SERUM COPPER AND MAGNESIUM AND THE EFFECT OF ORAL CONTRACEPTIVE AGENTS

THESIS

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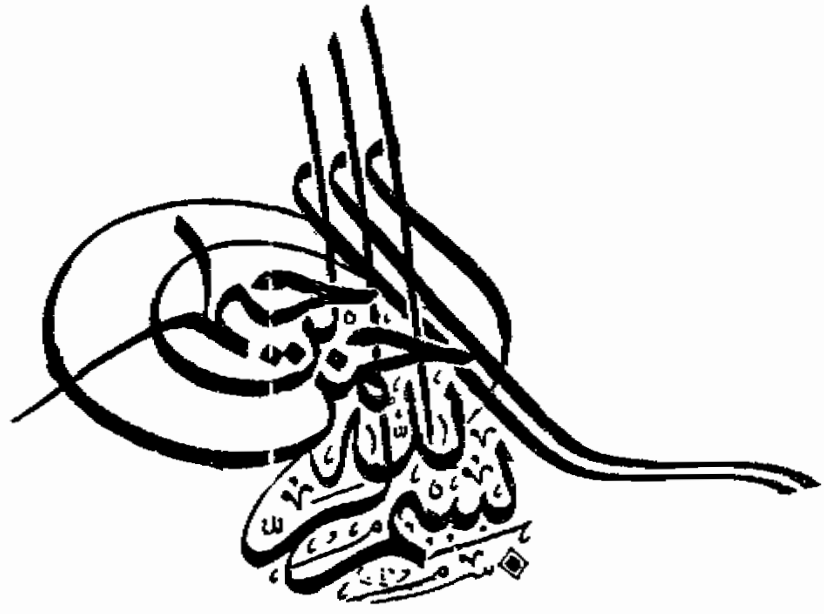

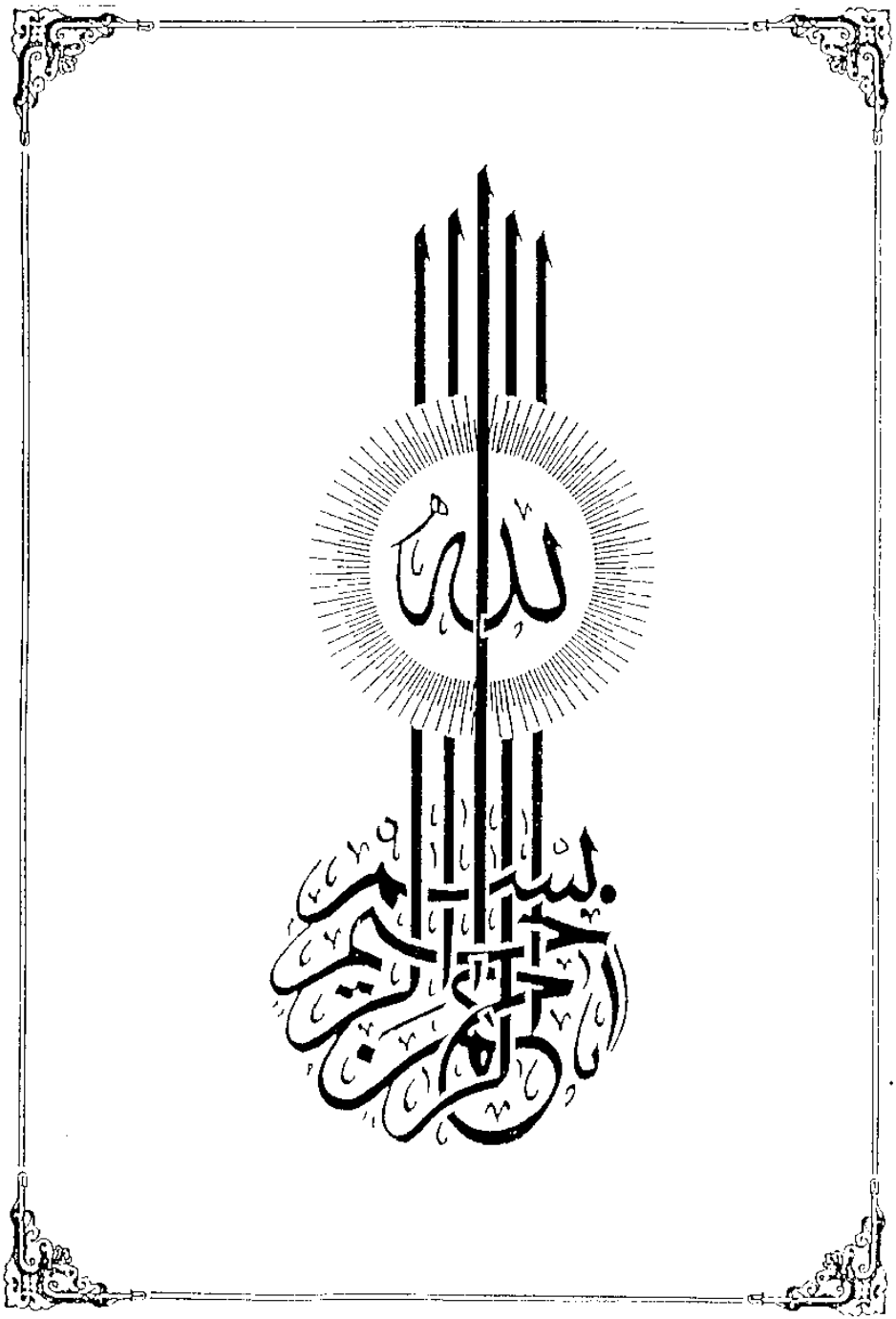

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C O N T E N T S

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AIM OF THE WORK

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The determination of trace elements was limited by method up to last decade. This resulted in a lesser knowledge of concentrations of these metals in many physiological and pathological conditions. But this problem is solved greatly by atomic absorption spectrophotometry that makes study of these metal concentrations in hand.

The increased usage of oral contraceptive pills ~~that~~ have effects on many features of human metabolism including trace elements such as iron, magnesium, zinc, copper, phosphorus and iodine (El-Tawil et al., 1969; Schenker et al., 1971).

The effect of the regular intake of O.C.A. on plasma copper and magnesium of women had been studied (Oleary and Spellacy, 1969; Halsted et al., 1968; Prasad et al., 1975; Schenker et al., 1971) and effect of O.C.A. on plasma zinc had been studied by (Nabeih et al., 1985). So:

The aim of this work:

Is to study the effect of O.C.A. usage on serum copper, magnesium levels of middle aged women, as regards composition of pills.

O.C.A. = Oral Contraceptive Pills

REVIEW OF LITERATURE

TRACE ELEMENTS

Introduction:

Trace elements are certain elements although present in minute amounts in tissues, they are essential nutrients with total concentrations in 70 kilogram man is less than 4 grams.

Trace elements include: iron, copper, iodine, cobalt, manganese, flourine, molybdenum, zinc, selenium, chromium, nickel, lead and cadmium.

Trace elements are essential to many vital processes including maintenance of life, growth and reproduction.

The field of trace element physiology and metabolism - over past few years - has grown rapidly. This occured with help of recently developed technique (flameless atomic absorption, spectrophotometry), which allowed reliable measurements of several trace elements in different tissues.

This technique is hindered by factors as lack of convenient methods for handling of samples, expense of equipment and difficulties with contamination of samples.

Copper:

The presence of copper in animal tissues was recognised 150 years ago (Underwood, 1977; and Prasad, 1978) and its dietary importance was known by (Prasad, 1978).

Biochemistry and Physiology:

Copper was known as a component of many enzymes, as it is essential for the synthesis of heme A, a component of cytochrome oxidase enzyme. Copper was established as a significant catalyst.

Ceruloplasmin contains essentially all the plasma copper and it probably plays a role in copper transport from liver to the extrahepatic organs (O'Dell, 1976).

Metabolism of Copper:

1. Requirement:

Daily copper requirement for human adult is estimated as about 2-5 mg/day. Average diets contain about 2-5mg copper that is considered as arich copper supply (Scheinberg, 1976).

2. Absorption:

Absorption of copper occurs mainly at duodenum as stated by (Sacks et al , 1943) but (Evans, 1972) stated that copper absorption occurs in stomach and upper intestine and each is of certain mechanism. Smaller

amount of copper is absorped in stomach as energy dependent process but the great part of copper is absorped from upper intestinal mucosa bounded to two protein fractions. About 32% of orally taken copper is absorped in normal human subjects (Cartwright and Wintrobe, 1964).

Copper absorption depends on chemical valency of ingested metal, level of other minerals in ingested diets and acidity of intestinal mucosa (Underwood, 1977). This is explained as high calcium carbonate and ferrous sulphide in diet depress copper absorption. This suggest competition between different cations at same sites of intestinal mucosa (Underwood, 1977).

Dietary zinc exerts antagonistic effect on copper absorption from small intestine (Peter W.F. et al., 1981). This is because zinc induces synthesis of a copper binding ligand may be a thionein in mucosal cells that sequestres copper from these cells.

3. Excretion:

Copper is mainly excreted in biliary system (0.5-1.3mg) as stated by (Van-Ravesteyn, 1944). High amount is excreted in faeces of about (0.1-0.3mg). 0.01-0.06mg is excreted in urine (Cartwright and Wintrobe, 1964). Increased urine excretion occurs in patients of

liver cirrhosis associated with biliary obstruction (Bearn and Kunkel, 1954). About 0.5mg is excreted through menstruation (Prasad, 1978).

4. Distribution in tissues and body fluids:

Adult human body contains about 100-150mg of copper (Tipton and Cock, 1963) but (Cartwright and Wintrobe, 1964) stated that this content is about 80mg. Some organs as liver, brain, heart and kidney have in ascending order highest concentrations of copper and intermediate concentrations are in lungs, intestine and spleen (Tipton and Cock, 1963). Also organs as muscles, bone and endocrine glands have lowest concentrations. Liver, heart, spleen, kidneys and brain contain about 23mgm copper (Cartwright and Wintrobe, 1964). Of this amount, 8mgm is present in liver and some amount in brain.

Copper in Blood:

Copper is bounded to ceruloplasmin (large glycoprotein alpha2 globulin), plasma albumin and to erythrocytes.

The fixed part of copper in plasma caeruloplasmin forms about 95% of total plasma copper and is synthesized in liver to be released to blood (Owen and Hazerling, 1966). The normal plasma caeruloplasmin concentrations is about 20-50mgm/100ml Blood

(cartwright, 1977). Caeruloplasmin transfers copper to be excreted in bile and G.I.T. (Gault et al., 1966). Copper is also found in some enzymes in plasma as cytochrome oxidase and monamine oxidase enzymes. A small amount of copper is present freely in plasma and is bounded to amino acids (Sass-Kortsak, 1965). Copper concentration in plasma is not changed with food or by fasting (Prasad, 1978).

Copper concentration in whole blood is 98 (72-125)ugm/100ml and in plasma 109 (75-145)ugm/100ml as stated by (Adelsten et al., 1961) plasma copper concentration in females is higher (114 ± 4.67ugm/100ml) than men (105 ± 5.03ugm/100ml) (Lahey, 1953).

Copper is present in erythrocytes in form of a colourless protein called erythrocuprein that forms about 60% of total red cell copper as called by (Cartwright and Wintrobe, 1964). This amount is found freely in erythrocytes but remainder of erythrocyte copper is loosely bounded to undifferentiated protein and is more labile than erythrocuprein (Prasad, 1978).

Copper deficiency:

A syndrome of copper deficiency that affecting patients with sickle cell anaemia who receive 150mgm zinc daily orally for nearly 2 years and this

deficiency is characterized clinically by hypochromic microcytic anaemia and neutropenia (Prasad, 1978).

Copper Excess:

Human copper toxicity may occur in these conditions:

(1) Wilson's disease.

(2) The use of copper containing intrauterine contraceptive devices.

(3) Addition of copper salts to animal feeds.

(4) Use of copper sulphate as fungiside, algiside and molluscaside.

(Scheinberg and Sternlieb, 1976).

Wilson's disease:

According to Tourian (1985) there is a defect in biiliary excretion of copper causing accumulation of copper in liver, brain and other tissues. The majority of patients show decreased concentrations of caeruloplasmin in serum, that is main pathogenic finding in Wilson's disease.

This rare disease is characterised by degenerations in brain in basal ganglia particularly and liver cirrhosis (Tourian, 1985). The mutant gene of Wilson's disease is an abnormal intracellular protein that has increased affinity for copper (Uzman et al., 1956) the disease is inherited as an autosomal