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The Application of Two-dimensional Centrifugation to Clinical Chemistry Testing

James T. Holen, Steven G. Schultz and Sie Ting Wong

Abbott Laboratories, Diagnostics Division, Department 93M, Abbott Park, IL, USA

ABSTRACT

We have developed a new clinical chemistry analyzer, the VISION System, which uses centrifugal force to separate whole blood, measure reagent and plasma volumes, and complete all steps required for a spectrophotometric analysis. The system is based on a multichambered test pack containing liquid reagents, which can be centrifuged in two planes oriented at right angles to each other. The analyzer regulates the temperature, timing and optical measurements for up to 10 different test packs in the same run. We have demonstrated good precision and accuracy on 6 clinical chemistry analytes, 2 enzymes, potassium and theophylline using this system.

INTRODUCTION

We have previously reported on the use of two-dimensional centrifugation for clinical chemistry blood testing (1). This concept includes the use of a unique test pack (Fig. 1) in which all of the essential steps in running a blood test can be performed automatically. We report here on the preliminary evaluation of several clinical chemistry tests using the VISION System.

METHODS

Details of the VISION System operation have been previously described (1). Briefly, test packs are injection molded in acrylic as a cover and multichambered body which can be ultrasonically welded together. A sealed polypropylene cup containing diluent and a stabilized reagent is located inside the test pack (Figure 1A). The specimen well can accomodate 40-120 uL of whole blood, plasma or serum.

During initial centrifugation (Fig. 1, B-D) the reagent cup moves within the test pack, and the sealing membrane, which is affixed by posts, peels away from the cup, releasing diluent and reagent. The combined reagent volume is measured exactly by the reagent measuring chamber, with excess being trapped

in a reagent overflow chamber. The specimen collects in a blood separating chamber where red blood cells separate from plasma at 500 x g during the first 45 seconds of the run. Excess specimen is trapped in a blood overflow chamber. The test pack is then rotated (Fig. 1, E-F) by an electromagnetic rotation system, during which reagent moves to a mixing chamber and plasma moves to a sample delay chamber. Rotation back to the initial position (Fig.1,G-H) moves reagent through a series of mixing slots to the cuvette. The plasma moves to a sample measuring chamber where either 3.6 or 9.4 uL of liquid is measured (test packs are designed to dilute plasma either 1:75 or 1:28). After reagent integrity is checked optically and the reagent has reached the appropriate test temperature (37°C. for enzyme rate reactions) the test pack is rotated once again (Fig. 1, I-J) and plasma is added to the reagent. The test pack then returns to the initial position, where the test reaction is monitored optically.

A cutaway diagram of the optics system (Fig.2) shows the orientation of the test pack in relation to the xenon flash lamp. The optics system can monitor 8 different wavelengths of light from 340 to 633 nm with a custom made diode array assembly. Analyzer software is designed to measure either endpoint or rate assays, store data from calibration runs and print out test results in user units. The analyzer also reports information on sample interferences, out-of-range samples or controls and instrument self diagnostic checks.

Clinical chemistry tests have been optimized and stabilized for use in the VISION System and are based on known or recently published solution chemistry methods. The following methods are used: Glucose (Hexokinase); Cholesterol (Esterase/oxidase/peroxidase); Uric acid, Uricase/microperoxidase method (2); Urea Nitrogen (Urease/GlDH, UV kinetic); Triglycerides (Lipase/Glycerol Kinase, UV); Creatinine (Alkaline picrate); Alkaline Phosphatase (p-Nitrophenyl Phosphate); SGOT (UV kinetic, activated with pyridoxal phosphate); Potassium by crown ether extraction (3); Theophylline by Enzyme Inhibition Immunoassay, (U.S. Patent 4273866). We compared VISION results on a wide variety of sera from hospitalized patients to methods available on the Abbott VP or TDx Analyzer (Abbott Laboratories Irving, TX 75062); the DuPont aca (DuPont Company, Wilmington, DE 19898); or the IL 443 Flame Photometer (Instrumentation Laboratory, Inc., Lexington, MA 02173).

RESULTS

Typical within day and between day precision on control serum is summarized in Table 1 for several tests. Comparable within-day precision is observed for whole blood specimens (Data not shown). Clinical correlation data is summarized in Table 2.

TABLE 1. VISION System Precision on Control Sera

ASSAY, UNITS	Control Conc.	%CV Within Day*	%CV Between Day**
Glucose, mg/L	770	1.0	2.4
Cholesterol, mg/L	960	1.4	1.6
Uric Acid, mg/L	37	2.7	2.4
Urea Nitrogen, mg/L	144	3.8	3.3
Triglycerides, g/L	3.6	3.5	3.8
Creatinine, mg/L	11	5.5	5.7
Alkaline Phosphatase, U/L	100	3.3	2.3
SGOT, U/L	200	2.7	2.7
Potassium, mmol/L	4.3	2.6	3.6
Theophylline, mg/L	12	3.4	1.1

* n=12, 2 runs ** n=12 x 5 days

TABLE 2. VISION System Clinical Correlation Data

VISION Test	Ref. Inst.	No. Sera	Y-intercept	Slope	r
Glucose	VP	193	55 mg/L	0.988	.998
Cholesterol	VP	150	20 mg/L	1.010	.980
Uric Acid	VP	219	2 mg/L	0.980	.980
Urea Nitrogen	VP	112	6 mg/L	1.020	.998
Triglycerides	VP	200	2 mg/L	1.020	.996
Creatinine	aca	254	1 mg/L	0.998	.999
Alkaline Phosphatase	aca	200	-8 U/L	0.88	.998
SGOT	VP	50	4 U/L	0.989	.995
Potassium	IL443	168	.02 mmol/L	1.02	.940
Theophylline	TDx	260	.27 mg/L	0.989	.986

DISCUSSION

The VISION System is capable of performing a wide range of clinical chemistry tests on whole blood specimens. Data shown here on precision and clinical correlation is comparable to that of batch serum analyzers used in clinical laboratories. The test pack and the analyzer have sufficient flexibility to perform not only typical endpoint assays, but also rate reactions, enzyme immunoassays, and organic extraction assays.

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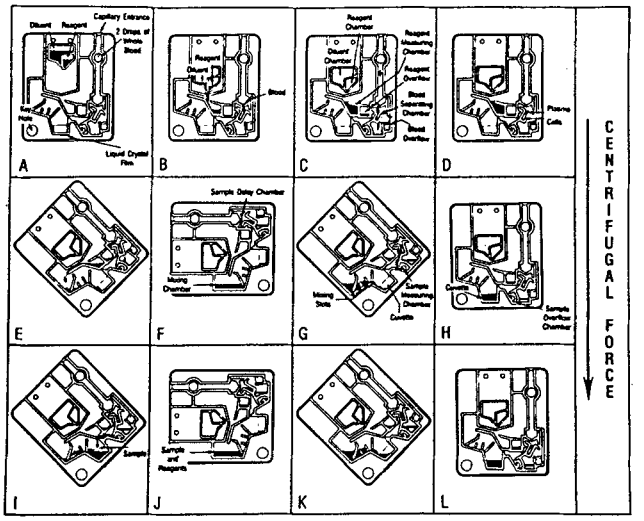

Figure 1. Details of the fluid movement inside the test pack. Refer to Methods Section for narrative description.

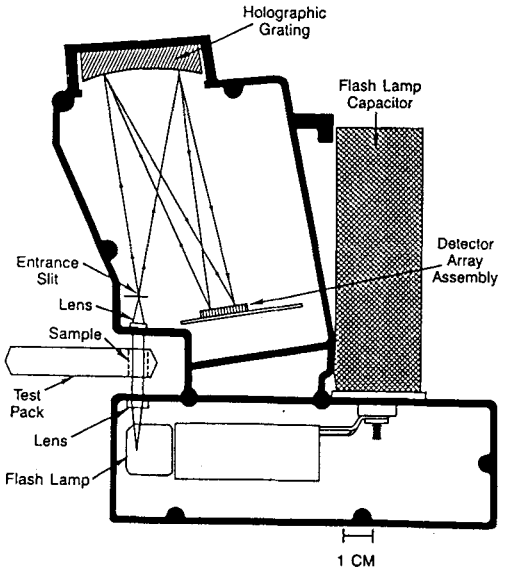

Figure 2. Optics arrangement of the VISION photodiode array spectrometer.