

## Nutrient and drug interactions in case of diabetes

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### Abstract

Diabetes is a complex condition with a variety of causes and pathophysiology. The current one target approach has not provided much clinical outcomes for the treatment of the disease and its complications. Herbal medicine has been used for the management of various diseases over centuries. Many diabetic patients are known to use herbal medicines with anti-diabetic properties in addition to their treatments, which may present both a benefit as well as potential risk to effective management of their disease.

**Keywords:** drug-nutrient interactions, antidiabetic drugs, antidiabetic herbs, pharmacokinetic interaction, pharmacodynamics interaction, bioavailability, herb – drug interactions

### Introduction

The FDA defines a drug, in part, as “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease”<sup>[1]</sup>. As per NCI, Nutrition is - The taking in and use of food and other nourishing material by the body<sup>[2]</sup>. Drug-nutrient interactions involve changes to a drug caused by a nutrient, or changes to a nutrient as a result of the drug<sup>[3]</sup>.

### Types of Nutrient-Drug interactions

1. Pharmaceutical Interactions – Drug-Nutrient interaction affects Compatibility, solubility and stability of Drugs
2. Pharmacokinetic Interactions – These interactions affect Absorption, Distribution, Metabolism and Excretion.
3. Pharmacodynamic Interactions – These interactions alter signal transductions, genetic polymorphism, Enzymes, Transporters, Receptors etc.<sup>[4]</sup>

Mechanistically, drug–nutrient interactions occur because of altered intestinal transport, altered metabolism, systemic

distribution and excretion, as well as additive or antagonistic effects<sup>[5]</sup>. Majority of Drug-Nutrition interactions alter the bioavailability of drugs.

### Examples

For example, Pioglitazone- Anti-Diabetic drug is an acidic drug with dissociation constant value (pKa) of 5.19. Caffeine – one of the nutrients increases gastric and ileac blood flow, which may have resulted in increased bioavailability of Pioglitazone<sup>[6]</sup>.

Certain interactions are useful to control and manage diabetes effectively i.e. Combination of garlic with Metformin (500mg – twice day) - typical antidiabetic remedy has shown to improve glycemic control in addition to antihyperlipidemic activity. Garlic may be a good addition in the management of patients with type-2 diabetes.<sup>[8]</sup>

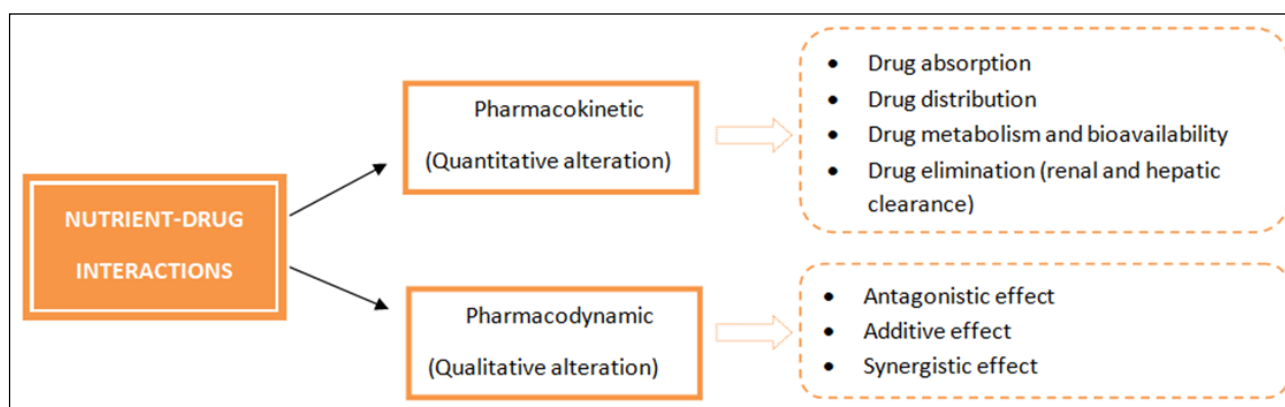


Fig 1

Repaglinide (RPG) a rapid-acting meglitinide analogue, is an oral hypoglycemic agent for patients with type 2 diabetes mellitus. The oral absorption of Repaglinide is rapid and complete but its bioavailability is low because of considerable first-pass metabolism. Quercetin (QCT) is a well-known antioxidant and antidiabetic flavonoid that has

been used as an important ingredient in many functional foods and complementary nutrient. QCT can inhibit the hepatic metabolism of RPG *in vitro* via a mixed mechanism. Furthermore, the *in vivo* systemic exposure of RPG following intravenous and oral administration in rats was significantly increased by the concurrent administration of

QCT. Based on the FDA guidelines, the magnitude of *in vivo* clinical herb–drug interactions between RPG and QCT was predicted to be a 1.03–1.54-fold increase in the AUC of RPG. These results suggest that clinically significant pharmacokinetic interactions between QCT and RPG could occur and that enhance bioavailability of Repaglinide <sup>[9]</sup>.

Ref: *Diabetol Metab Syndr* <sup>[7]</sup>

Oral hypoglycemic drugs like Avandia, Glucophage, Prandin affects folic acid and vitamin B12. Drug induced depletion occurs. Some dietary supplements have potential for interactions with specific drug class and/or cause additive blood glucose lowering effects and increase risk of hypoglycemia when used in combination. For example alfalfa, aloe vera, alpha lipoic acid, bilberry, CoQ10, chromium, garlic, ginkgo biloba, ginseng, green tea, melatonin, milk thistle, niacin, st. John's wort and vitamin K1 <sup>[10]</sup>.

The most common medications used to treat Gastroesophageal reflux disease GORD are proton pump inhibitors (PPIs) and antagonists of histamine selective H2 receptors (H2RAs), both of which independently affect vitamin B12 and magnesium status. Research indicates that co-prescribing metformin with either PPIs or H2RAs can have further deleterious effects on vitamin B12 status. Vitamin B12 deficiency related to metformin and poly pharmacy is likely to contribute to the symptoms of diabetic neuropathy. <sup>[11]</sup>

#### Side effects of drugs and other medications

**Taste and Smell Alterations:** Some drugs may alter one's ability to taste and smell certain foods. Food intake may be affected due to alteration of taste sensation, reduced acuity to taste, or undesirable after taste.

**Gastrointestinal (GI) Effects:** Some drugs can cause irritation to the digestive tract that includes stomach upset, nausea, vomiting, diarrhea, constipation, ulcers, and gastric bleeding. Some drugs may alter gastric acidity and damage mucosal surfaces leading to decreased nutrient absorption.

**Appetite Changes:** Alterations in appetite may include suppression or stimulation of hunger leading to weight loss or weight gain.

**Organ Toxicity:** Since many drugs must pass through the liver and kidney upon excretion, hepatotoxicity (liver damage) and nephrotoxicity (kidney damage) are of primary concern.

**Metabolic Effects:** Some drugs may affect blood glucose levels by stimulating the production of glucose or inhibiting its uptake. Other drugs may inhibit insulin secretion, decrease insulin sensitivity, or increase insulin clearance from the blood. This may lead to conditions known as hyperglycemia (high blood glucose), hypoglycemia (low blood glucose), or diabetes. Other medications may lead to abnormal lipid levels, causing elevated cholesterol or triglycerides <sup>[12]</sup>.

#### Benefits of minimizing drug interactions

- Medications achieve their intended effects
- Improved compliance with medications
- Less need for additional medication or higher dosages
- Fewer caloric or nutrient supplements are required
- Adverse side effects are avoided
- Optimal nutritional status is preserved
- Accidents and injuries are avoided
- Disease complications are minimized

- The cost of health care services is reduced
- There is less professional liability
- Licensing agency requirements are met

#### Food and drug interaction education

**High Priority for Food–Drug Counseling:** Certain food–drug counseling must be done before the patient is placed on the drug regimen outside the hospital setting. These are interactions that may cause potentially serious illness or problems over a short period of time.

A variety of drugs are introduced every year. Food / Nutrient and drug interactions can cause negative effects in efficacy and safety of drugs also altering nutritional status of the patient. Like drugs, foods are not tested in detail so they may interact with over the counter drugs. Clinical dietitians can take best roles to educate ordinary people and patients about the right food choices and nutraceuticals.

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