

**BIOCHEMICAL STUDIES ON CARBOHYDRATE
METABOLISM IN NORMAL AND
EXPERIMENTALLY DIABETIC RATS**

THESIS

Submitted to
The Faculty of Science
Ain Shams University

In Partial Fulfilment of the Degree
of
MASTER OF SCIENCE

By
AZZA AHMED ATEF MAHMOUD

Demonstrator
In the Department of Biochemistry
Ain Shams University

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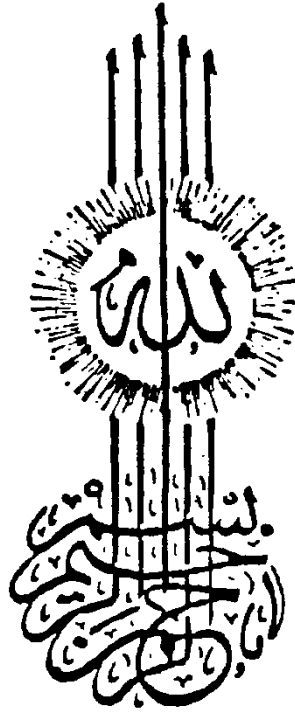
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1985





وَقُلْ اَعْمَلُوا فَسَيَرَى اللّٰهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ
۝ وَسِعَتْ قَاعَهُ الْمَقَامُ ۝

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PART I

THEORETICAL SECTION

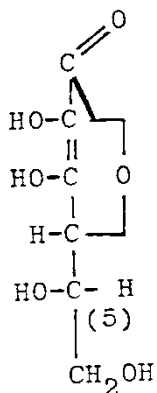
A - CHEMICAL AND BIOCHEMICAL STUDY

B - REVIEW OF LITERATURE

A. CHEMICAL AND BIOCHEMICAL STUDIES

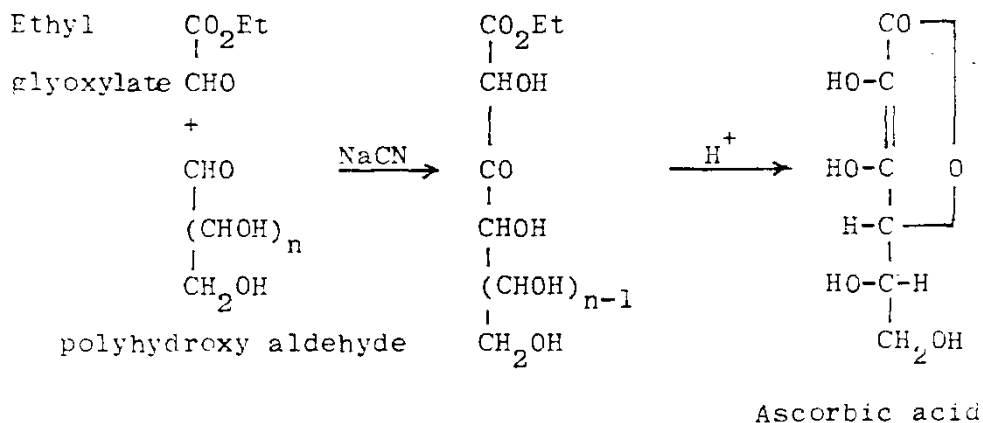
Ascorbic acid

Vitamin C or ascorbic acid was first isolated in pure crystalline form from lemon juice by the American Biochemists King & Waugh in 1932. It is one of the simplest vitamins in structure, being a lactone of a sugar acid, (Lehninger, 1975).

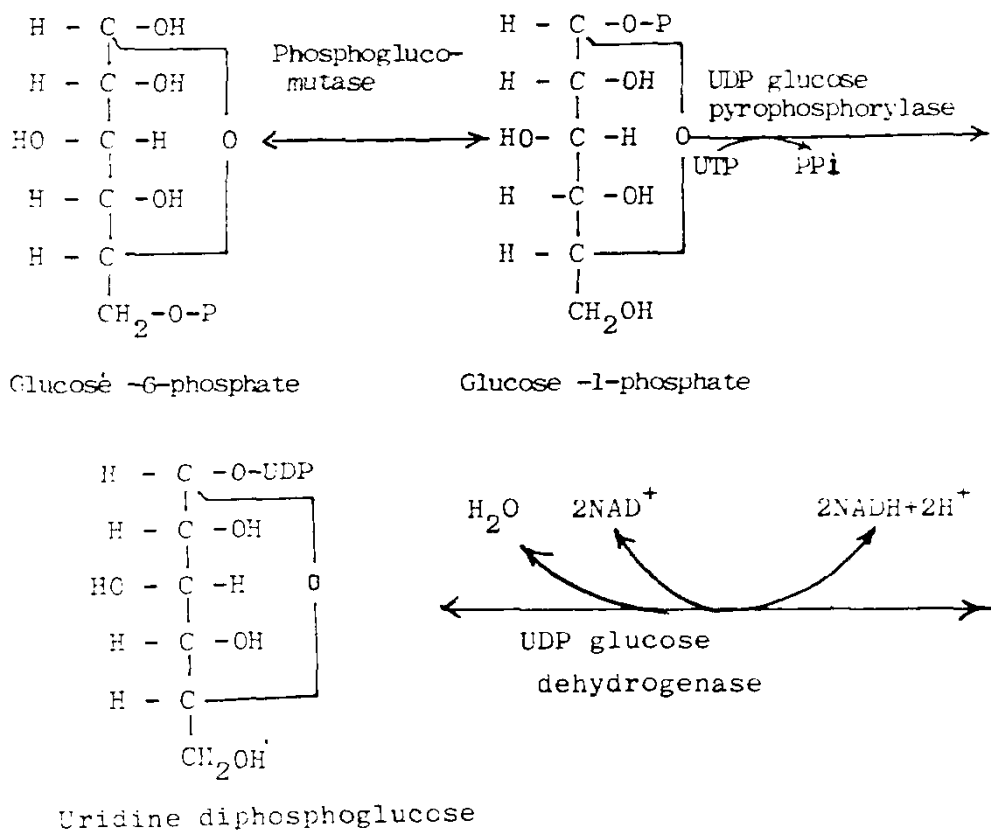


Ascorbic acid.

A general method of preparing ascorbic acid involves the condensation between polyhydroxy aldehyde e.g. L-threose ($n=2$) and ethyl glyoxylate in the presence of sodium cyanide. The intermediate 3-oxo-derivative (not isolated) is then hydrolyzed with acid. (Finar, 1975).



Most species of animals can synthesize ascorbic acid except guinea pig and man. They synthesize the vitamin from D-glucose via the glucuronic acid pathway Fig. (1). (Harper, et al. 1977).



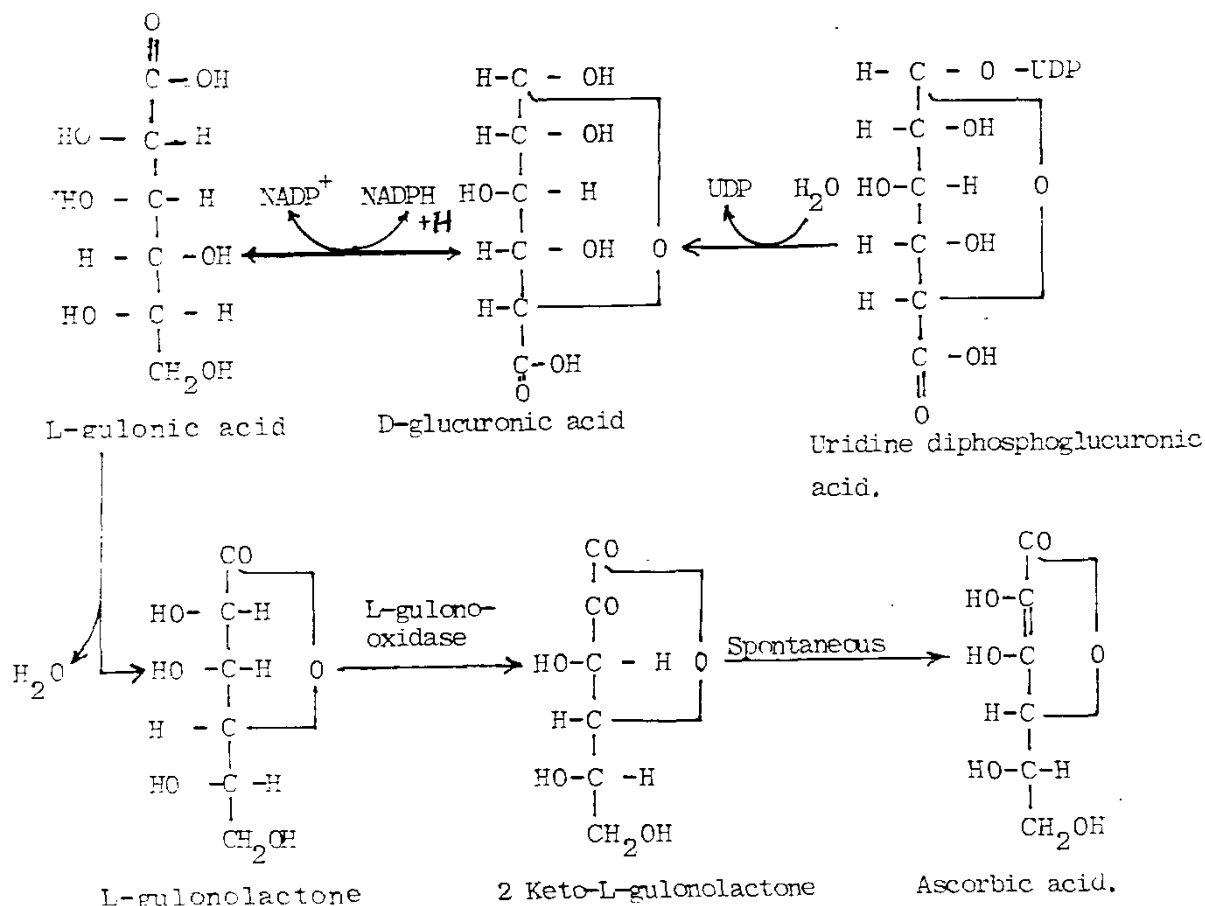
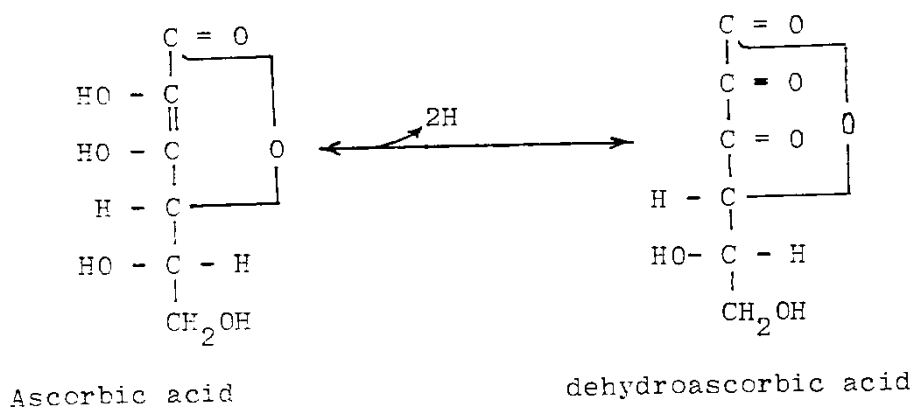


Fig. (1) Glucuronic acid pathway.

Pure ascorbic acid is a white crystalline solid freely soluble in water. The molecular formula was shown to be $\text{C}_6\text{H}_8\text{O}_6$ and m.p. 192°C . (Finar, 1975).

Vitamin C is readily oxidized to the dehydroform. Both forms are physiologically active and both are found in the body fluids. The enediol group of ascorbic acid (from which removal of hydrogen occurs to produce the dehydroform) may be involved in the physiologic function of this vitamin. It is conceivable that this chemical

grouping functions in a hydrogen transfer system; a role of the vitamin in such a system. (Harper, et al. 1977).



Studies with L-ascorbic labeled in the various positions with isotopic carbon 14 have shown that the vitamin is extensively oxidized to respiratory CO_2 in **rat**. Correspondingly, ascorbic acid disappears slowly in man; it has a half-life of about 16 days in man compared to a half life of about 4 days in the guinea pig.

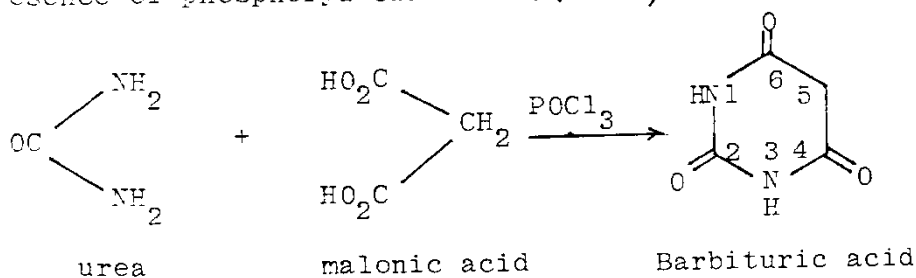
L-ascorbic acid -1- ^{14}C is converted to labeled urinary oxalate in man, guinea pig and rats. In man conversion of ascorbic acid to oxalate may account for the major part of the endogenous urinary oxalate. (Harper, et al. 1977).

The biochemical function of ascorbic acid is still not known. Probably the most clearly established functional role of the vitamin is in maintaining the

normal intracellular material of cartilage, dentine, and bone. There are also a number of reports of a possible function of ascorbic acid in oxidation - reduction systems, coupled with glutathione, cytochrome C, pyridine nucleotides or flavin nucleotids. The vitamin has been reported to be involved in the oxidation of tyrosine and in the metabolism of adrenal steroids and of various drugs. (Harper, et al 1977).

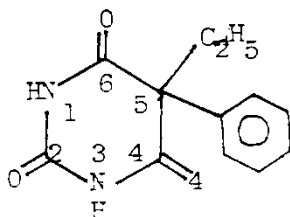
Barbituric acid

Barbituric acid (malonylurea) was originally prepared by condensing urea with malonic acid in the presence of phosphoryl chloride . (Finar, 1975).



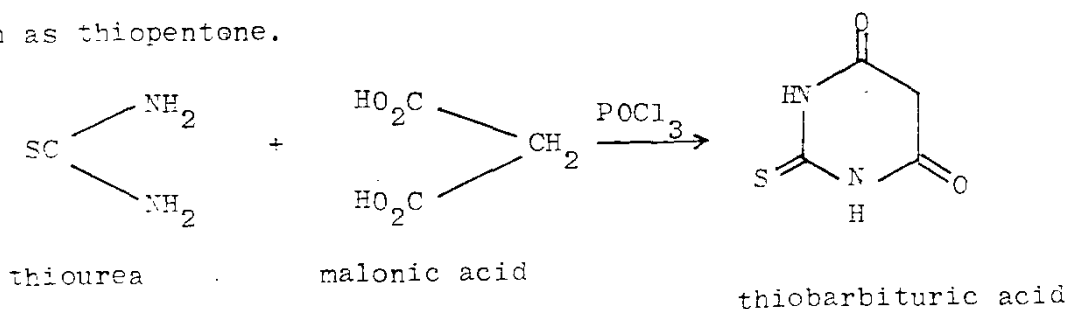
Barbituric acid is a solid substance, m.p. 253°C and is not very soluble in water. It is soluble in distilled water, heated to 75°C the solution then cooled to 40 - 45°C and immediately used. (Martinz, 1955).

Barbituric acid is the parent compound of the barbiturate series. The majority of the clinically useful barbiturates are obtained by making appropriate substitutions at position (5) in the molecule e.g. phenobarbitone is ethylphenylbarbituric acid.



Phenobarbitone

If thiourea instead of urea is combined with malonic acid, the resulting thiobarbituric acid is the parent compound of ultra short acting intravenous anaesthetics such as thiopentone.



An increase in the potency and a decrease in the duration of action can be produced by increasing the length of the alkyl groups on C₅, by the substitution of alicyclic, branched, or unsaturated side chains for alkyl groups on C₅ and by the attachment of an alkyl group to one of the nitrogen atoms of the ureide.

For many years, the therapeutically useful barbiturates have been classified according to their duration of action this being based on animal experiments. They were divided up into ultra short, short, medium and long acting barbiturates.

I. Long acting (8 to 12 hours or longer).

Barbitone ——— 5,5 diethylbarbituric acid.

