

IDEXX Catalyst Bile Acids for point-of-care assessment of total bile acids in dogs and cats



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Introduction

Measurement of total bile acids concentration is used to evaluate liver function by estimating the efficiency of enterohepatic circulation, which can be affected by hepatic parenchymal disease, vascular anomalies (e.g., portosystemic shunts), and cholestatic liver disease.^{1,2} Improved sensitivity and specificity are achieved by assessing bile acids concentrations before, as well as two hours after, feeding the patient.

The IDEXX Catalyst® Bile Acids assay is designed to allow measurement of bile acids concentration in serum or lithium heparin plasma (or whole blood using the lithium heparin whole blood separator) in dogs and cats. It is designed to provide a wide reportable range (1–180 $\mu\text{mol/L}$) and allow reliable, accurate bile acids results within the veterinary practice setting.

The objectives of this study were to evaluate:

- Performance of Catalyst Bile Acids by a method comparison to a reference method* used in veterinary reference laboratories.
- Precision of the assay using control fluids.
- Influence of common interfering substances (haemolysis, lipaemia, and icterus) on reported results.
- Bias of bile acids measurement between serum and plasma on Catalyst Bile Acids.

Method comparison

Materials and methods

Serum samples from 70 dogs and 29 cats were analysed as follows:

1. Reference method: Diazyme Total Bile Acids Assay* (enzyme cycling method) run on the chemistry analyser used in IDEXX Reference Laboratories. Samples were analysed twice with the reference method, and an average bile acids concentration was calculated for use in the comparison.
2. Catalyst Bile Acids assay: Each sample was analysed once on one Catalyst One® Chemistry Analyser and one Catalyst Dx® Chemistry Analyser to give a maximum total of two comparisons per sample. The analysers were used in a random order.

Both the reference method and Catalyst Bile Acids assays were conducted according to the manufacturers' specifications. Results from each Catalyst Bile Acids assay run were compared to the average concentration from the reference method. Correlation plots were constructed with calculation of r and slope. The slope of this correlation directly speaks to the overall bias, and r is a statistical technique that evaluates the relationship between two series of events. In this context, an r of one and a slope of one are a perfect correlation with zero bias.

Results

The results of the method comparison study are summarised in figure 1.

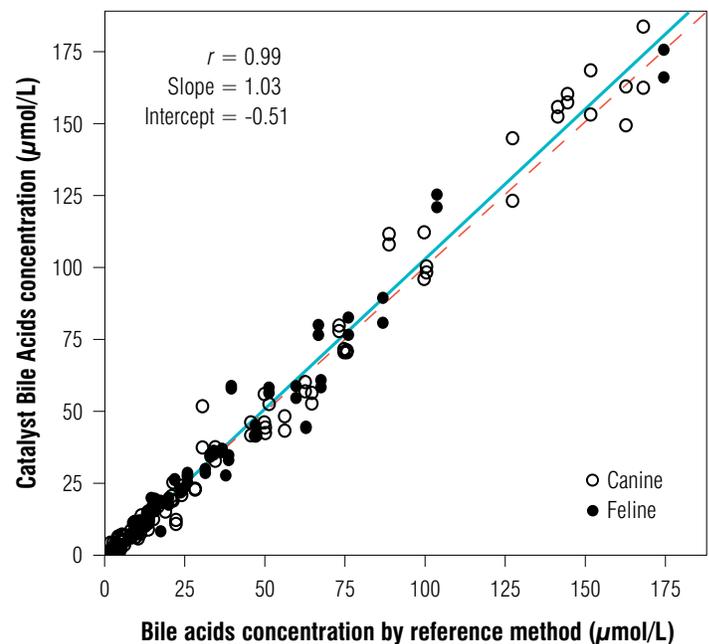


Figure 1: Correlation graph of pairwise comparisons for bile acids in canine and feline samples measured by the two assays. The line of best fit (linear regression) for the data is shown on the graph (solid line) with the slope and r value. The $x = y$ is shown as the dashed line in the graph.

Precision

Materials and methods

Precision was assessed using control fluid at three concentrations of bile acids. All concentrations were evaluated eight times per day for 10 days on each of two Catalyst One® and two Catalyst Dx® chemistry analysers. The mean concentration and standard deviation were calculated.

Results

Results of the precision study are summarised in table 1.

	Mean concentration (µmol/L)	Standard deviation (µmol/L)
Catalyst Dx analyser	9.7	1.4
	22.2	1.6
	78.9	3.1
Catalyst One analyser	11.0	1.3
	22.2	1.6
	76.7	2.7

Table 1: Summary of results from precision study.

Interfering substances study

Materials and methods

Interference caused by the presence of haemoglobin, lipids, or bilirubin was assessed per CLSI EP07-A2 method guidelines.³ Canine plasma samples, which were visibly clear of interferents, were collected, pooled, and spiked with bile acids. Canine red blood cell hemolysate[†], Intralipid^{®‡}, and ditaurobilirubin[§] were used for investigating potential impact by haemolysis, lipaemia, and icterus, respectively. Aliquots of the pooled sample were prepared and spiked with varying concentrations of the interfering substances (as shown in table 2). Each aliquot was then analysed

either two times (haemolysis), or one time (lipaemia, icterus), on each of 4 Catalyst One analysers.

Results

Results of the interfering substances study are outlined in table 2. No interference was observed with lipaemic samples. Interference leading to increased bile acids results may be observed in samples with moderate to marked haemolysis (≥ 250 mg/dL) and in icteric samples.

Haemolysis		Lipaemia		Icterus	
Haemoglobin concentration (mg/dL)	Mean bile acids concentration (µmol/L)	Intralipid [®] concentration (mg/dL)	Mean bile acids concentration (µmol/L)	Ditaurobilirubin concentration (mg/dL)	Mean bile acids concentration (µmol/L)
Not spiked	27.4	Not spiked	27.5	Not spiked	26.1
128	31.6	62.5	26.8	3.72	28.1
250	34.7	125	27.1	7.14	29.1
385	37.3	250	27.3	14.97	32.2
497	41.2	500	27.4	23.43	33.6

Table 2: Summary of results of interfering substances study.

Serum-to-plasma bias

Materials and methods

Whole blood samples from 26 canines were spiked with bile acids, split, and processed as either serum or plasma. The Catalyst Bile Acids assay was then performed on both serum and plasma samples. A regression plot was prepared by pairing serum results on the x-axis and plasma results on the y-axis.

Results

The results are summarized in figure 2 and show good correlation and minimal bias between serum and plasma samples.

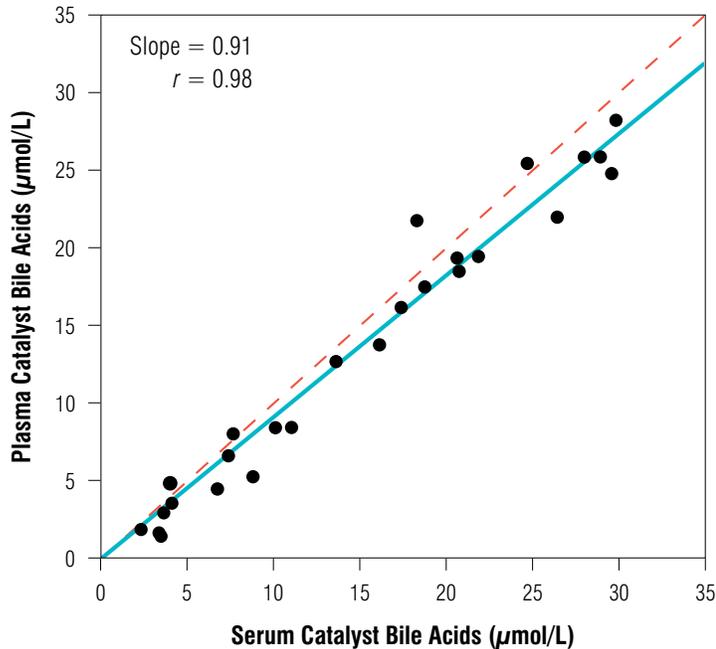


Figure 2: Correlation graph of pairwise comparisons for bile acids in canine plasma and serum samples ($n = 26$). The line of best fit (linear regression) for the data is shown on the graph (solid line) with the slope and r value. The $x = y$ is shown as the dashed line in the graph.

Conclusion

The assay demonstrates excellent correlation with the Diazyme Total Bile Acids method with minimal bias ($r = 0.99$; slope = 1.03). Catalyst Bile Acids results may be impacted by samples with moderate to marked levels of haemolysis or icterus. Clinically, if bilirubin concentration is elevated or if the animal is icteric, there is little additional value in performing a bile acids test by any methodology as bile acids are expected to be elevated when hyperbilirubinaemia associated with hepatobiliary disease is present.²

Catalyst® Bile Acids provides veterinarians with an accurate and precise point of care option in the assessment of hepatobiliary disease in dogs and cats.

References

1. Cocker S, Richter K. Diagnostic evaluation of the liver. In: Ettinger SJ, Feldman EC, Côté E, eds. *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat*. 8th ed. St Louis, MO: Elsevier; 2017:1611–1621.
2. Stockham SL, Scott MA. Liver function. In: Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, IA: Blackwell; 2008:675–706.
3. CLSI. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI document EP07-A2.

*Reference method consisted of the Diazyme Total Bile Acids Assay Kit (Enzyme Cycling Method) (Diazyme Laboratories, Inc. Poway, California, USA; catalog number: DZ042A) performed on the Beckman Coulter AU5800 (Beckman Coulter, Brea, California, USA).

[†]Lysate from canine red blood cells washed in saline and lysed in water with no surfactant.

[‡]Intralipid® (Sigma-Aldrich, Inc., St. Louis, Missouri, USA), a phospholipid-stabilized soybean oil.

[§]Bilirubin conjugate (Scripps Laboratories, San Diego, California, USA; catalog number: B0114), a synthesized ditaurobilirubin.

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