

# Anticoagulant effects of phytotherapeutic drugs and their importance in surgical dental procedures

*Efeitos anticoagulantes de drogas fitoterapicas e sua importância em procedimentos odontológicos cirúrgicos*

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## ABSTRACT

*Phytotherapeutic drugs are plant-derived products with medicinal properties. They are used for treating or preventing several diseases. However, patients who use these substances and even health professionals are unaware of their negative effects. One of the most common negative effects of phytotherapeutic drugs reported in the literature is the inhibition of natural coagulation factors in the human body. Therefore, the aim of this study was to perform a brief review of the literature concerning the anticoagulant effects of phytotherapeutic drugs and their importance in surgical dental procedures. Preventive measures, clarification and monitoring of patients taking phytotherapeutic drugs are recommended before performing surgical dental procedures, in order to prevent against complications such as hemorrhage.*

**Indexing terms:** Blood coagulation factors. Phytotherapeutic drugs. Surgical dental procedures

## RESUMO

Fitoterápicos são produtos derivados de plantas com propriedades medicinais. Eles são utilizados para o tratamento ou a prevenção de diversas doenças. No entanto, os pacientes que fazem uso destas substâncias, na sua grande maioria, desconhecem seus efeitos negativos. Portanto, o objetivo deste estudo foi realizar uma breve revisão de literatura sobre os efeitos anticoagulantes de fitoterápicos e sua importância diante da realização de procedimentos odontológicos cirúrgicos. Medidas de prevenção, esclarecimento e acompanhamento de pacientes que se utilizam destes medicamentos são recomendados antes da realização destes procedimentos a fim de prevenir complicações como processos hemorrágicos.

**Termos de indexação:** Fatores de coagulação sanguínea. Fitoterápicos. Procedimentos odontológicos cirúrgicos.

## INTRODUCTION

Alternative substances for treating or preventing several diseases have aroused the interest of the population around the world, including natural substances and phytotherapeutic drugs<sup>1-5</sup>.

Phytotherapeutic drugs are plant-derived products with medicinal properties. The literature contains several medical indications for their use, with significant positive results that include antimicrobial, anti-inflammatory and anti-oxidant effects<sup>6-7</sup>. Nonetheless, considering the many countries where they are produced and marketed<sup>8</sup>, it could be reasonably assumed that the general population may use them without a medical or dental prescription,

or even without appropriate dosing. About two-thirds of the patients who use phytotherapeutic drugs are unaware of their negative effects<sup>9</sup>. In addition, in general, health professionals have a small knowledge about the negative effects of phytotherapeutic drugs<sup>2,4,9</sup>.

One of the most common negative effects of phytotherapeutic drugs reported in the literature is the inhibition of natural coagulation factors in the human body. Phytotherapeutic drugs, whether alone or combined with allopathic substances, may result in hemorrhage during and after surgical procedures<sup>7,10-11</sup>. Consequently, the aim of this study was to carry out a brief review of the literature concerning the anticoagulant effects of phytotherapeutic drugs and their importance in surgical dental procedures.

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### Garlic (*Allium sativum*)

*Allium sativum* can be consumed in the form of tablets or capsules containing powder or oil, or else applied topically. Several medicinal properties have been reported, such as antimicrobial, anti-hypertensive, antithrombotic, antimutagenic and fibrinolytic effects, as well as glucose-reducing platelet activity. It is also indicated for decreasing cholesterol and treating arteriosclerosis<sup>12</sup>. However, its anticoagulant effect has been proven in studies that have demonstrated a reduction in platelet activity, leading to hemorrhage<sup>4,13</sup>. This effect may be further heightened by its combined use with allopathic medications, such as acetylsalicylic acid, warfarin and other drugs<sup>12,14-15</sup>.

Therefore, it is recommended that *Allium sativum* be suspended at least one week before a surgical dental procedure<sup>10</sup>. In case of combined use with warfarin, this recommendation is even more important, because of the likelihood of high interaction<sup>5,10</sup>.

### Chilean boldo (*Peumus boldus*)

Concentrated *Peumus boldus* solution is widely used for the treatment of digestive and liver disorders<sup>5</sup>. However, its possible antiplatelet effects have already been described in the literature<sup>5,16-17</sup>. When *Peumus boldus* is used alone in high doses and/or in association with allopathic drugs, platelet dysfunctions may be even greater. Therefore, it is recommended that the use of *Peumus boldus* be suspended before performing surgical dental procedures<sup>18</sup>.

### Chamomile (*Matricaria recutita*)

*Matricaria recutita* can be used as an essential oil, in capsule or liquid form. It has several medicinal properties, such as anti-inflammatory, antispasmodic<sup>18-19</sup> sedative and antiseptic effects. It is indicated for the treatment of flatulence, digestive disorders and nasal mucositis<sup>19</sup>. However, *Matricaria recutita* also may act on platelet function, and consequently increase the risk of hemorrhage<sup>11,14</sup>. Although cases of interaction with warfarin have already been reported as leading to hemorrhage<sup>20</sup>, this link has not yet been clearly established. Nevertheless, because of its possible antiplatelet action and probable interaction with other drugs<sup>5,20</sup>, its use should be suspended preventively prior to surgical dental procedures.

### Indian horse chestnut (*Aesculus hippocastanum*)

*Aesculus hippocastanum* can be taken in the form of tablets, capsules, gels or creams. This substance is used

as an adjuvant in capillary treatment, and for the treatment of varicose veins and hemorrhoids<sup>18-19</sup>. It interferes with platelet function and with the coagulation action of warfarin<sup>5,21</sup> and other drugs<sup>18</sup>. Therefore, its use must be avoided before surgical dental procedures.

### Ginkgo biloba (*Ginkgo biloba*)

*Ginkgo biloba* is a substance widely used by the population around the world in the form of gel and capsules to treat vascular disorders<sup>18</sup>, aid cognitive development<sup>14</sup>, prevent dementia<sup>12</sup> and Alzheimer's disease<sup>10</sup>, and treat macular degeneration, tinnitus and erectile<sup>10</sup>. Its antiplatelet action has already been reported<sup>1-5</sup>, although there are controversies on this matter<sup>22</sup>.

The anticoagulant effects of *Ginkgo biloba* have been reported mainly when this substance is used in combination with allopathic drugs, such as warfarin<sup>5</sup>, heparin<sup>18</sup>, aspirin<sup>1,11,19,23</sup>, and ibuprofen<sup>24</sup>. Therefore, dentists must be attentive to patients taking *Ginkgo biloba*, particularly when this substance is associated with other drugs of high hemorrhagic potential, before performing surgical procedures.

### Ginseng (*Panax ginseng*)

*Panax ginseng* is used for preventing against states of physical and mental fatigue<sup>18</sup>, for strengthening the immune system<sup>19</sup>, for its aphrodisiac, antidepressant and diuretic properties, and for preventing cardiovascular disorders<sup>4</sup>. Its interaction with warfarin has already been established<sup>25</sup>. However, some studies do not corroborate these findings<sup>26-27</sup>. Therefore, further studies are needed on this subject.

In brief, many studies have found scientific evidence regarding the antiplatelet properties or drug interactions regarding the substances addressed in this study. These properties and interactions have demonstrated the potentiation of their hemorrhagic effects. Therefore, preventive measures, clarification and monitoring of patients taking these substances are recommended before performing surgical dental procedures, in order to prevent against complications such as hemorrhage.

### Collaborators

L COSME-SILVA, JR OLIVEIRA, FD MARTINHO and CH FERRARI participated in the design, organization and writing of the article. LF CUBA and RICARDO MACHADO were responsible for critical review and writing of the article.

## REFERENCES

1. Vaes LP, Chyka PA. Interactions of warfarin with garlic, ginger, ginkgo, or ginseng: nature of the evidence. *Ann Pharmacother*. 2000;34(12):1478-82.
2. Wynn RL, Bergman SA. Drugs and herbal remedies that affect blood clotting. *Gen Dent*. 2002;50(6):484-8.
3. Varona F, Morales M. Ginkgo biloba y hemorragia cerebral. *An Med Interna*. 2005;22(4),199.
4. Shankland II WE. Four common herbs seen in dental practice: properties and potential adverse effects. *Cranio*. 2009;27(2):118-24.
5. Ge B, Zhang Z, Zuo Z. Updates on the clinical evidenced herb-warfarin interactions. *Evid Based Complement Alternat Med*. 2014;2014:957362. doi: 10.1155/2014/957362
6. Winslow LC, Kroll DJ. Herbs as medicines. *Arch Intern Med*. 1998;158:2192-9.
7. Pribitkin EA. Herbal medicine and surgery. *Sem Integ Med*. 2005;3(1):17-23. doi: 10.1016/j.sigm.2005.01.005
8. Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, et al. The complete german commission e monographs: therapeutic guide to herbal. Austin: Am Botanical Council; 1988.
9. Bardia A, Nisly NL, Zimmerman MB, Gryzlak BM, Wallace RB. Use of herbs among adults based on evidence-based indications: findings from the National Health Interview Survey. *Mayo Clin Proc*. 2007;82(5):561-6. doi: 10.4065/82.5.561
10. Ang-Lee MK, Moss J, Yuan C-S. Herbal medicines and perioperative care. *JAMA*. 2001;286(2):208-16. doi: 10.1001/jama.286.2.208
11. Saw JT, Bahari MB, Ang HH, Lim YH. Potential drug-herb interaction with antiplatelet/anticoagulant drugs. *Complement Ther Clin Pract*. 2006;12(4):236-41. doi: 10.1016/j.ctcp.2006.06.002
12. Nizarali N, Rafique S. Dental management of patients with drug-related acquired bleeding disorders. *Dent Update*. 2013;40(9):711-2.
13. Borrelli F, Capasso R, Izzo AA. Garlic (*Allium sativum* L.): adverse effects and drug interactions in humans. *Mol Nutr Food Res*. 2007;51(11):1386-97. doi: 10.1002/mnfr.200700072
14. Heck AM, Dewitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *Am J Health Syst Pharm*. 2000;57(13):1221-7
15. Little JW. Complementary and alternative medicine: impact on dentistry. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2004;98(2):137-45. doi: 10.1016/j.tripleo.2004.05.011
16. Teng CM, Hsueh CM, Chang YL, Ko FN, Lee SS, Liu KCS. Antiplatelet effects of some aporphine and phenanthrene alkaloids in rabbits and man. *J Pharm Pharmacol*. 1997;49(7):706-11.
17. Lambert JP, Cormier J. Potential interaction between warfarin and boldo fenugreek. *Pharmacotherapy*. 2001;21(4):509-12. doi: 10.1592/phco.21.5.509.34492
18. Nicoletti MA, Oliveira-Júnior MA, Bertasso CC, Caporossi PY, Tavares APL. Principais interações no uso de medicamentos fitoterápicos. *Infarma*. 2007;19(1/2):32-40.
19. Abebe W. Herbal medication: potential for adverse interactions with analgesic drugs. *J Clin Pharm Ther*. 2002;27(6):391-401. doi: 10.1046/j.1365-2710.2002.00444.x
20. Segal R, Pilote L. Warfarin interaction with matricaria chamomilla. *CMAJ*. 2006;174(9):1281-2. doi: 10.1503/cmaj.051191
21. Ulbricht C, Tiffany N, Boon H, Ulbricht C, Basch E, Bent S, et al. Horse chestnut: a multidisciplinary clinical review. *J Herb Pharmacother*. 2002;2(1):71-85
22. Koch E. Inhibition of platelet activating factor (PAF)-induced aggregation of human thrombocytes by ginkgolides: considerations on possible bleeding complications after oral intake of Ginkgo biloba extracts. *Phytomedicine*. 2005;12(1-2):10-6. doi: 10.1016/j.phymed.2004.02.002
23. Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of Ginkgo biloba extract. *N Engl J Med*. 1997;336(15):1108. doi: 10.1056/NEJM199704103361518
24. Meisel C, John A, Roots I. Fatal intracerebral mass bleeding associated with Ginkgo biloba and ibuprofen. *Atherosclerosis*. 2003;167(2):367. doi: 10.1016/S0021-9150(03)00015-7
25. Janetzky K, Morreale AP. Probable interaction between warfarin and ginseng. *Am J Health Syst Pharm*. 1997 Mar 15;54(6):692-3.
26. Jiang X, Williams KM, Liauw WS, Ammit AJ, Roufogalis BD, Duke CC, et al. Effect of St John's wort and ginseng on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. *Br J Clin Pharmacol*. 2004;57(5):592-9. doi: 10.1111/j.1365-2125.2003.02051.x
27. Yuan CS, Wei G, Dey L, Karrison T, Nahlik L, Maleckar S, et al. Brief communication: American ginseng reduces warfarin's effect in healthy patients: a randomized, controlled trial *Ann Intern Med*. 2004;141(1):23-7.

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