



# Medicinal Plants, Precautions for Their Use in the Elderly

Geuny Vázquez Bandomo, Ana Elena Rodríguez Cadalso, Regina de la Caridad Rodríguez MuñozI, Eduardo Rafael Aguila Turiño, Viviana Silvia Rodríguez Jiménez and Reimundo Eugenio Fernández Abril  
*Filial of Medical Sciences Elena Fernández de Castro Unit, Trinidad 62600, Sanctis Spiritus, Cuba*

**Abstract: Objective:** To relate physiologic changes and presence of illnesses in older adults, with the risk of appearance of adverse reactions and pharmacological interactions as consequence of the use of medicinal plants. **Methods:** To carry out a search in the last 5 years and to present a general vision about what have been published related to the use of medicinal plants with risk of appearance of adverse reactions and interactions in older adults. **Conclusions:** Technological prevision based on the search of articles in the Virtual Library in Health (BVS) and using the words key “medicinal plants”, “older adult”, “pharmacokinetics”, “adverse reactions”, “elderly”, “pharmacological interactions”, and the association among them.

**Key words:** Medicinal plants, older adult, elderly, pharmacokinetics, adverse reactions and pharmacological interactions..

## 1. Introduction

The World Health Organization (WHO) defines the term active aging as the process of optimization of opportunities of health, participation and security with the purpose of improving quality of life while people is aging, making reference to the term active as the continuous participation in the individual’s social roles and not only in their physical capacity or laboral activity [1].

The use of grasses for cure diseases has a very long origin. There are differences among diverse historical texts about the origin of cure by means of plants. The certain thing is that among the first peoples benefitted with grasses were the Asians, as for example China. Later it was the Egyptians and Hebrews, as well as the Greeks and Romans. The earliest descriptions of medicinal plants appear in the writings of Hipocrates, Teofrasto, Galeno, and Celso [2].

Over the years, with the invention of microscope it has been able to carry out more investigations of several vegetables and to know their properties, what

takes to procreate synthetic substances by means of active principles arising an indifference for the natural thing and giving place to the consumption of what it is known today as medications. However, the side effects caused by many synthetic substances are sometimes more serious than the wrong things they combatted. This bring us to the exploration of natural medicine, because organisms can always tolerate such side effects better [3].

In recent years there has been a remarkable growth in the interest for fitomedications, not only limited, national development and results, domestic and international markets, but health authorities and public opinion are interested in the fixation and quality of these drugs [4].

According to the World Health Organization, 80% of the world’s population, more than 4 billion people, use plants as their main medicine [5].

Worldwide, the number of people over 65 years of age is increasing, and it is predicted that by the year 2050, the elderly population will account for 21% of the total population [6].

Older persons are considered to be at risk due to their biological deterioration and the reduction of their

---

**Corresponding author:** Ana Elena Rodríguez Cadalso, Ph.D., research field: medical sciences.

physical resources, as well as the political treatment and prevalence of chronic diseases [7].

Additionally, the bibliography reports that consumption of medicinal plants by older adults has increased during the last decade [7].

A study on the use of medicinal plants by the elderly in Canada found that 80% of the elderly use medicinal plants [8].

A study carried out in the United States on older adults belonging to Hispanic and non-Hispanic elderly found that the 49% of them consumed medicinal plants [9].

A study in Switzerland of 1380 elderly people found that 19.1% of them used at least one medicinal plant [10]. A study carried out in the community of Toa Payoh in Singapore found that 25.3% of the elderly had consumed medicinal plants in the year before the study [11].

A study of pensioners in Brazil of the city of Belo Horizonte found that 10.6% of them consumed medicinal plants in the 15 days before the study [12].

Aging is a physiological process of irreversible change that varies from person to person, and it is important to bear in mind that science has offered multiple theories to explain this problem [13]. The key is to recognize and know that aging organisms are not necessarily sick. Healthy aging is possible and many problems can be alleviated or recovered, although this issue remains controversial as it is difficult to separate the physiological aspects from the pathological aspects at this age [14].

Epidemic and demographic transitions in the developed countries and Latin America, including the Mexican population, are, in a sense, a meditation on the importance of increasing life expectancy in favour of increasing the elderly population; along with this change, the presence of chronic degenerative diseases such as hypertension, diabetes, renal insufficiency, senile insanity, depression, tumatotide arthritis, degenerative arthritis, neoplasms, arrhythmias, dyslipidemia, etc., has greatly worsened the

population [15].

The use of plants is often based on general knowledge, and many times patients do not associate their use with a health professional [16].

Therapy with medicinal plants among adults seems to be excelled, mainly as self-medication practice, the same happens when there are availability and access to industrialized medications [17, 18].

## 2. Development

### 2.1 Aging of the Eldest Adult

Aging is an irreversible life process characterized by the gradual loss of its physiology and physiological functions and ending at death. Besides a complex mixture of external factors (such as diet, lifestyle and genetic factors), many of these factors end up causing older people becomes dependent, cannot be been worth by itself, causing their own distrust and becoming susceptible people in society.

### 2.2 Theories of Aging

- Accumulation of damages in genes and chromosomes
- Hormonal changes
- Perversion of protean molecules
- Cellular death caused by alterations in the synthesis of DNA, of RNA and of proteins
- Lost of effectiveness of the immune system
- Alterations of the epigenetic mechanisms that maintain the cellular integrity

### 2.3 Biological Changes in Older Adult

Consequently, the musculoskeletal system no longer works in the same way, losing its functions of mobility, elasticity, strength and lack of inclusive adipose tissue, leading to bone weakness, older people tending to fracture, and inclusive column deformation.

Similarly, the skin will also change, sebaceous glands and sweat glands are reduced, resulting in reduced allergies and antibodies, there are obvious wrinkles, redness, fear of delay and other phenomena,

affecting the touch [19].

Aging carries a series of changes, including dependence, psychological rigidity, reduced interpersonal relationships, participation in social activities and negative attitudes.

#### 2.4 Types of Aging

Everyone's social, physical and psychological age is in many cases inconsistent with his or her chronological age. In connection with this, there are three components of aging:

**Biological aging:** Considered as the progressive loss of the physiologic reservations of a person.

**Psychological aging:** Is understood as a deterioration in the adaptability and intellectual capacity of a subject.

**Social aging:** It would assume that everyone has a loss in fulfilling their social and cultural roles.

These differences show us the importance of behavior of an older adult in emphasizing the presence of ageing factors as a way to intervene in their declining physical, mental or social capacities [20].

#### 2.5 Main Illnesses in Older Adult

It can be then concluded that, over the years, living organisms complete their life cycle from birth to the moment they complete senescence, presenting numerous health problems associated with the existence of physiological changes and organic degradation, which lead to the existence of chronic diseases. We can provide assistance to the following people:

- Arthritis
- Hypertension
- Auditory impediments
- Illnesses of the heart
- Visual impediments (including cataracts)
- Deformities or orthopedic impediments
- Diabetes mellitus
- Chronic sinusitis
- Fever of the hay and allergic rhinitis (without

asthma)

#### ➤ Varixes

Almost all older adults have at least a chronic illness, and generally, they have multiple types of illness, called "comorbidity", which force them to manage the care of several dysfunctions at the same time. Many people have some restrictions in their daily life activities due to chronic pain. Just like adults, they are more likely to encounter difficulties in personal care and independent living [21].

Primary aging refers to changes or unavoidable diseases of the older adults that are related to heredity, while secondary aging refers to the loss of ability due to trauma or inevitable falls [22].

By this way, it would be possible to know the difficulties experienced by the elderly life and process, the disease is severe and chronic, it is the biggest problem for them, because most of the time they do not have the appropriate knowledge, now select a treatment and choose not to correct treatment, or cannot make them benefit as a result, therefore, they have been told to improve their quality of life as the goal of benefit their alternatives.

### 3. Importance of Keeping in Mind Polipharmacy in Older Adult

The increase of the expectation of life, multimorbidity and the strict implementation of guides of clinical practice based on evidence are the reasons of the polipharmacy in old man/woman that potentially can have important negative consequences, such as adverse reactions to medications, medication-illness interaction, inappropriate dosage or reduction of the effectiveness. Adverse reactions to medication represent 7% of the causes of derivation of those older than 75 years old, and 25% of hospitalized patients over 80 years old.

Although aging hepatic physiologic alterations have been described as the decrease of the hepatic sanguine flow, it would be necessary to dose keeping in mind, any drug metabolism in the liver has been more or less

eliminated the half-life, which minimize the care, since can't metabolize drugs in the right way, hemoglobin should flow in the liver, secondary to cardiac dysfunction [1].

As the growth of the age, to participate in social activities, and a negative attitude will occur a series of changes, the benefits are positive, help the elderly because exercise can help reduce the loss of muscle and bone mass, also allows the formation of new social groups, and maintain new friendships, active social and cultural fusion, witness psychological

benefits, to relieve stress and anxiety, relaxed atmosphere and a good sense of humor, so as to improve self-esteem [1, 23].

Medicinal plants carry out their pharmacological effect by the affinity of their molecules to receptors, unchaining biochemical processes.

In medicinal plants, active metabolites responsible for the pharmacological effect, act in the same way.

Changes in the pharmacokinetics and pharmacodynamics of medications and medicinal plants in the eldest adult (Table 1).

**Table 1 Adapted from bibliography [24].**

Parameter	Effect by the age	Clinical Implications
Absorption	Not very affected	Interactions among medications
Distribution	quotient fat/water albumin	- Fat-soluble pharmacies (benzodiazepines) have a large distribution volume and a long stay. - Water-soluble drugs (paracetamol, digoxin, etc.), small volume distribution, high risk of toxicity - The binding of a drug to a protein
Metabolism	Mass and hepatic sanguine flow pharmacy metabolism	- Metabolism-related drugs are more susceptible to oxidation: diazepam, phenytoin, antidepressants, verapamil. - The metabolism for conjugation is not affected (lorazepam, oxazepam, etc.).
Excretion	Appraises glomerular filtration	- Use of formulas for estimating glomerular filtration. Serum creatinine is not good indicator of renal function. - Dosage adjustments in drug. The serum creatinine is not good indicator of renal function. - Dosage adjustments in drugs of renal excretion (many antibiotics, digoxin, etc.)
Pharmacodynamics	Less predictable Alteration in sensitivity and number - of the receivers	More intense effects - Morphine: lingering effect. - Benzodiazepines: greater sedation. - Beta stimulation in sensitivity recipients.

#### 4. Ways of Using Natural Medicine

**Bathing:** With plants has effect of aromatic, cure to airframe, stimulant, embellish skin. It is boiled in water with a small amount of prescribed plants, prepared to be filtered, and added to the bathtub water, which can be general or local.

**Hot drink or water decoctions:** Boil the plants for three minutes to slow the fire, then remove them from the heat and leave to rest; recipients should cover the pot within 10 minutes. It applies to the hard, compact parts of plants (roots, bark, seeds, etc.).

**Compresses:** A very clean cloth of cotton or gauze is impregnated in liquid (obtained by infusion) and once squeezed, it is applied on the affected area. It can

be covered with a wool piece or even to blindfold it.

**Cataplasms:** The plant or dried roots are ground in a mortar and mixed with water and enough flax powder or flax seeds so that the whole preparation can cover the affected area. They manifest as pain, inflammation, maturation of abscesses, rheumatism, neuralgia, colds, and breathing problems.

**Emulsions:** A drug extracted from crushed seeds suspended in water to form a milky white substance with therapeutic value. Some may be applied in the form of catalysis or repression.

**Infusion:** This is the most convenient way to prepare the tender and soft parts of the plant. Put it in a cup, put hay on it, sprinkle boiling water on it, cover it, and let it sit for about ten minutes.

批注 [A1]: Wool or wood?

Dusts: Mortar is extracted from the trituración of hay. It can be eaten directly or mixed with other foods.

Juices: They are obtained from crushed or pressed fresh plants. If they are thick, dilute them with water. It is important to remember that it is not very protective and therefore must be taken immediately.

Maceration: The plants can be soaked in cold water for several hours. It can extract unstable active ingredients before heating, but in water [25-27].

### **5. Examples of Results of Uses of Plants in Older Adult**

Medicinal plants was welcomed by the elderly, because they provide benefits for their lives, the survey, conducted in Cuba, as part of the main attention to health, the plant has become the active use of medicinal plant growth or to grow in their habitat, in this way will the vegetables for the treatment of disorders which their communities. Recent research confirms the ongoing research on flora, the purpose of which is to find the properties of these substances, regardless of whether they are beneficial or not, to try to reduce the use of chemical prototypes, and to use natural substances [25].

An investigation carried out in Paraguay by Soria N, and Ramos P showed that the use of medicinal plants as a primary health concern in Paraguay shows that traditional medicines are almost unacceptable to health workers and are welcomed by some. Although previous studies have proven its effectiveness, due to its acceptability, effectiveness, accessibility, readiness and low cost, WHO has sought to include razors in traditional medicines as part of essential health care programmes. This is why it was concluded that its use should be pre-studied to determine its type, source and appropriate dosage to ensure its benefits [28].

An article published in Cuba by Espinosa A, the medical center and personalized medicine point out that some current medical abilities are not enough to confirm the diagnosis at the time of consultation, because nowadays medical consultation is conducted

to the user in a fast manner and only focuses on the disease or pain he/she shows. This is why it is necessary to try to change the medical concept and treat the patient as a unique existence, instead of comparing the disease with the previous diagnosis. Carry out more personalized research, accurately and detailedly analyze the functions of the body, the reasons for its psychological state, and the interpersonal relationship besides investigating the irritability of users. Therefore, a group of students tried to rescue the new progress and progress of drugs. To ensure that the patient's health is good and complete [29].

Another article published in Chile by Leighton N, there are also restrictions on the use of medicinal herbs. A study learned that not all medicinal plants are beneficial to organisms, and that over-consumption and misuse may even cause adverse effects. People don't know anything about this, and they always think that the use is only for them. There are benefits and contributions to health. However, it is well known that people who take it with medicated water will show the loss of the efficacy of the medicine, or in turn cause a negative impact on the body's health. The reason is to prevent population growth and point out that the use of any Medicinal plants are good for everyone, except those who suffer from chronic health, embarrassment, nursing and even chronic diseases of children under 12 years old are contraindicated. This is why the Ministry of Public Health strives to establish a list of poisonous plants and prohibits the use of poisonous plants. For the purpose of planting, using and selling to avoid damage to health [30, 31].

### **6. Pharmacological Interactions between Medicinal Plants and Medications**

Knowledge about the pharmacological interactions between medicinal plants and drugs is limited. There are many responsible factors that have been mentioned: proper identification and responsible actor characteristics, lack of standardization of active

ingredients, lack of formal studies of interactions, lack of integration of medicinal plant systems into pharmacovigilance programmes, lack of vigilant attention to medicines. For the consumption of these products, the doctor's part may have little clinical significance in most interactions. However, enough cases have been documented to suggest caution, especially when patients try drugs (anticoagulants, antiepileptics, antiretrovirals, immunosuppressive agents) that may cause clinically excellent interactions.

In addition to publications and case reports, a variety of medicinal plant abstracts are available as sources of information, with varying degrees of scientific support depending on their nature. Some sources of gratitude are the German Medicines Agency's monograph on medicinal plants, ESCOP (European Plant Therapeutic Scientific Cooperation) [32], a recent monograph published by the WHO or the European Medicines Agency (EMA) [10].

The possibility of pharmacological interactions between medicinal plants and medicines has particular implications when targeting a particular field of patients with a disease or chronic disease. Chronic diseases patients are more susceptible to the influence of natural therapy, because they all condensed the motives and reasons, make the personal choice of orthodoxy on palliative care instead of pharmacology. A state of constant disease, more or less evidence that can be part of the recovery, only by pharmacological treatment and complications and adverse reaction in the process of materials cannot be ruled out. In a recent study conducted in the United States, plants approved for medicinal use agreed to use them: to treat symptoms, drugs, and mood; self-experimental assessment of disease progression; there is a separate drug regimen; and managing the stigma associated with the disease [33].

## 7. Interaction Mechanisms of Medicinal Plants with Medications

Pharmacological interactions between medicinal plants and drugs, like drug-drug interactions, have pharmacokinetic and pharmacodynamic properties.

Those of pharmacodynamic character are characterized by an increase or decrease of the pharmacological effect when it is administered in a concomitant way a medication and a medicinal plant. Basically, pharmacological effects caused by medicinal plants can result in a loss of the effectiveness or toxicity of the drug, but in some cases it can produce a positive synergistic effect or a reduction in toxicity. Pharmacological Interactions of pharmacokinetic character are the most frequent, giving place to changes in the absorption of medications (modulation of the transporters of flow like the P-glycoprotein, formation of complex, alterations of the gastrointestinal motility and affectation of the pH) and of the metabolism, mainly the hepatic one for inhibition or induction of different isoenzymes of the Cytochromes P450 that metabolize the medication.

The IF of pharmacokinetic character will be clinically excellent when considerable changes take place in the pharmacokinetic parameters (area under the curve concentration-time the concentration plasmatic maxim or the half life of elimination ( $t_{1/2}$ )) that without a doubt, will take place in medications with narrow therapeutic margin [34].

Because of the proper characteristics of the older adult's aging, chronic illnesses appears that increase the risk of adverse reactions and pharmacological interactions since in a general way they use a large quantity of medications and medicinal plants and for the vulnerability caused by modifications they suffer in their physiology.

### 7.1 Examples of Interactions between Medicinal Plants and Medications

Antithrombotic agents of the Grass of San Juan (*Hypericum perforatum*) decrease the anticoagulant effect of warfarine and fenprocumona by induction of

the CYP2C9 [35, 36].

The consumption of Garlic (*Allium sativum*) [37-40], Ginger (*Zingiber officinale*) [41], ginkgo (*Ginkgo biloba*) [42], and ginseng (*Panax ginseng*) [43] has been related with alterations in the sanguine clotting, although there is a notification of reduction of the effect of warfarina with ginseng (*Panax quinquefolium*) [44].

It has been postulated that zaragatona (*Plantago psyllium*) and ispagula (*Plantago ovata*) could inhibit the warfarina absorption [45].

There is a notification in literature of warfarina interaction with the fruit of mango in large quantities [27], the same thing as with large quantities of green tea [46].

Although interactions have not been described, the plants that contain salicylates like the ulmaria (*Filipendula ulmaria*) and sallow (*Salix* spp.) should be used carefully in anticoagulated patient, the same thing that some plants as melitoto (*Melilotus officinalis*), bean tonca (*Dipteryx odorata*) and asperilla (*Galium odoratum*) that contain coumarinic derivatives [47-50].

There is a potential additive effect with grasses that contain salicylates and with those that have antiplatelet activity like ginseng (*Panax ginseng*) or ginkgo (*Ginkgo biloba*) [49, 50].

Theoretically, the matricaria (*Tanacetum parthenium*), ginger (*Zingiber officinale*), kava (*Piper methysticum*) and dong quai, has antiplatelet effect *in vitro* [50].

It has also been described a case of ocular hemorrhage in a patient treated with aspirin and ginkgo (*Ginkgo biloba*), although this last one has been related with hemorrhage [51-53].

## 7.2 Cardiovascular System

### 7.2.1 Heart therapy

laxatives that contain sen (*Cassia senna* and other *Cassia* spp.), sacred shell (*Rhamnus purshiana*) can produce hypokalemia producing toxicity by digoxina

[47-50].

There is clinical evidence of reduction in digoxina levels by hiperico (*Hypericum perforatum*) [47-51]. y elevation of digoxina levels in combined treatment with Siberian ginseng (*Eleutherococcus senticosus*) [54].

Yohimbina (*Pausynistalia yohimbe*) can antagonize the guanabenz effects and metildopa by its antiadrenergic properties [55-59].

### 7.2.2 Blockers of the channels of calcium

It has been notified the theoretical interaction between nicardipino and ginkgo (*Ginkgo biloba*) by induction of the CYP3A2 where nicardipine, nifedipine and diltiazem are metabolized, in rats [60].

The antagonists of calcium are substrates of P450 isoenzima 3A4 for which, theoretically, their metabolism could be influenced by the St Johns' worth [48-50].

### 7.2.3 Agents that act on the Renina-Angiotensina system

There is potentiation of the hipotensive effect of lisinopil by garlic (*Allium sativum*) and of the cough by application of a capsaicina cream (*Capsicum* spp.) [61-62].

### 7.2.4 Agents that reduce serum lipids

The induction of the hepatic and intestinal CYP3A4 can diminish the plasmatic concentrations of simvastatina that is metabolized extensively in the intestine by this way. The pravastatina concentrations were not modified [63].

### 7.2.5 Analgesics.

There can be salicylates in several plants, as for example in the bark of the sallow (*Salix* spp.) and in the ulmaria (*Filipendula ulmaria*), although their potential toxicity seems to be much smaller than that of the aspirin. Salicylates can interact with thrombolytics and antiattaches and, although the dose adjustment is not usually recommended, the same considerations should be made for grasses that contain salicylates [64, 65].

The tamarind (*Tamarindus indica*) can increase the

absorption of aspirine [66].

There is a hemorrhage notification in a patient that received rofecoxib and ginkgo (*Ginkgo biloba*) [67].

The effect of levodopa would be reduced by the administration of alkaloids of the rauwolfia (as the reserpina) that alters the neurotransmitters' liberation.

The kava administration (*Piper methisticum*) can reduce the effectiveness of levodopa in the treatment of Parkinson because of its antagonistic effect on the dopamina [68].

An interaction has been observed between prociclidina and the nut of the areca (*Areca catechu*), with appearance of an extrapyramidal picture in a patient treated with flufenacina [69, 70].

#### 7.2.6 Medications used in diabetes

A variety of angelic, the *Angelica dahurica*, used in the Chinese traditional medicine, contains furanocoumarins and could retard the tolbutamida elimination by enzymatic inhibition [71].

Insulin and oral hipoglycemics would interact with the "stimulants" grasses as efedra (*Ephedra sinnica*) and products that contain caffeine like coke or guaraná since all these products increase sanguine glucose [68].

The fruit of the bitter melon or karela (*Momordica charantia*) has hipoglycemic properties that could interfere in the control of the glucemia by its additive effect with antidiabetics [72].

The doses of insulin and oral antidiabetic, could need adjustments due to the hipoglycemic effect of the ginseng (*Panax ginseng*) [73].

#### 7.2.7 Antibacterial for systemic use

A case of possible interaction has been published between the fennel (*Foeniculum vulgare*) and ciprofloxacin, being in a decrease of concentrations of this last one, in rats [74].

The khat, a grass chewed in África and Yemen could reduce the absorption of ampicillin and amoxicillin [75].

Rubber guar can reduce the absorption of penicillin V (*Cyamopsis tetragonoloba*).

Most of macrolide antibiotics are substrates of Cytochrome P450, which can be induced by hypericum (*Hypericum perforatum*). [76, 77].

## 8. Conclusions

Medicinal plants are not completely harmless, in the older adults, physiologic changes after the metabolism of medicinal plants. There is also happen that the mature patients bigger than general way suffer of several illnesses and the medications used to treat chronic illnesses they have many interactions with the medicinal plants.

For this reason, caution should be exercised when using medicinal plants in the elderly.

## References

- [1] Leocadio Rodríguez Mañas and Pedro Abizanda Soler. 2015. *Tratado de Medicina Geriátrica*. Vol. 1. Barcelona, Spain.
- [2] Juan Martínez Guijarro. 2005. *Las Plantas Medicinales y su seguridad*. Una guía para la utilización correcta de las drogas vegetales y sus preparaciones fitomedicinales. Barcelona: Nexus Médica. p. 320.
- [3] J. Sagrera Ferrandiz. 1996. "Enciclopedia de Medicina Natural: Medicinas Alternativas. Plantas Medicinales." Published by Iatros Ediciones, Santafé de Bogotá, Colombia. p. 99.
- [4] Lérica L. Acosta de La Luz. 2006. "La producción agrícola de plantas medicinales en Cuba garantiza de calidad en la producción de fitofármacos." Available from: <http://www.herbotecnia.com.ar/c-public-011.html>.
- [5] Beyra, Á., León, M. C., Ferrández, D., Herrera, R. 2004. "Estudios etnobotánicos sobre plantas medicinales en la provincia de Camagüey, Cuba." *Anales del Jardín Botánico de Madrid* 61 (2): 185-204.
- [6] La situación demográfica en el mundo. Nueva York: Naciones Unidas 2014.
- [7] de Souza Silva, J. E., Souza, C. A. S., da Silva, T. B., Gomes, I. A., Brito Gde, C., de Souza Araújo, A. A. et al. 2014. "Use of Herbal Medicines by Elderly Patients: A Systematic Review." *Arch Gerontol Geriatr* 59 (2): 227-33.
- [8] Levine, M. A., Xu, S., Gaebel, K., Brazier, N., Bédard, M., Brazil, K., Lohfeld, L. et al. 2009. "Self-reported Use of Natural Health Products: A Cross-sectional Telephone Survey in Older Ontarians." *Am J Geriatr Pharmacother* 7 (6): 383-92.
- [9] Zeilmann, C. A., Dole, E. J., Skipper, B. J., McCabe, M.,



- Low, D. T., Rhyne, R. L. 2003. "Use of Herbal Medicine by Elderly Hispanic and Non-Hispanic White Patients." *Pharmacotherapy* 23 (4): 526-32.
- [10] Stjemberg, L., Berglund, J., Halling, A. 2006. "Age and Gender Effect on the Use of Herbal Medicine Products and Food Supplements Among the Elderly." *Scand J Prim Health Care* 24 (1): 50-5.
- [11] Ng, T. P., Tan, C. H., Kua, E. H. 2004. "The Use of Chinese Herbal Medicines and Their Correlates in Chinese Older Adults: The Singapore Chinese Longitudinal Aging Study." *Age Ageing* 33 (2): 135-42.
- [12] Marlière, L., Brandão, M. G., Klein, C. H., Acurcio, F. A. 2008. "Herbal drug use by elderly people: results from a domiciliary survey in Belo Horizonte (MG), Brazil." *Revista Brasileira de Farmacognosia* 18 (Supl.): 754-60.
- [13] Coronado Arce, I. A., Alaya Gutiérrez, A. A. 2012. "Fisiología del Envejecimiento." *Rev Med Act Clin* 17: 813-818.
- [14] Allevato, M., Gaviria, J. 2008. "Envejecimiento." *Act Terap Dermatol* 31: 154-61. Available from: [http://www.atdermae.com/pdfs/atd\\_31\\_03\\_02.pdf](http://www.atdermae.com/pdfs/atd_31_03_02.pdf).
- [15] María Eugenia Guzmán-Pruneda. 2007. "Fisiopatología del paciente de edad avanzada." *Anestesia en el Paciente Geriátrico* 30 (1): S234-S236.
- [16] Oliveira, A. E., Dalla Costa, T. 2004. "Interações farmacocinéticas entre as plantas medicinais *Hypericum perforatum*, *Ginkgo biloba* e *Panax ginseng* e Fármacos Tradicionais." *Acta Farm Bonaer* 23 (4): 567-78.
- [17] Veiga-Junior, V. F. 2008. "Study of the Medicinal Plants Consumption in the Middle-North Region of the Rio de Janeiro State: Acceptance by Health Professionals, Way of Use of the Population." *Rev Bras Farmacog* 18 (2): 308-13.
- [18] Cascaes, E. A., Falchetti, M. L., Galato, D. 2008. "Perfil da automedicação em idosos participantes de grupos da terceira idade de uma cidade do sul do Brasil." *Arq Catarin Med* 37 (1): 63-9.
- [19] Joaquín Jordan Bueso PAS. Medicina Geriátrica. 1.ª ed. Vol. 1. Madrid, España: ELSEIVIER- MASSON; 2012. 406 p.
- [20] Jose Carlos Millan Calenti. *Principios de Geriatria y Gerontología* McGraw-Hill Interamericana de España S. L. Vol. 1. p. 635.
- [21] Charlotte Eliopoulos. 2014. *Enfermería Gerontologica*. 1.ª ed. Vol. 1. Lippincott Williams & Wilkins.
- [22] Karen Dayana Rodriguez Daza. 2011. *Vejez y Envejecimiento*. Bogotá Editorial Universidad del Rosario, 2010. 42 p.— (Documento de Investigación; 12).
- [23] Genua, M. I. et al. 2000. pp. 959-992. Available from: <https://www.sefh.es/bibliotecavirtual/ftomo2/CAP08.pdf>.
- [24] Martín Alcalde, E. 2008. "La Farmacoterapia en el Paciente Anciano." *Boletín Farmacoterapéutico de Castilla-La Mancha* 9 (3).
- [25] Jose Agustin Ramirez Calderon. 2004. "La Huerta Organica y Plantas Medicinales." primera. Vol. 1. Bogota: Grupo Editorial Niño de America Ltda.
- [26] J. Sagrera Ferrandiz. "Enciclopedia de Medicina Natural Medicinas Alternativas." Colombia: PEV-IATROS; 1996. 99 p.
- [27] Gilberto Adhemar Garcia. et al. 2000. "Guía Moderna de Medicina Natural." 2.ª ed. Vol. 1. Peru: Asdimor. 368 p.
- [28] Cardoso Soler, A. B., Porto Verdecia, M. 1997. "Experiencia cubana en el estudio y aplicación de medicamentos herbarios." *Rev Cuba Plantas Med* 2 (1): 30-4.
- [29] Nidia Soria, Pasionaria Ramos. 2015. "Use of Medicinal Plants in Primary Health Care in Paraguay: Some Considerations for Its Safe and Effective Use." *Mem Inst Investig Cienc Salud* 13 (2): 8-17.
- [30] Alfredo Daró Espinosa Brito. 2015. "Person-centered Medicine and Personalized Medicine." *MediSur*. 13 (6): 920-4. Available from: <http://scielo.sld.cu/pdf/ms/v13n6/ms17613.pdf>.
- [31] Paula, Leighton, N. 2015. "Las hierbas medicinales también tienen restricciones de uso." Available from: <http://www.chilevivesano.cl/noticias/las-hierbas-medicinales-tambien-tienen-restricciones-de-uso>.
- [32] ESCOP. Available from: <http://www.escop.com/> [Consultado mayo de 2012].
- [33] Busse, J. W., Heaton, G., Wu, P., Wilson, K. R., Mills, E. J. 2005. "Disclosure of Natural Product Use to Primary Care Physicians: A Cross-sectional Survey of Naturopathic Clinic Attendees." *Mayo Clin Proc* 80 (5): 616-23.
- [34] Moron Rodríguez, F. *Farmacología Clínica*. La Habana, Cuba. Editorial Ciencias Médicas. 2008.
- [35] Yue, Q. Y., Bergquist, C., Gerden, B. 2000. "Safety of St. John's wort (*Hypericum perforatum*)." *Lancet* 355 (9203): 576-7.
- [36] Monitoring the Safety and Quality of Medicines. Herbal safety news. St. John's wort [on line]. Available from URL: <http://medicines.mhra.gov.uk>.
- [37] Vaes, L. P., Chyka, P. A. 2000. "Interactions of Warfarin with Garlic, Ginger, Ginkgo or Ginseng: Nature of the Evidence." *Ann Pharmacoter* 34 (12): 1478-82.
- [38] Mohammad, S. F., Woodward, S. C. 1986. "Characterization of a Potent Inhibitor of Platelet Aggregation and Release Reaction Isolated from *Allium sativum* (garlic)." *Thromb Res* 44 (6): 793-806.
- [39] Lawson, L. D., Ranson, D. K., Hughes, B. G. 1992. "Inhibition of Whole Blood Platelet-aggregation by Compounds in Garlic Clove Extracts and Commercial

- Garlic Products." *Thromb Res* 65 (2):141-56.
- [40] Sunter, W. H. 1991. "Warfarin and garlic." *Pharm J* 246: 722.
- [41] Harrell, B. B. 1980. "Chinese Food and Platelets." *N Eng J Med* 303(13): 756.
- [42] Matthews, M. K. 1998. "Association of Ginkgo biloba with Intracerebral Hemorrhage." *Neurology* 50 (6): 1933-4.
- [43] Janetzky, K., Morreale, A. P. 1997. "Probable Interaction between Warfarin and Ginseng." *Am J Health Syst Pharm* 54 (6): 692-3.
- [44] Yuan, C-S., Wei, G., Dey, L., Karrison, T., Nahlik, L., Maleckar, S. et al. 2004. "Brief Communication: American Ginseng Reduces Warfarin's Effect in Healthy Patients." *Ann Intern Med* 141 (1): 23-27.
- [45] Robinson, D. S., Benjamin, D. M., McCormack, J. J. 1971. "Interaction of Warfarin and Non-systemic Gastrointestinal Drugs." *Clin Pharmacol Ther* 12 (3): 491-5.
- [46] Taylor, J. R., Wilt, V. M. 1999. "Probable Antagonism of Warfarin by Green Tea." *Ann Pharmacother* 33 (4): 426-8.
- [47] Miller, L. G., Murray, W. J. Editors. *Herbal Medicinals: A Clinician's Guide*. New York. Pharmaceutical Products Press. 1998.
- [48] Rowin, J., Lewis, S. L. 1996. "Spontaneous Bilateral Subdural Hematomas Associated with Chronic Ginkgo biloba Ingestion." *Neurology* 46 (6): 1775-6.
- [49] Chung, K. F., McCusker, M., Page, C. P., Dent, G., Guinot, P., Barnes, P. J. 1987. "Effect of a Ginkgolide Mixture (BN 52063) in Antagonising Skin and Platelet Responses to Platelet Activating Factor in Man." *Lancet* 1 (8527): 248-51.
- [50] Barnes, J., Phillipson, J. D., Anderson, L. A. *Herbal Medicines*. 2nd ed. London: The Pharmaceutical Press, 2002.
- [51] Rosenblatt, M., Mindel, J. 1997. "Spontaneous Hyphema Associated with Ingestion of Ginkgo biloba Extract." *N Engl J Med* 336 (15): 1108.
- [52] Matthews, M. K. 1998. "Association of Ginkgo biloba with Intracerebral Haemorrhage." *Neurology* 50 (6): 1933-4.
- [53] Vale, S. 1998. "Subarachnoid Hemorrhage Associated with Ginkgo Biloba." *Lancet* 352 (9121): 36.
- [54] McRae, S. 1996. "Elevated Serum Digoxin Levels in a Patient Taking Digoxin and Siberian Ginseng." *Can Med Assoc J* 155 (3): 293-5.
- [55] Kim, Y. I., Paik, Y. H., Kang, S. S., Kim, J. H. 1982. "Effects of Alpha-adrenoceptor Antagonists Administered Intraventricularly on Central Hypotensive Action of Clonidine and on Central Hypertensive Action of Methoxamine in Rabbits." *Arch Int Pharm Ther* 257 (1): 66-76.
- [56] Imai, Y., Nolan, P. L., Johnston, C. I. 1986. "Tachycardic and Hypertensive Effects of Centrally Administered Clonidine in Conscious Rats." *Clin Exp Hypertension A* 8 (2): 239-58.
- [57] Peter, A. G. M. De Smet, Konstantin Keller, Rudolf Hänsel, R. Frank Chandler. 1997. *Adverse Effects of Herbal Drugs*. vol. 3, Springer-Verlag, Berlin.
- [58] Musso, N. R., Vergassola, C., Pende, A., Lotti, G. 1995. "Yohimbine Effects on Blood Pressure and Plasma Catecholamines in Human Hypertension." *Am J Hypertens* 8 (6): 565-71.
- [59] Grossman, E., Rosenthal, T., Peleg, E., Holmes, C., Goldstein, D. S. 1993. "Oral Yohimbine Increases blood Pressure and Sympathetic Nervous Outflow in Hypertensive Patients." *J Cardiovasc Pharmacol* 22 (1): 22-6.
- [60] Shinozuka, K., Umegaki, K., Kubota, Y., Tanaka, N., Mizuno, H., Yamauchi, J. et al. 2002. "Feeding of Ginkgo Biloba Extract (GBE) Enhances Gene Expression Hepatic Cytochrome P-450 and Attenuates the Hypotensive Effects of Nicardipine in Rats." *Life Sci* 70 (23): 2783-92.
- [61] McCoubrie, M. 1996. "Doctors as Patients: Lisinopril and Garlic." *Br J Gen Pract* 46: 107.
- [62] Hakas, J. F. 1990. "Topical Capsaicin Induces Cough in Patient Receiving ACE Inhibitor." *Ann Allergy* 65 (4): 322-3.
- [63] Sugimoto, K., Ohmori, M., Tsuruoka, S., Nishiki, K., Kawaguchi, A., Harada, K. et al. 2001. "Different Effects of St John's Wort on the Pharmacokinetics of Simvastatin and Pravastatin." *Clin Pharmacol Ther* 70 (6): 518-24.
- [64] Harder, S., Klinkhardt, U. 2000. "Thrombolytics: Drug Interactions of Clinical Significance." *Drug Saf* 23 (5): 391-9.
- [65] Abebe, W. 2002. "Herbal Medication: Potential for Adverse Interactions with Analgesic Drugs." *J Clin Pharm Ther* 27 (6): 391-401.
- [66] Mustapha, A., Yakasai, I. A., Aguye, I. A. 1996. "Effect of Tamarindus Indica L. on the Bioavailability of Aspirin in Healthy Human Volunteers." *Eur J Drug Metab Pharmacokin* 21 (3): 223-6.
- [67] Hoffmann, T. 2001. "Ginkgo, Vioxx and Excessive Bleeding: Possible Drug Interactions: Case Report." *Hawaii Med J* 60 (11): 290.
- [68] Stockley, I. H., editor. *Stockley's drug interactions*. 6th ed. London: The Pharmaceutical Press, 2002.
- [69] Schelosky, L., Raffauf, C., Jendroska, K., Poewe, W. 1995. "Kava and Dopamine Antagonism." *J Neurol Neurosurg Psychiatry* 58 (5): 639-40.
- [70] Deahl, M. 1989. "Betel Nut Induced Extrapramidal Syndrome: An Unusual Drug Interaction." *Mov Disord* 4

- (4): 330-2.
- [71] Ishihara, K., Kushida, H., Yuzurihara, M., Wakui, Y., Yanagisawa, T., Kamet, H. et al. 2000. "Interaction of Drugs and Chinese Herbs: Pharmacokinetic changes of Tolbutamide and Diacepam Caused by Extract of *Angelica dahurica*." *J Pharm Pharmacol* 52 (8): 1023-9.
- [72] Aslam, M., Stockley, I. H. 1979. "Interaction between Curry Ingredient (Karela) and Drug (Chlorpropamide)." *Lancet* 1 (8116): 607. doi: 10.1016/s0140-6736(79)91028-6.
- [73] Sotaniemi, E. A., Haapakoski, E., Rautio, A. 1995. "Ginseng Therapy in Non-insulin-dependent Diabetic Patients." *Diabetes Care* 18 (10): 1373-5.
- [74] Zhu, M., Wong, P. Y., K, Li, R. C. 1999. "Effect of Oral Administration of Fennel (*Foeniculum vulgare*) in Ciprofloxacin Absorption and Disposition in the Rat." *J Pharm Pharmacol* 51 (12): 1391-6.
- [75] Abdel Ghani, Y. M., Etman, M. A., Nada, A. H. 1999. "Effect of Khat Chewing on the Absorption of Orally Administered Amoxicillin." *Acta Pharm* 49 (1): 43-50.
- [76] Wang, Z., Gorski, J. C., Hamman, M. A., Huang, S. M., Lesko, L. J., Hall, S. D. 2001. "The Effects of St John's Wort (*Hypericum perforatum*) on Human Cytochrome P450 Activity." *Clin Pharmacol Ther* 70 (4): 317-26.
- [77] Markowitz, J. S., Donovan, J. L., DeVane, C. L., Taylor, R. M., Ruan, Y., Wang, J. S. et al. 2003. "Effect of St John's Wort on Drug Metabolism by Induction of Cytochrome P450 3A4 Enzyme." *JAMA* 290 (11): 1500-4.