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# BIOCHEMICAL ASPECTS OF KETOSIS: AN OVERVIEW

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**Abstract:** The metabolic diseases reduce productivity of animals. Ketosis is one of the important metabolic disease encountered in animals at high production though not limited to it. Production of ketone bodies is a normal and regular process occurring in animal body but the excess production may bring associated hazards to the animal. The biochemical basis of the disease is important in handling and management of the suffering animals. Here, the biochemical aspects of genesis and management of ketosis is being briefly discussed.
**Keywords:** Ketosis, metabolic diseases, high production, biochemical basis.

## Introduction

though the ketogenic acidosis is being clinically handled very efficiently but proper diagnosis and treatment are always determinant of the prognosis in such cases. Ketosis is a phenomenon pertaining to the abnormal levels of ketone bodies (i.e. acetone, acetoacetic acid and β-Hydroxy butyric acid) in body fluids. The hazard comes through the acidosis associated with these ketone bodies when present in excess in the body fluids. Out of these volatile fatty acids, β-Hydroxy butyric acid can only exhibit certain level of stereoisomerism [D (-)]. The striking sweetish smell from ketotic animals are due to the released acetone which is volatile in nature. Acetone is nonionisable but whereas others exists in ionized form at physiological pH. Further acetone and acetoacetic acids are readily soluble in water but β-Hydroxy butyric acid can be dissolved at certain proportions only. Synthesis of ketone occurs largely in liver though not exclusively. Extra-hepatic ketogenesis is well documented in the organs like heart, kidney, mammary glands and rumen of the ruminants (McSherry *et al*., 1960).

## Biosynthesis of Ketones

It is a regular product of metabolism. The source is mostly fatty acids. Specifically, long chain fatty acids (LCFA) with more than 16 carbons. The LCFA gets coupled with Co-A in cytosol and can form either triacyl glycerol or can form acetyl co-A by β-Oxidation of fatty

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acids. In the absence of needed amount of oxaloacetic acid (OAA) or in presence of excess citrate two molecules of acetyl Co-A condenses two form ketone bodies (Shaw, 1956). Out of the four enzymes involved in ketone body synthesis, thiolase is present in both cytosol and mitochondria but rest are confined to mitochondria.

HMG-CoA synthase is the rate limiting enzyme and exclusive to liver. The concentration of this enzyme rises with cAMP, glucagon and decreases with higher level of succinyl CoA. Though the synthesis of ketone bodies is augmented by volatile fatty acids (VFA) but the influence of propionate is indirect and mediated by Carnitine acyltransferase-I. Further, Butyrate is a precursor of β-Hydroxy butyric acid where as acetate is converted to acetyl CoA prior to conversion to ketone bodies.

Enzymes like HMG CoA synthase, HMG CoA lyase and β-Hydroxy butyrate dehydrogenase are present in ruminal epithelium too along with Butyryl CoA synthase which can form acylated butyrate. The acylated butyrate can be converted to aceto-acetate and β-Hydroxy butyrate later via β-oxidation. Additionally, rumen epithelium does contain Keto acid Co-A transferase which can transfer the CoA directly to the succinate from that of aceto acetyl CoA, thus generating acetoacetate. Ketotic cows were found to produce more acetoacetate in their mammary glands. By estimating the arterio-venous difference of β-Hydroxy butyrate and aceto-acetate concentration it was found that keto conversion is the process that occurs in mammary gland rather than ketogenesis.

Interestingly, ketogenesis will only start with high level of LCFA. Even if a fall in mitochondrial OAA level can't initiate the synthesis by itself.

Though the glucose concentration increases during diabetes mellitus but due to lack of insulin, increased lipolysis and increased gluconeogenesis occur. These two favour ketogenesis (Brockman, 1979).

During pregnancy and lactogenesis also, there is chance of ketosis due to heavy drainage of glucose from the dam for the foetus and milk sugar synthesis respectively (Baird, 1982). Another form of ketosis is found in humans and rats known as post exercise ketosis (Johnson *et al*., 1969). Mostly the amateur persons show ketonemia and ketonuria after a prolonged exercise. Supplementation of diet rich in carbohydrate can decrease the level of formation (Koeslag, 1982). Factors like enhanced gluconeogenesis and decreased level of ketone oxidation may further contribute to this after exercise.

**Factors affecting ketogenesis:**

- Excess feeding of silage (Spoiled /having more butyrate) (Andersson,1988)

- Starvation
- Poor quality food with low propionate and high butyrate
- Less fodder in the diet
- Production stress (Milched animals)
- Breed susceptibility (H. *Friesians)*
- Due to some other precipitating factors (i.e. diseases like mastitis, abomasal displacement and TRP)
- Deficiency of insulin

**Detection of ketosis:**

The methods can be broadly classified into two broad categories as (I) qualitative and (II) quantitative

(I) Qualitative: This determines the presence or absence of ketone bodies in body fluids. Alkaline nitroprusside test (Rothera's test) is such a test which has been an established tool for such diagnosis. This test detects acetone and acetoacetic acid while nonresponsive towards β-hydroxy butyrate (Geishauser, 1998). This test is also available in the forms of strips which is commonly used for detection of ketones in urine. The chemicals with aldehyde /ketone groups can yield false positive for this test.

(II) Quantitative: It can be done by two different approaches (I) Micro-dilution: For acetone (Reaction to vanillin) (II) Enzymatic: For acetoacetate and β-hydroxy butyrate. For determination, whole blood or plasma is preferred over serum. As per Wiliamsons *et al*., (1962) the enzymatic method for detection of acetoacetate or β-hydroxy butyrate is accurate enough and used in commercial spectrophotometers. The assay is based on the change in absorbance at 340 nm (Indirectly measures NADPH oxidation).

**Biochemical basis of treatment:**

The treatment of spontaneous ketosis with glucocorticoids can be explained by the proteolytic effects on enzymes which utilize glucose in muscles by providing gluconeogenic precursor and glucose. The administration of concentrated glucose solution can control the condition. Apart from that the glucose precursors like propionate (as sodium salt), propylene glycol and glycerol can be used to treat such conditions. They all support the possibility of ketosis attributed by hypoglycaemia. Treatment with somatotropin in a penultimate lactation period may decrease the chances too as contributed by lesser fat deposition in the animal. This limits the flow of LCFA from the body sources.

## Conclusions

Ketosis is preventable. Proper management of feeding to the animals, exercise and treatment of alimentary disease can help in prevention. To deal with these factors a proper knowledge of the biochemical aspects of this disease is essential. That can help both the diagnosis and treatment of ketosis. Clinical detection of the ketones in body fluids always contribute towards better prognosis in affected animals.

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