Antech SDMA immunoassay performs well in comparison study with IDEXX SDMA and Liquid Chromatography Mass Spectrometry (LCMS).

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INTRODUCTION

SDMA is the acronym for Symmetric Dimethylarginine. SDMA is a methylated form of the amino acid arginine. SDMA is produced at a constant rate as proteins are broken down by cells in the body. SDMA is exclusively excreted by the kidneys.[1] Given its steady rate of production and free filtration by the kidneys, SDMA measurement can act as a surrogate measure of a test called Glomerular Filtration Rate, or GFR, which evaluates kidney function in dogs[2,3] and cats.[4,5] Measurement of GFR can be expensive and not easy to perform from a practical perspective. Given that SDMA can be evaluated using a single blood sample, this test provides a rapid and efficient means by which a clinician can evaluate kidney function.

In contrast to creatinine, SDMA detects a decrease in kidney function, and subsequent decrease in GFR, earlier.[2,3,5] SDMA increases when there is an average loss of 40% of kidney function, whereas creatinine does not increase until there is a 75% or more decrease in kidney function. SDMA can be increased in acute kidney injury (AKI) and chronic kidney disease (CKD) in both dogs and cats. SDMA is also not affected by the loss of lean muscle mass.[6,7] Whereas in thin patients with loss of lean muscle, creatinine does not accurately estimate a decrease in kidney function. For these reasons, SDMA is a more reliable and sensitive indicator of loss of kidney function than creatinine.

The importance of SDMA measurement is highlighted by its inclusion in the International Renal Interest Society (IRIS) guidelines for diagnosing, staging, and monitoring chronic kidney disease (CKD) in dogs and cats. The IRIS guidelines can be found on the website: http://www.iris-kidney.com/. It is imperative to always evaluate kidney function biomarkers, like creatinine and SDMA, with a complete urinalysis to determine if there is a pre-renal, renal, or post-renal cause of the patient's azotemia and increased SDMA. Azotemia and increased SDMA can occur due to pre-renal causes, such as dehydration, and post-renal causes, such as urethral obstruction. In both scenarios, the decrease in GFR is potentially treatable and does not necessarily signal a sustained loss in renal function. If the change in biomarkers is determined to be renal in origin, SDMA is a more sensitive biomarker for both staging and monitoring disease progression.

SDMA can be measured using different methodologies. Antech SDMA is measured using an automated homogeneous enzyme immunoassay that has been validated in dogs and cats. Antech SDMA is rapid, sensitive, reproducible, and can be analyzed using high throughput technology, allowing for faster turnaround times.

STUDY DESIGN

Reference Interval Study

The reference interval study for dogs and cats was performed using 99 dogs and 97 cats. All dogs and cats were between the ages of 2 and 6 years. The creatinine range for the dogs used was < 1.6 mg/dl (141.4 umol/L) and the creatinine range for the cats used was < 2.4 mg/dL (212.2 umol/L).

Correlation Study with IDEXX SDMA

Antech SDMA was correlated with IDEXX SDMA reference laboratory testing using 76 dogs and 73 cats. Dogs were between 3 months and 18 years of age, and cats were between the ages of 2 and 18 years. The creatinine in dogs ranged from 0.2-10.1 mg/dL (17.7 umol/L - 892.8 umol/L), and the creatinine in cats ranged from 0.6-28.3 mg/dL (53.0 umol/L - 2501.7 umol/L).

Correlation between Antech SDMA and Liquid Chromatography Mass Spectrometry was performed by an external medical laboratory in Austria, EUROLyser (eurolyser.com).

RESULTS

Reference Interval Study

The normal reference ranges for Antech SDMA in dogs is < 14 ug/dL, and in cats < 15 ug/dL.

Reference Interval for Canine SDMA

	Reference Interval
Normal	< 14.0 µg/dL
Mild Increase	14.0 - 16.0 µg/dL
High	> 16.0 µg/dL

Reference Interval for Feline SDMA

	Reference Interval
Normal	< 15.0 µg/dL
Mild Increase	15.0 - 20.0 µg/dL
High	> 20.0 µg/dL

The Antech SDMA reference intervals for dogs and cats are similar to those reported from other reference laboratories, but are not identical due to differences in proprietary methodologies.

Correlation study with IDEXX SDMA

When comparing the Antech SDMA to the IDEXX SDMA, the correlation coefficient in cats is 0.98, and the correlation coefficient is 0.98 in dogs.

Figure 1 (below) shows the plotted data and correlation statistics using a Deming regression model to compare IDEXX SDMA (ug/dL) on the x-axis with Antech SDMA (ug/dL) on the y-axis for cats.

Feline Data: n = 73, R = 0.98, Bias -0.3%

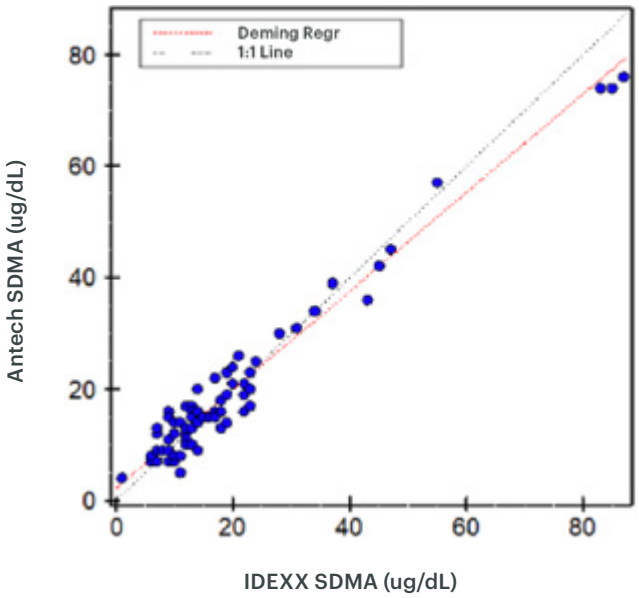
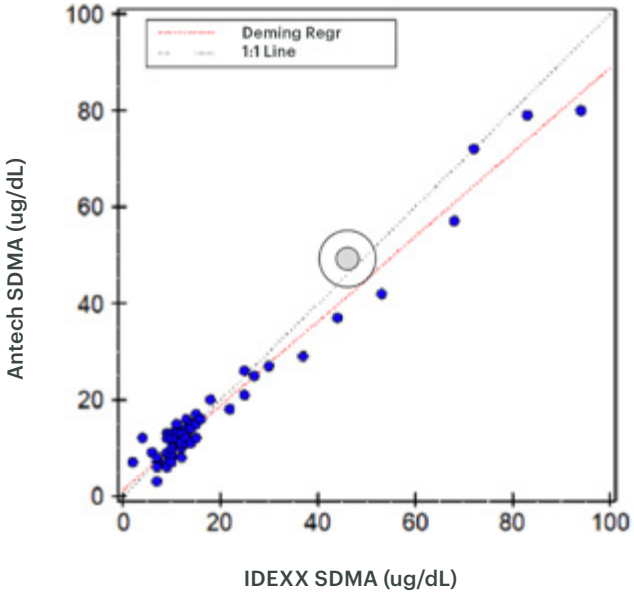


Figure 2 (below) shows the plotted data and correlation statistics using a Deming regression model to compare IDEXX SDMA (ug/dL) on the x-axis with Antech SDMA (ug/dL) on the y-axis for dogs.

Canine Data: n = 76, R = 0.98, Bias -5.2%



Correlation study with LCMS SDMA

Correlation studies performed with the Antech SDMA and Liquid Chromatography Mass Spectrometry (LCMS) are excellent, with a correlation coefficient of 0.98 in dogs and 0.99 in cats.

Figure 3 (below) shows the plotted data and correlation statistics using a Deming regression model to compare LCMS SDMA (ug/dL) on the x-axis with Antech SDMA (ug/dL) on the y-axis for dogs.

Canine Data: n = 49, R = 0.98

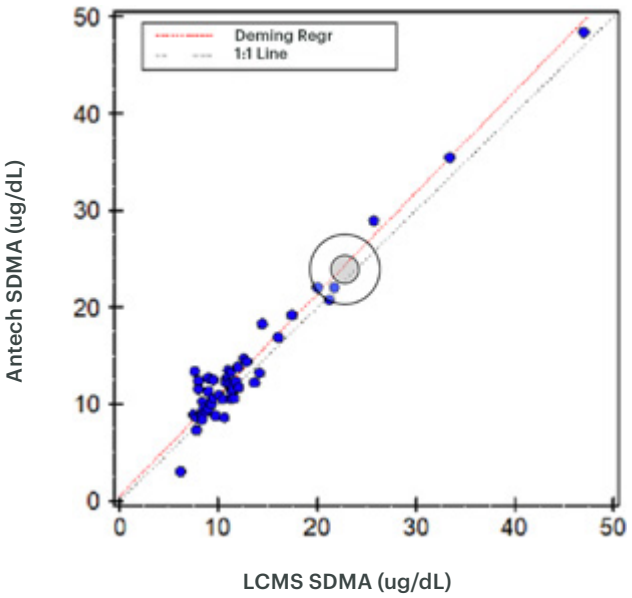
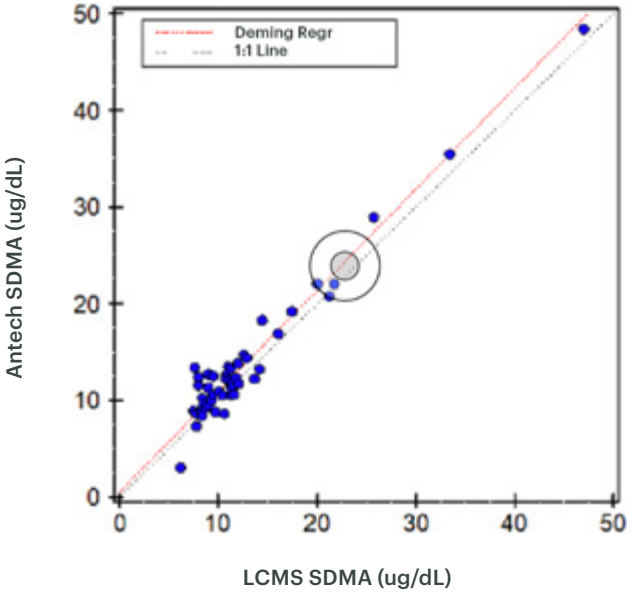


Figure 4 (below) shows the plotted data and correlation statistics using a Deming regression model to compare LCMS SDMA (ug/dL) on the x-axis with Antech SDMA (ug/dL) on the y-axis for cats.

Feline Data: n = 48, R = 0.99



DISCUSSION

The physiological processes that lead to the formation of SDMA are highly conserved across species, and SDMA values above 14-16 ug/dL in dogs and 15-20 ug/dL in cats warrant further investigation into the underlying cause of an increased SDMA. Additionally, repeat testing of SDMA in 2 to 4 weeks is recommended to evaluate trends and persistence of abnormal SDMA results.

Correlation studies performed internally have shown that the IDEXX SDMA and Antech SDMA tests have a very high degree of correlation in both dogs and cats, with R values greater than and equal to 0.98. Correlation coefficients were interpreted as follows: r = 0.90–1.0, defined very high correlation; 0.70–0.89, high correlation; 0.50–0.69, moderate correlation; 0.30–0.49, low correlation; and 0–0.29, little, if any, correlation.

Liquid Chromatography Mass Spectrometry (LCMS) is considered the gold standard methodology for measuring SDMA. SDMA has been shown to have very high correlation with the measurement of glomerular filtration rate. LCMS is an advanced analytical technique that is used to accurately identify and quantify molecules within a sample. It is not used routinely by commercial laboratories because it cannot process the large volumes of samples that are received. LCMS correlation with the Antech SDMA was very high, with an R-value of 0.98 and above.

Precision refers to the repeatability of a measurement of an analyte. This is different from accuracy, which refers to how close the value reported for an analyte is to the true value. The Antech SDMA shows a total coefficient of variation (CV) range of 5.1% to 13.3%. This is acceptable and is consistent with that reported for IDEXX SDMA.

CONCLUSIONS

SDMA is an earlier, more sensitive, and reliable biomarker signaling a decrease in kidney function in dogs and cats compared with creatinine. The Antech SDMA immunoassay compares extremely well with IDEXX SDMA immunoassay in dogs and cats with a coefficient correlation of greater than 0.98. Antech SDMA is also highly correlated with LCMS, with a coefficient correlation that is greater than 0.98. The reference ranges for dogs and cats with Antech SDMA are comparable to IDEXX SDMA, with normal reference values of < 14 ug/dL in dogs and < 15 ug/dL in cats.

REFERENCES

1. Kielstein JT, Salpeter SR, Bode-Boeger SM, Cooke JP, Fliser D. Symmetric Dimethylarginine (SDMA) as endogenous marker of renal function—a meta-analysis. Nephrol Dial Transplant. 2006;21(9):2446–2451.
2. Nabity MB, Lees GE, Boggess M, et al. Symmetric Dimethylarginine assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. J Vet Intern Med. 2015;29(4):1036–1044.
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric Dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. J Vet Intern Med. 2016;30(3):794–802.
4. Braff J, Obare E, Yerramilli M, Elliott J, Yerramilli M. Relationship between serum symmetric Dimethylarginine concentration and glomerular filtration rate in cats. J Vet Intern Med. 2014;28(6):1699–1701.
5. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. Comparison of serum concentrations of symmetric Dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. J Vet Intern Med. 2014;28(6):1676–1683.
6. Hall JA, Yerramilli M, Obare E, Yerramilli M, Yu S, Jewell DE. Comparison of serum concentrations of symmetric Dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. Vet J. 2014;202(3):588–596.
7. Hall JA, Yerramilli M, Obare E, Yerramilli M, Melendez LD, Jewell DE. Relationship between lean body mass and serum renal biomarkers in healthy dogs. J Vet Intern Med. 2015;29(3):808814.

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