1. GENERAL PHARMACOLOGYIC ULCER

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PHARMACOLOGY

- **DEFINATION:** "THE STUDY OF THE DRUGS (ORIGIN, NATURE, CHEMISTRY) AND THEIR ACTIONS ON LIVING ANIMALS, ORGANS AND TISUUES"

- **DRUG:** IT IS ACTIVE SUBSTANCE.

- **MEDICINE:** IT IS THE SUBSTANCE USED TO DELIVER DRUG IN STABLE AND ACCEPTED FOR

- **SOURCE OF DRUGS:**

SOURCE	SPC. & DRUGS	CATEGORY
PLANTS	FOX GLOVE: DIGITALIS	CARDIAC GLYCOSIDE
MICROBES	PENICILLIUM NOTATUM: PENICILLIN	ANTIBIOTIC
ANIMALS	PORK, BEEF: INSULINE	ANTIDIABETICS
MINERALS	GOLD	ANTIARTHRITIS
SYNTHETICS	ASPIRIN	ANTI-INFLAMMATORY
GENETICAL	HUMAN RECOMBINANT GENE	

DIFFERENT THERAPEUTICS USES OF DRUGS

CURATIVE USE:

- DRUG REMOVE CAUSES & ELIMINATE DISEASE.
- ANTI BIOTICS KILL ORGANISMS & REMOVE THE CAUSES OF INFECTION.

SUPPRESSIVE & SYMPTOMATIC USE:

- DO NOT CURE DISEASE BUT SUPPRESS SYMPTOMS.
- ANALGESIC RELEIVE PAIN IN ATHRITIS BUT DO NOT CURE IT.

PROPHYLACTIC OR PREVENTIVE:

- PREVENT SPECIFIC PATHOLOGICAL CONDITION.
- ANY VACCINE

DIAGNOSTIC USES:

- DIAGNISIS OR IDENTIFY UNDERLYING PATHOLOGY OR CAUSE OF DESEASE.
- X-RAY FILM, BARRIUM SULPHATE.

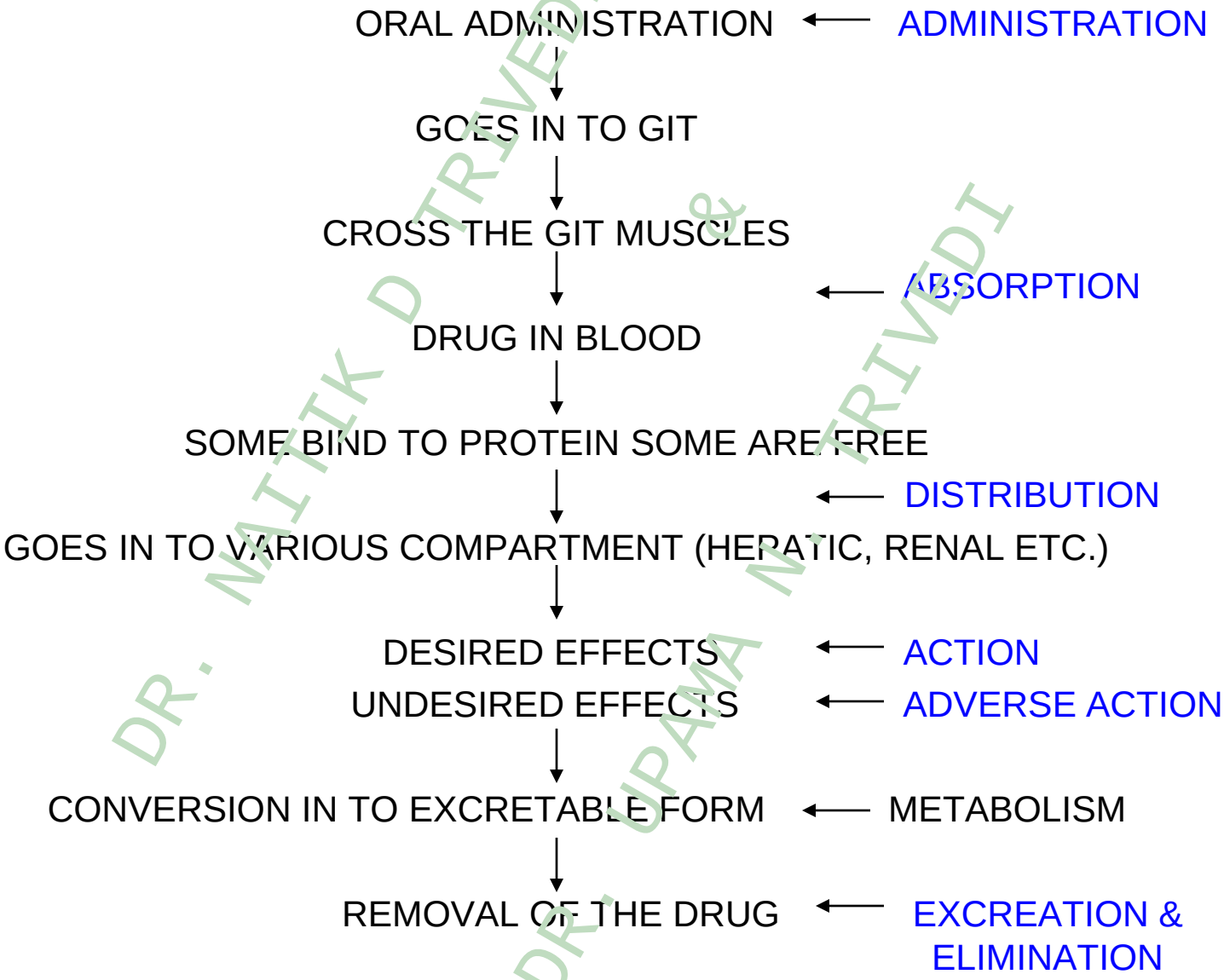
AUXILLIARY USE:

- TWO DRUG ADMINISTRATE TOGETHER.
- ONE DRUG SUPORT OTHER.
- PENICILLIN AND PROBENECID- PENICILLINE KILLS ORGANISM, PROBENECID REDUCE RENAL ELIMINATION.

PLACIBO:

- NO ACTIVE CONSTITUTE, ONLY PSYCOLOGICAL TREATMENT.

WHATS HAPPENS TO A DRUG WHEN IT ENTERS IN TO BODY?



GENERAL TERMINOLOGY

ADMINISTRATION: "INTRODUCTION OF DRUG IN TO HUMAN BODY".

ABSORPTION: "TRANSPORT OF DRUG FROM SITE OF ADMINISTRATION IN TO CIRCULATION".

DISTRIBUTION: "TRANSPORT OF DRUG FROM CIRCULATION TO VARIOUS COMPARTMENT".

DESIRED EFFECTS: "SPECIFIC AND WANTED EFFECT PRODUCE BY DRUG FOR WHICH IT IS ADMINISTERED".

UNDESIRED EFFECTS: "HARMFUL OR UNWANTED EFFECT OF DRUGS".
MINODIXIL-VASODILATOR, HAIR GROW IS UNDESIRED EFFECT.

METABOLISM: "CONVERSION OF DRUGS INTO A FORM THAT GETS EXCRETED EASILY".

EXCREATION OR ELIMINATION: "REMOVAL OF DRUG FROM BODY".

PHARMACOKINETICS: "WHAT A BODY DOES TO A DRUG".
PHARMACODYNAMICS: "WHAT A DRUGS DOES TO A BODY".

OD: ONCE A DAY, **BD (BID) :** TWICE A DAY, **TDS (TID) :** TRICE A DAY,
QDS (QID) : FOUR TIMES A DAY, **HS (ON) :** EVERY NIGHT, **OM :** EVERY MORNING,
AC : BEFORE FOOD, **PC :** AFTER FOOD, **SOS :** IF NECESSARY.

PHARMACOKINETICS

"WHAT A BODY DOES TO A DRUG"

- ✓ABSORPTION
- ✓DISTRIBUTION
- ✓METABOLISM
- ✓EXCREATION

ABSORPTION

"SITE OF ADMINISTRATION TO SYSTEMIC CIRCULATION"

BIOAVAIBLITY:

- ALL DRUG THAT IS ADMINISTERED MAY NOT GO INTO THE CIRCULATION (EXCEPT INTRAVANOUS ROUTE), SOME FRACTION IS WASTED.

"FRACTION OF TOTAL ADMINISTERED DRUG THAT ENTERS INTO CIRCULATION"

- IT IS **THE PARAMETER** THAT **MEASURES THE RATE AND EXTENT OF ABSORPTION.**
- IT IS **ALTER BY VARIOUS FACTORS.**

FACTOR AFFECTING ABSORPTION OR BIOAVAIBILITY

NATURE OF DRUGS

MOLECULAR WEIGHT

LIPID SOLUBLITY

PHARMACEUTICAL

PARTICAL SIZE

ADDITIVES

FORMULATION TECHNIQUE

HOST FACTORS

GENETIC FACTORS

DISEASE STATUS

ADMINISTRATION RELATED

ROUTE

CONCENTRATION

PH AT SITE

ONLY FOR ORAL ROUTE

DISINTEGRATION

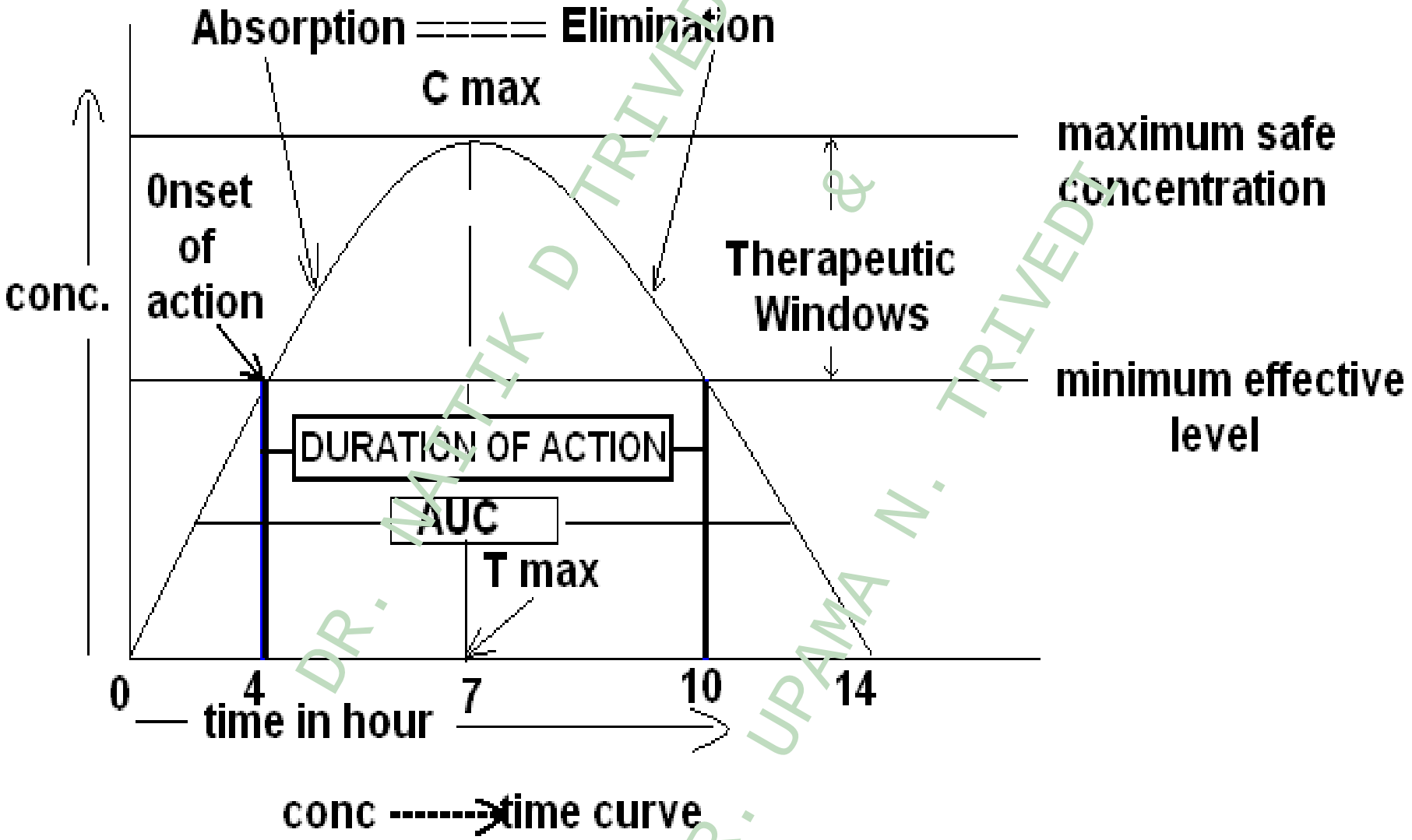
DISSOLUTION

ENTERO HEPETIC CIRCULATION

FOOD & DRUG INTERACION

FIRST PASS EFFECTS

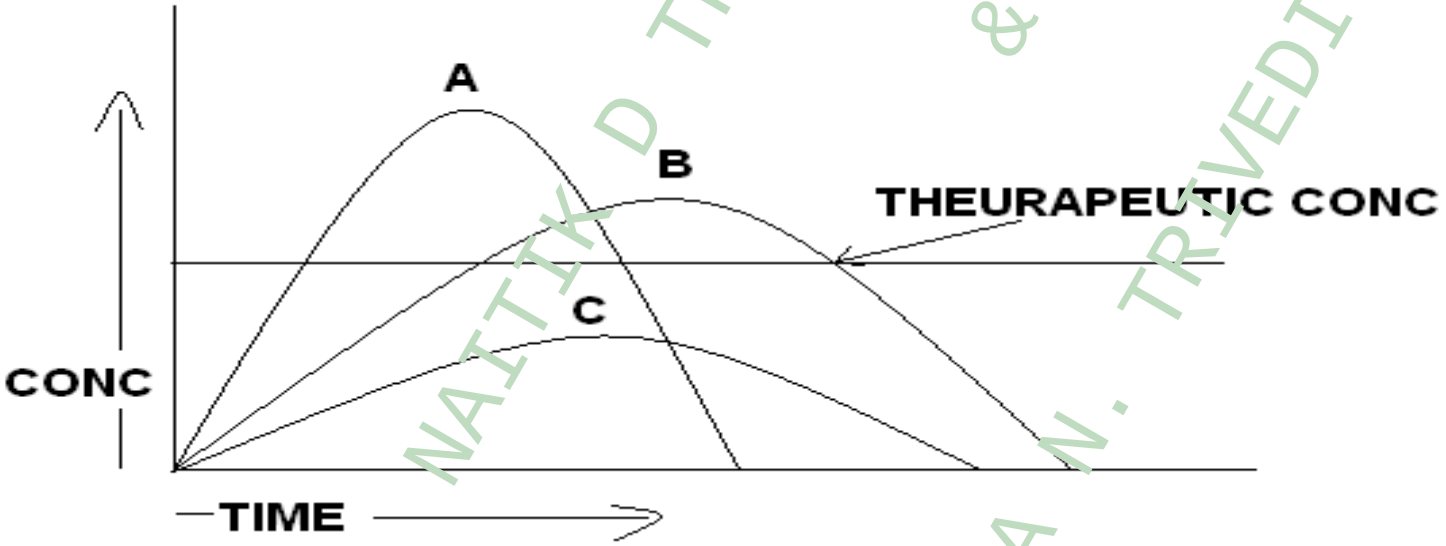
ABSORPTION PATTERN OF A DRUG



- **BIOAVAIBLITY OF DRUG BY ORAL ROUTE (F):**

$$F = \frac{\text{AUC AFTER ORAL ADMINISTRATION}}{\text{AUC AFTER INTAVENOUS ADMINISTRATION}}$$

CONCENTRATION CURVE OF THREE DIFFERENT DRUGS



- **DRUG A:** EARLY ONSET—SHORT DURATION
- **DRUG B:** LATE ONSET --- LONG DURATION
- **DRUG C:** NOT EFFECTIVE THERAPEUTICALLY

DISTRIBUTION

"TRANSPORT OF DRUG FROM CIRCULATION TO VARIOUS COMPARTMENT"

VOLUME OF DISTRIBUTION:

- **AFTER ABSORPTION, A FRACTION ATTACHED TO PLASMA PROTEINS AND A FRACTION REMAINS FREE.**
- **FREE PORTION IS AVAILABLE FOR DISTRIBUTION ALL OVER BODY.**
- **TRANSFERRED INTO DIFFERENT COMPARTMENTS LIKE EXTRACELLULAR FLUID OR INSIDE THE CELLS OF DIFFERENT ORGANS.**

"SO THE TERM VOLUME OF DISTRIBUTION COVER THE FREE FRACTION OF DRUG INTO THE CIRCULATION"

IT IS ALSO KNOWN AS APPERENT VOLUME OF DISTRIBUTION BECAUSE IT DOESN'T INDICATE REAL VOLUME.

$$Vd = \frac{\text{DOSE ADMINISTERED IV}}{\text{PLASMA CONCENTRATION}}$$

Eg: SUPPOSE 500 mg DRUG IS ADMINISTERED BY IV ROUTE AND PLASMA CONC. PRODUCE BY IT IS SUPPOSE 10mg/L THE APPERENT VOLUME OF DISTRIBUTION IS 500/10 = 50L.

FACTOR AFFECTING THE DRUG DISTRIBUTION

- ✓ PLASMA PROTEIN BINDING.
- ✓ RATE OF BLOOD FLOW IN VARIOUS ORGANS.
- ✓ CELLULAR BINDING.
- ✓ CONCENTRATION IN FATTY TISSUE.
- ✓ BLOOD BRAIN BARRIER.

PLASMA PROTEIN BINDING

- MOST DRUGS IN THE VASCULAR COMPARTMENT BIND REVERSIBLY TO MACROMOLECULES IN THE PLASMA.
- THESE ARE ALBUMIN, GLOBULIN, TRANSFERRIN, CERULOPLASMIN, GLYCOPROTEINS AND α AND β LIPOPROTEINS.
- ACIDIC DRUGS MAINLY BINDS TO ALBUMIN, WHEREAS BASIC DRUGS BINDS TO PLASMAPROTEIN AND ALBUMIN.
- BINDING INFLUENCES DRUG DISTRIBUTION, METABOLISM AND ELIMINATION BECAUSE ONLY FREE DRUG TAKE PART IN P'COKINETIC PROCESSES.
- SO, DRUG CIRCULATE IN BOTH FREE AND BOUND FORM AND HAS DYNAMIC EQUILIBIRIUM BETWEEN THESE TWO FORMS.

FREE DRUG + PROTEIN ⇌ DRUG PROTEIN COMPLEX

- ONLY FREE FORM OF THE DRUG IS PHARMACOLOGICALLY ACTIVE FORMAND DIFFUDE THROUGH CAPILLARY WALLS TO REACH THE SITE OF ACTION.
- SO THE EXTENSIVE BINDING REDUCE THE INTENSITY OF DRUG ACTION.

CELLULAR BINDING

- SOME DRUGS ARE DISTRIBUTED TO SITES OTHER THAN THE PLASMA.
- LIPID SOLUBLE DRUGS MAY ENTER FAT STORES.

Eg: VERAPAMIL, LIGNOCAIN ETC.

- TISSUE BINDING ALSO SEEN AND THIS DELAYS ELIMINATION FROM THE BODY AND PROLONG THE $t_{1/2}$ OF THE DRUG.

Eg. DIGOXIN BINDS TO CARDIAC MUSCLES AND CHLOROQUINE TO RATINA.

RATE OF BLOOD FLOWS INTO VARIOUS ORGANS

- IT INFLUENCE DRUG DELIVERY TO THE SITE OF ACTION.

Eg. IV INJECTION OF A LIPID SOLUBLE DRUG, THE BRAIN CONC. RISE

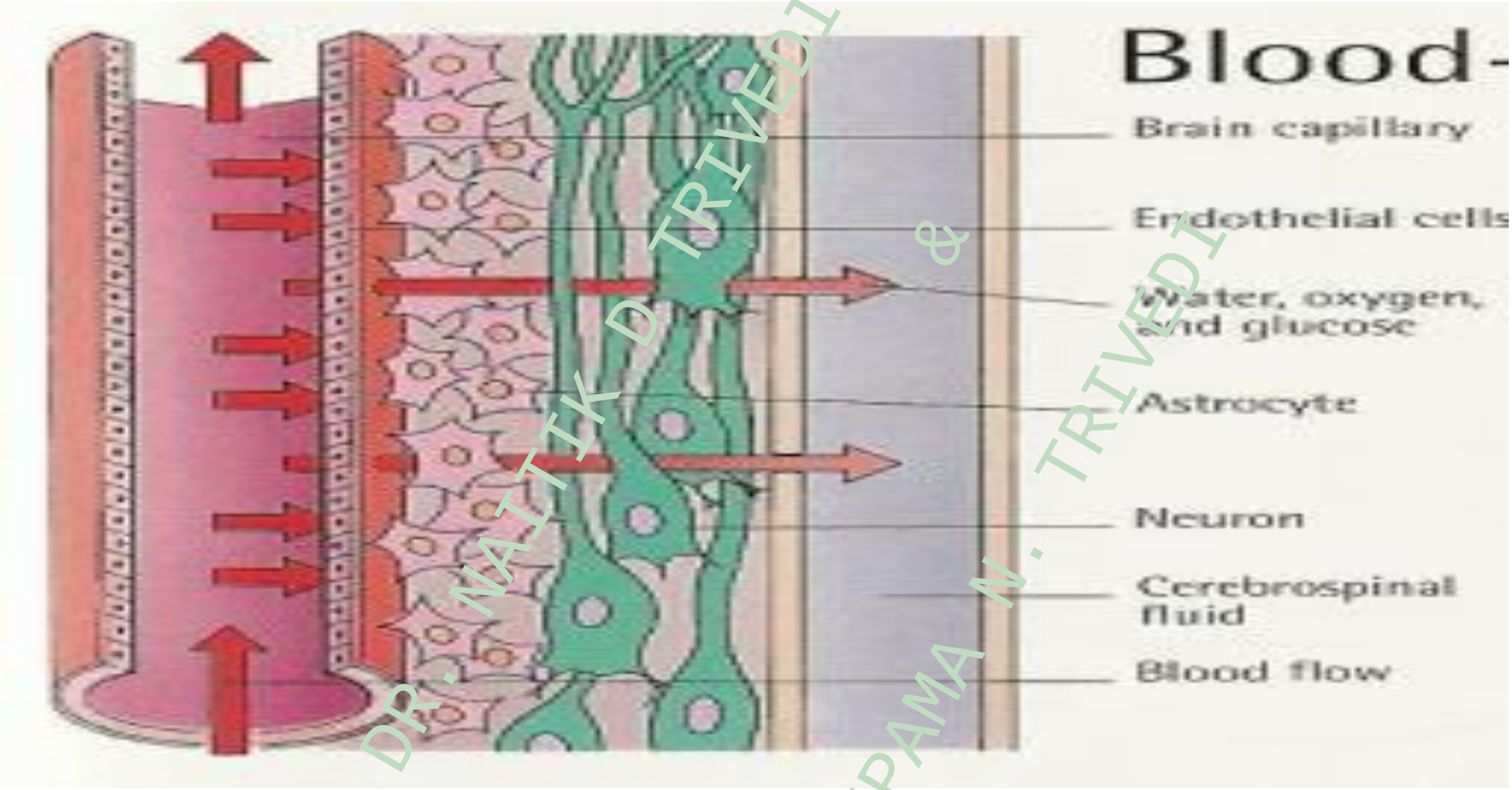
- RAPIDLY DUE TO GOOD TISSUE PERFUSION AND EQUILIBRIUM BETWEEN FREE AND BOUND DRUG IS ATTAINED.
- IN MUSCLES THESE PHENOMENON HAPPENS SLOWLY.
- SO THE FAT CONTENT MUSCLES RESTRICTED THE BLOOD FLOW SO DRUG ABSORB SLOWLY.

CONC. IN FATTY TISSUE

- CONC. OF DRUGS IN FATTY TISSUE IT ALSO INFLUENCES DRUG DISTRIBUTION.

- DRUGS WITH HIGH LIPOPHILICITY GLUTHIMIDE IS STORED IN FAT AND SERVE AS DEPOT. WHEN PLASMA LEVEL OF THE DRUG ARE LOWERED BY METABOLISM, PLASMA LEVEL ARE PROMPTLY RESTORED BY METABOLIZATION OF DEPOT STORAGE SITES.

THE BLOOD BRAIN BARRIER



- CAPILLARIES FOUND IN OTHER PARTS OF THE BODY THE CAPILLARIES IN THE BRAIN ARE HIGHLY SPECIALIZED AND MUCH LESS PERMEABLE TO WATER-SOLUBLE DRUGS.

- THE BRAIN CAPILLARIES CONSIST OF ENDOTHELIAL CELLS WHICH ARE JOINED TO ONE ANOTHER BY CONTINUOUS TIGHT INTERCELLULAR JUNCTIONS COMPRISING WHAT IS CALLED AS THE **BLOOD-BRAIN BARRIER.**

- MOREOVER, THE PRESENCE OF SPECIAL CELLS CALLED AS *ASTROCYTES*, WHICH ARE THE ELEMENTS OF THE SUPPORTING TISSUE FOUND AT THE BASE OF ENDOTHELIAL MEMBRANE, FORM A SOLID ENVELOPE AROUND THE BRAIN CAPILLARIES.

- AS A RESULT, THE INTERCELLULAR PASSAGE IS BLOCKED AND FOR A DRUG TO GAIN ACCESS FROM THE CAPILLARY CIRCULATION INTO THE BRAIN, IT HAS TO PASS THROUGH THE CELLS RATHER THAN BETWEEN THEM.

METABOLISM OR BIOTRANSFORMATION OF THE DRUG

"CONVERSION OF DRUGS INTO A FORM THAT GETS EXCRETED EASILY"

DEPENDING UPON THE **BIOLOGICAL ACTIVIRY** IT IS CLASSIFIED IN FOLLOWING WAYS:

1) INACTIVTON:

- CONVERSION OF ACTIVE DRUG IN TO INACTIVE METABOLITES.

2) ACTIVATION:

- IN THIS SITUATION THE METABOLITE IS BIOLOGICALL ACTIVE.

Eg: DIAZEPAM AFTER METABOLISM CONVERT IN TO OXAZEPAM IS ALSO BIOLOGICAL ACTIVE.

- IN SOME CASE PHARMACOLOGICALLY INACTIVE SUBSTANCE AFTER METABOLISM CONVERT IN TO ACTIVATION FORM.

Eg: L-DOPA IS INACTIVE BUT ITS METABOLITE DOPAMINE IS ACTIVE. THIS TYPE OF DRUG IS KNOWN AS PRO DRUG.

SIGNIFICANCE OF PRODRUGS

1) PRODRUGS ARE SOMETIMES BETTER ABSORBED THAN DRUGS.

Eg: TALAMPICILLIN IS THE PRODRUG OF AMPICILLIN IS BETTER ABSORBED THAN AMPICILLIN.

2) PRODRUG REDUCE TOXICITY.

Eg: BENORYLATE PRODUCES LESS GI ADVERSE EFFECTS THAN ASPIRIN.

3) USEFUL FOR THE PROPER DISTRIBUTION.

Eg: L-DOPA CROSS THE BBB WHILE DOPINE NOT.

DEPENDING UPON THE CHEMICAL REACTION

ACCORDING TO CHEMICAL REACTION IT IS DEVIDED IN TO TWO PHASE

PHASE I	PHASE II
1) NON SYNTHETIC REACTION 2) INCLUTE PROCESS LIKE OXIDATION, REDUCTION HYDROLISIS. 3) METABOLITES OF IT CAN BE ACTIVE, INACTIVE OR TOXIC.	1) SYNTHETIC REACTION 2) CONJUGATION IS THE MAIN CHEMICAL PROCESS 3) METABOLITES OF PHASE II REACTION NECESSARILY INACTIVE.

DRUGS ARE ELIMINATED FROM THE BODY BY 4 DIFFERENT ALTERNATIVES

1) ELIMINATED UNCHANGED WITHOUT METABOLISM
2) ELIMINATED ONLY BY PHASE I REACTION.
3) ELIMINATE ONLY BY PHASE II REACTION.
4) ELIMINATE BY PHASE I AND II REACTION.

PHASE I REACTION

1) HYDROLYSIS:

DRUG CONTAINIG FUNCTIONAL GROUPS SUCH AS CABOXYLIC ACID, ESTER, AMIDE, THIOESTER, ACID ANHYDRIDE UNDERGO HYDROLYSIS.

2) REDUCTION:

DRUG CONTAINING AN ALDYHIDE, KETONE, DISULFIDE, SULFOXIDE, QUININE, ALKENE ETC ARE UNDERGO REDUCTION.

3) OXIDATION:

IN THIS PROCESS CYTOCHROME P450, NADPH, Fe+3 ETC ARE INVOLVED.

PHASE II REACTION

THESE CONJUGATION REACTION INCLUDE GLUCORONIDATION,SULFONATION, ACETYLATION, METHYLATION, CONJUGATION WITH GLUTATHION AND WITH AMINO ACID SUCH AS GLYCIN, GLUTAMIC ACID.

PHASE II REACTION ARE GENERALLY FASTER THAN PHASE I

ELIMINATION OR EXCRETION

"REMOVAL OF DRUG FROM BODY"

DRUGS ARE EXCRETED BY DIFFERENT ROOTS:

1) RENAL EXCRETION:

A) GLOMERULAR FILTRATION B) TUBULAR SECRETION C)TUBULAR REABSORPTION

2) FECAL ELIMINATION:

- UNABSORBED PART OF THE DRUGS.
- SOME DRUGS DIFFUSE BACK FROM BLOOD IN TO INTESTINE
- MANY DRUGS GOING TO LIVER ARE SECRETED IN TO BILE AND ELIMINATED.

Eg: NEOMYCIN, DOXYCYCLINE.

3) PULMONARY ELIMINATION:

- MAINLY ALCOHOLIC AND VOLATILE DRUGS.

4) ELIMINATION IN BREAST MILK:

- IT IS NOT SIGNIFICANT FOR THE MOTHER BUT TOXIC FOR BABY.
- MILK IS SLIGHTLY ACIDIC IN NATURE SO BASIC DRUGS ARE PREFERBLY CONCENTRATED IN MILK.

Eg: CORTICOSTEROID SUPPRESS ADRENAL FUNCTION

CHLORAMPHENICOL GRAY BABY SYNDROM/BONE MARROW DEPRESION

SALIVA, TEARS ARE ALSO THE ADDITIONAL ROUTE OF ELIMINATION

CONCEPT OF CLEARANCE

ELIMINATION RATE:

- AMOUNT OF **SUBSTANCE REMOVAL** FROM THE CIRCULATION **PER UNITE TIME.**

CLEARANCE (ML/MIN):

- VOLUME OF **PLASMA** THAT IS **CLEARED OF DRUG PER UNIT TIME.**

THE RELATION BETWEEN CLEARANCE, ELIMINATION RATE AND PLASMA CONCENTRATION, EXPRESSED AS;

CL=ELIMINATION RATE (µg/min) / PLASMA CONCENTRATION (µg/ml)

TOTAL BODY CLEARANCE = $CL_{Renal} + CL_{Hepatic} + CL_{Lungs}$

ELIMINATION KINETICS

FIRST ORDER KINETICS OR EXPONETIAL KINETICS:

- WHEN CONCENTRATION OF DRUGS IN BODY INCREASES ELIMINATION RATE IS ALSO INCREASES.
- HERE, THE RATE OF ELIMINATION IS DIRECTLY PROPOSNAL TO CONCENTRATION.

ZERO ORDER KINETICS:

- HERE, DRUG ELIMINATION RATE IS NOT DEPEND ON TO CONCENTRATION.
- MEANS IF THE CONC. OF DRUGS INCREASE IN BLOOD ELIMINATION DOES NOT INCREASE IN SAME PROPOSION.
- THIS TYPE OF KINETIC KNOWN AS SATURATION KINETICS.

ELIMINATION HALF LIFE

"TIME TAKEN FOR ITS PLASMA CONCENTRATION TO HALF OF ITS ORIGINAL AMOUNT"

FOR ZERO ORDER:

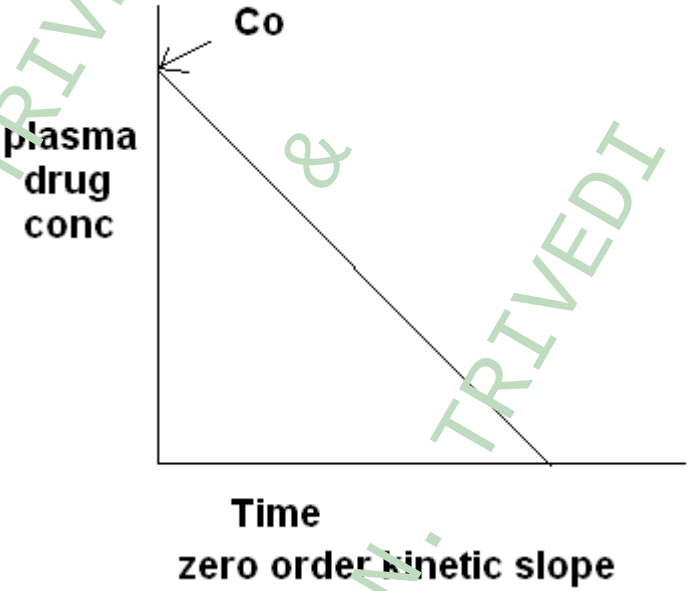
$dc/dt = - K_0C_0$

$dc = - K_0 * dt$

Integration,

$C-C_0 = - K_0 * dt$

$C = C_0 - K_0 * dt$



HALF LIFE:

TAKE $t = t_{1/2}$ **AND** $C = C_{o/2}$

$C_{o/2} = Co - K_0 * t_{1/2}$

$$t1/2 = \frac{Co}{2 * Ko}$$

FOR FIRST ORDER:

$$C = Co\ e^{-K * t}$$

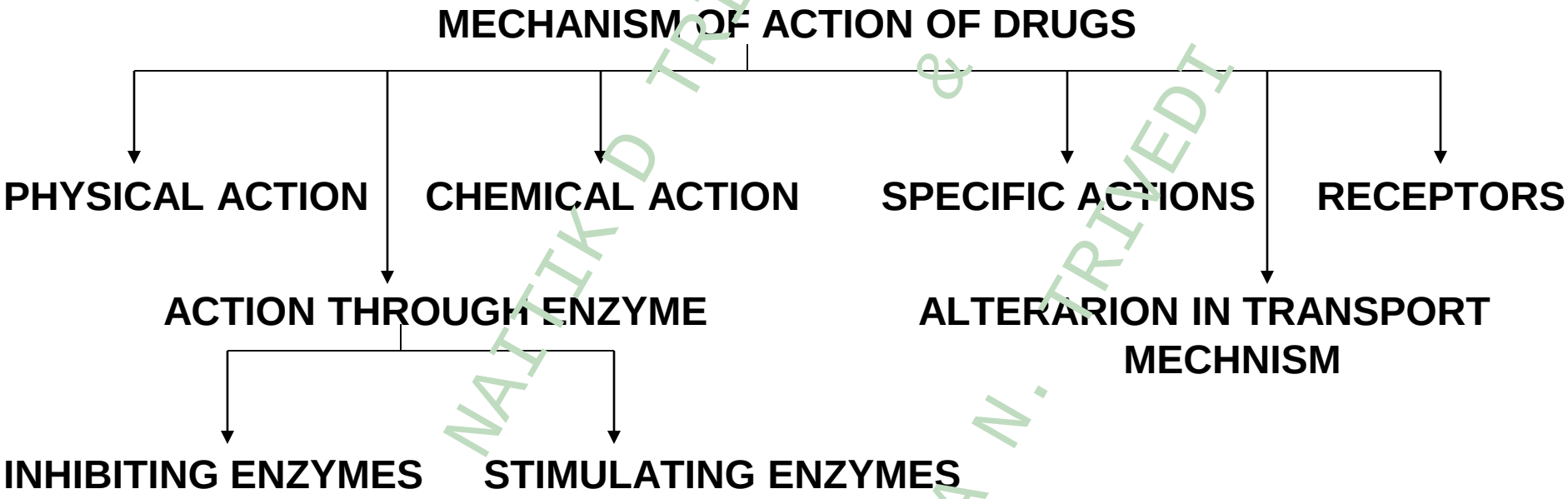
HALF LIFE:

$$t1/2 = \frac{0.6909}{K}$$

PHARMACODYNAMIC

"WHAT A DRUG DOES TO A BODY"

DRUGS CAN PRODUCE THEIR EFFECTS IN A VARIETY OF WAYS:



➢ **PHYSICAL ACTION:**

- BULK **LAXATIVE ABSORB WATER** AND SWELL.
- FORM MASS IN LARGE INTESTINE AND **FACILITATE THE PASSAGE OF STOOLS.**

➢ **CHEMICAL ACTION:**

- **ANTACIDS NEUTRALIZE ACID** IN STOMACH AND REDUCE ACIDITY.

➢ **ACTION THROUGH ENZYME:**

- MOST COMMON MODES OF ACTION

A) COMPETITIVE ACTION:

- **ANGIOTENSIN I** CONVERT IN **TO ANGIOTENSIN II BY** THE HELP OF **ANGIOTENSINOGEN CONVERTING ENZYME (ACE),** WHICH **PRODUCE VASOCONSTRICTION.**
- **LISINOPRIL** IS **STRUCTURLY SIMILAR TO ANGIOTENSIN I** SO ACE BIND WITH LISINOPRIL AND **INHIBIT THE CONVERSION FROM IANGIOTENSIN I TO II.**

B) NON COMPETITIVE ACTION:

- **CYCLOOXIGENASE** IS THE ENZYME **PRODUCE PROSTAGLANDIN**, THE SUBSTANCE **REQUIRE FOR THE INFLAMATION.**
- **NSAIDS** (IBUPROFEN, DICLOFENAC, ETC) **INHIBITE THE ENZYME** AND PREVENT FORMATION OF ENZYME AND **REDUCE INFLAMATION**.

C) ACTION BY STIMULATING ENZYME:

- DRUGS LIKE **STEPTOKINASE OR UROKINASE STIMULATE** ENZYME **PLASMINOGEN** AND **PROMOTE BREAKDOWN OF BLOOD CLOT.**

➢ **ALTERATION IN TRANSPORT SYSTEM:**

- DRUG CAN **ALTER ENTRY AND EXIT** OF DIFFERENT IONS INSIDE CELLS.

Eg: **CALCIUM CHANNEL BLOCKERS** LIKE NIFEDIPINE, VERAPAMIL **PREVENT ENTRY OF CALCIUM** INSIDE CELL AND PREVENTS CONTRACTION OF MUSCLES.

➢ **SPECIFIC ACTION:**

A) DRUGS CAN ALTER CONSTITUTION OF CELL MEMBRANE.

Eg: **GENERAL ANEASTHETICS ALTER** LIPIDS, PROTEINS AND WATER IN THE NERVE CELL MEMBRANE AND PRODUCE ANEASTHETICS ACTION.

B) DRUGS CAN ALTERS SPECIFIC METABILIC PROCESSES INSIDE THE HUMAN CELL AND AFFECT THE MICROORGANISM.

Eg: **PENICILLINS INHIBIT THE CELL WALL SYNTHESIS** OF THE MICROORGANISM BUT NOT THAT ACTION ON HUMAN CEL WALL.

RECEPTORS

- MOST OF THE DRUGS PRODUCE THEIR ACTION THROUGH RECEPTORS.
- IT IS A MACROMOLECULES RESIDE ON THE SURFACE OF THE CELL OR INSIDE THE CELLS.
- BINDS TO SPECIFIC MOLECULES AND PRODUCE SPECIFIC EFFECTS.

"IT IS THE SITE THAT PROVIDES SPACE FOR ATTACHMENT OF SOME SUBSTANCE AND REGULATE THE FUNCTIONING OF THE CELL"

✓ **PHYSIOLOGICAL RECEPTORS:**

- PROVIDE SITE FOR PHYSIOLOGICAL SUBSTANCE ATTACHMENT

Eg: ADRENERGIC RECEPTORS PROVIDE SPACE FOR ADRENALINE.

✓ **DRUG RECEPTORS:**

- PROVIDE SITE FOR SPECIFIC DRUG ATTACHMENT

Eg: BENZODIAZEPINE GET ATTACHED TO BENZODIAZEPINE RECEPTORS.

✓ **AFFINITY:**

- CAPACITY OF SUBSTANCE TO GET ATTACHED TO THE RECEPTORS

Eg: ADRENALINE HAS AFFINITY FOR ADRENERGIC RECEPTORS.

✓ INTRINSIC ACTIVITY:

- CAPACITY OF SUBSTANCE TO BRING OUT SOME CHANGES (OR PRODUCE SOME ACTION) AFTER GETTING ATTACHED TO RECEPTORS.

Eg: ADRENALINE AFTER ATTACHED TO ADRENERGIC RECEPTORS GENERATE CYCLIC AMP AND INCREASE FORCE OF CONTRACTION AND HEART RATE.

- ACTION AND EFFECT ARE TWO DIFFERENT, ACTION MEANS CHANGES AFTER BINDING AND EFFECT MEANS BIOLOGICAL EFFECTS OBSERVED AFTER ADMINISTRATION OF DRUG.

✓ AGONIST:

- ATTACED TO RECEPTORS AND PRODUCE CONFERMATIONAL CHANGES IN RECEPTORS.
- IT HAS AFFINITY AND INTRINSIC ACTIVIRY.

Eg: ADRENALINE AFTER ATTACHED TO ADRENERGIC RECEPTORS GENERATE CYCLIC AMP AND INCREASE FORCE OF CONTRACTION AND HEART RATE, SO IT IS THE AGONIST OF ADRENERFIC RECEPTORS.

✓ COMPETITIVE ANTAGONIST:

- SUBSTANCE HAVE AFFINITY BUT NOT INTRINSIC ACTIVITY.

Eg: PROPANOLOL PREVENT THE ATTACHMENT OF ADRENALINE AND PREVENT INCREASE HEART RATE OR REDUCE HEAR RATE.

- THESE SUBSTANCE ARE STRUCTURLY SIMILAR

✓ **PARTIAL AGONIST:**

- IT HAS BOTH AFFINITY AND INTRINSIC ACTIVITY BUT INTRINSIC ACITIVITY IS LESS THAN AGONIST.

✓ **INVERSE AGONIST:**

- PRODUCE ACTION BUT OPPOSITE TO AGONIST.

✓ **SPARE RECEPTORS:**

✓ **SILENT RECEPTORS:**

REGULATION OF RECEPTORS

1) DOWN REGULATION:

- WHEN RECEPTORS EXPOSED TO AGONISTS FOR A LONG TIME, THE NUMBER OF RECEPTORS AND THEIR SENSITIVITY FOR AGONIST ARE REDUCED.
- WHEN THE AGONIST IS DISCONTINUED, THE ACTIVITY OF RECEPTORS REAPPEARS.
- Eg: SALBUTAMOL IS USFUL FOR ASTHAM WHEN IT GIVEN IT PRODUCE DILATION OF BRONCHIAL MUSCLES THROU RECEPTORS BUT AFTER A PROLONG TIME ITS ACTION GET DECREASED BY DECREASIN SENSITIVITY TOWARDS THE RECEPTORS.

2) UP REGULATON:

- RECEPTORS ARE BLOCKED FOR A LONG TIME, THE NUMBER AND SENSITIVITY OF THE RECEPTORS FOR AGONIST ARE INCREASED.

MECHNISMS OF RECEPTORS ACTION

- ACCORDING TO MECHANISM OF ACTION THEY ARE CLASSIFIED AS BELOW:

1) RECEPTORS WITH INTRINSIC ION CHANNELS:

- THESE RECEPTORS ARE ON THE SURFACE OF THE CELL AND CONTAIN ION CHANNELS.
- DIFFERENT RECEPTORS HAVE DIFFERENT ION CHANELS BY WHOM THEY REGULATE CELLULAR ACTION.

Eg: NICOTINIC RECEPTORS, 5-HT RECEPTORS.

2) ENZYME RECEPTORS:

- THESE RECEPTORS ACTUALLY ENZYME (Eg. TYROSINE RECEPTORS).
- ONE PART OF THE RECEPTOR IS OUT SIDE THE CELL AND ONE IS INSIDE.
- DRUG BINDS TO OUTER PART AND STIMULATE THE RECEPTORS AND PHOSPHORYLATE OHER PART, AND START THE SIGNALING PROCESS AND GIVES ACTION.

Eg: INSULINE RECEPTORS.

3) GENE ASSOCIATED RECEPTORS:

- THESE RECEPTORS ARE SITUTED INSIDE THE CELL AND ARE ACCOSIATED WITH GENES.

Eg: STEROID.

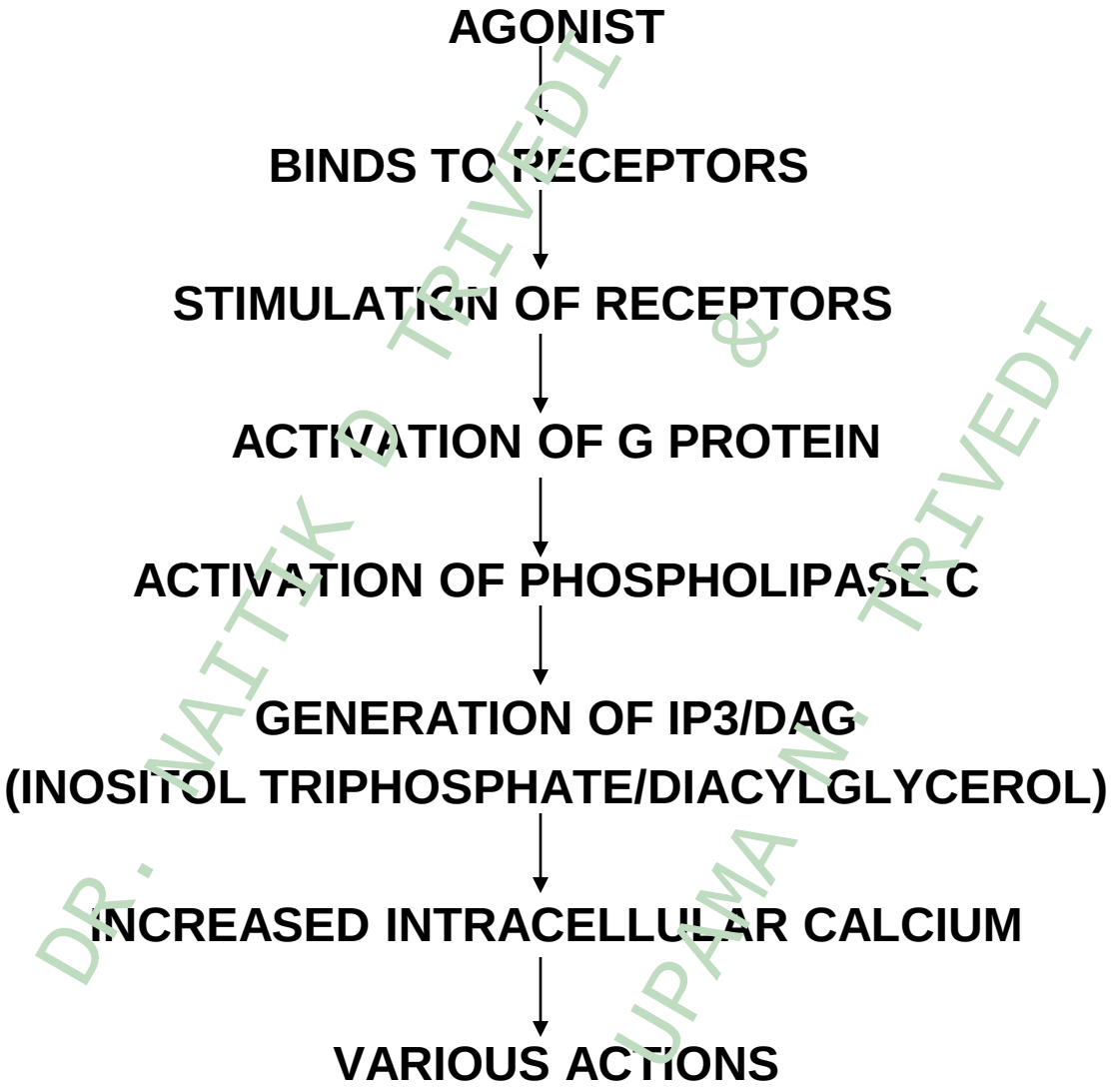
4) G PROTEIN COUPLED RECEPTORS:

- **G** PROTEINS MEANS GTP ACTIVATED RECEPTORS.
- G PROTEIN ARE OF DIFFERENT TYPES.
- AGONIST STIMULATE RECEPTORS, STIMULATED RECEPTORS PRODUCE ACTION G PROTEIN IN FOLLOWING PATHWAY:

A) ACTION THROUGH ADENYL CYCLASE AND Camp:

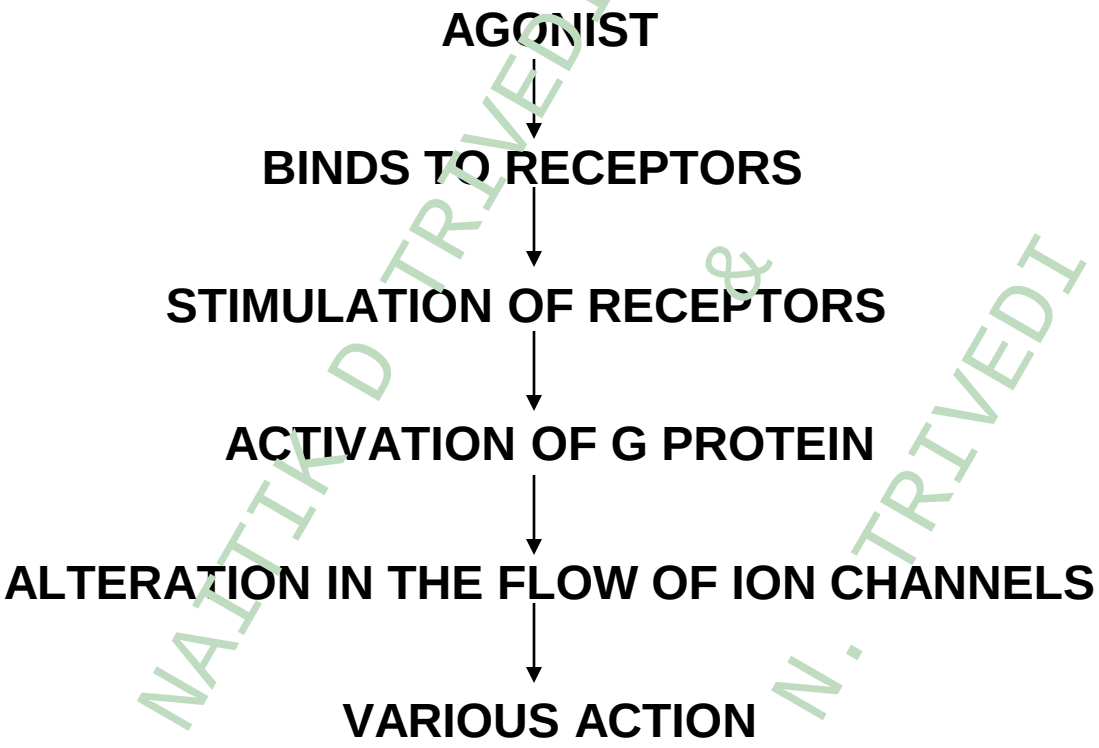
Eg: DOPAMINE RECEPTORS, H2 RECEPTORS.

B) ACTION THROUGH IP3/DAG:



Eg: BETA RECEPTORS (B1), H1 RECEPTORS.

C) ACTION THROUGH G PROTEIN ASSOCIATED ION CHANNELS:



Eg: B2 RECEPTORS