VIJAYA INSTITUTE OF PHARMACEUTICAL SCIENCES FOR WOMEN
Enikepadu, Vijayawada-521108

MECHANISMS OF DRUG INTERACTION AND INTERACTIONS MEDIATED THROUGH ADME

presented by

Mr. S.VENKATESWARA RAO, M. Pharm
Assoc. Professor,
Department of Pharmaceutics.

DRUG:

- A drug is a substance which may have medicinal, intoxicating, performance enhancing or other effects when taken or put into a human body.

DRUG INTERACTIONS:

- Alter pharmacological activity of one drug by administration of another drug or presence of food, drink or by exposure to environmental chemicals
- The altered drug is called as object drug.
- The agent that produce the interaction is called as precipitant.

EXAMPLES:

- For increasing pharmacological activity of drug

  E.g.: Increasing anticoagulant effect of Warfarin by concominent administration with Probencid

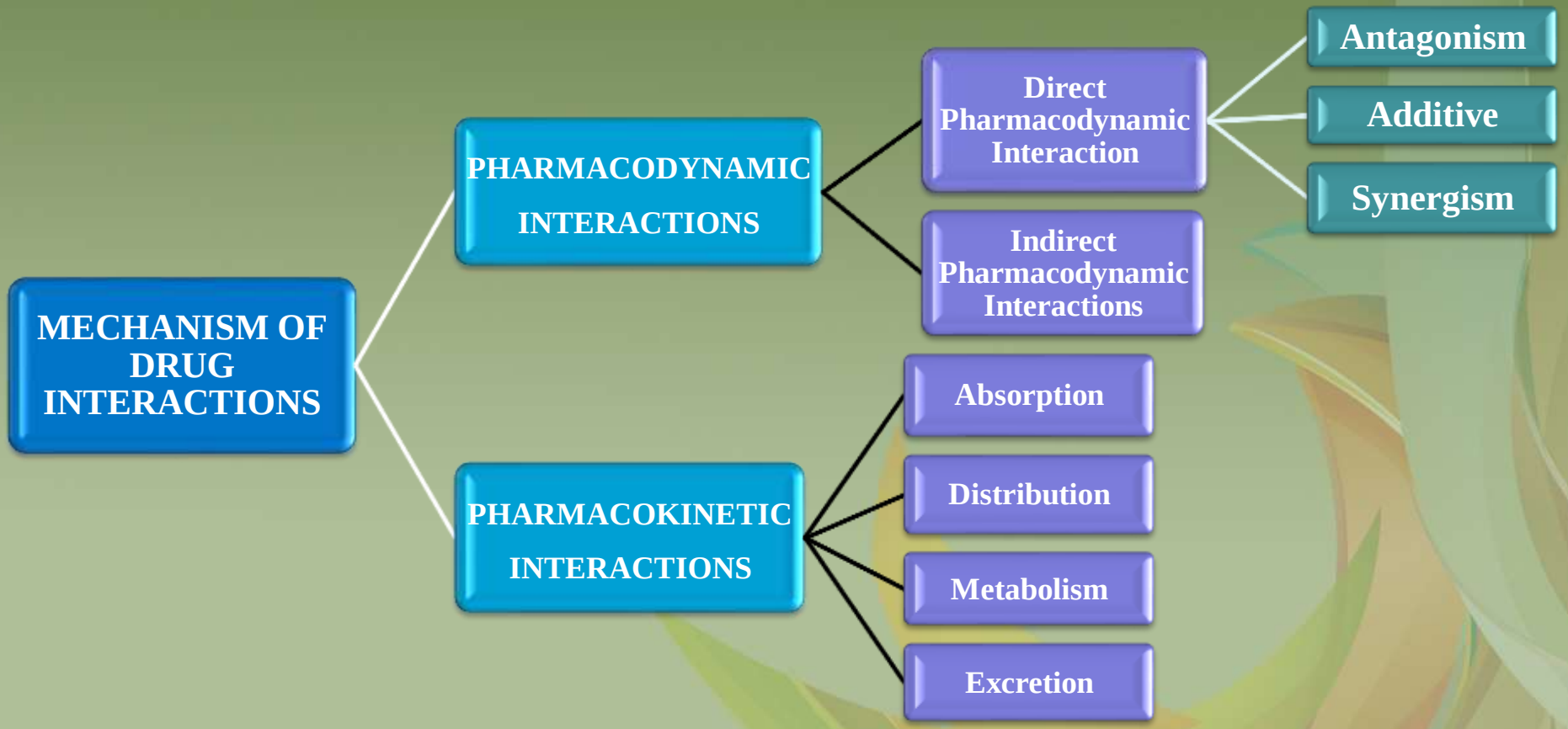
- For decreasing pharmacological activity of drug

  E.g.: Decreasing activity of tetracycline in presence of food, drink and mineral supplements with metal ions

- Sometimes drug interactions are beneficial

  E.g.: Increasing activity of Penicillin by administration with Probencid

MECHANISM OF DRUG INTERACTIONS



PHARMACODYNAMIC INTERACTIONS

DIRECT PHARMACODYAMIC INTERACTION

Antagonism:

The object and precipitant having opposite activity.

E.g.:

- C.N.S stimulant + Phenobarbitol –reduced sedative effect of Phenobarbitol
- Diuretic + Oral hypoglycaemic or Insulin – increased blood glucose level

Additive:

The object and precipitant having similar activity and effect is sum of individual drugs

E.g.:

- Sedative + alcoholic beverages – increased CNS depressant effect.
- Aminoglycoside + Diuretics – Ototoxicity develops quickly.

Synergism:

The activity of one drug is increased by another drug.

E.g.:

- Aspirin + Alcohol – enhanced analgesic activity of Aspirin.
- Ibuprofen + Codeine – enhanced analgesic activity of codeine.

INDIRECT PHARMACODYAMIC INTERACTION

Both object and precipitant having unrelated activity

E.g.:

- Salicylates decrease the activity of platelet aggregates when Warfarin increase anticoagulant effect.

PHARMACOKINETIC INTERACTIONS

ABSORPTION

- Commonly absorbed in oral route of administration
- Decreasing rate of absorption is significant in ‘acute conditions’ and not significant in ‘chronic conditions’.
- Parenteral route absorption is rare when adrenergic drug is administrated with cholinergic drugs.
- Various mechanism involved in alteration of mechanism involved in GIT.

S.No	OBJECT DRUG	PRECIPITANT DRUG	EFFECT PRODUCED
I.	**Complexation and absorption:**		
1.	Tetracycline, Penicillin	Certain foods (e.g.: milk), Drugs (e.g.: antacids containing Mg, Al, Ca, Fe)	Complexation of tetracycline with metal ion results decrease in absorption.
2.	Fluoroquinolones e.g.: Ciprofloxacin	Antacids and Sucralfate	Complexation of Fluoroquinolones With metal ions results in decreased absorption.
II.	**Changes in GI pH:**		
1.	Aspirin, Sulfonamides	Antacids	Improved dissolution and rate of absorption
2	Tetracycline, Ketoconazole	Antacids	Reduced dissolution and bioavailability.
III.	**Changes in GI motility:**		
1.	Aspirin, Paracetamol	Metoclopramide	Increased GI motility and reduced absorption.
2.	Levodopa, Lithium	Anticholinergic	Decreased GI motility and increased absorption
IV.	**Changes in GI Microflora:**		
1.	Digoxin	Antibiotics	Enhanced bioavailability due to destruction of bacterial flora.
V.	**Malabsorption:**		
1.	Vitamin A, B_{12}, Penicillin, Digoxin	Neomycin	Inhibition of absorption of object drug.

DISTRIBUTION

- When Two drugs capable of protein binding are given then one drug having greater affinity towards the binding protein may displace the other drug from its binding sites thereby it increases the distribution
- Such competitive displacement causes highly significant interactions , when the displaced drug
  - Is more than 95%binding
  - Has small of volume distribution
  - Has narrow therapeutic index

S.No	OBJECT DRUG	PRECIPITANT DRUG	EFFECT PRODUCED
1.	Phenytoin	Valproate	Increased plasma concentration of Phenytoin leads to toxicity.
2.	Tolbutamide	Sulfonamides	Increased hypoglycemic activity
3.	Warfarin	Phenylbutazone	Increased in anticoagulant activity of drug

METABOLISM

ENZYME INDUCTION

Increase metabolism of active drug and results decrease in plasma concentration and increase toxicity of metabolites.

ENZYME INHIBITION

Increasing the accumulation of drug results in toxicity

S.No	OBJECT DRUG	PRECIPITANT DRUG	EFFECT PRODUCED
I.	**Enzyme inducer:**		
1.	Coumarin, Anti coagulants	Phenobarbital and other Barbiturates	Reduced plasma concentration of object drug and results in metabolic toxicity.
2.	Corticosteroids , Theophylline	Phenytoin	Reduced plasma concentration of object drug and results in metabolic toxicity.
II.	**Enzyme inhibition:**		
1.	Alcohol	Disulfiram	Increased plasma concentration of object drug.
2.	Carbamazepine, Theophylline	Erythromycin	Increased clinical efficacy due to inhibition of hepatic metabolism.

EXCRETION

- Occurred when drugs or metabolites are excreted in urine.
- Due to alteration of glomerular filtration rate, passive tubular reabsorption, active tubular secretion, renal blood flow, urine pH.
- It influence reabsorption of sodium, lithium, and results in toxicity.
- Some other excretion mechanisms like bile excretion is altered due to the bile transport or bile flow rate.

S.No	OBJECT DRUG	PRECIPITANT DRUG	EFFECT PRODUCED
I.	**Alteration in active tubular secretion:**		
1.	Penicillin, Cephalosporins	Probencid	Elevated plasma levels of object drugs due to blockage of their tubular secretion.
II.	**Alteration in urinary pH:**		
1.	Amphetamine, Quinidine	Antacids, Thiazides	Increased passive reabsorption and toxicity.
III.	**Alteration in renal blood flow:**		
1.	Lithium	NSAIDS	Reduced renal clearance and results toxicity.

THANK YOU