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Message: from the President of BioNatural Healing College (BNHC)



Greetings!

First and foremost, I am extremely thankful to Almighty God for granting me this opportunity to present the BioNatural Healing College (BNHC), BNHC E-Magazine to our dear readers. Also, I would like to thank you all, especially those that are the dear readers that send us their valuable feedback and support. The information in this magazine is solely for educational purposes.

We hope this BNHC- E-Magazine will be useful to you based on the contribution and dedication of many other respected researchers and colleagues around the globe. Thanking and wishing you all have the best health and prosperous life.

Best regards,

Dr. Nadir Sidiqi Ph.D.



BioNatural Healing College

BioNatural Healing College Hope you and your loved ones are staying healthy and safe during this pandemic (COVID-19). What we need to do especially during this uncertain time as follows:

1. Vaccination, Sanitation and Isolation from Social Interaction.
2. Positive Attitude will Increase the Power of Mind and Immune System.
3. Healthy Diet and Drink Plenty of Water (Honey with green tea, vitamin D₃, vitamin C), Get Enough Sleep.
4. Exercise (any type of physical activity for 30 minutes daily).
5. A Lot of Prayer to Almighty God (be patient, calm).

May Almighty God bless, guide us all (Humanity) and grant us the ability to find a cure for the elimination of COVID-19.

Understanding: Drug- Herb-Vitamin Interactions

By: Dr. Nadir Sidiqi Ph.D.

Introduction

The demand for natural and herbal supplements is currently a high health concerns issue among the public because many herbal remedies are familiar and are used by the general public. However, many people have the misconception that a natural substance is always naturally safe and can be used as a part of natural medicine; this is a wrong perception because that leads many users to herbs, vitamins, and supplements such as prescription and nonprescription medicines. As a result of that combination usage of drug-herb and vitamin unaware act for possible interaction can occur.

For instance, plants can be both useful and harmful, and even poisonous, however, everything depends on preparation and dose. It is highly important to understand that toxicity can arise for various reasons, but here is to consider two main reasons: (1) Endogenous toxicity of herbal or food products due to their chemical composition. (2) Exogenous toxicity caused by external agents such as microbial contamination, pesticide residues, and the presence of adulterants or contaminants¹. According to the book “A-Z Guide to Drug-Herb-Vitamin Interactions: Edited by Dr. Alan R. Gaby and the HealthNotes Team (2006)”. The authors of the above book stated that an herb or supplement causes a negative reaction and becomes highly publicized by the media, which then warns people against the substance in question, rather than educating them about specific risks and safe usage. Furthermore, while people interested in natural remedies often don’t know to ask their healthcare providers about interactions, those who do may find that practitioners don’t know how to access reliable information.

It's important to note that the other types of interactions that are not included in the above book and the authors bring our attention such as Side effects that may be caused by a drug only (Over counter drug package insert for this information), Interactions between two or more drugs, Interactions between alcohol and specific nutrients, and Interactions between drugs and water (e.g. drugs inducing dehydration)².

Understanding interactions and depletions: The human body functions because numerous reactions are constantly taking place inside the body. For instance, a person having breakfast, lunch, dinner, drinking (water), medications, and herbal supplements; all of these influence those reactions. The concept of interaction refers to the possibility that when two (or more) substances are given concurrently, one substance may interact with another, or alter its bioavailability or clinical action. The net result may be increased or a decrease in the effectiveness of one or both substances. It is important to understand that interactions may impact positive effects (achieving better therapeutic effects at a lower dosage) or negative results (creating unwanted side effects or adverse reactions). Most of the possible interactions may be classified into two major categories: Pharmacokinetic and pharmacodynamic^{3,4,5}.

Pharmacokinetic interactions: Can be defined as the study of the time course of drug absorption, distribution, metabolism, and excretion. Clinical pharmacokinetics is the application of pharmacokinetic principles to the safe and effective therapeutic management of drugs in an individual patient⁶.

Pharmacodynamic interactions: Refers to the relationship between drug concentration at the site of action and the resulting effect, including the time course and intensity of therapeutic and adverse effects. The effects of a drug present at the site of action are determined by that drug's binding with a receptor⁷. The human body in both situations either pharmacokinetic or pharmacodynamic interactions is primarily using drugs to treat illness. Therefore, drugs are designed by the manufacturer with the intention to help correct the body's temporary health problems caused by illness or genetic makeup. Drugs' mode of action in the body is various, when the body is not working properly the drug mode of action often replaces a chemical that is missing, blocks an unwanted reaction, or enhances the desired reaction. Therefore, in the process, a drug may also cause the body to lose nutrients or need more important nutrients, such as potassium, sodium, calcium, or some of the vitamins⁸. For instance, taking an herb or nutrient with a drug at the same time may cause a harmful reaction, however, in some situations an herb or nutrient might actually improve the action of a drug. When taking herbs or nutrients at the same time along a drug, consequently, might reduce the amount of medication absorbed into the body, reducing its effectiveness.

It would be wise by taking the drug and the herb or nutrient at different times. All drugs have side effects with the potential to cause unwanted symptoms or side effects. As the authors of the A-Z Guide to Drug-Herb-Vitamin Interaction indicate that some herbs or nutrients when taken with a drug, might help to prevent the side effects or make them less severe. In addition, depletion happens when a drug causes the body to lose a nutrient. The drug might also interfere with the nutrient's absorption. For example, the diuretic drug Furosemide causes the body to lose potassium, so people taking Furosemide might need to supplement with potassium to avoid unwanted problems such as muscle cramps, fatigue, or heart rhythm disturbances⁹. The rest of this study will focus on a case study based on clinical evidence according to Angelo Izzo and other researchers "Interactions between Herbs and Conventional Drugs: Overview of the Clinical Data (2012)"¹⁰.

Interactions between herbs and drugs: It is important to shed some light on the complexity of herbs and drugs interactions and also a mistake that many people don't understand regarding herb-to-drug interactions according to the clinical case study as follows:

Aloe vera (*Aloe barbadensis*): Historically aloe vera record goes back 6,000 years to early Egypt, where the plant was depicted on stone carvings. Known as the “plant of immortality” aloe vera was presented as a burial gift to deceased Pharaohs¹¹.



Courtesy: Steven Foster Source: <https://nccih.nih.gov/health/aloevera>

Medicinal uses: Aloe vera (Family: *Liliaceae*) is used in western countries as a laxative (*A. vera latex*, which contains anthraquinones) and for dermatologic conditions (*A. vera gel*, containing mainly mucilages).^{12, 13} In traditional Chinese medicine, *A. vera* is mainly used for inflammatory conditions, diabetes, and hyperlipidaemia¹⁴.

Black cohosh (*Cimicifuga racemosa*: Family: *Ranunculaceae*): Black cohosh is a member of the buttercup family. Native to North America.

Medicinal uses: Black cohosh has a history of usage for rheumatism (arthritis and muscle pain). Mostly used as rhizome and roots to treat symptoms of menopause as well.^{16, 17} It has been associated with serious safety concerns, such as hepatotoxicity, which urgently requires further investigation.^{18, 19}

Black cohosh and drug interactions: The effect of black cohosh extract on the activity of human CYP (the Cytochrome P450 isoenzymes CYPs are a superfamily of haemoprotein enzymes found on the membrane of the endoplasmic reticulum) enzymes as well as on P-glycoprotein has been evaluated in a number of clinical trials^{20, 21} using different probe drugs, including caffeine, midazolam, chlorzoxazone, debrisoquine, and digoxin. The results suggest that black cohosh is unlikely to affect the pharmacokinetics of conventional drugs that are metabolized by CYP1A2, CYP3A4, CYP2E1, and CYP2D6 or are substrates of P-glycoprotein. In addition, seven different brands of commercial black cohosh products were found not to affect human CYP using an in vitro liver microsomal technique²². It seems that black cohosh only has minor risks in patients undergoing conventional pharmacotherapy.



Courtesy: Steven Foster Source: <https://nccih.nih.gov/health/blackcohosh>

Cat's claw (*Uncaria tomentosa*, Family: *Rubiaceae*): Grows wild in many part of the world, especially Central and South America, particularly in the Amazon rainforest.

Medicinal uses: Cat's claw has effective immunostimulant and antiviral effects; it has been used for conditions, such as rheumatoid arthritis and AIDS²³.

Cat's claw and drug interactions: Cat's claw has been shown to increase the plasma concentration of the protease inhibitors atazanavir, ritonavir, and saquinavir²⁴. In vitro, a cat's claw has been shown to inhibit CYP3A4, which is responsible for the metabolism of the protease inhibitors. However, no human data on the possible modulation of CYP enzymes by cat's claw has been provided as of the dated 2012 reported by Angelo Izzo²⁵.

Chamomile (*Matricaria recutita*, Family: *Asteraceae*): Two types of chamomile have been used for health conditions: German chamomile and Roman chamomile²⁶.

Medicinal uses: Chamomile is used both externally (for skin and mucous membrane inflammations) and internally (for the treatment of gastrointestinal spasms and inflammatory disease of the gastrointestinal tract.^{27, 28}

Chamomile and drug interactions: Chamomile contains coumarins which can be found in many plants. Some, but not all coumarin compounds may exert an anticoagulant effect²⁹. A case of the rectus sheath and retroperitoneal haematomas were reported in a patient under warfarin therapy³⁰. Researchers believed, but have not proved, that the coumarin constituents of chamomile may have worked synergistically or additively with warfarin, resulting in over-anticoagulation.



Cat's claw

www.auntiedogmasgardenspot.wordpress.com

<https://nccih.nih.gov/health/chamomile/atagance.htm>

Cranberry (*Vaccinium macrocarpon*, Family: *Ericaceae*): Cranberries are the fruit of a native plant of North America³¹.

Medicinal uses: Historically, cranberry fruits and leaves were used for a variety of problems, such as wounds, urinary disorders, diarrhea, diabetes, stomach ailments, and liver problems. More recently has been a natural remedy for urinary tract infection or *Helicobacter pylori* (*H. pylori*) infection that can lead to stomach ulcers or to prevent dental plaque³².

Cranberry and drug interactions: According to multiple study cases (including 2 cases of fatal interaction) as the report stated increased international normalized ratio which is an standard test for prothrombin PT (INR: is a standardized number that's figured out in the lab. If you take blood thinners, also called anti-clotting medicines or anticoagulants, it's especially important to check your INR. The INR is figured out using the results of the prothrombin time (PT) test. This measures the time it takes for your blood to clot as defined by the University of Rochester Medical Center) and haemorrhage,^{33,34} serious concerns have been raised regarding a possible interaction with the anticoagulant warfarin. However, the report also indicates that these warnings may possibly be attributed to misleading conclusions³⁵. With the exception of one study, which showed that capsules containing concentrated cranberry juice increased the area under the INR-time curve of warfarin by 30%³⁶, a number of clinical trials have consistently shown that cranberry juice, even administered at high doses, did not cause any clinically relevant changes in warfarin pharmacokinetics and pharmacodynamics.^{37, 38} Clinical evidence indicates the lack of interaction between cranberry juice and CYP isoenzymes (e.g. CYP2C9, CYP1A2 and CYP3A4)^{39, 40} necessary for warfarin metabolism.⁴¹ Finally, a clinical trial found that pomelo juice, but not cranberry juice, affected the pharmacokinetics of cyclosporine (CYP3A4 and P-glycoprotein substrate) in humans.⁴²



Courtesy Steven Foster Source: <https://nccih.nih.gov/health/cranberry>

Danshen (*Salvia miltiorrhiza*, Family: *Lamiaceae*): Native to China and Japan also known as Chinese salvia or red salvia.

Medicinal uses: Danshen is widely used in traditional Chinese medicine to prevent and treat cardiovascular conditions such as acute ischemic stroke and myocardial infection.^{43,44}

Danshen and drug interactions: Danshen can affect haemostasis in several ways, including inhibition of platelet aggregation. Researchers have highlighted the possibility of interactions between warfarin and danshen, as a result in an increased anticoagulant effect.^{45, 46} A pharmacokinetic mechanism seems unlikely since danshen has been shown to induce intestinal CYP3A4 in 14 healthy volunteers.⁴⁷

Dong quai (*Angelica sinensis*, Family: *Apiaceae*): Other *Angelica* species are in Southeast Asia such as *Angelica acutiloba*, which is predominantly found in Japan, and *Angelica gigas*, which is mainly found in Korea. These three species are similar; however, the chemicals they contain are different⁴⁸.

Medicinal uses: Dong quai is one of the most popular traditional Chinese medicines. Preparations from its roots are used mainly for dysmenorrhoea, amenorrhoea, or excessive menstrual flow.⁴⁹

Dong quai and drug interactions: The mode of action of dong quai is due to the presence of a number of chemical constituents especially coumarins⁵⁰, which may have anticoagulant actions⁵¹. Two studies suggest that over anticoagulation following co-administration of warfarin and dong quai.^{52, 53}



Danshen Sources: <http://consciouslifeneeds.com/> Dong quai:
<http://medicinalherbinfo.org/herbs/DongQuai.htm>

Echinacea (*Echinacea spp*, Family: *Asteraceae*): Native to the

United States and southern Canada with having nine known species.

Medicinal uses: Echinacea has been used traditionally for colds, flu, and other infections, to improve the immune system and fight infection⁵⁴.

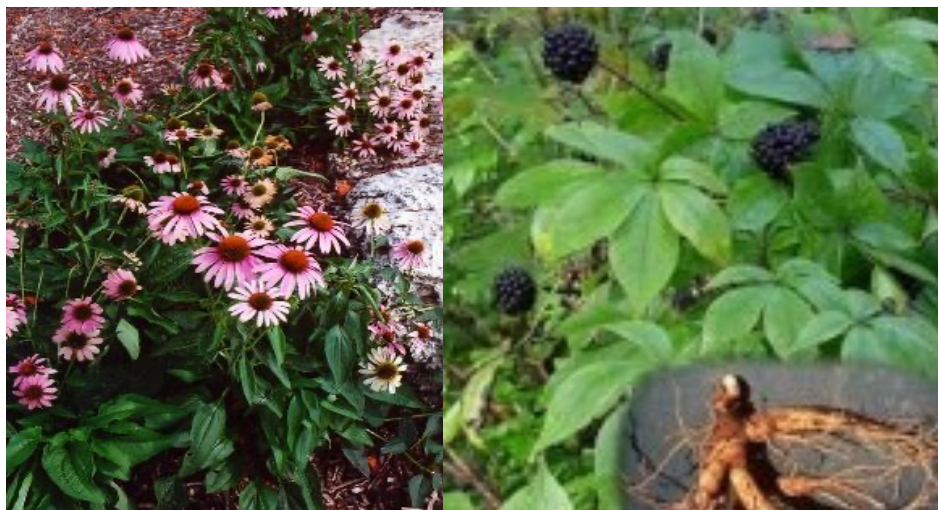
Echinacea and drug interactions: As of 2012 report by Angelo Izzo has not shown verifiable reports of drug-to-herb interaction with any Echinacea species according to the review “Interactions between Herbs and Conventional Drugs: Overview of the Clinical Data”. According to studies, Echinacea did not change the pharmacokinetics of digoxin, a P-glycoprotein substrate,⁵⁵ nor did it alter the pharmacokinetics of chlorzoxazone (CYP2E1 probe),⁵⁶ debrisoquine (CYP2D6 probe),^{57, 58} dextromethorphan (CYP2D6 probe),⁵⁹ or tolbutamide (CYP2C9 probe).⁶⁰ Another studies have found that Echinacea affects caffeine (CYP1A2 probe) and midazolam (CYP3A4 probe) pharmacokinetics; however, this has not been confirmed by other clinical trials.^{61, 62}

A recent clinical trial showed that *E. purpurea* root extract did not affect the overall darunavir or ritonavir (a combination of protease inhibitors) pharmacokinetics in HIV patients.⁶³ Protease inhibitors are mainly metabolized by CYP3A4 and are P-glycoprotein substrates⁶⁴.

Eleuthero (*Eleutherococcus senticosus* Family: *Araliaceae*): Native to eastern Asia and also known as Siberian ginseng, and also Asian ginseng (*Panax ginseng*) belong to the same family.

Medicinal uses: Both Asian ginseng and Eleuthero have the capacity to promote health and relieve fatigue and also remedy during convalescence⁶⁵.

Eleuthero and drug interactions: Eleuthero, at generally recommended over-the-counter dose, is unlikely to alter the disposition of co-administered medications primarily metabolized by CYP2D6 or CYP3A4.⁶⁶ A study indicates that increased levels of digoxin have been associated with ingestion of eleuthero⁶⁷. According to the report the patient was asymptomatic for digoxin toxicity despite high plasma levels of the cardiotonic drug. Since eleuthero contains glycosides with structural similarities to digoxin that interfere with digoxin assays, this is not a real clinical herb-to-drug interaction, but rather represents an artifact of digoxin assays.⁶⁸



Echinacea Sources: <http://medicinalherbinfo.org/herbs/Echinacea.html>

Eleuthero <http://www.maisonterre.net/eleuthero-root/>

Garlic (*Allium sativum* L., Family: *Alliaceae*): Garlic has been used by humans throughout history, and garlic is native to central Asia⁶⁹.

Medicinal uses: Garlic has been used as a food and medicine for thousands of years to treat many diseases such as colds, flu, coughs, ringworm (fungal infections), fever, a digestive disorder. Recently, garlic is used in modern science indicates that taking garlic can slightly lower blood cholesterol levels; studies have suggested in the prevention of heart diseases or stroke, slightly lower blood pressure, regular garlic consumption lowers the risk of certain cancers as reported by NCCIH⁷⁰.

Garlic and drug interactions: Garlic may thin the blood. It should be discontinued seven days before surgery and should be taken cautiously if taking anticoagulant medications such as warfarin (Coumadin) and clopidogrel (Plavix). In addition, garlic might decrease the effectiveness of some medications used for HIV/AIDS including nevirapine (Viramune), delavirdine (Rescriptor), and Efavirenz (Sustiva). Taking garlic along with saquinavir (Fortovase, Invirase) might decrease the effectiveness of this drug as pointed out by Dr. Weil⁷¹.

Ginger (*Zingiber officinale*, Family: *Zingiberaceae*): Ginger has a long history of use as a culinary spice as well as medicine that can be found in ancient Arabic, Chinese, Greek, and Indian writings.

Medicinal uses: Ginger is well known in traditional medicine as an anti-inflammatory agent, nausea reliever, and digestive aid. For instance, the use of ginger ale for easing an upset stomach relieves.

Ginger and drug interactions: Ginger may act as a blood thinner, so use caution if a person is currently taking anticoagulants⁷².



Garlic Sources: Courtesy Steven Foster <https://nccih.nih.gov/health/garlic>
<https://nccih.nih.gov/health/ginger>

So, for the partial names of the herbs and drugs interactions that have been mentioned, it would be useful to better understand these complex herb-drug-vitamin interactions. It is better to mention a few more herb names instead of a description of each one of them: For instance, Ginkgo (*Ginkgo biloba*), Ginseng (Korean Ginseng, *Panax ginseng*), Ginseng (American Ginseng, *Panax quinquefolius*), Goldenseal (*Hydrastis Canadensis*), Green Tea (*Camellia sinensis*), Kava (*Piper methysticum*), Licorice (*Glycyrrhiza glabra*), Milk Thistle (*Silybum marianum*), Peppermint (*Mentha piperita*), Red Yeast Rice, Saw Palmeto (*Serenoa repens*), Schisandra chinensis, Schisandra sphenanthera, Soy (*Glycine max*), St. John's Wort (*Hypericum perforatum*), and Valerian (*Valeriana officinalis*)⁷³.

Herbal and dietary supplement- drug interactions: According to the National Center for Complimentary and Alternative Medicine (NCCAM), a dietary supplement can be a vitamin, a mineral, an herb or other botanical, an amino acid, or other such substances or their constituents.

These supplements have demonstrated pharmacologic action used to produce therapeutic results.⁷⁴ Even supplements that do not have a documented pharmacologic action can affect the absorption, metabolism, and disposition of other drugs as pointed out by the authors of publication “Herbal and Dietary Supplement- Drug Interactions in Patients with Chronic Illnesses (2008)⁷⁵”. The most common cases that have been reported such as asthma, insomnia, depression, chronic gastrointestinal disorders, pain, memory problems, and menopausal symptoms are the medical conditions for supplements are most commonly used.^{76.77} A study indicates that patients at high risk for interactions, such as those with seizure disorders, cardiac arrhythmia, or congestive heart failure, often report dietary supplement use⁷⁸.

These patients tend to take more prescription medications, especially medications with a narrow therapeutic index. However, interactions in the case of dietary supplements can be of two types: Pharmacodynamic interactions occur when the intrinsic action of a dietary supplement augments or antagonizes the activity of another drug. Pharmacokinetic interactions result from changes in metabolism, excretion, or (infrequently) absorption or protein binding of the active aspect of the dietary supplement or the drug, resulting in more pronounced or diminished pharmacologic activity⁷⁹. The evidence-based studies to support dietary supplement-drug interactions are similar to drug-drug interactions and vary widely. There is a gap, due to incomplete knowledge of interactions based on animal studies, case reports, case series, historical contraindication, and many recommendations regarding dietary supplement-drug interactions are based on a guess rather than clinical trial⁸⁰.

Many drugs can cause nutritional deficiencies, for instance, antacids deplete calcium; aspirin depletes vitamin C and folic acid; diuretics deplete minerals (especially calcium, magnesium, potassium, and zinc); some cholesterol-lowering drugs interfere with the absorption of fat-soluble vitamins such as A, D, and E; corticosteroids such as prednisone deplete vitamin D, potassium and some of the B vitamins. In addition, some lowering cholesterol-lowering drugs deplete coenzyme Q10 and vitamin E; and conventional hormones replacement therapy and birth control with progestins deplete magnesium, the B vitamins, and folic acid according to the authors (Mindell and Hopkins) of the “Book: Prescription Alternatives (2009)⁸¹”.

Furthermore, alcohol is not just a drink for pleasure but rather a life-threatening drug and has effects on the body especially when alcohol is drunk with any drugs which will cause harmful interactions. For instance, acetaminophen may cause liver damage, aspirin can cause stomach bleeding, SSRI antidepressants can increase effects of alcohol, barbiturates can cause extreme sedation, and bupropion increased risk of seizures and don't assume it does not interact for any drug as pointed out by the above authors.

Conclusion: Understanding the interactions of drug-herb-vitamin is a very important issue in the health care systems. It is important to inform the doctor if you are taking any type of medicinal herbs or natural supplement before his or her doctor prescribes medications. It is necessary to avoid the use of unnecessary drugs and also mix taking with medicinal herbs for the possibility of interactions, resulting in health problems. Furthermore, research is needed for many other types of drug and herbs interaction which are not been experimented with yet and also requires experiments within the various herb and herb interactions that may occur themselves.

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