ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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# Drug-Nutrient Interactions: This Clinical Consideration Will Continue To Grow

Great progress has been made during this century in the worldwide prevention of premature death, with large decreases in childhood mortality, and resulting large increases in life expectancy. As shown in Table 1, over the last 40 years, the life expectancy of man has increased by 20 years in the less developed regions and by 10 years in the more developed regions of the world.

It is well known that as man lives longer, the incidence of chronic diseases, such as arthritis, hypertension, coronary artery disease, and adult onset diabetes will continue to increase. As the incidence of chronic disease rises, the use of long-term drug therapy to palliate or fight the effects of chronic disease will continue to escalate. It is well known that there are numerous interactions that take place between drugs and nutrients (foods, beverages, and nutritional supplements). Many nutrients substantially interfere with pharmacotherapeutics, and drugs can interfere with the goals of nutritional therapeutics. There are many routes by which drugs and nutrients interact. Knowledge of significant drug-nutrient interactions is crucial to the control of chronic disease, and maintenance of general health.

The nutritional status of an individual can have a major influence on the success of modern drug therapy. The same is true of animals. Dr. Robert Coffey has found that approximately 20% of the animals in the herds he routinely vaccinates do not develop immunity because of deficiency of copper, zinc, and manganese. When he supplements their diets with copper, zinc, and manganese amino acid chelates, the animals are then able to develop their immune systems after being vaccinated. Well nourished individuals are less likely to contract disease, and when they encounter specific diseases, their illness is less severe, and their response to drug therapy is more favorable. As the above statement on drug-nutrient interactions infers, the foods and nutritional products being consumed in conjunction with drug therapy can have a significant impact on the over-all course of therapy. Thus, the potential for interactions between drugs and nutrients is becoming an ever increasing concern.

**Table 1**
**Forty Year Trends In Mortality**

| | Life Expectancy in Years | | |
|---|---|---|---|
| | 1950-55 | 1970-75 | 1990-95 |
| China | 40.8 | 63.2 | 70.9 |
| India | 38.7 | 50.3 | 60.4 |
| Africa | 37.7 | 45.9 | 54.1 |
| All less developed areas | 42.2 | 55.2 | 63.3 |
| United Kingdom | 69.2 | 72.0 | 76.1 |
| United States | 69.0 | 71.3 | 76.4 |
| Former Soviet Union | 64.1 | 68.6 | 71.3 |
| All more developed areas | 66.0 | 71.1 | 74.9 |
| World Average | 47.5 | 58.5 | 65.5 |

*Peto, R. Nature Vol 356-16 April, 1992 pp 557-558

# Drugs and Nutrients Can Interact in Many Ways

A drug-nutrient interaction can be defined as events that result from the chemical, physiological, or pathophysiological relationships between nutrients and drugs. These interactions are significant when they diminish the intended purpose of the drug; when they impair the nutritional status of the individual; or when they cause acute or chronic drug toxicity. A drug can impair the nutritional status of an individual, with consequent profound effects upon the body's response to the drug.

*Drugs can affect the nutritional status of an individual in many ways. They can:*

1. *Stimulate appetite, and thus increase nutrient intake.*
2. *Suppress appetite, and thus decrease nutrient intake.*
3. *Effect carbohydrate metabolism*
   a. *Hypoglycemic effect*
   b. *Hyperglycemic effect*
4. *Alter lipid metabolism, causing increases or decreases in serum lipids.*
5. *Have anabolic or catabolic effects on protein metabolism.*
6. *Effect absorption, thus altering nutrient bioavailability, through altering intestinal lumen environment, mucosal morphology, interfering with other nutrient metabolism, interfering with digestive enzymes, or forming insoluble and unabsorbable complexes.*

In addition, certain nutrients are known to have a negative impact on drug therapy. In a recent study, reported in the Journal of the American Dietetic Association 95 (3): 309-315, March of 1995, patients at three health facilities were assessed for drug-nutrient interactions over the course of 6 months. These patients were being treated for various chronic disorders. They were receiving on the average between 4 and 5 different medications. The researchers concluded that chronically ill individuals who consume multiple medications are at notable risk for drug-nutrient interactions. The most commonly observed potential drug-nutrient interactions were gastrointestinal interactions affecting the drug bioavailability and the mineral status of the patients. Virtually every individual on multiple drug long term therapy incurs drug-nutrient interactions.

In the April, 1995 edition of American Family Physician, Dr. Julienne Kirk authored a review article entitled "Significant Drug-Nutrient Interactions". In this article, the tremendous negative impact that certain nutrients can have on the course of drug therapy received in depth coverage. It was stated in this article that there is much documentation concerning the ability of certain nutrients to interact with medications in the gastrointestinal tract and have a negative effect on the medication's bioavailability or activity. The absorption rates of certain medications reviewed had their bioavailabilities decreased by factors of from 40% to 80% by various food components. Many medications have narrow blood level margins between effective and non-effective concentrations. Obviously, decreases in bioavailability of the magnitude seen in this review could lead to the failure of the drug therapy. One of the most significantly mentioned types of drug-nutrient interactions is the direct chemical interaction between polyvalent cations, such as calcium or iron, and the drug, causing a complexation that either deactivates the drug or blocks its absorption.

## Nutritionally Functional Mineral Chelates May Be the Answer

In all of the research on interactions between minerals and drugs, it has been seen that the minerals are in their ionic state when they react with the drugs. Most mineral supplements are in a form that produces ionic forms of the mineral when exposed to the gastrointestinal tract's environment. Because of this, the researchers caution against the co-ingestion of any mineral containing products with medications. It should be pointed out that only the ionic forms of the minerals are known to cause this negative drug-nutrient interaction. There is no evidence to indicate that electro-chemically neutral forms of a mineral would cause any such interaction problem. Albion

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Laboratories produces nutritionally functionalmineralaminoacidchelates. Nutritionally functional mineral amino acid chelates. Nutritionally functional mineral chelates are electrochemically neutral. They do not ionize in the gastrointestinal system the way other mineral forms do. In formulating Albion's mineral chelates, the ligands have been selected that have stability constants that when properly chelated to the various minerals, will predictably allow the mineral chelates to remain intact throughout the various pH's found in the gastrointestinal system. This has been further demonstrated in simulated gastric experiments. The chelate bonds in Albion's mineral chelates do not break apart in the various pH environments of the gut.

# Iron Supplements: A Common Cause of Drug Interactions

In an article by Norman Campbell and Brian Hasinoff (Br. J. Clin. Pharmac. [1991], 31, pp. 251-255), the impact potential of iron-drug interactions was reviewed extensively. Although all polyvalent minerals have the same negative impact potential on the course of drug therapy, iron is one mineral that has been most studied. According to this report, iron-drug interactions of clinical significance may occur in many people and with a large number of different medications. Concurrent ingestion of ionic iron (from salts, such as ferrous sulfate, gluconate, fumarate, and the like), causes marked decreases in the bioavailability of a number of drugs, while at the same time decreasing the bioavailability of the ingested iron. The major mechanism of these iron-drug interactions is the formation of unabsorbable iron-drug complexes through ionized iron's ability to irreversibly complex with certain functional groups on the drug's molecular structure. Functional groups on the drugs to which ionic iron binds tightly include phenolic, catechol, carboxyl, amine, and sulphydryl groups. Table 2 contains a partial list of medications that are known to bind with iron, or have a predictable potential to bind strongly with iron.

In addition to ionic iron's ability to complex with many drugs, ionic iron can also catalyze oxidation and reduction reactions that can destroy many drugs prior to their absorption. Most drugs have two functional groups that bond to the one iron ion. Iron has a coordination number of six, which indicates that it has a strong tendency to bind six functional groups. Thus one mole of ionic iron can bind to as many as three moles of a drug. The higher the stability constant is for the iron-drug complexes, the less free drug there will be for absorption. In addition, the less soluble the iron-drug complex, the greater the decrease in absorption. In most cases, the formation of the iron-drug complex not only decreases absorption, but

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**Table 2**
**Ionic Iron Interactions**

A partial list of orally administered drugs which bind with iron:

- Acetaminophen
- Ampicillin
- Captopril
- Carbidopa
- Ciprofloxacin
- Ethambutol
- Folic Acid
- Indomethacin
- Isoprenaline
- Salicylates
- Levodopa
- Methyldopa
- Minoxidil
- Nalidixic Acid
- Norfloxacin
- Penicillamine
- Rifampicin
- Tetracycline
- Thyroxin

A partial list of orally administered drugs which have the potential to bind strongly to iron based on binding with copper or on functional groups present:

- Antazoline
- Bephenium
- Chlorpheniramine
- Cyclosporins
- Dicumarol
- Digoxin
- Diethylstilbestrol
- Diphenhydramine
- 17-Ethinylestradiol
- Furosemide
- Hexylresorcinol
- Methotrexate
- Oxazepam
- Pheniramine
- Tonzylamine

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deactivates the drug. The higher the iron cation content ingested relative to the drug, the more the overall interference.

The timing of the ingestion of iron and drug is important. The reactions between drugs and iron cations have been seen to be significant when the iron salts are ingested for up to 3 hours before or 2 hours after the ingestion of many drugs. Since many therapeutic courses of iron therapy require multiple daily doses, it is obvious that this potential negative drug-nutrient interaction is impossible to avoid, when employing iron that ionizes in the gastrointestinal tract. Iron cation studies are listed that show drug bioavailability reductions by factors ranging from 50% to as high as 88% induced by the ionic iron.

All polyvalent mineral cation forms are capable of inducing the same drug-nutrient interactions as iron. Ionic calcium is well known for its ability to decrease the bioavailability of many antibiotics. Copper and zinc have been shown to react with many drugs in the same way as iron. In a study by R.E. Polk (Antimicrob. Agents Chemother. 33, 1989), the administration of a supplement containing zinc and copper was demonstrated to decrease the bioavailability of an antibiotic by 24%. What would be the effect of administering a product that contained a complete selection of all the nutritionally required minerals in forms that ionize in the gastrointestinal system at RDA levels?

It should be remembered that all published mineral cation-drug interactions have shown marked reductions in both the drug and the mineral bioavailability. It is possible that there are many more mineral cation-drug interactions of clinical significance then those already discussed. Researchers feel that many people are receiving inadequate therapy based on these mechanisms.

## Closing Thought

Albion recognizes the need for caution when one is taking medications. The negative potential interactions between medications and nutritional factors have been clearly demonstrated. The particular negative effects of mineral cations on the course of drug therapy have been shown to be significant. It is important to follow all warnings that accompany medications. It may be wise to consider using nutritionally functional mineral chelates over other mineral forms, when one is taking supplements in conjunction with medications, but this should be discussed with a physician.

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