PHG 322

PHG 322 Practical course

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Lab# 4 Tutorial

Herbs-Drugs Interaction

Pharmacognosy
Department

Herb	Drug	Interacting Rate	Interaction
Garlic	**Antiplatelet/Anticoagulants drugs** e.g. **aspirin**, **clopidogrel** (Plavix), **dalteparin** (Fragmin), **enoxaparin** (Lovenox), **heparin**, i**ndomethacin** (Indocin), **ticlopidine** (Ticlid), **warfarin** (Coumadin), and others.	**Moderate** Do not take this combination	Garlic might enhance the effects of warfarin (Coumadin) as measured by the International Normalized Ratio (INR). Theoretically, garlic might also enhance the effects and adverse effects of other anticoagulant and antiplatelet drugs.
Senna	**Digoxine**	**Moderate** Be cautious with this combination	Theoretically, overuse/abuse of this product increases the risk of adverse effects of cardiac glycoside drugs by depleting potassium
	Warfarin	**Moderate** Be cautious with this combination.	Senna has stimulant laxative effects. In some people senna can cause diarrhea. Diarrhea can increase the effects of warfarin, increase international normalized ratio (INR), and increase the risk of bleeding. In one report, excessive use of senna for 3 weeks resulted in diarrhea, bloody stools, and an elevated INR of 11.9. Advise patients who take warfarin not to take excessive amounts of senna.
Echinacea	Immunosuppressant drugs include **azathioprine** (Imuran), **basiliximab** (Simulect), **cyclosporine** (Neoral), **Sandimmune,** **daclizumab** (Zenapax), **sirolimus** (Rapamune), **prednisone** (Deltasone,	**Moderate** Be cautious with this combination	Theoretically, echinacea may interfere with immunosuppressant therapy because of its immuno-stimulating activity.

	Orasone), and **other corticosteroids** (glucocorticoids)		
German Chamomile	**Tamoxifen** (Nolvadex)	**Moderate** Be cautious with this combination.	Theoretically, large doses of German chamomile might interfere with tamoxifen because of its potential estrogenic effects
	Warfarin	**Moderate** Be cautious with this combination	Taking German chamomile and warfarin together might increase the effects of warfarin and increase the risk of bleeding.
	Contraceptive Drugs (e.g. Microgynon 30**)**	**Moderate** Be cautious with this combination.	
Valerian roots + Hops extract	**CNS Depressant** Some CNS depressants are: **benzodiazepines**, **pentobarbital** (Nembutal), **phenobarbital** (Luminal), **secobarbital** (Seconal), **thiopental** (Pentothal), **fentanyl** (Duragesic, Sublimaze), **morphine**, **propofol** (Diprivan), and others.	**Major** Do not take this combination	Theoretically valerian and hops, concomitant use of valerian and drugs with sedative and anesthetic properties may cause additive therapeutic and adverse effects
Soya Extraction	**Monoamine oxidase inhibitors**		Fermented soy products such as tofu and soy sauce contain tyramine. Tyramine is an amino acid that is involved in blood pressure regulation. Tyramine is metabolized by monoamine oxidase. MAOIs decrease the breakdown of tyramine. Consuming more than 6 mg of tyramine while taking a MAOI can increase the risk of hypertensive crisis. The amount of tyramine in fermented soy products is usually relatively small, often less than 0.6 mg per serving; however, there can be significant variation depending on the specific product used, storage conditions, and length of storage. Storing one

Cont' Soya Extraction			brand of tofu for a week can increase tyramine content from 0.23 mg to 4.8 mg per serving. Advise patients taking MAOIs to avoid fermented soy products that contain high amounts of tyramine. Some MAOIs include phenelzine (Nardil), tranylcypromine (Parnate), and others.
	Antibiotics	**Moderate** Be cautious with this combination.	Antibiotics may decrease the action of isoflavones in soy, because intestinal bacteria are responsible in part for converting the isoflavones into their active forms. Antibiotics may decrease the ability of intestinal bacteria to convert the isoflavones
	Tamoxifen (Nolvadex)	**Moderate** Be cautious with this combination.	There is concern that soy might interfere with tamoxifen due to the estrogenic effects of soy isoflavones. Preliminary evidence suggests that soy isoflavones genistein and daidzen can antagonize the antitumor effects of tamoxifen under some circumstances; however, soy isoflavones might have different effects when used at different doses. A relatively low in vitro concentration of soy isoflavones such as 1 microM/L seems to interfere with tamoxifen. High in vitro concentrations such as those >10 microM/L might actually enhance tamoxifen effects. People on a high-soy diet have soy isoflavones levels ranging from 0.1-6 microM/L. Until more is known, advise patients taking tamoxifen to avoid therapeutic use of soy products.
	Warfarin	**Moderate** Be cautious with this combination	Soy milk has been reported to decrease the international normalized ratio (INR) in a patient taking warfarin. The mechanism of this interaction is not known. Soy may also inhibit platelet aggregation . Dosing adjustments for warfarin may be necessary.
St. John's wort	**Contraceptive Drugs (**e.g. Microgynon 30**)**	**Major** Do not take this combination	St. John's wort can decrease norethindrone and ethinyl estradiol levels by 13% to 15%, resulting in breakthrough bleeding, irregular menstrual bleeding, or unplanned pregnancy. Bleeding irregularities usually occur within a week of starting St. John's wort and regular cycles usually return when St. John's wort is discontinued. Unplanned pregnancy has occurred with concurrent use of oral contraceptives and St. John's wort extract. St. John's wort is thought to induce the cytochrome P450 1A2 (CYP1A2), 2C9 (CYP2C9), and 3A4 (CYP3A4) enzymes, which are responsible for metabolism of progestins and estrogens in contraceptives. Women taking St. John's wort and oral contraceptives concurrently should use an additional or alternative form of birth control.
	Warfarin	**Major** Do not take this combination	St. John's wort can decrease the therapeutic effects of warfarin. Taking St. John's wort significantly increases clearance of warfarin, including both the R-isomer and S-isomer of warfarin. This suggests that St. John's wort induces CYP1A2 and CYP3A4, which metabolize R-warfarin and CYP2C9,

Cont' St. John's wor	**Warfarin**		which metabolizes S-warfarin. St. John's wort can also significantly decrease International Normalized Ratio (INR) in people taking warfarin. In addition, warfarin physically interacts with hypericin and pseudohypericin, active constituents of St. John's wort. When the dried extract is mixed with warfarin in an aqueous medium, up to 30% of warfarin is bound to particles, reducing its absorption. Taking warfarin at the same time as St. John's wort might reduce warfarin bioavailability.
	Digoxine	**Major** Do not take this combination	Concomitant use can reduce serum levels and the therapeutic effects of digoxin, requiring dosing adjustments when St. John's wort is started or stopped. St. John's wort extract 900 mg daily can reduce serum digoxin levels by 25% after 10 days in healthy people.
	Antidepressant Drugs	**Major** Do not take this combination	Concomitant use can lead to increased adverse effects and increase the risk of serotonergic side effects, including serotonin syndrome. Although this effect has only been reported with nefazodone (Serzone), paroxetine (Paxil), and sertraline (Zoloft), it might also occur with other antidepressants. Use of St. John's wort with other antidepressants should only be done with close supervision.
Ginseng Panax	Immunosuppressant drugs include **azathioprine** (Imuran), **basiliximab** (Simulect), **cyclosporine** (Neoral), **Sandimmune, daclizumab** (Zenapax), **sirolimus** (Rapamune), **prednisone** (Deltasone, Orasone), and **other corticosteroids** (glucocorticoids)	**Moderate** Be cautious with this combination	Theoretically, concurrent use might interfere with immunosuppressive therapy. Panax ginseng might have immune system stimulating properties.
	Insuline	**Moderate** Be cautious with this combination	There is some concern that Panax ginseng might have additive hypoglycemic effects when used with insulin. Insulin dose adjustments might be necessary in patients taking Panax ginseng); use with caution.

Ginkgo	**Antiplatelet/Anticoagulants drugs** e.g. **aspirin**, **clopidogrel** (Plavix), **dalteparin** (Fragmin), **enoxaparin** (Lovenox), **heparin**, i**ndomethacin** (Indocin), **ticlopidine** (Ticlid), **warfarin** (Coumadin), and others.	**Major** Do not take this combination	Ginkgo leaf has been shown to decrease platelet aggregation and might increase the risk of bleeding when combined with antiplatelet or anticoagulant drugs. It is thought that the ginkgo constituent, ginkgolide B, displaces platelet-activating factor (PAF) from its binding sites, decreasing blood coagulation. Short-term use of ginkgo leaf might not significantly reduce platelet aggregation and blood clotting. Also, a single dose of ginkgo plus clopidogrel (Plavix) does not seem to significantly increase bleeding time. However, single doses of ginkgo plus cilostazol (Pletal) does seem to prolong bleeding time. It has been suggested that ginkgo has to be taken for at least 2-3 weeks to have a significant effect on platelet aggregation. Use ginkgo cautiously or avoid in patients who are taking antiplatelet or anticoagulant drugs.
	Ibuprofen	**Major** Do not take this combination	Gingko has antiplatelet effects and has been associated with several cases of spontaneous bleeding. Combining ginkgo with ibuprofen might have additive antiplatelet effects and increase the risk of bleeding.

Major = Do not use combination; contraindicated; strongly discourage patients from using this combination; a serious adverse outcome could occur.

Moderate = Use cautiously or avoid combination; warn patients that a significant interaction or adverse outcome could occur.

INR (International normalized ratio)

The international normalized ratio (INR), prothrombin ratio (PR) and prothrombin time (PT) are measures of the extrinsic pathway of coagulation. They are used in the measure of warfarin dosage, liver damage and vitamin K status. The reference range for prothrombin time is 7-10 seconds, the range for the INR is 0.8-1.2.

The prothrombin time is the time it takes plasma to clot after addition of tissue factor (obtained from animals). This measures the quality of the extrinsic pathway (as well as the common pathway) of coagulation.

The speed of the extrinsic pathway is very affected by levels of factor VII in the body. Factor VII has a short half-life and its synthesis requires vitamin K. Deficiencies in vitamin K, which can be caused by warfarin, liver damage, or an immature liver in newborns, result in an increased prothrombin time

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Tamoxifen

Tamoxifen is an antagonist of the estrogen receptor in breast tissue. It has been the standard endocrine (anti-estrogen) therapy for hormone-positive early breast cancer, although aromatase inhibitors have been proposed for postmenopausal women.[1]

Some breast cancer cells require estrogen to grow. Estrogen binds to and activates the estrogen receptor in these cells. Tamoxifen is metabolized into compounds that also bind to the estrogen receptor but do not activate it. Furthermore tamoxifen prevents estrogen from binding to its receptor. Hence breast cancer cell growth is blocked.

Tamoxifen was discovered by ICI Pharmaceuticals[2] (now AstraZeneca) and is sold under the trade names Nolvadex, Istubal, and Valodex. However, the drug, even before its patent expiration, was and still is widely referred to by its generic name "tamoxifen."

Fluoxetine

Fluoxetine (trade name Prozac) is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. Fluoxetine is approved for the treatment of major depression (including pediatric depression), obsessive-compulsive disorder (in both adult and pediatric populations), bulimia nervosa, anorexia nervosa, panic disorder and premenstrual dysphoric disorder.[1] Despite the availability of newer agents, it remains extremely popular. Over 22.2 million prescriptions for generic formulations of fluoxetine were filled in the United States in 2007, making it the third most prescribed antidepressant

Monoamine oxidase inhibitors (MAOIs)

Monoamine oxidase inhibitors (MAOIs)are a class of powerful antidepressant drugs prescribed for the treatment of depression. They are particularly effective in treating atypical depression, and have also shown efficacy in smoking cessation.

Due to potentially lethal dietary and drug interactions, MAOIs had been reserved as a last line of defense, used only when other classes of antidepressant drugs (for example selective serotonin reuptake inhibitors and tricyclic antidepressants) have failed.