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Review Article

Ascorbic Acid Metabolisms: A review

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Abstract

Ascorbic acid (vitamin C) is a water-soluble, hexonic sugar, with a molecular weight of 176. It is known to play vital roles in numerous functions of the body, especially in hydroxylation reactions. Its requirement by animals may be increased when challenged in the form of immune and metabolic stress. The main objective of this brief review is to outline the catabolic and anabolic pathways of ascorbic acid as well as its metabolic functions.

Keywords:
Epidermolysis bullosa,
Genetically determined, Recessive dystrophic subtype.

1. Analytical Methods

The determination of ascorbic acid in various matrices can be carried out by several analytical techniques. Of these, high-pressure liquid chromatography [1] and spectrophotometry [2] are the most common techniques applied. The former is preferable, as the spectrophotometric determination is very difficult and requires tedious pre-treatment to eliminate interfering substances. The “Chemistry of Ascorbic Acid” by Szent Gyorgi [3] has reported the discovery of a carbohydrate derivative from the adrenal cortex of the ox, this derivative possessing strong reducing properties. The physiological activity appeared to be associated with the reducing power [4]. Ascorbic acid is a fine crystalline, white or slightly yellow odorless powder with a tart taste. It is easily oxidized in air. Chemically, ascorbic acid is the enolic form of 3-oxo-L-gulofuranolactone, which is optically active in water and is highly labile as it is easily oxidized by the enzyme dehydroascorbate reductase to dehydroascorbic acid. Both the oxidized and reduced forms are physiologically active [5].

Blood samples for ascorbic acid determination should be deproteinized and stabilized immediately after collection. Lykkesfeldt *et al* [6] showed that a concentration of 5% metaphosphoric acid stabilizes ascorbic acid and dehydroascorbic acid during a two-month storage at 200^{0}C. Unless reduced back to ascorbate, dehydroascorbic acid undergoes irreversible ring opening to 2,3-diketogulonic acid. According to Dhariwal *et al* [7], the two-electron oxidation product of ascorbate, dehydroascorbate, is labile at physiological pH and temperature (half life 5-7 min.). Dehydroascorbate can be reduced or recycled to ascorbate in blood by both erythrocytes [8] and neutrophils[9].

2. Ascorbic Acid Biosynthesis

L-ascorbic acid is biosynthetically formed in almost all mammals studied, except in man, several other primates and guinea pigs [10]. Ascorbic acid is a product of glucose metabolism in the glucuronate pathway [11]. The anabolic pathway of ascorbic acid utilizes glucose as the initial substrate [12].

3. Ascorbic Acid Catabolism

The metabolic fate of ascorbic acid and its derivative in animals depends on a number of factors including animal species, route of ingestion, quantity and nutritional status. The catabolic pathways of ascorbic acid proceed through xylitol or through L13 ribulose to D-xylose as initial step for the conversion of L to D-sugars. Another pathway for the catabolism of ascorbate is by C2 - C3 carbon cleavage, to give rise to oxalate and a 4-carbon compound as intermediates. The major two ascorbic acid degradation pathways at physiological pH are the oxidative and the non-oxidative ones. The major pathway has erythrulose as is the major product of the non-oxidative degradation of dehydroascorbic acid (DHA), and also 2,3-diketogulonic acid [12]. DHA rapidly hydrolyzes in solution at pH 7.0 to L-diketogulonate (2,3-DKG), which is very unstable and degrades further [6]. Analysis showed that L-erythrulose (ERU) and oxalate were the primary degradation products of ascorbic acid regardless of which compound was used as the starting material. In the presence of high concentrations of H2O2, 2,3-DKG produces L-threonate, oxalate, and CO2. In the absence of H2O2, 97 % of the products consist of ERU and oxalate [12].

4. Metabolic Functions of Ascorbic acid

Over the last few years, it has been recognized that ascorbic acid is involved in a great variety of biochemical processes beyond the scope of prevention of scurvy [13]. The metabolic functions of ascorbic acid in cattle have been repeatedly reviewed [14-16]. Apart from fermentation of dietary ascorbic acid in the rumen, fundamental differences between ruminants and monogastric animals with respect to ascorbic acid metabolism are not known.

5. Hydroxylation reactions

In most cases, ascorbic acid assists biosynthetic processes and regulatory mechanisms which comprise hydroxylation reactions according to the mixed function type [17]. Apart from its participation in collagen formation, ascorbic acid is a co-substrate for a variety of mono- and dioxygenases for redox reactions in biochemical processes, such as the conversion of dopamine to noradrenaline and for the metabolism of cholesterol and carnitin [13]. L- ascorbic acid participates in the biosynthesis of collagen, carnitin, catecholamines, cartilage, skin, skeletal and connective tissues [18]. The synthesis of carnitin could be of special importance for cows in the postpartum phase, because at that time large amounts of stored fat are mobilized [19]. Carnitin enables fatty acids to enter the mitochondria, where they are broken down to acetyl-coA by β-oxidation. Vitamin C also participates in the modulation of complex biochemical pathways, which are an essential part of the normal metabolism of immune cells [20]. Ascorbic acid functions in cholesterol metabolism in that it is required for the transformation of cholesterol into bile acids which in turn facilitate fat absorption [21].

6. Anti-oxidant function

One of the major metabolic roles of ascorbic acid is its participation as antioxidant agent and free radical scavenger in numerous cellular oxidation processes [22]. This activity is attributed to its properties as an electron donor. Vitamin C is capable of protecting against oxidative injuries in the aqueous compartments and lipid bilayer of cell membranes [23]. It also scavenges aqueous-phase reactive oxygen radicals (ROS) by very rapid electron transfer and thus inhibits lipid peroxidation [24]. Vitamin C plays an important role in the defence against oxidative damage, especially in leukocytes. It also protects the structural integrity of the cells of the immune system [25]. Vitamin C was found to be effective against superoxide, hydroxyl radicals, hydrogen peroxide, peroxy radicals and singlet oxygen, thereby protecting phagocytes from oxygen radicals entering the cytoplasm from the phagosome [26]. Vitamin C also functions in reducing the tocopheroxy radical, thereby restoring the radical scavenging activity of vitamin E [26]. The ascorbate radical (semi-dehydroascorbate) is reduced to ascorbate by NADH-dependent semi-dehydroascorbate reductase[27].

Furthermore, vitamin C serves as a radical scavenger and general antioxidant for cellular metabolites including unsaturated fatty acids, vitamins A and E, and carotenoids [28]. The anti-oxidative function of ascorbic acid is evident when treating nitrate poisoning in cattle. Nitrate from the feed is reduced to nitrite in the rumen and leads to the formation of methaemoglobin in the blood [29]. Due to its antioxidant potential, ascorbic acid was proved to be effective in curing post parturient haemoglobinurea in buffaloes [30].

7. Role of Vitamin C in the metabolism of minerals

Vitamin C is necessary for iron metabolism, maintenance of normal tyrosine oxidation and acts as a hydrogen transport agent [31]. It plays a role in the maturation of erythrocytes, absorption and mobilisation of iron and in keeping constant the haemoglobin content [32]. Ascorbic acid keeps iron in the reduced, bivalent form and thus methaemoglobin is reduced [33]. The relations between iron, as a generator of free radicals, and vitamin C have been studied [34,35]. In addition to the influence of cortisol on the synthesis of ascorbic acid [36], it has also been hypothesized that ascorbic acid itself could influence adrenal gland function. Ketotic cows injected subcutaneously/intravenously with ascorbic acid showed a transient elevation of the glucose level and a lowering of the ketone level in the blood [37]. An effect of ascorbic acid on the metabolism of calcium could also be relevant for dairy cows. By administering high doses of ascorbic acid, the hypocalcaemia of cows at an early stage of lactation has been successfully treated [38].

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