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Foods and Herbs That May Interact with Medications Used for Arterial Hypertension and Dyslipidemia

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Abstract

The aim of this review was to verify the risks of drug-nutrient interactions in the elderly. This is an integrative literature review, with a descriptive approach, carried out through research in indexed databases, legislation and pharmacopoeias. Data collection took place in the year 2022, through the analysis of literature collected of the last 10 years collected. The data showed that many of the continuous drugs use by the elderly can lead to interactions of different orders with nutrients, increasing the risk of plasmatic fluctuation as grapefruit, orange, lemon and lime interact with systemic arterial hypertension, increasing the risk of drug intoxication in the elderly. The action of the health team is essential, through the careful evaluation of the administered drugs, diet therapy and the interaction between them, to benefit the elderly with better use of the therapy and improvement of nutritional conditions.

Keywords

Elderly, Integrative Literature Review, Interactions, Nutrients, Drugs

1. Introduction

Consumption of certain foods and herbs may interfere with the effect of drugs [1]. The elderly often portrays multiple morbidities and less functional reserve of

organs; therefore, the food effects may be exacerbated. In-depth knowledge of the elderly's clinical presentation will certainly promote a safer and more accurate interactive panel and pharmacological prediction.

Most of the pharmacokinetic and pharmacodynamic divergence from standard parameters is observed in the elderly population, which tends to have comorbidities that might alter nutrient absorption, distribution, utilization, and drug interactions. Prescribed drugs not only have the potential to interact with each other, but also with molecules present in certain foods and alter the metabolic capacity of enzymes that process the drugs/prodrugs. For these reasons, it is necessary for patients and caregivers to monitor the consumption of foods and herbs that may trigger interactions with prescribed medications for the control of hypertension and/or dyslipidemia.

The elderly often presents with altered pharmacodynamics due to changes in tissue response, which depends on the number and affinity of receptors, on the activation of effector mechanisms, and on the body's homeostatic mechanisms that will determine the drugs' overall effects. Processes such as pharmacokinetics, absorption, metabolism, distribution, and elimination may also be altered in the elderly population. Main changes that are observed as follows [2] [3] [4].

2. Method

This was a study carried out through a bibliographical survey and based on the experience lived by the authors when carrying out an integrative review.

To produce this article, a bibliographical analysis was carried out of scientific material obtained from the following databases: US National Library of Medicine-National Institutes of Health (PubMed), Virtual Health Library (Latin American and Caribbean Literature in Health Sciences—LILACS), Web of Science and Google® Scholar, laws and pharmacopoeias, in a retrospective investigation of the last 10 years.

3. Discussion

3.1. Characterization of the Elderly Population [5]

Body composition: Reduction of total volume of water in the body water; reduction of lean mass; increase in body fat; decrease in serum albumin.

Cardiovascular system: Decreased myocardial sensitivity to β-adrenergic stimulation; increase in total peripheral resistance; decreased activity of baroreceptors, which are mechanoreceptors located in the carotid sinus and aortic arch. Baroreceptors sense and respond to moment-to-moment blood pressure adjustments by detecting sudden changes in blood pressure and transmitting this information to the central nervous system.

Central Nervous System: Decrease in weight and brain volume, which may later pathways involved in the renin-angiotensin system (RAS) [6].

Endocrine system: Decreased thyroid gland volume/function; decreased pancreatic function associated to increased incidence of diabetes mellitus; menopause-

associated hormonal changes; prostatic hypertrophy due to androgenic hormonal alteration.

Digestive System: Increase in gastric pH; decreased blood flow/absorption from the digestive tract; reduction of intestinal transit; changes in microbiome and signaling in the gut-brain axis [7].

Immune system: Decreased cell-mediated immunity secondary to thymic atrophy.

Liver: Decrease in the size of the liver; decreased hepatic blood flow.

Lungs: Decreased respiratory muscle force; decreased maximum respiratory capacity; decreased total alveolar surface.

Kidneys: Decreased glomerular filtration; decreased renal blood flow; decreased tubular secretory function; reduction of renal mass.

Comorbidities in the elderly and the concomitant use of medicinal plants and/or foods with prescription drugs for the treatment of non-communicable chronic diseases is a common scenario. There is a prevalent misconception that medicinal plants/herbs do not cause harm because they originate in nature. Therefore, many times medicinal plants and/or herbs and/or food are used with the purpose of aiding in the control of health issues that have already been medicated using prescription drugs. Worldwide, the two most common non-communicable chronic diseases are dyslipidemia and systemic arterial hypertension, therefore, the objective of this short communication was to bring patient awareness of commonly used foods/herbs/supplements and their interactions with hypertension and dyslipidemia prescription drugs. Long these lines, it is important to prevent additive or synergistic effects that can further jeopardize the elderly population's health.

3.2. Garlic, or *Allium sativum* L. (Uses Dyslipidemia and Systemic Arterial Hypertension) [4] [8] [9]

Main active components: terpenes, fatty acids, organosulfates, saponins and phenylpropanoids.

Mechanism of action: Therapeutic indication (Memento): Coadjuvant in the treatment of chronic bronchitis, asthma, as an expectorant, and as a preventive measure for vascular alterations. Supportive in the treatment of hyperlipidemia, mild to moderate arterial hypertension, flu and cold symptoms and aiding in the prevention of atherosclerosis.

Sulfur compounds show vasodilatory activity *in vitro* mediated by nitric oxide release. The use of garlic may reduce the expression of CYP cytochrome enzymes CYP3A4, CYP3A5, CYP3A7, CYP2C9, CYP2C19 and CYP2E1 isoforms and P-glycoprotein, and may increase expression of CYP2C9, CYP3A1 and CYP1A1. CYP enzymes are important for biotransformation of drugs, metabolites, and toxins.

Drug interactions: Synergistic interaction with beta-blocker antihypertensive drugs, which work by reducing cardiac output and reducing renin and catecholamine secretion at nerve synapses. Beta-blockers also act on vasodilation by in-

creasing the synthesis and endothelial release of nitric oxide. Garlic, a sulfur-containing plant, exert a similar effect triggering potentiation of the antihypertensive drugs. Beta-blockers (ex: Propranolol) are metabolized by the CYP2D6 isoform of cytochrome enzymes, which is also affected by garlic.

Concomitant use of garlic with the antihypertensive inhibitors of the angiotensin-converting enzyme, causes an increase in the hypotensive effect of the drugs. Similarly, use of garlic with calcium channel antagonists enhances the drugs actions by interfering with the rate of clearance. Calcium channel blockers are also metabolized via CYP450 enzymes, with verapamil being mainly metabolized by the CYP3-A4 isoform.

Allium sativum cannot be used in combination with oral anticoagulants, heparin, thrombolytics, antiplatelets, warfarin, and non-steroidal anti-inflammatory drugs (NSAIDs) due to increased risk of bleeding. Association of this herbal medicine with yet another class of drugs, the antiviral protease inhibitors, may reduce serum concentrations of those drugs, increasing the risk of viral resistance and treatment failure. In addition, garlic can reduce the effectiveness of chlorzoxazone by inducing its metabolism. Chlorzoxazone is a strong oxidizing agent that is used as a skeletal muscle relaxant and as an analgesic.

3.3. Shell Ginger, or *Alpinia zerumbet* (Pers.) B.L. Burtt & R.M. Sm. (Use: Systemic Arterial Hypertension) [9] [10] [11] [12]

Main active components: Shell ginger essential oil contains mono and sesquiterpenes, with a higher concentration of terpinen-4-ol and 1,8-cineol, which are responsible for the hypotensive and vasodilator action, respectively. Presence of flavonoids contribute to the anti-hypertensive action.

Mechanism of action: The essential oil (terpinen-4-ol and 1.8 cineole) improves cardiovascular hemodynamics. Terpineol works as a calcium channel blocker. Catechins act on vascular smooth muscle by inhibiting cell proliferation, therefore potentially preventing the development of atherosclerosis [13]. The alkaloids have diuretic action, therefore decreasing blood pressure.

Drug Integrations: Terpineol works similarly to antihypertensive calcium channel antagonists, by preventing calcium from entering cells. When the essential oil is used with antihypertensive drugs, it can cause hypotension due to incrementation of the antihypertensive effect. Catechins have a pharmacological effect like the mechanism of action of direct vasolytic antihypertensives and may enhance the action of such drugs.

3.4. Citrus Species, Such as Grapefruit, Oranges, Lemons and Limes (Use: Systemic Arterial Hypertension) [7] [8]

Main active components: Orange contains phenols, tannins, flavonoids (anthocyanidins, flavones, flavanols, narirutin, hesperidin, naringin and neohesperidin), xanthones, saponins, steroids, and triterpenoids.

Mechanism of action: Hesperidin blocks beta-adrenergic receptors (drugs that act to reduce cardiac output), reduces renin secretion by juxtaglomerular

cells (kidney granular cells), and has a central nervous system action by decreasing sympathetic activity. Hesperidin contributes to the effect of beta-blockers by providing an antihypertensive effect and inhibiting angiotensin converting enzyme (ACE) activity. Grapefruit is known to inhibit CYP3A4, therefore increasing the bioavailability of drugs that are metabolized via that pathway. Moreover, immature *Citrus unshiu* (satsuma mandarin) fruits have anti-allergic effects against the Type I, II and IV hypersensitivity reactions [14].

Drug interactions: Possible synergistic interactions with beta-blocking antihypertensive drugs (atenolol, bisoprolol, metoprolol, propranolol, pindolol, carvedilol, nadaolol and labetalol) as well as with ACE inhibitors (benazepril, captopril, delapril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril and trandolapril) most likely by increased bioavailability due to decreased degradation.

3.5. Artichoke, or *Cynara scolymus* L. (Uses: Dyslipidemia and Systemic Arterial Hypertension) [4] [8] [9] [10]

Main active components: Phenolic acids, phenylpropanoids, saponins, flavonoids, sesquiterpenes, and steroids.

Mechanism of action: Antidyspeptic, antiflatulent, diuretic. Help in the prevention of atherosclerosis. Adjuvant in the treatment of mild to moderate mixed dyslipidemia and as an aid in the symptoms of irritable bowel syndrome.

In vitro showed that the dry aqueous extract of artichoke leaves inhibited cholesterol biosynthesis in cultured rat hepatocytes. Cynaroside and its aglycone, luteolin, are primarily responsible for this activity. Phase IV clinical studies conducted in patients with dyspepsia or hepatic or biliary dysfunction using standardized extract of *C. scolymus*, with a minimum of 2.5% caffeoylquinic acid derivatives expressed as chlorogenic acid, demonstrated a significant reduction in symptoms of generalized pain, discomfort, abdominal pain, gas and nausea. In addition, intraduodenal biliary secretion increased significantly after 90 minutes of treatment.

Drug Interactions: Reduces the effectiveness of drugs that interfere with blood clotting, such as aspirin and coumarin anticoagulants (warfarin). May decrease the blood concentrations of drugs metabolized by CYP3A4, CYP2B6, and CYP2D6 because *C. scolymus* is an inducer of these enzymes.

Artichoke interacts with other medications when associated with diuretics, especially loop diuretics (furosemide) and thiazides (chlorthalidone, hydrochlorothiazide, indapamide). This can be explained by the diuretic effect of low polar compounds present in the artichoke leaves that cause causing a decrease in blood volume culminating in a drop in blood pressure and hypovolemia. The diuretic effect of artichoke also leads to a large amount of potassium excretion.

3.6. Passionflower, or *Passiflora* sp. (Use: Systemic Arterial Hypertension) [4] [8] [9] [10]

Main active components: Flavonoids (di-C-heteroside flavones: vitexin and

apigenin), indole alkaloids and saponin.

Mechanism of action: The antioxidant properties of phenolic compounds improve endothelial function and normalize vascular tone, resulting in a hypotensive effect. Phenolic compounds potentiate the hypotensive effects of drugs that have the same mechanism of action.

Drug Interactions: Concomitant use of passionflower with caffeine, guarana or ephedra may cause an increase in blood pressure. Potentiates the effects of drugs of the direct vasodilator class (hydralazine, minoxidil).

3.7. St. John's Wort, or Hypericum Perforatum (Use: Kidney and Lung Ailments, Insomnia, Depression, Menopausal Symptoms, Anxiety, Obsessive Compulsive Disorder, and to Aid Wound Healing)

Main active components: Two major active molecules have been identified: hypericin (a naphtodianthrone) and hyperforin (a phloroglucinol). However, nearly 20% of extractable compounds are considered biologically active [15].

Mechanism of action: Hyperforin plays an important role in the induction of cytochrome P450 enzymes. Hyperforin also induces the P-glycoprotein transporter (P-gp), therefore affecting the pharmacokinetics of many drugs [16].

Drug Interactions: By stimulating CYP450 enzymes, St. John's wort can weaken the effects of many drug classes that depend on that pathway for degradation, including warfarin and other anticoagulants, statins (sholesterol-lowering drugs). St John's wort significantly reduces the bioavailability of verapamil (which is used to prevent angina and arrhythmia pain) as well as the bioavailability of similar calcium channel blockers [17].

Although *H. perforatum* is sold as over-the-counter drug through US and Europe, scientific literature has been advising for its potential toxicity and drug-interaction. Thus, the use of this plant should done with careful, especially in elderly [18].

Observation: Plants with warning for hypertensives [4]: *Glycyrrhiza glabra* L./*Glycyrrhiza inflata* Batalin/*Glycyrrhiza uralensis* Fisch ex DC./*Cyanara carduncul*us L./*Paulllinia cupana* Kunth ex H.B.K. var. Sorbilis (Mart.)/*Zingiber officinale* Roscoe./*Achillea millefolium* L./*Allium sativum* L./*Baccharis trimera* (Less. DC.)/*Bidens pilosa* L./*Rosmarinus officinalis* L./*Zea mays* L./*Panax ginseng* C. A. Meyer.

4. Conclusions

We conclude that in order to avoid the side effect resulting from the interaction between food and medication, the work of the multidisciplinary health team is essential, especially with regard to the elderly. The use of medicines by the elderly happens in large quantities, thus being a polypharmacy patient [19].

The foods listed are common foods in the daily life of any individual, thus increasing the risk of interaction between herbal medicines and foods listed in this article. The careful evaluation of administered drugs, diet therapy and the inte-

raction between them, is to benefit the elderly with better use of therapy and improvement of nutritional conditions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bushra, R., Aslam, N. and Khan, A.Y. (2011) Food-Drug Interactions. *Oman Medical Journal*, **26**, 77-83. https://doi.org/10.5001/omj.2011.21

[2] Beyth, R.J. and Shorr, R.I. (2002) Principles of Drug Therapy in Older Patients: Rational Drug Prescribing. *Clinics in Geriatric Medicine*, **18**, 577-592. https://doi.org/10.1016/S0749-0690(02)00017-4

[3] Jacob Filho, W. and Kikuchi, E.L. (2011) Geriatria e gerontologia básicas. Elsevier, Brasil.

[4] Sanitária, A.N.D.V. (2016) Memento terapêutico. Farmacopeia Brasileira.

[5] Bogacka, A., Heberlej, A., Usarek, A. and Okoniewska, J. (2019) Diet and Nutritional Status of Elderly People Depending on Their Place of Residence. *Roczniki Panstwowego Zakladu Higieny*, **70**, 185-193. https://doi.org/10.32394/rpzh.2019.0069

[6] Santos, R.A.S., *et al.* (2019) The Renin-Angiotensin System: Going beyond the Classical Paradigms. *American Journal of Physiology Heart and Circulatory Physiology*, **316**, H958-H970. https://doi.org/10.1152/ajpheart.00723.2018

[7] Parker, A., *et al.* (2022) Fecal Microbiota Transfer between Young and Aged Mice Reverses Hallmarks of the Aging Gut, Eye, and Brain. *Microbiome*, **10**, Article No. 68. https://doi.org/10.1186/s40168-022-01243-w

[8] Nicoletti, M.A., *et al.* (2007) Principais interações no uso de medicamentos fitoterápicos. *Infarma*, **19**, 32-40.

[9] Porto, J.C.F., *et al.* (2021) Plantas medicinais x medicamentos anti-hipertensivos: Interação medicamentosa. *Research, Society and Development*, **10**, e126101623414. https://doi.org/10.33448/rsd-v10i16.23414

[10] Souza, J.B.P., *et al.* (2017) Interações planta medicinal x medicamento convencional no tratamento da hipertensão arterial. *Infarma Ciências Farmacêuticas*, **29**, 90-99. https://doi.org/10.14450/2318-9312.v29.e2.a2017.pp90-99

[11] Pinto, N.V., Assreuy, A.M.S., Coelho-de-Souza, A.N., Ceccatto, V.M., Magalhães, P.J.C., Lahlou, S. and Leal-Cardoso, J.H. (2009) Endothelium-Dependent Vasorelaxant Effects of the Essential Oil from Aerial Parts of *Alpinia zerumbet* and Its Main Constituent 1,8-Cineole in Rats. *Phytomedicine*, **16**, 1151-1155. https://doi.org/10.1016/j.phymed.2009.04.007

[12] Santos, B.A., Roman-Campos, D., Carvalho, M.S., Miranda, F.M.F., Carneiro, D.C., Cavalcante, P.H., Cândido, E.A.F., Xavier Filho, L., Cruz, J.S. and Gondim, A.N.S. (2011) Cardiodepressive Effect Elicited by the Essential Oil of *Alpinia speciosa* Is Related to L-Type Ca^{2+} Current Blockade. *Phytomedicine*, **18**, 539-543. https://doi.org/10.1016/j.phymed.2010.10.015

[13] Won, S.M., *et al.* (2006) Catechins Inhibit Angiotensin II-Induced Vascular Smooth Muscle Cell Proliferation via Mitogen-Activated Protein Kinase Pathway. *Experimental & Molecular Medicine*, **38**, 525-534. https://doi.org/10.1038/emm.2006.62

[14] Fujita, T., *et al.* (2008) Comparative Evaluation of 12 Immature Citrus Fruit Extracts

for the Inhibition of Cytochrome P450 Isoform Activities. *Biological and Pharmaceutical Bulletin*, **31**, 925-930. https://doi.org/10.1248/bpb.31.925

[15] Klemow, K.M., *et al.* (2011) Medical Attributes of St. John's Wort (*Hypericum perforatum*). In: Benzie, I.F.F. and Wachtel-Galor, S., Eds., *Herbal Medicine*: *Biomolecular and Clinical Aspects*, CRC Press, Boca Raton.

[16] Soleymani, S., *et al.* (2017) Clinical Risks of St John's Wort (*Hypericum perforatum*) Co-Administration. *Expert Opinion on Drug Metabolism & Toxicology*, **13**, 1047-1062. https://doi.org/10.1080/17425255.2017.1378342

[17] Agbabiaka, T.B., *et al.* (2018) Prevalence of Drug-Herb and Drug-Supplement Interactions in Older Adults: A Cross-Sectional Survey. *British Journal of General Practice*, **68**, e711-e717. https://doi.org/10.3399/bjgp18X699101

[18] Marrelli, M., Statti, G. and Conforti, F. (2020) *Hypericum* spp.: An Update on the Biological Activities and Metabolic Profiles. *Mini-Reviews in Medicinal Chemistry*, **20**, 66-87. https://doi.org/10.2174/1389557519666190926120211

[19] de Oliveira, H.S.B. and Corradi, M.L.G. (2018) Aspectos farmacológicos do idoso: Uma revisão integrativa de literatura. *Revista de Medicina*, **97**, 165-176. https://doi.org/10.11606/issn.1679-9836.v97i2p165-176