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ORIGINAL ARTICLE

Comparison of Clot Activator Gel Biochemistry Tubes

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Abstract

Introduction: The clinical laboratory testing process has three phases, and one of the most common errors that adversely affect the accuracy of laboratory test results occurs in the pre-analytical phase. Different brands of blood collection tubes used in laboratories can adversely affect the accuracy of the parameters. This study aims to compare the clot activator gel biochemistry tubes for selected clinical parameters.

Methods: Fifty healthy volunteers aged between 18-70 years were included who didn't have any chronic or inflammatory disease, any clinical or pathological disease, and didn't use any medication. The biochemical parameters such as serum albumin, creatinine (crea), urea, triglyceride (TG), calcium (Ca), sodium (Na), potassium (K), and chloride (Cl) levels; aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) activity were measured by an autoanalyzer. Student's t-test and Bland-Altman plot methods were used for statistical data analysis by SPSS software.

Results: There was no statistical difference between the two different tube brands in terms of all evaluated clinical parameters that could affect the accuracy of the test results.

Discussion and Conclusion: When the BD® brand tube is taken as a reference, it is thought that AYSET® tubes give the same or close values, and the clinical use of AYSET® brand tubes will not cause an error in laboratory tests.

Keywords: Biochemical analyzes; blood collection tube; clinical laboratory; lab test errors.

Clinical laboratory analyses aid clinicians in diagnosing, treating, and monitoring diseases, and also play a vital role in ensuring quality and continuity in health systems[1]. The main task is to provide reliable and high-quality analysis results[2]. The laboratory testing cycle encompasses all steps between clinicians' requests to perform a laboratory test and the test results. The cycle consists of three phases: pre-analytical, analytical, and post-analytical[3]. A wide variety of pre-analytical variables also affect the reliability of the laboratory test report, such as sample quality, sample collection, handling, storage, and physiological and endogenous interaction factors[4]. The post-analytic phase in the clinical testing process includes critical value reporting, result reporting, manual transcription of results, and data entry[5]. Because the laboratory testing process is multi-phase, testing errors are difficult to detect and are innately uncertain as they are less easily understood than other types of medical errors[6]. The test errors that may take place at any step during the entire testing process must be accurately identified, detected, and minimized, which is vital for clinical laboratories[7]. Most errors in laboratory test results occur in the pre-analytical phase, as the pre-analytical

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phase involves more human intervention than the other phases, and many of these errors are avoidable[8].

Another variable that is often poorly recognized in the pre-analytical phase of testing is blood collection tubes. Since different brands produce sample collection tubes with different materials and in different shapes in terms of components such as clot activator, separating gel, surfactant, and stopper, performance evaluation is needed for the tubes produced. Although well-designed, these may not be suitable for all clinical tests[9,10]. Blood samples are taken into different sample tubes according to the analysis method of the planned parameter during the blood collection stage. The selection of blood tubes used for the collection of samples is essential for the pre-analytical phase because of its effects on all subsequent steps[11]. The choice of blood collection tube is critical to minimize pre-analytical and analytical errors[12]. False selection and utilization of blood collection tubes can adversely affect laboratory results, and the components from the blood collection tubes can also change the stability of the parameter. In this sense, investigating the effect of blood collection tubes on laboratory results emphasizes the importance of comprehending the differences between blood tubes[13].

The gray-capped tubes contain fluoride ions that prevent glycolysis and are used for the determination of glucose and lactate. Though containing lithium heparin as an anticoagulant, the green-capped tubes are used to separate blood and plasma and obtain plasma[14]. While purple-capped whole blood/plasma containing ethylene-diamine-tetra-acetic acid (EDTA) is used to obtain whole blood/plasma, blue-capped sample tubes which contain sodium citrate are used in samples taken for use in coagulation devices[15]. The clot activator gel biochemistry tubes with yellow caps are used to obtain serum from blood samples taken for testing. These tubes contain separating gels that form a barrier between the packed cells and serum obtained by centrifugation, and the gel used in the tubes is relatively inert. Tubes of different brands may affect analyte concentrations or stability, causing inaccurate results[16,17]. The most preferred sample type for laboratory tests is serum; besides samples such as plasma, urine, cerebrospinal fluid, plasma, urine, stool, saliva, cerebrospinal fluid, and joint fluid[18]. The serum is obtained without anticoagulants from the blood collection tube, which is free of anticoagulation factors and fibrin. The serum has a cleaner structure compared to the other parts because it does not contain fibrin or anticoagulant factors.

Nowadays, different brands of tubes for blood collection are used in laboratories, and it is thought that the difference between the tubes affects the accuracy of the parameters to be measured. Therefore, validation of blood collection tubes is essential for the integrity of the results[19]. The verification affirms clinical test results of blood collection tubes using local instrumentation and reagents, revealing a source of bias in test results that was evaluated by statistical analysis of laboratory data obtained[20]. This study aimed to compare the results of two different brands of blood collection tubes (BD® Vacutainer Serum Separation Tubes II and AYSET® Tube clot activator & Gel) for some selected biochemical parameters.

Materials and Methods

Study Design

The volunteers who came to the Medical Biochemistry Blood Collection Unit of the University of Health Sciences, Haydarpasa Numune Health Application, and Research Center signed an informed consent form and agreed to participate between May and June 2022 in the study. The number of volunteers was calculated as a minimum of 50 volunteers by power analysis to get 80% power at the α=0.05 significance level in this study. Fifty healthy volunteers aged between 18-70 years were included in this study; who didn't have any chronic or inflammatory disease, any clinical or pathological disease, and didn't use any medication. People who have any chronic, inflammatory, clinical, or pathological disease and use blood thinners were excluded. The study has been confirmed by the Local Ethics Committee of the University of Health Sciences Türkiye, Faculty of Medicine (12/9 decision number, 22/238 registration number) on the date 22.04.2022. The study was conducted according to the principles of the Declaration of Helsinki.

Sample Collection

AYSET® clot activator & gel (AYSET® Medical Devices, Türkiye; Ref number: 70658) and BD® Vacutainer Serum Separation Tubes II advance (Becton, Dickinson and Company, Franklin Lakes, USA; Ref number: 367955) tubes for comparison by performing biochemical analyzes used. Approximately 3 mL of blood was drawn into these sterile blood tubes for each tube. Afterward, these blood samples were centrifuged for 10 minutes at 3000 x g to separate the serum then biochemical analyzes were made.

Biochemical Analysis

Serum albumin, creatinine (crea), urea, triglyceride (TG),

calcium (Ca), sodium (Na), potassium (K), chloride (Cl), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) were measured using a Roche-Hitachi autoanalyzer (Abbott Architect Ci 4100 autoanalyzer, California, USA) at the clinical biochemistry laboratory.

Statistical Analysis

After the biochemical measurements were taken, statistical analyzes of all data were performed with SPSS version 25.0 (IBM, Armonk, NY, USA). Parametric data were expressed as mean±standard deviation (SD). The difference between groups was detected using the Student's t-test. The Bland-Altman plot was used to detect differences in mean values between two tubes, and $p<0.05$ values were considered statistically significant.

Results

In our study, there was no statistically significant difference between the two biochemistry tubes in terms of the parameters given in Table 1, as a result of the measurements made in the blood samples taken into the AYSET® and BD® tubes.

Bland-Altman is used to show acceptable clinical agreement for all analytes between the two different blood collection tubes. All results of the nine biochemical parameters (albumin, crea, urea, TG, Na, Ca, K, Cl, AST, ALT,

Table 1. Comparison of BD® and AYSET® tubes with regards to biochemical parameters

	BD® Mean±SD	AYSET® Mean±SD	p
ALB g/L	51.06±3.63	51.13±3.61	0.948
Crea mg/dL	0.87±0.82	0.87±0.81	0.994
Urea mg/dL	20.08±5.49	20.04±5.48	0.982
TG mg/dL	108.72±27.17	109.20±27.65	0.951
Ca mg/dL	44.66±15.97	44.66±15.96	1.000
Na mmol/L	140.80±1.38	141.00±1.38	0.612
K mmol/L	1.44±1.51	1.42±1.47	0.964
Cl mmol/L	103.29±1.39	103.34±1.43	0.905
AST U/L	20.32±4.61	20.28±4.42	0.975
ALT U/L	19.16±3.59	18.80±4.01	0.740
LDH U/L	212.92±27.73	210.28±28.99	0.744

P<0.05 is considered statistically significant. SD: Standard deviation; ALB: Albumin; Crea: Creatinin; TG: Triglyceride; Ca: Calcium; Na: Sodium; K: Potassium; Cl: Chloride; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDH: Lactate dehydrogenase.

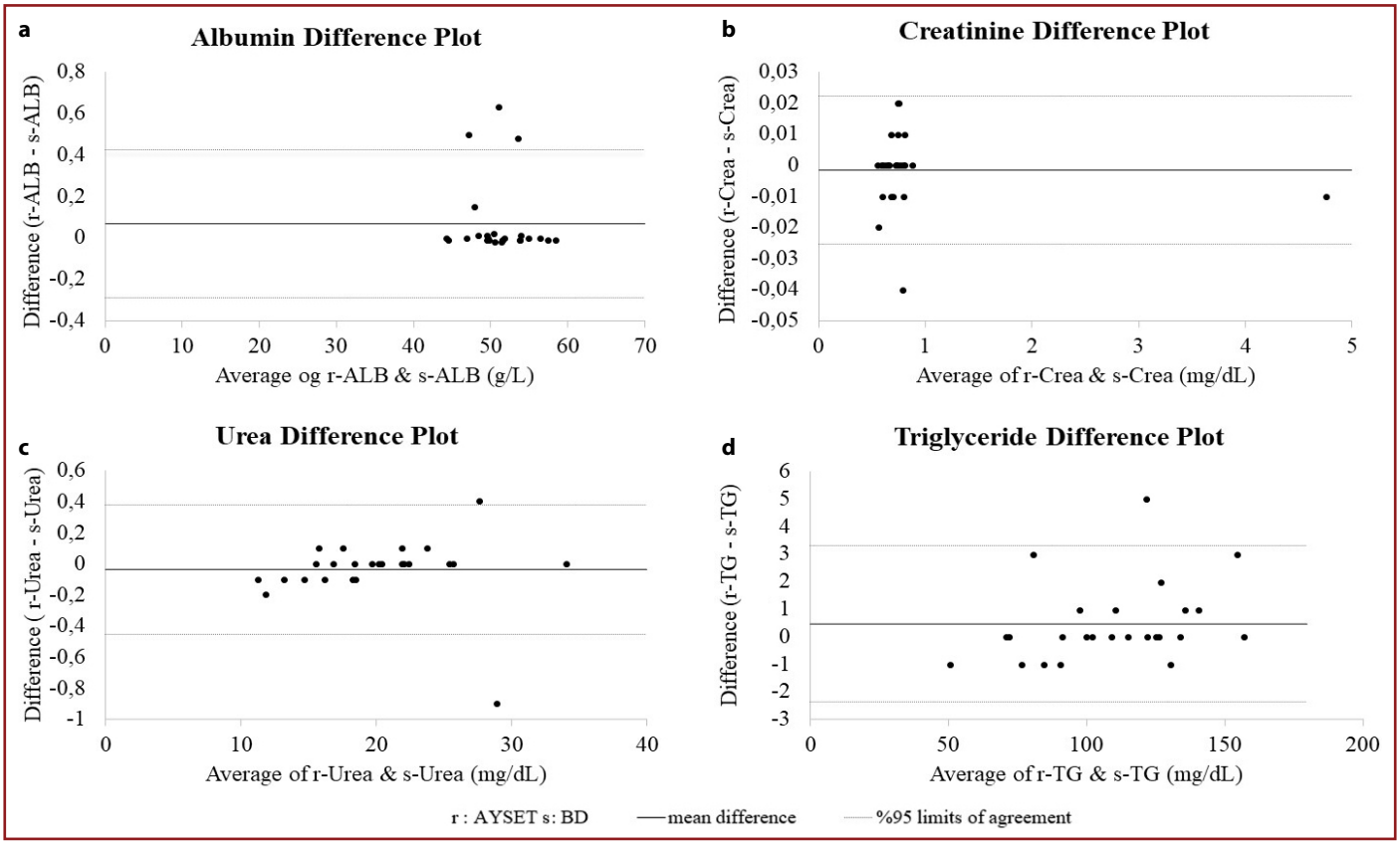

Figure 1. Comparing the AYSET® and BD® tubes with Bland-Altman difference plots for **(a)** albumin, **(b)** creatinine (crea), **(c)** urea, and **(d)** triglyceride (TG) parameters.

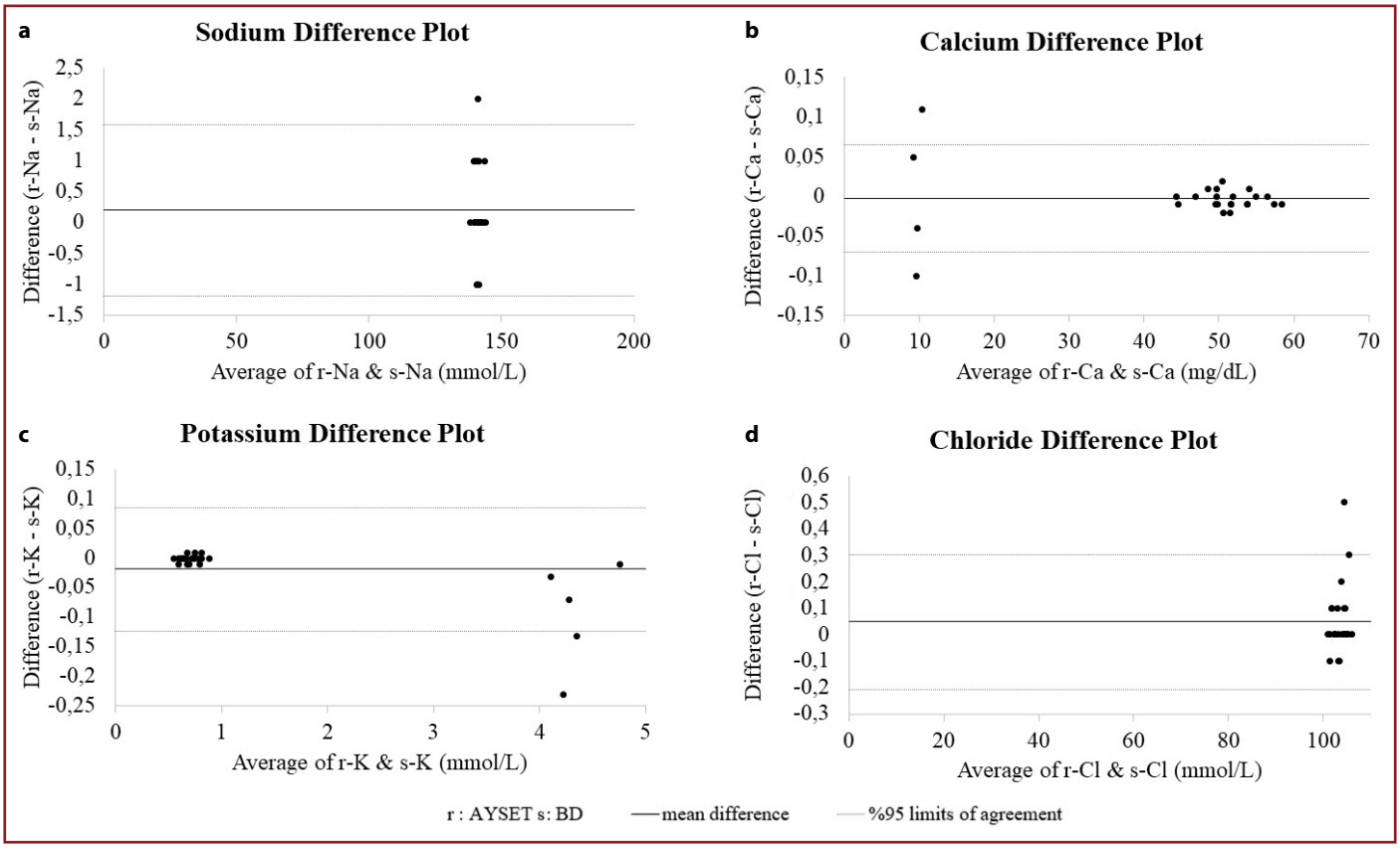

Figure 2. AYSET® and BD® tubes are compared using Bland-Altman difference plots for the parameters sodium (Na), calcium (Ca), potassium (K), and chloride (Cl).

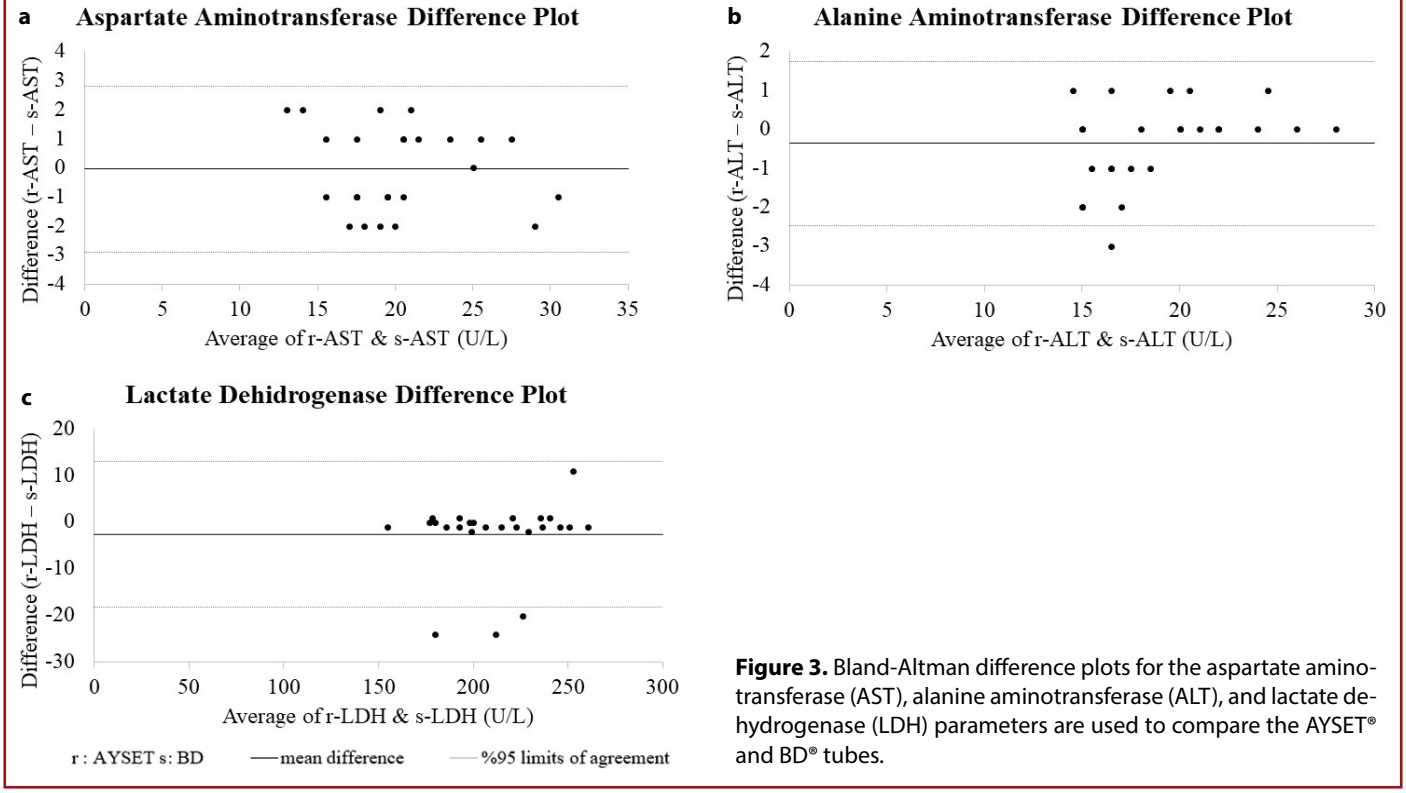

Figure 3. Bland-Altman difference plots for the aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) parameters are used to compare the AYSET® and BD® tubes.

and LDH) that were examined for both AYSET® and BD® brand blood tubes were not statistically different and were consistent. The albumin, crea, urea, and TG parameters are in Figure 1. Additionally, the mean differences for these parameters were 0.06 g/L (95% CI: 0.117 to 0.003), -0.0016 mg/dL (95% CI: -0.0008 to -0.00312), -0.036 mg/dL (95% CI: -0.0702 to -0.0018), and 0.48 mg/dL (95% CI: 0.024 to 0.936), respectively.

The Na, Ca, K, and Cl parameters are in Figure 2, and the percentages of bias were very low. In addition, mean differences for these parameters were 0.20 mmol/L (95% CI: 0.39 to 0.01), -0.0024 mg/dL (95% CI: -0.00012 to -0.00468), -0.0192 mmol/L (95% CI: -0.00096 to -0.03744), and 0.048 mmol/L (95% CI: 0.0024 to 0.0936), respectively.

The AST, ALT, and LDH parameters are in Figure 3. The mean differences for these parameters were -0.04 U/L (95% CI: -0.078 to 0.002), -0.36 U/L (95% CI: -0.702 to -0.018), and -2.64 U/L (95% CI: -5.148 to 0.132), respectively. In line with the results of our study, there are no significant differences in the data sets in the Bland-Altman difference plot.

Discussion

Laboratory tests provide the basic information necessary for the evaluation of the disease process in the clinical sense; the accuracy and reliability of the results are vital for patient health as well[21]. The clinical laboratory testing process has three steps: pre-analytical, analytical, and post-analytical. Ordering the test, taking the sample, processing, transporting, and delivering the sample are pre-analytical phases; the analytical stage is the laboratory that takes and analyzes the sample; reporting is also the post-analytic stage[22]. Laboratory test error is defined as an error that may occur during the entire test process, from the test request to the reporting of the results, that may affect the quality of laboratory services in any way and pose a severe danger to the health of the patient[23]. The test errors are often seen in the pre-analytical phase[24]. One of the most common errors that adversely affect the accuracy of laboratory test results in the pre-analytical phase is using incorrectly designed tubes[25]. Validation and verification of blood collection tubes are essential for the accuracy of test results, as different brands of blood collection tubes used in laboratories can adversely affect the accuracy of the parameters[26]. To date, blood collection tubes of many different brands have been evaluated for many different clinical biochemical parameters. In the literature, two tubes have not been compared with regard to the biochemical parameters we determined for this study. In our study, we aimed to compare the clot activator gel biochemistry tubes used for serum collection, which is a widely utilized sample in biochemical laboratories, for eleven clinical parameters. As a result, there was no difference between the two different brands of tubes in terms of clinical parameters that could affect the accuracy of the test results.

The separating gels in the tubes are produced from a polymeric material and, due to its specific density between serum/plasma. Therefore, it forms a layer that allows the samples to be separated into their serum after centrifugation[27]. Serum separator tubes provide many advantages, such as ease of transport and storage of samples, shortening of centrifugation time, improvement in serum analyte stability, and better separation of blood plasma from blood cells[28]. Separation gels inside blood tubes are highly hydrophobic. Interactions with hydrophilic biochemistry parameters such as proteins, peptides, or electrolytes can be minimized. In a study investigating the stability of some therapeutic compounds and drugs in samples in two different types of blood tubes, it was noted that separator blood collection tubes were associated with a decrease in the concentration of many drugs[29]. There are also studies showing that gel tubes are suitable for antibiotic, antiepileptic, cardioactive, and asthma drug measurements, but not for antidepressant drug measurements[30]. In a study in which gel-containing BD Vacutainer® Serum Separation Tubes II Plus and BD Vacutainer® serum glass tubes were compared for special protein testing, it was stated that blood samples taken into serum separator tubes should be evaluated in the laboratory's own environment. It has been said that the reason for this is the clinically significant changes in analyte concentrations in serum separator tubes due to pre-analytical errors[31]. In the study of Ozdemir et al.[9], the performances of BD Vacutainer® Serum Separation Tubes II Advance and KWS (Shijiazhuang Kang Weishi Medical Instrument Co., China) branded tubes were compared for some clinical biochemical parameters and the stability of the production quality was tested. They revealed that the results other than the Ca and K tests were acceptable in the routine process. However, Ercan et al.[32] revealed that they compared BD® and AYSET® brand gel biochemistry tubes for thyroid function tests, and there was no statistical difference between the two tubes for these parameters. When BD® and AYSET® were compared, it was seen that there was no difference in AST, ALT, and LDH enzyme activities between the two brands. However, serum albumin, crea, urea, and TG; Ca, Cl, K, and Na electrolyte levels were statistically insignificant, as were the parameters in the previous study between both tubes.

The limitations of the study are the small number of patients and the need to evaluate more clinical parameters in order to evaluate different brands of clot activator gel biochemistry tubes.

Conclusion

Blood collection tubes of different brands and contents are available from various manufacturers for routine clinical laboratories. The existence of these differences may affect the test results, so each laboratory should verify the tubes of different new brands before using them. Verification is of great magnitude in clinical laboratories, which have vital importance in terms of patient health. In this study, when the BD® brand tube was taken as a reference, it was seen that AYSET® tubes gave the same or close values to this brand, and there was no statistically significant difference. In this sense, AYSET® brand tubes are also considered to be clinically useful. Considering the limitations of the study, future research should be conducted with more volunteers, a wider age range, and more clinical biochemical parameters to better evaluate different brand sample tubes.

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Ethics Committee Approval: The study was approved by the University of Health Sciences Faculty of Medicine Ethics Committee (no: 12/9, date: 22/04/2022).

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