

## Potassium Assay for Cedex Bio and Cedex Bio HT Analyzers

*Reliable and convenient control of the important cation in cultures*

In cell culture and microbial fermentation, potassium is the 2<sup>nd</sup> most relevant cation after sodium. Control of the potassium concentration within a narrow operating range is important to gain healthy and fast growing cultures and to obtain high yields of products in biomanufacturing processes.

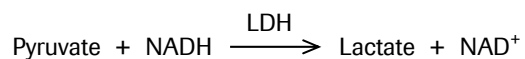
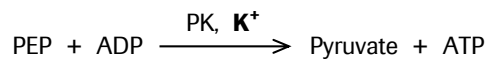
A common method for potassium determination is the use of an ion-selective electrode. However, the electrodes are susceptible for various interferences and require continuous maintenance. Therefore, an enzyme-based assay with photometric detection is the preferable method for the integration in the common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

### 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 – 20 µL used

### Assay principle

The assay is based on the K<sup>+</sup> dependent enzymatic activity of pyruvate kinase (PK). The rate of the conversion of the substrate phosphoenolpyruvate (PEP) to pyruvate by PK correlates to the potassium concentration. The pyruvate formation is monitored photometrically at 340 nm by the consumption of NADH in presence of lactate dehydrogenase (LDH).



### Test range designed for cell culturing and fermentation

Protocol	Potassium concentration range
KB, normal range	2 – 30 mmol/L, 78 – 1,173 mg/L
KD, high range	25 – 300 mmol/L, 978 – 11,730 mg/L, and up to 3 mol/L, 117 g/L with auto-dilution



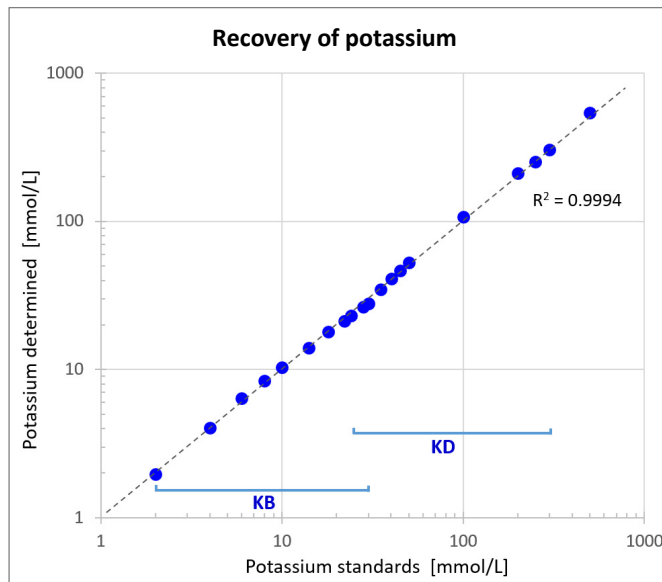
## High precision

	Level 1	Level 2	Level 3
Potassium conc. [mmol/L]	5.62	10.6	16.4
CV in-run	4.6 %	2.8 %	1.9 %
CV, inter-run	3.6 %	2.8 %	3.2 %

Potassium was determined in spiked culture media samples on a Cedex Bio HT Analyzer. Coefficients of variation (CV) are calculated for 21 replicates in one run, and repeated determination on 10 days. (Evaluation data of Roche Diagnostics)

## High accuracy

Over a wide test range, potassium concentrations can be determined accurately in various culture media formulations.



**Figure 1:** Potassium was determined on a Cedex Bio HT Analyzer in a row of standards with increasing KCl concentrations spiked to a CHO cell culture medium. The two protocols KB and KD were used for the lower and higher range, respectively. The results show a good linearity of the test and all samples are determined with deviations < 8% from the target concentrations. (Evaluation data of Roche Diagnostics)

## Method comparison

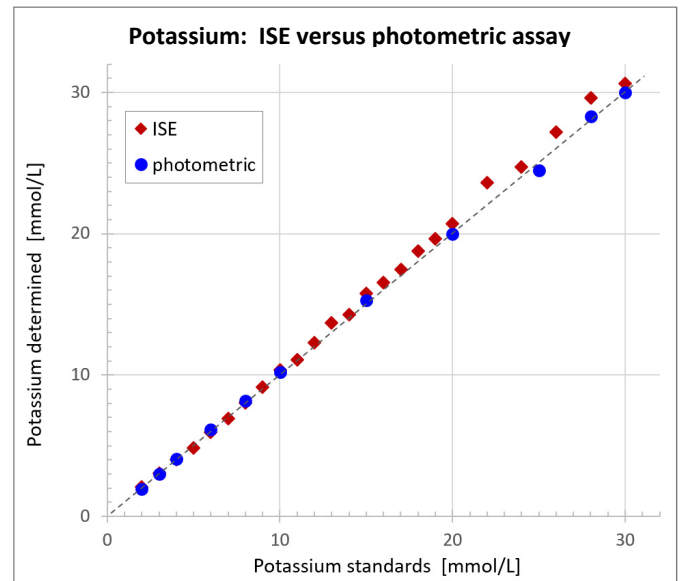
For determination of potassium, the Cedex Analyzers used an ion-selective electrode (ISE) in the past, measuring an electrical potential of a membrane sensor in contact to the sample, compared to another sensor in a reference solution.

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  $K^+$  ions to the membrane (e.g. other cations, chelators, lipophilic compounds).

The enzymatic potassium test 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 robust against interferences.

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



**Figure 2:** Potassium was determined on a Cedex Bio HT Analyzer in samples of culture media spiked with different KCl concentrations, using the ISE electrode and the photometric potassium test, respectively.

The results show a good consistency of the potassium recovery of the two methods with deviations < 5%. (Evaluation data of Roche Diagnostics)

## Potential interferences

**Sodium:** The assay is designed for an accurate determination of potassium in the presence of 100 to 200 mmol/L sodium, covering the typical conditions in upstream and downstream procedures of cell culture and microbial fermentation. Working with samples of < 100 or > 200 mmol/L sodium, the accuracy must be verified for that specific sample matrix.

Using the KD protocol, the instrument automatically prepares a sample predilution in 154 mmol/L NaCl solution, which is the optimal matrix for accurate potassium determination.

**Ammonium:** To prevent an interference by  $NH_4^+$  ions, the Cedex test protocol automatically uses a preceding reaction step to eliminate  $NH_4^+$  from the sample.

Tested interferences: The following substances are checked for a potential interference in the potassium assay.

Substance	Critical concentration ⇒ effect
Sodium, Na <sup>+</sup>	No effect in the range of <b>100 – 200 mmol/L Na<sup>+</sup></b> , <b>&lt; 100 mmol/L Na<sup>+</sup></b> ⇒ possible underestimation of K <sup>+</sup> , <b>&gt; 200 mmol/L Na<sup>+</sup></b> ⇒ possible overestimation of K <sup>+</sup>
Magnesium, Mg <sup>2+</sup>	<b>&gt; 50 mmol/L</b> ⇒ possible overestimation of K <sup>+</sup>
Ammonium, NH <sub>4</sub> <sup>+</sup>	No effect (tested up to 100 mmol/L)
Calcium, Ca <sup>2+</sup>	No effect (tested up to 100 mmol/L)
Iron, Fe <sup>3+</sup>	No effect (tested up to 10 mmol/L)
Pyruvate	No effect (tested up to 20 mmol/L)
Lactate	No effect (tested up to 50 mmol/L)
Alanine	No effect (tested up to 60 mmol/L)
Lactate dehydrogenase	No effect (tested up to 10 kU/L)

(Evaluation data of Roche Diagnostics)

## Ordering information

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

Product	Pack size	Cat. no.
Potassium Bio	4 x 50 tests	08 881 367 001
Potassium Bio HT	165 tests	08 881 731 001
Calibrator K Bio	6 x 1 mL	09 336 699 001
Control F Level 1 Bio	6 x 1 mL	08 377 995 001
Control F Level 2 Bio	6 x 1 mL	08 378 002 001
Control F Level 3 Bio	6 x 1 mL	08 378 029 001

## Regulatory disclaimer

For use in quality control/manufacturing process only.

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### Published by

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