sore outbreaks, seems to be effective against the virus. In a study by Morag [45] an extract from *Sambucus nigra* was tested against HSV-1 and demonstrated to have completely inhibited the replication virus strains. The black elder may strongly stimulate the immune system by inducing cytokine production in healthy subjects and in patients with influenza, or in other immunocompromised patients, such as those with cancer or HIV. Formulas containing *Sambucus* have a strong stimulating effect on the production of anti-inflammatory and inflammatory cytokines (IL-1 β , TNF α , IL-6, IL-8, IL-10). The production of all 5 cytokines by a drug containing *Sambucus* increased between 1.3 and 1.6 times when compared to the placebo [46]. No type of interaction with the *Sambucus nigra* was found in the literature about which it is well documented.

The groundsell bush (*Baccharis genistelloides*) is commonly used to treat liver problems, digestive disorders, malaria, ulcers, diabetes, anemia, diarrhea, urinary inflammations, tonsillitis, worms, hypercholesterolemia, erectile dysfunction, female infertility and rheumatism. It is also used as an abortive drug [47]. The main use of the groundsell in current study was the disappearance of digestive disorder symptoms. The main toxic effects reported for *B. genistelloides*

is the induction of abortion, commonly reported and experimentally proven in animals, attributed to an uterotonic activity of its compounds [48]. Although studies fail to indicate any problems with kidney or liver toxicity, the use of the groundsell should be prohibited for pregnant women due to its proven abortion risks and for patients on drugs for blood pressure due to its hypotension effects [49].

The lemon balm (*Melissa officinalis*) was mentioned by the interviewed for the treatment of intestinal and menstrual cramps. The literature reports that that lemon balm may interact with other medicines containing herbs, especially kava (*Pipermethysticum G. Forst*). In fact, it interacts with depressants on the central nervous system and on thyroid hormones (thyrotropin-releasing hormone) [50].

There are few studies on the adverse reactions and contraindications for the tansy (*Tanacetum vulgare L*). Empirical information was more abundant than scientific information and it is believed that one should be careful with the plant's consumption by pregnant women, infants and children. The components of the tansy, such as taneacetona acid, are toxic. High doses may cause poisoning and the necessary cautions in its consumption are highly recommended.

The aniseed (*Pimpinella sp*), the third plant used for stomach pain, is used to treat heartburn, stomach ache, digestion difficulties and dyspepsia [50]. No interactions with the aniseed were found in the literature which is well documented on the subject.

The chamomile (*Matricaria recutita*) is mostly used as a tranquilizer. In a study by Farnsworth (1972) [51], in which flavored oil of chamomile was used, it was shown that it had a sedative effect and a positive effect on mood. The flavonoid apigenin, found in chamomile, proved to be a ligand for central benzodiazepine receptors exerting anxiolytic and slight sedative, albeit not anticonvulsant or myorelaxing [51,52]. The interaction between chamomile anticoagulants and cyclosporine is found in the literature. Seagal and Pilote [52] report that one patient who intook warfarin had severe internal injuries after using chamomile, probably due to coumarin compounds which act synergistically with warfarin, resulting in suprathereapeutic anticoagulation. In another study, one patient had a high concentration of cyclosporine after drinking from 1 to 1.5 L/day of tea. When the same patient ceased ingesting the tea, concentrations returned to their former level [53]. The use of aspirin as a painkiller should also be taken into account by patients. Since ASA has anticoagulant-antiplatelet properties, the same type of interaction that occurs with warfarin as an anticoagulant may also occur with this drug. In addition, allergic reactions to this plant are not uncommon. These reactions include symptoms such as abdominal cramps, tightness in the throat, angioedema of the lips and eyes, hives, itching, upper airway obstruction and pharynx edema [54].

Several other plants were cited in current study besides those mentioned above, or rather, within the list of the ten major plants reported by the population. Due to the importance of the topic and to the lack of extant studies on the subject, a review of the literature on other medicinal plants cited in current study but not part of the ten most important ones will follow.

- The aloe (*Aloe arborescens*) was mentioned by the interviewed patients primarily as a treatment for gastritis symptoms by drug infusion. Documented in the literature, there is no drug interaction when the medicinal plant is used, although some adverse effects such as contact dermatitis are mentioned [55]. In addition, it is contraindicated for pregnant women, breastfeeding mothers and children [55,56], intestinal obstruction, ulcerative

colitis, appendicitis, abdominal pain of unknown origin [57], hemorrhoids and kidney diseases [58].

- The leaves of the sweet orange (*Citrus sinensis* L) were used as an infusion for the treatment of pain and bronchitis. The literature mentions allergies (caused by volatile oils of fruits and flowers) [59], erythema, blisters, pustules, skin and pigmented spots (caused by furanocumarins found in the juice and peels of fruits) [60] as adverse reactions. Its use is contraindicated during pregnancy and lactation [61].
- Fennel leaves (*Foeniculum vulgare* Mill.) were prepared by infusion and used for the treatment of insomnia. Some therapeutic uses of the plant have been proven. They include coughs, bronchitis [56,57,62], mild gastrointestinal problems with spasms in the upper respiratory phlegm and flatulence [56]. One study suspects a likely interaction between ciprofloxacin and *Foeniculum vulgare*, with reduces plasma concentrations of the antibiotic [62].
- The leaves of the Brazilian cherry (*Eugenia uniflora*) were used by the interviewed patients to treat bleeding gums. The literature shows a contraindication in its use for patients with arrhythmias and heart failure [61].
- The lemon, often in the form of juice, may also be used for the treatment of throat pain due to its antimicrobial action, probably because it contains citral and linalool [63,64]. A drug interaction was detected between the lemon and chloroquine, a drug used for the treatment and the clinic prophylaxis of malaria [65]. In the interaction, plasma concentration of chloroquine is reduced and its therapeutic effects decreased [65]. Another interaction occurred with Fe which may increase iron absorption by the body [66].

Further studies addressing this issue are necessary, coupled to a conscience-raising education policy for the population, both to users of herbal medicines and to health care professionals, with regard to the high potentiality in the adoption of this practice.

Conclusion

It is important to educate the people on the adverse effects of the concomitant use of herbal and allopathic medicines as these problems occur without the users' awareness. This is more serious because people tend to self-medicate themselves with herbal medicines and health professionals do not have sufficient knowledge on their correct use.

Authors' contributions

SGDO was responsible for the administration of the questionnaires; she analyzes the results, literature, writing, and review of the scientific paper. RGL and EP were responsible for the administration of the questionnaires; they analyze the results, literature, writing and review of the scientific paper.

References

1. Tirona RG, Bailey DG (2006) Herbal product-drug interactions mediated by induction. *Br J Clin Pharmacol* 61: 677-681.
2. Henderson L, Yue QY, Bergquist C, Gerden B, Arlett P (2002) St John's wort (*Hypericum perforatum*): drug interactions and clinical outcomes. *Br J Clin Pharmacol* 54: 349-356.
3. Farnsworth NR, Akerele O, Bingel AS, Soejarto DD, Guo Z (1985) Medicinal plants in therapy. *Bull World Health Organ* 63: 965-981.
4. Akerele O (1988) Medicinal plants and primary health care: an agenda for action. *Phytotherapy* 5: 355-363.
5. Brito AR, Brito AA (1993) Forty years of Brazilian medicinal plant research. *J Ethnopharmacol* 39: 53-67.
6. Calixto JB (2000) Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). *Braz J Med Biol Res* 33: 179-189.
7. Wayland C (2001) Gendering local knowledge: medicinal plant use and primary health care in the Amazon. *Med Anthropol Q* 15: 171-188.
8. Wayland C (2003) Contextualizing the Politics of Knowledge: Physicians' Attitudes toward Medicinal Plants. *Med Anthropol Q* 17: 483-500.
9. Brazilian Ministry of Health
10. Clement YN, Morton-Gittens J, Basdeo L, Blades A, Francis MJ, et al. (2007) Perceived efficacy of herbal remedies by users accessing primary healthcare in Trinidad. *BMC Complement Altern Med* 7: 4.
11. Dergal JM, Gold JL, Laxer DA, Lee MS, Binns MA, et al. (2002) Potential interactions between herbal medicines and conventional drug therapies used by older adults attending a memory clinic. *Drugs Aging* 19: 879-886.
12. Brazier NC, Levine MA (2003) Drug-herb interaction among commonly used conventional medicines: a compendium for health care professionals. *Am J Ther* 10: 163-169.
13. Cordeiro CHG, Chung MC, Sacramento LVS (2005) Drug interactions between herbs and medicines: *Hypericum perforatum* and *Piper methysticum*. *Braz J Pharmacol* 15: 272-278.
14. Oliveira SGD, Moura FRR, Demarco FF, Nascente PS, Del Pino FAB, et al. (2012) An ethnomedicinal survey on phytotherapy with professionals and patients from Basic Care Units in the Brazilian Unified Health System. *J Ethnopharmacol* 140: 428-437.
15. Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, et al. (1993) Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med* 328: 246-252.
16. Saw JT, Bahari MB, Ang HH, Lim YH (2006) Potential drug-herb interaction with antiplatelet/anticoagulant drugs. *Complement Ther Clin Pract* 12: 236-241.
17. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, et al. (1998) Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA* 280: 1569-1575.
18. Bensoussan A, Myers SP (2015) Towards a safer choice. The practice of traditional Chinese medicine in Australia. Sydney.
19. Kuo GM, Hawley ST, Weiss LT, et al. (2004) Factors associated with herbal use among urban multiethnic primary care patients: a cross-sectional survey. *BMC Complementary Alternative Medicine* 4: 18.
20. (2002) Department of Economic Development, Data from the City of Pelotas, RS, Brazil.
21. Vendruscolo GS, Mentz LA (2006) Study the agreement of the use of quotations and importance of families and species used in traditional medicine by the Ponta Grossa neighborhood community, Porto Alegre, RS, Brazil. *Acta botanica brasílica* 20: 367-382.
22. Brasileiro BG, Pizziolo VR, Matos DS, Germano AM, Jamal CM (2008) Medicinal plants used by the population assisted by the "Programa de Saúde da Família" (Family Health Program) in Governador Valadares County-MG, Brazil. *Braz J Pharm Sci* 44: 629-636.
23. Mahady GB (2001) Global harmonization of herbal health claims. *J Nutr* 131: 1120S-1123S.
24. Kuhn MA (2002) Herbal remedies: drug-herb interactions. *Crit Care Nurse* 22: 22-28,30,32.
25. Miller LG (1998) Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions. *Arch Intern Med* 158: 2200-2211.
26. Seidl PR (2002) Pharmaceuticals from natural products: current trends. *An Acad Bras Cienc* 74: 145-150.
27. van Andel T, Westers P (2010) Why Surinamese migrants in the Netherlands continue to use medicinal herbs from their home country. *J Ethnopharmacol* 127: 694-701.
28. Travassos C, Viacava F, Fernandes C, Almeida CM (2000) Social and geographical inequalities in health services utilization in Brazil. *Sci & Health* 5:133-149.
29. Lima-Costa MF, Barreto SM, Giatti L (2003) Health status, physical functioning, health services utilization, and expenditures on medicines among Brazilian elderly: a descriptive study using data from the National Household Survey. *Reports in Public Health* 19: 735-743.

30. Peng CC, Glassman PA, Trilli LE, Hayes-Hunter J, Good CB (2004) Incidence and severity of potential drug-dietary supplement interactions in primary care patients: an exploratory study of 2 outpatient practices. *Arch Intern Med* 164: 630-636.
31. Namsa ND, Tag H, Mandal M, Kalita P, Das AK (2009) An ethnobotanical study of traditional anti-inflammatory plants used by the Lohit community of Arunachal Pradesh, India. *J Ethnopharmacol* 125: 234-245.
32. Teklehaymanot T (2009) Ethnobotanical study of knowledge and medicinal plants use by the people in Dek Island in Ethiopia. *J Ethnopharmacol* 124: 69-78.
33. Zheng XL, Xing FW (2009) Ethnobotanical study on medicinal plants around Mt. Yinggeling, Hainan Island, China. *J Ethnopharmacol* 124: 197-210.
34. Ribeiro MCSA, Barata RB, Alemida MF, Silva ZP (2006) Sociodemographic profile and utilization patterns of the public health care system (SUS)-PNAD 2003. *Sci and Health* 11: 1011-1022.
35. DellaGreca M, Cutillo F, D'Ambrosia B, Fiorentino A, Pacifico S, et al. (2009) Antioxidant and radical scavenging properties of *Malva sylvestris*. *Nat Prod Commun* 4: 893-896.
36. Souza GC, Haas AP, von Poser GL, Schapoval EE, Elisabetsky E (2004) Ethnopharmacological studies on antimicrobial remedies in the south of Brazil. *J Ethnopharmacol* 90: 135-143.
37. Ritter MR, Sobierajsky GR, Schenkel EP, Mentz LAC (2002) Used as medicinal plants in the municipality of Ipe, RS, Brazil. *Braz J Pharm* 12: 51-62.
38. Freitas AG, Costa V, Farias ET, Lima MCA, Sousa IA, et al. (2002) Anti-staphylococcal activity of the *Plantago major* L. *Braz J Pharm* 12: 64-65.
39. Samuelsen AB (2000) The traditional uses, chemical constituents and biological activities of *Plantago major* L. A review. *J Ethnopharmacol* 71: 1-21.
40. Martins CHG, Moreti, DLC, Vieira RGL, Stoppa MA, Ambrósio Junior GN, et al. (2003) Hematological study in rats treated with medicinal plants. XVIII. *Achyrocline satureioides* (Lam.) D.C. *Braz J Pharmac Sci* 39: 215.
41. Quercia V, Bucci B, Iela G, Terracciano M, Pierini N (1978) [Determination of boldine by HPLC (high pressure liquid chromatography) in *Boldus* extracts]. *Boll Chim Farm* 117: 545-548.
42. Salati R, Lugli R, Tamborino E (1984) [Evaluation of the choleric property of 2 preparations containing extracts of boldo and cascara]. *Minerva Dietol Gastroenterol* 30: 269-272.
43. Backhouse N, Delporte C, Givernau M, Cassels BK, Valenzuela A, et al. (1994) Anti-inflammatory and antipyretic effects of boldine. *Agents Actions* 42: 114-117.
44. Lambert JP, Cormier J (2001) Potential interaction between warfarin and boldofenugreek. *Pharmacotherapy* 21: 509-512.
45. Morag A, Mumcuoglu M, Baybikov T, Schelsinger M (1997) Inhibition of sensitive and acyclovir-resistant HSV-1 strains by an elderberry extract in vitro. Xth International Congress of Virology Jerusalem, Israel 11-16 August 1996. *Phytoparasitica* 25: 1.
46. Barak V, Birkenfeld S, Halperin T, Kalickman I (2002) The effect of herbal remedies on the production of human inflammatory and anti-inflammatory cytokines. *Isr Med Assoc J* 4: 919-922.
47. Suttisri R, Kinghorn AD, Wright AD, Otto S (1994) Neoclerodane diterpenoids and other constituents from *Baccharis genistelloides*. *Phytochemistry* 35: 446-446.
48. Ruiz ALTG, Taffarello D, Souza VHS, Carvalho JE (2008) Pharmacology and Toxicology and *Peumus boldus* e *Baccharis genistelloide*. *Braz J Pharmac* 18: 295-300.
49. Betoni JE, Mantovani RP, Barbosa LN, Di Stasi LC, Fernandes Junior A (2006) Synergism between plant extract and antimicrobial drugs used on *Staphylococcus aureus* diseases. *Mem Inst Oswaldo Cruz* 101: 387-390.
50. Tepe B, Akpulat HA, Sokmen M, Daferera D, Yumrutas O, et al. (2006) Screening of the antioxidative and antimicrobial properties of the essential oils of *Pimpinella anisetum* and *Pimpinella flabellifolia* from Turkey. *Food Chemistry* 97: 719-724
51. Viola H, Wasowski C, Levi de SM, Wolfman C, Silveira R, et al. (1995) Apigenin, a component of *Matricaria recutita* flowers, is a central benzodiazepine receptors-ligand with anxiolytic effects. *Planta Medica* 61: 213-216.
52. Segal R, Pilote L (2006) Warfarin interaction with *Matricaria chamomilla*. *CMAJ* 174: 1281-1282.
53. Nowack R, Nowak B (2005) Herbal teas interfere with cyclosporin levels in renal transplant patients. *Nephrol Dial Transplant* 20: 2554-2556.
54. Benner MH, Lee HJ (1973) Anaphylactic reaction to chamomile tea. *J Allergy Clin Immunol* 52: 307-308.
55. Der Marderosian A (2001) The review of natural products: The most complete source of natural products information Saint Louis: Facts and Comparisons.
56. (1997) ESCOP-European Scientific Cooperative on Phytotherapy. Monographs on the medicinal uses of plant drugs. Exeter: Centre for Complementary Health Studies.
57. Blumenthal M (1998) The complete German commission and monographs: Therapeutic guide to herbal medicines. Austin, Texas: American Botanical Council.
58. Newall CA, Anderson LA, Phillipson JD (2002) Medicinal Plants: A Guide for health professionals. Londres: Editorial Premier.
59. Tkachenko KG, Dazarinova NV, Muzychenko LM, Shurgaya AM, Pavlova OV, et al. (1999) Sanation properties of essential oils of some plant species. *Rastitelnye-Resursy* 35: 11-24.
60. Gruenwald J, Brendler T, Jaenicke J (2000) PDR for Herbal Medicines (Physicians' Desk Reference). Montvale, New Jersey: Medical Economics Company.
61. Blumenthal M, Goldberg A, Brinkmann J (2000) Herbal medicine - Expanded commission and monographs. Newton, MA: Integrative medicine Communications.
62. Zhu M, Wong PY, Li RC (1999) Effect of oral administration of fennel (*Foeniculum vulgare*) on ciprofloxacin absorption and disposition in the rat. *J Pharm Pharmacol* 51: 1391-1396.
63. Fisher K, Phillips CA (2006) The effect of lemon, orange and bergamot essential oils and their components on the survival of *Campylobacter jejuni*, *Escherichia coli* O157, *Listeria monocytogenes*, *Bacillus cereus* and *Staphylococcus aureus* in vitro and in food systems. *J Appl Microbiol* 101: 1232-1240.
64. Manners GD (2007) Citrus limonoids: analysis, bioactivity, and biomedical prospects. *J Agric Food Chem* 55: 8285-8294.
65. Mahmoud BM, Ali HM, Homeida MM, Bennett JL (1994) Significant reduction in chloroquine bioavailability following coadministration with the Sudanese beverages Aradaib, Karkadi and Lemon. *J Antimicrob Chemother* 33: 1005-1009.
66. Ballot D, Baynes RD, Bothwell TH, Gillooly M, MacFarlane BJ, et al. (1987) The effects of fruit juices and fruits on the absorption of iron from a rice meal. *Br J Nutr* 57: 331-343.