

PRESCRIPTION DRUGS INTERACT WITH ORANGES

Many people have heard about some of the grapefruit interactions with prescription drugs, but now we are learning about orange juice and apple juice. Here are two

Allegra (fexofenadine)

- **Why shouldn't I take Allegra with fruit juices?**

"Allegra should be used as directed according to the product label. Maximum effectiveness has been demonstrated when Allegra is taken with water. Taking Allegra with fruit juice IS NOT a safety risk, but the effectiveness of the medicine may be reduced."

Source: www.allegra.com/faqs.aspx

Vyvanse (lisdexamfetamine)

Avoid taking this drug with fruit juices or vitamin C as this can cause your body to absorb less of the drug.

Professor David Bailey at the University of Western Ontario told the American Chemical Society back in 2008 that orange juice could reduce the power of some medicines. Read more:

www.dailymail.co.uk/health/article-1046915/Drinking-fruit-juice-stop-medication-working.html#ixzz1OckkbKEa

Now the research is accumulating so that the *Pharmacist's Letter* (at www.pharmacistsletter.com – subscription required) has developed a chart of six prescription drugs that have their absorption affected by more than 10% by which is the cut off for no current concerns. In the case of Allegra (fexofenadine) the effect on absorption is said to be 40%. Other prescription drugs are Teckturna (aliskiren) for blood pressure – 60%; Cipro (ciprofloxacin) a synthetic antibiotic – 40%; Tenormin (atenolol)

a beta blocker for high blood pressure – 40%; Synthroid (levothyroxine) to treat low thyroid activity – 11%; and Singulair (montelukast) for asthma – 22%.

The mechanism at work with orange juice is different than the mechanism with grapefruit that increases plasma levels through inhibiting the CYP3A4 pathway. Orange juice works through organic anion transporting peptides (OATPs). There are several OATPs now identified. OATP activity can vary because of genes. OATP works the opposite of the CYP3A4 and at the same time, along with other chemical reactions which makes it difficult to figure out what is going on. Several fruit juices inhibit OATP and the effect seems to be for about four hours. With grapefruit the effects can last days.

So avoid using grapefruit, orange or apple juice for four hours if taking one of these prescription drugs. Ask your health care provider if you have any questions.

FDA CONCERNED WITH LIQUID VITAMIN D SUPPLEMENTS

In a letter to manufacturers of liquid vitamin D supplements, FDA advised that safeguards were needed to protect from overdoses. Some medicine droppers will hold more than an infant should receive according to FDA, so FDA suggests the droppers be marked to measure 400 IU only. FDA recommends that droppers be used that can hold no more than this amount.

Also, FDA's letter stated, "Vitamin D is a generic term that is used to refer to the secosterols, ergocalciferol or Vitamin D2, and cholecalciferol or Vitamin D3 and their metabolites and analogues. Vitamin D is normally produced in the skin from a pro-vitamin using ultraviolet B (UV-B), and with

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adequate sun exposure, Vitamin D is not required in daily dietary intake. Vitamin D is the principal regulator of calcium, and is therefore important for skeletal development, bone mineralization and bone homeostasis, among other functions.”

“The Institute of Medicine’s (IOM) recommended Upper Limit (UL) for chronic Vitamin D intake for infants (children less than 1 year of age) is 25 mcg/day (1,000 IU/d), and for children age 1 year and older the recommended UL is 50 mcg/day (2,000 IU/d), based upon the specific vitamin D molecule being D3 from naturally occurring substances, such as fatty fish and fish liver oils. The UL for pregnancy and lactation is the same as for non-pregnant adults at 50 mcg/day (2000 IU/d). The UL value for adults ages 18 and older was based on a safety factor of 1.2 applied to a no adverse effect level (NOAEL) of 60 mcg/d. The lowest adverse effect level (LOAEL) in the IOM analysis was 95 mcg/d. The adverse effect used in the risk assessment was hypercalcemia, serum calcium elevated above the normal range, specified as above 2.75 mmol/liter (11 mg/dL)¹.”

“In 2008 the American Academy of Pediatrics (AAP) recommended that all breast-fed and partially breast-fed infants (beginning in the first 2 months after birth) consume 400 IU/day of Vitamin D. Initial symptoms of Vitamin D toxicity are usually associated with resultant high serum calcium and include weakness, fatigue, lassitude, headache, nausea, vomiting, and diarrhea; mental status changes and coma may also develop. Renal function may be affected early. Cardiac arrhythmias may also ensue. Prolonged hypercalcemia can lead to soft tissue deposition of calcium; favored areas include the kidney, resulting in other associated problems such as hypertension. Additionally, other soft tissues that are affected include blood vessels, heart, lungs, and skin. Osteomalacia may also occur. Blood chemistry changes include elevated calcium and urea, with inconsistent elevation of phosphorus. If the problem is caught early, treatment may completely reverse the symptoms. Residual sequelae may include permanent renal impairment, and osteoporosis, among others².”


Joshua M. Sharfstein, M.D., Principal Deputy Commissioner of Food and Drugs, signed the letter.

1. Institute of Medicine, National Academy of Sciences, *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press, 1997.
2. Daniel D. Federman, M.D., Elizabeth G. Nabel, MD, eds. 2010. *ACP Medicine*. New York, NY. BC Decker Inc. ISBN 0-9703902-9-7. ISSN 1548-9345. STAT!Ref Online Electronic Medical Library.
<http://online.statref.com/document.aspx?fxid=48&docid=630>.
4/9/2010 12:41:40 PM CDT (UTC -05:00).

The letter may be downloaded at:


www.fda.gov/Food/DietarySupplements/GuidanceComplianceRegulatoryInformation/ucm215527.htm.

BIPHOSPHONATE DRUGS WORK BETTER IF VITAMIN D IS HIGHER




In a study presented at the early June 2011 meeting of the Endocrine Society in Boston, Richard Bockman, M.D., Ph.D., chief of the Endocrine Service at Hospital for Special Surgery (www.hss.edu) presented the results of a new study concluding bone building bisphosphonate drugs work much better with high vitamin D levels. This report was released by Newswire.com with its embargo until June 6, 2011. The Hospital for Special Surgery posted a June 6 story that was written from information in the *LA Times*.

What the study showed was reported in the *LA Times* as, “However, in the study, 83% of people with vitamin D levels less than 20 ng/ml had a poor response to bisphosphonates compared with 77% of people with levels between 20 ng/ml and 30 ng/ml, 42% of people with levels of 30 ng/ml to 40 ng/ml and 24% of those exceeding 40 ng/ml.”



The Institute of Medicine report on vitamin D was that “levels of 20 ng/ml to 30 ng/ml are adequate for most normal, healthy adults.” Dr. Bockman’s study showed that higher levels of vitamin D caused these drugs to work seven times better.



[These bisphosphonates include: Fosamax, Boniva, Actonel and Zometa otherwise called alendronate, ibandronate, residronate, and zoledronate. The downside of these drugs was not mentioned in either the Hospital web site or the Newswire.com articles mentioned above. There are reports of jaw bone necrosis and broken femurs. Malpractice attorneys are looking for patients with these problems with TV ads. The level of calcium is also coming

increase heart problems and kidney stones in some, not all, people. Some health professionals still recommend 1000 mg to 1200 mg of dietary calcium per day taking into account that 300 mg comes from dairy (milk or fortified orange juice) and 300 mg from other non-dairy food. – Ed.]

REANALYSIS OF VITAMIN D PLUS CALCIUM IN MELANOMA

This reanalysis is important for women concerned about melanoma of the skin. Women in the Women’s Health Initiative (WHI) Study, aged 50 to 79, took vitamin D 400 IU and calcium 100 mg (elemental calcium) for a mean follow-up period of seven years. There was an annual self-report for nonmelanoma skin cancer (NMSC) and melanoma. Physicians adjudicated the melanoma reports. The WHI Study contained more than 36,000 women.

Treatment and placebo groups differed only slightly in outcomes, but in the subgroup with NMSC assigned to calcium and vitamin D had a reduced risk of melanoma over the placebo group. The hazard ratio was 0.43. The researchers recommend more studies to confirm that women with NMSC will benefit from low dose calcium and vitamin D to prevent melanoma.

Researchers were: Jean Y. Tang, Teresa Fu, David Feldman, Eleni Linos, and Marcia L. Stefanick, Stanford School of Medicine, Stanford University, Stanford, CA; Erin LeBlanc, Northwest Kaiser Center for Health Research, Portland, OR; JoAnn E. Manson, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; Mara Z. Vitolins, Wake Forest University Health Sciences,

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Winston-Salem, NC; Nathalie C. Zeitouni, Roswell Park Cancer Institute and University at Buffalo, NY; and Joseph Larson, Women's Health Initiative Clinical Coordinating Center, Fred Hutchinson Cancer Research Center, Seattle, WA.

More information may be obtained from: Jean Y. Tang, MD, PhD, Department of Dermatology, Stanford University School of Medicine, 450 Broadway, Pavilion C, MC 5334, Redwood City, CA 94305; e-mail: tangy@stanford.edu.

VITAMIN D IMPROVES PANCREAS FUNCTION

Researchers at Tufts-New England Medical Center, Boston, Massachusetts, have completed a controlled trial comparing four separate groups: 1) Vitamin D3 2000 IU daily with calcium carbonate 400 mg twice a day; 2) Vitamin D3 2000 IU daily with a calcium placebo; 3) Vitamin D3 placebo with calcium carbonate 400 mg twice a day; and 4) Vitamin D3 placebo and calcium placebo daily. Patients were all 40 years old and at risk for type 2 diabetes. The BMI mean was 32 and glycated hemoglobin (Hb A1c) 5.9%. The outcomes showed no significant difference in calcium and no calcium, but the Vitamin D3 group had improved beta-cell function and a marginal effect on attenuating the rise of Hb A1c.

A large number of patients were recruited to obtain an estimated 112, but the pool ended up being small. According to ClinicalTrials.gov, this study NTC00436475, started in September 2007 and ended in November 2009. The researchers anticipated that additional studies would be required. The lead researcher was

Anastassios G. Pittas, M.D., M.S., with Joan Mitri, Bess Dawson-Hughes, and Frank B. Hu. The study was reported in *Am J Clin Nutr* 2011 *ajcn*.011684; first published online June 29, 2011. Doi:10.3845/ajcn.111.011684.

PROBIOTICS SEIZED

On June 7, 2011 FDA announced that the agency with assistance from U. S. Marshals seized probiotic products from UAS Laboratories, Inc., of Eden Prairie, Minn. because the company markets the products as drugs.

The seized products include DDS Acidophilus, DDS Plus, Probioplus DDS, DDS Junior, and Cran-Gyn DDS, in capsule, powder, and tablet forms.

UAS Laboratories said the products could treat or prevent colds, flu, respiratory infections, urinary tract infections, yeast infections, ulcers, and high cholesterol. The company markets the products in the United States and internationally.

The FDA has warned UAS Laboratories that its products were in violation of federal law. During a March 2011 inspection, the agency discovered that the company continued to make disease claims for the products, despite previous warnings from the FDA.

The Federal Food, Drug, and Cosmetic Act restricts the use of disease claims to approved, or otherwise legally marketed, drugs. The seized products are misbranded under the Act because their labeling does not have adequate directions for use.

To make a claim that a product prevents, treats, cures, or mitigates disease, companies generally must submit a New Drug Application and demonstrate to the FDA that the product is safe and effective for the particular claim. Companies may also market an over-the-counter drug under a monograph.

UAS Laboratories' products did not conform to any existing monograph, nor did the company file or receive approval of a new drug application, and the products are not generally recognized as safe and effective for their recommended uses, according to the complaint filed in U.S. District Court for the District of Minnesota.



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