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ECPHARMACOLOGYANDTOXICOLOGY
Review Article

Poison-Drug Enigma

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Received: April 23, 2018; **Published:** June 19, 2018

Abstract

In the past poisons were considered harmful biological chemicals secreted by plants and animals. These poisons produced a number of medicinal remedies that later evolved to become drugs we know today. These drugs were usually considered harmless substances, but in reality, even a drug can become a poison. Initially, scientist thought that only dose greater than therapeutic range can convert it into a poison, but recent researches changed this former concept and highlighted various other contributing factors. In order to counter all these factors, we need to assess keenly these poisonous agents biologically and clinically to be used effectively.

Keywords: *Drug; Poison; Dose; Organ Response; Interactions; Otc Drugs*

Introduction

Fossil records shows around the time when dinosaurs went extinct number of plant species that exist were few. At that time only wind and air pollinated flowers like ferns and cycads and few insect species (cockroaches and dragonlies) which did not need flowers were present. Then suddenly plants started using insects for pollination and flowers of different shapes and colors evolved. With this abundant and diverse food source of plants, insects exploded themselves in diversity.

As new insect spp. was plant eaters, so plants developed chemical compounds to protect them some of them acted like poisons while other repellents. Then humans started using them as food spice, medicinal plants, poisons etc. Lily (*Scadoxus puniceus*) belongs to Amarylis family consist of many poisonous plants like *Clivia* and *Crinum* but still bulb of plant was used in traditional medicine for the treatment of cough, gastrointestinal problems as well as for safe delivery which indicate a fine line between medicine and poison.

"A pill for every ill" is a common call of pharmacist and physicians. It is very true as there is a pill for every ill and many pills are under the way of discovery. Many active researchers are searching solutions of the unsolved medical conditions. Although drugs are saving lives of living beings around the globe, they are also the cause of many deaths.

A drug can be utilized in one way or the other for example, one pill to have babies while the other to prevent them, some are responsible for baldness while other to grow hair etc. People are using them on the basis of daily advertisements and recommendations from friends. However, a drug can only produce beneficial effects under favorable conditions but also have both harmful as well as healthy effects at the same time as we can see this in the case of NSAIDs (non-steroidal anti-inflammatory drugs) that act as anti-inflammatory agent but also ulcer causing agent. So, improper use of a drug makes them unhealthy and poisonous.

Practically, it is observed that the entire nature of a human body is to maintain a state of equilibrium i.e., homeostasis. Whereas diseased state is characterized by breaking of this equilibrium. A drug helps to restore this balance, but it shows unintended off-target side-effects either using same doses or higher doses. In health care system biological chemicals interrupting homeostasis are considered as Poisons.

Poisons can also be used as drugs for example many chemotherapeutic agents are fighting against undesirable cell but on the other hand tend to kill off healthy dividing cells. Normally term poison evoke thoughts of murder and mayham but for centuries healers and scientists have shown the power of toxins, poisons and venoms to be utilized as medicine.

Poisons are also in practice for good. Anticoagulants tyrofabin and hirudin derived from animal resources. The diabetes drug Exenatide lowers blood sugar and increases insulin production a synthetic version of an important component found in saliva of a lizard.

Drug-or Poison Overlapping Medical Terms

Drugs and medicine are two overlapping medical terms like side effects and adverse effects. Medicine are used with intent to cure imparts positive effects where as a drug can have positive or negative effects. Similarly, poison and drug are overlapping though independent terms.

Therapeutic window gives a range of doses (sub dose, therapeutic dose, overdose) in a biological system providing safe effective therapy. Therapeutic window is a ratio between minimum effective concentration (MEC) and minimum toxic concentration (MTC). It is the therapeutic dose at which a biological chemical can cure and give expected effects while at overdose can be lethal and is often termed as Poison.

Poisons act by gradually affecting the organs by clotting of blood or clumping blood vessels and result in loss of motor and sensory nervous system however, drugs (overdose/addict dose) act slowly by weakening immune system.

Any chemical substance (natural or synthetic) capable of producing psychological and physiological effects is a drug, on contrary poison is capable of causing illness and even death when enters or absorbed. So, we can say neither all drugs are poisonous, nor all poisonous substances are drugs. Fentanyl is an example of a medical purpose drug which can technically poison. Similarly, heroin a recreation and an illicit drug never prescribed by physician can technically poison when taken in large doses. Besides above mentioned even many prescription drugs are too potentially dangerous to many organs of the body (kidney, heart, liver) so considered to be a poison without causing death.

So, can we call a drug a poison? the answer is if medications or chemical substances when taken with intent to produce harm is classified as poison but if taken with the intent to provide health benefit is considered as a drug.

Poisons	Effects	Occurence
Arsenic	Cause and cure cancer, Poisonous in high doses, Treat blood cancer acute promyelocytic leukemia, Also, a part of chemotherapy drug anthracyclins,	Pesticides, building products
Foxglove	Strengthen the heart, controls rhythm, improves circulation, poisonous leaves cause low blood pressure, irregular heartbeat	Biennial plant, tall dramatic spikes of tubular flowers
Radiations	Murder the cancer cells Damage the DNA of cancer cells Lethal in high doses (blistering and darkening of skin,)	High energy radiations, X-ray, gamma rays, radioactive substances
Yew Plant	Potentially toxic treatment of cancer is in yew tree, poisonous to humans, contain a chemical to treat lung and breast cancer at cellular level Paclitaxel – treat lung, breast, AIDS related kaposi's sarcoma	Seeds, leaves, bark
Mercury	In past used to prepare remedies like teething powder, infant's purgative formula	
Botulinum toxin - Botox	Respiratory failure. It is a neurotoxin - enters the nerves and destroys vital proteins.	Bacteria

Table 1: *Medicinally Active Poisons used in Cancer Therapy and Heart Diseases.*

Dietary Poisons

Sugar makes things sweet and taste better and people if try to cut back on sugar experience withdrawal because it causes overstimulation of reward centres of our brain with the release of dopamine and as a result people become addicted to sugar just like cocaine/heroin. Consumption of sugar is on the rise around the world in the form of soda and drinks. But only six teaspoons of sugar are sufficient for woman and nine teaspoons are healthy for men. Sugar is the major cause of obesity.

Added sugar is also a poison having no nutritional value lacking essential proteins, minerals and vitamins. Added sugar being toxic in nature effects our metabolism ultimately link to many diseases. High fructose corn syrup is the biggest culprit and is a part of many canned products, peanut butter, salads, dressings etc. It is better to go for natural source of sugar present in fruits rather in processed foods.

Very commonly used tomatoes (Amygdalin, 0.6 gm/kg of seed), potatoes (Solanin, 0.2 gm/kg), Pears (Formaldehyde, 0.06g/kg), Courgettes (Cucurbitacin E, variable) do have toxic compounds.

Apitherapy-Poison as Medicine

There are multiple references available in science when poisons are used as medicines. Bees and many species of order hymenoptera (ants, jelly fish and wasps) have few specific compounds in their venom 29 amino acid peptide called melitten that gives body a burning sensation. At high temperature body releases inflammatory compounds by activating certain channels like TRPV1 in sensory neurons melitten follows the same path. Tradition of using toxins as medicine is centuries old in many cultures like Chinese, Indian, romans and has treated many diseases from eczema, epilepsy to stop bleeding (steppe viper venom). Melitten is now utilized as potent antimicrobial agent and scientist are working to utilize it in HIV patients because of its ability to pop up cells (as virus needs protective coating to be effective).

The terrible and tremendous power of venoms consisting of cocktail of compounds of proteins, peptides and many more chemical constituents, the content of these cocktails depend upon many factors such as how the animal uses them i.e. immobilization, defence etc. and other factors for example location, age, diet etc.

Pharmaceuticals derived from venom

Captopril peptide present in venom of Brazilian viper (*Bothrops jararaca*) with potent blood thinning ability which is a first oral ACE (Angiotensin converting enzyme)-inhibitor to treat hypertension.

Byetta/Exenatide from the venom of lizard the gila monster to treat Type 2 diabetes to stimulate release of insulin and reduces the sugar overproduction as well as reverses the hormonal changes by diseases.

It takes a long way to develop a safe and working medicine even after discovery. It requires large volume of venom but at the moment only snake is among the venomous species from which venom can be extracted in large amount. Currently work is being done to find advance techniques of extracting small amount of venom. Many scientists believe that there are solutions to many neurological problems lies in venoms. Various species containing venom exist on this planet like venomous primates, venomous snails but many become extinct every year the safest way to preserve these species lies in conservation through commercialization as it's a resource and is important economically [1].

Specie	Cure	Cause	Stages of Clinical Trials	References
Pufferfish spiky fish	Chronic pain Toxin 3000 times more potent than morphine Cancelling chemopain	Tetrodotoxin target nervous system result in fatal paralysis of muscles that control breathing and heart rate	Before approval from FDA are under comparative study with existing chemotherapeutic agents	[2]
Shark skin	Making bacteria feel unwelcome Urinary catheters mimic the texture of shark skin ward of microbes like staphylococcus aureus, methicillin resistant staphylococcus aureus, pseudomonas aeruginosa		Companies are making medical devices	
King cobra	Pain reliever, 20 to 200 times more potent than morphine	Can kill human	Animal testing: mice experienced twice the thermal pain	
Tick burries in flesh, spits saliva	Clearing up clots Drug 70 times more potent than natural blood thinning agents in the body		Tested successfully in animal and require bit more evidence and will enter in human trials	
Sea anemone	Retraining immune cells. Treat autoimmune diseases	Compound ShK-186 affects potassium channels in body, regulate metabolism and treat obesity	Toxin inspired drug is in first phase of clinical trials	
Fire bellied toad	Healing wounds Secrete venom laced sweat when provoked but certain proteins in perspiration will heal wounds. Peptide promote growth of blood vessel. A drug using this toxin cure scar		Potential drug patented in china and USA and about to enter in human trials	
Waxy-monkey Frog Toxin is embedded in skin	Keeping blood vessels in check. Frog's venom control blood vessel growth known as angiogenesis Antiangiogenic properties are useful to treat diabetes related blindness		Set for human trials within a year	

***Table 2**: Poison to Potion.*

Supplements are safe or poisonous?

Often due to side effects people turn away from pharmaceuticals and start placing there hope in the curative powers of drugs of natural origin e.g. herbs or vitamins and minerals.

Vitamins and Minerals

Various evidence shows when people become sick using vitamin overdoses. If these agents have power to heal then they must be powerful enough to cause harm. Now an authority in almost every country is trying to regulate these drugs as well. We should consider all the claims and counter claims related to this.

Vitamin E is found safe when taken in doses of 400 I.U. daily but is not recommended without prescription for people with high blood pressure as it strengthens the heart muscle ultimately pumps large volume of blood and have stronger contractions. Similarly, diabetics should also use in modest doses as it improves glucose tolerance, so insulin intake must be reduced.

Vitamin A nutritional component of beef liver, sweet potatoes, carrots etc., although used for smooth healthy glowing skin but also act as a poison. Science has linked taking vitamin A with better health and lowering incidence of diseases even like cancer but still it is more known for poisonings. As it is Fat soluble so store in the body like other fat-soluble vitamin i.e., D, E, K. Its poisoning effects are not only from supplements but also from eating raw food like eating liver of a polar bear having high content of Vitamin A. Similar cases are seen in children when fed with fish or chicken liver excessively. Vitamin D a sunshine vitamin used to treat rickets but cause hypercalcemia when taken in higher doses.

S/No.	Vitamin	Max daily dosage
1.	A	25,000 I.U.
2.	Thiamine (B1)	25 mg
3.	Riboflavin (B2)	25 mg
4.	Niacin	50 mg
5.	B6	50 mg
6.	B12	25 mcg
7.	Folate	800-1,200 mcg
8.	C	1,000 mg
9.	D	500 I.U.
10.	E	600 I.U.
11.	Calcium	1,200 mg
12.	Chromium	200 mcg
13.	Iron	30 mg
14.	Magnesium	400 mg
15.	Selenium	200 mcg
16.	Zinc	35 mg

Table 3*: Safe limits for Supplements.*

Spell of Herbs

Health effects of many herbs are well known as they have occupied a space in modern pharmaceuticals either consist of plant parts or their chemical copies for example anesthetics, quinine, aspirin, morphine, reserpine, digitalis and various anticancer agents like vincristine and vinblastine.

Besides healthy effects certain herbs do have dangerous effects such as comfrey (liver cancer). Garlic is also a potent herb against atherosclerosis. Recent revolution is trying to merge synthetic with the natural and scientists are showing interest in exploring plant species on earth that remain untested. But still self-medication using herbs are not safe due to lack of complete information. These should also be utilized with thought. These days' Chinese herbs are occupying space on the shelves of health food stores as Chinese herbology is thousands of years old. There is a long list of dangerous herbs some are enlisted below.

Herbs	Poisonous	Refferences
Aconite	Queen mother of poisons	Using medicines wisly, The Prevention Total Health System, Chp: "Drugs" at the Health Food Store)
Aloe	Fresh juice is safe for wounds/burns but internally toxic cause purge	
Angelica	Devilish nature,carcinogens,induce abortion	
Arnica	Toxic to heart	
Belladonna	Poisonous	
Bittersweet	Just two berries to kill	
Blue cohosh	Cannot safely used to stimulate menstruation and child birth and toxic to heart muscles and intestines	
Broom	Slows heart beat & dangerous drug	
Calamus	Heart and liver damage	
Celandine	Cause severe stomach and intestine irritation even death	
Coltsfoot	Toxins cause liver cancer	
Henbane	Poison cause racing heart beat	
Juniper	Effective in tiny doses but cause kidney damage when repeated doses	
Life root	Ease child birth pain but damage liver	
Lobelia	Helps in Weight loss but fatal and deadly	
Mandrake	European type destroys heart and American intestines	
Mistletoe	Berries and leaves cause agonizing disruption of heart beat and eventually death	
Strychnine	Poisoning moles	
Periwinkle	Valuable source of modern drugs but depresses bone marrow functions	
Tonka beans	Interfere with blood clotting	
Wormwood	CNS depressant causes stupor, convulsions	

Table 4: *List of Dangerous Herbs.*

Plants and animals are constantly manufacturing a large complex compound in light as well as in darkness. Nature itself is a laboratory synthesizing compounds beneficial not only for producer but also for human for example. Artemisinin antimalarial drug derived from a sweet wormwood herb *Artemisia annua*, salicylic acid important component of aspirin found in willow tree *Salix alba* etc.

Microbes are too busy in creating antibiotics to fight against various types of infections similarly, fungi, algae and molds if are producing toxins must also produce medicines [3].

Horrors in the pill

We have to keep this in mind that drugs developed and marketed must be used with extreme care otherwise will produce more harmful effects than beneficial effects.

Thalidomide a harmless sleeping pill proves to be an example of destructive fury of some pharmaceuticals and caused phocomelia (deformed limbs) in infants. Diethylstilbestrol (DES) alternative to female hormone estrogen used to decrease the chances of miscarriage resulted in physical deformities and various types of cancers.

Toxicity of Metabolites

Many poisonous substances are not injurious directly but after their metabolism they are converted into metabolites in liver that may or may not be toxic to human body. Although genetic variability of liver enzymes does effect production of metabolites. So, in some individuals more toxic metabolites are produced while in other less toxic metabolites of same agents will produce [4,5].

Poison /Drug	Metabolises	Reactions
Methanol (wood alcohol)	Formaldehyde and formic acid (Liver)	Metabolic Acidosis
Acetaminophen (paracetamol)	Glucuronidation and Sulfation pathways High doses these pathways saturated and metabolism on other pathways P450 dependent glutathione conjugation (Liver)	Glutathione cannot regenerate quickly as glucoronic acid and sulfateresult in toxicity in liver.
Codeine (pain relieving agent) little effect on pain relieving pathways and have analgesic effect	Nor-codeine, morphine, codeine-6-glucuronide (Liver) Morphine most active act through enzyme CYP2D6 pathway [6]	Effects vary individual to individual depending upon presence of enzymes in individuals.

Hormonally Active Compounds

Recent researchers revealed variable effects of hormones at different doses for example exposure of gene to different doses of estradiol (natural human hormone) that exist in human blood bounded up by proteins. In its bound form estradiol don't interact with hormone receptors and in turn don't turn on genes of interest. With increase in dose there will be concurrent increase in response [7]. But as receptor occupancy increases a feedback loop cuts in reducing the availability of additional receptors. Any further increase in dose will cause toxicity to the cell. A non-monotopic curve of dose response will be generated i.e., with increase in dose there will be an increase in response however, any further increase will disrupt system.

Similarly, an enzyme aromatase (Testosterone → estrogen→ masculinize the brain of male mammals) if supplied insufficiently disrupts natural process. Another example of histamine and cytokines release exacerbation by low levels of environmental contaminants just like estradiol is seen [8]. Influx of Calcium into cells and concurrent release of prolactin too follow non-monotonic patterns [9].

Similar non-monotonic pattern of prostate cells is observed by a scientist when exposed to pesticides (organochlorine hexa chlorobenzene) it's increased concentration decreases androgenic activity and vice versa [10].

Effect of Organ Response

Another most important of considerations in defining a drug or poison is impaired organs e.g. liver or kidney can also responsible for converting therapeutic dose to a poison. So, it's not only the dose defining poison but organ response too.

Ricin in a dose as low as few salt grains when taken through any route i.e., I/V, orally or through inhalation act by inhibiting proteins from reproduction by killing the ribosomes in your cells resulting in multiple organ failure within a week and is very hard to be traced.

At high dose even, oxygen too interferes with the operations of CNS eventually lead to death.

Effect of Drug Disposition and Drug Action

Pharmacokinetics referred to drug disposition whereas pharmacodynamics referred to drug effects and the mechanism of action.

Drugs or nutrient upon entering the body binds to plasma protein (albumin). There are some barriers that need to be crossed before producing therapeutic activity.

Plasma protein binding - plasma protein bound drug effects the duration of action as it slows its distribution and ultimately elimination. Plasma proteins of patient's blood are a key factor for the drug or a nutrient [11].

First Pass Effect: Venous drainage of other organs (intestines and stomach) differs from the venous drainage of GIT i.e., directly to the heart and enroute to portal circulation delivering to liver respectively. The second route is of clinical significance as liver is the site of active biotransformation (metabolism) and interactions. Oral medications undergo extensive first pass effect. Drug metabolizing enzymes play key role in biotransformation of drug [12].

Blood Brain Barrier: It restricts the passage of nutrients that are more hydrophilic or lipophilic. Many drugs have limited ability to bind to blood brain barrier because of its structure and complex transport mechanism of drug exit [13].

Biological Membranes: Phospholipid bilayer of cholesterol, proteins and constituents. Passive diffusion if the drug is lipophilic (no energy is required), filtration molecular sieves allow molecules of different sizes. Facilitated diffusion i.e., carrier mediated diffusion is characterized by small number of molecules carriers that allow some drug to pass while restricts others.

Active transport allows the passage of drug against concentration gradient i.e. up regulation.

Endocytosis in -this drug is transported in the form of pits and vesicles used by mostly sucrose and insulin. Multiple factors are responsible for the drug disposition in the body.

Drug actions depend on physiological response going on in the body. However, basically drug adopts four ways to become pharmacologically active by

- Killing invading organism.
- Killing aberrant cells.
- Neutralizing the cells.
- Modifying physiological processes.

Arien's categorises interacting phases resulting in different physiologic response (bioavailability, volume of distribution, clearance and biomarkers). Pharmaceutical (compatibility, solubility, and stability), Pharmacokinetic (ADME) and pharmacodynamics effects (signal transduction, genetic polymorphism, enzymatic transport receptors) are the vital phases need to be considered as they effect patient outcome which can be negative as well as positive.

OTC Drugs- Good self-help tools

Over the counter drugs should not be taken for granted though inexpensively and conveniently we can treat ourselves as they too are the real drugs. There are thousands of drugs available both in the form of generic as well as fashion brands, but few key steps must be followed while picking an OTC drug [14-16].

Read Drug Facts label

- Active ingredient
- Purpose
- Uses
- Warnings
- Directions
- Other information
- Inactive ingredients

Acne products

No bacterial soap, liquid cleanser or scrub can cure acne because these are not formed due to surface oils and often plugged deep. FDA approved only few non-prescription drugs as safe and effective in acne treatment. These are sulphur, combination of sulphur/resorcinol and benzoyl peroxide. Sulphur and sulphur/resorcinol can't prevent pimples however benzoyl peroxide is most effective but still not a silver bullet only best among available brands.

Antacids

Sodium bicarbonate cheapest antacid around the globe but only occasional use is recommended because higher level of sodium disturb acid base balance and increases urinary tract infections in women. Calcium carbonate on the other hand is a major helper but not for extended period as increase calcium level impaired kidney functions. Milk of Magnesia (Magnesium hydroxide) causes diarrhea so people use it as a laxative but in combination with aluminium hydroxide act as constipating agent. Aluminium pull out calcium and in return weakens the bones ultimately causes skeletal deformities.

Aspirin and Acetaminophen

A very common white pill aspirin and acetaminophen are also available over the counter. Aspirin interferes with prostaglandins (unsaturated fatty acids) of the body. Aspirin and acetaminophen both act differently. Aspirin subdues prostaglandin within the injured tissue whereas acetaminophen works on prostaglandins in brain and central nervous system. Dose and duration plays a vital role while using these drugs. Aspirin causes GIT upset and Rey's syndrome (brain swelling) in child while acetaminophen effects liver besides offering healthy effects of pain killer as well as anti-inflammatory agents. So, we can say every drug is safe unless abused. Can we prefer acetaminophen over aspirin? the answer to this question is no as aspirin prevents heart attack, stroke and binds to proteins in the lens of eye and prevent cataract but may interact with other drugs like, antidiabetic drugs, heparin, anticoagulants etc.

Cough and Cold Remedies

We can't cure cold but just can endured caused by more than 100 different viruses. Antihistamines are most commonly used OTC drug act by blocking action of histamine a substance responsible for redness, itching and swelling wherever it is released. But it should be used with extreme care as it causes side effects like drowsiness.

Rebound effect of many decongestants is very often seen. Rhinitis medicamentosa a very common disease is due to addiction `to decongestant sprays or drops so it must not be used for more than three days maximum. As we all know cough is a necessary evil serves useful purpose of clearing air passages. Drugs used in treatment tranquilize the brain and control the reflexes. Suppressants containing codeine or dextromethorphan are effective and safe in correct doses otherwise not. People often take antihistamine which in return dry out lining of the throat and bronchial passages. Trite but true advice is rest, keep yourself warm and drinking plenty of fluids. Hidden sugar in many cough candies and syrups is just villainous. Non-cariogenic (non-cavity forming) substances must be included in sweetened or unsweetened liquid medicine used by children or adults.

Foot Care Products

Ins and outs of foot problems: Calluses and Corns both are made up of dead, toughened tissue. Calluses protrude outward whereas corns inward i.e., into the foot. Both are treated with same products: foot pads. Salicylic acid in foot pads dissolves dead tissue but don't distinguish between dead cells and living tissue so must be harmful may cause chemical burn. Pumice stone can also be very helpful. Similarly, antifungals to treat athlete's foot must be used with caution. Podiatrist must be consulted before using any OTC foot care products.

Hemorrhoid and Diarrhea Treatments

FDA approves only two chemicals used in local anesthetics i.e., benzocaine and pramoxine hydrochloride. Prolong use illicit allergic responses. Hemorrhoid naturally pop up and naturally disappear recent researches have shown. Calcium polycarbophil is one safe drug recommended by FDA.

Laxatives

Chemical stimulants like senna, phenolphthalein, danthrone, bisacodyl and castor oil strongest laxative but causes malnutrition when used to achieve non-medical benefits.

Phenolphthalein must be used with care as it's cure is worse than disease. Cells of the colon weep under assault and secrete a ropy, gluey liquid –mucus mixing with fecal mass making it more liquid. Osmotic and saline laxative like magnesium hydroxide in small doses is effective but high levels of magnesium is a threat for people with kidney problems similarly increased level of sodium effects people having heart problems so preferably use glycerine suppositories. Mineral oil deprives the body of all fat-soluble vitamins (A, D, E, K), rectal leakage and aspirated in the lungs of elderly and bedridden patients. DDS (dioctyl sodium sulfosuccinate) doesn't interfere with the absorption of nutrients. However, the safest are bulk forming laxative e.g., psyllium preparations and calcium polycarbophil.

Oral Hygiene Products

Like mouth washes and mint toothpastes are not the actual cures for oral health it is the good habits that prevent oral problems. Healthy mouth never gives bad odours.

Salves, Balms and Ointments

Hydrocortisone is used to treat itching and available over the counter better to use a petroleum jelly. Lidocaine and benzocaine most common anaesthetics to treat itching but overuse sensitize skin. Antiseptics like benzalkonium chloride, iodine or alcohol fight against few minor infections.

Sleep Aids and wakeup

Diphenhydramine hydrochloride and doxylamine succinate (antihistamines) are most commonly used and well-suited sleeping aids. All of this blunt awareness physically and mentally. Although they have wide margin of safety but still can be a source of potential poisoning. Too much pills excite the nervous system and ultimately cause insomnia. Sleeping pills should be avoided in asthma, glaucoma, heart diseases and pregnancy. Caffeine is the only non-prescription stimulant and is safe when taken in low doses [17,18].

Clinically significant interactions

Lastly, it is observed from recent research data even interactions too convert a drug into toxic biochemical. Medicines are used to cure so must be non-toxic, specific to organ, and must show linear potency but such ideal drug still not discovered and same drug shows different responses in different individuals.

Variable Effects of a drug are due to many types of interactions. Such interactions may result from changes in pharmaceutical and biopharmaceutical properties (pharmacokinetics and pharmacodynamics) categorized as Hansten's interactions [19]. So, interactions too convert a therapeutically effective drug into a poison [20].

Categories of Drug Interactions

Co administration of more than one drug or even a single drug may act individually, interact to enhance or decline the desired therapeutic effects and even can initiate unexpected reactions in a biological system.

Drug - Food interactions

Food is a undeniable part of a healthy lifestyle. Basic reason of food-drug interaction is due to physicochemical and physiological relationship between a drug and food/nutrient (botanically derived food/dietary supplement) [21].

Food-drug interactions can be avoided if taking drug one hour before and two hours after taking meal. Bran or insoluble fibers, vitamins/minerals, dietary fibers, pectin soluble fibers and intake of large green leafy vegetables do affect many drugs due to increase level of Vit K. Similarly, dietary supplements are not considered as drugs but food, but they do effect prescription and OTC drug and result in drug toxicity. Alcohol interact with almost every drug [22].

Many factors contribute to these interactions like dosage of the drug, age of a person, BMI, health of a person. But it doesn't mean avoidance of drug. It is always advised to ask doctor/pharmacist before taking a medication [23].

S/ No	Drug	Effects	Recommendations
1.	Dicumerol	Delays gastric emptying	With food
2.	Griseofulvin	Lipid soluble	With high fat food
3.	Propranolol	Food reduce first pass effect with metabolism	With food
4.	Acetaminophen	High pectin food (adsorbent andprotectant)	Intake -Empty stomach
5.	Digoxin	High fiber, high pectin food binds drug	Not with high fiber food
6.	Isoniazid	Foods raises gastric pH ↓ dissolution and absorption	Intake – empty stomach
7.	Levodopa/ Methyldopa	Competes with amino acids	Avoid proteinous diet
8.	Penicillamine/ Tetracyclines	Chelate form with Ca and Fe	Dairy products and Fe-rich foods/supplements
9.	Riboflavin / ascorbic acid	Protein-calorie malnutrition/ obesity effects drug disposition	Active component of microsomal enzyme system for drug metabolism

Table 6: *Drug-Food interactions- Accelerate / Delays drug absorption.*

Drug-Beverage Interactions

Cardio-protective benefits of alcoholic beverages supported its consumption. But they do interact for example alcohol and metronidazole. Antioxidant properties due to the presence of high flavonoids and polyphenols along this alteration of CYP activity [24].

Red wine from grape (*Vitis vinifera* L.) is known to inhibit hepatic CYP3A in vitro due to its components trans-resveratrol and gallic acid. Beer due to different types of phenolic acids and prenyl-flavonoids used as flavoring and preserving agent showed maximum inhibition of CYP3A4-mediated metabolism [25]. Tea (*Camellia sinensis* L.) due to presence of its high polyphenolic content showed effect on CYP activity (Roth M., *et al*. 2011). Catechins obtained from tea have shown effects on OATP2BI or OATP1A2- mediated estrone-3-sulfate uptake. But still research in this area is required to proof its clinical significance [26].

Drug - Lab Test Interactions

Drug Laboratory interactions major source of laboratory errors for example I-DOPA and Uric Acid [20]. There are many types but the most common are, Antibiotics (Penicillin), psychotropic medications (Clozapine), antihypertensive drugs (Hydrochlorothiazide and metoprolol), hormones (Birth control pills and steroids –prednisone and dexamethasone).

Drug Infusion fluid Interactions

It is also an important type of interactions for example between Ampicillin and Glucose. Plastic container fluid interaction, oily covering of syringe though solved by flouro-resin laminated rubber etc [27].

Drug –Disease Interactions

In this effect of participant drug on object drug are evaluated for example drug induced renal and hepatic dysfunction. Several cytochrome P450 enzymes activity is inhibited by disease states. Cytokine concentration is enhanced in diseased conditions like trauma, ischemia, infections, toxins etc. result in reduction of drug metabolism and enhanced levels in body which will later produce poisonous effects in biological system [28].

Nasal Decongestants –Hypertension – High Blood Pressure
NSAID's – Asthmatic- Increases Nasal Obstructions
Aspirin- Ulcer – worsens ulcer
Minoxidil –Heart Failure-Fluid retention
Ca Channel Blocker –Heart failure –Negative inotropic effect
Metformin –Heart failure- Increased lactate level
Beta blocker- Heart failure- Worsen asthma
Metoclopramide, antipsychotics – parkinson's- worsening parkinsons

Similarly, many disease conditions like obesity (alters Vd of lipophilic drugs), Ascites (Alters Vd of hydrophilic drugs), renal and liver impairment effects the drug metabolism and excretion. A drug-disease condition can worsen a medical condition.

Drug-Host Interactions

Antimicrobial drugs interact and release by products toxic to human body can even cause death. However, following are the responses observed through these interactions.

Organ Toxicity

Allergic Responses to drugs
Suppression and Alteration of Microbiota by Antimicrobials
Effects of Drug combinations
e.g. Antimicrobial drugs – act as an allergen e.g. penicillin allergies, Antibiotics –Slows the growth of or kills a bacterium etc. [29].

Drug –Parasite Interactions

Parasites (protozoans) are responsible for large number of deaths annually. There is a lack of effective vaccines and it is highly desired to have parasite resistant medications [30].

Drug-Ecochemical Interactions

These kinds of interactions are observed between plants and phytopathogenic zoospores [31].

Drug-Herb Interactions

Botanicals extracted are utilized by humans since old age. Very important group of drugs like, morphine, reserpine, vinca alkaloids etc. proved to be potent therapeutic agents. Concept that All-natural drugs are safe is incorrect they should be monitored too for their efficacy.

Herb	Drug	Interaction	Refferences
Black cohosh	Atorvostatin, Acetaminophen Alcohol	Liver toxicity accumulate products in body	[32]
CoenzymeQ10 (found in liver, pancreas, kidney) Cranberry Saw palmetto Green TeaGinger	Warfarin	↓ blood thinning effect, ↑clot formation	[32]
Echinaceae	Caffeine	Alters drug metablism	[33]
Evening Primrose Oil	Antiseizure medications Phenothiazine	↑ risk of seizure	[32]
Valerian	Antidepressants Pain killers Antianxiety drugs	↑ Insomnia & anxiety	[32]
St.John's Wort	Selective serotonin reuptake inhibitors (SSRIs), Tricyclic antidepressants (TCA), Monoamine oxidase (MAO), Triptans for migraine, dextromethorphan, birth control pills, HIV medications	Numerous and dangerous effects with OTC and prescription medications.	[34]
Melatonin	Muscle relaxer,Benzodiazipine, opioids,antihistamine	Drowsiness	[32]
Kava	Buprenophinec	Coma	[35]
Yohimbine	Selective serotonin reuptake inhibitors (SSRI)	↑ blood pressure	[36]
Fever few	Asprin Heparin Warfarin	Blood clotting disorders	[32]
Ginko biloba	Seizure medications Diabetic drugs	Alters liver metabolism of drugs	[37]
Golden seal	Antipsychotic drugs	↑ drug levels, Irregular heart rhythm	[38]

Table 7: *Drug- Herb Interactions [39].*

Drug overdose leads to poisonous effects

Overdose is another cause of converting medicine to poison. Risks associated with overdose depend upon type of substance, amount taken and characteristics of body. It includes cases of intentional and unintentional poisoning.

Medicines commonly causing poisoning are sedative, hypnotic medicines, psychotropic drugs (Benzodiazepines (tranquilizers), antidepressants, antipsychotics, neuroleptics (schizophrenia), psychostimulants, pain killers (paracetamol, NSAIDs), narcotics and hallucinogens.

Know the Dose and Know what you are taking

Drug awareness will be required immensely in days to come for a healthy life. It will help us in preventing blindly accepting the drugs unless one read and know about the drug. This is required due to multiple reasons like as follows.

The Pharmaceutical industry

Drug battle is going on as many companies are fighting or themselves only as we know if a drug proves to be a life saver it will bring cash to a company but if not a big loss. So, they are running in market and even adopting absurd means to run their business no thinking about the health of a patient.

- Over advertisement
- Free drug samples
- High priced gifts for physicians
- Publishing wares in journals
- Preprinted pads of the product to sell

Choose pharmacy as you choose a doctor

After having official piece of paper (Prescription) we assume that diagnostic part of illness is over, and healing begins but ignore the most important part pharmacy a place of utmost importance. Careful preparation of drugs by pharmacist is also an essential part of a healthier life. Pharmacist assist you in how and when to take medication and its side effects. He guides you about side effects of many OTC drugs. So, pharmacist and pharmacy must be considered as a potential health resource. They are the integral part of health care triad [40].

Applications of Sequencing to Medicines from Poisons

Cyclic peptides are polypeptide chains containing circular sequence of bonds. Such compounds are antimicrobials and toxic and exist in nature and in medicine they are used as immunosuppressive and antibiotic agents. Cyclic peptides are resistant to the process of digestion and so survive well in digestive tract. A team of scientists has discovered an enzyme (POPB-it converts linear shape toxin peptide to cyclic peptide ultimately billions of variant molecules) with ability to create molecules which can target a single organ only. This enzyme has the ability to synthesize chemical compounds known as cyclic peptides a pharmaceutically important molecule for creating new drugs which will help in finding single-minded medicines with least adverse effects e.g. Mushrooms [41,42].

Conclusion

Use of prescription and non-prescription drugs is very common especially elderly patient use it disproportionately. Polypharmacy increases the adverse reactions and risk lives. Medication reviews identifies high risk medications and drug interactions. It will reduce medication burden. So, a proper drug regimen and periodic pharmacist review of all medicines, prescriptions and non-prescriptions should be followed.

Future Prospective

Quality of life will be improved by managing our medicine wisely and responsibly.

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Volume 10 Issue 7 July 2018