

**CHAPTER
18**

DRUG INTERACTION

¹Dr. SHAIVAD SHABEEHUL HASAN ABADI

¹Assistant Professor, School of Pharmaceutical Sciences, Apeejay
Stya University, Gurugram

²Dr. MOHAMMAD RASHID IQBAL

²Assistant Professor, School of Pharmaceutical Sciences, Apeejay
Stya University, Gurugram

Ch.Id:-ASU/NSP/EB/HOP/2022/Ch-18

DOI: <https://doi.org/10.52458/9789391842529.nsp2022.eb.asu.ch18>

INTRODUCTION

A drug interaction is a change in a drug's action or side effects caused by taking it with food, drink, supplements, or another medication. We put ourselves at risk of potentially dangerous interactions every time we take a drug with another prescription medicine, OTC medicine, food item, or herb. The likelihood of a drug-drug interaction rises as the number of drugs used increases.

The "Object Drug" is the drug whose activity is affected by the interaction, while the "Precipitant" is the agent that causes the interaction.

Drug interactions are as follows:

- Mainly unfair and unbalanced
- Rarely desirable (beneficial) for example, increasing penicillin activity when given with probenecid

Causes of Drug Interactions

There are various causes of drug interactions. For example, one drug may alter the pharmacokinetics of another drug. Alternatively, drug interactions can also be caused by competition for a single receptor or signalling pathway.

Main factors contributing to drug interactions are-

- ◆ Multiple drug therapy
- ◆ Multiple prescribers
- ◆ Drug related factors
- ◆ Multiple pharmacological effects of drug
- ◆ Poor patient compliance
- ◆ Multiple diseases / illness
- ◆ Advancing age of patient

Types of Drug Interactions

Important types of drug interactions are:

1. Drug-drug interactions
2. Drug -food interactions
3. Drug-disease interactions
4. Drug-laboratory test interactions

5. Drug-chemical interactions

The over all effect of a drug- interaction is:

- Generally quantitative – increased or decreased effect.
- Rarely qualitative – faster or slower effect.
- Precipitation of newer or increased adverse effect.

Drug Interaction Mechanisms

Drug-drug interaction in the brain: altered compliance, when one drug changes a patient's behaviour in order to alter compliance with another. For example, as symptoms improve, a depressed patient taking an antidepressant drug may become more compliant with the medication.

Outside the body, pharmaceutical drug-drug interactions. It's a physicochemical interaction that occurs when drugs are mixed with intravenous infusions, resulting in the precipitation or inactivation of active principles before they're given out. Precipitation of sodium thiopentone in an intravenous dose, for example.

Drug-drug interactions pharmacokinetics: altered concentration or effect when one drug alters the systemic concentration of another, it changes how much or how long it is present at the site of action.

Pharmacodynamic drug-drug interactions occur when interacting drugs have either additive effects (overall effect increased) or opposing effects (overall effect decreased or even cancelled out).

Pharmacodynamic Interactions

When two drugs are combined, their effects can be additive (the result is what you would expect if you added the effects of each drug separately), synergistic (combining the drugs produces a larger effect than expected), or antagonistic (the drugs have opposite effects) (combining the drugs leads to a smaller effect than expected). Because the individual effects of each drug can vary from patient to patient, there is sometimes confusion about whether drugs are synergistic or additive. Patients may benefit from a synergistic interaction, but it may also increase the risk of overdosing. During various stages of a drug's interaction with an organism, both synergy and antagonism can occur. When synergy occurs at the level of a cellular receptor, for example, this is known as agonism, and the substances involved are known as agonists. The substances involved in antagonism, on the other hand, are known as inverse agonists. The various responses of a receptor to a drug's action have led to a variety of

classifications, such as "partial agonist," "competitive agonist," and so on. These ideas are crucial in understanding the pharmacodynamics of these interactions. Pharmacodynamic interactions are influenced by changes in an organism's response to drug administration. There is a strong suspicion that there are more unknown interactions than known interactions.

Pharmacodynamic interactions can occur on:

1. Pharmacological receptors: Receptor interactions are the most easily defined, but they are also the most common. From a pharmacodynamic perspective, two drugs can be considered to be:
 - a) Homodynamic, if they act on the same receptor. They in turn can be pure agonists, partial agonists or antagonists, and
 - b) Heterodynamic competitors, if they act on distinct receptors.
2. Signal transduction mechanisms:

These are molecular processes that start after a drug interacts with a receptor. Hypoglycemia (low blood glucose) in an organism, for example, causes the release of catecholamines, which trigger compensation mechanisms and raise blood glucose levels. Catecholamines release also causes a series of symptoms, which allow the organism to recognise what is going on and act as a motivator for preventative action (eating sugars).

3. Physiological systems Antagonist:

Consider drug A, which targets a specific organ. With higher levels of physiological substance S in the body, this effect will become stronger. Consider a drug B that increases the amount of substance S by acting on another organ. If both drugs are taken at the same time, drug A may cause an adverse reaction in the body because its effect will be increased indirectly by drug B's action. The use of digoxin and furosemide at the same time is an example of this interaction. The former acts on cardiac fibres, and its effect is amplified if blood potassium (K) levels are low.. Furosemide is a diuretic that lowers arterial tension but favours the loss of K⁺. This could lead to hypokalemia (low levels of potassium in the blood), which could increase the toxicity of digoxin.

Pharmacokinetics interactions:

Differences in the absorption, transport, distribution, metabolism, or excretion of one or both drugs cause changes in their effect when compared to the expected behaviour of each drug when taken separately. These adjustments are essentially drug

concentration adjustments. Two drugs are said to be homergic if they have the same effect on the body and heterergic if they have different effects.

Absorption interactions

Prokinetic agents, for example, increase the rate at which a substance passes through the intestines. If a drug is present in the absorption zone of the digestive tract for a shorter period of time, its blood concentration will decrease. Drugs that reduce intestinal motility will have the opposite effect. When certain drugs are taken with high-fat foods, their absorption is drastically reduced. Oral anticoagulants and avocado are examples of this.

Transport and distribution interactions

Competition for plasma protein transport is the primary interaction mechanism. In these cases, the first drug binds to the plasma protein, leaving the second drug dissolved in the plasma, changing its concentration. These situations are usually not clinically relevant because the organism has mechanisms to counteract them (for example, increasing plasma clearance). However, these circumstances should be considered if there are other issues present, such as when the excretion method is affected.

Metabolism interactions:

Drug interactions are frequently caused by changes in drug metabolism. Furthermore, nuclear receptors are typically used to activate human drug-metabolizing enzymes. The enzyme system containing the cytochrome P450 oxidases is one notable system involved in metabolic drug interactions.

CYP450

Cytochrome P450 is a large family of haemoproteins (hemoproteins) known for their enzymatic activity and role in drug metabolism. CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 are the most important enzymes among the various families found in humans. The majority of enzymes are also involved in the metabolism of endogenous substances like steroids and sex hormones, which is important if these substances cause problems. Enzyme function can be stimulated (enzyme induction) or inhibited (enzyme inhibition) as a result of these interactions (enzyme inhibition).

Enzymatic inhibition

If drug A is metabolised by a cytochrome P450 enzyme and drug B inhibits or reduces the enzyme's activity, drug A will remain high in the plasma for longer because inactivation is slower.

As a result, enzymatic inhibition will boost the drug's effectiveness. This can result in a variety of negative consequences.

Enzymatic induction

If drug A is metabolised by a cytochrome P450 enzyme and drug B induces or increases the enzyme's activity, drug A concentrations in blood plasma will rapidly fall as inactivation occurs more quickly. As a result, enzymatic induction will reduce the drug's effectiveness.

Excretion Interactions

Renal excretion

The kidneys can only remove the free fraction of a drug that is dissolved in blood plasma. As a result, drugs that are tightly bound to proteins are not excreted by the kidneys unless they are metabolised and then eliminated as metabolites. Creatinine clearance is used to assess kidney function, but it is only useful when the drug is excreted in its natural state in the urine. The properties of drug excretion from the nephrons of the kidney are the same as for any other organic solute: Active secretion, reabsorption, and passive filtration. Drug secretion in the latter phase is an active process that is influenced by factors such as the saturability of the transported molecule and substrate competition. As a result, these are critical sites where drug interactions may occur.

Bile excretion

Bile excretion differs from kidney excretion in that it always involves active transport across the bile duct epithelium against a concentration gradient, which requires energy expenditure. If the drug's plasma concentrations are high, this transport system can become saturated. Drugs that have a molecular weight greater than 300 and contain both polar and lipophilic groups are mostly excreted in the bile.

CONCLUSION

Positive drug interactions can be used to your advantage. Negative interactions, on the other hand, are usually of greater interest due to their pathological significance as well as the fact that they are frequently unexpected and may even go undiagnosed. It should be possible to prevent or at least diagnose interactions by studying the conditions that favour their appearance. The following are some of the factors or conditions that predispose the appearance of interactions:

Old age

Serious diseases

Polypharmacy

Hepatic or renal diseases

Genetic factors