

Sodium Assay for Cedex Bio and Cedex Bio HT Analyzers

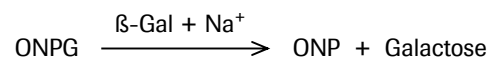
Reliable and convenient control of the most important cation in cultures

In cell culture and microbial fermentation, sodium is the most important cation in the culture medium. Control of the sodium concentration within a narrow operating range is substantial to gain healthy and fast growing cultures and to obtain high yields of products in biomanufacturing processes.

A common method for sodium determination is the use of an ion-selective electrode. However, the electrodes are susceptible for various interferences and require continuous maintenance. Therefore, a robust enzyme-based assay with photometric detection is the preferable method for the integration in typical laboratory workflows.

Assay principle

The assay is based on the Na⁺ dependent enzymatic activity of β-galactosidase (β-Gal). Using the enzyme substrate o-nitro-phenyl-β-D-galactopyranoside (ONPG), the release of the yellow o-nitro-phenolate (ONP) correlates to the Na⁺ concentration and can be measured photometrically.



Process control based on fast and reliable analytics

- Automated assay with highly reproducible results
- Wide measuring range, option for on-board dilution
- No sample filtration or other pretreatment required
- Low sample volume of 2.5 – 40 µL used

Test range designed for cell culture control

Protocol	Sodium concentration range	
NAB, normal range	50 – 275 mmol/L,	1.15 – 6.32 g/L
NAD, high range	250 – 1375 mmol/L,	5.75 – 31.6 g/L up to max. solubility with auto-dilution

High precision

	Level 1	Level 2	Level 3
Sodium conc. [mmol/L]	100	150	200
CV in-run	0.9 %	0.9 %	1.2 %
CV, inter-run	1.3 %	1.0 %	1.4 %

Sodium was determined in spiked culture media samples. Coefficients of variation (CV) were calculated for 21 replicates in one run, and repeated determination on 10 days.
(Evaluation data of Roche Diagnostics)



For use in quality control/manufacturing process only.

High accuracy

Over the whole test range, sodium concentrations can be determined with an inaccuracy of less than 3% in common culture media formulations.

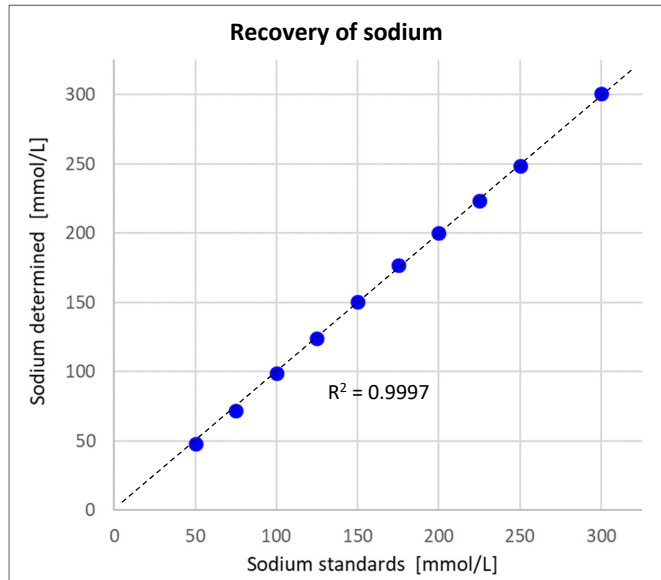


Figure 1: Sodium was determined in a row of standards with increasing NaCl concentrations using a Cedex Bio HT Analyzer with the enzymatic sodium assay. The results show a good linearity of the test and all standards are found with deviations < 2.5% from the target concentrations.
(Evaluation data of Roche Diagnostics)

Method comparison

For determination of sodium, the Cedex Analyzers used an ion-selective electrode (ISE) in the past, measuring an electrical potential of a membrane sensor in contact to the sample, compared to another sensor in a reference solution.

ISE sensors require continuous maintenance for correct function and frequent recalibration to compensate fluctuations. Furthermore, there is a considerable risk of interferences of various substances affecting the affinity of Na⁺ ions to the membrane (e.g. other cations, chelators, lipophilic compounds).

The enzymatic sodium assay is designed as a more convenient alternative. The photometric detection format fits perfectly into the analyzer concept, no special maintenance is required, and the assay is very robust against interferences.

Results of the enzymatic assay perfectly match to ISE results. Replacement of ISE testing by the enzymatic assay is easy and does not require revalidation of established procedures.

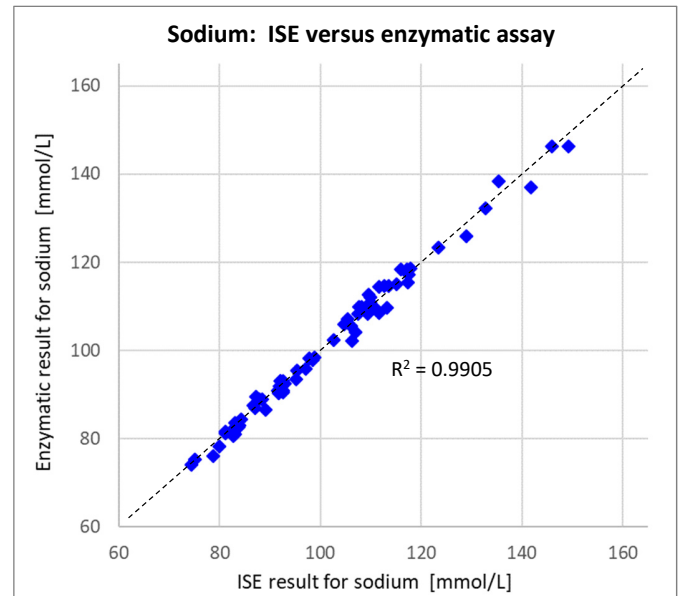


Figure 2: 70 samples of fermentation supernatants of various culture media were tested for sodium on a Cedex Bio HT Analyzer using the ion-selective electrode and the enzymatic sodium assay for comparison. The differences are all within $\pm 4\%$, with an average difference close to zero (ISE 0.3% higher than enzymatic), confirming the equivalence of the two methods.
(Data generated with culture samples of Roche Pharma)

Potential interferences

The following substances were tested for a potential interference in the enzymatic sodium assay:

Substance	Critical concentration \Rightarrow effect
Potassium, K ⁺	> 30 mmol/L \Rightarrow underestimation Na ⁺ , max. -10%
Ammonium, NH ₄ ⁺	No effect (tested up to 20 mmol/L)
Calcium, Ca ²⁺	No effect (tested up to 100 mmol/L)
Magnesium, Mg ²⁺	No effect (tested up to 100 mmol/L)
Copper, Cu ²⁺	No effect (tested up to 1 mmol/L)
Iron, Fe ³⁺	No effect (tested up to 10 mmol/L)
Galactose	No effect (tested up to 100 mmol/L)
Lactose	> 40 mmol/L \Rightarrow underestimation Na ⁺
MIT, methylisothiazolinone (common biocide and enzyme inhibitor)	> 0.2 g/L \Rightarrow underestimation Na ⁺

(Evaluation data of Roche Diagnostics)

Ordering information

For determination of sodium the following products are required in addition to the Cedex instrument with the general system reagents and accessories:

Product	Pack size	Cat. no.
Sodium Bio ⁽¹⁾	4 x 50 tests	08 881 863 001
Sodium Bio HT ⁽¹⁾	200 tests	08 881 871 001
Calibrator F Bio ⁽²⁾	6 x 1 mL	08 377 987 001
Control F Level 1 Bio ⁽²⁾	6 x 1 mL	08 377 995 001
Control F Level 2 Bio ⁽²⁾	6 x 1 mL	08 378 002 001
Control F Level 3 Bio ⁽²⁾	6 x 1 mL	08 378 029 001

Regulatory disclaimer

⁽¹⁾ For quality control/manufacturing of IVD/medical devices/ pharmaceutical products only.

⁽²⁾ For use in quality control/manufacturing process only.

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