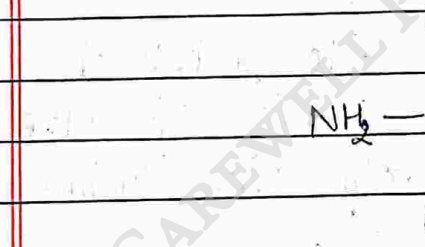
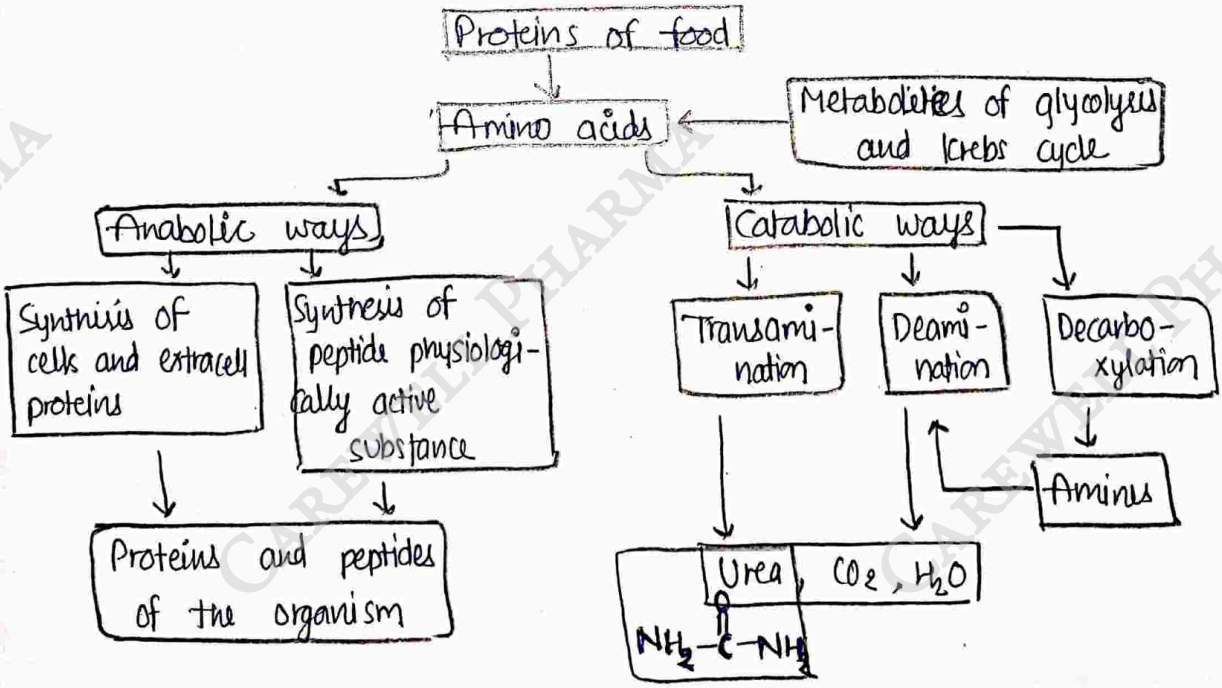
Amino Acid

An amino acid is an organic compound charateized by having a carboxyl group, amino group, and side chain attached to the central carbon atom.



General Pathway of Amino Acids Metabolism.



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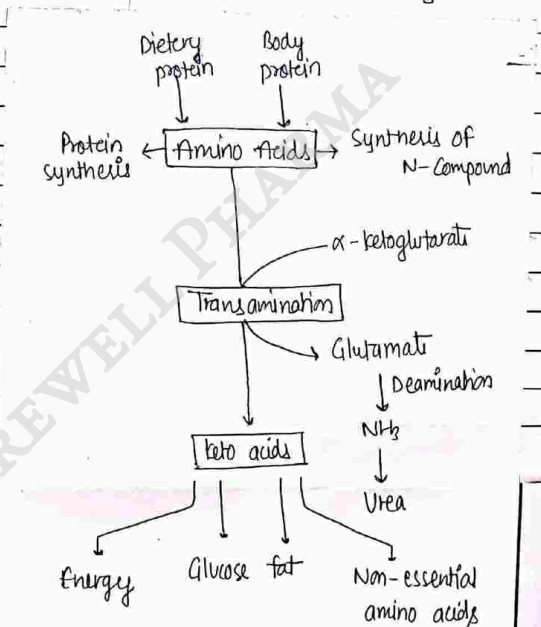
Amino acid metabolism

The amino acid undergoes certain common reaction like transamination followed by deamination for the liberation of ammonia. The amino group of the amino acid is utilized for the formation of urea which is an excretory end product of protein metabolism. The carbon skeleton of the amino acids is first converted to keto acids (by transamination) which meet one or more of the following fates.

(i) Utilized to generate energy.
(ii) Used for the synthesis of glucose
(iii) Diverted for the formation of fat or ketone bodies.
(iv) Involved in the production of non-essential amino acids.

Transamination

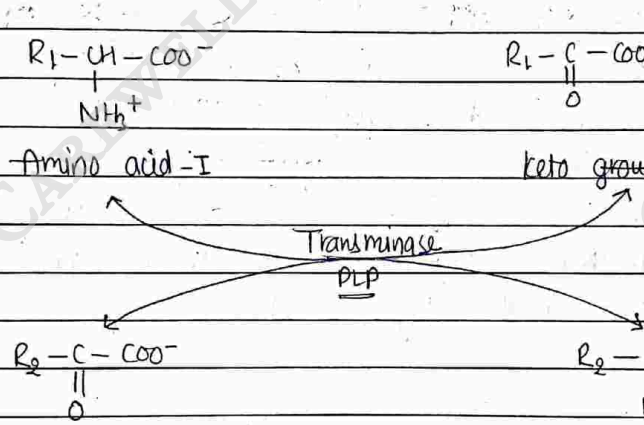
The transfer of an amino ($-NH_2$) group from an amino acid to a keto group is known as transamination. This process involves the interconversion of a pair of amino acids and a pair of keto acid, catalysed by a group of enzyme called transaminases (recently aminotransferase)



An overview of amino acid metabolism.

Salient features of transamination

1) All transaminase require ~~pyridoxal~~ pyridoxal phosphate (PLP), a coenzyme derived from vitamin B_6.
2) Specific transaminases exist for each pair of amino acid and keto acids. However, only two — namely, aspartate transaminase and alanine transaminase — make a significant contribution for transamination.
3) There is no free NH_3 liberated, only the transfer of amino group occurs.
4) Transamination is reversible



Transamination reactions

5) It is important for production of non-essential amino acids, as per the requirement of the cells. It involves catabolism & anabolism both.
6) Transamination diverts the excess amino acid towards energy generation.

• Deamination

The removal of amino group from the amino acids as NH_3 is deamination. Transamination involves only the shuffling of amino groups among the amino acids. On the other hand, deamination result in the liberation of ammonia for urea synthesis. Simultaneously, the carbon skeleton of amino acid is converted of keto

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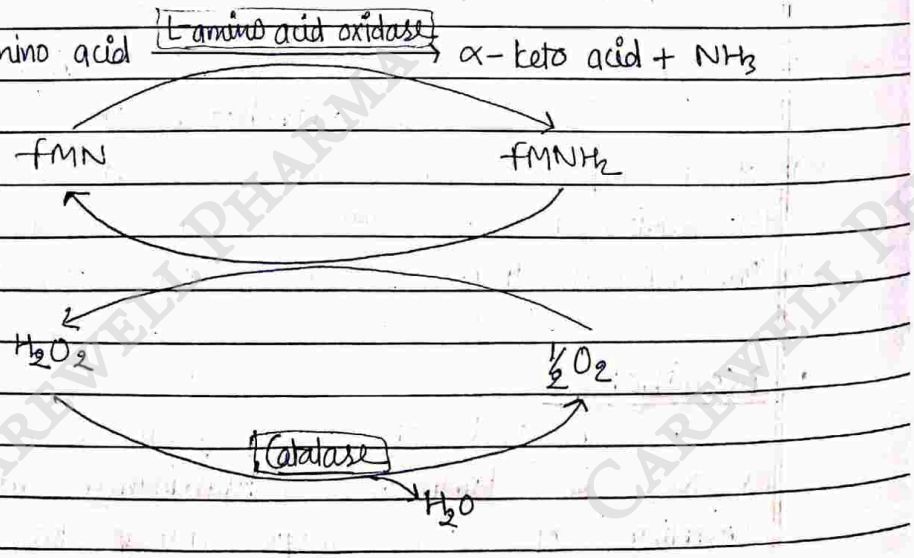
acids. Deamination may be either oxidative or non-oxidative.

I. Oxidative deamination

It is the liberation of free ammonia from the amino group of amino acids coupled with oxidation. This takes place mostly in liver & kidney. The purpose of oxidative deamination is to provide NH_3 for urea synthesis and α-keto acids for a variety of reactions, including energy generation.

- **Oxidative deamination by amino acid oxidases:**

L-Amino acid oxidase and D-Amino acid oxidase and flavoproteins, possessing FMN and FAD, respectively. They act on the corresponding amino acid (L or D) to produce α-keto acids and NH_3. In this reaction, oxygen is reduced to H_2O_2, which is later decomposed by catalase.



∴ Oxidative deamination of amino acids

The activity of L-amino acid oxidase is much low while that D-amino acid oxidase is high in tissue (mostly liver and kidney). L-Amino acid oxidase does not act on glycine and dicarboxylic acids. This enzyme, due to its very low activity, does not appear to play any significant role in the amino acid metabolism.

II. Non-oxidative deamination

Some of the amino acids can be deaminated to liberate NH_3 without undergoing oxidation.

a) Amino acid dehydrates: Serine, threonine and homoserine are the hydroxy amino acids. They undergo non-oxidative deamination catalysed by PLP-dependent dehydrases (dehydratases).

Serine
threonine homoserine $\xrightarrow[NH_3]{\text{dehydratase}}$ Respective α-keto acids

b) Amino acid desulfhydrases: The sulfur amino acids, namely cysteine and homocysteine, undergo deamination coupled with desulfhydration to give keto acids.

Cysteine $\xrightarrow[NH_3 + H_2S]{\text{Desulfhydrases}}$ Pyruvate

c) Deamination of histidine: The enzyme histidase acts on histidine to liberate NH_3 by a non-oxidative deamination process.

Histidine $\xrightarrow[NH_3]{\text{Histidase}}$ Urocanate

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Metabolism of ammonia

a) formation of ammonia → The production of NH_3 occurs from transamination & deamination of amino acids.

b) Transport & storage of NH_3 → The maintanance of NH_3 conc. in circulation is done by its transportation between various tissue and the liver mostly occurs in the form of glutamine or alanine & not as free NH_3

c) function of NH_3 → Inspite of being waste product of nitrogen metabolism, it is involved directly for the synthesis of many compounds in the body like purines, pyramidine etc.

d) Disposal of NH_3 → Urea is non-toxic and soluble compand & hence easily excreted in humans.

Toxicity of Ammonia

Ammonia when accumulates in the body results in
↓
Speech slurring & blurring of vision.
↓
which leads to coma, & finally death.

Hyperammonia Elevation of blood NH_3 level
↓
Cause hepatic coma & mental retardation.

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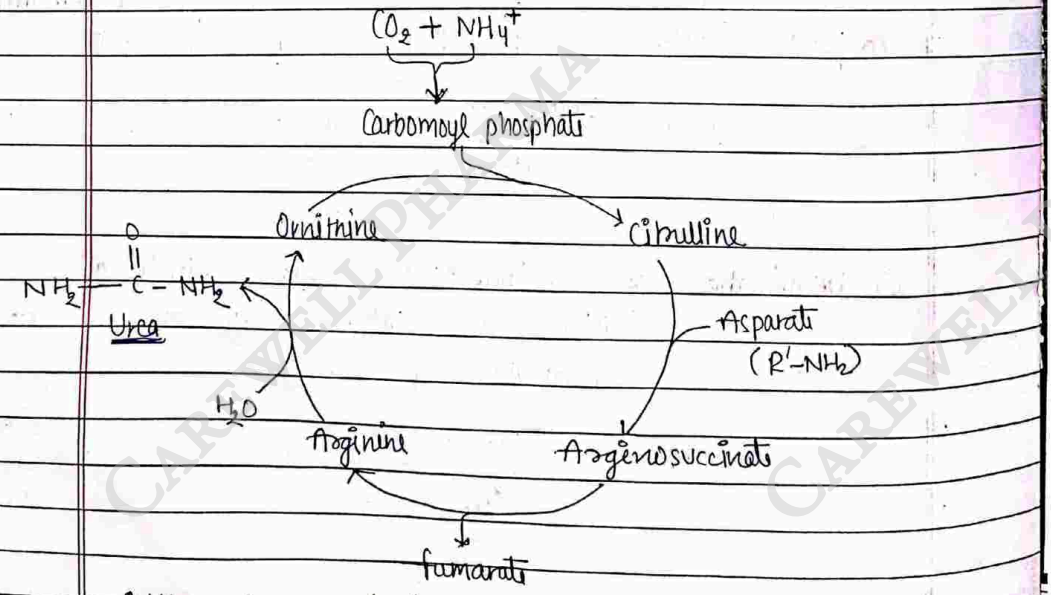
UREA CYCLE

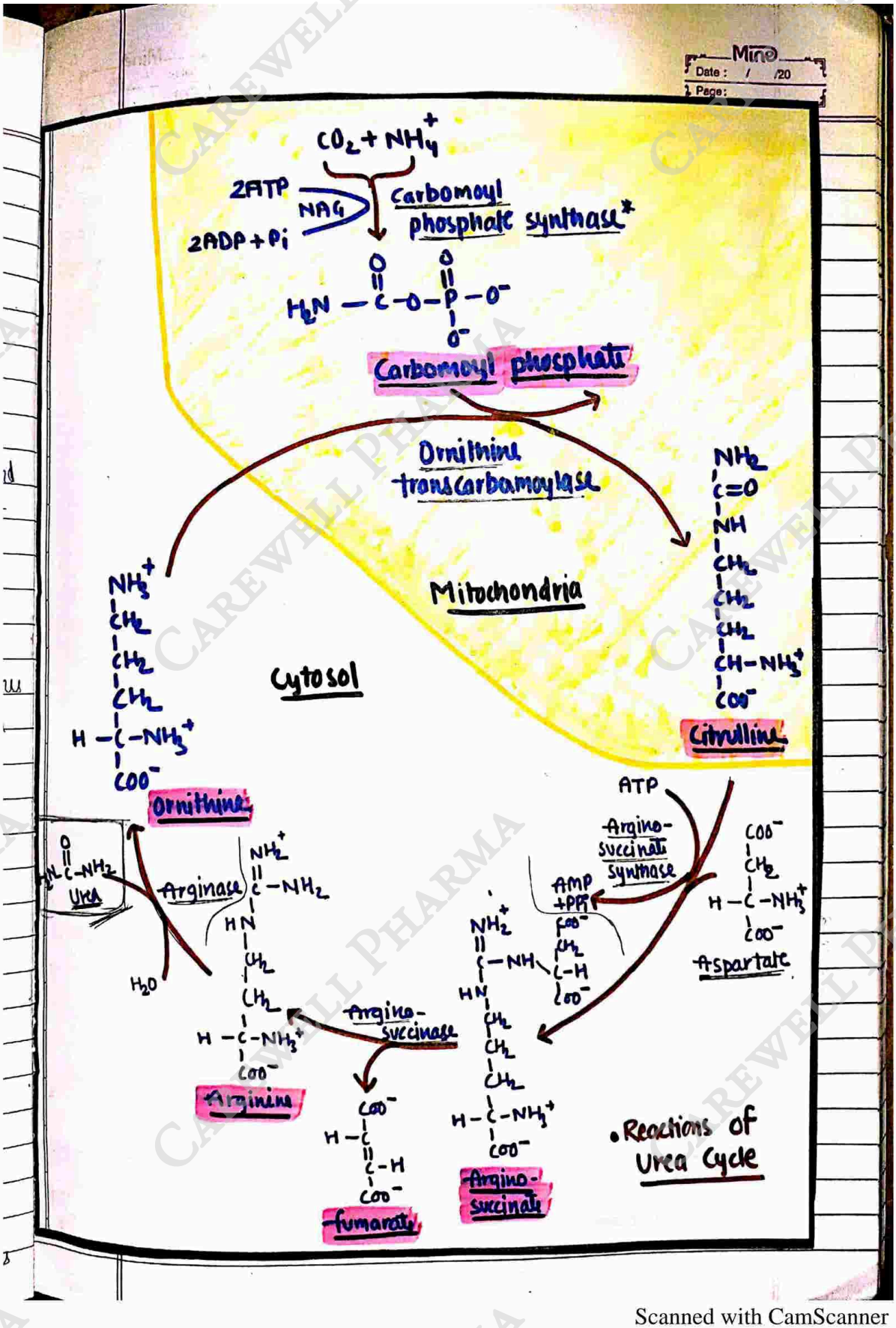
Urea is the end product of protein metabolism (amino acid metabolism). The nitrogen of amino acids, converted to ammonia, as described is toxic to the body. It is converted to urea and detoxified. As such, urea account for 80-90% of the nitrogen containing substance excreted in urine.

Urea is synthesized in liver and transported to kidney for excretion in urine. Urea cycle is the first metabolic cycle that was elucidated by Hans Krebs and Kurt henseleit (1932), hence it is known as Krebs-Henseleit cycle.

Urea has two amino ($-NH_2$) groups, one derived from NH_3 and the other from aspartate. Carbon atom is supplied by CO_2. Urea synthesis is a five-step cyclic process, with five distinct enzymes. The first two enzymes are present in mitochondria while the rest are localized in cytosol.



- Outline of urea cycle (In the synthesis of urea one amino group comes from ammonium ion while the other is from aspartate).



1. Synthesis of carbomoyl phosphate →
Carbomoyl phosphate synthase I (CPS I) of mitochondria catalyses the condensation of NH_4^+ ions with CO_2 to form carbomoyl phosphate. This step consumes two ATP and is irreversible, and rate-limiting. CPS I requires N-acetylglutamate for its activity. Another enzyme, carbomoyl phosphate synthase II (CPS II)- involved in pyrimidine synthesis - is present in cytosol. It accepts amino group from glutamine and does not require N-acetylglutamine for its activity.

2. Formation of Citrulline → Citrulline is synthesized from carbomoyl phosphate and ornithine by ornithine transcarbomoylase. Ornithine is regenerated and used in urea cycle. Ornithine and citrulline are basic amino acid. Citrulline produced in this reaction is transported to cytosol by a transporter system.

3. Synthesis of arginosuccinate :→
Arginosuccinate synthase condenses citrulline with asparate to produce arginosuccinate. The second amino group of urea is incorporated in this reaction. This step requires ATP which is cleaved to AMP and pyrophosphate (PPi). The latter is immediately broken down to inorganic phosphate (Pi).

4. Cleavage of arginosuccinate : Arginosuccinase cleaves arginosuccinate to give arginine and fumarate. Arginine is the intermediate precursor of urea. Fumarate liberated here provide a connecting link with TCA cycle, gluconeogenesis etc.

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5. formation of urea:- Arginase is the fifth and final enzyme that cleaves arginine to yield urea and ornithine. Ornithine, so regenerated, enters mitochondria for its reuse in the urea cycle. Arginase is activated by Co^{2+} and Mn^{2+}. Ornithine and lysine competes with arginine (competitive inhibition). Arginase is mostly found in the liver, while the rest of the enzymes (four) of urea cycle are also present in other tissue for this reason, arginine synthesis may occurs to varying degree in many tissue. But only the liver can ultimately produce urea

- Overall reactions and energetics

The urea cycle is irreversible and consumes 4 ATP. Two ATP are utilized for the synthesis of carbomoyl phosphate. One ATP is converted to AMP and PPi to produce argino succinate which equal to 2 ATP. Hence 4 ATP are actually consumed.

$$NH_4^+ + CO_2 + \text{Asparate} + 3ATP \longrightarrow \text{Urea} + \text{fumarate} + 2ADP + 2Pi + AMP + PPi$$

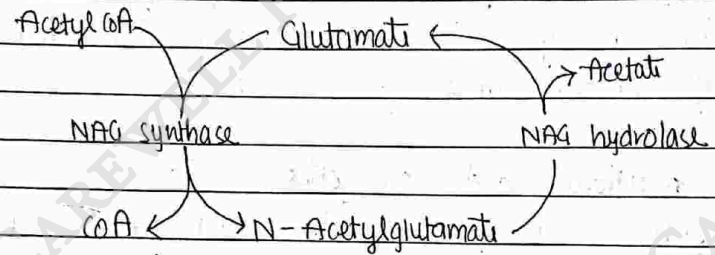
- Regulation of urea cycle.

The first reaction catalysed by carbamoyl phosphate synthase I (CPS 1) is rate-limiting reaction or committed step in urea synthesis. CPSI is allosterically activated by N-acetylglutamate (NAG). It is synthesized from glutamate and acetyl CoA by synthase and degraded by a hydrolase

The rate of urea synthesis in liver is correlated with the concentration of N-acetylglutamate. High concentrations of arginine increase NAG. The consumption

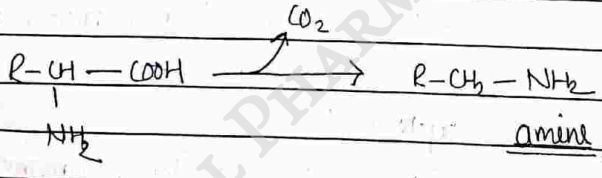
of a protein-rich meal increases the level of NAG in liver, leading to enhanced urea synthesis.

Carbamoyl phosphate synthase I and glutamate dehydrogenase are localized in the in the mitochondria. They coordinate with each other in the formation of NH_3, and its utilization for the synthesis of carbamoyl phosphate. The remaining four enzymes of urea cycle are mostly controlled by the concentration of their respective substrate



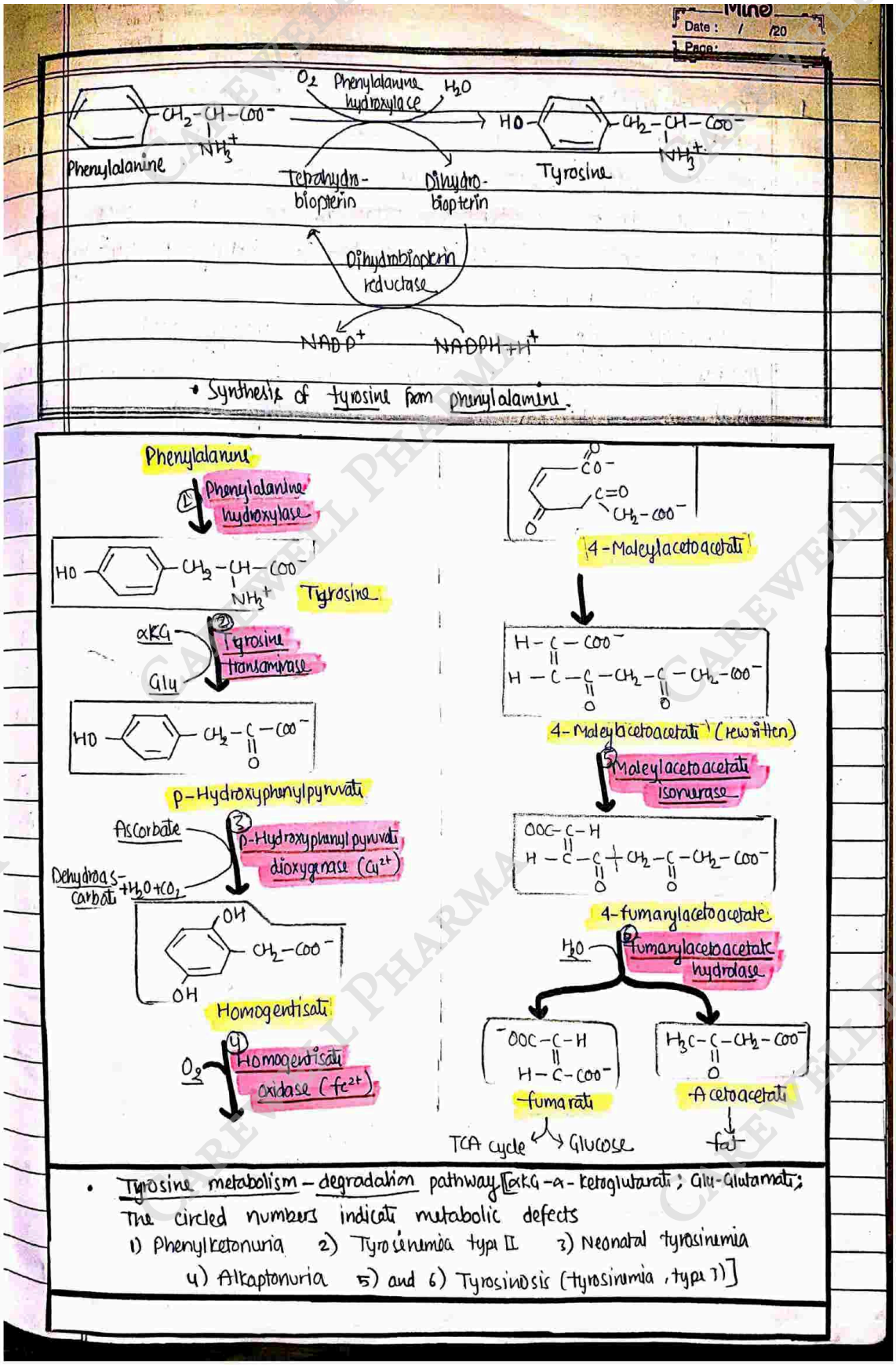
- formation and degradation of N-acetylglutamate.

- **Decarboxylation:** It is the removal of carbon dioxide from amino acids with formation of amines.



- **Degradation (Catabolism) of Tyrosine (Phenylalanine)**

The metabolism of phenylalanine and tyrosine is considered together. The sequence of the reaction in the degradation of these amino acids,



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1. As phenylalanine is converted to tyrosine, a single pathway is responsible for degradation of both these amino acids, which occurs mostly in liver.
2. Tyrosine first undergoes transamination to give p-hydroxyphenylpyruvate. This reaction is catalyzed by tyrosine transaminase (PLP dependent).
3. p-Hydroxyphenylpyruvate hydroxylase (or dioxygenase) is a copper-containing enzyme. It catalyses oxidative decarboxylation as well as hydroxylation of the phenyl ring of p-hydroxy phenylpyruvate to produce homogentisate. This rxn involves a a shift in hydroxyl group from para position to meta position, and incorporates a new hydroxyl group at para position. This step in tyrosine metabolic required ascorbic acid.
4. Homogentisate oxidase (iron metalloprotein) cleaves the benzene ring of homogentisate to form 4-maleylacetoacetate. Molecular oxygen is required for this rxn to break the aromatic ring.
5. Maleylacetoacetate undergoes isomerization to form 4-fumaryl acetoacetate and this rxn is catalyzed by maleylacetoacetate isomerase to form 4-fumarylacetoacetate.
6. Fumaryl acetoacetase (fumaryl acetoacetate hydrolase) brings about the hydrolysis of fumaryl acetoacetate to liberate fumarate and acetoacetate.

Fumarate is an intermediate of citric acid cycle and can also serve as precursor for gluconeogenesis. Acetoacetate is a ketone body from which fat can be synthesized. Phenylalanine and tyrosine are therefore, both glucogenic and ketogenic.

The inborn errors of phenylalanine and tyrosine metabolism are indicated in ~~cycle~~ pathway.

Disorders of Tyrosine & Phenylalanin Metabolism

	Disorder	Enzyme defective	Cause symptoms
1)	Phenylketonuria	a) Phenylalanine hydroxylase b) Dihydrobiopterin reductase	Growth failure, seizures, mental retardation
2)	Tyrosinemia Type-II	Tyrosine transaminase	Eye lesion, Dermatitis
3)	Neonatal Tyrosinemia	p-Hydroxyphenyl pyruvate dioxygenase	Mental retardation, Growth retardation
4)	Alkaptonuria. (Black urine disease)	Homogentisate oxidase	Urine resemble colour of coke. Ochronosis Arthritis.
5)	Tyrosinosis Tyrosinemia Type-I	a) Fumarylacetoacetate hydroxylase b) Maleylacetoacetate isomerase	Liver failure, Diarrhea, Vomiting polyneuropathy
6)	Albinism	Tyrosinase responsible for synthesis of melanin	photophobia

Phenylalanine (Phe, F) and tyrosine (Tyr, Y) are structurally related aromatic amino acids. Phenylalanine is an essential amino acid while tyrosine is non-essential. Besides its incorporation into proteins, the only function of phenylalanine is its conversion to tyrosine for this reason, ingestion of tyrosine can reduce the dietary requirement of phenylalanine. This phenomena is referred to as 'sparing action' of tyrosine on phenylalanine. The predominant metabolism of phenylalanine occurs through tyrosine. Tyrosine is incorporated into proteins and is involved in the synthesis of a variety of biological important compounds - epinephrine, norepinephrine, dopamine, thyroid hormones - and the pigment melanin.

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Disorders of Tyrosine (Phenylalanine) Metabolism.

1) Phenylketonuria → (PKU) It is the most common metabolic disorder in amino acid metabolism. The incidence of PKU is 1 in 10,000 births. It is due to deficiency of the hepatic enzymes, phenylalanine hydroxylase, caused by an autosomal recessive gene.

Phenylalanine metabolism in PKU:-

Phenylketonuria primarily caused the accumulation of phenylalanine in tissues and blood, and results in its increased excretion in urine.

Due to disturbance in the routine metabolism, phenylalanine is diverted to alternate pathways, resulting in the excessive production of phenylpyruvate, phenylacetate, phenyllactate and phenyl glutamine. All these metabolites are excreted in urine in high concentration in PKU.

Phenylacetate gives the urine a mousy odour.

2) Tyrosinemia type II

This disorder also known as Richner-hanhart syndrome, is due to a defect in the enzyme tyrosine transaminase. The result is a blockade in the routine degradation pathway of tyrosine. Accumulation and excretion of tyrosine and its metabolites- namely p-hydroxyphenyl pyruvate, p-hydroxyphenyllactate, phydroxyphenylacetate, N-acetyltyrosine- and tyramine are observed.

Tyrosinemia type II is characterized by skin (dermatitis) and eyes lesions and rarely mental retardation. A disturbed self-coordination is seen in these patients.

iii) Alkaptonuria (Black Urine disease)

Enzyme defect → The defective enzyme in alkaptonuria is homogentisate oxidase in tyrosine metabolism. Homogentisate accumulates in tissue and blood, and is excreted into urine. Homogentisate, on standing, gets oxidized to the corresponding quinones, which polymerize to give black or brown colour. For this reason, the urine of alkaptonuria patients resembles coke in colour.

iv) Albinism →

Albinism (Greek: albino - white) is an inborn error, due to the lack of synthesis of the pigment melanin. It is an autosomal recessive disorder with a frequency of 1 in 20,000.

- Hypopigmentation

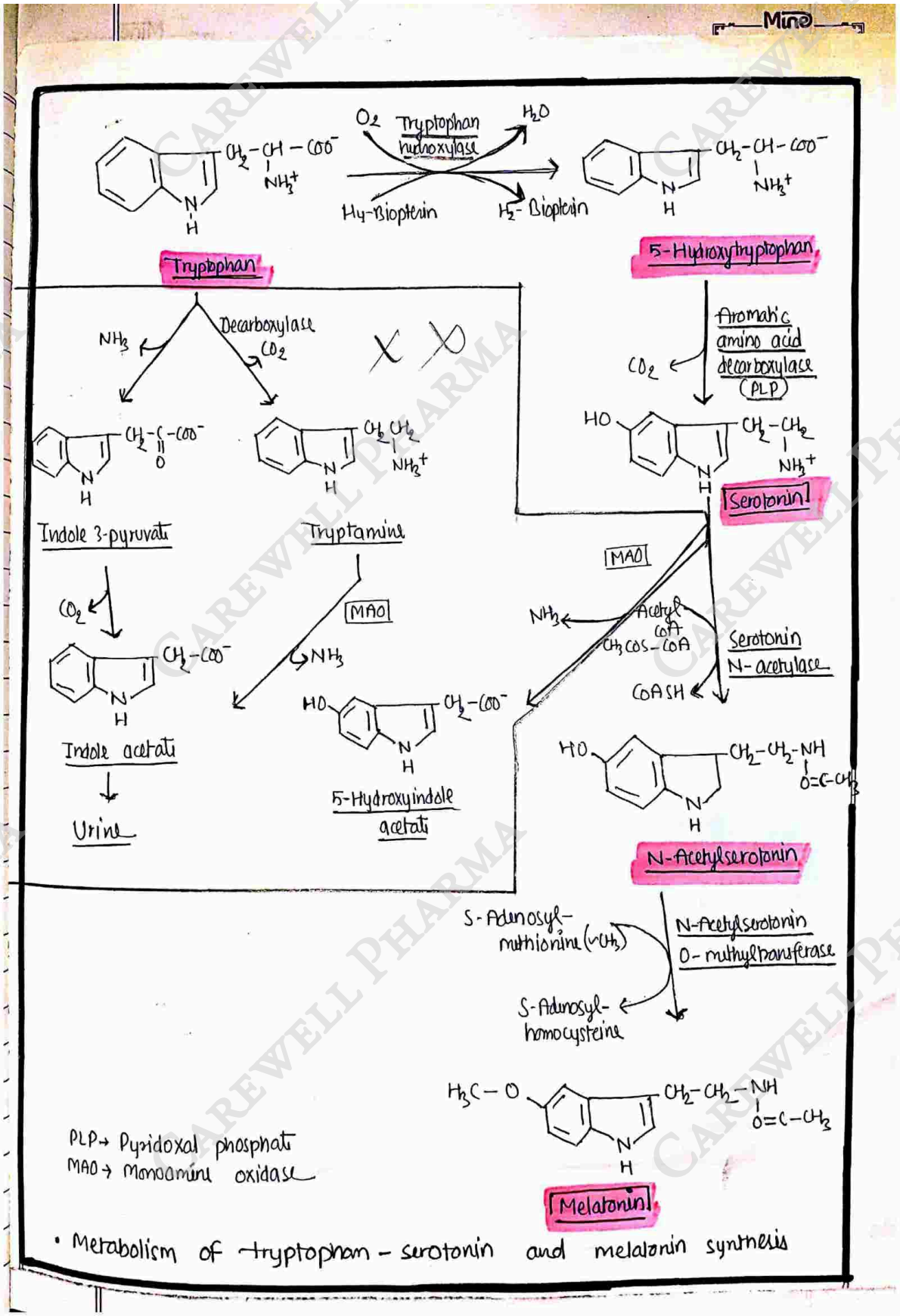
A good example of diffuse hypopigmentation is oculocutaneous albinism which is mostly due to mutations in the tyrosinase gene. The degree of hypopigmentation depends upon the type and severity of mutated genes.

⇒ Synthesis or Significance of biological substance

1) Serotonin pathway

Serotonin or 5-Hydroxytryptamine is a neurotransmitter, synthesized from tryptophan.

- Synthesis of serotonin: In mammals, the largest amount of serotonin is synthesized in the intestinal cells.



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Reactions of serotonin pathway

Serotonin is a neurotransmitter and performs a variety of functions.

- It is a powerful vasoconstrictor and result in smooth muscle contraction in bronchioles and arterioles
- It is closely involved in the regulation of cerebral activity (excitation)
- Serotonin controls the behavioural patterns, sleep, blood pressure and body temperature
- It evokes the release of peptide hormones from gastrointestinal tract.
- It is also necessary for the motility of GIT (peristalsis)

→ When tryptophan hydroxylase enzyme hydrolised tryptophan to 5-Hydroxytryptophan, further Aromatic Amino acid decarboxylase enzyme act on it and it produced a Serotonin.

→ Then Serotonin N-acetylase (the rate limiting enzyme) acted on serotonin and give N-Acetylserotonin. The latter undergoes methylation in the presence of enzyme N-Acetylserotonin O-methyl transferase, it give melatonin.

- Melatonin is a harmone, mostly synthesized by the pineal gland.
- It is involved in circadian rhythms or diurnal variations (24 hr cyclic process) of the body. It plays a significant role in sleep and wake process.
- Melatonin inhibits the production of melanocyte stimulating harmone (MSH) and adrenocorticotropic harmone (ACTH).
- It also performs a neurotransmitter function.

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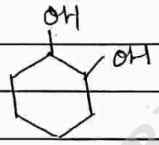
- Biosynthesis of catecholamines (dopamine, norepinephrine, epinephrine).

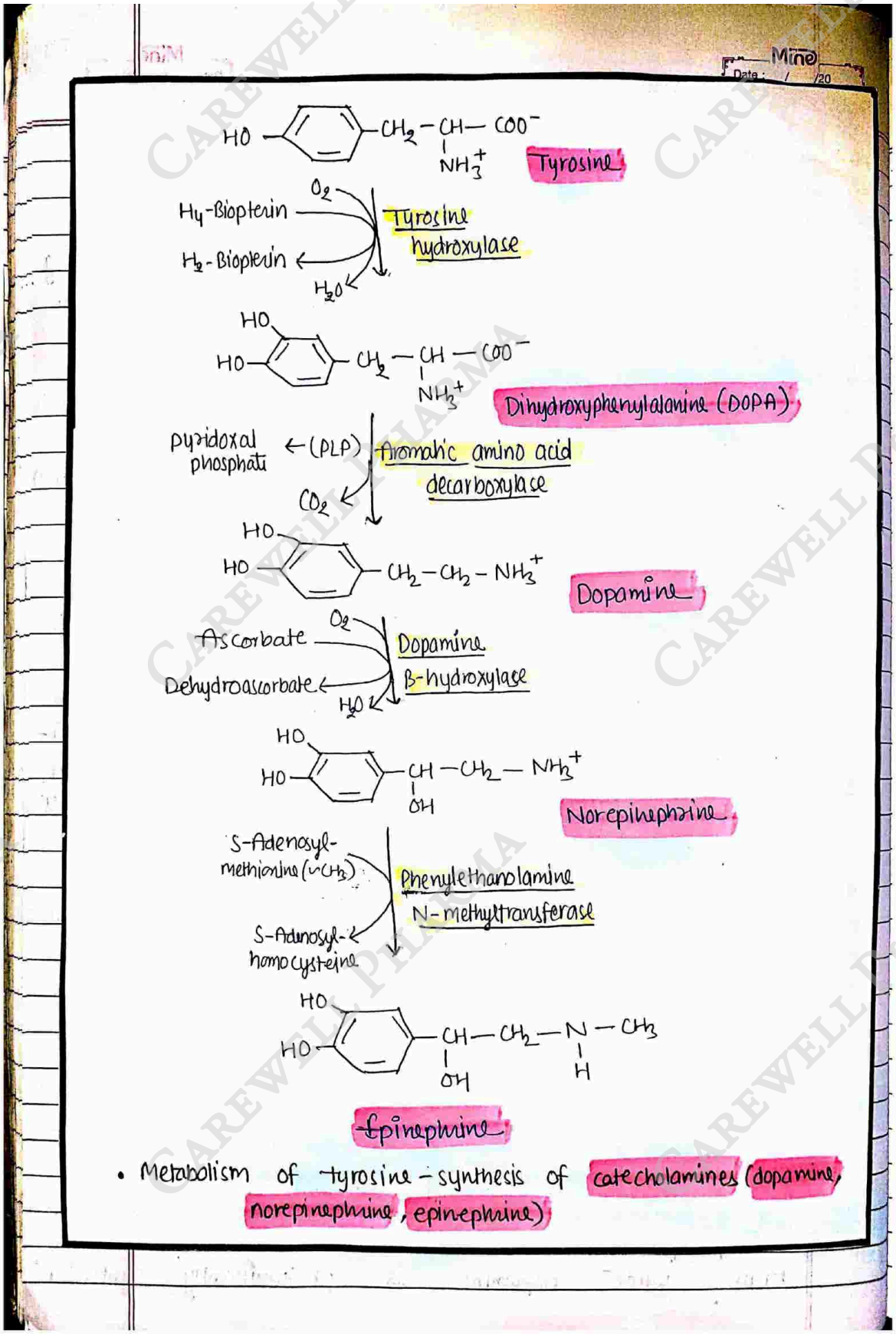
The name catechol refers to the dihydroxylated phenyl ring. The amine derivatives of catechol are called catecholamines.



Tyrosine is the precursor for the synthesis of ~~cate~~ catecholamines, namely dopamine, norepinephrine (noradrenaline) and epinephrine (adrenaline).

The conversion of tyrosine to catecholamines occurs in adrenal medulla and central nervous system involving the following reactions (in pathway on next page).

- Tyrosine is hydroxylated to 3,4-dihydroxyphenylalanine (DOPA) by tyrosine hydroxylase. This enzymes catalyses the rate limiting reaction and requires tetrahydro-biopterin as coenzyme (like phenylalanine hydroxylase). In contrast to this enzyme, tyrosinase present in melanocytes convert tyrosine to DOPA. Hence, two different enzymes system exist to convert tyrosine to DOPA.
- DOPA undergoes PLP-dependent decarboxylation to give dopamine which, in turn, is hydroxylated to produce norepinephrine. Methylation of norepinephrine by S-adenosyl methionine gives epinephrine. The difference b/w epinephrine is only a methyl group (remember that norepinephrine has no methyl group).
- There exists tissue specificity in the formation of catecholamines. In adrenal medulla, synthesis of the harmones, norepinephrine and epinephrine is prominent. Norepinephrine is produced in certain areas of the brain while dopamine is predominantly synthesized



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References - Internet

in substantia nigra and coeruleus of brain.

- funchion of catecholamines: Norepinephrine and epinephrine regulate carbohydrates and lipid metabolisms. They stimulate the degradation of triacylglycerol and glycogen. They cause an increase in the blood pressure. Dopamine and norepinephrine serves as neurotransmitters in the brain and autonomous nervous system.

- **CATABOLISM of HEME:**

Hemoglobin
- Globin
- Heme
  - Heme oxygenase + Fe^{2+}
  - Biliverdin
  - Biliverdin reductase
  - Bilirubin
    - Urobilinogen in kidney
      - Urobilin excreted in urine.
    - Bilirubin diglycuronide in intestine
      - Urobilinogen
      - Stercobilinogen
      - Stercobilin excreted in stools / feces

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- **Hyperbilirubinemia** → The condition having high bilirubin level is called Hyperbilirubinemia.

The cause of hyperbilirubinemia are Intrahepatic cholestasis and extrahepatic obstruction of biliary tract which prevent bilirubin from moving to intestine.

- **Jaundice** → It is caused by build up of bilirubin (waste material in blood). An inflamed liver or obstructed bile duct can lead to jaundice. ~~symptoms~~

Symptoms → Yellowing of eyes.
Dark urine
itching

	Types:-	Symptoms
1)	Pre Hepatic Jaundice	Abdominal pain, fever, dark urine
2)	Hepatic Jaundice	Bloody Nose, weakness, fever apelite
3)	Post hepatic Jaundice	Diarrhea, fever, Abdominal swelling, weightloss.

Unit-III

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LIPID METABOLISM

A lipid is a chemically defined as a substance that insoluble in water and soluble in alcohol ether and chloroform. Liquid lipid are an important component are living cells together with carbohydrates, and protein lipid are the most abundent lipid compauses 85-90% of body lipids. Most of the triglyceride are stored in the adipose tissue and served as energy reciever wize of the body.

- fatty acid oxidation :- The fatty acid in the body are mostly in the oxidation may be defined as the oxidation of fatty acid on the carbon atoms. This results in the sequential removal of 2 carbon compound, β-oxidation involves (acetyl CoA).

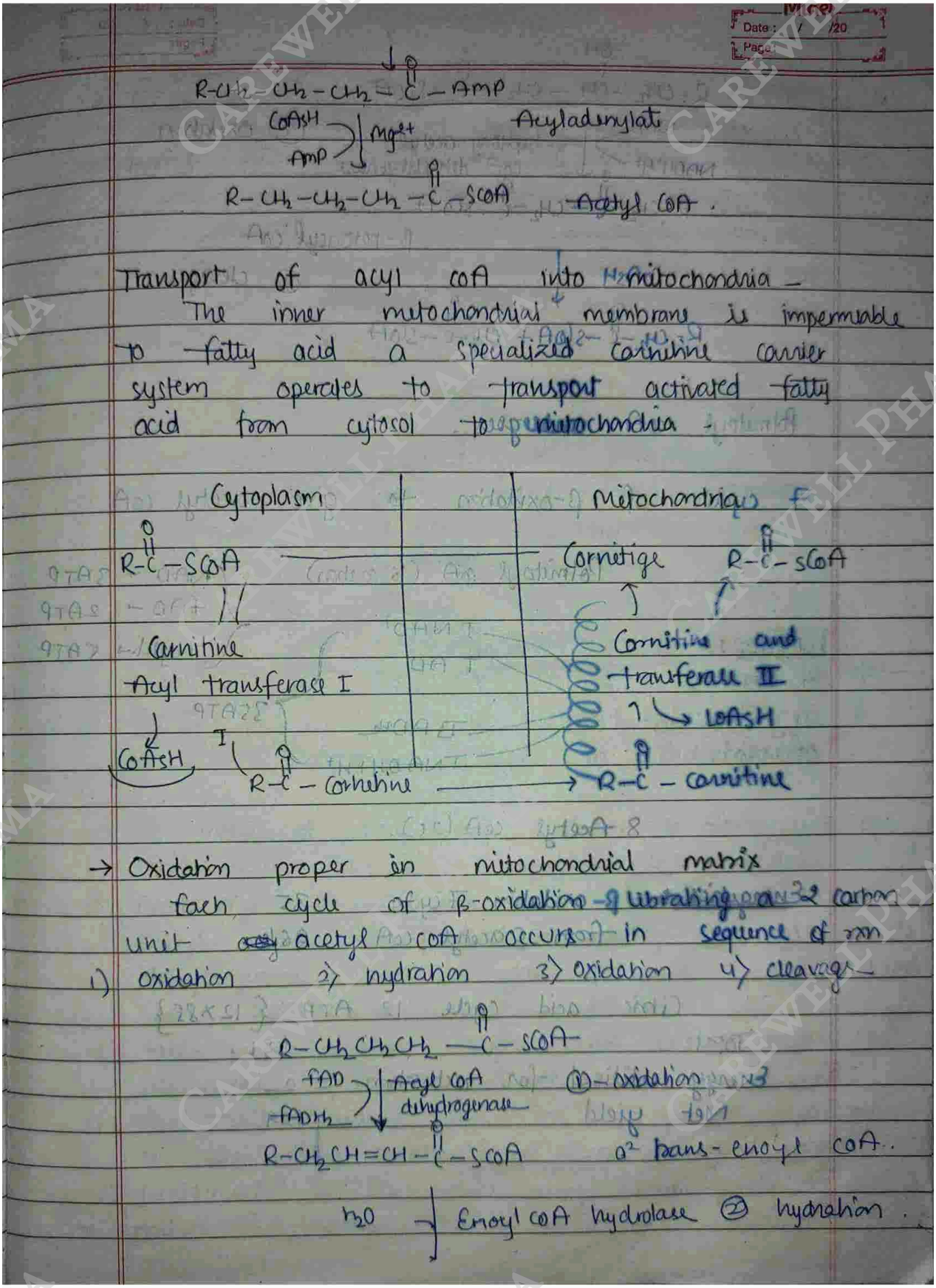
i) Activation of fatty acids occurs in the cytosol.
ii) Transport of fatty acid into mitochondria.
iii) β-oxidation proper in the mitochondrial matrix.

fatty acid activation :-
fatty acid are activated to acyl CoA by thiokinase or acyl CoA synthetic the rxn occurs in 2 steps and require ATP co-enzymes A and magnesium enzyme fatty acid react with ATP to form acetyl adenynate which them combine with co-enzymes A to produce acetyl CoA.

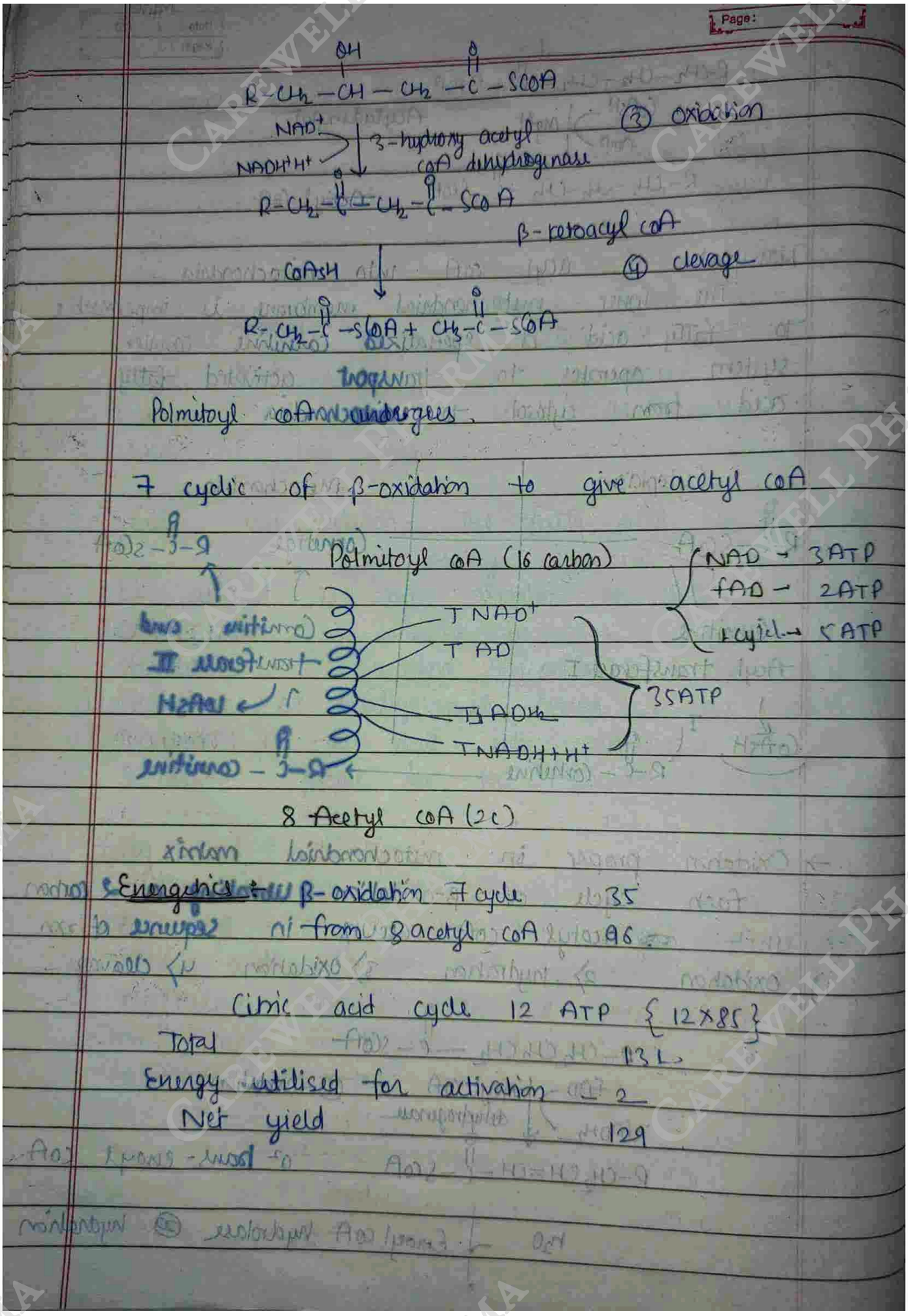
$R-CH_2-CH_2-CH_2-COOH$

ATP
PPi
Thiokinase

References - Internet

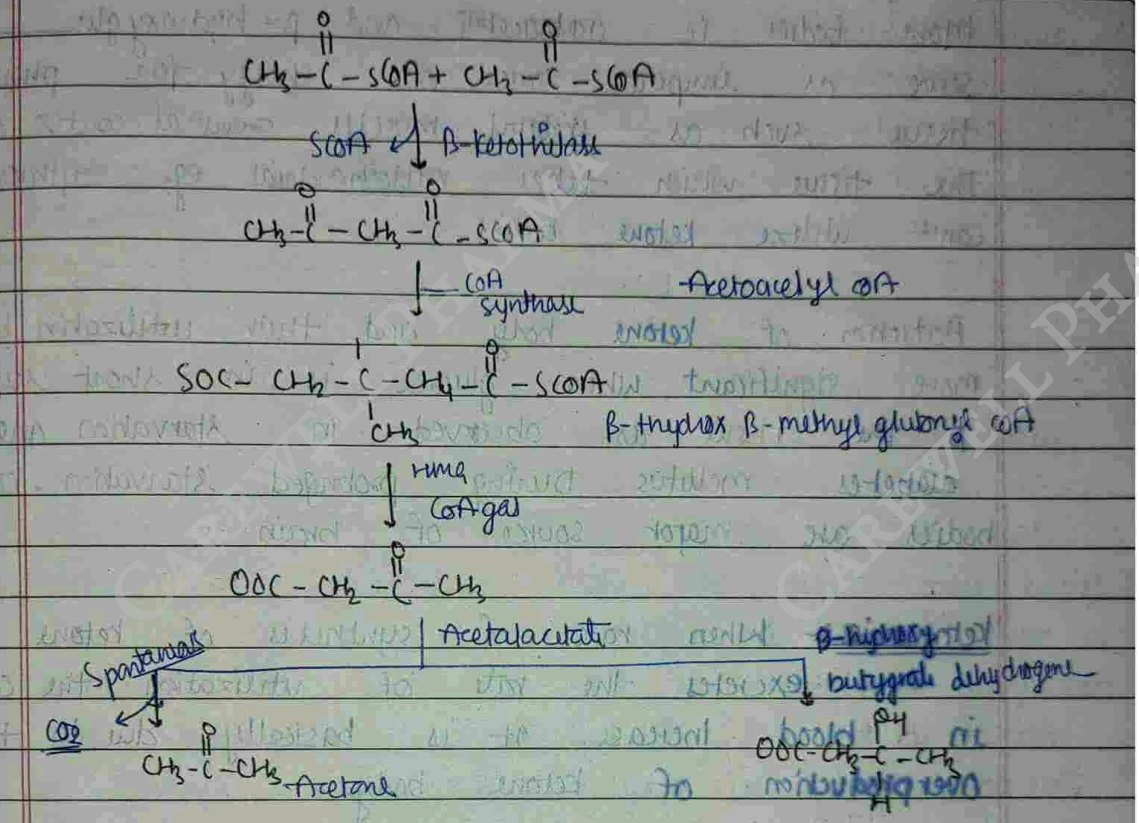


References - Internet



References - Internet

* Ketogenesis - Synthesis of ketone bodies occurs in the liver. The enzymes where ketones synthesis are located in mitochondrial matrix.



i) To moles of acetyl CoA condenses to form acetoacetyl CoA this rxn is catalysed by the enzyme thiolase
ii) Acetoacetyl CoA combine with another molecules of acetyl CoA to produce β-hydroxy β-methyl-glutarate dehydrogenase CoA in the presence of enzyme HMG CoA synthesis
iii) HMG CoA lygase cleave HMG CoA to produce acetoacetate and a molecule acetyl CoA
iv) Acetoacetate undergo the the spontaneous decarboxylation of to form acetone
v) Acetoacetate can be reduced by adehydrogenase to produce β-hydroxybutyrate.

References - Internet

Utilization of ketone bodies :- The ketone body being water soluble are easily transported from the liver to various tissue. The 2 ketone bodies i.e acetoacetate and β-hydroxy glu serve as import source of energy for pheripheral tissue such as skelatal muscle, renal cortex etc. The tissue which takes mitochondrial eg. erythrocytes can't utilize ketone bodies.

Production of ketone body and their utilization became more significant when glucose is in short supply to the tissue as observed in starvation and diabetes mellitus. During prolonged starvation, ketone bodies are major source of brain.

Ketonemia :- When rate of synthesis of ketone body excretes the rate of utilization the conc. in blood increase. It is basically due to the overproduction of ketone body.

Ketonuria :- It represent the excretion of ketone bodies in urine.

Ketoacedose :- Both acetoacetate and β-hydroxy butyrate are strong acids. Increase in their conc. in blood would cause acetoses. The ketone body in blood desociate released H^+ ion which lowers the pH.

Biosynthesis of fatty acids :- The dibicarbohyd and amino acid when consumed in excess can be converted to fatty acid and stored as can be

converted to fatty acid and stored as triglycerides. The de novo biosynthesis of fatty acid occurs predominately in occur in adipose tissue & kidney the enzyme machinary for fatty acid synthesis is located in cytosomal fraction of cells. The fatty acid synthesis takes place in 3 step

i) Production of acetyl CoA and NADPH.
ii) Conversion of Acetyl CoA to malonide CoA.
iii) Rxn of fatty acid synthesis complex.

i) Production of acetyl CoA and NADPH

Acetyl CoA is the main requirement for fatty acid synthesis. It is produced by oxidation of pyruvate in the mitochondria during TCA cycle, amino acid degradation and also from ketone bodies. In TCA cycle, the first product is citrate that is transported to cytosol. In this reaction step, acetyl CoA and oxaloacetate is synthesized by the cleaved reaction of citrate with citrate lyase enzyme oxaloacetate is further converted into pyruvate with the formation of NADPH. Therefore, acetyl CoA and NADPH are both important for the initative steps for synthesis of fatty acids.

Conversion of acetyl CoA to malonyl CoA 7 acetyl CoA + NO_2 + 7 ATP

Carbohydrate and aminoacids.

Acetyl CoA and NADPH are presiquist for fatty acids synthesis Acetyl CoA produced in mitochondria

Mitochondria power are not permeable to acetyl CoA An alternati or by pass arrangement is made for the transfer of acetyl CoA to cytosol.

Cytosol
Pyruvate → mitochondrial Matrix
Pyruvate

NADP+H+ / NADP+ — Matrix enzyma
Malate

Acetyl CoA + Oxaloacitate → Citrate → citrate synthase

NAD+ / NADH+H — HOH
Oxabacitate

ADP / ATP — citrate cyase
Citrate

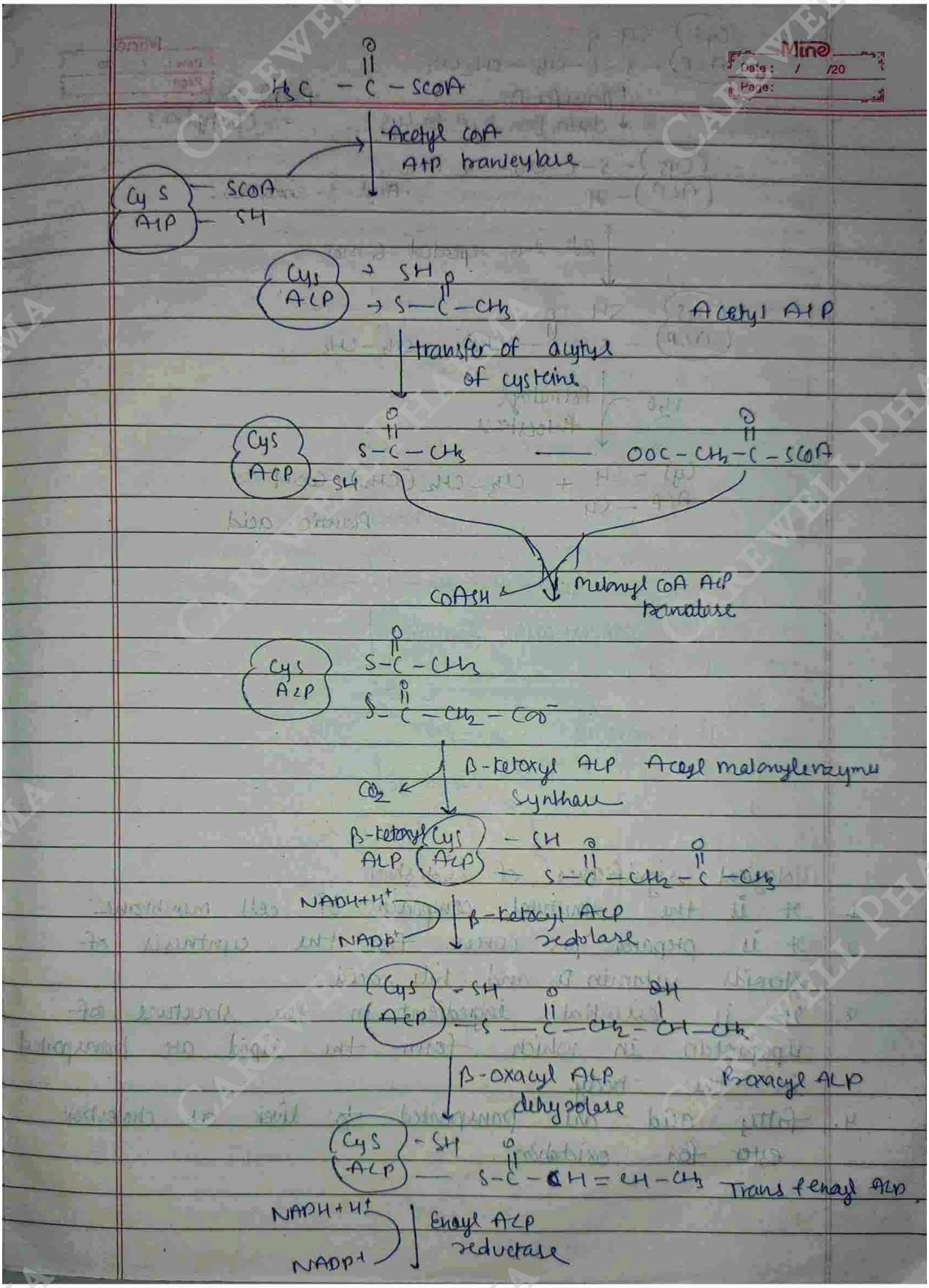
2. formation of malonyl CoA :-
Acetyl CoA is carboxylated to malonyl CoA

$CH_3 - C(=O) - SCOA$

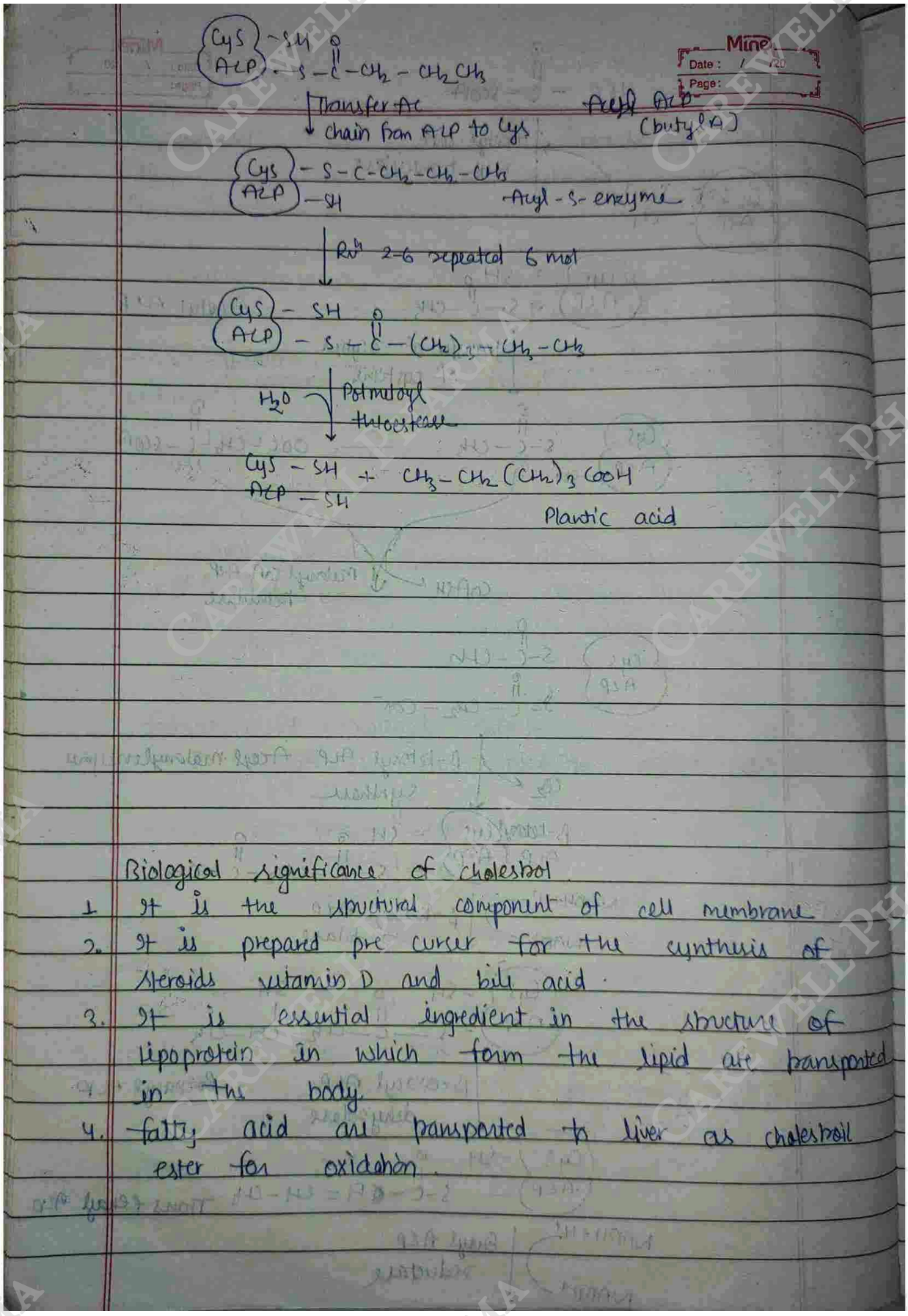
ATP / ADP — Acetyl CoA
Carboxybase

$OOC - CH_2 - C(=O) - SCOA$

3. Reaction of fatty acid synthase complex :-
The remaining reaction of fatty acid synthesis are catalysed by a multifunction enzyme known as fatty acid synthesis complex (FAS).

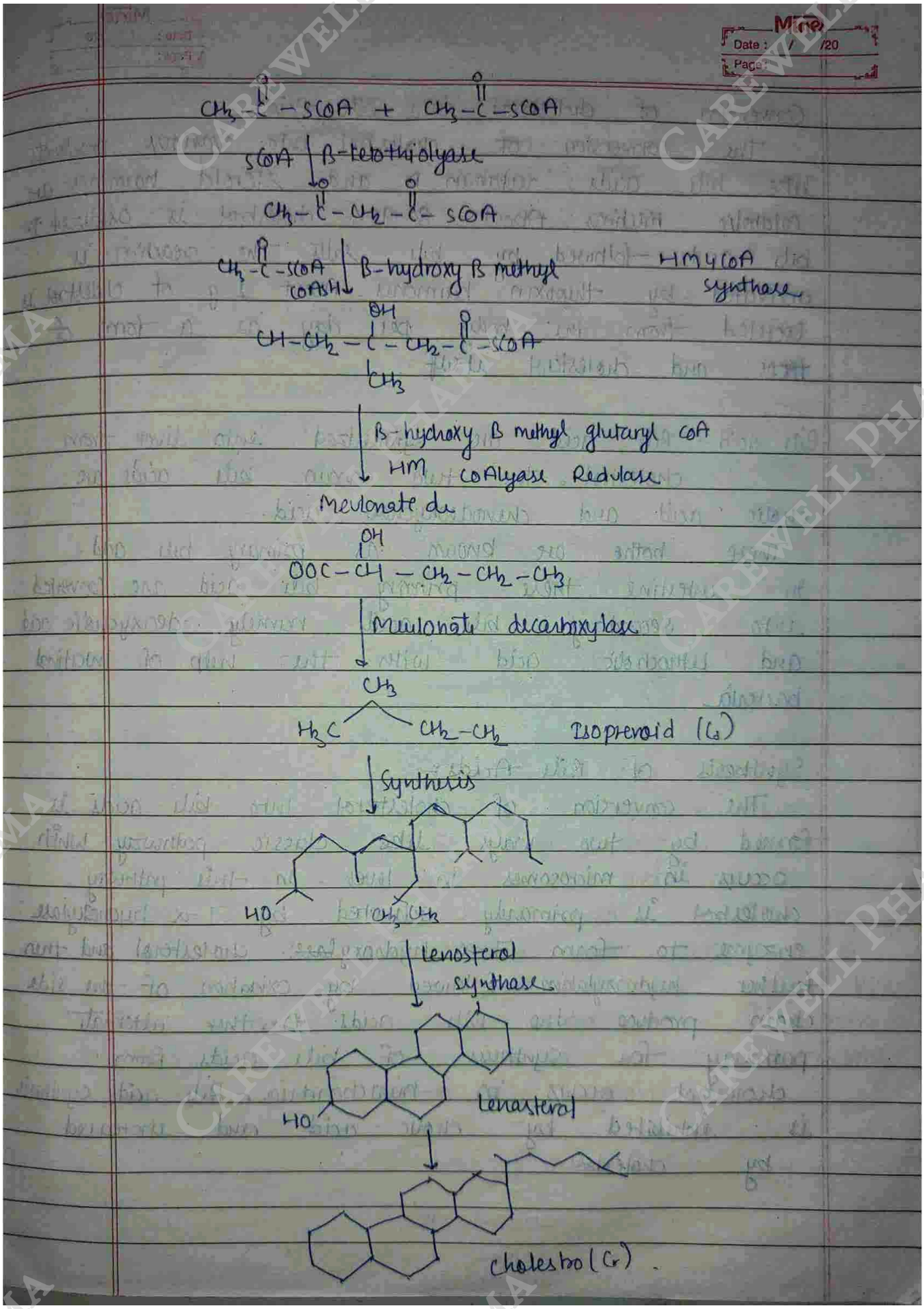


References - Internet



Biological significance of cholesterol

1. It is the structural component of cell membrane
2. It is prepared pre curser for the synthesis of steroids vitamin D and bile acid.
3. It is essential ingredient in the structure of lipoprotein in which form the lipid are transported in the body.
4. fatty acid are transported to liver as cholesterol ester for oxidation.



References - Internet

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Conversion of cholesterol into bile Acids

The conversion of cholesterol into various products like bile acids, vitamin D and steroid hormones are catabolic reactions. About 80-90% cholesterol is oxidized to bile acids, followed by bile salts. The reaction is activated by thyroxin hormone. About 1 g of cholesterol is excreted from the body per day as a form of feces and cholesterol itself.

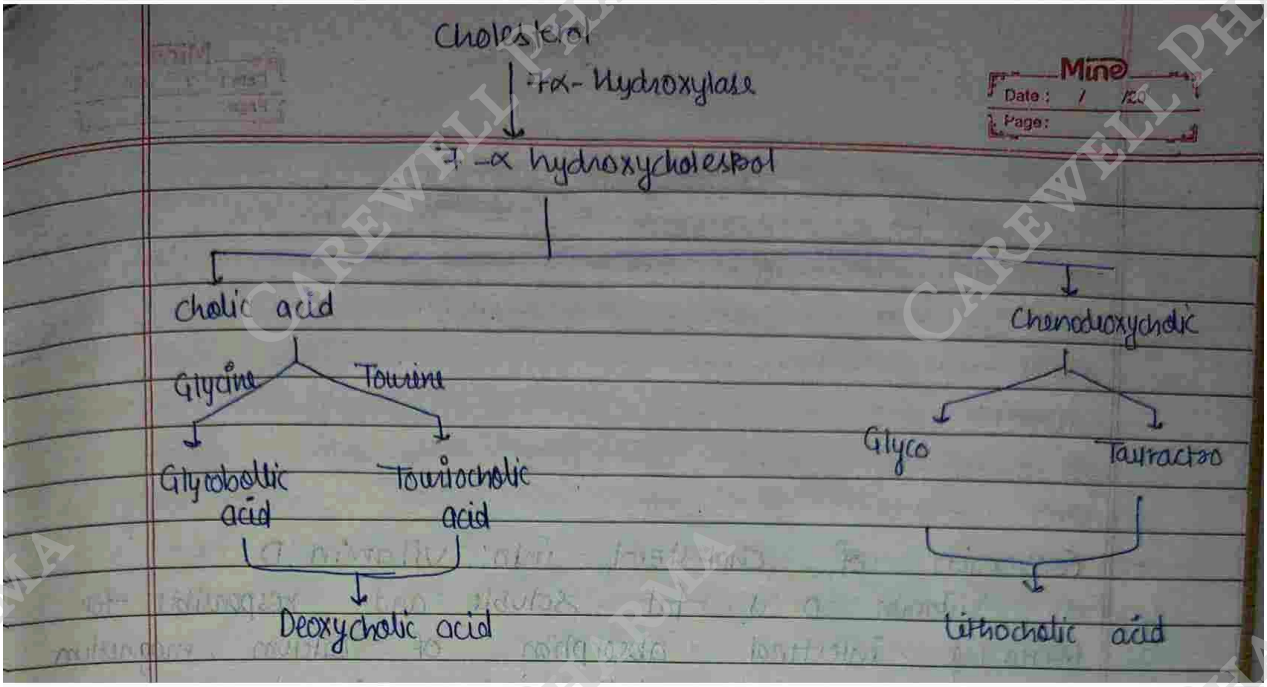
Bile acid → Bile acid are synthesized into liver from cholesterol. The two main bile acids are cholic acid and chenodeoxycholic acid.

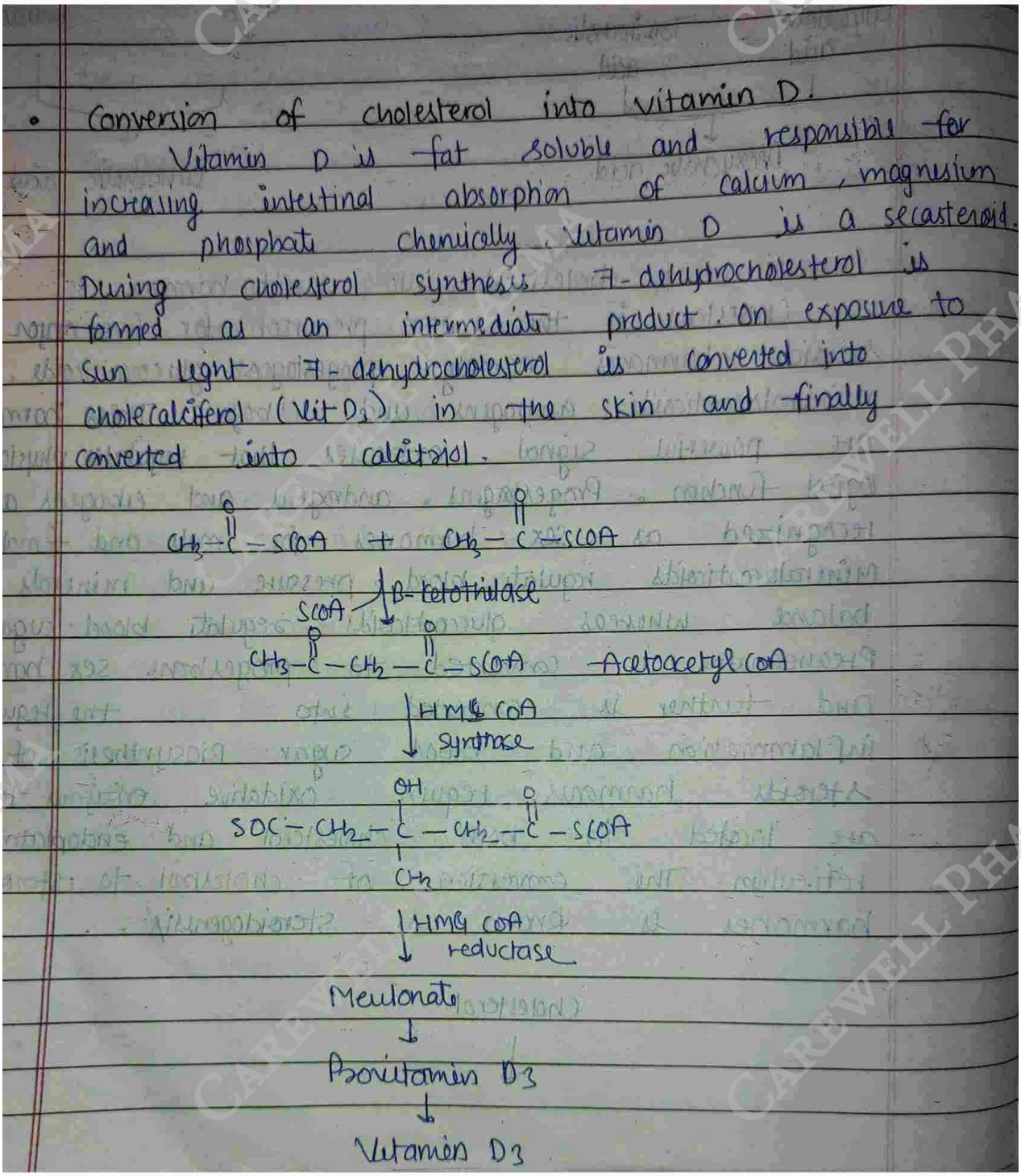
These bothe are known as primary bile acid. In intestine, these primary bile acid are converted into secondary bile acids namely deoxycholic acid and Lithocholic acid with the help of intestinal bacteria.

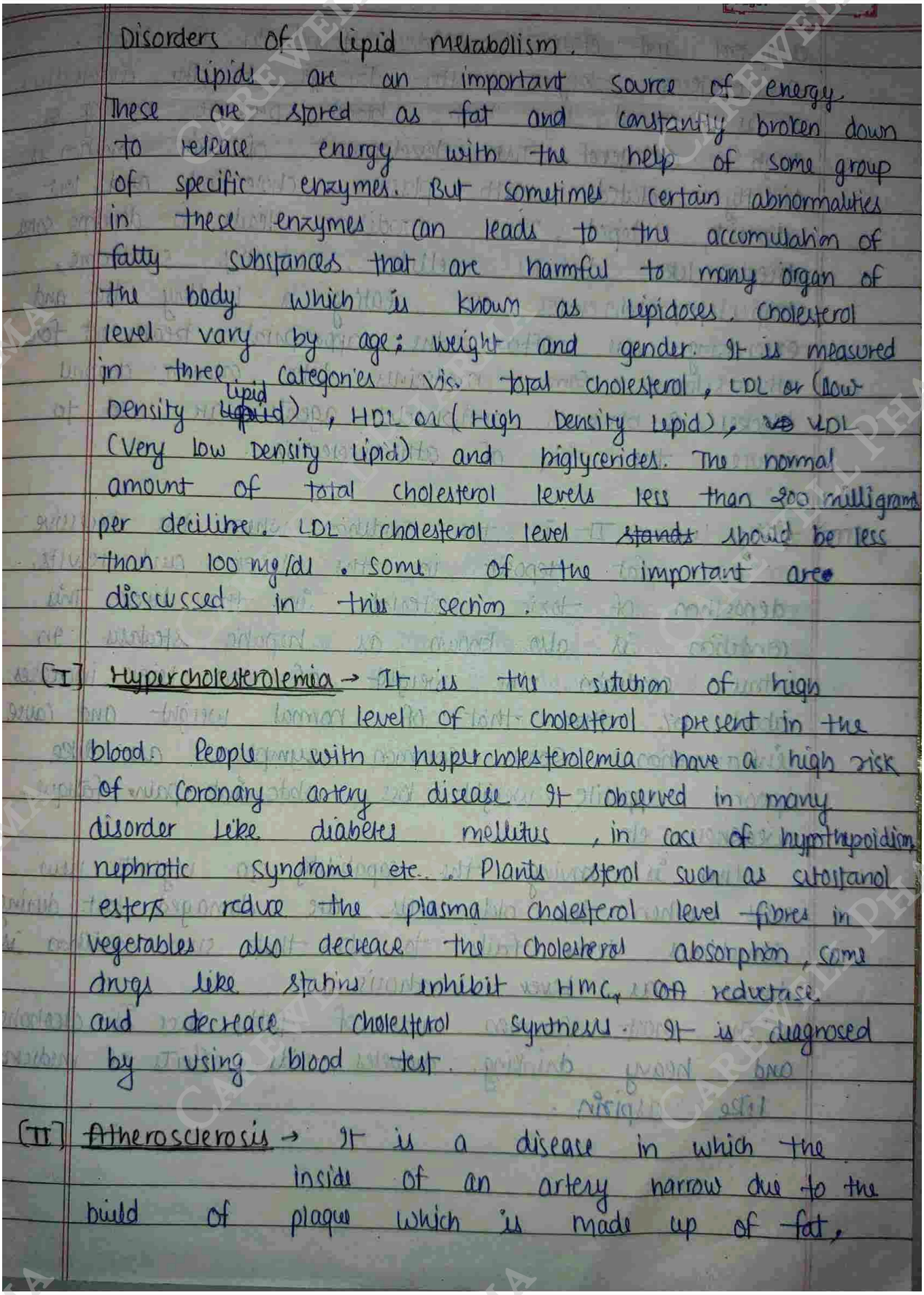
Synthesis of Bile Acids:-

The conversion of cholesterol into bile acids is formed by two ways like classic pathway which occurs in microsomes in liver. In this pathway, cholesterol is primarily activated by 7-α hydroxylase enzyme to form 7-α hydroxy~~late~~ cholesterol and then further hydroxylation followed by oxidation of the side chain produce the bile acids. Another alternate pathway for synthesis of bile acids from cholesterol occurs in mitochondria. Bile acid synthesis is inhibited by cholic acid and increased by cholesterol.

References - Internet





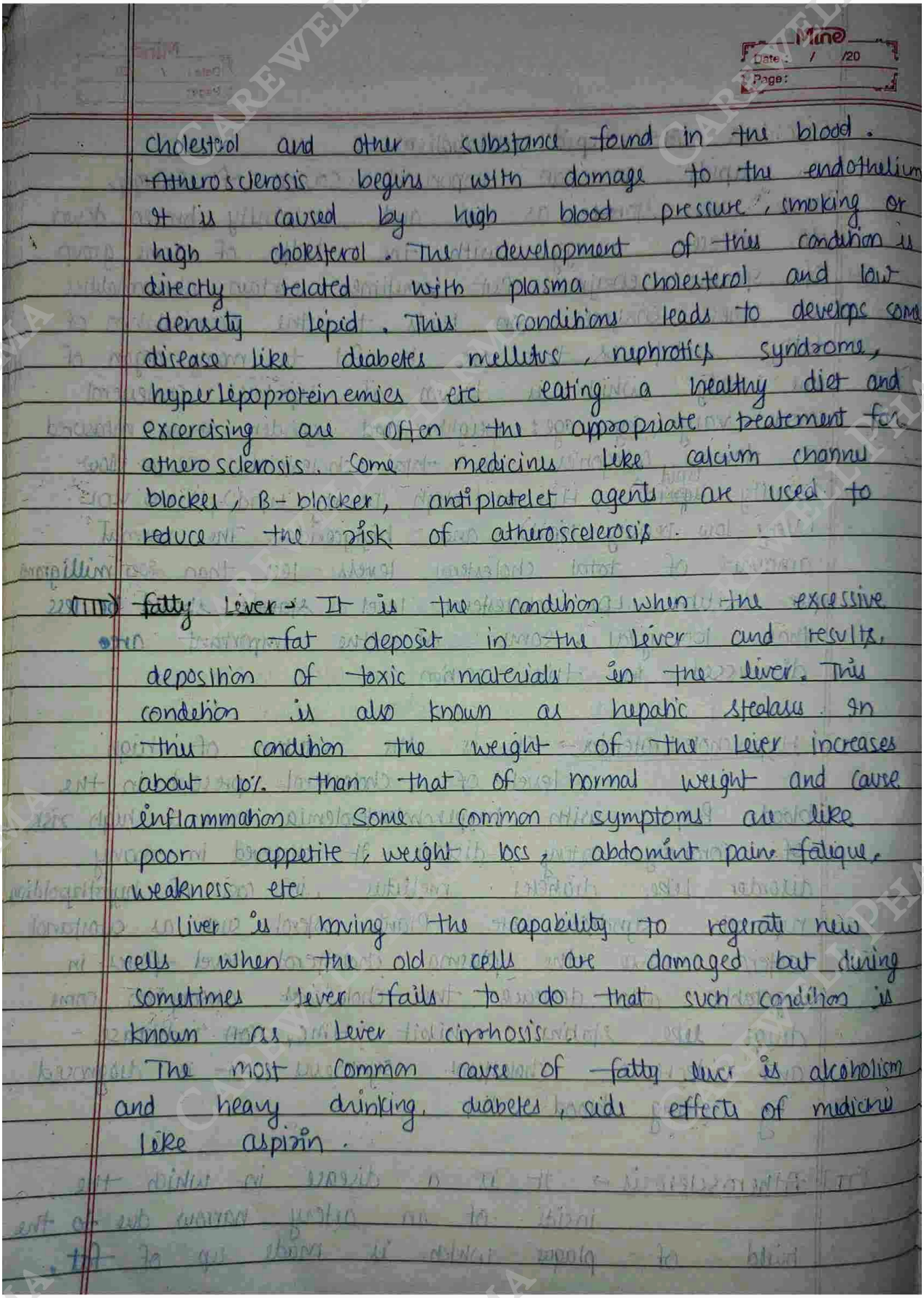


Disorders of lipid metabolism.

Lipids are an important source of energy. These are stored as fat and constantly broken down to release energy with the help of some group of specific enzymes. But sometimes certain abnormalities in these enzymes can leads to the accumulation of fatty substances that are harmful to many organ of the body which is known as Lipidoses. Cholesterol level vary by age; weight and gender. It is measured in three categories viz. total cholesterol, LDL or (low Density lipid), HDL or (High Density Lipid), VLDL (Very low Density Lipid) and biglycerides. The normal amount of total cholesterol levels less than 200 milligram per deciliter. LDL cholesterol level should be less than 100 mg/dl. Some of the important are discussed in this section.

[I] Hypercholesterolemia → It is the situation of high level of cholesterol present in the blood. People with hypercholesterolemia have a high risk of coronary artery disease. It observed in many disorder like diabetes mellitus, in case of hypothyroidism, nephrotic syndrome etc. Plants sterol such as sitostanol esters reduce the plasma cholesterol level fibres in vegetables also decrease the cholesterol absorption, some drugs like statins inhibit HMG, CoA reductase and decrease cholesterol synthesis. It is diagnosed by using blood test.

[II] Atherosclerosis → It is a disease in which the inside of an artery narrow due to the build of plaque which is made up of fat,

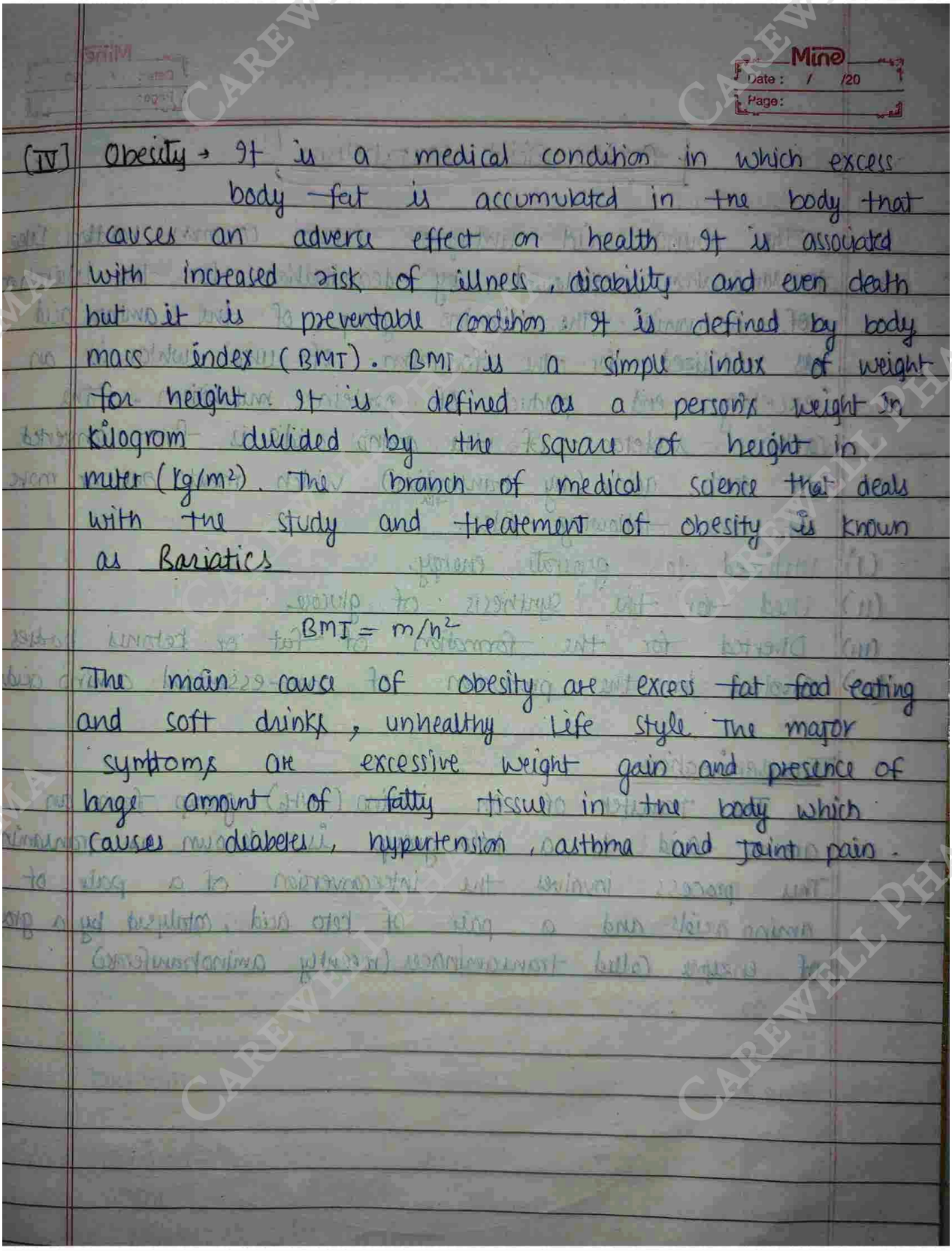


cholesterol and other substance found in the blood. Atherosclerosis begins with damage to the endothelium it is caused by high blood pressure, smoking or high cholesterol. The development of this condition is directly related with plasma cholesterol and low density lepid. This condition leads to develops some disease like diabetes mellitus, nephrotics syndrome, hyperlipoproteinemies etc eating a healthy diet and excercising are often the appropriate treatement for atherosclerosis. Some medicines like calcium channel blockers, β-blocker, antiplatelet agents are used to reduce the risk of atherosclerosis.

Fatty Liver - It is the condition when the excessive fat deposit in the liver and results deposition of toxic materials in the liver. This condition is also known as hepatic steatosis. In this condition the weight of the liver increases about 10% than that of normal weight and cause inflammation. Some common symptoms are like poor appetite, weight loss, abdominal pain, fatigue, weakness etc.

Liver is having the capability to regerate new cells when the old cells are damaged but during sometimes liver fails to do that such condition is known as liver cirrhosis.

The most common cause of fatty liver is alcoholism and heavy drinking, diabetes, side effects of medicine like aspirin.



[IV] Obesity → It is a medical condition in which excess body fat is accumulated in the body that causes an adverse effect on health. It is associated with increased risk of illness, disability and even death but it is preventable condition. It is defined by body mass index (BMI). BMI is a simple index of weight for height. It is defined as a person's weight in kilogram divided by the square of height in meter (kg/m^2). The branch of medical science that deals with the study and treatement of obesity is known as Bariatics

$$BMI = m/h^2$$

The main cause of obesity are excess fat food eating and soft drinks, unhealthy Life style. The major symptoms are excessive weight gain and presence of large amount of fatty tissue in the body which causes diabetes, hypertension, asthma and joint pain.