Product Introduction

Small Electrode Type Glucose Analyzer "Antsense Duo"

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There is growing emphasis on POCT (Point of Care Testing) which brings in-situ test results to the treatment because it enables the provision of immediate and effective medical care. HORIBA, Ltd. has started the sales of a new model Antsense Duo, a small electrode type glucose analyzer deriving from the conventional cartridge-type analyzer. Hereunder, we describe the features, improvements and the performance evaluation.

Introduction

POCT (Point of Care Testing) means the immediate in-situ test carried out by medical professionals at the patient's side. As the results obtained in real time enable the provision of immediate and effective medical care, it is carefully watched in recent years.[1] POCT is often effective for measuring blood glucose level in hospitals such as wards, emergency department or operation rooms. HLWM (Health, Labor and Welfare Ministry) distinguishes clearly SMBG (Self-Monitoring Blood Glucose) device manufactured for the patients who measure blood glucose level by themselves at home, from POCT device used in laboratories of hospitals.[2] In fact, for in-hospital tests, especially the tests carried out at bedside, not POCT glucose analyzers but SMBG devices are widely diffused.

Antsense is the series of POCT glucose analyzers, which have been sold since 1991. Since they provide highly accurate results, they have become widely used. Antsense Duo developed following Antsense III has been sold since 2013. Deriving the conventional measurement technologies, Antsense Duo has improved in user-friendliness under the product concept of highly accurate measurement and reduction of infection risk. Hereafter, we will introduce the basic structure of Antsense and the improved utility functions for the Antsense Duo.

Measurement Principle

Antsene Duo, as well as the conventional Antsense series products, has attained highly accurate measurement using the same measurement principle as that of dedicated glucose analyzers used in laboratories. The measurement system is based on the amperometric system of GOD (Glucose Oxidase) - hydrogen peroxide electrode method, which integrates hydrogen peroxide electrode with glucose oxidase immobilized membrane. Glucose contained in plasma penetrates the cap membrane on which glucose oxidase is immobilized. The glucose is decomposed to gluconic acid and hydrogen peroxide by catalysis of glucose oxidase. Hydrogen peroxide penetrates the H_2O_2 permselective membrane and makes contact with the platinum surface of electrode. H_2O_2 is decomposed on the platinum surface of electrode and detects the generated electron as electric current. The blood glucose level of the sample is calculated using the differential value of electric current. (Figure 1)

The cap membrane consists of three-layers: diffusion restricting membrane, GOD immobilized membrane and hydrogen peroxide permselective membrane. The diffusion restricting membrane restricts the amount of penetrating glucose in the sample to prevent over-range of the detection sensitivity and controls the measurement range. GOD immobilized membrane is Polyacrylonitrile (PAN) membrane which is chemically combined with GOD. Glucose is, as described above, decomposed to gluconic acid and hydrogen peroxide by GOD. H_2O_2 permselective membrane penetrates only generated hydrogen peroxide to the electrode and prevents any substance of which the molecular weight is high, including a substance that has an affect on reaction. Based on the same measurement principle as that of a large desktop type analyzer, Antsense is a portable small POCT

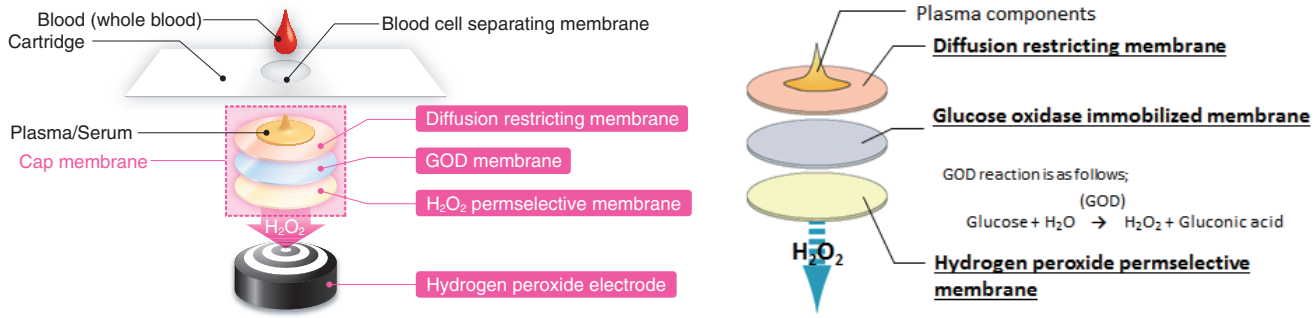

Figure 1 Measurement principle and membrane structure

glucose analyzer and is designed to easily measure whole blood. Hereafter, we introduce the technologies.

Blood cell separating function

Large-scale analyzers in laboratories measure the plasma after centrifugation. On the other hand, it is required for POCT devices to measure whole blood to provide results in a short time. Antsense Duo uses a unique operation procedure: Place a drop of blood sample on the dropping area of the dedicated cartridge. A blood cell separating membrane is used for this cartridge, which filtrates the blood cells and only plasma components penetrate the electrode.

Refreshing mechanism

Large-scale analyzers in laboratories have mechanism to refresh the measurement systems: priming and draining a certain amount of buffer solution after every measurement. In Antsense Duo, a small buffer tank placed on the electrode keeps optimum moisture and refreshes on the surface of cap membrane. After measurement, the electrode itself moves up and down. When it touches the buffer tank, the reactant waste on the electrode is diffused into the tank. This refreshing mechanism keeps the surface of electrode clean at all times, which enables consecutive measurements without carryover. For that, the buffer tank should be replaced at regular intervals as the reactant waste is accumulated in the tank.

Specifications and Improvement in Operability

Table 1 shows the basic specifications of Antsense Duo. The visible range is wide; 10 to 999 mg/dL. The sampling method is characteristic; dropping the blood sample on the blood cell separating membrane of cartridge. Accuracy is secured in the high glucose level by two point calibration using calibrator H. A large color LCD is used. ID management and communication function with Bluetooth are added.

Table 1 Specifications

General name	Glucose analyzer
Sales name	Antsense Duo
Type name	LP-150G
Parameter	Glucose concentration in blood
Medical instrument class	General medical device, Specially designated maintenance management required medical device
Measurement principle	GOD · hydrogen peroxide electrode method
Sampling method	Dropping blood sample on the blood cell separating membrane of cartridge
Substance measured	Whole blood (capillary blood, venous blood, arterial blood) *Blood plasma/serum cannot be measured.
Hct	Measurement value ±10% or less at 20% to 60% (whole blood measurement mode)
Sample amount	5 µL to 20 µL
Measurement time	45 seconds per sample (from start of measurement until display of measurement result)
Visible range	10 mg/dL to 999 mg/dL (0 mmol/L to 55.5 mmol/L)
Data storage	Sample measurement data: 300 results Calibration data: 300 results Control test data: 300 results (L, N, H combined) Event logs: 100 results (Internal data, effective only in communication)
Dimensions	205 (W) mm × 125 (D) mm × 55 (H) mm
Mass.	Approx. 750 g (with buffer tank, CAP membrane, rechargeable battery installed)
Measurement condition	Ambient temperature: 10°C to 35°C, relative humidity: 25% to 85% (No condensation)
Input	Input switches ×6 (operation switches ×5, power switch(, new tank detection switch, USB (program writing using special USB memory stick)
Output	Ethernet (data communication) RS-232C USB (acquisition of data in internal memory using special USB memory stick)
Display	3.5-inch color LCD Sample drop assist light (during sample measurement: blinks green; during calibration/control testing: blinks red)

Operation procedure

As well as those of other Antsense devices, the operation procedure is simple. Drop 5 to 20 µL on the cartridge and press the start measurement button. The cartridge is

Structure

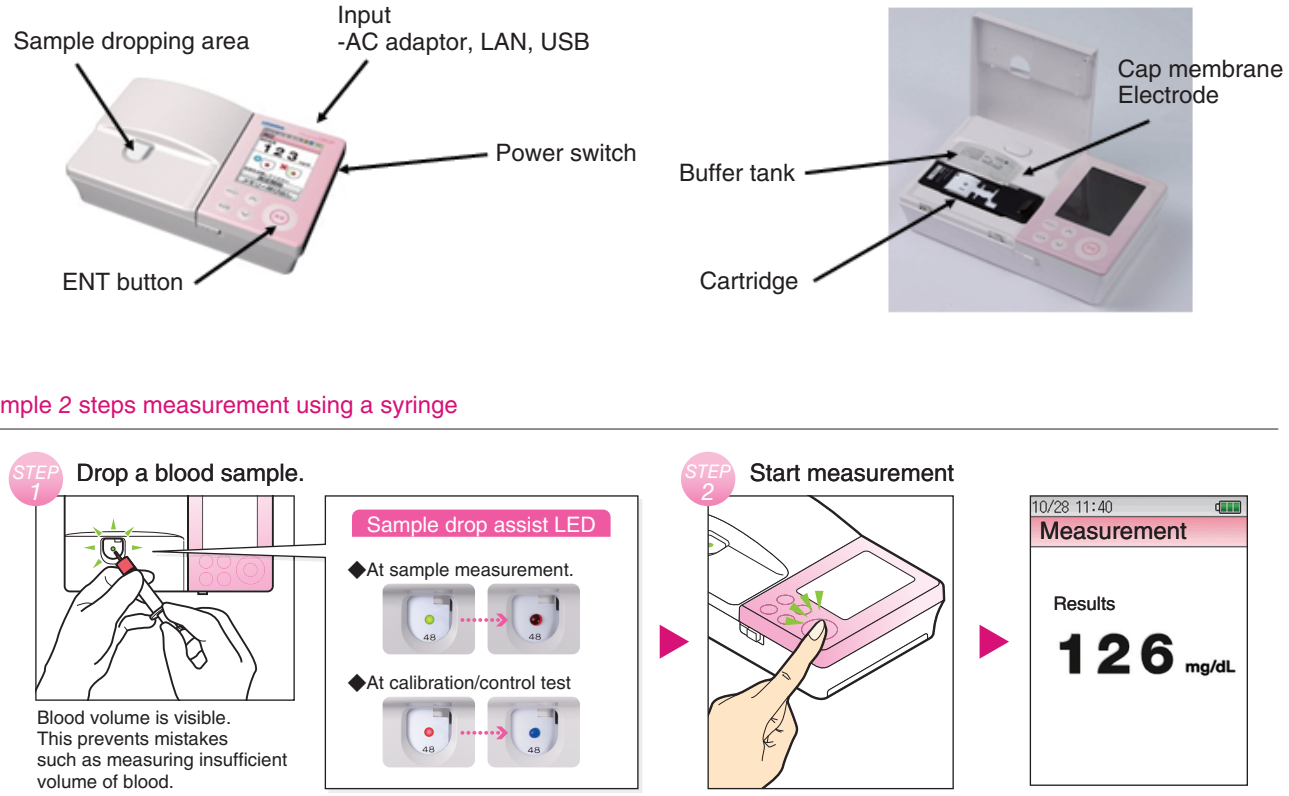

Figure 2 Structure and Operation procedure.

activated and the blood sample is transferred to the measurement position inside the device. Electrochemical cleaning and check of residual current are carried out on the electrode. As soon as the device is ready for measurement, the electrode moves and makes contact with the blood sample. When the glucose level is detected, the electrode moves back to the buffer tank position for electrode surface cleaning. The residual blood sample is rolled in the cartridge. Blood that may become a source of infection is never exposed on the surface and the cartridge is ready for next measurement.

As described above, the measurement principle of Antsense Duo is the same as that of dedicated analyzers in laboratories and the quality is assured by the calibration carried out with the dedicated calibrator once per 24 hours. Together, the control measurement is carried out to check the conditions of both calibration and device. To avoid unreliable results, the device is designed not to be measured if calibration is not carried out for more than 24 hours.

Reduction of blood infection risk

Normally, simple glucose analyzers such as SMBG aspirate blood using a disposable sensor attached to the main body. Once the blood sampling is detected, the electric current value is measured. If a device is used for a large number of patients, sufficient care is required to prevent cross-infection by cleaning the device after every measurement.

On the other hand, for the measurement with Antsense, any possible device infection source is not placed close to a patient because only a new sampling tool is placed close to a patient for every sampling and the sampled blood is dropped onto the main body of the device. This unique operation procedure has realized significant risk reduction for blood sample cross-infection via the main body of device.

Improvement for increasing operability

Since POCT testing is conducted outside a laboratory, users are nurses or doctors rather than laboratory technicians in most of cases. Then, a simpler and more user-friendly device is important in the clinical site. Antsense Duo has a large 3.5 inch color LCD to increase the operability from the conventional device. The LCD displays not only the operation procedure but also the procedure for replacement of consumables or troubleshooting. This display helps users or service personnel to deal with maintenance and troubleshooting in the field. Moreover, the sample drop assist LED is

added for the support of sample drop, which enables users to check the sample amount easily. This is the accessory function for the visual check by an operator. The risk hedge function to detect the short sample amounts by the sensor to prevent an incorrect measurement is an issue in the future.

Stabilization of measurement time

Antsense Duo completes the measurement: from sample dropping to the result display and ready state for next measurement in approximately 45 seconds. The basic structure is the same as that of the conventional device. Improvement in the measurement sequence slightly shortens the measurement time of blood samples at normal levels. The conventional devices had problems: Consecutive measurements of extremely high levels of blood samples required gradually a longer time for cleaning and stabilization of electrode. Antsense Duo is programed to change the frequency of cleaning according to the glucose level of the measured sample. Even after the consecutive measurements of samples with high glucose levels, it takes a constant measurement time for results to display. Then, Antsense Duo is used at the stationary condition not only in the clinical site but also in the places where many samples of high glucose level are measured for a clinical trial study or animal study.

For the introduction of IT

The introduction of IT in hospitals is dramatically developing. It is unexceptional also in the area of diabetic management. In the diabetic care system centered on the team medical care: doctors are in charge of instructions for blood glucose testing and medical care, nurses are in charge of blood glucose testing on site and care of patients, pharmacists are in charge of the management of medicine and laboratory technicians are in charge of the management of the devices, it is becoming essential to construct a network with which they share test results immediately using electronic charts. Even though management with paper medical charts has transitioned to that of electronic charts, in most of the present circumstances where nurses manually input the results in the system, their workloads increase and problems such as missed blood glucose testing or input errors occur. To reduce such risks, the POCT device is required to be adapted to the construct of the system where results are automatically transferred. Antsense Duo, has the ability to read Operator ID and Patient ID using the dedicated barcode reader, link them with the date and the results, store and send the data to the upper system via Ethernet.

Another important point in using a network, for POCT where the immediate test results are directly linked with the medical care, the provision of test results based on quality control and data assurance is required. In most of the cases, nurses and doctors are in charge of blood glucose testing at the clinical site and it is important that knowledgeable laboratory technicians get involved in device or quality control at the clinical site. First, the device information is consolidated via the internal network to "Glucose Analyzer Management System Roselink (option)", by the system architecture from which the test data are sent to the upper system, from the places where an administrative PC is placed such as a laboratory, multiple devices are able to be effectively managed in an integrated fashion.

Table 2 Within-run reproducibility of glucose solution

	Whole blood glucose level (mg/dl)			
MAX	46	177	654	812
MIN	45	179	645	797
MEAN	45.3	178.1	651	805.2
SD	0.5	0.7	3.7	5.0
CV	1.1%	0.4%	0.6%	0.6%

Evaluation

Finally, we present the evaluation of measurement performance.

Within-run reproducibility

After leaving whole blood samples for 24 hours and confirming the complete glycolysis, we added sodium fluoride and then, high-level glucose solution to prepare whole blood samples in levels from low to high. We measured the blood samples 10 times and evaluated the reproducibility. We confirmed a good reproducibility in all ranges: less than 50 mg/dL of glucose low level: CV1.1%, medium to high glucose level: less than CV0.6%. (Table 2)

Comparison with reference method (GOD immobilized membrane, hydrogen peroxide electrode method). We present the correlation between the results of whole blood samples measured with Antsense Duo and the plasma results of the same samples measured with the reference analyzer. (Figure 3) We confirmed a good correlation: y=1.016x-0.343, R2=0.997 for 100 samples. We used GA 1171(manufactured by Arkray) as reference analyzer.

Influence of hematocrit

We centrifuged whole blood samples of different glucose levels, and isolated plasma and other components. Then, we mixed the plasma and the components to prepare the samples of which the Hct value became the target value. We measured these samples with Antsense DUO.

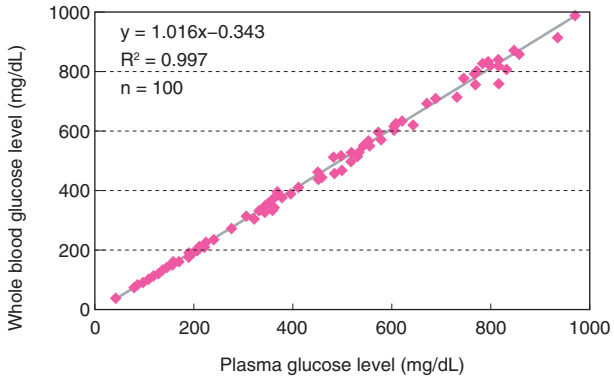

Figure 3 Correlation with the reference method (GOD immobilized membrane, hydrogen peroxide electrode method)

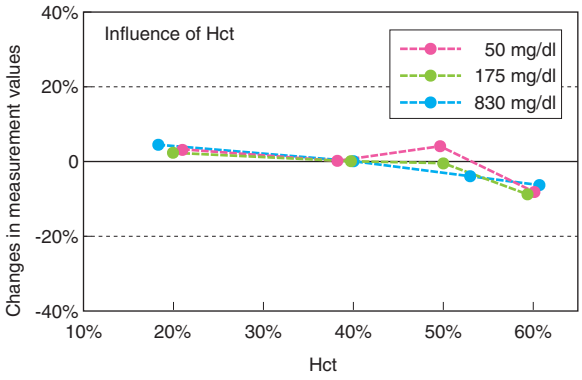

Figure 4 Influence of Hematocrit

Measure the sample with Antsense Duo. Based on the measurement value at Hct 40%, we compared the measurement values at different Hct values. (Figure 4) We confirmed that the changes in measurement values were within +/-10% at 20 to 60% of Hct, the specification range of the device.

Conclusions

Antsense Duo is a POCT glucose analyzer that provides equivalent level of results to those measured in laboratories by a simple operation using a drop of whole blood sample in a short time. In the performance evaluation, a high correlation with a reference glucose analyzer is also confirmed. Antsense Duo is not easily influenced by any coexisting material of blood sample such as dissolved oxygen, type of tubes or ascorbic acid, and is suggested to be useful in the clinical site. Compared with the conventional devices, the supplementary function is enhanced for the improvement in operability. Even though, it is true that there is a hurdle for the SMBG users to introduce the device of which utility is very different. It is a big issue in the future to develop a more user-friendly device with which anyone can provide correct results on the concept of quality assurance and measurement accuracy that is important for test data linked with medical care. Together with that, we aim to propose a total solution including not only blood glucose testing but also the construction of a control system of devices and a smooth control system of diabetic care by using the data transmission and the linkage with electronic charts in hospitals.

Furthermore, it is important to understand the demands of POCT and highly accurate blood glucose testing since there is a rapidly increasing diabetic population and the market is expanding in the world, to collaborate in the global development of blood glucose testing in different countries and thereby creating a foothold for the future promotion of our diabetes business.

References

[1] Kaoru Yuasa, Makoto Kaneko, et al, Utility of various types of POCT blood glucose devices in the clinical site, *PRACTICE*, **31-3**, 378(2014)

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