Multidisciplinary

Self-study CPD activity

Activity Reference Number
G1(26)

Topic
Basic Pharmacology

Article(s)
Basic Pharmacology at a glance and the use and misuse of OTCs, prescription drugs and Supplements

Part 1 is approved for **THREE (3)** ***Clinical*** Continuing Education Units (CEU's)
Part 2 is approved for **THREE (3)** ***Clinical*** Continuing Education Units (CEU's)
Part 3 is approved for **THREE (3)** ***Clinical*** Continuing Education Units (CEU's)
Part 4 is approved for **THREE (3)** ***Clinical*** Continuing Education Units (CEU's)
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Part 6 is approved for **THREE (3)** ***Clinical*** Continuing Education Units (CEU's)

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Basic pharmacological considerations

Introduction

Pharmacology is the scientific discipline concerned with the actions of drugs on living systems, and it provides the foundation for rational and effective therapeutic practice. At its core, drug action is governed by several general principles that explain how medicines produce their intended effects and why variability in response is common across individuals. The first fundamental principle is that drugs exert their effects by interacting with **specific biological targets**. These targets—receptors, enzymes, ion channels, and transport proteins—serve as the molecular sites at which drugs initiate their actions. The structure of a drug determines its affinity for these targets, and this specificity underlies both the therapeutic mechanisms and potential off-target interactions.

The second principle is that the **magnitude of a drug's effect is directly related to the concentration that reaches its site of action**. Drug concentration is not determined solely by the administered dose; instead, it is shaped by the pharmacokinetic processes of absorption, distribution, metabolism, and excretion. These processes influence how quickly a drug becomes available, how long it persists in the body, and the degree to which it accumulates at its target tissues. Consequently, understanding pharmacokinetics is essential for predicting the onset of action, therapeutic efficacy, and the need for dosage adjustments in different clinical contexts.

The third overarching principle is that **all drugs can produce both beneficial and adverse effects**. Even when acting on well-defined targets, drugs may affect multiple physiological systems, especially at higher concentrations. Variability in patient factors—such as age, genetics, comorbidities, and concomitant medication use—further contributes to differences in therapeutic and toxic responses. This duality underscores the importance of assessing the benefit–risk ratio, personalising therapy, and monitoring patients during treatment.

Together, these principles provide a conceptual framework for understanding how drugs behave in the body and why responses differ among individuals. They also form the basis for more detailed exploration of pharmaceutical preparations, pharmacokinetics, and pharmacodynamics, which collectively determine the clinical success of pharmacological interventions.

A drug taken orally passes through three phases for its action to take effect, namely:

- The pharmaceutical or dissolution phase
- The pharmacokinetic phase (absorption, distribution, metabolism and extraction)
- The pharmacodynamic phase (drug action, receptors, enzymes and hormones)

The Pharmaceutical Phase (Drug Administration and Disintegration Phase)

The **pharmaceutical phase** is the **first step** in the sequence of drug action and refers to the **processes that occur before a drug is absorbed into the body**. It encompasses the **formulation, release, and disintegration** of a drug after administration, determining *how the drug becomes available for absorption*.

This phase is most relevant to **oral dosage forms**—tablets, capsules, suspensions, and solutions—because these must physically break apart in the gastrointestinal tract before the active ingredient can be absorbed. Parenteral (e.g., IV) or gaseous drugs bypass this phase since they do not require disintegration.

1. Drug Formulation and Design

The pharmaceutical phase begins with the **physicochemical properties** of the drug and how it has been formulated. A tablet, capsule, or other dosage form contains not only the active pharmaceutical ingredient (API) but also excipients such as:

- **Binders** (help hold the tablet together)
- **Disintegrants** (help the tablet break apart)
- **Fillers**, **lubricants**, **coating agents**, etc.

How these components interact influences the **rate and extent of drug release**.

2. Disintegration of the Dosage Form

Once administered (e.g., swallowed), the dosage form enters an aqueous environment.
The first important event is **disintegration**—the tablet or capsule ruptures into smaller granules. This increases the surface area exposed to fluids, enabling the next step (dissolution).

Factors affecting disintegration include:

- Manufacturing method (compression force)
- Type and amount of disintegrants
- GI tract conditions (pH, motility, presence of food)
- Coatings (enteric coatings delay disintegration)

3. Dissolution of the Active Ingredient

After disintegration, the API must **dissolve in the gastrointestinal fluids**.
Dissolution is crucial because **only dissolved drug molecules can cross biological membranes** and be absorbed.

Dissolution rate depends on:

- Drug solubility (hydrophilic vs. lipophilic)
- Particle size (smaller dissolves faster)
- pH and temperature of GI fluids
- Presence of food, bile salts, and enzymes
- Formulation technologies (e.g., micronisation, sustained-release matrices)

Dissolution is often the rate-limiting step in drug absorption for poorly soluble drugs.

4. Bioavailability Implications

The pharmaceutical phase directly influences:

- **Onset of action**
  Faster disintegration/dissolution → faster absorption.
- **Bioavailability**
  Poor dissolution → reduced amount reaching systemic circulation.
- **Consistency of therapeutic effect**
  Well-formulated drugs provide predictable plasma concentrations.

5. Special Formulations

Some dosage forms are specifically engineered to modify the pharmaceutical phase:

- **Enteric-coated tablets** (protect drug from stomach acid; delay release)
- **Sustained/controlled-release formulations** (slow dissolution for prolonged action)
- **Immediate-release tablets** (optimised for rapid disintegration)

These products deliberately alter the rate and site of disintegration and dissolution.

Summary

The **pharmaceutical phase** is the stage in which a drug **is released from its dosage form, disintegrates, and dissolves** before being absorbed. It determines how quickly and efficiently the active ingredient becomes available for the **pharmacokinetic phase** (absorption, distribution, metabolism, and excretion). Proper formulation and dissolution characteristics are

essential to ensure consistent therapeutic outcomes.

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Pharmacokinetics and Pharmacodynamics

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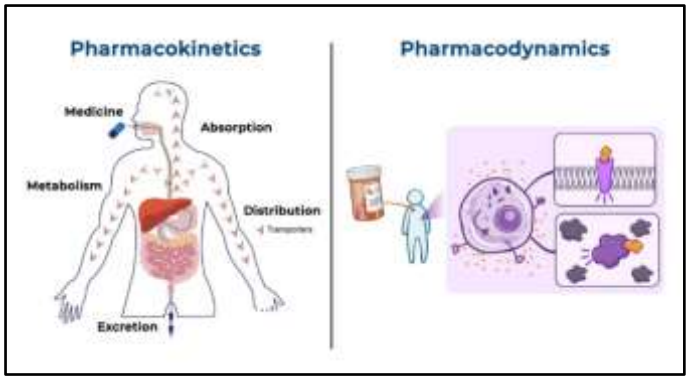

Overview

Pharmacokinetics – Examining the Interaction of Body and Drug

Pharmacokinetics is the term that describes the four stages of absorption, distribution, metabolism, and excretion of drugs. **Drugs** are medications or other substances that have a physiological effect when introduced to the body. There are four basic stages a medication goes through within the human body: absorption, distribution, metabolism, and excretion. This entire process is sometimes abbreviated **ADME**.

Absorption is the first stage of pharmacokinetics and occurs after medications enter the body and travel from the site of administration into the body's circulation. **Distribution** is the second stage of pharmacokinetics. It is the process by which medication is spread throughout the body. **Metabolism** is the third stage of pharmacokinetics and involves the breakdown of a drug molecule. **Excretion** is the final stage of pharmacokinetics and refers to the process by which the body eliminates waste. Each of these stages is described separately in the following sections of this chapter.

Research scientists who specialise in pharmacokinetics must also pay attention to another dimension of drug action within the body: time. Scientists do not have the ability to visualise where a drug is going or how long it is active. To compensate, they use mathematical models and precise measurements of blood and urine to determine where a drug goes and how much of the drug (or breakdown product) remains after the body processes it. Other indicators, such as blood levels of liver enzymes, can help predict how much of a drug is going to be absorbed.

Principles of chemistry are also applied while studying pharmacokinetics because the interactions between drugs and body molecules represent a series of chemical reactions. Understanding the chemical encounters between drugs and biological environments, such as the bloodstream and the oily surfaces of cells, is necessary to predict how much of a drug will be metabolised by the body.

Pharmacodynamics – Examining the effects of drugs in the body

Pharmacodynamics refers to the effects of drugs in the body and the mechanism of their action. As a drug travels through the bloodstream, it exhibits a unique **affinity** for a drug-receptor site, meaning how strongly it binds to the site. Drugs and receptor sites create a lock and key system (see Figure 1) that affects how drugs work and the presence of a drug in the bloodstream after it is administered. This concept is broadly termed as drug **bioavailability**.

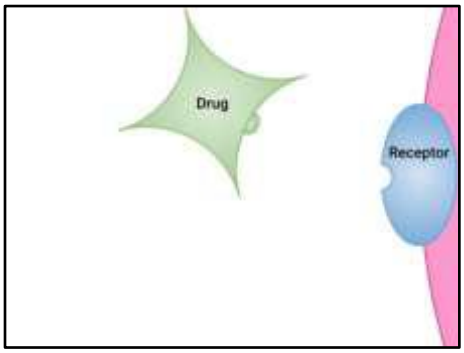

Fig 1: Pharmacodynamics: Drug and Receptor Binding

The bioavailability of drugs is an important feature that chemists and pharmaceutical scientists keep in mind when designing and packaging medicines. However, no matter how effectively a drug works in a laboratory simulation, the performance in the human body will not always produce the same results, and individualised responses to drugs have to be considered. Although many responses to medications may be anticipated, a person's unique genetic makeup may significantly impact their response to a drug. **Pharmacogenetics** is defined as the study of how people's genes affect their response to medicines.

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Pharmacokinetics and pharmacodynamics

Stages of pharmacokinetics

1. Absorption

The first stage of pharmacokinetics is known as absorption. Absorption occurs after drugs enter the body and travel from the site of administration into the body's circulation. Medications can enter the body through various routes.

1.1 Common routes to administer medications include the following examples:

- Oral (swallowing an aspirin tablet)
- Enteral (administering medication into the gastrointestinal tract via a nasogastric tube)
- Rectal (administering an acetaminophen suppository)
- Intranasal (spraying allergy medication into the nose)
- Inhalation (breathing in asthma medication from an inhaler)
- Intramuscular (injecting an influenza vaccine into the deltoid muscle)
- Subcutaneous (injecting insulin into the subcutaneous tissue in the abdomen)
- Transdermal (wearing a nicotine patch that is absorbed through the skin)
- Intravenous (administering antibiotics directly into a vein)

1.2 First-Pass Effect

When a medication is administered orally or enterally, absorption may be significantly hindered in the gastrointestinal (GI) tract. For example, when medications made of protein are introduced into the GI tract, they can be quickly deactivated by enzymes as they pass through the stomach and duodenum. If some of the drug is absorbed from the intestine into the bloodstream, part of the

absorbed portion may be broken down by liver enzymes, whereas the remaining part escapes into the general circulation. The portion of the drug that enters the general circulation will either become protein-bound (and thus inactive) or remain free to circulate and create an action at a receptor site. This entire process that results in reduced concentration of active drug available in an individual's circulation is known as the **first-pass effect**. Due to the first-pass effect, prescribing providers and nurses administering medications must understand that several doses of an oral medication may be needed before enough free drug stays active in the circulation to exert the desired effect. These metabolic effects are further described in the "Metabolism" section later in this chapter.

1.3 Alternate Routes

A workaround to the first-pass effect is to administer medication using alternate routes to the GI tract. Examples of alternative routes that avoid the first-pass effect include transdermal, nasal, inhalation, injection, or intravenous administration of medication. Alternative routes of medication administration bypass the first-pass effect by entering the bloodstream directly or via absorption through the skin or lungs. For example, pain relievers may be administered directly into the bloodstream (referred to as intravenous medications) so they are quickly available for distribution to tissues within the body.

Transdermal application of medication is an alternate route that has the primary benefit of slow, steady drug delivery directly to the bloodstream, without passing through the liver first. Drugs delivered transdermally enter the blood via a meshwork of small arteries, veins, and capillaries in the skin. This makes the transdermal route of drug delivery particularly useful when a medication must be administered over a longer period of time to control symptoms. For example, transdermal application of fentanyl, a pain medication, can provide effective pain management over several hours; a scopolamine patch can control motion sickness over the duration of a cruise ship vacation; and a nitroglycerin patch is used to prevent chronic chest pain. Despite their advantages, transdermal patches have a significant drawback in that only very small drug molecules can enter the body through the skin, making this application route inappropriate for some types of medications.

1.4 Life Span Considerations

Neonate and Paediatric

Gastric absorption in neonates and pediatric clients varies from adults. In infants, the acid-producing cells of the stomach are immature until around the age of one to two years. Additionally, gastric emptying may be decreased because of slowed or irregular peristalsis (coordinated muscle movements of the intestines).

The liver of infants and children is not fully mature, resulting in a decrease in first-pass elimination and subsequently higher drug levels in the bloodstream.

Older adult

As a natural result of aging, older adults will experience decreased blood flow to tissues within the GI tract. In addition, there may be changes in the gastric (stomach) pH that may alter the absorption of certain medications. Older adult clients may also experience variations in available plasma proteins, which can impact drug levels of medications that are highly protein-bound.

Consideration must also be given to the use of subcutaneous and intramuscular injections in older clients experiencing decreased cardiac output because decreased drug absorption of medications can occur when peripheral circulation is decreased. Additionally, as adults age, they often have less subcutaneous fat, resulting in decreased absorption of medication from transdermal patches that require adequate subcutaneous fat stores for proper absorption.[5]

1.5 Route Considerations

1.5.1 Oral (PO) or Enteral (NGT, GT, OGT) Ingestion

- Oral route is a convenient route for the administration of solid and liquid formulations.
- Additional variables that may influence the rate and extent of absorption include enteric coating or extended-release formulations, acidity of gastric contents, gastric emptying rate, dietary contents, and the presence of other drugs.
- First-pass effect: Blood containing the absorbed drug passes through the liver,

which can deactivate a substantial amount of the drug and decrease its bioavailability (the percentage of dose that reaches the systemic circulation).

1.5.2 Topical and Transdermal Application

- Topical creams, lotions, and ointments are generally used for local effect; transdermal patch formulations are used for systemic effect.

- Absorption through the buccal or sublingual membranes may be rapid and is used for systemic effect.

- Absorption through skin is generally slower but produces a steady, long-term effect that avoids the first-pass effect. However, absorption of medication is affected by blood flow to the skin.[6] For this reason, heat and cold applications should not be used over transdermal medications.

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2. Distribution

The second stage of pharmacokinetics is the process known as **distribution**. Distribution is the process by which a drug is dispersed throughout the body's blood and tissues. After a drug enters into systemic circulation by absorption or direct administration, it will pass from vascular spaces to tissues where a drug-receptor interaction will occur, creating the effect of the drug.

Drugs are designed to primarily cause one effect, meaning they bind more strongly to one specific receptor site and predictably cause or block an action. However, side effects and adverse effects can occur when the drug binds to other sites in addition to the target tissue, causing an unintended action. These side effects can range from tolerable to unacceptable and can result in the discontinuation of the medication. For example, a person might take the pain reliever ibuprofen (Advil) to treat a sore leg muscle, and the pain may be subsequently relieved, but there may also be stomach irritation as a side effect.

The distribution of a drug throughout the body is dependent on many body-related factors such as blood flow, tissue differences, plasma protein-binding, the blood-brain barrier, and the placental barrier.

2.1 Blood Flow

The circulatory system transports medications throughout the body in the bloodstream. Many factors can affect the blood flow and delivery of medication, such as decreased blood flow (due to dehydration), blocked vessels (due to atherosclerosis), constricted vessels (due to uncontrolled hypertension), or weakened pumping by the heart muscle (due to heart failure). As an example, when administering an antibiotic to a client with diabetes who has an infected toe, it may be difficult for the antibiotic to move through the blood vessels all the way to the area of the toe that is infected because of blocked vessels in the legs and feet due to atherosclerosis.

2.2 Tissue Differences

Distribution occurs most rapidly into tissues with a greater number of blood vessels that allow high blood flow (such as the lungs, kidneys, liver, and brain). Distribution occurs least rapidly in tissues with fewer numbers of blood vessels (such as fat), resulting in low blood flow.

The permeability of capillaries is tissue-dependent. Capillaries of the liver and kidney are porous,

allowing for greater permeability. Distribution rates are relatively slower or nonexistent into the central nervous system because of the tight junction between capillary endothelial cells and the blood-brain barrier.

2.3 Protein-Binding

After a drug enters the bloodstream, a portion of it exists as free drug, dissolved in plasma water, but a portion of it becomes bound to proteins. This is important because only free and unbound drugs will pass from the bloodstream to tissues where drug-receptor interactions will occur, thus producing the first effects of a medication. The other portion of the drug that becomes "protein-bound" is inactive while it is bound. For many drugs, these bound forms can account for 95-98% of the total.[1]

Protein binding can also act as a reservoir, as the drug is released slowly, causing a prolonged action. When considering drug distribution, it is important to consider both the amount of free drug that is readily available to tissues, as well as the protein binding that causes the drug to be released over time.

Albumin is one of the most important proteins in the blood. Albumin levels can be decreased by several factors such as malnutrition and liver disease. Therefore, clients with low albumin levels may experience differences in the desired actions of administered medication because of the consequence effect on protein-binding and distribution.

Competition for plasma binding can also impact the effects of drugs. For example, aspirin and warfarin are anticoagulants that compete for the same plasma protein-binding site. Administering both drugs at the same time will increase the amount of unbound drug, thereby increasing their effects and increasing the client's risk for bleeding.[2]

The proportion of the drug that is bound is inactive, because it is not available to receptors, and the portion that remains unbound is the free, active drug. Only free drugs (not bound to protein) can cause a pharmacological response. As the free drug in the blood circulation decreases, more bound drug is released from the protein to maintain the balance of free drug.

As an analogy of how protein binding affects the distribution of medications, consider passengers at a bus stop going to their destination. Many passengers (i.e., drug molecules) want to take a ride on the bus. Everyone is eager to get to their destination (i.e., receptor sites) and tries to find a seat. Some passengers are stronger than others and take all the seats first (such as drug molecules with greater protein-binding ability). When there aren't enough seats on the bus, some passengers are left at the bus stop and become "free" to move around or walk to their destination. In a similar way, "free" drug molecules that are not protein-bound circulate freely in the bloodstream. The "free" passengers in this analogy may go directly to their destination, or they may stop at other locations along the route. In a similar manner, "free" drug molecules produce the first intended or unintended effects in the body when they attach to receptors. Furthermore, similar to the passengers who had seats on the bus and then later got off at their destination, the medication molecules attached to proteins are eventually released and attach to the receptor sites.

2.4 Blood-Brain Barrier

Medications destined for the central nervous system (the brain and spinal cord) face an even larger hurdle than protein-binding; they must also pass through a nearly impenetrable barricade called the **blood-brain barrier**. This blockade is built from a tightly woven mesh of capillaries that protect the brain from potentially dangerous substances, such as poisons or viruses. Only certain medications made of lipids (fats) or those with a "carrier" can get through the blood-brain barrier.

Scientists have devised ways for medications to penetrate the blood-brain barrier. For example, the brand-named medication Sinemet® is a combination of two drugs: carbidopa and levodopa. Carbidopa is designed to carry the levodopa medication across the blood-brain barrier, where it enters the brain and is converted into dopamine to exert its effect on symptoms related to Parkinson's disease.

Some medications inadvertently bypass the blood-brain barrier and impact an individual's central nervous system function as a side effect. For example, diphenhydramine is an antihistamine used to decrease allergy symptoms. However, it can also cross the blood-brain barrier, depress the central nervous system, and cause the side effect of drowsiness. In the case of a person who has difficulty falling asleep, this drowsy side effect may

be useful, but for a person trying to carry out daily activities, drowsiness can be problematic.

2.5 Placental Barrier

The placenta links mother and fetus, and the blood-placental barrier regulates the transfer of molecules between maternal and fetal circulation to protect the fetus. Drug transporters are involved in the transport of drugs through the placenta, affecting potential drug distribution to the fetus.[4] The placenta is known to be permeable to some medications, and furthermore, some drugs can cause significant harm to the fetus. However, many medications have not been specifically studied in pregnant clients, and their effects on the fetus are unknown.

2.6 Life Span Considerations

Neonate and Paediatric

Fat content in infants and children is decreased because of greater total body water. Additionally, protein-binding capacity is decreased, and the developing blood-brain barrier allows more drugs to enter the central nervous system.

Older Adult

At the same body mass index, older adults, on average, tend to have more body fat than younger adults. This increased body fat can result in a longer duration of action for many medications that accumulate in fatty tissues. Serum albumin also decreases, resulting in more active free drug circulating within the body. For these reasons related to distribution, many older adult clients require lower dosages of medication.

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3. Metabolism

After a drug has been absorbed and distributed throughout the body, it is broken down by a process known as **metabolism** so that it can be excreted from the body. Drugs undergo chemical alteration by various body systems to create compounds that are more easily excreted.

As previously discussed in this chapter, medications that are swallowed or otherwise administered into the gastrointestinal tract are inactivated by the intestines and liver, known as the first-pass effect. Additionally, everything that enters the bloodstream, whether swallowed, injected, inhaled, absorbed through the skin, or produced by the body itself, is metabolised by the liver. See Figure 2 for an image of the liver. These chemical alterations are known as biotransformations. The biotransformations that take place in the liver are performed by liver enzymes.

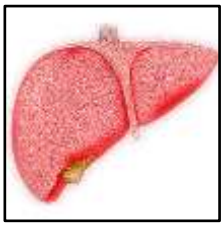

Fig 2. Liver

Biotransformations occur by mechanisms categorised as either Phase I (modification), Phase II (conjugation), and in some instances, Phase III (additional modification and excretion.)[2]

Phase I biotransformations alter the chemical structure of the drug. Many of the products of enzymatic breakdown, called metabolites, are less chemically active than the original molecule. For this reason, the liver is referred to as a "detoxifying" organ. An example of a Phase I biotransformation is when diazepam, a medication prescribed for anxiety, is transformed into desmethyldiazepam and then to oxazepam. Both

these metabolites produce similar physiological and psychological effects to diazepam.[3]

In some instances, Phase I biotransformations change an inactive drug into an active form called a "prodrug." Prodrugs improve a medication's effectiveness. They may also be designed to avoid certain side effects or toxicities. For example, sulfasalazine is a medication prescribed for rheumatoid arthritis. It is a prodrug that is not active in its ingested form but becomes active after Phase I modification.

Phase II biotransformations involve reactions that couple the drug molecule with another molecule in a process called conjugation. Conjugation typically renders the compound pharmacologically inert and water-soluble, so it can be easily excreted. These processes can occur in the liver, kidneys, lungs, intestines, and other organ systems. An example of Phase II metabolism is when oxazepam, the active metabolite of diazepam, is conjugated with a molecule called glucuronide so that it becomes physiologically inactive and is excreted without further chemical modification.

Following Phase II metabolism, Phase III biotransformations may also occur, where the conjugates and metabolites are excreted from cells.

3.1 Factors Affecting Metabolism

Critical factors in drug metabolism are the type and concentration of liver enzymes. The most important enzymes for medical purposes are monoamine oxidase and cytochrome P450. These two enzymes are responsible for metabolising dozens of chemicals.[6]

Drug metabolism can be influenced by a number of factors. One major disruptor of drug metabolism is depot binding. Depot binding is the coupling of drug molecules with inactive sites in the body, resulting in the drug not being accessible for metabolism. This action can also affect the duration of action of other medications susceptible to depot binding. For example, tetrahydrocannabinol (THC), the main psychoactive component of marijuana, is highly lipid-soluble and depot binds in the adipose tissue of users. This interaction drastically slows the metabolism of the drug, so metabolites of THC can be detected in urine weeks after the last use.[7]

The metabolic conversion of drugs is generally enzymatic in nature. The enzyme systems involved are localised in the liver, although many tissues have some metabolic activity.

The cytochrome P450 enzyme family is the major catalyst of drug biotransformation.

Factors affecting biotransformation include the concomitant use of other drugs, causing enzyme induction or enzyme inhibition.

Enzyme induction

Enzyme induction leads to an increased rate of biotransformation and corresponding decreases in the availability of the parent drug.

In some cases, a given compound can induce both the transformation of other compounds and its own metabolism. A well-characterised example of this so-called auto-induction occurs with the anticonvulsant carbamazepine. The antiretroviral nevirapine also demonstrates auto-induction properties.

Enzyme inhibition

Inhibition of drug biotransformation enzymes results in elevated levels of the parent drug, prolonged pharmacological effects, and increased drug-induced toxicity

Additionally, drugs that share metabolic pathways can "compete" for the same binding sites on enzymes, thus decreasing the efficiency of their metabolism. For example, alcohol and some sedatives are metabolised by the cytochrome P450 enzyme, and only a limited number of these enzymes exist to break these drugs down. Therefore, if a client takes a sedative after drinking alcohol, the sedative is not well-metabolised because most of cytochrome P450 enzymes are filled by alcohol molecules. This results in reduced excretion and high levels of both drugs in the body with enhanced effects. For this reason, the co-administration of alcohol and sedatives can be deadly.

3.2 Clinical Significance

When administering medication, nurses must know how and when the medication is metabolised and eliminated from the body. Most of the time, the rate of elimination of a drug depends on the concentration of the drug in the bloodstream. However, the elimination of some drugs occurs at a constant rate that is independent of plasma concentrations. For example, the

ethanol contained in alcoholic beverages is eliminated at a constant rate of about 15 mL/hour regardless of the concentration in the bloodstream.

3.3 Half Life

Half-life refers to the rate at which 50% of a drug is eliminated from the body. Half-life can vary significantly between drugs. Some drugs have a short half-life of only a few hours and must be given multiple times a day, whereas other drugs have half-lives exceeding 12 hours and can be given as a single dose every 24 hours. See Figure 3 for an illustration of half-life affecting the blood concentration of medication over time.

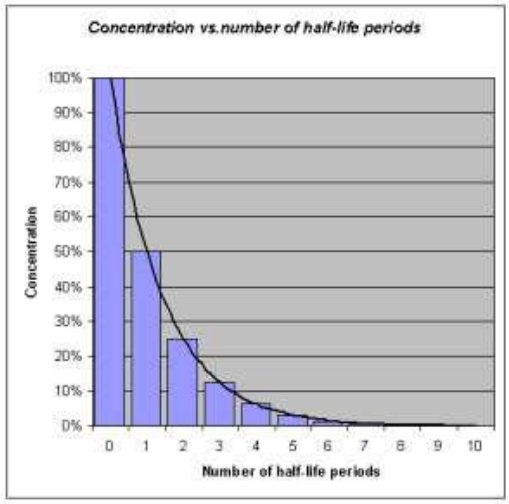

Fig 3. Half-Life Affecting Blood Concentration of Medication Over Time

Half-life affects the duration of the therapeutic effect of a medication. Many factors can influence half-life. For example, liver disease can prolong the half-life if it no longer effectively metabolises the medication. Information about the half-life of a specific medication can be found in evidence-based medication references. For example, the South African Medicines Formulary (SAMF)

3.4 Life Span Considerations

Neonatal and Paediatric

The developing liver in infants and young children produces decreased levels of enzymes. This may result in a decreased ability of the young child or neonate to metabolize medications. In contrast, older children may experience increased metabolism and require higher doses of medications once the hepatic enzymes are fully produced.[12]

Older Adult

Metabolism by the liver may significantly decline in the older adult. As a result, dosages should be adjusted according to the client's liver function and their anticipated metabolic rate. First-pass metabolism also decreases with aging, so older adults may have higher "free" circulating drug concentrations and thus be at higher risk for side effects and toxicities.[13]

3.5 Did You Know?

Did you know that, in some people, a single glass of grapefruit juice can alter levels of drugs used to treat allergies, heart diseases, and infections? Fifteen years ago, pharmacologists discovered this "grapefruit juice effect" by luck, after giving volunteers grapefruit juice to mask the taste of a medicine. Nearly a decade later, researchers figured out that grapefruit juice affects the metabolizing rates of some medicines by lowering levels of a drug-metabolizing enzyme called CYP3A4 (part of the CYP450 family of drug-binding enzymes) in the intestines. This is also called enzyme induction.

Paul B. Watkins of the University of North Carolina at Chapel Hill discovered that other juices like Seville (sour) orange juice—but not regular orange juice—have the same effect on the liver's ability to metabolize using enzymes. Each of ten people who volunteered for Watkins' juice-medicine study took a standard dose of felodopine, a drug used to treat high blood pressure, diluted in grapefruit juice, sour orange juice, or plain orange juice. The researchers measured blood levels of felodopine at various times afterward. The team observed that both grapefruit juice and sour orange juice increased blood levels of felodopine, as if the people had received a higher dose. Regular orange juice had no effect. Watkins and his coworkers have found that a chemical common to grapefruit and sour oranges, dihydroxybergamottin, is likely the molecular culprit. Thus, when taking medications that use the CYP3A4 enzyme to metabolize, clients are advised to avoid grapefruit juice and sour orange juice.[14]

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3. This work is a derivative of Medicines by Design by US Department of Health and Human Services, National Institutes of Health, National Institute of General Medical Sciences and is available in the Public Domain.

4. Excretion

Excretion is the final stage of a medication interaction within the body. The body has absorbed, distributed, and metabolized the medication molecules – now what does it do with the leftovers? Remaining parent drugs and metabolites in the bloodstream are often filtered by the kidney, where a portion undergoes reabsorption back into the bloodstream, and the remainder is excreted in the urine. The liver also excretes byproducts and waste into the bile. Another potential route of excretion is the lungs. For example, drugs like alcohol and the anesthetic gases are often eliminated by the lungs.[1]

4.1 Routes of Excretion

4.1.1 Kidney

The most common route of excretion is through the kidneys. As the kidneys filter blood, the majority of drug byproducts and waste are excreted in the urine. The rate of excretion can be estimated by taking into consideration several client factors, including age, weight, biological sex, and kidney function. There are known sex differences in the three main renal functions of glomerular filtration, tubular secretion and tubular reabsorption. Renal clearance is generally higher in men than in women.[2]

Kidney function is measured by lab values such as serum creatinine, glomerular filtration rate (GFR), and creatinine clearance. If a client's kidney function is decreased, then their ability to excrete medication is affected, and drug dosages must be altered for safe administration.

Renal disorders, such as chronic kidney disease, can reduce kidney function and hinder drug excretion. As kidney function decreases with age, drug excretion becomes less efficient, and dosing adjustments may be needed. Other medical conditions that impact blood flow to the kidneys can also affect drug elimination. For example, heart failure can affect systemic blood flow to the kidney, resulting in decreased filtration and elimination of drugs.

4.1.2 Liver

As the liver filters blood, some drugs and their metabolites are actively transported by hepatocytes (liver cells) to the bile. Bile moves through the bile ducts to the gallbladder and then on to the small intestine. During this process, some drugs may be partially absorbed by the intestine back into the bloodstream. Other drugs are biotransformed (metabolised) by intestinal bacteria and reabsorbed. Unabsorbed drugs and byproducts/metabolites are excreted in the faeces.

If a client has decreased liver function, their ability to excrete medication is affected, and drug dosages must be adjusted. Lab studies used to evaluate liver function are called liver function tests and include measurement of alanine transaminase (ALT) and aspartate aminotransferase (AST) enzymes that the body releases in response to damage to or disease of the liver.

Conditions that cause decreased blood flow to the liver can also affect the metabolism and excretion of drugs. For example, conditions such as shock, hypovolemia, or hypotension cause decreased liver perfusion and may require adjustment of dosages of medication.

4.1.3 Other Routes to Consider

Sweat, tears, reproductive fluids (such as seminal fluid), and breast milk can also contain drugs and byproducts/metabolites of drugs. This can pose a toxic threat, such as the exposure of an infant to breast milk containing drugs or byproducts of drugs ingested by the mother. Therefore, nurses must refer to a drug reference and contact a health care provider with any concerns before administering medications to a mother who is breastfeeding.[3]

4.2 Life Span Considerations

Neonate and Paediatrics

Neonates and children have immature kidneys with decreased glomerular filtration, resorption, and tubular secretion. As a result, they do not excrete medications as efficiently from the body. Dosing for most medications used to treat infants and pediatric clients is commonly based on weight in kilograms, and a smaller dose is usually prescribed. In addition, pediatric clients may have higher levels of free circulating medication than anticipated and may become toxic quickly. Therefore, it is vital for nurses to diligently recheck dosages before administering medications and closely monitor infants and children for early identification of adverse effects and drug toxicity.[4]

Older Adult

Kidney and liver function often decrease with age, which can lead to decreased metabolism and excretion of medications. Subsequently, medication may have a prolonged half-life with a greater potential for toxicity due to elevated circulating drug levels. Some medications may be avoided or smaller doses recommended for older clients due to these factors, which is commonly referred to as "Start low and go slow."[5]

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Pharmacodynamics

So far in this chapter, we have learned the importance of pharmacokinetics in how the body absorbs, distributes, metabolises, and excretes a medication. Now let's consider how drugs act on target sites of action in the body, referred to as **pharmacodynamics.**

Mechanism of action is a medical term that describes how a medication works in the body. For example, did you know that an osmotic laxative like magnesium citrate attracts and binds with water? The mechanism of action for this medication is it pulls water into the bowel, which softens stool and increases the likelihood of a bowel movement.

A drug's mechanism of action may refer to how it affects a specific receptor. Many drugs bind to specific receptors on the surface of cells to cause an action. For example, morphine binds to a specific receptor that inhibits transmission of nerve impulses along the pain pathway and decreases a client's feelings of pain.

Other medications inhibit specific enzymes for a desired effect. For example, earlier in this chapter we discussed how monoamine oxidase inhibitors (MAOIs) are prescribed as antidepressants because they block monoamine oxidase, the enzyme that breaks down serotonin and dopamine. This blockage increases the concentration of serotonin and dopamine in the central nervous system and increases a client's feelings of pleasure.

1. Agonist and Antagonist Actions

Drugs have agonistic or antagonistic effects on receptor sites. An **agonist** binds tightly to a receptor to produce a desired effect.
An **antagonist** competes with other molecules and blocks a specific action or response at a receptor site. See Figure 4 for an illustration of how a beta-blocker, an antagonist cardiac medication, blocks a specific action on the beta receptors of a cardiac cell.

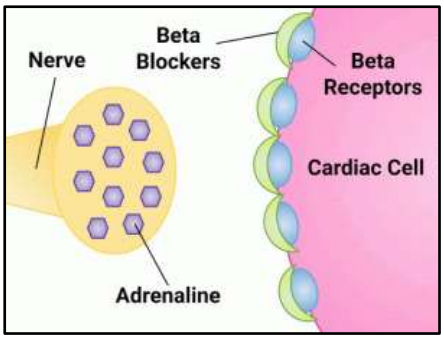

Fig 4. Antagonist Action of Beta-Blockers on Beta Receptors of a Cardiac Cell

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1. "Mechanism of Action" by Dominic Slausen at Chippewa Valley Technical College is licensed under CC BY 4.0.

2. Types of medications

There are a variety of drugs and substances that clients may utilise for symptom management or to enhance their wellness. Nurses document clients' use of prescription medications, over-the-counter medications, herbal substances, and other supplements in the medical record. Some substances have a long half-life and have the potential to interact with new medications, so accuracy is vital. Ensuring an accurate medical record and knowledge of the different types of substances a client is taking is important for an effective nursing plan of care.

2.1 Prescription Medications

Drugs are prescribed by a licensed prescriber for a specific person's use and regulated through the South African Products Regulatory Authority (SAHPRA). For more information, visit their website at https://www.sahpra.co.za.

2.2. Generic Medications

Generic medications can be safe and effective alternatives to their brand-name counterparts at a significantly reduced cost. By law, generic medications must have the same chemically active ingredient in the same dose as the brand-name (i.e., they must be "bio-equivalent"). However, the excipients (the base substance that holds the active chemical ingredient into a pill form, such as talc) or the flavouring can be different. Some clients do not tolerate these differences in excipients very well. When prescribing a medication, the provider must indicate that a generic substitution is acceptable. Nurses are often pivotal in completing insurance paperwork on the client's behalf if the brand-name medication is more effective or better tolerated by that particular client.[2]

2.3 Over-the-Counter Medications

Over-the-counter (OTC) medications do not require a prescription. They can be bought at a store and may be used by multiple individuals. OTC medications are also regulated through the FDA. Some prescription medications are available for purchase as OTC in smaller doses. For example, diphenhydramine (Benadryl) is commonly prescribed as 50 mg every 6 hours, and the prescription strength is 50 mg. However, it can also be purchased OTC in 25 mg doses (or less for children).

2.4. Herbals and Supplements

Herbs and supplements may include a wide variety of substances, including vitamins, minerals, enzymes, and botanicals. Supplements such as "protein powders" are marketed to build muscle mass and can contain a variety of substances that may not be appropriate for all individuals. Herbals and supplements are often considered complementary and alternative medications (CAM). **Complementary and alternative medications (CAM)** are types of therapies that are commonly used in conjunction with, or as an alternative to, traditional medical therapies. These herbal and supplement substances are not regulated, and most have not undergone rigorous scientific testing for safety for the public. While clients may be tempted to try these herbals and supplements, there is no guarantee that they contain the ingredients listed on the label. It is also important to remember that there is a potential for adverse effects or even overdose if the herbal or supplement contains some of the same drugs that were also prescribed to a client.[4] By understanding the use of CAM therapies, nurses can help their clients make informed decisions and take a holistic approach to their care. Additionally, being knowledgeable about CAM therapies can help nurses to better educate their clients on the potential benefits and risks associated with these therapies, which can help improve client outcomes and satisfaction.

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3 Efficacy, dose-response, onset, peak and duration

Dosing considerations play an important role in understanding the effect that a medication may have on a client. Additionally, the nurse must be aware of the overall **dose-response** based on the dosage selected. Dose response is the dose of medication required to achieve the desired response to the medication. As the dose increases, the response of the drug may increase, as well as the potential for toxicity. This response helps determine the therapeutic index of a drug, or the effective dose range.

3.1 Onset, Peak, and Duration

Three additional principles related to the effect a medication has on a client are onset, peak, and duration.

Onset of medication refers to when the medication first begins to take effect. The time of onset is affected by the route of administration. For example, a diuretic given intravenously will begin to take effect much faster than a diuretic administered orally because the intravenous route delivers the drug directly to the systemic circulation and avoids the first-pass effect.

Peak refers to the maximum concentration of medication in the body, and the client shows evidence of the greatest therapeutic effect. For example, a client taking ibuprofen can anticipate maximum pain relief in one to two hours when the medication reaches peak serum levels.

Duration refers to the length of time the medication produces its desired therapeutic effect. For example, the duration of oral acetaminophen is four to six hours, at which time the client will likely require an additional dose for pain.

3.2 Duration, Dosing, and Steady State

Now, let's consider the implications of duration and dosing. Remember, the duration of medication is correlated with the elimination. Half-life is the amount of time that it takes for half of the drug to be eliminated from the body.

If a medication has a short half-life (and is therefore eliminated more quickly from the body), the therapeutic effect is shorter. These medications may require repeated dosing throughout the day in order to achieve steady blood levels of active free drug and a sustained therapeutic effect.

Other medications have a longer half-life (and therefore are eliminated more slowly from the body, resulting in longer therapeutic duration) and may only be administered once or twice per day. For example, oxycodone immediate release is prescribed every 4 to 6 hours for the therapeutic effect of immediate relief of severe pain, whereas oxycodone ER (extended release) is prescribed every 12 hours for the therapeutic effect of sustained relief of severe pain.

Steady state refers to the point at which the amount of drug entering the body is equal to the amount of drug being eliminated, resulting in a stable drug concentration.[2] When steady state is achieved, there is a state of equilibrium in the body and the concentration of the drug remains constant, resulting in optimal therapeutic effect.

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4 Therapeutic levels

4.1 Therapeutic Window

For every drug, there exists a dose that is minimally effective (the Effective Concentration) and another dose that is toxic (the Toxic

Concentration). Between these doses is the **therapeutic window**, where the safest and most effective treatment will occur. For example, see Figure 5 for an illustration of the therapeutic window for warfarin, a medication used to prevent blood clotting. Too much warfarin administered causes bleeding, and vitamin K is required as an antidote. Conversely, not enough warfarin administered for a client's condition can cause clotting. Think of the therapeutic window (the green area on the graph) as the "perfect dose," where clotting is prevented and yet bleeding does not occur.

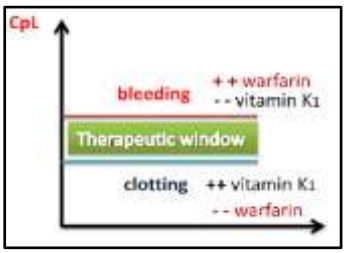

Fig 5: Therapeutic window

The effect of warfarin is monitored using a blood test called the international normalised ratio (INR). For clients receiving warfarin, nurses vigilantly monitor their INR levels to ensure the dosage appropriately reaches their therapeutic window and does not place them at risk for bleeding or clotting.

4.1.1 Peak and Trough Levels

Now let's apply the idea of therapeutic window to the administration of medications requiring the monitoring of peak and trough levels, which is commonly required in the administration of specific IV antibiotics. The dosage of these medications is **titrated**, meaning adjusted for safety, to achieve a desired therapeutic effect for the client. Titration is accomplished by closely monitoring the peak and trough levels of the medication. A drug is said to be within the "therapeutic window" when the serum blood levels of an active drug remain consistently above the level of effective concentration (so that the medication is achieving its desired therapeutic effect) and consistently below the toxic level (so that no toxic effects are occurring).

A **peak** drug level is drawn after the medication is administered and is known to be at the highest level in the bloodstream. A **trough** level is drawn when the drug is at its lowest in the bloodstream, right before the next scheduled dose is given. Medications have a predicted reference range of normal values for peak and trough levels. These numbers assist the pharmacist and provider in gauging how the body is metabolising, protein-binding, and excreting the drug and are used to adjust the prescribed dose to keep the medication within the therapeutic window. When administering IV medications that require peak or trough levels, it is vital for the nurse to plan the administration of the medication according to the timing of these blood draws.[2]

4.2 Therapeutic Index

The **therapeutic index** is a quantitative measurement of the relative safety of a drug. It is a comparison of the amount of drug that produces a therapeutic effect versus the amount of drug that produces a toxic effect.

- A large (or high) therapeutic index number means there is a wide therapeutic window between the effective concentration and the toxic concentration of a medication, so the drug is relatively safe.
- A small (or low) therapeutic index number means there is a narrow therapeutic window between the effective concentration and the toxic concentration. A drug with a narrow therapeutic range (i.e., having little difference between toxic and therapeutic doses) often has the dosage titrated according to measurements of the actual blood levels achieved in the person taking it.

For example, phenytoin has a narrow therapeutic index between the effective and toxic concentrations. Clients who start taking phenytoin to control seizures have frequent peak and trough drug levels to ensure they achieve steady state with a therapeutic dose to prevent seizures without reaching toxic levels.

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3.

5. Evaluating Effects

The medical practitioner is responsible for assessing the client, monitoring lab values, and recognising side effects and/or adverse effects of medications. Drug dosages should be verified to ensure all are within recommended safe ranges according to the client's current status, as well as for their potency.

Potency refers to the amount of the drug required to produce the desired effect. A drug that is highly potent may require only a minimal dose to produce a desired therapeutic effect, whereas a drug that has low potency may need to be given at much higher concentrations to produce the same effect. Consider the example of opioid versus nonopioid medications for pain control. Opioid medications often have a much higher potency in smaller doses to produce pain relief; therefore, the overall dose required to produce a therapeutic effect may be much less than that for other analgesics.

The nurse preparing to administer medications must also be cognizant of drug selectivity and monitor for potential side effects and adverse effects. **Selectivity** refers to the separation between the desired and undesired effects of a drug. Drugs that are selective will search out target sites to create a specific drug action, whereas nonselective drugs may impact many other types of cells and tissues, thus increasing the risk for unintended side effects and/or adverse effects. Selective beta-1 blockers search out specific receptors on the heart to create their effect, whereas nonselective beta-blockers may affect receptors in the lungs in addition to those in the heart, causing potential respiratory side effects like a cough.

A **side effect** occurs when the drug produces effects other than the intended effect. A side effect, although often unintended, is generally anticipated by the provider and is a known potential consequence of the medication therapy. Examples of common side effects are nausea, vomiting, diarrhoea, and drowsiness. In some situations, however, side effects may have a beneficial impact. For example, a side effect of hydrocodone is drowsiness. A client who is having difficulty sleeping due to pain and takes hydrocodone at bedtime may find the drowsiness beneficial in helping them fall asleep.

Conversely, unanticipated effects can occur from medications that are harmful to the client. These harmful occurrences are known as **adverse effects**. Adverse effects are relatively unpredictable, severe, and are a reason to discontinue the medication.[1] For example, an adverse effect of ciprofloxacin is tendon rupture. Adverse effects should be reported to the pharmacy and tracked as a client safety concern according to agency policy.

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Concurrent use of herbal and prescribed medicine by patients in primary health care clinics, South Africa

African Journal of Primary Health Care & Family Medicine
ISSN: (Online) 2071-2936, (Print) 2071-2928

Introduction

People worldwide have been using medicinal herbs to improve or treat their health conditions before the inception of conventional medicine. Over time, the world has seen an increased demand for herbal products.[1] African traditional medicine (ATM), particularly herbal medicine (HM), has been part of health care in African countries, and its contributions to the primary health care (PHC) system are well known in some parts of the African continent.[2] South Africa categorises indigenous HM as ATM, whereas Homoeopathy, Ayurveda, Traditional Chinese Medicine, Unani Tibb, and Western Herbal Medicine, as complementary medicine (CM).[3] However, these modalities are not acknowledged as part of the national healthcare system.[4] South Africa, which is a country rich in indigenous medicinal plants, has approximately 30,000 plant species, accounting for almost 10% of the world's higher plant species.[5] A large proportion (60%–80%) of the South African population uses herbal products for the treatment of ailments and cultural practices.[6]

These practices are derived from the indigenous knowledge and experiences possessed by communities. Indigenous knowledge (IK) is regarded as the knowledge that has been acquired outside the educational system. It is easily transferred in a community that shares common cultural concepts and speaks the same language.[7] Indigenous knowledge is central to the social, cultural and spiritual beliefs of these communities.[8] The deep-rooted indigenous knowledge of HM is evident in the decision-making and usage of HM.[9] Moreover, a personal, family and community-positive experience, ease of availability, perceived lack of side effects and patients' experience or witness of unfavourable behaviour of healthcare providers (HCPs) is a push factor towards using HM.[10]

Herbal products can either be obtained from a traditional health practitioner (THP), herbal markets or pharmacies as well as being available as home-made remedies.[11] South Africa has taken various initiatives to promote the safety, efficacy, labelling and traditional use of HM.[12] However, most of these are not registered by the South African Health Products Regulatory Authority (SAHPRA) and have not undergone quality control tests, and their safety is unknown.[13,14] According to the World Health Organisation (WHO), HM comprised herbs, herbal materials and preparations and finished products that contain plants as active constituents.[15] These herbs may contain more than 150 active constituents that may affect the pharmacokinetics of prescribed medicines and cause adverse effects.[16] These adverse effects range from an allergic reaction, gastrointestinal upset, coagulation abnormalities, cerebral haemorrhage, liver damage and possible death.[17,18]

In South Africa, herbal products are sold at herbal markets or by THP as herbal concoctions, packaged in recyclable plastic bottles or paper with labels that do not provide the full ingredients of the herb.[19] These herbal concoctions are a mixture of different plant species or a single plant to treat various health ailments.[20] Patients use these herbal concoctions concurrently with prescribed medicines without the knowledge of the implications of HDIs.(herb-drug-interactions)[21,22] Research shows that desperate patients use HM to complement prescribed medicines such as antihypertensives, hypoglycaemics, antiarrhythmics, anticoagulants, antiretrovirals and antidepressants.[12,16] Moreover, a review conducted to assess the severity of HDIs in patients who co-administer HM and prescribed medicines showed that patients taking warfarin, insulin, aspirin and/or statins, reported evident interactions with herbal products including: (1) sage, (2) flaxseed, (3) cranberry, (4) *Camelia sinesis,* (5) *Hypericum perforatum*, (6) *Ginkgo biloba* and (7) *Matricaria chamomile*.[23,24] For example, acetylsalicylic acid, as an antiplatelet agent, is the drug that most interacts with HMs, followed by warfarin, which can interact with *Ginkgo biloba* and *Hypericum perforatum,* leading to increased bleeding.[25] Amlodipine, an antihypertensive drug, when combined with *Ginkgo biloba,* changes the pharmacokinetic interactions of amlodipine through the metabolism of the CYP3A4 enzyme [26]

Several studies conducted in South Africa confirmed that consumers do not disclose the use of HM to their healthcare providers.[27,28,29] The non-disclosure prevents the discussion and recording of potential HDIs by HCPs.[30] Additionally, the non-registration of most HM exacerbates the risk of HDIs.[14] Several studies have explored the reasons why patients use HM[31,32,33], but within the South African context, there is a dearth of information regarding patients' knowledge about herb-drug interaction.

This study sought to provide an in-depth description of the use of HM through focus group discussions (FGD) with patients attending PHC clinics in three provinces – Gauteng, Free State and Mpumalanga, South Africa.

Discussion

The study revealed that the driving force behind the use of HM is easy accessibility, lower cost and the perception of having no side effects. The findings also found that respondents follow what their forefathers have been doing by using HM. These findings are similar to studies conducted in South Africa[38,39] and support the notion that HM plays a role in the lives of the population of South Africa. Because of the lack of knowledge and personal perceptions, respondents raised their concerns about the side effects they are experiencing while using prescribed medicine.[40,41,42] As part of the consultation and the right of the patient to be informed, HCPs need to discuss the benefits and risks of the prescribed medication with patients.[43,44] In order to better understand HM and HDIs, an expansion of knowledge of the pharmacodynamics and pharmacokinetics of HM is essential. Patients need to hear about HM directly from HCPs to limit HDIs.

Respondents reported that they started using HM upon recommendation by people who have personal experience with HM and television advertisements. This finding indicates that HM in the community and society at large is an important issue, as people are sharing information about medicinal plants or herbs among themselves. This can be attributed to the historical African culture of sharing information about medicinal herbs orally from generation to generation.[46] Moreover, various media advertisements have increased awareness and have given HM respect and credibility.

During the discussion, most FG respondents confirmed the co-administration of HM and prescribed medication. Concurrent use of these modalities is a common practice, especially in patients with chronic conditions.[23] This is because of patients simultaneously seeking treatment from both conventional and traditional or complementary health systems for the same ailment.

Even though a small fraction of respondents felt that using HM and prescribed medicine is wrong, they took this decision because of how they felt, not necessarily because they had the knowledge regarding HDI. This highlights the importance of educating patients about the danger of co-administering HM and prescribed medicines and possible HDIs.

Herbal medicines contain hundreds of active ingredients that may interact and cause modifications to prescribed medication.[48] This study revealed a low awareness of potential herb-drug interactions, where most of the respondents mentioned that they were not aware of the potential interaction of herbs and prescribed medication. A similar study carried out by Ezuruike and Prieto[51] showed that 60% of participants who took HM alongside prescribed medicine are unaware of the identity of HM being taken, which exacerbates the risks of the HDIs. A study conducted in South Africa showed similar results, where consumers purchase HM products from herbalists and traditional healers, packaged in containers with the contents not being stated.[20] These findings demonstrate that patients do not have knowledge of HDIs, and there is a need for continuous education of patients about HDIs.

Respondents in this study mentioned that they do not disclose the use of HM to their HCPs. This shows that patients are not forthcoming with their use of HM when consulting in the PHC clinics. A possible reason could be the perceived unpleasant behaviours of PHC nurses mentioned in the study.[27,31] Respondents confirmed that they experience unpleasant behaviours from nurses during clinic visits. This behaviour of PHC nurses could weaken the ability of the health system and compromise the quality of patient care.
Respondents also mentioned that doctors and nurses do not have time to give an explanation about their conditions or treatment during the consultation. This may be because of a few HCPs having to deal with the volume of patients in a short time.[52] A study conducted in a hospital in South Africa reported that nurses experience a high patient load, staff absenteeism and burnout.[53] This calls for stakeholders to come up with interventions to combat workload and absenteeism to create favourable conditions for both patients and HCPs. Education about the use of HM requires a sensitive approach that depends on listening and spending time with the patients.

Conclusion

The findings of this study revealed that there is a lack of knowledge and awareness of the risks that may be with the co-administration of HM and prescribed medicines. Within the identified themes, participants believed anecdotes from community members and family, cultural background and positive experiences of HM. These findings can be used to develop interventions aimed at preventing possible HDIs.

Natural product pharmacology: the British Journal of Pharmacology perspective

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Received: 14 June 2024 Accepted: 15 July 2024; DOI: 10.1111/bph.17300

Overview

Natural products (NPs) have long been used as a rich source of bioactive compounds for drug development. Recent technological advancements have revitalised natural products research, as evidenced by increased publications in this field. In this editorial review, we highlight key points from the British Journal of Pharmacology (BJP) practical guide, which outlines standards for natural products research reports, and provide papers published in the BJP between years 2020 to 2023 that demonstrate adherence to these guidelines.

Introduction

Natural products (NPs) provide an important source of bioactive compounds in drug discovery. Despite the significance of natural products, past research encountered numerous challenges, particularly regarding the isolation, identification and synthesis of these compounds, which prompted a decline in natural product-based drug discovery. In recent years, accelerated technological developments exemplified by the advent of advanced analytical tools, multi-omics techniques, sophisticated synthesising strategies and refined microbial culturing practices have opened new avenues for overcoming the traditional hurdles faced in natural products research (Atanasov et al., 2021). These advancements have not only expanded the scope of pharmaceutical research but have also rekindled interest in natural products, as one of the most promising yet challenging areas of study.

Despite the rise of synthetic chemistry and molecular biotechniques, the discovery of natural products remains a crucial pathway for the development of novel pharmaceuticals. This is especially evident in the search for new antimicrobials, anticancer agents and anti-inflammatory compounds, in which complex molecules with potent biological activities are found but not easily replicated by synthetic analogues.

Considering the aforementioned changes in natural product research and its implications for drug discovery, the aim of this editorial review is to summarise the previous practical guide for transparent reporting of research on natural products published in 2020 by the BJP (Izzo et al., 2020). This practical guidance and review will serve as a blueprint for researchers, by providing a set of standards for enhancing the quality, reproducibility and transparency of natural product research. As the field continues to evolve, it is imperative to evaluate and explain the latest scientific advancements of natural product papers published in BJP.

This editorial review makes a connection between traditional approaches and modern technologies, providing guidelines for current and future investigations aimed at developing novel therapeutics based on natural products research.

Consequently, we underscore the necessity of continuous innovation and adaptation in the methodologies employed, ensuring that the field attracts significant attention from researchers.

The 2020 BJP practical guide aimed at ensuring transparent reporting in natural product pharmacological research. The guide highlights the pivotal role that natural products play in drug discovery (Izzo et al., 2020).

Besides highlighting the various research categories that are preferred by the BJP, the 2020 BJP practical guide offers explicit advice on methodological rigour. For instance, it requires the comparison of concentration–response curves for both the vehicle and the investigated compound, and insists on the inclusion of a positive control.

The significance of selecting and testing in vitro concentrations that are appropriate to pharmaceutical development and drug discovery is also highlighted. For in vivo studies, the 2020 BJP practical guide specifies that dosages should bear translational significance, with correct extrapolation between animals and humans, emphasising that the route and timing of administration should align with the natural product's intended use. These guidelines aim to increase the translational relevance of research findings, thereby supporting the mission of the BJP to advance transparency and reproducibility in natural product research.

Outlook

In future research, the potential of natural products in disease prevention and treatment will be exploited not only through their diversity and complexity but also based on how precisely their mechanisms of action can be understood. While traditional research methods have succeeded in identifying connections between natural products and disease prevention/treatment, they often overlook a broad target spectrum of natural products due to their structural characteristics.

This raises the question of which targets have direct biological significance in the development of specific diseases. To address this issue, more systematic and refined research approaches need to be brought in. Chemical proteomics has emerged as a new method to comprehensively screen and identify the protein targets of active small molecules, including natural products, involving two crucial steps in target identification: chemical probe design and synthesis, as well as target fishing and identification (Chen et al., 2020). In the ABPP approach, probes are designed and synthesised from parent molecules based on structure-activity relationships to ensure that the probes retain the pharmacological activity of the original molecules.

Overall, the steps in chemical proteomics approaches involve probe design and synthesis, incubation with target samples, enrichment of bound proteins, identification of protein targets, validation of target information and pharmacological effects. This strategy can reveal the direct relationship between natural products and key targets in specific diseases, laying a solid foundation for precision treatment.

Moreover, studies using animal models or human samples can be conducted to corroborate the key targets and validate natural product effects on the treatment progress.

Conclusion

In summary, by adopting new research strategies, researchers will be able to gain a deeper understanding of the effects and mechanisms of natural products in prevention and disease treatment, thereby paving the way for discovering new therapeutic targets.

Looking ahead, we remain committed to supporting and publishing ground-breaking natural product work that not only meets but exceeds our standards. We encourage authors to take advantage of the insights and feedback provided through the editorial process to enrich their research contributions. Our goal is to advance the field of natural product research by disseminating research of the highest quality and of significant impact on the scientific community and beyond.

As we move forward, we are optimistic that the collective efforts of our contributors will continue to push the boundaries of what is possible in natural product research. Together, we can build on the progress achieved thus far, ensuring that the BJP remains at the forefront of publishing innovative and influential research in this ever-important area of pharmacological science.

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Off-label use of medicines in South Africa: a review

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Received: 8 July 2024 Accepted: 20 November 2024

Background

Off-label use of medicinal products has become an important part of mainstream and legitimate medical practice worldwide. This practice is common in oncology, obstetrics, paediatrics, and in the management of infectious diseases (notably HIV), and inflammatory conditions, as well as in rare and/or orphan diseases. However, the off-label use of medicines has recently raised many clinical and legal difficulties, not only among medical practitioners but also among pharmacists and other healthcare professionals.

Introduction

In South Africa, the Medicines Act 101 of 1965, as amended, gives the South African Health Products Regulatory Authority (SAHPRA) the powers to assess the scientific evidence, often provided by the applicant, and to decide whether to register medicines or not.

Usually, the criteria which SAHPRA uses include evidence on: (i) the effectiveness (or efficacy) of medicine for the management of specific indication(s), (ii) safety profile in the specific population for which registration is sought, and (iii) the quality of the health products to be administered without further manipulations. Similar criteria are used globally by other similar regulatory bodies, such as the Food and Drug Administration (FDA) in the United States of America (USA), as well as the Therapeutic Goods Administration (TGA) in Australia.

However, medicines such as amitriptyline are often prescribed on an off-label basis. This is also known as off-label drug use (OLDU). Meaning, such medicines are prescribed and utilised for additional indications for which regulatory authorities have not registered or approved. The OLDU has become an important part of mainstream and legitimate medical practice worldwide. It is commonly practised in disciplines and specialities such as oncology, obstetrics, paediatrics, infectious diseases, notably human immunodeficiency virus (HIV), pain and inflammatory conditions, as well as in rare and/or orphan diseases. In numerous cases of perinatally HIV-1-infected children, OLDU has been an optimal strategy to prevent immunological and clinical deterioration in the early start of highly active antiretroviral therapy (HAART).

However, while OLDU use can provide necessary treatment options in certain situations, it is fraught with potential risks and challenges, not only among medical practitioners but also for pharmacists and other healthcare professionals. Clinicians must weigh these risks carefully, rely on the best available evidence, and ensure transparent communication with patients and/or caregivers regarding the off-label use of medications. Therefore, in this narrative review, scientific evidence regarding the advantages and disadvantages of prescribing and utilising medicines to treat diseases for which they are not registered is synthesised to make the vast body of knowledge comprehensible to healthcare providers and regulatory authorities.

Regulatory framework

While off-label and unlicensed practices are well-characterised in several developed countries and regions, there are concerns about the limited number of studies addressing these practices in developing countries.
including South Africa. Recent reviews indicate that unlicensed use of medicines can account for

up to 75% of medication use among hospitalised children in some studies. However, Oshikoya et al. reported that off-label prescriptions were only 7.7% among children with chronic diseases attending speciality paediatric clinics in Nigeria. Despite this, earlier studies highlighted a higher risk of drug-drug interactions among paediatric patients. Additionally, there were significant concerns regarding the off-label use of pentazocine among paediatric surgical patients in Nigeria, with most children experiencing between two and seven adverse events.

Developing countries, including South Africa, are particularly affected by off-label and unlicensed medicine use. This is due to the significant proportion of the population aged 0 to 18 years and their higher susceptibility to infectious diseases. For example, Southern Africa has a high incidence of children born to mothers with HIV, which contrasts with the situation in higher-income countries.

Studies have reported that 17% to 40% of prescription drugs in ambulatory care are prescribed for conditions that are not approved by the FDA or other regulatory agencies, meaning they are used for indications that have not received official approval.

Medicines are commonly prescribed on an off-label basis. There is considerable evidence regarding medical practitioners' regular reliance on OLDU. This practice is to a greater extent applied in the non-traditional management approaches for pain, mental disorders and cardiovascular diseases, among others.

Gabapentin

The FDA approved gabapentin's clinical use in 1994 as an adjunct therapy for the treatment of partial seizures in adults with epilepsy. Gabapentin reduces neuronal excitability in patients with epilepsy. However, it is often prescribed for the management of neuropathic pain (ICD-10: M79.2), bipolar disorder (ICD-10: F31) and migraine (ICD-10: G43.909). Recently, Tubog et al. reported that gabapentin is effective in the management of postoperative pain in the first 24 h after surgery. However, there is a need for randomised clinical trials to assess the effectiveness of gabapentin in the management of chemotherapy-induced neuropathy.

Carbamazepine

Carbamazepine regulates the voltage-gated sodium channel, which results in an inhibition of action potential and reduced synaptic transmission. The FDA has approved it for acute manic and mixed episodes in bipolar disorder (ICD-10: F31. 2). Carbamazepine is used on an off-label basis for refractory schizophrenia (ICD-10: F20. 5), restless leg syndrome (ICD-10: G25.81) and severe alcohol withdrawal syndrome (ICD-10: F10. 239) among many others. Winkelmann et al. reported carbamazepine as one of the pharmacological agents that improve both positive and negative symptoms in schizophrenic patients.

Carbamazepine has been reported to be a tolerable and effective pharmacological agent for the treatment of restless leg syndrome. The treatment of neuropathic pain and fibromyalgia is another prominent off-label use of carbamazepine. Saeed et al. suggested that carbamazepine has clinically significant pain relief (in patients with diabetic neuropathy) with improved quality of life and good tolerability. Carbamazepine has been reported to have efficacy of carbamazepine in the treatment of agitation and aggression associated with dementia. However, the response to treatment is patient-dependent (patient-tailored treatment).

Imipramine and fluoxetine

Tertiary amine tricyclic antidepressants such as imipramine prevent norepinephrine and serotonin from being reabsorbed. Although imipramine is FDA approved for the treatment of depression (ICD- 10: F32. 9), it is now used on an off-label basis for the treatment of nocturnal enuresis (ICD- 10: F98. 02), panic disorder (ICD- 10: F41. 0), and neuropathic pain (ICD-10: M79. 2) to mention a few. Imipramine is a treatment option for children over the age of six who suffer from nocturnal enuresis.

Fluoxetine has been approved by the FDA for its significant effect in the management of major depressive disorder (ICD-10: F33.1) and obsessive–compulsive disorder (ICD-10: F42. 9). Unregistered uses for fluoxetine include social anxiety disorder (ICD- 10: F40. 10), post-traumatic disorder (ICD-10: F43.1) in adults borderline personality disorder (ICD- 10: F60. 3), and Raynaud phenomenon (ICD-10: I73. 0). Martin et al. reported the use of fluoxetine at a dosage of 20–80 mg is effective in the management of posttraumatic disorder. Fluoxetine has been reported to efficiently and effectively treat and prevent the relapse of PTSD symptoms. Sohel et al., confirm the tolerability of

fluoxetine (20 mg daily) and suggest that it would be effective as a novel treatment for Raynaud's phenomenon. Interestingly, Li et al., strongly suggested that the use of fluoxetine by males can counteract the contraction of the vas deferens, thereby, delaying ejaculation i.e. premature ejaculation.

Propranolol and timolol

B-adrenoreceptor antagonists, such as propranolol are registered for the treatment of cardiovascular failure (ICD- 10: I50. 9), atrial fibrillation (ICD- 10: I48.91), and coronary artery disease (ICD- 10: I25. 41) Propranolol can enhance the sympathetic response in angina and tachyarrhythmias while preventing acute ischemic attacks This it has been demonstrated to improve mortality and morbidity in individuals with hypertension complicated by heart failure, angina, or any history of previous myocardial infarctions.Shahrokhi and Gupta (2023), reported the use of propranolol at doses 40–120 mg a day in the treatment for restless leg syndrome. Propranolol (40–320 mg daily) can also be used for migraine prophylaxis. The therapeutic benefits may take up to 12 weeks to become apparent when using an adequate dose of the medication.

Timolol is a nonselective β-blocker that can be taken orally or topically. It is mainly used to diminish intraocular pressure in patients with open-angle glaucoma (ICD- 10: H40. 11) and ocular hypertension (ICD- 10: H40. 05). Timolol has likewise been displayed to successfully treat and limit slight, superficial juvenile hemangiomas (ICD-10: D18. 0). A study by Carcel et al., recommended the use of timolol, 10 mg twice daily, for the prophylactic treatment of migraines.

Wiysonge, reported timolol as an essential antihypertensive agent. The study showed that an average daily dosage of 15—30 mg will help achieve optimal levels of blood pressure with no significant side effects.

Atorvastatin

Atorvastatin is a lipid-lowering agent indicated for hypercholesterolaemia (ICD- 10: E78. 00), and prevention of cardiovascular disease. However, atorvastatin has been used on an off-label basis for chronic heart failure (ICD- 10: I50. 22), diabetic retinopathy (ICD- 10: E11. 319), prevention of atrial fibrillation, and rheumatoid arthritis (ICD- 10: M06. 9).

Advantages of off-label use of medicines

Prompt utilisation of new treatment options.

Off-label prescribing gives medical practitioners the freedom to promptly use new treatment options based on the latest evidence. This means medical practitioners can prescribe, albeit with certain restrictions or conditions, unapproved medicines relying mainly on the available scientific data and appropriate medical practice for certain conditions. For example, isosorbide dinitrate is often used to treat patients with acute strangulated internal haemorrhoids – thereby avoiding the risk of incontinence disorders after conventional surgical treatment. On the other hand, metformin, an effective fertility drug in non-obese women with polycystic ovary syndrome, has several advantages over other first-line treatments for non-ovulatory infertility such as clomiphene. For women who are resistant to clomiphene, metformin alone or in combination with clomiphene is an effective next step.

New and rare diseases

OLDU is useful in patients with rare diseases and may be the only treatment available.. Many anti-cancer drugs that were first approved to treat one type of cancer have been tried to treat another type of cancer. Numerous studies have found that off-label cancer drug use is more prevalent in regions where clinicians are located near clinical trial units. These studies further noted that off-label use increases by 85% when randomized controlled trials demonstrate that an off-label use of a cancer drug improves patient survival Mitomycin is indicated, for example, for the treatment of gastric and pancreatic cancers. In addition, it meets standard treatments approved for the management of lung, bladder, breast, cervical, and other carcinomas. However, it is not approved by the FDA for these additional indications.

Populations where medicines are needed but difficult to conduct research

The use of drugs outside of the package insert recommendations for indications, age, route, dose, and frequency is the most common definition of off-label use. Often, drugs may not have been studied and approved for a particular population, for example, in paediatric, geriatric or pregnant patients.

Obstetricians often prescribe medications for indications other than those listed on the product label.

Medicines such as nifedipine, isosorbide dinitrate, betamethasone, and aspirin are often used on an off-label basis among pregnant patients.
Another population that often benefits from OLDU is the geriatrics. In this group of patients, the effects of drugs are affected by age-related changes in pharmacokinetics, pharmacodynamics, and homeostasis, making them more susceptible to the side effects of drugs. Evidence shows that the use of drugs to support the effect is particularly important. In elderly care, prescribers should consider costs and choose the drug with the highest potential for success. The use of unapproved, non-indications of drugs can be safely carried out if the accepted practices are followed. However, it is advisable to notify the patient (or caregiver) that the drug is being prescribed without approval to avoid liability for later problems. This provides clear information about potential benefits, potential problems, and alternative treatment options.

Disadvantages

Insufficient evidence
In some cases, OLDU is practised in the absence of appropriate scientific data. For example, paclitaxel was originally approved for the treatment of ovarian cancer, but after published reports on breast cancer showed its effectiveness, it was used in the treatment of breast cancer years before regulatory approval for this indication.

Clinicians' non-disclosure
Discussions on off-label use of medicines are primarily conducted by consultants per specialty and clinical pharmacologists. Patients and patient caregivers are rarely involved in the most technical issue(s). This is unsatisfactory from an ethical point of view. The affected persons should know drug approval status including many other things. Patient knowledge and decisions regarding off-label treatment are especially important for alternative therapies where one drug is not approved, and the other drug is approved. But both alternatives are deemed equivalent from a medical point of view. From an ethical point of view, the ethical requirement of 'informed consent' means that patients should be informed of any pharmaceutical product used on an off-label basis. Therefore, clinicians are at risk of lawsuits due to the adverse effects associated with when medicines are used on an off-label basis. A study involving 46,021 patients at primary care clinics in Quebec, Canada, found that the rate of adverse drug events was 44% higher for OLDU compared to on-label use.

This finding held even after accounting for factors such as drug class, drug age, patient age and comorbidities, polypharmacy, and continuity of care. The legal theories used include the unregulated use of research drugs, the failure to obtain informed consent for OLDU, and medical malpractice.

Conclusion

It is not illegal for medical practitioners to use medicines on an off-label basis. However, it is illegal for pharmaceutical companies to promote drugs and their health products for off-label use. According to the FDA, approved medicines and/or devices advertised for unauthorised use have been incorrectly labelled or tampered with. Thus, discourages the distribution and/or advertisement by any pharmaceutical companies as this can be legally deemed misleading and non-factual. Some may believe that pharmaceutical companies provide transparency with regard to treatment choice, as opposed to the opinion that it poses a significant risk to public health and well-being.

The OLDU can be compared to a double-edged sword that can be utilised fruitfully by medical practitioners.
However, if there is uncertainty about the scientific relevance of off-label use, it can expose the patient to unauthorised experiments, unknown health risks and exposure to ineffective medicines. Therefore, there is an urgent need for guidance in South Africa on the regulatory framework for OLDU. Furthermore, timeous processing and approval of additional indications of medicines, where there is sound scientific evidence to do so, is needed. This will alleviate a heavy burden and possible risks that medical practitioners inherently carry when they compassionately use medicines on an off-label basis.

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On request.

Review Article

Herbal medicines and drug interactions: A growing concern in healthcare

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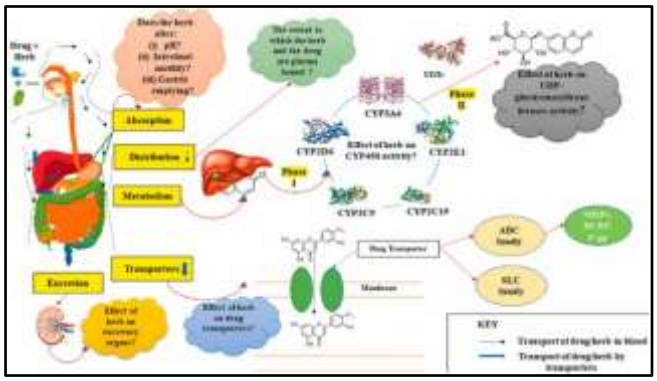

Introduction

"According to the World Health Organisation, herbal remedies are defined as finished, labelled pharmaceutical products that contain plant parts, airborne substances, or preparations derived from plants, whether in their raw form or as processed materials, or mixtures thereof". Juices, gums, fatty oils, essential oils, and any other similar things are considered to be plant material. Excipients may be added to herbal remedies in addition to the pharmaceutical active ingredients. The growing prevalence of herbal medical products (HMPs) in communities where prescription drugs are also widely used raises the possibility of serious public health consequences from unfavourable herb-drug interactions.

Herb-drug interactions have been identified by regulatory bodies around the world, including the Therapeutic Goods Administration, U.S. Food and Drug Administration, Medicines Control Agency, and the Medical Products Agency, as a significant safety concern. A lot of prescription medications and herbal remedies can be hazardous at certain doses while being beneficial at others. The pharmacological or toxicological effects of each constituent can be altered by the interaction of herbs and drugs. The synergistic therapeutic effects of long-term medications may make their administration more challenging. For example, herbs have historically been used to lower blood glucose levels in diabetics could potentially cause hypoglycemia if combined with traditional medications.

Herbal medications are widely used, but the scarcity of reported side effects and interactions is likely attributed to two factors: underreporting and the generally safe nature of the herbs commonly used. In the realm of herb-drug interactions, there is a dearth of experimental evidence, case reports are few, and case series are uncommon. "There is also a lack of data on drug-drug interactions, as most clinical studies on this topic are limited to case reports. Randomised controlled trials are scarce due to ethical concerns about intentionally assigning patients to studies that investigate potential adverse effects." Although significant, the actual frequency of medication interactions is unknown. A study of 1000 senior patients admitted to the hospital from the emergency room revealed alarming rates of drug-drug interactions.

Specifically, 538 patients (53.8%) experienced a total of 1087 drug-drug interactions, and notably, 30 patients (5.6% of those with interactions) suffered adverse effects as a direct result of these interactions. As of right now, the primary alternate method for carrying out research on Herbal Drugs is gathering real-world evidence through observational research. The data used to compile this proof came from actual sources such as

administrative claims databases, medical records, and polls. Real-world studies, especially those conducted at the population level, enable researchers to investigate the effects of herb-drug combinations outside of controlled settings, despite significant constraints. Observational studies are essential to fill in this knowledge gap by providing accurate data on the application, safety, and efficacy of HMs as well as investigating any potential therapeutic implications of any interactions with conventional medications. In order to assess the usefulness of practical data analysis in observational research examining the clinical implications of concurrent use of HMs and conventional drugs, this review article set out to address the lack of a comprehensive review that concentrates on real-world evidence of positive or negative effects from the combined use of HMs and conventional drugs in prior literature. This was primarily achieved by providing clarification on the selected data sources and study methodologies, as well as by indicating potential directions for more research.

Mechanism of Action of Herbal Drug Interaction

Drug-herb interaction is the same as pharmacokinetic and pharmacodynamic drug-drug interaction.

Pharmacokinetic interaction

It involves Absorption, Distribution, Metabolism, and Elimination of the drug molecule.

Absorption: Absorption means the process by which a drug moves from the administration site into the bloodstream. Herbal medication and drugs, when administered by the oral route, are absorbed into the blood through the gastrointestinal route, i.e stomach and intestine. The herbal constituents may alter the physicochemical environment of the stomach and intestine, such as changes in intestinal pH, complexing mechanism and intestinal motility, which leads to changes in the concentration of the drug that enters the bloodstream. For example, common ingredients in herbal weight loss products are laxative herbal constituents such as Aloe vera leaf, Guar gum and Senna, which may result in a decrease in the intestinal transit time and reduction of drug absorption. Mucilage and gum are water-soluble but poorly absorbable. The psyllium, rhubarb, flaxseed, marshmallow, and aloe are the gum and mucilage-containing plants that can bind to other various types of drugs and reduce their action. E.g. the absorption of lithium is inhibited by psyllium, rhubarb and Aloe vera can cause diarrhoea, resulting in a reduction of their action of drugs having a narrow therapeutic index. It can be avoided by taking the drugs one hour before or two hours after consumption of herbal medications.

Distribution: Distribution means the process by which a drug moves from the bloodstream to its target site in the body. Herbal constituents such as Meadowsweet and Black willow can bind to plasma proteins and contain pain-reducing salicylates. These herbs have the ability to dislocate highly protein-bound drugs such as carbamazepine and warfarin and increase serum drug levels. Thus, the adverse effects of these drugs are enhanced when taken concurrently.

Metabolism: The process by which the body breaks down a drug into a new form, called a metabolite. Upon entering the bloodstream, drugs undergo metabolism in the liver, where they are either converted into their active therapeutic forms or broken down and eliminated from the body. Herbal drugs have the ability to alter hepatic metabolism by induction or inhibition of liver enzymes. Thus, herbal medicament can alter the count of therapeutically active drugs in two ways: Enzyme Induction activity: the herbs have activity to stimulate the production and the activity of enzymes leading to degradation and elimination of drug residues from the plasma. It decreases the amount of drugs, e.g St. John's Wort, as it induces the activity of the cytochrome P450 enzymes. It could lower the concentration of warfarin, digoxin, protease inhibitors, theophylline, carbamazepine, etc., or the effectiveness of oral contraceptives.

The enzyme needed to break down the medicine may be inhibited by herbs, which would raise the drug's levels. While enzyme inhibition might happen in two to three days, the process of enzyme induction can take days or weeks. For instance, liquorice reduces the metabolism of corticosteroids, which can have harmful and toxic effects. According to an in vitro investigation, cytochrome P450 and the isoenzyme CYP3A4 may be inhibited by herbs such as chamomile and echinacea. Combining medications such as simvastatin, alprazolam, calcium-channel blockers, and protease inhibitors may result in negative side effects and elevated serum drug levels. P-glycoprotein and cytochrome P450 enzymes play a crucial role in drug metabolism and transport, affecting drug absorption, distribution, and elimination. Such as P-glycoprotein is an ATP-binding cassette (ABC) transporter found in various tissues, including the intestine, liver, kidney and

blood-brain barrier. Cytochrome P450 (CYP) Enzymes are a family of heme-containing enzymes primarily found in the liver and intestine, responsible for the metabolism of many drugs.

Elimination:

Elimination is the process by which the body removes a drug from the body. A few drugs are excreted through the renal route. The herbal medicaments may alter the renal function and may influence the drug level in the blood. The drug level found in blood may increase if the herbal medications reduce renal function, while it may decrease if the herb increases renal function. The serum drug levels are affected due to changes in excretion. E.g chronic liquorice consumption can interfere with antihypertensive and antiarrhythmic medications by causing hypokalaemia and water retention.

Pharmacodynamic interaction

Pharmacodynamic interactions occur when two or more substances (e.g., herbs, medications) affect the same biological pathway or mechanism, resulting in an altered response.

Additive interaction

Herbs can have an impact that is comparable to that of drugs and can intensify their effects. Therefore, using herbal sedatives, anticoagulants, and antihypertensives at the same time as prescription medications may enhance their effects. Combined effects of two substances, resulting in a response that is the sum of their individual effects.

Antagonistic interactions

This indicates that the herb may have the opposite effect of the drug, minimising the effects of the treatment. For example, ephedra and other herbs high in caffeine, such as cola nut, guarana, mate, and green tea, which are frequently used in weight-loss products, may oppose the effects of antihypertensive medications.

Synergistic

The desired effect of the drugs is enhanced when used together. For example, a combination of antihypertensives can be prescribed to reduce blood pressure.

Other Antihypertensive Medicines Interact with Herbs

Ephedra

This strong decongestant, which contains epinephrine, effectively widens bronchial passageways, but its potent stimulant properties can cause sleeplessness, elevated blood pressure, and other adverse effects, making it a contentious substance that should be avoided when taking cardiac medications or receiving treatment for glaucoma, thyroid issues, or hypertension.

Ginseng

This supplement is often adopted to help lower cholesterol, increase energy, improve stamina, and reduce stress. However, it can elicit feelings of anxiety and excitement, and excessive use may result in adverse effects such as headaches, sleeplessness, and palpitations. Additionally, it can raise blood pressure levels. Therefore, it is not recommended for individuals taking coumarin or high blood pressure medication.

Licorice

Used to cure stomach ulcers, colds, and coughs. Excessive dosages may cause potassium loss, water retention, and elevated blood pressure. Use caution while taking digoxin or diuretics together since this may induce further potassium loss, which is detrimental to heart health.

Cayenne Pepper

Reports of potential interactions between antihypertensive medication, which lowers blood pressure, and MAO inhibitors. When taken in excess, it may harm the kidneys and liver.

Implications of drugs that interact with herbs in drug development

Anticipating drug interactions with herbal supplements is difficult for drug scientists because of the general dearth of knowledge describing their pharmacologic activities and composition. Current understanding suggests that many herbal remedies must not be taken at the same time with many other drugs that are substrates for cytochrome P3A4 and P-glycoprotein. The dramatic increase in the use of herbal medicine worldwide means that many more patients on conventional medicines are being exposed to herbal medicines, so it is important to identify drugs in a timely manner that can interact with herbs. These drug interactions could pose a safety risk to drug scientists.

There is little information available about who is using these products and for what purposes, since they are unwilling or do not believe it is necessary to disclose to clinicians the kinds and dosages of

herbal treatments being used. Because of this, drug interactions with herbal remedies are probably more common than drug-drug interactions and are very likely to be greatly underreported and undervalued. The oxidative metabolism of more than 50% of currently prescribed pharmaceuticals involves CYP3A4; therefore, herbal medicines that activate this enzyme are likely to interact with a much greater number of medications than previously known. Only a very tiny percentage of currently marketed medications have been looked at for possible interactions with human botanicals like ginkgo and St. John's wort.

Therefore, more carefully thought-out clinical research is undoubtedly needed to learn more about how drugs interact with herbs. The crucial study of interactions between herbs and medications depends on the ability to accurately detect the presence of altered anabolism and transport, as well as the ability to measure the level of inter-mutualism and its scientific significance in drug development. The creation of novel compounds that are categorised as "strong drugs," or those that are not transported by P-gp or cytochrome-Ps, is one possible tactic to resolve undesirable drug interactions with herbal remedies. Ariens was the one who originally put up the idea of "hard drugs." These medications have easy kinetics of excretion through the kidney or bile because they are non-metabolizable. Their pharmacokinetics are therefore straightforward and typically predictable.

There will be much less chance of interactions when these medications are used in conjunction with natural medicines. If medications must be taken in addition to herbal therapies, there are situations in which reasonable drug usage is required. This establishes a safe protocol for combining drugs, modifying dosages, and discontinuing therapy when detrimental interactions occur between drugs and herbs. When used with drugs that enable continuous evaluation of plasma drug concentrations and related toxicities, herbs with a limited pharmacological index are recommended.

Risks Associated With Herb-Drug Interactions

Drug interactions typically result in a wide range of outcomes, from serious side effects, potentially deadly adverse effects, or even death. Regretfully, anecdotal data from misquoted published papers and misunderstandings have led to irrational inferences being made about the potential hazards associated with several herbal treatments. A case in point is the coumarin-containing herb *Melilotus officinalis*, also referred to as sweet clover. Initially, it was thought that the coumarin content of this herb caused bleeding disorders. [Jogi / International Journal of Pharmaceutical Chemistry and Analysis 2025;12 (1)].

But it was eventually found that dicoumarol, a molecule produced from coumarin by bacteria in hay that had been destroyed, was the cause of the illness. Sweet clover loses its anticoagulant properties when it is thoroughly dried because it does not contain dicoumarol. Even when the insufficient reporting of side effects in the herbal industry is taken into account, well-documented and credible examples of harm caused by the use of herbal medicines continue to be extremely few. However, there are safety concerns related to herbal medications that should be properly evaluated in light of reliable information. The inclusion of a distinct system for classifying the safety of herbal medicines, which primarily addresses pharmacokinetic herb-drug interactions. The significance of these interactions in assessing the safety of herbal products is emphasised in the second edition of the Botanical Safety Handbook by the American Herbal Product Association. When a therapeutic plasma level is raised above the maximum hazardous concentration or when its drug's plasma level is not reached, the pharmacokinetic herb-drug interaction severity is typically determined by these two factors.

Patients who use medications with limited therapeutic windows are more vulnerable since even slight variations in the blood levels of these medications might have harmful side effects or fail to produce the desired results. Furthermore, while using herbal remedies in addition to prescription medications, some circumstances and diseases could necessitate routine patient monitoring. The most susceptible patient groups are those receiving treatment with medications with low therapeutic indexes (such as theophylline, phenytoin, phenobarbital, warfarin, immunosuppressive drugs, digoxin, and certain antiretroviral drugs), patients with impaired hepatic and renal function, older persons, newborns, new mothers, organ transplant recipients, and those with specific genetic diseases. Some individuals are in particular need of additional and alternative therapies to either treat their conditions or lessen the adverse side effects of traditional medicines. Cancer patients are more susceptible in this sense because, compared to the general population, they take complementary and

alternative treatments more frequently. When undergoing chemotherapy, some cancer patients take up to eight herbal supplements.

Polypharmacy and complementary therapies, especially herbal remedies, are commonly linked. There is a higher chance of interactions when patients use multiple allopathic medications (polypharmacy) in addition to natural medications (occasionally, many herbal medications). Based on proven cases and clinical studies, it is interesting to note that only a small fraction of regularly used herbal medications are contraindicated for usage when used in combination with allopathic drugs, when taken in normal doses. In recent years, a number of reliable, scientifically supported sources have emerged to categorise herbal remedies according to how safe they are to take in addition to prescription medication.

Limitations of Herb-Drug Interaction

Case reports provide the majority of the information that is currently available regarding the interactions between herbal medicines and prescription medications. But now, clinical research is also starting to show up in the literature. Given that causality is rarely proven beyond a reasonable doubt, even case reports with documentation should be regarded with caution. In accordance with the Fugh-Berman and Ernst scoring system, 68.5% of the reported cases were classified as "unevaluable" (meaning that there was not enough information in the reports to determine the likelihood of an interaction), 18.5% as "possible" (meaning that the reports suggested an interaction but there might have been other factors contributing to the event), and 13% as "well documented" (meaning that the reports seemed to offer solid evidence for an interaction).

Misidentification, Adulteration, and Contamination

The composition of herbal items may not always be fully disclosed on their labels, and negative responses or interactions linked to particular herbs may really be the result of mislabelled plants, prescription medications, or heavy metals. Examining a "Siberian ginseng" (Eleutherococcus senticosus) product associated with a case of neonatal androgenization, for example, turned out to be Chinese silk vine (Periploca sepium), an unrelated species. Empathy and neuropathy linked to a Chinese herbal remedy allegedly prepared from long-dan-cao (Gentiana rigescens) roots in Hong Kong were demonstrated to be brought on by Podophyllum emodi, a distinct plant. Guangfang-ji (Aristolochia fangchi), a weight-loss supplement, was actually the source of more than 48 cases of renal toxicity that were reported to fang-ji (Stephania detrandra). Erythrolochic acid is known to be a nephrotoxin. In the latter instance, the Chinese names' similarity appears to have caused the error.

The mix of medications and "herbal" goods is an issue with Chinese patent medications. Two-thirds of the 2609 traditional Chinese medicine samples that were taken from eight Taiwanese hospitals contained pharmaceutical adulterants, the most common of which were caffeine, paracetamol, indomethacin, hydrochlorothiazide, and prednisolone. Non-steroidal anti-inflammatory medicines (NSAIDs) and benzodiazepines are included in several Chinese prescription medications that are distributed outside of Asia. Among these substances are Chuifong Toukuwan, Tung Shueh, and Miracle Herb. A number of formulations have been available since 1974; these include aminopyrine, hydrochlorothiazide, phenylbutazone, indomethacin, diazepam, diclofenac, mefenamic acid, and dexamethasone.

Heavy metal contamination is common in Asian herbal products. In California, USA, herbal shops yielded a total of 251 Asian patent medications with lead (at least 1 ppm), arsenic, and mercury.

Conclusion

With ramifications for both medicine and the economy, phytopharmaceuticals, or herbal medicine, are a subject of growing international interest. Most people agree that herbal medications are secure and efficient treatments. Because they think plant medicines have no negative side effects, people are therefore turning more and more to herbal medicine. On the other hand, medicinal plants may be hazardous on their own or in conjunction with other medicines. The adverse effects of herbal medicines can vary in severity, causing mild to severe side effects such as rashes and allergic responses, headaches, nausea, vomiting, and diarrhoea. Research indicates that there may be harmful side effects from herbal medications. According to a study, certain users of herbal medicines may have liver damage and kidney failure as a result of the dangerous interactions they have with other medications or the presence of heavy metals or toxic compounds.

References

Available on request

Appendices of quick guides to dug-interactions

Primary Health Care Drug-Drug Interactions: Printable Summary

Focussed on commonly used scheduled medicines in PHC. Evidense-based quick reference with numbered citations

Medicine / Class	Interacting Partners(s)	Type (PK/PD)s	Clinical Effect / Action (Refs)
ACE inhibitors (enalapril, lisinopril, perindopril)	Potassium salts, spironolactone; ARBS; NSAIDs	PD, PK/PD	Hyperkalaemia reduced antihypertensive effect and renal injury with NSAIDs. Check K+ creatinine, avoid chronic NSAIDs use {1,2]
ARBs (losartan, valsartan)	Potassium salts, spironolactone: NSAIDs	PD, PK/PD	Additive hyperkalaemia: reduced BP control /AKI with NSAIDs. Monitor K+, renal function [1,2]
Thiazide diuretic (HCTZ)	Lithium, corticosteroids	PK (renal clearance). PD	Increased lithium levels/toxicity, additive hypokalaemia and hyperglycaemia. Monitor lithium/K+ [1,3]
Beta-blockers (atenolol/propranolol)	Verapamil/diltiazem: insulin/sulfonylureas	PD	Bradycardia/AV block: masks hypoglycaemia symptoms. Avoid non-DHP CCB + beta-blocker combo [1,3]
Macrolides (erythromycin/clarithromycin)	Simvastatin/atorvastatin: theophylline, warfarin, QT-prolongers	PK 9CYP3A4 inhibition); PD	Increased statin/myopathy risk increased theophylline, increased INR, QT risk. Consider pravastatin/rosuvastatin, monitor. [4-7]
Rifampicin	Oral contraceptive: warfarin: many antiretrovirals; azoles; methadone	PK (potent induction)	Reduced exposure and failure of co-meds (e.g. QC failure). Adjust therapy/choose alternatives. [8-11]
Metronidazole	Alcohol; warfarin	PD: PK/PD	Disulfiram-like reaction, increased INR. Avoid alcohol; monitor INR [12,13]
Co-trimoxazole (TMP-SMX)	Warfarin; ACE/ARBs/spironolactone	PK; PD	Increased INR via CYP2C9 inhibitors, hyperkalaemia. Monitor INR and K+ [14-16]
Fluoroquinolones (ciprofloxacin)	Antacids/calcium/iron/magnesium, theophylline	PK (chelation CYP1A2)	Reduced antibiotic absorption (separate by 2-4h); increased theophylline toxicity [17,18]
Metformin	Cimetidine	PK (renal transport)	Increased metformin levels. Lactic acidosis risk (rare). Prefer alternatives or monitor [19]
Sulfonylureas (glibenclamide)	NSAIDs: warfarin; alcohol	PK/PD	Increased hypoglycaemia risk. Counsel; monitor glucose [3]
Insulin	Beta-blockers	PD	Masks adrenergic symptoms of hypoglycaemia. Educate patient [3]
NSAIDs (ibuprofen/diclofenac/naproxen)	ACE/ARB + diuretic (*triple whammy*); warfarin; SSRIs	PK/PD	AKI, loss of BP control; GI bleed esp. with warfarin/SSRIs. Avoid triple combo; gastroprotection if needed [2,20,21]
Paracetamol	Chronic alcohol; rifampicin; isoniazid	PK (Induction)	Increased hepatotoxicity risk: use lower max dose: monitor LFTs IF RISKS [22]
SSRIs (fluoxetine/sertraline)	Tramadol, linezolid/MAOIs; NSAIDs/warfarin	PD; PD/PK	Serotonin syndrome, increased bleeding. Avoid tramadol combo, monitor bleed risk. [22-25]
TCAs (amitriptyline)	Antihistamines; alcohol; antihypertensives	PD	Increased sedation, anticholinergic effects; orthostasis. Caution in elderly [3]
Benzodiazepines (diazepam)	Opioids; alcohol; antihistamines	PD	Additive respiratory depression. Avoid co=prescribing where possible [3]
Warfarin	Metronidazole; TMP-SMX; macrolides; azoles; NSAIDs; SSRIs	PK/PD	Increased INR and bleeding. Check INR within 3-5 days of changes, avoid NSADs [6,13-16,21]
Statins (simvastatin / atorvastatin)	Macrolides: azoles; amiodarone	PK (CYP3A4)	Increased statin exposure > myopathy. Prefer pravastatin/rosuvastatin [4-7]
Theophylline	Macrolides; ciprofloxacin	PK (CYP1A2)	Increased theophylline levels > toxicity. Consider alternatives, monitor. [18]
Salbutamol	Non-selective beta-blockers	PD (antagonism)	Reduces bronchodilation; avoid propranolol if possible [3]
Inhaled corticosteroids (budesonide / fluticasone)	Ritonavir; itraconazole	PK	Increased systemic steroid exposure (Cushingold). Prefer beclomethasone; avoid strong CYP3A inhibitors [27]

Supplements and Herbal Preparations: Drug–Interaction Quick Reference

Evidence-based (peer-review style) summary with numbered citations

Scope and Methods. This reference lists common supplements and herbal preparations with clinically meaningful interactions with scheduled medicines, prioritising agents with stronger human evidence and/or frequent reports (for example, antiplatelet effects or CYP/P-gp modulation). Evidence was drawn from peer-reviewed reviews, clinical trials, pharmacokinetic studies, case series, and reputable drug-interaction monographs. Numbers in square brackets refer to the full references in the References section.

Supplement / Herb	Mechanism (abridged)	High-risk co-medications	Expected clinical effect
St. John's Wort	Potent inducer of CYP3A4 and P-glycoprotein [1-5]	Oral contraceptives; immunosuppressants (cyclosporine, tacrolimus); anticoagulants; many CYP3A substrates including some HIV/chemo agents [1-6]	Decreased exposure leading to loss of efficacy (for example, transplant rejection, pregnancy, virologic failure) [1-4]
Ginkgo biloba	Antiplatelet/anticoagulant effects; possible pharmacokinetic interactions [7-10]	Warfarin/DOACs; antiplatelets (aspirin, clopidogrel); NSAIDs; SSRIs/SNRIs; antiepileptics [7-10;	Increased bleeding risk; rare seizure reports [7-10]
Ginseng (Panax spp.)	Hypoglycaemic effects; decreases warfarin effect; stimulant properties [11-13]	Insulin/oral hypoglycaemics; warfarin; MAOIs/stimulants [11-13]	Hypoglycaemia; reduced INR/anticoagulation; increased BP/HR [11-13]
Garlic (high dose)	Antiplatelet effects; possible enzyme induction [14-16]	Warfarin/DOACs; antiplatelets [14-16]	Increased bleeding risk; possible reduced exposure of some substrates [14-16]
Kava	CNS depression; hepatotoxicity signals [17-19]	Benzodiazepines, barbiturates, opioids, alcohol; hepatotoxic drugs [17-19]	Excess sedation; liver injury [17-19]
Valerian	GABAergic/sedative effects [20-21]	CNS depressants including benzodiazepines, barbiturates, opioids, sedating antihistamines, alcohol [20-21]	Additive sedation/respiratory depression [20-21]
Echinacea	Immunomodulation; mild CYP effects [22-24]	Immunosuppressants (cyclosporine, tacrolimus); selected chemo [22-24]	Reduced immunosuppression; variable pharmacokinetic effects [22-24]
Vitamin K	Directly antagonises vitamin K antagonists [25]	Warfarin, acenocoumarol [25]	Decreased anticoagulation leading to thrombosis risk [25]
Vitamin E (high dose)	Antiplatelet effects [26-27]	Warfarin/DOACs; antiplatelets [26-27]	Increased bleeding risk [26-27]
Fish Oil (high dose)	Antiplatelet effects at pharmacologic doses [28-29]	Anticoagulants/antiplatelets [28-29]	Increased bleeding tendency (usually modest) [28-29]
Iron salts	Chelates certain drugs in the gut; decreased absorption [30-33]	Tetracyclines, fluoroquinolones, levothyroxine, bisphosphonates [30-33]	Decreased exposure/efficacy of co-medication [30-33]
Calcium salts	Chelation/complexation; decreased absorption [30-33]	Tetracyclines, fluoroquinolones, levothyroxine, bisphosphonates [30-33]	Decreased exposure/efficacy of co-medication [30-33]
Magnesium salts	Chelation; electrolyte effects (digoxin risk) [30-34]	As for calcium + digoxin, some antiarrhythmics [30-34]	Decreased absorption; potential digoxin toxicity [30-34]
Saw Palmetto	Antiplatelet activity signals [35]	Anticoagulants/antiplatelets [35]	Increased bleeding risk [35]
Black Cohosh	Hepatotoxicity signals [36-37]	Hepatotoxic drugs (for example, statins, isoniazid, methotrexate) [36-37]	Increased liver injury risk [36-37]
Liquorice (glycyrrhizin)	Mineralocorticoid effects leading to hypokalaemia/hypertension [38-40]	Diuretics, corticosteroids, digoxin, antihypertensives [38-40]	Decreased potassium, arrhythmias; increased BP [38-40]
Evening Primrose Oil	Antiplatelet; lowers seizure threshold [41-42]	Anticoagulants/antiplatelets; antiepileptics [41-42]	Increased bleeding; seizures [41-42]
Yohimbine	Alpha-2 antagonist; sympathomimetic [43-44]	MAOIs; stimulants; antihypertensives [43-44]	Hypertensive crisis; tachycardia [43-44]

Clinical caution: Highest concern with narrow therapeutic index drugs (warfarin, digoxin, calcineurin inhibitors, antiepileptics, HIV/chemo agents). Always reconcile supplements and scheduled medicines; consider INR/drug-level monitoring when applicable.

Primary Health Care Drug–Drug Interactions

Category	Drug Combinations	Main Risk	Why it matters	PHC Action
Anticoagulation	Warfarin/DOAC + NSAIDs or aspirin/clopidogrel	Major bleeding	Additive antiplatelet + anticoagulant effect	Avoid chronic NSAIDs; use paracetamol; consider PPI; monitor
Anticoagulation	Warfarin + macrolides/azoles/quinolones	INR increases leading to bleeding	Enzyme inhibition	Check INR after start/stop; dose adjust
TB treatment	Rifampicin/rifapentine + oral contraceptives	Contraceptive failure	Enzyme induction	Use non-hormonal method; counsel
TB treatment	Rifampicin/rifapentine + warfarin	INR decreases leading to thrombosis	Enzyme induction	Frequent INR; increase dose if needed
TB/HIV	Rifampicin + many ART regimens	HIV under-treatment/toxicity	Enzyme induction	Check HIV-specific guidance; consider rifabutin
HIV (boosted)	Ritonavir/cobicistat + simvastatin/lovastatin	Myopathy/rhabdomyolysis	CYP3A4 inhibition	Avoid; use safer statin/dose
HIV (boosted)	Boosted ART + sedatives/antiarrhythmics/etc.	Toxicity or failure	Strong enzyme inhibition	Always check interaction list
Kidney risk	ACE-I/ARB + diuretic + NSAID	Acute kidney injury	Reduced renal perfusion + prostaglandin block	Avoid NSAIDs; hydrate; check creatinine
Electrolytes	Spironolactone/ACE-I/ARB + potassium supplements	Hyperkalaemia	Additive potassium retention	Avoid routine potassium; monitor potassium
Diabetes	Sulfonylurea + TMP-SMX or alcohol	Hypoglycaemia	Potentiated glucose-lowering	Monitor glucose; dose adjust
Diabetes	Metformin + dehydration/AKI-risk drugs	Lactic acidosis (rare)	Reduced clearance	Sick-day rules; pause if very ill
Psychiatry	SSRI/SNRI + NSAIDs/anticoagulants	Bleeding	Platelet inhibition	Avoid NSAIDs; consider PPI
QT risk	Multiple QT-prolonging drugs	Torsades de pointes	Additive QT prolongation	Avoid stacking; check ECG/electrolytes
Respiratory	Frequent beta-2 agonist + diuretics/steroids	Hypokalaemia	Potassium shifts	Check potassium if high dose
Absorption	Dairy/iron/calcium/antacids + tetracyclines/quinolones	Treatment failure	Chelation	Separate dosing by hours
Herbal	St John's Wort + many medicines	Treatment failure	Enzyme induction	Avoid unless approved
Herbal	Ginkgo/garlic/ginseng + anticoagulants/NSAIDs	Bleeding	Antiplatelet effects	Avoid; stop before procedures
Screen every patient for TB medicines, boosted HIV therapy, blood thinners, NSAIDs, and herbal/OTC products.				

Traffic-Light Quick Reference – 2025

Risk	Drug Combination	Main Concern	PHC Action
RED (Avoid)	Warfarin/DOAC + NSAIDs or aspirin/clopidogrel	Major bleeding	Avoid NSAIDs; use paracetamol; consider PPI; Monitor
RED (Avoid)	Ritonavir/cobicistat + simvastatin/lovastatin	Rhabdomyolysis	Contraindicated; switch statin
RED (Avoid)	ACE-I/ARB + diuretic + NSAID	Acute kidney injury	Avoid triple combo; stop NSAID
AMBER (Caution)	Warfarin + macrolides/azoles/quinolones	INR increase → bleeding	Check INR; dose adjust
AMBER (Caution)	Rifampicin + warfarin	INR decrease → thrombosis	Frequent INR; adjust dose
AMBER (Caution)	Sulfonylurea + TMP-SMX or alcohol	Hypoglycaemia	Monitor glucose; adjust dose
AMBER (Caution)	SSRI/SNRI + NSAIDs/anticoagulants	Bleeding	Avoid NSAIDs; consider PPI
AMBER (Caution)	Multiple QT-prolonging drugs	Torsades risk	Avoid stacking; ECG/electrolytes
GREEN (Usually OK)	Most antihypertensives + other chronic meds	Minimal interaction	Continue; routine monitoring
GREEN (Usually OK)	Metformin + most antibiotics (non-AKI)	Low interaction risk	Continue; apply sick-day rules
GREEN (Usually OK)	Inhaled respiratory meds + most chronic meds	Minimal interaction	Continue
Always screen for TB medicines, boosted HIV therapy, blood thinners, NSAIDs, and herbal/OTC products.			

QUESTIONNAIRE
G1(26) Part 1 of 6
Basic Pharmacology at a glance and the use and misuse of OTCs, prescription drugs and Supplements

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Introduction

Question 1: A drug's *primary* therapeutic action begins when it interacts with which biological target(s)?

- **A:** Receptors, enzymes, ion channels, and transport proteins
- **B:** Keratin, collagen, and elastin
- **C:** Red blood cells only
- **D:** Bone marrow only

Question 2: A clinician is explaining why patient response varies even when the same dose is prescribed. Which principle best supports this?

- **A:** Drug effect depends only on the labelled dose
- **B:** Drug effect depends on concentration reaching the site of action (shaped by ADME)
- **C:** Drug effect depends primarily on route of administration
- **D:** Drug effect is identical across individuals, unless the drug is administered IV

Question 3: A prescriber asks a colleague why two patients on the same dose can have different effects. Which combined concept best explains this?

- **A:** Pharmacodynamics and patient factors
- **B:** The pharmaceutical phase
- **C:** Pharmacokinetics (ADME), pharmacodynamics + patient factors (age, comorbidities, concomitant meds)
- **D:** Excretion that may be delayed

The pharmaceutical phase

Question 4: In the pharmaceutical phase, "disintegration" refers to:

- **A:** Chemical breakdown of the drug by liver enzymes
- **B:** Tablet/capsule rupturing into smaller granules after administration
- **C:** The rate at which the dosage form dissolves
- **D:** Binding of drug to plasma proteins

Question 5: Why is dissolution crucial in the pharmaceutical phase?

- **A:** Only dissolved drug molecules can cross biological membranes to be absorbed
- **B:** It determines whether a drug binds to receptors
- **C:** It converts a drug into its inactive metabolite
- **D:** It prevents first-pass metabolism

Question 6: The pharmaceutical phase primarily determines:

- **A:** How quickly and efficiently the active ingredient becomes available for the pharmacokinetic phase
- **B:** Which receptor the drug binds to
- **C:** Whether the drug will be excreted in urine or bile
- **D:** Whether the drug is an agonist or antagonist

Question 7: A patient reports that: "this tablet doesn't work as fast as the other one." Which concept best explains differences in onset related to the dosage form?

- **A:** Pharmacodynamics only
- **B:** Pharmaceutical (dissolution) phase influencing availability for absorption
- **C:** Genetic polymorphisms
- **D:** Therapeutic index

Question 8: You are counselling a patient about a delayed-release product. What is the key practical implication of delayed disintegration/dissolution?

- **A:** Faster onset than immediate release
- **B:** Slower availability for absorption → altered onset and timing of effect
- **C:** Avoidance of adverse effects
- **D:** No difference in clinical effect timing

Question 9: A patient crushes an oral controlled-release tablet to "make it work quicker." Based on the pharmaceutical phase, the main risk is:

- **A:** The drug becomes highly protein-bound
- **B:** Altered release/dissolution characteristics leading to unintended exposure
- **C:** The drug cannot be absorbed at all
- **D:** The drug is fully inactivated by the liver

Question 10: From a medication-safety perspective, why is dissolution clinically important for oral therapy?

- **A:** Only dissolved drug can be absorbed and reach systemic circulation
- **B:** Dissolution determines whether a drug is an agonist
- **C:** Dissolution prevents drug–drug interactions
- **D:** Dissolution guarantees no first-pass effect

Pharmacokinetics and pharmacodynamics

Question 11: A clinician teaching interns asks what ADME stands for. Which one of the following is correct?

- **A:** Absorption, Distribution, Metabolism, Excretion
- **B:** Administration, Diffusion, Metabolism, Elimination
- **C:** Absorption, Dissolution, Metabolism, Excretion
- **D:** Adsorption, Distribution, Modification, Excretion

Question 12: Which clinical lab consideration is explicitly discussed as useful for predicting drug absorption in the body?

- **A:** Serum sodium only
- **B:** Blood levels of liver enzymes as indicators
- **C:** ABO blood grouping
- **D:** ECG intervals

Question 13: TRUE or **FALSE.** Pharmacodynamics describes how the body absorbs, distributes, metabolises, and excretes a drug.

- **A:** TRUE
- **B:** FALSE

Question 14: Which statement best distinguishes pharmacokinetics (PK) from pharmacodynamics (PD) clinically?

- **A:** PK = what the drug does to the body; PD = what the body does to the drug
- **B:** PK = what the body does to the drug (ADME); PD = what the drug does to the body (effect/mechanism)
- **C:** PK applies only to injectables; PD applies only to orals
- **D:** PK is irrelevant to dose adjustment

Stages of pharmacokinetics
First pass effect

Question 15: A clinician chooses a non-oral route to avoid reduced active drug levels due to hepatic breakdown after absorption. What phenomenon is being avoided?

- **A:** Therapeutic index
- **B:** First-pass effect
- **C:** Depot binding
- **D:** Protein binding

Question 16: TRUE or **FALSE**. The document notes that oral/enteral medications may require several doses before enough “free drug” remains active due to the first-pass effect.

- **A:** TRUE
- **B:** FALSE

THE END

QUESTIONNAIRE
G1(26) Part 2 of 6
Basic Pharmacology at a glance and the use and misuse of OTCs, prescription drugs and Supplements

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Life-span considerations

Question 1: An older adult has reduced GI perfusion. What clinical impact is highlighted?

- **A:** Absorption of some medications may decrease
- **B:** Absorption of all medications increases
- **C:** First-pass effect is eliminated
- **D:** Rate of dissolution is irrelevant

Question 2: An older adult has decreased peripheral circulation. Which administration routes may show reduced absorption?

- **A:** Inhaled only
- **B:** Subcutaneous and intramuscular
- **C:** Rectal only
- **D:** Oral only

Distribution
Tissue differences

Question 3: Which of the following can affect blood flow and thus the delivery of medication?

- **A:** Dehydration
- **B:** Blocked vessels
- **C:** Heart failure
- **D:** None of the above

Question 4: A provider wants to know why a drug reaches the heart quickly but the CNS slowly. Which distribution factor is emphasised?

- **A:** Tissue blood flow and capillary permeability differences
- **B:** Tablet colour
- **C:** Patient mood state
- **D:** Presence of food only

Question 5: TRUE or **FALSE**. Only protein-bound drug crosses into tissues to produce pharmacological effects.

- **A:** TRUE
- **B:** FALSE

Question 6: A patient with liver disease has low albumin. What is the most clinically relevant implication?

- **A:** Increased protein binding always reduces free drug
- **B:** Lower albumin can change drug distribution/effects due to altered protein binding
- **C:** Low albumin prevents drugs from dissolving
- **D:** Low albumin eliminates the need for monitoring

Question 7: A patient is on warfarin and starts aspirin without telling anyone. What risk is highlighted?

- **A:** Reduced anticoagulant effect due to increased binding
- **B:** Increased free drug → increased anticoagulant effect → bleeding risk
- **C:** Guaranteed clotting due to antagonism
- **D:** No interaction because they bind different proteins

Question 8: Which statement best matches the text's explanation of protein binding as a "reservoir"?

- **A:** Protein binding makes all effects immediate
- **B:** Bound drug can be released slowly, prolonging action
- **C:** Bound drug is permanently inactive
- **D:** Protein binding prevents metabolism

Blood brain barrier

Question 9: A CNS-targeting medication must cross an additional barrier beyond protein binding. Which is it?

- **A:** Placental barrier
- **B:** Blood-brain barrier
- **C:** Alveolar barrier
- **D:** Hepatic barrier

Question 10: TRUE or **FALSE**. Lipid-based drugs or drugs with a "carrier" are more likely to cross the blood-brain barrier.

- **A:** TRUE
- **B:** FALSE

Metabolism

Question 11: In clinical terms, metabolism (biotransformation) is best described as:

- **A:** Movement of drug from plasma into tissues
- **B:** Breakdown of a drug molecule
- **C:** Release of drug from a capsule
- **D:** Binding of drug to receptors

Question 12: A prescriber explains a prodrug to a patient. Which statement aligns with the text?

- **A:** A prodrug is active as administered and needs no conversion
- **B:** Prodrugs improve a medication's effectiveness
- **C:** A prodrug cannot be absorbed
- **D:** A prodrug is always excreted unchanged

Question 13: A female patient has been taking the oral contraceptive tablet (parent) for several months. A week ago, she started taking St. John's Wort, a potent inducer of the P450 enzyme system. What will happen?

- **A:** Less metabolism of parent → more parent drug available
- **B:** More metabolism of parent → less parent drug available = risk of falling pregnant
- **C:** No effect on parent drug levels

Question 14: The text's "depot binding" example is most clinically similar to which phenomenon?

- **A:** THC stored in fat tissue with delayed release
- **B:** Insulin stored in bone marrow
- **C:** Warfarin stored in lungs
- **D:** Antibiotics stored in stomach acid

Question 15: TRUE or **FALSE**. Enzyme inhibition can raise parent drug levels and increase toxicity risk.

- **A:** TRUE
- **B:** FALSE

THE END

QUESTIONNAIRE
G1(26) Part 3 of 6
Basic Pharmacology at a glance and the use and misuse of OTCs, prescription drugs and Supplements

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Question 1: A patient has been taking simvastatin 40mg, one tablet daily for a number of years. The patient is prescribed cimetidine (an enzyme inhibitor) for reflux symptoms for one month. The prescription is repeated for three months as the patient will be going overseas for work shortly. Before leaving the patient asks a pharmacist to sell him the three packets as he would not be able to fill it where he is going. Against this background, which of the following statements are **TRUE?**

- **A:** The metabolism of cimetidine will be inhibited, leading to raised cimetidine level
- **B:** Simvastatin is not metabolised in the liver, and cimetidine will thus not affect it
- **C:** The metabolism of simvastatin will be inhibited, leading to raised simvastatin levels, and possible toxicity
- **D:** The patient may complain of the typical myopathy type symptoms associated with statin use

Question 2: Is it **TRUE** or **FALSE** that the half-life of a drug has very few clinical implications?

- **A:** TRUE
- **B:** FALSE

Question 3: A patient of yours has recently begun with an antihypertensive. After four weeks' treatment and very little response to treatment, you start checking compliance and eventually establish that the patient takes his tablet each morning between 7-8am with a glass of grapefruit juice. The patient takes another glass of grapefruit juice around mid-morning when he takes some vitamins and supplements. Is the grapefruit juice a reason why the antihypertensive does not achieve its desired effect?

- **A:** No, fruit juices have no effect of medicines taken
- **B:** Yes, grapefruit juice increased the acidity level in the GI tract and less medicine is absorbed
- **C:** Yes, grapefruit juice induces the metabolism of the antihypertensive rendering it less effective
- **D:** No, grapefruit juice enhances the dissolution of the tablet

Question 4: Besides urinary elimination, which excretion route is included in the text's examples?

- **A:** Hair
- **B:** Sweat or breast milk
- **C:** Nails
- **D:** Earwax

Life-span considerations

Question 5: A clinician is adjusting a dose in an older adult. Which rationale best fits the text's life-span considerations?

- **A:** Older adults absorb all drugs faster
- **B:** First-pass effect disappears in older adults
- **C:** Distribution is identical across all ages
- **D:** Reduced organ function can alter metabolism/excretion and thus dosing needs

Question 6: The "start low and go slow" approach in older adults is linked to:

- **A:** Increased absorption in older adults
- **B:** Guaranteed absence of side effects
- **C:** Reduced organ function affecting metabolism/excretion and dosing needs
- **D:** All the above

Pharmacodynamics

Question 7: TRUE or **FALSE**. An antagonist binds to a receptor and activates it to produce the intended effect.

- **A:** TRUE
- **B:** FALSE

Question 8: A clinician asks for a "mechanism of action" description. Which example aligns with the text's pharmacodynamics illustration?

- **A:** Magnesium citrate draws water into the bowel (osmotic effect)
- **B:** Magnesium citrate inhibits hepatic enzymes to prevent metabolism
- **C:** Magnesium citrate increases albumin binding to reduce free drug
- **D:** Magnesium citrate blocks the blood–brain barrier

Types of medication

Question 9: A medical practitioner counsels a patient worried about switching from brand to generic. Which statement is most consistent with the text?

- **A:** Generic drugs contain another active ingredient
- **B:** Generic drugs are always less effective
- **C:** Generic drugs cause less adverse effects
- **D:** Generic drugs contain the same active ingredient as the brand drug

Question 10: A patient reports intolerance after changing to a generic formulation. What explanation is supported?

- **A:** Excipients can differ and some patients may not tolerate them
- **B:** The active ingredient must have changed
- **C:** The blood–brain barrier became permeable
- **D:** The first-pass effect was eliminated

Question 11: **TRUE** or **FALSE**. The text states that herbals/supplements are regulated by the FDA and most have undergone rigorous scientific testing for safety

- **A:** TRUE
- **B:** FALSE

Efficacy, dose-response, onset, peak and duration

Question 12: A nurse explains "peak" levels when timing blood draws. Which definition best matches the text?

- **A:** Lowest serum level just before the next dose
- **B:** Time when tablet disintegrates
- **C:** Highest serum level after administration
- **D:** Time when metabolism begins

Question 13: A prescriber asks why a medication takes several doses to stabilise. What is "steady state"?

- **A:** When absorption stops
- **B:** When first-pass metabolism disappears
- **C:** When the drug has been metabolised
- **D:** When the amount of drug entering the systemic circulation equals drug eliminated → stable concentration

Therapeutic window

Question 14: When monitoring warfarin therapy, what concept explains the "safe and effective range" between ineffective and toxic dosing?

- **A:** First-pass effect
- **B:** Therapeutic window
- **C:** Depot binding
- **D:** Disintegration time

Question 15: A trough level for a titrated IV antibiotic should be drawn:

- **A:** Right before the next scheduled dose
- **B:** Immediately after the dose is given
- **C:** Only after the drug is fully excreted
- **D:** During tablet dissolution

THE END

QUESTIONNAIRE
G1(26) Part 4 of 6
Concurrent use of herbal and prescribed medicine by patients in primary health care clinics, South Africa

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Introduction

Question 1: South Africa categorises indigenous herbal medicine (HM) as which of the following?

- **A:** Complementary medicine (CM)
- **B:** African traditional medicine (ATM)
- **C:** Conventional medicine
- **D:** Homeopathy

Question 2: Approximately what proportion of the South African population uses herbal products for ailments/cultural practices?

- **A:** 5%–10%
- **B:** 20%–30%
- **C:** 40%–50%
- **D:** 60%–80%

Question 3: TRUE or **FALSE**: Indigenous knowledge (IK) is described as knowledge acquired outside the educational system.

- **A:** TRUE
- **B:** FALSE

Question 4: Which of the following is listed as a push factor towards using herbal medicine (HM)?

- **A:** Ingredient labelling
- **B:** Perceived lack of side effects
- **C:** Mandatory South African Health Products Regulatory Authority (SAHPRA) registration
- **D:** Inclusion in the national health care system

Question 5: Many herbal medicines are not registered by which South African authority?

- **A:** Health Professions Council of South Africa (HPCSA)
- **B:** The South African Medical Research Council (SAMRC)
- **C:** SAHPRA
- **D:** The Allied Health Professions Council of South Africa (AHPCSA)

Question 6: According to the WHO description, herbal medicine (HM) includes which of the following?

- **A:** Only purified single-molecule extracts
- **B:** Herbs, herbal materials/preparations, and finished products containing plants as active constituents
- **C:** Only OTC products dispensed in pharmacies
- **D:** Only products prescribed by medical practitioners

Question 7: Herbs may contain more than how many active ingredients that could affect pharmacokinetics and cause adverse effects?

- **A:** 10
- **B:** 25
- **C:** 50
- **D:** 15

Question 8: TRUE or **FALSE. "**Coagulation abnormalities" are listed among possible adverse effects linked to herbal medicines.

- **A:** TRUE
- **B:** FALSE

Question 9: Which prescribed medicine classes are explicitly mentioned as being complemented with HM by "desperate patients"?

- **A:** Propulsive and anti-propulsives
- **B:** Antibiotics
- **C:** Antihypertensive, hypoglycaemic, antiarrhythmic, anticoagulant, antiretroviral, and antidepressants
- **D:** Analgesics and antipyretics

Question 10: Which set of herbal products is specifically listed as having evident interactions in patients taking warfarin/insulin/aspirin/statins?

- **A:** Sage, flaxseed, cranberry, camellia sinensis, hypericum perforatum, ginkgo biloba, matricaria chamomile
- **B:** Aloe vera, echinacea, ginger, turmeric, valerian, peppermint, rosemary
- **C:** Garlic, ginseng, kava, liquorice, saw palmetto, yohimbine, oregano
- **D:** Only Hypericum perforatum and ginkgo biloba

Question 11: Warfarin can interact with ginkgo biloba and hypericum perforatum leading to which of the following **TWO**?

- **A:** Increased sedation
- **B:** Increased bleeding
- **C:** Reduced anticoagulant effect (clotting)
- **D:** Reduced absorption of warfarin with no clinical impact

Question 12: TRUE or **FALSE** Non-disclosure of HM use prevents discussion/recording/prevention of potential herb–drug interactions (HDIs) by healthcare providers.

- **A:** TRUE
- **B:** FALSE

Question 13: The study notes that respondents commonly began using HM after recommendation by:

- **A:** Medical practitioners
- **B:** People with personal experience and television advertisements
- **C:** Nurses during chronic care visits only
- **D:** All the above

Natural product pharmacology

Question 14: The natural product pharmacology piece describes natural products (NPs) as a rich source of:

- **A:** Inert excipients
- **B:** Bioactive compounds for drug development
- **C:** Only vitamins and minerals
- **D:** Synthetic analogues exclusively

Question 15: The editorial review highlights key points from which guide?

- **A:** The 2010 WHO essential medicines list
- **B:** The 2020 British Journal of Pharmacology (BJP) practical guide
- **C:** The 1996 Medicines Act guidance note
- **D:** The 2023 FDA black box warning compendium

THE END

QUESTIONNAIRE
G1(26) Part 5 of 6
Concurrent use of herbal and prescribed medicine by patients in primary health care clinics, South Africa

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Question 1: The introduction notes that past natural product research faced challenges particularly regarding:

- **A:** Pricing and reimbursement
- **B:** Isolation, identification, and synthesis
- **C:** Patient consent procedures
- **D:** Hospital formulary design

Question 2: Recent technological developments include which of the following combinations?

- **A:** Advanced analytical tools, multi-omics, sophisticated synthesising strategies, refined microbial culturing
- **B:** Improved hospital acceptance
- **C:** Ease of manufacturing
- **D:** All the above

Question 3: Which therapeutic discovery areas are explicitly mentioned as examples where natural products remain crucial?

- **A:** Dermatology
- **B:** Antimicrobials, anticancer agents, anti-inflammatory compounds
- **C:** Antacids
- **D:** Vaccine

Question 4: The document positions the 2020 BJP guide primarily as a standard for:

- **A:** Transparent reporting on natural product pharmacological research
- **B:** Off-label prescribing
- **C:** Diagnosing adverse drug reactions
- **D:** All the above

Off-label use of medicines in South Africa: A review

Question 5: In the off-label review, its use is described as being common in which of the following area specialties?

- **A:** Orthopaedics
- **B:** Oncology
- **C:** Dentistry
- **D:** Ophthalmology

Question 6: The South African law mentioned as giving SAHPRA powers to assess evidence and register medicines is:

- **A:** Medicines and Related Substances Act 101 of 1965 (as amended)
- **B:** POPIA 4 of 2013
- **C:** National Health Act 61 of 2003
- **D:** Pharmacy Act 53 of 1974

Question 7: TRUE/FALSE. There were significant concerns regarding the off-label use of pentazocine among paediatric surgical patients in Nigeria, with most children experiencing between two and seven adverse effects.

- **A:** TRUE
- **B:** FALSE

Question 8: Which international regulators are named as using criteria similar to that of SAHPRA?

- **A:** EMA and MHRA
- **B:** FDA (USA) and TGA (Australia)
- **C:** CDC and WHO
- **D:** NIH and CDC

Question 9: Off-label drug use (OLDU) is explained as prescribing medicines for:

- **A:** Only paediatric patients
- **B:** Only hospital inpatients
- **C:** Additional indications not registered/approved by regulators
- **D:** A number of “listed” conditions

Question 10: Which of the following statements are **TRUE?**

- **A:** Gabapentin is often prescribed for the management of neuropathic pain, bipolar disorder and migraine
- **B:** *Tubog et al*. recently reported that gabapentin is effective in the management of postoperative pain in the first 24 h after surgery
- **C:** Carbamazepine is NOT used off-label for the treatment of restless leg syndrome
- **D:** Carbamazepine has been reported to have efficacy in the treatment of agitation and aggression associated with dementia, however response to treatment is patient-dependent

Question 11: Unregistered uses for fluoxetine include:

- **A:** Social anxiety disorder
- **B:** PTSD in adults
- **C:** Borderline personality disorder
- **D:** Schizophrenia

Question 12: TRUE/FALSE. *Li et al*. strongly suggested that the use of fluoxetine by males can counteract the contraction of the vas deferens, thereby delaying ejaculation, i.e. premature ejaculation.

- **A:** TRUE
- **B:** FALSE

Question 13: Atorvastatin has been used off-label for ……..?

- **A:** Chronic heart failure
- **B:** Diabetic retinopathy
- **C:** Impotence
- **D:** Rheumatoid arthritis

Question 14: According to the conclusion, what is stated as illegal?

- **A:** Clinicians promoting off-label use, instead of prescribing medicines indicated and approved for that particular condition
- **B:** Pharmacists dispensing medicines for off-label use
- **C:** Pharmaceutical companies promoting drugs for off-label use
- **D:** None of the above

Question 15: OLDU ……?

- **A:** Gives medical practitioners the freedom to promptly use new treatment options based on the latest evidence
- **B:** Is not useful in patients with rare disease
- **C:** May benefit the geriatric population
- **D:** All the above

THE END

QUESTIONNAIRE
G1(26) Part 6 of 6
Concurrent use of herbal and prescribed medicine by patients in primary health care clinics, South Africa

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer**; in which case you must mark all the correct answers.

Question 1: Regarding off-label use:

- **A:** For women who are resistant to clomiphene, metformin alone or in combination with clomiphene is an effective next step
- **B:** Mitomycin is used for the management of lung, bladder, breast, cervical and other carcinomas
- **C:** Nifedipine, betamethasone and aspirin are often used for pregnant patients
- **D:** None of the above

Question 2: The conclusion compares OLDU to:

- **A:** A "single-use tool"
- **B:** A double-edged sword
- **C:** A dangerous practice
- **D:** An experimental activity that is prohibited

Question 3: The conclusion states there is an urgent need in South Africa for:

- **A:** Guidance on the regulatory framework for OLDU
- **B:** More direct-to-consumer advertising
- **C:** Timeous processing and approval of additional indications where there is sound scientific evidence to so
- **D:** Replacing SAHPRA with the SAMRC for OLDU approvals

Herbal medicines and drug interactions: A growing concern in healthcare

Question 4: TRUE/FALSE. The herbal-interactions article defines herbal remedies (per WHO) as finished, labelled pharmaceutical products containing plant parts/materials or plant-derived preparations/mixtures.

- **A:** TRUE
- **B:** FALSE

Question 5: Which of the following statements are **TRUE** regarding herbal medicines?

- **A:** Widely used, but a scarcity of reported side effects and interactions
- **B:** Underreporting of side- and adverse effects
- **C:** There are many case reports, but few randomised, controlled trials
- **D:** All the above

Question 6: The text provides an example that herbs used to lower blood glucose in diabetics could potentially cause which issue if combined with traditional medications?

- **A:** Hyperglycaemia
- **B:** Hypoglycaemia
- **C:** Hypertension
- **D:** Arrhythmia

Mechanism of action of herbal drug interactions

Question 7: With reference to absorption ……?

- **A:** Herbal weight loss products containing aloe vera and senna, can result in a decrease in intestinal transit time and the reduction in absorption of other drugs
- **B:** The absorption of lithium is inhibited by psyllium, rhubarb and aloe vera
- **C:** It is not useful to take a herbal medicine two hours before or after administration of a scheduled medicine
- **D:** None of the above

Question 8: The herbal constituents meadowsweet and black willow ……..?

- **A:** Contain pain reducing salicylates
- **B:** Is highly protein bound
- **C:** Has the ability to displace other highly protein bound drugs, such as carbamazepine and warfarin
- **D:** Is well studied through double-blind trials

Question 9: Regarding metabolism ……?

- **A:** Herbals do not have the ability to inhibit or induce the metabolism of parent (other) drugs
- **B:** St. John's Wort is an enzyme inducer, and can lower the concentration of drugs such as warfarin, carbamazepine, the oral contraceptive pill and other
- **C:** Enzyme inhibition manifests quicker than enzyme induction
- **D:** Chamomile and echinacea can inhibit liver enzymes

Question 10: Which of the following statements are **TRUE?**

- **A:** Chronic liquorice consumption can interfere with antihypertensive and antiarrhythmic medication by causing hypokalaemia and water retention
- **B:** Ephedra and other herbs high in caffeine, such as green tea, may oppose the effects of antihypertensive medication
- **C:** Herbal preparations seldom result in a response that is the sum of their individual effects
- **D:** All the above

Question 11: Ephedra ……?

- **A:** Is a strong decongestant and contains epinephrine
- **B:** Effectively widens bronchial passageways
- **C:** Does not cause elevated blood pressure, or sleeplessness
- **D:** Should be avoided when taking treatment for glaucoma, thyroid or hypertension

Risks associated with herb-drug interactions

Question 12: Susceptible patient groups are those …….. ?

- **A:** Who use medicines with a broad therapeutic range
- **B:** With impaired renal and hepatic function
- **C:** Who is older
- **D:** Who are being treated for cancer

Question 13: TRUE/FALSE. The herbal-interactions text states that NSAIDs and benzodiazepines are included in several Chinese prescription medications distributed outside Asia.

- **A:** TRUE
- **B:** FALSE

Question 14: The text mentions heavy metal contamination in Asian herbal products, with examples including:

- **A:** Iron and calcium only
- **B:** Lead, arsenic, and mercury
- **C:** Sodium and potassium
- **D:** Chloride and bicarbonate

Question 15: (TRUE/FALSE): The document includes an "Appendices of quick guides to dug-interactions" section in Part 2.

- **A:** TRUE
- **B:** FALSE

THE END