# Estimation of Sulfur-Containing amino acids In patients of uncompansated liver diseases

# THESIS

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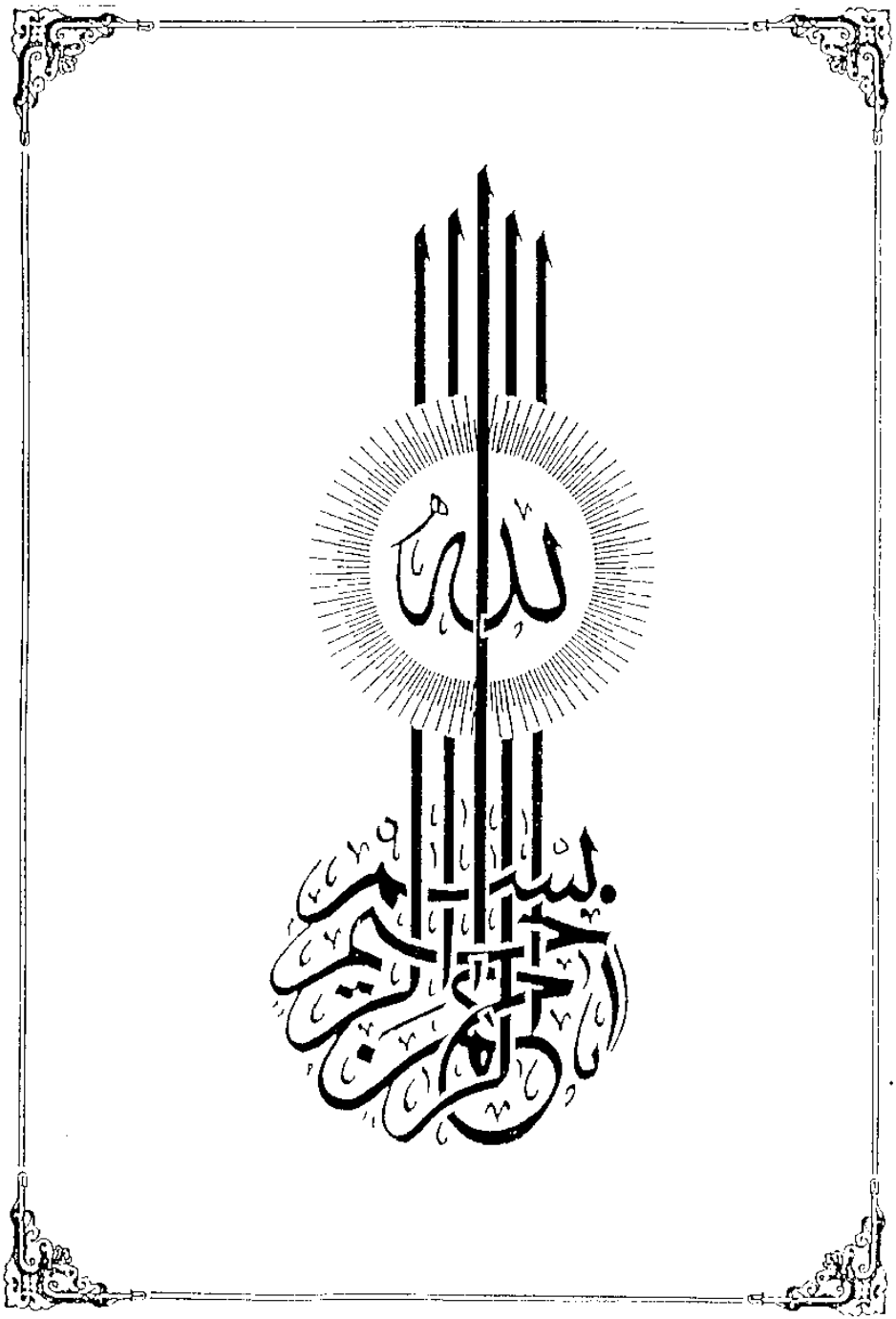

# A C K N O W L E D G E M E N T

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# C O N T E N T S

# Introduction

# I N T R O D U C T I O N

The sulfur-containing amino acids (Methionine, cystine and cysteine ) are catabolised mainly in the liver. their raised values in patients with chronic liver disease probably result from impaired hepatic metabolism and portal systemic shunting of blood.

In cirrhotic subjects a distinctive pattern of plasma amino acids concentration has been observed. The distorted pattern of essential amino acids in cirrhosis will result in changes in amino acids availability to the brain. Entery of amino acids into the brain depends on several carriers each charged by group of amino acids.

Sulfur-containing amino acids have been long associated with hepatic encephalopathy. The role of methionine particularly in its pathogenesis has been investigated extensively, increased levels of methionine have been reported in the plasma of patients with hepatic encephalopathy. ( Phear EA, et al. 1956).

The substances that have been incriminated in the induction of hepatic coma are methionine and its degradation products, other amino acids, certain short-chain fatty acids, biogenic amines, indoles, skatoles and ammonia. ( Chen, Sieve and Mahadevan, 1970).

## Proteins and Amino Acids

Proteins are the most characteristic compounds found in the living cell. They are organic substances of high moleculor weight consisting largely of a number of amino acids united by peptide linkage (Wahba, 1969).

### Protein Digestion:

Protein digestion begins in the stomach, where pepsins cleave some peptide linkages. Like many of the other enzymes concerned with protein digestion pepsins are secreted in inactive precursors of proenzyme form and actived in the intestinal tract. The pepsin precursors are called pepsinogens and are activated by gasteric Hcl. Human gasteric mucosa contains 3 chromatographically distinct pepsinogens which produce 3 pepsins with slightly different properties(pepsins I, II, and III) pepsins hydrolyze the bonds between aromatic amino acids such as phenylalanine or tyrosine and a second amino acid. So the products of peptic digestion are polypeptides of very diverse sizes. (Ganong, 1977).

Because pepsins have apH optimum of (1.6-3.2) their action is terminated when the gasteric content are mixed with the alkaline pancereatic juice in the duodenum.

The PH of the duodenum is about 6.5, in the small

intestine, small polypeptides ( oligopeptides), are formed by the action of the powerfull protein-splitting enzymes trypsin and chemotrypsins. The pancr eatic carboxy peptidase and the intestinal amino peptidase and dipeptidase split these fragments into smaller peptides and free amino acids. Some free amino acids are librated in the intestinal lumen, but others are librated at the cell surface by the amino-peptidase and dipeptidase that line the luminal border of the mucosal cells. Some di- and tri- peptides are actively transported into the intestinal cells and hydrolysed interacellularly, with the amino acids entering the blood stream. ( Gamong, 1977).

Absorption:

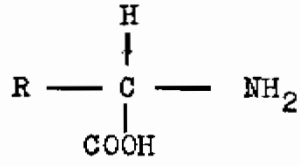
After ingestion of protein meal there is a sharp transient rise in the amino nitrogen content of the portal blood. L. amino acids are absorped more rapidly than the corresponding isomers. Amino acid transport, like sugar transport, is facilitated by high $Na^+$ concentration on the mucosal side of the intestinal epithelial cells.

The transported amino-acids accumulate in the mucosal cells, and from these cells they apprantly diffuse passively into the blood. Absorption of amino acids is rapid in the duodenum and jejunum but slow in the ileum.

Approximately 50% of the digested proteins comes from ingested food, 25% from proteins in digestive juices, and 25% from desquamated macosal cells. Some of the ingested protein enters the colon and eventually digested by bacterial action. The protein in the stools is not of dietary origin but comes from bacteria and cellular debris. ( Ganong, 1977) .

Amino acids :

The alpha-amino acids are the fundamental structural units of proteins. They have both an amino group and carboxyl group attached to the same ( $\alpha$ ) carbon atom.



The amino acids may be classified according to the number of their amino and carboxyl groups into three groups :

1. Neutral amino acids = Monoamino - mono carboxylic a,a.

2. Acidic amino acids = Monoamino - dicorboxylic a.a.

3. Basic Amino acids = Diamino - mono corboxylic a.a.

The amino acids in each group may further be sub-divided according to whether the radical R - in the general formula represents an aliphatic, aromatic or heterocyclic nucleus.

1. Neutral Amino Acids :

A) With aliphatic side chains:

Glycine (Gly): Alanine (Ala): Valine (VAL):

Leucine (Leu) Isoleucine (Ile)

B) With side chains containing hydroxylic groups:

Serine ( Ser) and Thereonine ( Thr).

C) With side chains containing sulfur atoms:

Cysteine (Cyste.), Cystine (Cyst.) and Methionine (Met.).

D) With side chains contains aromatic ring. (A.A.A):

Phenylalanine ( Phe), Tyrosine (Tyr) and Tryptophan (Trp.).

E) Imino acids :

Proline ( Pro) and Hydroxy proline ( Hyp).

II. Acidic amino acids:

Aspartic acid ( Asp) and Glutomic acid (Glu).

III. Basic amino acids:

Arginine ( Arg), Lysine ( Lys), Hydroxylysine (Hyl) and Histidine ( His). (Rodwell, 1977).

Essential Amino acids:

Certain amino acids are called " essential" or "indispensable" in the diet. These essential amino acids can't be synthesized by the organism from substances ordinarily present in the diet at a rate to supply fully . The physiological requirements of the animal. They must be supplied in the diet.

The list of essential amino acid varies with the animal species. It may also vary with the physiological state of the animal.

The ten essential amino acids required by the man are: Tryptophan, Phenylalanine, Lysine, Methionine, Valine, Leucine, Isoleucine, Threonine, Arginine and Histidine.

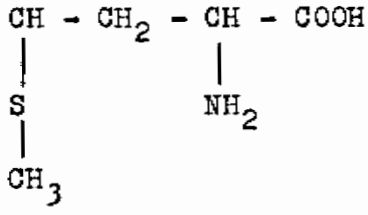
The remainder, called " non-essential" or "dispensable" amino acids, are also required by the organism since they are found in the protein of the tissues, but they can be synthesized in the body e.g glycine, cysteine and tyrosine.

The nutritive value of aprotein is now known to depend on its content of essential amino acids. (Wahba, 1969).

## The sulfur containing amino acids

The sulfur containing amino acids include Methionine, Cysteine and Cystine.

Methionine:



L. Methionine

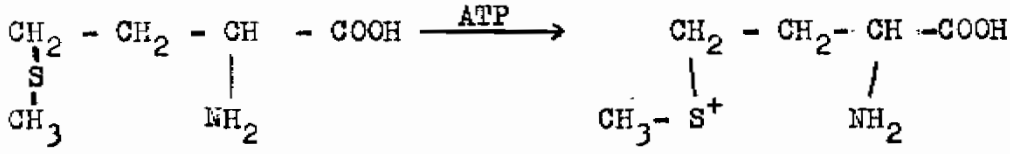
Synthesis:

Methionine is synthesized from homocysteine by transmethylation and by a mechanism in which a one carbon unit is utilized by reactions involving folic acid and vit. $B_{12}$.

Metabolism:

The metabolism of methionine includes reactions in which its sulfur atom and methyl group are transfer to other molecules. Trans-sulfuration involves the formation of cystathionine which is an intermediate in both degrative and synthetic pathways.

L. Methionine condenses with ATP, forming S - adensylmethionine or Active methionine".




L. Methionine

S- adenosyl methionine
"Active methionine"

Methionine in the form of S-adenosylmethionine is the principal source of methyl groups in the body.

It is the key compound in the transmethylation which leads to the formation of methyl groups of N - methylnicotinamide, methylhistamine, creatine, choline, anserine, epinephrine , metanephrine, ergosterol, certain purines Alkaloids and other compounds.

Methionine as amethyl donner used in synthesis of choline act as lipotropic agent in curing fatty liver due to choline deficency, and conversely, processes that utilize methyl groups exoessively or diets poor in protein (Containing methionine) will all tend to favor the production of fatty liver.

Methionine gives cysteine in the body as follows: