

## Original Articles

# Comparison of the Dilute Russell's Viper Venom Time by A Conventional Method with an Automated Kit Assay for the Detection of Lupus Anticoagulants

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**Abstract:** Lupus anticoagulants (LA) are a mixture of acquired antibodies interfering with phospholipid dependent coagulation tests. They are associated with an increased risk of thrombosis. The dilute Russell's viper venom time (dRVVT) is the most common and widely used test for the detection of LA. A number of commercial dRVVT kits are now available. This study was undertaken to compare a conventional dRVVT method with a commercial automated assay to determine their sensitivity and specificity for the identification of LA. Blood samples of 30 LA positive patients and of 30 LA negative healthy subjects by the standard method were analyzed. The conventional dRVVT method used in-house reagent detected by a semi-automated instrument (650C MDA) and the commercial dRVVT kit assay used a single set of reagent detected by an automated instrument (ACL 200). Of the 30 LA positive samples, 15 and 2 were positive by the commercial kit assay, and by the conventional method, respectively. Of the 30 LA negative samples, two gave positive results by the commercial kit assay whereas all were negative by the conventional method. The sensitivity and specificity of the conventional method were 6.67% and 100%, respectively, whereas of the commercial kit assay were 50% and 93.3%, respectively. This difference in the sensitivity of the two methods was statistically significant ( $p = 0.004$ ).

**Key Words :** ● Russell's viper venom time ● Lupus anticoagulants

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## Introduction

Lupus anticoagulants (LA) are acquired antibodies that belong to the family of antiphospholipid antibodies (APA).<sup>13</sup> They are directed against phospholipid (PL) bound to various plasma proteins or lipid-protein products.<sup>46</sup> They are a mixture of immunoglobulins (IgG, IgM, IgA), which have the ability to prolong one or more of the *in vitro* coagulation tests by inhibiting the activity of FXa-FVa-Ca<sup>++</sup>-PL complex, which are required for the conversion of prothrombin to thrombin in the coagulation cascade.<sup>79</sup> LA are associated with an increased risk of both venous and arterial thrombosis,<sup>10-14</sup> recurrent spontaneous abortions,<sup>15-17</sup> and thrombocytopenia.<sup>18-20</sup> They occur in about 10% to 35% of patients with systemic lupus erythematosus,<sup>21</sup> and may be detected in healthy population. The dilute Russell's Viper Venom Time (dRVVT) is the most common test and is widely used for the diagnosis of LA. Since the venom directly activates FX, it is unaffected by the presence of antibodies to factors VIII, IX or XI. In addition, the limiting concentration of phospholipid will also increase the sensitivity of the test.<sup>22</sup> A number of commercial dRVVT kits are now available. A simplified dRVVT method containing venom, calcium, a heparin neutralizer and phospholipid combined into a single reagent has been introduced. This modification allows the performance of the assay on automated coagulation instruments. The number of requests for LA screening in clinical laboratories has been increasing. Therefore, we decided to introduce a

commercial kit with automation technique into our laboratory instead of a conventional assay which used in-house reagents and performed by semi-automated instrument. This study was undertaken to compare the performance of a conventional dRVVT method with a commercial automation one in order to determine their sensitivity and specificity for the detection of LA in patients previously identified to have LA, and in LA negative healthy subjects.

## Materials and methods

### Subjects

We studied plasma samples of 30 patients (22 females, 8 males; mean age 37.2 yrs) which were previously diagnosed to have LA according to the SSC criteria.<sup>23-24</sup> The underlying medical problems of the patients included thrombotic events (n = 10), systemic lupus erythematosus (n = 10) and other diseases (primary phospholipid syndrome, chronic renal failure, hypertension, thyrotoxicosis, headache and graft versus host disease) (n = 10). None of the plasma contained heparin or warfarin. Plasma samples were also obtained from 30 healthy subjects (19 females, 11 males; mean age 30.4 yrs) with negative LA.

### Blood collection

Blood samples of patients and normal subjects were collected into plastic tubes containing 0.109 M sodium citrate (9:1 ratio) using two syringe technique and double centrifuged at 4 °C for 20 min at 2,000 g to obtain platelet poor plasma with platelet count below 10x10<sup>9</sup>/L. The plasma

was either tested immediately or freezed at -80°C until assay. Normal pooled plasma from 20 healthy subjects was prepared in the same manner.

### Coagulation tests

The standard procedure for previous diagnosis of LA consisted of screening, mixing and confirmatory steps. Screening tests were activated partial thromboplastin time (APTT)<sup>25</sup> using kaolin-inosithin suspension (1:100, V:V, of 3.8% inosithin in 0.15 M sodium chloride and 2.5 mg% kaolin suspension in veronal buffer), kaolin clotting time (KCT) using 2 gm% kaolin suspension in saline according to Exner et al,<sup>26</sup> and 1:5 dilute APTT. The assays were carried out by manual technique for the first two tests, whereas the third one used semi-automated machine (MLA 650 C, Medical Laboratory Automation, Pleasantville, NY, USA). When the clotting time exceeded normal range, the test was repeated with a 1:1 mixture of patient's and normal plasma. If the mixing test remained outside the normal range, confirmatory test using platelet neutralization procedure (PNP)<sup>27</sup> was performed. A plasma sample was diagnosed to have LA when at least one of the screening tests was prolonged which was not corrected by mixing with normal plasma and showed neutralization after adding excess phospholipid in the confirmatory test.

Conventional dRVVT method was carried out with 1:200 Russell viper venom (Murex Diagnostic Ltd, Temple Hill, Dartford, England) in Tris buffer saline pH 7.5 and 1:8 kaolin-inosithin sus-

pension (APTT reagent) according to Thiagarajan et al.<sup>22</sup> The test was performed on MLA 650 C coagulometer. Mixing and confirmatory tests were done on plasma samples with prolonged clotting time. The same criteria was also used for the diagnosis of LA.

Commercial dRVVT assay was performed on ACL 200 coagulometer using IL Test™ LAC screen and confirm (Instrumentation Laboratory, Milano, Italy). LAC screen contained Russell viper venom, phospholipids, calcium, polybrene (heparin neutralizing agent), buffer, stabilizers, dyes and preservative. LAC confirmed contained the same components but more phospholipids. If LAC screen clotting time of patient was 20% longer than the mean of screen normal range (i.e. ratio >1.2), the presence of LA would be confirmed with LAC confirm. The plasma sample was considered to have LA if normalized LAC ratio (screen ratio/confirm ratio) was equal or more than 1.2.

### Results

Of 30 LA positive samples previously diagnosed by the standard method, the conventional dRVVT method showed positive result in only two samples (Table 1). In contrast, for LA negative samples, no positive result was seen. For the commercial dRVVT assay, the positive result was found in 15 out of 30 LA positive samples whereas two gave positive results in LA negative samples (Table 2). The distribution of LA positive and negative sample results performed by the conventional method compared

**Table 1** Comparison of dilute Russell's viper venom time (dRVVT) by conventional assay with standard method for the diagnosis of lupus anticoagulants (LA)

Conventional method	Standard method		
	LA Positive	LA Negative	Total
LA Positive	2	0	30
LA Negative	28	30	30
Total	30	30	60

**Table 2** Comparison of dilute Russell's viper venom time (dRVVT) by commercial kit assay with standard method for the diagnosis of lupus anticoagulants (LA)

Commercial kit assay	Standard method		
	LA positive	LA negative	Total
LA positive	15	2	30
LA negative	15	28	30
Total	30	30	60

**Table 3** Sensitivity, specificity and receiver operating characteristic (ROC) area of the two dilute Russell's viper venom time (dRVVT) methods

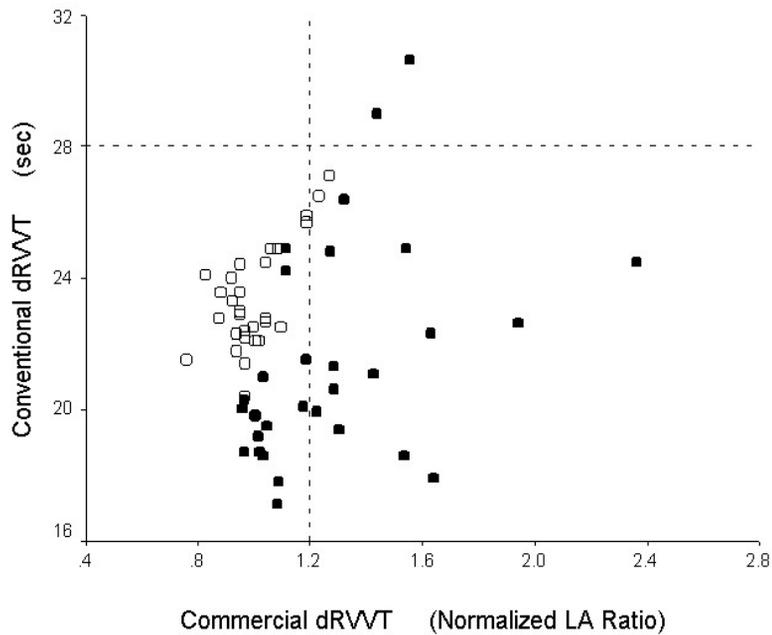
Test	Sensitivity (%)	Specificity (%)	ROC area	P - value
Conventional method	6.67	100	0.5333	0.004
Commercial kit method	50	93.3	0.7167	

with the commercial kit is shown in Figure 1. The receiver operating characteristic (ROC) curves were generated for each test and the sensitivity and specificity of them were calculated. The ROC area under ROC curve of the conventional method was 0.533, whereas that of the commercial assay was 0.7167 (Figure 2). The sensitivity and specificity of the conventional dRVVT method relative to the standard method was 6.67% and 100%, respectively (Table 3). The sensitivity and the specificity of the commercial dRVVT assay relative to the standard method

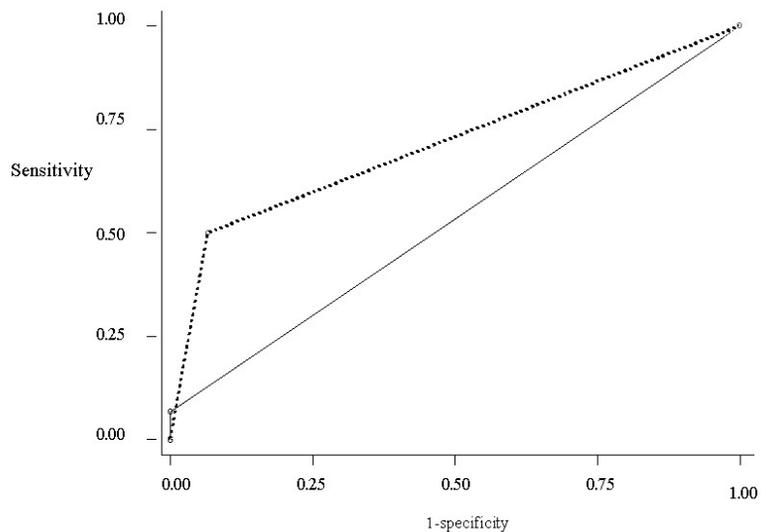
were 50% and 93.3%, respectively. The difference of the two methods was statistically significant ( $p = 0.004$ ).

### Discussion

The accuracy of LA identification is obviously important because of their association with an increased risk of thrombosis. The high demand of LA tests contributes to an increasing workload. The commercial reagents with automated analyzers are used to ease this workload. The dRVVT is one of the most widely used tests



**Figure 1** Comparison of the conventional dilute Russell's viper venom time (dRVVT) method with the commercial dRVVT assay. Closed circles are patients with lupus anticoagulants (LA) positive. Open circles are reference population. Dashed lines indicate upper normal range of the tests.



**Figure 2** Receiver operating characteristic (ROC) area of the conventional dilute Russell's viper venom time (dRVVT) method under the solid line was 0.533. ROC area of the commercial dRVVT assay under the dashed line was 0.716. The difference of the two methods for detecting lupus anticoagulants (LA) in patients with LA positive and in healthy subjects was statistically significant ( $p = 0.004$ ).

since it is a reproducible, sensitive and relatively specific method for LA. We compared the test obtained by an automated commercial kit assay with that by a home made reagent method for the identification of LA in the LA negative and positive plasma samples by the "standard" method. LA negative samples were from healthy volunteers with normal coagulogram to ensure that there were no confounding factors. For the LA negative group, the commercial kit assay showed two positive results while none was shown by a home made reagent assay. The two methods had a good specificity (93.3% for the IL kit assay and 100% for the in-house reagent method). The marked difference in sensitivity of the two methods was seen when the tests were performed using LA positive samples. The commercial kit method was more sensitive than the conventional one (50% versus 6.67%). The p-value from ROC curve generation showed a significant difference of the two methods in detecting LA ( $p = 0.004$ ).

The discrepancy of dRVVT results between different reagents and different instruments have been reported. Luddinurton et al<sup>28</sup> performed in-house dRVVT on the CAM-MTX coagulometer (Organon Teknika) by using viper venom and platelet substitution from Diagnostic Reagents Ltd, Oxon, UK. The samples were collected from 12 LA positive patients, 15 warfarin treated patients, 10 heparin treated patients, 11 patients with liver disease and 23 patients with positive anticardiolipin antibody but negative LA. Their study showed good sensitivity (91.7%) and

specificity (100%) of the dRVVT test. Lawrie et al<sup>29</sup> studied five sets of dRVVT reagents on Amelung KC 4A coagulometer (mechanical system) and Sysmex CA-6000<sup>TM</sup> (photo-optical system) in LA positive samples ( $n = 10$ ) and in samples from patients receiving oral anticoagulants with and without LA ( $n = 30$ ). Sensitivity of all reagents from both instruments ranged from 62 to 97% and specificity ranged from 23 to 100%. The sensitivities of IL reagent on CA-6000<sup>TM</sup> and KC 4A were all 90%, whereas the specificities were 42 and 46%, respectively. The variation of dRVVT results were summarized by Triplett<sup>30</sup>. The analysis was performed in samples from LA positive ( $n = 23$ ), heparinized ( $n = 20$ ), oral anticoagulant treated ( $n = 20$ ), factor inhibitors ( $n = 14$ ) and hemophilia ( $n = 14$ ) patients. The sensitivity of seven commercial screening dRVVT tests ranged from 96 to 100%, whereas the specificity ranged from 48 to 73%. For IL reagent the sensitivity and specificity were 100 and 64%, respectively. Jennings et al<sup>31</sup> reported the results of United Kingdom National Quality Assessment Scheme Survey in one LA positive sample and one LA negative sample prepared from a pool of normal donors. Nine commercial kits and one in-house dRVVT reagents were used by 228 centers. The correct diagnosis was achieved by 97% of the participants for the LA negative samples and 81.7% for the LA positive samples. There were variation of sensitivities among these reagents whereas the specificities were similar. The study of Tripodi et al<sup>32</sup> also showed the variation of dRVVT tests. They re-

ported the results of a survey of the Italian Federation of Anticoagulant Clinics and the Italian Committee for Standardization of Laboratory Methods of 70 participants. Three commercial dRVVT tests were used by 66 laboratories. Twenty of them used IL reagent. As a screening test, the sensitivities of the three reagents for normal plasma with purified anti- $\beta$ 2-GPI added in high, intermediate and low LA potency were 85-94%, 78-93% and 44-87%, respectively. The sensitivities of IL reagent for each LA potency plasma were 85, 85, and 60%, respectively. The specificities of the dRVVT reagents in LA negative lyophilized normal plasma with and without heparin added, and in artificial coagulation deficiency plasma were 100% and 93-100%, respectively. For IL reagent, the specificity in each LA negative plasma were 100, 100, and 95%, respectively. In confirmatory test, the specificity of IL reagent in low potency LA increased from 95 to 100%.

From the afore-mentioned studies, the difference of dRVVT results were not only from different reagents, but also from different instrumentations. The variability of the results expressed the heterogeneity of the Russell's viper venom utilized in preparation of the reagents among manufacturers. Russell's viper snake is prevalent in India and Southeast Asia. Depending on geographical location where Russell's viper venom are collected, there is important difference of the venom. The marked difference of the sensitivity of the reagents used in our study might be affected by this reason. Furthermore,

the different source of phospholipid used in each test was also another explanation.<sup>31</sup> In the conventional method freeze-thawed platelet was used as phospholipid source, while in the IL test the source of phospholipid was from vegetable. Another reason was the different detection technique of the two methods, one was semi-automated while the other was fully automated. Although there was much different in the sensitivity of different dRVVT tests, the specificity in LA negative group obtained from normal subjects was rather similar in most studies including ours. In conclusion, the commercial DRVVT kit assay was more sensitive than the conventional test for the detection of LA. Therefore, it can substitute the conventional method for the diagnosis of LA.

## Reference

1. Triplett DA. Protean clinical presentation of antiphospholipid-protein antibodies (APA). *Thromb Haemost* 1995;74:329-37.
2. Triplett DA. Antiphospholipid-protein antibodies: laboratory detection and clinical relevance. *Thromb Res* 1995;78:1-31.
3. Bevers EM, Galli M, Barbui T, Comfurius P, Zwaal RFA. Lupus anticoagulant IgG's (LA) are not directed to phospholipid only but to a complex of lipid bound prothrombin. *Thromb Haemost* 1991;66:629-32.
4. Mc Neil HP, Simpson RJ, Chesterman CN, Krilis SA. Antiphospholipid antibodies are directed against a complex antigen that includes lipid binding inhibitor of coagulation:  $\beta$ 2-glycoprotein I (apolipoprotein H). *Proc Natl Acad Sci (USA)* 1990;87:4120-4.
5. Keeling DM, Wilson AJG, Maekie JJ, Isenberg DA, Machin SJ. Lupus anticoagulant activity of some

- antiphospholipid antibodies against phospholipid bound  $\beta_2$ -glycoprotein I. *J Clin Pathol* 1993;46:665-7.
6. Margolius A Jr, Jackson DP, Ratnoff OD. Circulating anticoagulants. A study of 40 cases and a review of the literature. *Medicine* 1961;40:145-50.
  7. Thiagarajan P, Shapiro SS, De Marco L. Monoclonal immunoglobulin M coagulation inhibitor with phospholipid specificity. Mechanism of a lupus anticoagulant. *J Clin Invest* 1980;66:397-405.
  8. Pengo V, Thiagarajan P, Shapiro SS, Heine MJ. Immunological specificity and mechanism of action of IgG lupus anticoagulant. *Blood* 1987;70:69-76.
  9. Wahl DG, Guillemin F, de-Maistre E, Perret Guillaume C, Lecompte, Thibaut G. Meta analysis of the risk of venous thrombosis in individuals with antiphospholipid antibodies without underlying autoimmune disease or previous thrombosis. *Lupus* 1998;7:15-22.
  10. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. *J Rheumatol* 2002;29:2531-6.
  11. Kinuya K, Kakuda K, Matano S, et al. Prevalence of deep vein thrombosis in the lower limbs and the pelvis and pulmonary embolism in patients with positive antiphospholipid antibodies. *Ann Nucl Med* 2001;15:495-7.
  12. Owaidah TM, Qurashi FH, Al Nounou RM, et al. Single center review of clinicopathological characterization in 77 patients with positive lupus anticoagulant antibodies. *Hematology* 2003;8:249-57.
  13. Galli M, Luciani D, Bertolini G, Barbui T. Lupus anticoagulants are stronger risk factors of thrombosis than anticardiolipin antibodies in the antiphospholipid syndrome. A systematic review of the literature. *Blood* 2003;101:1827-32.
  14. Unger P, Plein D, Pradier O, LeClere JL. Thrombosis of aortic valve homograft associated with lupus anticoagulant antibodies. *Ann Thorac Surg* 2004;77:312-4.
  15. Granger KA, Farquharson RG. Obstetric outcome in antiphospholipid syndrome. *Lupus* 1997;6:509-13.
  16. Chakrabarti S, Bhunia C, Bhattacharya DK. The prevalence of antiphospholipid antibodies in cases of recurrent pregnancy loss. *Assoc Physicians India* 1999;47:496-8.
  17. Ogishima D, Matsumoto T, Nakamura Y, Yoshida K, Kuwabara Y. Placental pathology in systemic lupus erythematosus with antiphospholipid antibodies. *Pathol Int* 2000;50:224-9.
  18. Godeau B, Piette JC, Fromont P, Inrator L, Schaeffer A, Bierling P. Specific antiplatelet glycoprotein autoantibodies are associated with the thrombocytopenia of primary antiphospholipid syndrome. *Br J Haematol* 1997;98:873-9.
  19. Nojima J, Suehisa E, Kuratsune H, et al. High prevalence of thrombocytopenia in SLE patients with a high level of anticardiolipin antibodies combined with lupus anticoagulant. *Am J Hematol* 1998;58:55-60.
  20. Schmutz M, Revel-Vilk S, Hiraki L, Rand ML, Blanchette VS, Silverman ED. Thrombocytopenia and thromboembolism in pediatric systemic lupus erythematosus. *J Pediatr* 2003;143:666-9.
  21. Love PE, Santoro SA. Antiphospholipid antibodies : Anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and non-SLE disorders. Prevalence and clinical significance. *Ann Intern Med* 1990;112:692-8.
  22. Thiagarajan P, Pengo V, Shapiro S. The use of the dilute Russell viper venom time for the diagnosis of lupus anticoagulants. *Blood* 1986;68:869-74.
  23. Brandt JT, Triplett DA, Alving B, Scharrer I. Criteria for the diagnosis of lupus anticoagulants : an update. *Thromb Haemost* 1995;74:1185-90.
  24. Greaves M, Cahen H, Machiw SJ, Mackie I. Guidelines on the investigation and management of the antiphospholipid syndrome. *Br J Haematol* 2000;109:704-15.
  25. Atichartakarn V. Partial thromboplastin (for inosithin as platelet substitute). In: Mitrakul C, ed. *Laboratory Manual of Hemostasis* 1978:13-4.
  26. Exner T, Rickard KA, Kornenberg H. A sensitive test demonstrating lupus anticoagulant and its behavioural pattern. *Br J Haematol* 1978;40:143-51.
  27. Triplett DA, Brandt JT, Kaczor D, Schaeffer J. Labora-

- tory diagnosis of lupus inhibitors: a comparison of the tissue thromboplastin inhibitor procedure with a new platelet neutralization procedure. *Am J Clin Pathol* 1983;79:678-82.
28. Luddington R, Scales C, Baglin T. Lupus anticoagulant testing with optical end point automation. *Thromb Res* 1999;96:197-203.
29. Lawrie AS, Mackie IJ, Purdy G, Machin SJ. The sensitivity and specificity of commercial reagents for the detection of lupus anticoagulant show marked differences in performance between photo-optical and mechanical coagulometers. *Thromb Haemost* 1999;81:758-62.
30. Triplett DA. Use of the dilute Russell viper venom time (dRVVT): Its importance and pitfalls. *J Autoimmune* 2000;15:173-8.
31. Jennings I, Greaves M, Makie IJ, Kitchen S, Woods TAL, Preston FE. (on behalf of UK National External Quality Assessment Scheme of Blood Coagulation). Lupus anticoagulant testing: improvements in performance in a UK NEQAS proficiency testing exercise after dissemination of national guidelines on laboratory methods. *Br J Haematol* 2002;119:364-9
32. Tripodi A, Biasiolo A, Chantarangkul V, Pengo V. Lupus anticoagulant (LA) testing: Performance of clinical laboratories assessed by a national survey using lyophilized affinity-purified immunoglobulin with LA activity. *Clin Chem* 2003;49:1608-14.

## Comparison of the Dilute Russell's Viper Venom Time by A Conventional Method with an Automated Kit Assay for the Detection of Lupus Anticoagulants

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**บทคัดย่อ:** Lupus anticoagulants (LA) เป็นกลุ่มของภูมิคุ้มกันต้านทานที่เกิดขึ้นภายหลังซึ่งมีคุณสมบัติเป็น anti-phospholipid จึงสามารถรบกวนการตรวจการแข็งตัวของเลือดที่ต้องอาศัย phospholipid ในขบวนการ ผู้ป่วยที่มี LA จะมีความเสี่ยงในการเกิดหลอดเลือดอุดตันเพิ่มขึ้น การตรวจหา LA ที่ใช้กันทั่วไปอย่างกว้างขวางในปัจจุบันได้แก่ การทดสอบ dilute Russell's viper venom time (dRVVT) ซึ่งสามารถหาซื้อน้ำยาสำเร็จรูปได้ในท้องตลาด การศึกษาในครั้งนี้ต้องการเปรียบเทียบดูว่าวิธีการดั้งเดิมสำหรับการทดสอบ dRVVT ซึ่งใช้น้ำยาที่เตรียมเองและใช้เครื่องมือกึ่งอัตโนมัติ (650 MLA) กับวิธีที่ใช้น้ำยาสำเร็จรูปซึ่งใช้เครื่องมืออัตโนมัติ (ALC 200) แต่ละอย่างจะให้ความไวและความจำเพาะต่อการตรวจหา LA แตกต่างกันอย่างไร จากการตรวจวิเคราะห์ตัวอย่างเลือดจากผู้ป่วยที่มี LA และจากคนปกติที่ไม่มี LA อย่างละ 30 ราย จากตัวอย่างเลือดของผู้ป่วยที่มี LA พบว่าวิธีที่ใช้น้ำยาสำเร็จรูปสามารถตรวจพบ LA ได้ 15 ราย ขณะที่วิธีที่ใช้น้ำยาที่เตรียมเองสามารถตรวจพบ LA ได้เพียง 2 ราย สำหรับกลุ่มของคนปกติที่ไม่มี LA พบผลบวก 2 รายโดยวิธีที่ใช้น้ำยาสำเร็จรูปและผลลบทั้งหมดโดยวิธีที่ใช้น้ำยาที่เตรียมเอง ความไวและความจำเพาะของวิธีที่ใช้น้ำยาสำเร็จรูปคือร้อยละ 6.67 และร้อยละ 100 ตามลำดับ ขณะที่ความไวและความจำเพาะของน้ำยาสำเร็จรูปคือร้อยละ 50 และร้อยละ 93.3 ตามลำดับ ความแตกต่างในความไวของการตรวจสอบด้วยวิธีการทั้งสองแบบพบว่ามีนัยสำคัญทางสถิติ ( $p = 0.004$ )

**Key Words :** ● Russell's viper venom time ● Lupus anticoagulants

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