D-3 hydroxybutyrate (Ranbut)

High linearity and excellent sensitivity for the detection of ketosis in humans and animals
**What is Ketosis?**

When carbohydrates are not available, fat is utilised for energy production. Metabolism of fatty acids in the liver results in the production of ketone bodies, consisting of acetone (2%), acetoacetate (20%) and D-3 hydroxybutyrate (78%). Levels of ketone bodies in the blood are elevated (ketosis) when synthesis exceeds breakdown. Very high levels can be toxic causing damage to the kidneys and liver. Monitoring for ketosis is important in both human and veterinary medicine as ketosis has been associated with diabetes, hypoglycaemia, epilepsy and twin lamb disease.

**Why measure D-3 hydroxybutyrate?**

The nitroprusside method of ketone detection, used in semi-quantitative dipstick tests (e.g. Ketostix® and Acetest®), detects acetone and acetoacetate, but not D-3-hydroxybutyrate.

**Advantages over dipstick tests**

- D-3 hydroxybutyrate is the major ketone body in the blood.
- During ketosis, D-3 hydroxybutyrate levels increase more than the levels of acetone and acetoacetate, making D-3 hydroxybutyrate a more sensitive marker of ketosis.
- D-3 hydroxybutyrate is the most stable of the ketone bodies (7 days at +4°C) - acetone and acetoacetate are unstable, so serious errors can arise if analysis is delayed.
- Ketone tests usually measure one or more ketones and therefore their results may be different.

**One kit satisfies the needs of all laboratories**

The Ranbut assay from Randox offers high linearity and excellent sensitivity for the detection of ketosis in humans and animals.

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**Ketone Body Production**

Energy demand exceeds glucose supply

**FATS**

Fatty Acids

Liver

Alternative oxidation

D-3 hydroxybutyrate (Ranbut)

Measures D-3 hydroxybutyrate for the detection of ketosis in humans and animals.

% Composition of ketone bodies in the blood during ketosis

- 78% D-3 hydroxybutyrate
- 20% Acetoacetate
- 2% Acetone

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**Composition of ketone bodies in the blood during ketosis**

- D-3 hydroxybutyrate
- Acetoacetate
- Acetone
D-3 hydroxybutyrate (Ranbut) in human healthcare

The detection of ketosis is important in several human conditions. The most important use of Ranbut in humans is in the detection of potentially fatal ketoacidosis in diabetics.

- **Diabetic ketoacidosis** – is a serious complication of diabetes occurring when blood sugar levels are consistently high and insulin levels are severely low. Due to the lack of glucose entering the cells the body begins to use fat stores as an alternative source of energy as a result the body produces ketones in particular D-3 hydroxybutyrate. Symptoms of ketoacidosis include nausea, vomiting and abdominal pain. The condition can even lead to coma or death if the individual is not treated immediately.

- **In alcoholic ketoacidosis**, the ratio of D-3 hydroxybutyrate to acetoacetate is more than twice that in diabetic ketoacidosis. Therefore, monitoring levels of D-3 hydroxybutyrate is important when making a differential diagnosis between these two conditions.

- **Severe injury, illness or sepsis** - Many critically ill patients respond to starvation by metabolising fats and proteins, which leads to muscle wastage. Monitoring ketone body levels in these patients following an overnight fast allows diagnosis of this problem. Ranbut may be used to identify patients likely to benefit from nutritional support.

- **DiETING** - Monitoring D-3 hydroxybutyrate levels may be used to monitor patients’ dietary compliance.

- **Childhood epilepsy** - Regular monitoring of ketone body levels may be beneficial in maintaining a correct (ketogenic) diet for the control of epilepsy.

- **Ketotic hypoglycaemia** – refers to any circumstance in which hypoglycaemia is accompanied with ketosis. It is also used to define recurrent episodes of hypoglycaemia with ketosis in young children. Delayed feeding is the most common cause among children with symptoms including vomiting, lethargy, unresponsiveness and even seizures. The detection of D-3 hydroxybutyrate in the serum or plasma of infants may indicate ketotic hypoglycaemia.

What are the advantages of using Ranbut?

- **High linearity** - Ranbut is linear to 2.9 mmol/l
- **High sensitivity** - Ranbut can detect changes in concentration as low as 0.07 mmol/l
- **Only kinetic method available for the measurement of D-3 hydroxybutyrate making automation easier**
- **Easy to use**
- **Good stability of working reagents (7 days at +4°C)**
- **Specific for D-3 hydroxybutyrate** (the major circulating ketone body)
- **Measurement of ketones in serum rather than in urine** helps eliminate the risk of false negatives due to insensitivity and false positives due to drug interference
- **Quality controls and supporting EQA programme available**
- **Application sheets available for most clinical analysers**

D-3 hydroxybutyrate (Ranbut) in veterinary healthcare

Ketosis occurs during times of high energy demand. In animals, energy demand is high during milk production, pregnancy and immediately after birth.

- In dairy cows, ketosis can cause decreased milk yields, weight loss, infertility, excitability, and loss of appetite. These symptoms can lead to financial loss, so regular monitoring of dairy cows for ketosis has economic benefits.

- Pregnancy toxemia, also known as ketosis, is a metabolic disease that occurs in late pregnancy. It is most prevalent in ewes carrying two or more lambs or in very fat ewes. It is caused by a disturbance in carbohydrate usage in the animal. Ewes with ketosis are lethargic and have a poor appetite for one to two weeks at the end of pregnancy.

- In piglets, incorrect feeding at birth can lead to hypoglycaemia. Detection of ketosis will alert the farmer to the hypoglycaemia, allowing careful nutrition to return glucose levels to normal.
Performance characteristics

Sample Type – Suitable for use with both serum and plasma samples

Wide measuring range – 0.07mmol/l – 2.9 mmol/l

Excellent Sensitivity – 0.07mmol/l

Limited Interference – The following analytes were tested up to the following levels and found not to interfere:

- Total Bilirubin: 25mg/dl
- Direct Bilirubin: 25mg/dl
- Haemoglobin: 1000mg/dl
- Triglyceride: 750mg/dl
- Intralipid®: 600mg/dl

Standard – supplied with the kit

Excellent Precision

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<th>Level 1</th>
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Total Precision

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Excellent correlation to standard methods – A correlation coefficient of r=1.00 was obtained with a competitor method

Suitable for both manual and automated use - Fully automated applications are available for a wide range of clinical analysers including the RX series

How to order

Ranbut is currently available in the following pack sizes:

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(R3 hydroxybutyrate + NAD\(^+\) \rightarrow 3-hydroxybutyrate dehydrogenase \rightarrow Acetoacetate + H\(^+\) + NADH)

(The change in absorbance at 340 nm can be directly correlated with the D-3 hydroxybutyrate concentration.)

Technical support

To ensure quality, all Randox reagents and controls are manufactured in-house and undergo our own rigorous quality control procedures registered to the International Quality Standard ISO 9001. In-house development and manufacture ensures that our Technical Support division has detailed knowledge of each Randox product. Technical Support is available to all Randox customers and includes access to procedure information 24 hours a day, 7 days a week.