÷ Unit-4 ÷

÷ Adenohypophyseal Hormones ÷

Ch-1 Adenohypophyseal Hormones.
Ch-2 Thyraid Hormones.
Ch-3 Parathormone Calcitonin.
Ch-4 Insuline Glucagon.
Ch-5 ACTH and Corticosteroids.

÷ Chaper ÷ 1

Adenohypophyseal Hormone (Pituitary Gland)

Pituitary Gland ÷ Pituitary Gland is also known as hypophyseal gland which is present Hypothalamus part of brain.

- In the skull small depression is present which is known as sella tersica and inside the sella tersica small gland like 'pea' is hanging with the infondibulam.
- Which is known as pituitary gland.
- Its diameter is 1 cm only.
- The pituitary gland on the basis there size and function is devided into three part

(1) Anterior Pituitary
(2) Median Pituitary
(3) Posterior Pituitary.

1) Anterior Pituitary is also known as Adenohypophyseal Pituitary.

2) Median Pituitary is also known as Mesen Hypophyseal pituitary.

3) Posterior Pituitary is also known as Neuro Hypophyseal pituitary.

→ The Anterior Pituitary is release five hormone.

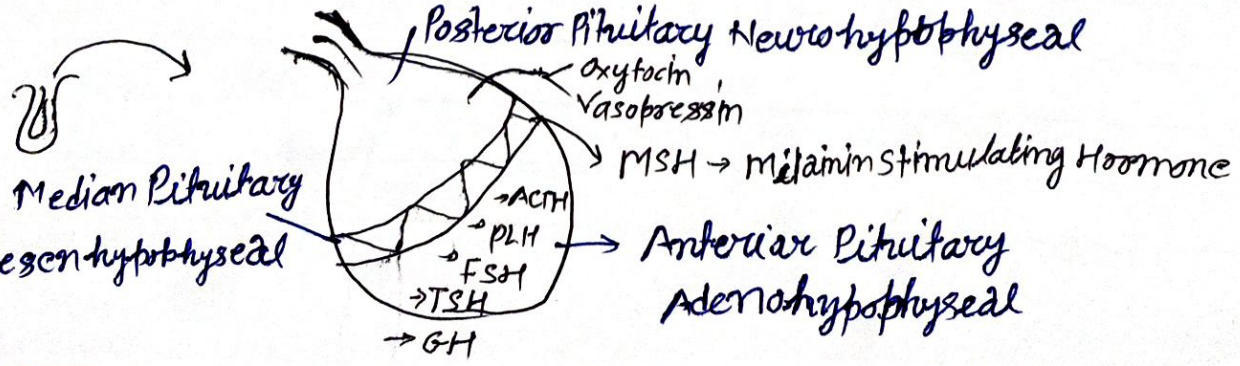
i) AcTH - Adreno Cardico tropic hormone.
ii) PLH - Prolactine hormone.
(iii) FSH - Follicular Stimulating hormone.
(iv) TSH - Thyroid Stimulating hormone.
(v) GH - Growth hormone.

→ The median Pituitary release one hormone.
(i) MSH → Milanin Stimulating hormone.
Which is decide the color of the body.

→ The last one is Posterior Pituitary or Neurohypophyseal release the two hormone.

(i) Oxylocin
(ii) Vasopressin.

→ Pituitary gland is also called master gland.
→ And hypothalamus is called master of master gland.



← Hypothalmic Control of Adenohypophysis :-

→ Because Pituitary Glands contrals the release of hormone of diff-2 glands. so they are called master gland.

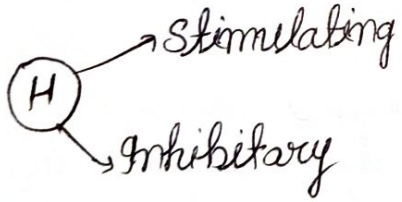
→ But the control of Pituitary gland hormone is regulated by the hypothalmus. so hypothalmus is known as the master of master gland.

→ Because hypothalmus secreate two types of hormone for the same gland.

(i) Stimulatory

(ii) Inhibitary.

→ Hypothalmus is a very highly vascular organ in which Hypophyseal pituitary gland is present and it is covered with the network of blood vessel capilary. this is called Hypothalmic - Hypophyseal Portal Capilary Network.



Hypothalmic Hypophyseal Portal Capilary Network.

→ Hypothalmus Secreate ten types of diff-2 hormone which contral the function of Anterior Pituitary.

(1) Growth hormone releasing factor.

(2) Growth hormone Inhibitary factor.

(3) Prolactin releasing factor.

(4) Prolactin Inhibitary factor.

(5) Gonadotrophin releasing factar

(6) Gonadotrophin Inhibitary factar.

(7) Thyratrophin releasing factar

(8) Thyratrophin Inhibitary factar.

(9) Milamin stimulating hormone releasing factar.

(10) Melamin stimulating hormone Inhibitary factar.

∴ Pathological disorder of Adenohypophysea.

⇒ The pathological disease appears the body when the hormone secreation is hyper or becomes hypo.

→ On the basis of hypathalmus hormone it is devided in to two categary.

(i) Trophic Hormone :- These hormone influence the function of other gland indirectly. Ex- TSH, ACTH.

(ii) Non Trophic Hormone :- These hormone affect the function of any gland directly. Ex GH.

- On the basis of Pathological disorder or Secreation of hormone disease can be classified into two type.

(i) Hyperpituitorism

(ii) Hypopituitarism.

(i) Hyperpituitarism :-

→ When the secereation of hormone becomes excess from the pituitary gland this is called hyperpituitarism.

Ex :- Exathalmic Gaitwre., Acromagelli.

(ii) Hypopituitarism.

When the hormone secreation from the Pituitary gland becomes less or hypo in nature this is called Hypopituitarism

Ex- Gaitwre, Dwarphism.

Adenohypophyseal Hormones

→ Group - 1 :-

Growth-hormone → 191 amino acid

Prolactin → 198 Amino Acid

Placental Lactogen → 191 Amino Acid.

Group - II :-

LH → 89 α-AminoAcid, 115 β-AminoAcid

FSH → 89 α-AminoAcid, 115 β-AminoAcid

Thyrotrophin → 89 α Amino Acid, 112 β-Amino Acid

Gonadotrophin → 92 α-Amino Acid. 145 β Amino Acid.

Group-III :-

ACTH → 39 Amino Acid

MSH → 13 α-Amino Acid 18 β-Amino Acid

Lipoprotein → 91 α-Amino Acid 58 β-Amino Acid.

÷ Thyroid Gland and their Hormone ÷

Thyroid Gland ÷ In the trachea of human both side two lobes are present basically they are called thyroid Gland

→ And it was discoverd by the Wharton in 1656.

→ It is a butterfly or H shaped gland which is located on both side of the thrachea. and on the anterior posteriar four corners of the thyroid gland Parathyroid gland is also present.

→ In the structure of thyroid gland a singal unit is called thyroglobulin.

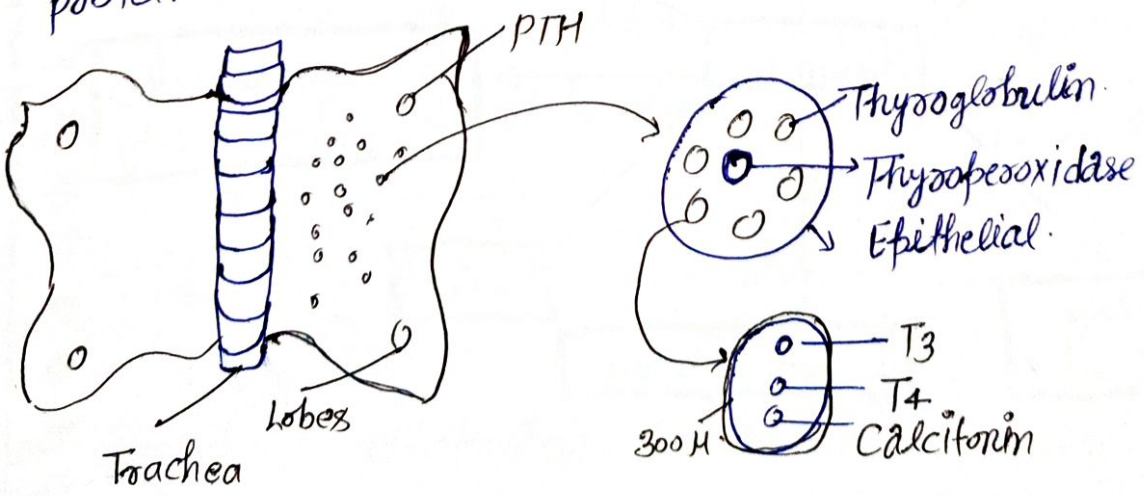
• And ~~in~~ inside the thyroglobulin it is a glycoprotein structure. thyroglobulin in which the enzymes are store

→ Basically there are three enzyme T_3, T_4, & Calcitonin.

→ T_3 means triiodo thyroxin., T_4 means Tetra Iodothyroxin.

→ The weight of the thyroid gland is about 25g and the gland size is slightly larger in female than male.

→ The diameter of thyroglobulin which is unit of thyroid gland have the size of 300 μ. and it is made by the colloidal protein.



Role of Thyroid Gland :-

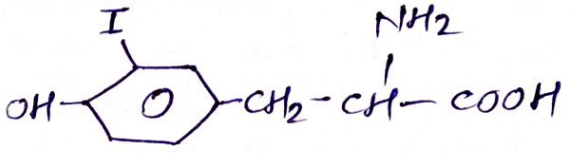
→ Thyroid gland play two major role in human body they have in the grouth and development of the body and it also controll the mental-health of any human.

→ The need of Iodine is very necessory for the production of thyroid hormone in our body.

→ Our body need 6 to 7 mg Iodine in per day and about these total quantity for the 90% of the quantity is uptake by the thyroid gland to produce these (T3, T4 & Calcitonin) hormone.

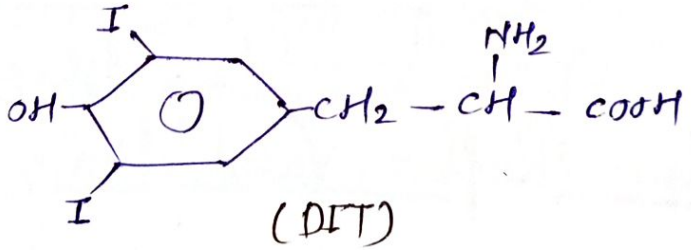
→ After the hydrolysis of the thyroglobulin it release the thyroid hormone. T4, T3, DIT & MIT.

(i) Mono Iodo Thyroxin.



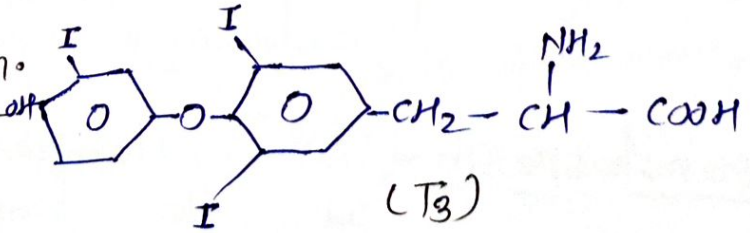
(MIT)

(ii) Di Iodothyroxin.



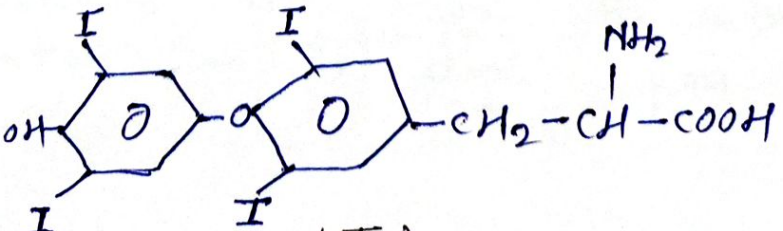
(DIT)

(iii) Tri Iodothyroxin.



(T_3)

(iv) Tetraiodothyroxin



(T_4)

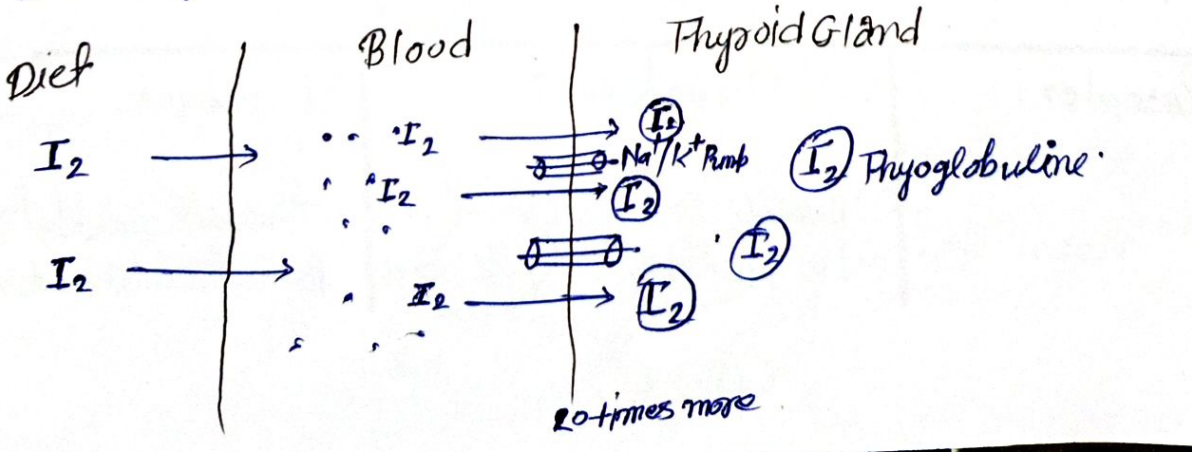
Biosynthesis Storage and Release of Thyroid Hormone:-

→ Biosynthesis of thyroid hormone takes place inside the thyroglobuline of thyroid gland and it involves following four steps -

(i) Iodine Uptake by the thyroid Gland.
(ii) Oxidation of Iodine and Iodination of Tyrosyl Group.
(iii) Oxidative Coupling of Iodo tyrosyls to form T_3 & T_4
(iv) Release of Thyroid Hormone.

(i) Iodine Uptake by the thyroid Gland:-

→ From the diet Iodine . is goes and absorb into the blood and its systemic circulation.
→ And from the blood Iodine is uptake by the thyroglobuline inside the thyroid gland by the active transport.
→ The conc. of iodine is 20 times more in thyroid gland than blood.
→ So the energy is required for the transport of iodine from blood to thyroid gland.
→ They contains Sodium Potassium ATPase pump and with the help of sodium potassium ATPase pump the iodine is uptaken by the thyroglobuline and goes inside the thyroid Gland.



(2) Oxidation of Iodine and Iodination of Tyrosyl Group :-

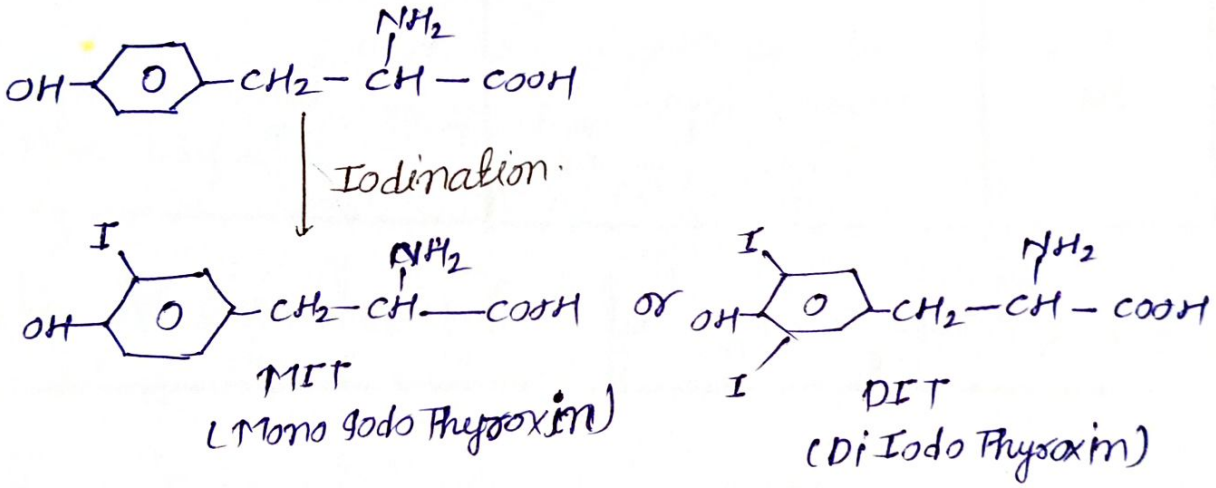
→ The enzyme Thyroperoxidase which is present inside the thyroglobuline it helps in the oxidation and cleavage of the iodine malecule.

→ And by this enzyme I_2 (Iodine) malicule is breaks into the iodo group.

$$I_2 \xrightarrow[\text{oxidation}]{\text{Enzyme Thyroperoxidase}} I^{\circ}\ I^{\circ}$$

or

I^+ (Iodo) I^- (Iodide)



(3) Oxidative Coupling of Iodo Tyrosyls to form T_3 & T_4

After the formation of MIT and DIT Precursor molecule withe the help of enzyme thyroperoxidase then they are coupled to each other and they form t_3 and T_4 hormones.

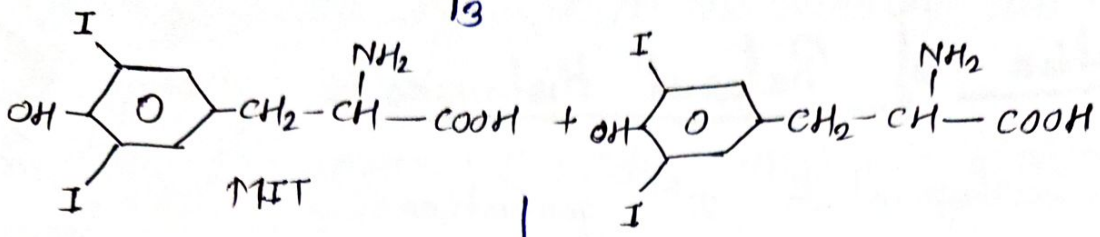
→ when the one malicule of MIT coupled with the one molicule of DIT inthe presence of Thyroperoxidase enzyme the form T_3 hormone (Tri Iodo Thyroxine).

→ And when the two molecule of DIT are coupled with eachother then they form t_4 hormone (Tetra Iodo thyroxine)

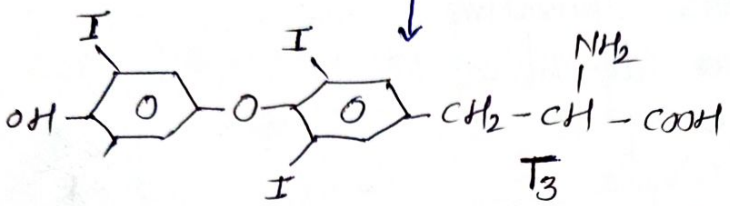
MIT + DIT

↓ Thyroperoxidase

T_3



MIT



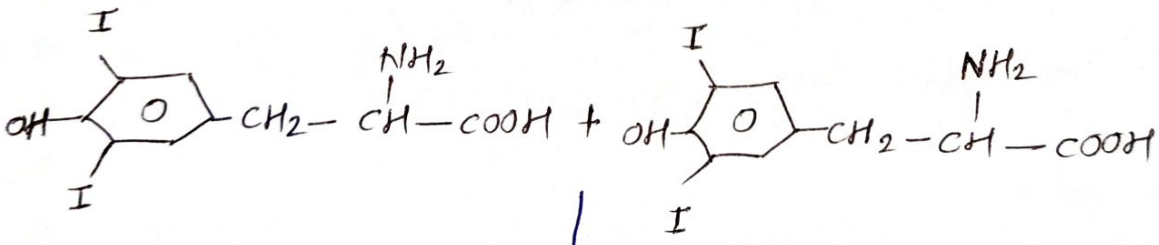
T_3

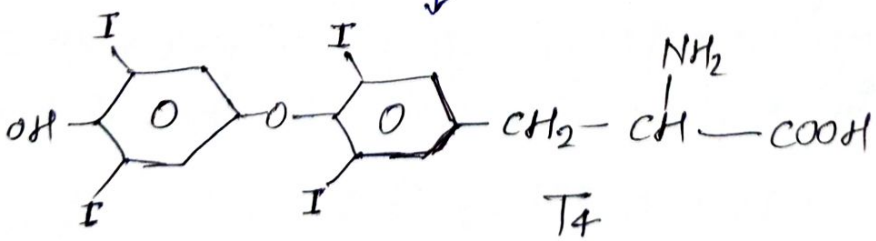
(Tri Iodo Thyroxin)

DIT + DIT

↓ Thyroperoxidase

T_4





T_4

(Tetra Iodo Thyroxin)

(4) Release of Thyroid Hormone:-

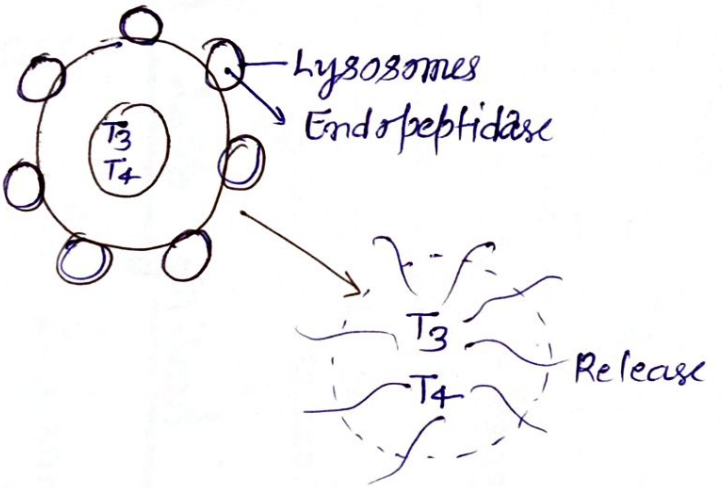
→ The release of Thyroid Hormone is basically controll by the Hormone TSH. which is released from the Anterior Pituitary of the Pituitary gland.

→ But they also control by the self method.

→ In the besides of the thyoglobuline lysosomes cells are present and these lysosome cells are release the enzyme endopeptidase

→ And when the enzyme endopeptidase is release

→ The thyoglobuline surface is raptured then the hormone T_3 & T_4 release in the systemic circulation.



Pharmacokinetics of Thyroid Hormone

→ When the thyroid gland release the hormone then it goes the systemic circulation. into blood. then they can't reach each and every tissue along.

→ So they bind with the globuline protein which is present in the blood and make a complex with the globulin protein.

→ And this globulin protein helps to carry the thyroid hormone to each and every organ of the body.

→ Untill the thyroid hormone is bonded with the globulin protein so they can't be metabolise with the various enzyme

→ So there duration of action inside body is increase.
and the average half life for the thyroid hormone in body is 6 to 7 hours.

→ And then after 6 to 7 hours when globulin protein is again released then Thyroid hormone is free and by the diff-2 Chemical reactions like-

→ Decarboxylation Reaction

→ Deamination Reaction.

they are metabolise and they are excreated from the urine.

Physiological Action of Thyroid Hormone:-

(1) Growth and Development.
(2) Calorigenic Effect.
(3) CVS Effect.
(4) Miscellaneous Effect.

(1) Growth and Development:-

→ Thyroid Hormone is basically involved in the Growth & development of the body and their body organ. by the effect of metabolism. When the thyroid hormone is not release in properly then the development of body and its part becomes diminished this is called cretinism.

(2) Calorigenic Effect :-

→ Because Thyroxin hormone helps in the metabolism then by the process of Gluconeogenesis, Lipolysis, Glycogenolysis they increase the production of energy which is called Calorigenic effect.

(3) CVS - cardio Vascular System Effect :-

→ They increase the force of contraction of CVS.

(4) Miscellaneous Effect :-

→ Breakdown of lipid, Cholesterol inside the body.

:- Disease of Thyroid Glands :-

When the level of thyroxin hormone either more or less it can cause diff-2 disease they are called disease of Thyroid gland.

→ When the hormone secreate less in quantity then it called Hyposecretion.

→ Due to hyposecretion basically three disease can occurs -

(i) Simple Goitre

(ii) Myxodema.

(iii) Critinism.

→ When the level of thyroxin hormone is more than the normal level then they called the hyper secretion. it causes to disease -

(i) Grave disease

(ii) Plummer's disease.

(i) Simple Goitre:- The term goiter denotes any enlargement of thyroid gland.

⇒ Normal secretion by thyroid Gland needs an adequate intake of iodine.

⇒ If the dietary supply of Iodine does not meet the daily requirement, Thyrotropin is released in higher concentration ⇒ which results into the enlargement of thyroid gland.

⇒ This enlarged thyroid gland is known as goitre.

:- Drug Used in therapy of Hyperthyroidism :-

(1) Radioactive Iodine.

(2) Antithyroid drug.

(A) Thioamides
(B) Aniline derivatives
(C) Polyhydric Phenol
(D) Ionic Inhibitor
(E) Miscellaneous — (i) Lithium Carbonate, (ii) Adrenergic Blocker.

(i) Thioamides:- Thiourea and thiouracil derivatives are among the primary drugs to treat thyroid hyperactivity.

⇒ The methyl and Propylthiouracil are effective drugs. they inactivate the peroxidase enzymes.

(ii) Aniline derivatives:- These agents interfere some of the processes catalyzed by thyroid peroxidases like iodine oxidation, organification and coupling of iodotyrosines. ex- includes sulfathiazole, Sulfadiazine, P-amino salicylic Acid.

(iii) Polyhydric Phenols:- The only clinical agent from this category is resorcinal.

→ It possesses some mechanism like that of thioamides.

(iv) Ionic Inhibitors:- These are all monovalent hydrated anions and resemble in size with iodide ions.

→ They effect the powder of thyroid gland to accumulate iodine by inhibiting the iodide transport mechanism. Ex- Thiocyanate, Perchlorate, Fluoborate.

(v) Miscellaneous Agents:-

(i) Lithium Carbonate:- Lithium appears to prevent the release of both hormonal and non hormonal iodine from the thyroid gland.

→ It is less preferred agent due to its adverse effects which include tremors with high risk of cardiac failure.

(ii) Adrenergic blockers:- Hyperthyroidism has some of the symptoms common with adrenergic overstimulation. due to this reason the adrenergic blockers are sometimes used in alleviating many of the signs and symptoms of hyperthyroidism usually for short term treatment.

Ex- Reserpine, Guanethidine, and Propanolol.

→ They may help in reducing tachycardia, tremor anxiety, sweating and heat intolerence associated with hyperthyroidism.

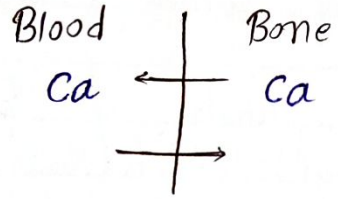
Parathyroid Hormones Calcitonin and Vitamin D:

Parathyroid Gland: Parathyroid Gland is small gland which is located on the four corner of the thyroid gland.

→ It is a yellow in colar so it is called yellow glandular body.

→ And the weight of these gland approx 0.05 to 0.3 gm it means 50mg to 300 mg.

→ The parathyroid hormone basically work to maintain the calcium level in both blood plasma as well as in bone.



→ When the calcitonin is release then they decrease the concentration of calcium level in blood and increase in the bone. they causes the hypokalemia.

→ And when the parathyroid Hormone is release they increase the Ca^{++} into the blood and decrease into the bone they called Hyperkalemia.

→ The total calcium level in our blood is on average 10 to 11 mg in per 100 ml of the blood.

→ And the total concentration of the calcium in the blood devided into two part.

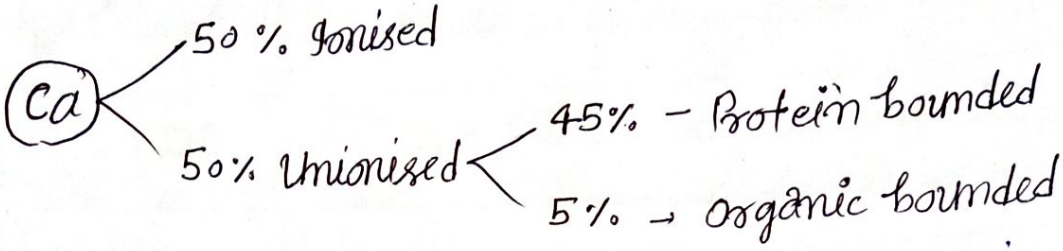
(i) 50% Ionised form

(ii) 50% Unionised form.

→ The 50% unionised form is further it can be devided into form.

→ (i) 45% of this protein bounded.

→ (ii) And the 5% of this is organic bounded.

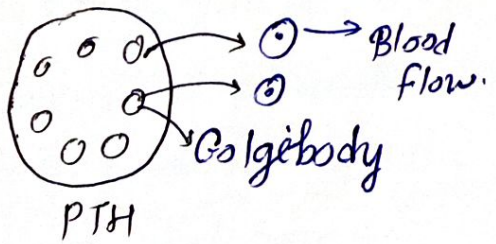


→ The parathyroid hormone is made up of the 84 amino acid in a singal chain sequence. and there molecular weight is about 9500.

⇐ Synthesis and Secretion of Parathyroid Hormone:-

→ It is decrived from the 84 amino acid sequence and they are synthesies inside the parathyroid gland.

→ Basically they are synthesies inside the parathyroid gland with the help of golgibody. and they secrete (with the help of) in the form of vessicles. and release into the systemic circulation.



→ The parathyroid hormone basically act on kidney bone and GIT. to maintain the blood plasma calcium level by the three method -

(i) Promoting Absorption of calcium from GIT.
(ii) Mobelising the calcium in bones.
(iii) Decrease Ca^{++} Excretion.

Physiological function of Parathormone on body :-

(i) Effect on bone :- Basically Parathormone by the mobelising the Ca^{++} ion into the bone they maintain the level of Ca^{++} and PO_4^- ion into the bone.

(ii) Effect on kidney :- It increase the rate of reabsorption.

(iii) Effect on GIT :- It converts the calcifodial into the calcitrial.

Disorder of Parathyroid Hormone :-

(i) Hyperparathyroidism :- The the Parathyroid hormone level is increase more than the normal range this is called hyperparathyroidism.

→ Decrease Plasma Concentration.
→ Skeleton abnormilis.
→ Bone deformation

(ii) Hypoparathyroidism :- If the level of Parathyroid hormone is decrease than the normal range this is called Hypoparathyroidism.

→ Muscle spasm.
→ Tetany
→ Tachycardia.

÷ Calcitonin ÷

→ Calcitonin is a hormone protein that lowers the concentrations of blood calcium when it has risen to an above normal level.

→ In humans and other mammals, calcitonin is secreted by the parafollicular cells of the thyroid gland while in fish, bird, and reptiles it is secreted by the Ultimobranchial gland.

÷ Pharmacological Actions ÷

The main actions of calcitonin are the lowering of blood calcium and the suppression of cell activity that causes calcium to be last from bones.

→ Some of the main actions of calcitonin are described below.

(1) In Postmenopausal Women With Osteoporosis ÷

→ Osteoporosis leads to brittle and easily fractured bones as a result of decreased bone mass along with architectural breakdown of the bones.

→ Common Fracture sites includs the vertebrae, hip, forearm and wrist.

→ The most common type of osteoporosis occurs in postmenopausal females, when the rate of bone resorption by osteoporosis is faster than the rate of bone formation by osteoblasts.

(2) Maintenance of Calcium balance in the body :-

→ Calcitonin opposes the effects of parathyroid hormone, which acts to increase the blood calcium level.

→ Calcitonin lowers blood calcium level by suppressing Osteoclast activity in the bones and increasing the amount of calcium excreted in the urine.

(3) Effect on the kidney :- Calcitonin also regulates the level of calcium and other minerals in the kidneys.

→ This hormone prevents the re-absorption of phosphates by the kidney and increases the kidney's re-absorption of calcium and magnesium.

(4) Calcitonin also affects hunger and appetite and has been shown to reduce the volume and acidity of gastric juice as well as the volume of the pancreatic juice and its trypsin and amylase content.

Pharmacokinetics of Calcitonin :- Calcitonin-Containing medicines are usually administered as solutions than can be injected but for the past couple of decades, they have also been available in the form of nasal sprays.

→ When used as a nasal spray, calcitonin takes around 13 to 15 minutes to be absorbed in to the blood.

→ The half life of commercially prepared calcitonin is around 18 to 20 minutes.

÷ Side effect of Calcitonin÷ Nasal spray use ing associated with side effects such as runny nose and nasal crusting, dryness, bleeding itching and redness.

→ The majority of these symptoms are mild and resolve as a patient adjust to using the spray.

→ There may be symptoms that mimic flu such as tiredness fever and chills.

→ Skin rash

→ Muscle Pain and arthritis.

→ Sinusitis, chest, tightness, difficulty breathing.

→ High blood pressure, chest pain, Palpitations.

→ Abdominal pain, nausea, Diarrhea, vomiting, Flatulence and decreased appetite.

← Vitamin D →

→ Vitamin-D is a fat soluble vitamin.

→ Vit. D is a sterol, it contains steroid nucleus.
(Cyclopentanoperhydro Phenanthrene ring)

→ Vitamin-D function like a hormone.

÷ Forms of Vitamin D÷

→ Vitamin D in the diet occurs in two forms.

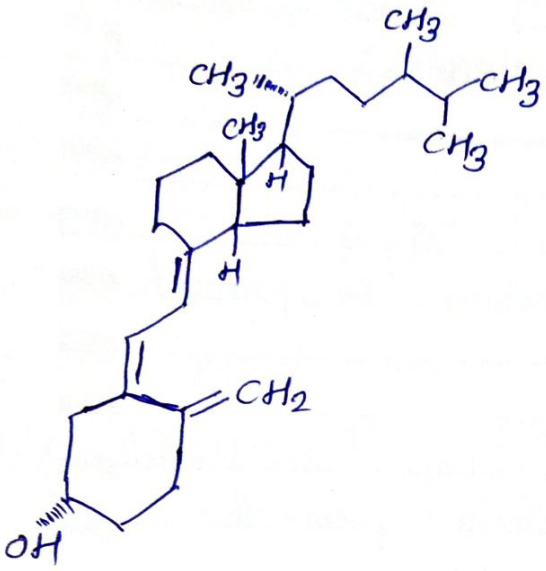
→ Vitamin - D_2 (Ergocalciferol)

→ Vitamin - D_3 (Cholecalciferol)

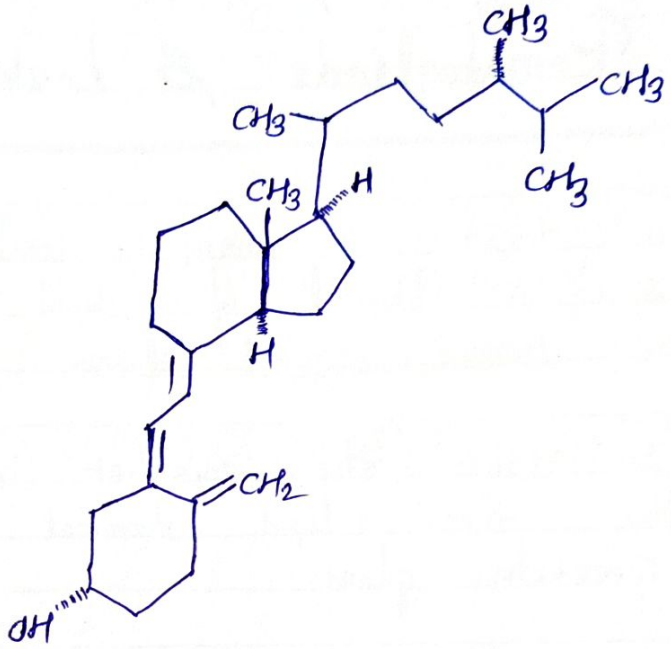
Chemistry

→ Ergocalciferal (Vit-D_2) is formed from ergosteral is present in plant

Vit-D_2



Vit-D_3



← Vitamin D is a sunshine →

→ During the course of cholesteral biosynthesis 7 dehydrocholesterol is formed as an intermediate.

→ On exposure to sunlight, 7-dehydrocholesterol is converted to cholecalciferal in the skin (dermis and epidermis)

→ Dark skin pigment (Melanin) Adversely influences the synthesis of cholecalciferol.

→ Skin is the largest organ in the body.

→ The production of vitamin D inthe skin is directly proportional to the exposure to sunlight and inversely proportional to pigmentation of skin.

→ Excessive exposure to sunlight does not result in vit. D toxicity since excess provitamin D_3 are destroyed by sunlight itself.

Absorption: → Diet from animal sources such as animal liver contains vitamin D_3.

→ Diet from plant sources contains vitamin D_2.

→ Vit. D_2 & D_3 are absorbed from upper small intestine and bile is essential.

Mechanism: Vitamin D_3 and D_2 form mixed micelles by combining with bile salts (Micelles).

→ Mixed micelles are presented to mucosal cells.

→ Absorption occurs by passive transport.

Transport: Vit. D-binding globulin - Vit D is transported from intestine to the liver by binding to vitamin D binding globulin.

→ 25-Hydroxy D_3 and 1,25-dihydroxy D_3 are also transported in the blood by binding to vitamin D binding globulin.

Storage: → 25 hydroxycholecalciferol is the major storage and circulatary form of vitamin D

Biochemical function:

→ Calcitrial (1,25 DHCC) Acts at three different levels to maintain plasma calcium.

Action on Intestine: Calcitrial increases the intestinal absorption of calcium and Phosphate

→ In the intestinal cells, calcitrial binds with a cytosolic receptor to form a calcitrial-receptor complex.

→ This complex interacts with a specific DNA leading to the synthesis of a specific calcium binding protein.
→ This protein increases calcium uptake by intestine.
→ The mechanism of action of calcitrial is similar to that of steroid hormone.

Action on bone :- In osteoblasts of bone, calcitrial stimulates calcium uptake for deposition as calcium phosphate

→ Recommended dietary Allowance (RDA)

→ Children – 10 gm/day or 400 IU/day
→ Adults – 5 gm/day or 200 IU/day
→ Pregnency lactation – 10 gm/day or 400 IU/day
→ Above the age of 60 years – 600 IU/day

Source of Vit-D :- → Exposure to sunlight produces cholecalciferol.
→ Good sources includes – Fatty fish, fish liver oils egg, yolk etc.
→ Milk is not a good source.

Deficiency of Vitamin-D :- Deficiency of vitamin D causes rickets in children and osteomalacia in adults.

→ Rickets.
→ It is a vitamin D deficiency state in children.

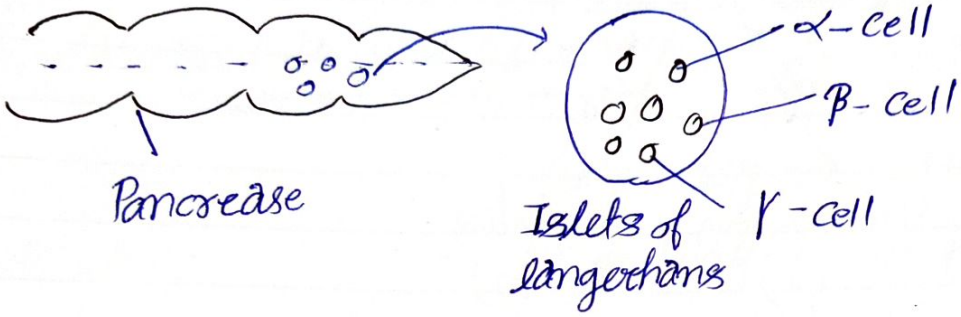
causes :- Dietary deficiency and non exposure to sunlight.
→ Rickets in children is characterized by bone deformities due to incomplete mineralization.

÷ Insulin and Oral Anti-Diabetic Drugs ÷

Insulin & Glucagon ÷ Insulin is the hormone secreted in the pancreas by the beta cells of islets of langerhans.

→ Insulin lowers blood sugar level.

→ Diabetes mellitus occurs in the absence of insulin secretion



α-Cell – Glucagon

β-Cell – Insuline

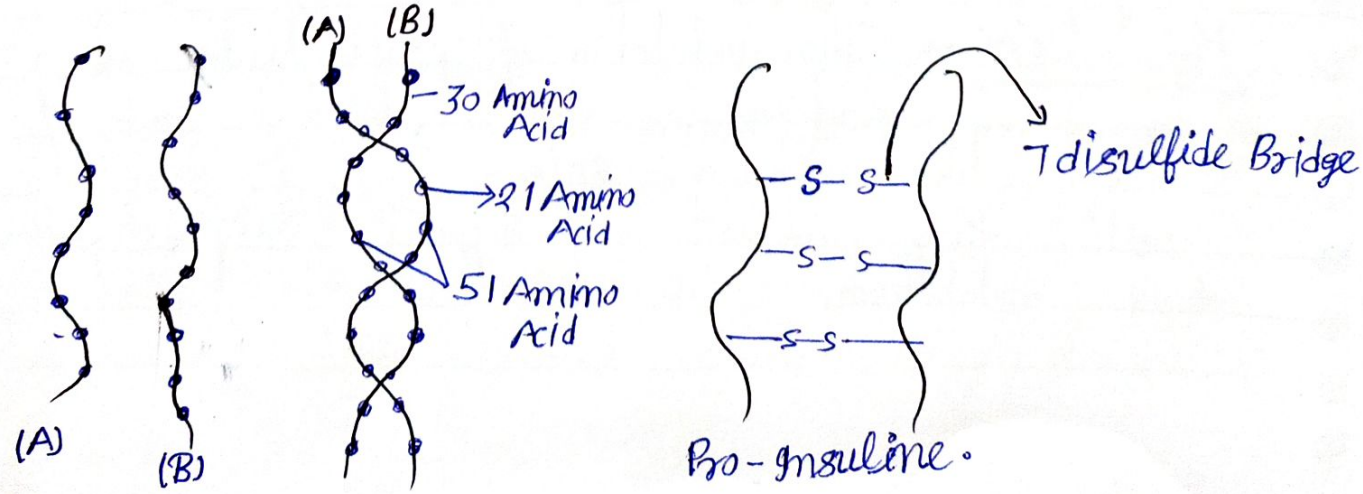
γ-Cell – Somatostatin (GH)

Chemistry ÷ Insuline is a polypeptide and it has a molecular weight of about 6000.

→ It contains 51 amino acid arranged in two chains viz.

→ A chain containing 21 amino acids and B chain containing 30 amino acid.

→ These two chains are linked by disulfide bridges.



Synthesis, Storage and release:- In the pancreas, insulin is synthesized by beta cells of islets of Langerhans.

→ Initially it is synthesised as a single chain polypeptide called proinsulin.

→ Proinsulin is 1/8th as active as insuline.

→ It is later cleaved into A and B chains which are connected by disulfide bridges.

→ Insulin is stored in the granules of beta cells.

→ It is released in response to a rise in blood glucose level.

→ The release of insulin is controlled by the concentration of glucose in blood.

Transport Fate and Extraction:- Insulin circulates in plasma partly in a protein bound form and partly in a free form.

→ It is taken up mostly by the liver, kidney and skeletal muscle. No insulin is taken up by red blood cells and brain.

→ Insulin is degraded by tissues like liver, kidney, testes and placenta.

→ It is metabolised by glutathione - insulin transhydrogenase (insulinase).

→ This enzymes separates the two chains.

→ The individual chains are degraded by proteolytic enzymes.

Action of Insulin:- (A) liver:- In the liver, insulin increases the activity of two enzymes :-

(1) Glucokinase which increases glucose uptake.

(2) Glycogen synthetase which increases glycogen deposition.

→ It decreases the activity of two other enzymes.

(1) Phosphorylase and cyclic AMP, Inhibition of which decreases, glycogenolysis (breakdown of glycogen).

(2) Enzymes concerned with gluconeogenesis (fresh synthesis of glucose from non-carbohydrate sources)

⇒ As a result the breakdown of liver glycogen and fresh synthesis of glucose is decreased.

⇒ But glucose is mobilised to the liver and deposited as glycogen.

(b) Adipose Tissue:- Insulin increases the permeability, uptake and metabolised of glucose in the fat cell.

⇒ Increased Glucose Utilisation leads to the synthesis of glycerol, Alpha glycerophosphate and fatty acid.

⇒ The later two compounds combine to form triglyceride (Storage form of fat).

⇒ Thus, insulin induces lipogenesis (Synthesis of fat).

⇒ But it prevents lipolysis (break-down of fat).

(c) Skeletal Muscle:- Insulin stimulates the uptake of glucose by the muscle cell.

⇒ It stimulates the entry of amino acid into the cell and its incorporation into protein (Anabolic effect).

⇒ But it prevents the breakdown of fat in the muscle (Anti-lipolytic Effect.

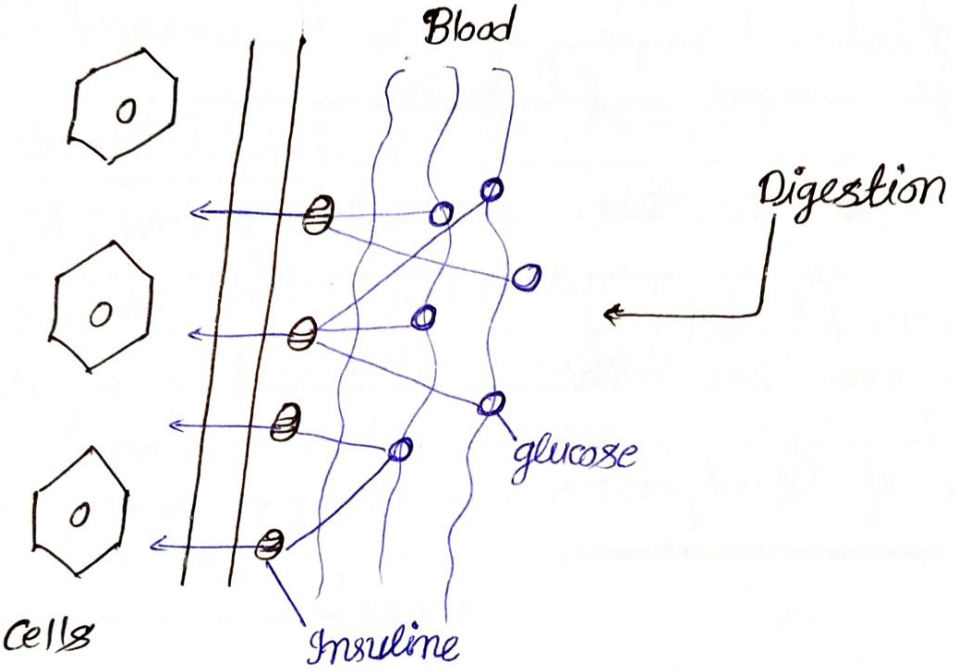
→ **Mechanism of hypoglycemic Action :-** Insuline lowers blood glucose level by the following mechanisms.

(1) Insulin promotes glycogen synthesis but prevents glycogen breakdown in the liver.

(2) It also prevents gluconeogenesis.

(3) It promotes the uptake and utilisation of glucose in the skeletal muscles.

(4) It also promotes the conversion of glucose to fat in adipose tissue.



Administration :- Insuline is destroyed by gastrointestinal enzyme.

→ So it is ineffective on oral administration.

→ It is given by parenteral route like subcutaneous injection.

:- Adverse Reaction :- (1) **Hypoglycemia :-** Which may lead to coma and convulsions.

(2) **Allergy :-** Characterised by itching redness and swelling at the site of injection.

(3) Lipodystrophy:- Due to Atrophy of subcutaneous tissue at the site of frequent injection.

(4) Presbiopia:- Due to alteration in the physical properties of lens (of the eyes).

(5) Obesity:- Leading to increase in body weight.

→ Therapeutic uses:- (1) Treatment of diabetes mellitus.

(2) Treatment of diabetes due to pancreatic diseases.

(3) In schizophrenia where insulin induced coma is useful (Insulin shock therapy)

(4) For improving appetite and increasing body weight.

÷ Preparation of Insulin:- Insulin is a will soluble.

→ It is rapidly absorbed and rapidly eliminated.

→ So it has short duration of action.

→ The addition of substances like protamine or zinc decreases the solubility of insulin, these preparations are slowly absorbed and hence have a long duration of action.

→ The common preparation of insulin can be classifies as -

Short Acting	Plain insulin Insulin zinc suspension (semilente)
Intermediate Acting	Globin zinc Insulin Isophane insulin Insuline zinc suspension (Ultralente)
Long Acting.	Protamine zinc insuline Insuline zinc suspension

Newer Insulins :- Those are purer form of neutral and stable preparations free from proinsulin.

⇒ Also they are less antigense and so can be used in patient allergic to beef insulin.

⇒ But these preparation are expensive.

⇒ The preparation are -

(1) **Nuso :-** It is bovine insulin in clear neutral solution.

(2) **Actrapid :-** It is a clear neutral solution of monocomponent porcine insuline.

(3) **Rapitard :-** It is a cloudy mixture of actrapid and bovine insulin.

(4) **Monotard :-** It contains highly purified porcine insuline. It is non antigenic.

(5) **Human Insulines :-** They are obtained by recombinant DNA technology from E-coli or yeast. They are widely used as present.

Advantages :- (1) More water soluble.

(2) Rapid S.C absorption.

(3) Useful in insuline resistance

(4) Useful in allergy to commercial insuline.

(5) Useful for short term use in surgery or infection.

(6) Useful in pregnancy (To treat Gastrointestinal Diabetes).

→

Insulin Analogues :- They are obtained by recombinant DNA technology.

→ They have similar Pharmacodynamics as commercial insulins.

→ But Pharmacokinetics on S.C injection can be modified so to produce less hypoglycemic episodes the insulin analogues are (1) Insulin lispro (2) Insulin aspart (3) Insulin glargine.

Newer Insulin delivery devices :- The following are the newer insulin delivery divices.

→ They have the advantages of easy and accurate administration

(1) Insulin Syringes.
(2) Jel injection.
(3) Pen devices.
(4) Insulin Pumps
(5) Implantable Pump.
(6) External Artificial Pancreas.

:- Glucagon :-

→ It is a polypeptide containing 29 amino acid and has a molecular weight of 3485.

→ It is secreted by the alpha cells of the islet of langerhans.

:- Actions :-

(1) A fall in blood glucose level and a rise in plasma amin acid level stimulates the release of glucagon.

(2) It produces glycogenolysis. as a result. there is a rise in blood glucose level.

(3) It stimulates glucogenesis the presence of glucocorticoids is necessary for this effect.

(4) It also stimulates lipolysis in peripheral tissue.

Administration :- It is destroyed by proteolytic enzyme of gastrointestinal tract. so it is administered by parenteral route.

Preparation And dose :- Glucagon hydrochloride 1 mg by subcutaneous or intravenous injection.

Therapeutic Uses :- It is mainly used in the treatment of insulin induced hypoglycemia.

÷ Oral Antidiabetic Drugs ÷

→ Insulin is ineffective orally and so it has to be injected but the oral antidiabetic drugs (oral hypoglycemic agent) lower blood glucose level on oral administration.

÷ Classification of drugs ÷

1. Sulfonylureas (a) First Generation	Tolbutamide Chlorpropamide
(b) Second Generation	Glibenclamide Glipizide Glyclazide Glymepiride
2. Biguanides	Metformin

Sulfonylureas :- These compounds are chemically related to sulfonamides.

→ They have the following basic structure : $R_1-SO_2NH-CONH-R_2$

Pharmacological Actions (1) These drugs lower blood suger level on oral Administration.

(2) They lower blood suger lower in diabetic (only in type-2 and nat in type-1) and in all non-diabetic individuals

(3) They are effective only in presence of functional pancreas

(4) They produce increase in body weight like insulin.

Mechanism of Action: Sulfonylureas act by the following mechanism.

(1) Stimulation of the synthesis and release of insulin from the betacells of islets of langerhans.

(2) Increase in the number of beta cells.

(3) Inhibition of glycogenolysis and gluconeogenesis.

(4) Decrease in the rate of insuline degradation

Absorption fate and Excretion: Sulfonylureas are rapidly absorbed from gastrointestinal tract.

→ They are partly bound to plasma proteins.

→ They are metabolised in liver and excreted in urine.

Adverse reaction: (1) Hypoglycemia and this effect is potentiated by salicylates.

(2) Allergic reactions leading to skin rashes.

(3) Bone marrow changes like leucopenia and thrombocytopenia.

(4) Hypothyroidism and goitre.

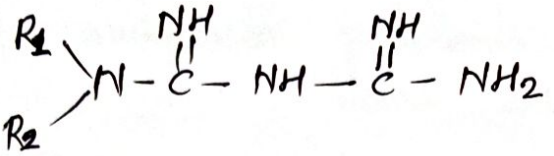
(5) Potentiation of barbiturates and other sedative hypnotics.

Preparation and dose: (1) Tolbutamide tablets - 0.5 g to 1 g daily

(ii) Chlorpropamide Tablets - 250 to 500 mg daily

Theraperutic Use:- In the treatment of matwity on set diabetes insulin resistant diabetes and diabetes insipidus

:- Biguanides:- Biguanides have the following general chemical structure.



Pharmacological Action:- (1) Biguanides lower blood suger level only is a diabetic individual but not in a noomar individual.

→(2) They patentiate the hypoglycemic action of insulin and sulfonylureas.

(3) They inhibit lipogenesis in adipose tissue.

(4) They increase fibrinolytic activity of plasma.

Mechanism of Action:- (1) The presence of exogenous or endogenous insulin is necessary for the action of biguanides but insulin release from panoreas is not stimulated.

(2) Perciphera utilisation of glucose is stimulated.

(3) Absorption of glucose from intestine is inhibited.

Absorption fate and excretion :- Biguanides are well absorbed from GIT maximum activity occurs in 4 hrs they are eliminated through urine within 24 hours.

Adverse Reaction:- (1) Unpleasent bitter or metallic taste.

(2) Abdominal discomfort anorexia and nausea.

(3) Lethargy and muscle weakness.

(4) Lactic acidosis it can be precipitated by alcohal.

Preparation and dose: Metformin tablet 500 to 2000 mg daily

Therapeutic Use: (1) Obese mild diabetics.
(2) Non-diabetic obese patients.
(3) In patients allergic to sulfonylureas.

α - Glucosidase Inhibitors:

Acarbose: It is an α - Glucosidase inhibitor. by reversibly binding with this enzyme, it prevents the absorption of glucose.
- This effect occurs in the brush border of small intestine it can be used with insulin sulfonylureas or biguanides.

Meglital: It is another α - Glucosidase inhibitor it acts by similar mechanism as acarbose.

ACTH And Corticosteroid

Pharmacological Action:

(1) Cabohydrate Protein and Fat Metabolism.
(2) Electrolyte and water Balance
(3) Cardio Vascular System.
(4) Nervous System.
(5) Skeletal Muscle.
(6) Anti - Inflammatory Action.
(7) Anti Allergic Immunosuppresion.

(1) Carbohydrates Protein and Fat Metabolism:-

→ Carbohydrates is the richest source of energy. and they produce ATP in our body.

→ And the corticosteroid basically Glucosteroid maintain the glucose level in our body by the process of breakdown of glucose into glycogen and again breakdown of Glycogen into glucose.

→ They also perform the Glycogenolysis, Glycolysis, Gluconeogenesis process and so maintain the glucose level.

→ They also in helps the breakdown of Protein into amino acid and into the fatty acid and alcohal in the body.

(2) Electrolyte and Water Balance :- The second hormone Mineralocorticoids is decrease the excretion of mineral & Water.

→ And it help in the balancing of the conc of mineral and water in our body.

(3) CVS :- They basically do not affect the directly into the heart but by the process of water and mineral balance

→ They increase the conc. of Na^+ and K^+, Ba^+ in body so it causes the vassoconstriction and they causes the hypertension in the CVS.

(4) Nervous System :- Basically they do not affect directly to the nervous system but by the increasing of conc of ions they helps in the reporrarisation and depolarisation rate.

(5) Skeletal Muscle :- Due to the prominent effect of corticoids upon electrolyte balance Gluconeogenesis and circulatory system the functioning of skeletal muscles is greatly influenced by alterations in plasma corticoid concentrations.

(6) Anti Inflammatory Properties :- Edema, Fibrin deposition, capillary dilation, migration of leucocytes into the affected area are the early signs of inflammation which are then associated with redness, swelling and increased pain sensation.

→ The glucocorticoid activity runs parallel with Anti-inflammatory effect of these steroid.

(7) Anti Allergic And Immunosuppressive Action :-

Besides their antiinflammatory activity, corticosteroids also have antiallergic activity and when given systemically they alleviate the symptoms of Asthma.

→ They modify the clinical course of a variety of diseases in which hypersensitivity is imp.