Venous thromboembolism (VTE) is the most prevalent cardiovascular disease in the world after myocardial infarction and stroke (1). VTE is silent but still potentially fatal disease which includes, deep vein thrombosis (DVT) and pulmonary embolism (PE) (2). The risk of VTE in Indian population (53.6%) is nearly similar to that of the global population (51.8%) (3).

Unfractionated heparin (UFH) and low molecular weight heparins (LMWHs) are the cornerstones in treatment and prophylaxis of thrombosis for more than 65 years (4). Prophylaxis for VTE by using pharmacologic agents like heparin (UFH), LMWHs and direct thrombin inhibitors (DTIs) reduces the relative risk of VTE by 45-63% and 60% in hospitalized medical and general surgery patients, respectively, as compared with no prophylaxis (4-8). As it requires long-term therapy of heparin, for the treatment of VTE, it causes a number of side effects, such as thrombocytopenia, bleeding, changes in lipid metabolism and osteoporosis (9).

To overcome these problems, newer anticoagulant drugs are required. Sulfated polysaccharides (SPS) are abundantly present in some of the marine organisms which exhibit anticoagulant and antithrombotic activities (10, 11). Green marine algae Codium dwarkense Borgesen is one of them which is commonly found on Indian waters (12). Bioassay-guided purification of sulfated polysaccharides from Codium dwarkense Borgesen, yielded two products, which contained arabinan sulfate and arabinogalactan sulfate. An in vitro study showed...
that the product containing arabinan sulfate exhibited stronger anticoagulant activity than product containing arabinogalactan sulfate (13). However, up to our best knowledge, there is no \textit{in vivo} study to support anticoagulant and antithrombotic activities of SPS obtained from \textit{Codium dwarkense} Borgesen. So, the present \textit{in vivo} study was planned to evaluate an anticoagulant effect of sulfated polysaccharides, obtain from \textit{Codium dwarkense} Borgesen in Wistar rats.

\textbf{MATERIALS AND METHODS}

\textbf{Materials}

Sulfated polysaccharides from \textit{Codium dwarkense} Borgesen was provided by the Central Salt and Marine Research Institute (CSMCRI), Bhavnagar, Gujarat. SPS was dissolved in distilled water and 50 mg/mL solution was prepared before dosing. \(\kappa\)-Carrageenan was purchased from Sigma Chemical Company, St. Louis, MO, USA; ether from Rachana Ether India Pvt. Ltd., Nasik, Maharashtra and heparin from Gland Pharma Ltd., Hyderabad, India. The main equipments used in this study included ELISA reader for FDP and D-Dimer ELISA kit (Washington St., Concordia, KS 66901, USA) and fibrinogen kit (Peary Court, Novi, MI 48377, USA).

\textbf{Animals}

Wistar albino rats (250 ± 50 g) of either sex and Swiss albino mice (25 to 30 g) of females were procured from central animal house of the institute. They were housed in standard transparent polypropylene cages and kept under controlled room temperature (25 ± 2°C) in a 12 h light-dark cycle. The animals were given standard laboratory diet and water \textit{ad libitum}. The animals were allowed to acclimatize to the laboratory conditions at least 7 days before starting of the experiments. The animal handling was performed according to Good Laboratory Practice (GLP) guidelines. Present study was started after approval from Institutional Animal Ethics Committee (IAEC), of Government Medical College, Bhavnagar, Gujarat, India [Approval No: IAEC 34/2014, dated 08/02/2014].

\textbf{Study design}

Before starting the study, an acute toxicity study was performed according to, “organization for economic co-operative development (OECD)” guidelines no. 423. Gradually increasing doses of 5, 50, 300, 1000 and 2000 mg/kg of sulfated polysaccharide was administered orally in female mice (3 animals for each dose). Mice were closely observed for development of signs of toxicity and mortality for 14 days. Sulfated polysaccharide was found safe.
Evaluation of anticoagulant effect of sulfated polysaccharide... 989

up to 2000 mg/kg. Two different doses 200 and 400 mg/kg were selected for evaluation of anticoagulant activity.

After that, forty eight Wistar albino rats (250 ± 50 g) were randomly divided (Computer generated software – Rando software) into six groups (n = 8 for each group). A single dose of κ-carrageenan intravenously in rat tail vein was given at pre-decided time in all the study groups for producing hypercoagulable state. The study groups were as follows: Group 1 (Disease control): rats received 1 mL distilled water orally for 3 days after injecting κ-carrageenan. Group 2 (Active control): received 300 units/kg heparin subcutaneously for 3 days after injecting κ-carrageenan. Group 3 (Treatment low dose): received 200 mg/kg sulfated polysaccharide orally for 3 days after injecting κ-carrageenan. Group 4 (Treatment high dose): received 400 mg/kg sulfated polysaccharide orally for 3 days after injecting κ-carrageenan. Group 5 (Preventive low dose): received 200 mg/kg sulfated polysaccharide orally for 3 days followed by single dose of κ-carrageenan on last day. Group 6 (Preventive high dose): received 400 mg/kg sulfated polysaccharide orally for 3 days followed by single dose of κ-carrageenan on last day.

Study procedure and outcome measures

Induction of thrombosis

κ-Carrageenan (dissolved in normal saline) (14) was injected intravenously in the dose of 3 mg/kg body weight of rat to produce thrombosis. In restrained rat, wax thread was tied at root of tail. Xylene was applied over the site to dilate the vein. After 10 min of injection, thread was removed. Animals were observed for gross finding of thrombosis in rat tail from 5 minutes to 6 hours of post injection period. Length of tail thrombosis was measured.

Serological parameters

Rats were anesthetized with inhalational ether anaesthesia. Blood samples were collected at 0 (baseline), 24, 48 and 72 h after κ-carrageenan injection alternatively from right and left retro-orbital plexus. All the samples collected into citrate vacutate and EDTA vacutate. They were sent to pathology laboratory for Prothrombin Time (PT), International Normalized Ratio (INR), activated Partial Thromboplastin Time (aPTT) and platelets count analysis. ELISA was used to determine the levels of the fibrinogen, fibrin/fibrinogen degradation products (FDPs) and D-dimer, which are sensitive indices of fibrinolytic activity in microbiology laboratory. The standard curve for FDP, FIB and D-Dimer was created by using curve expert professional software version 2.2 and from the standard curve, concentration of FDP, FIB and D-Dimer were calculated. As samples were diluted up to 1 : 2000, the concentration reading from the standard curve was multiplied by dilution factor (2000).
Histopathological analysis

After 72 h, rats were sacrificed after giving injection of ketamine (75 mg/kg; intraperitoneally) and injection of xylazine (10 mg/kg; intraperitoneally). Lung, liver, mesentery were removed and kept in formaldehyde (10% v/v) solution for 24 h. Five mm sections were taken and processed in a series of graded acetone and xylene, embedded in paraffin wax. Five µm thin sections were taken and stained with hematoxylin-eosin (H & E) and evaluated under optical light microscope for formation of microthrombi in lung, liver and mesentery. All slides were coded and blinded. Analysis was done blindly by the pathologist from our institute without knowledge of treatment plan.

Histological results were graded as following:

0 - no lesions; 1 - minimal lesions (individual or a few necrotic cells); 2 - mild lesions (10–25% necrotic cells or mild diffuse degenerative lesions); 3 - moderate lesions (25–40% necrotic or degenerative cells); 4 - marked lesions (40–50% necrotic or degenerative cells); 5 - severe lesions (more than 50% necrotic or degenerative cells). The second scale is based on the first scale, but simply considers sections with scores = 3 as significant liver lesions (15).

For lung, leukocyte infiltration was evaluated to determine the severity of alveolar inflammation. 0. no extravascular leukocytes; 1. < 10 leukocytes; 2. 10–45 leukocytes; 3. > 45 leukocytes. The average of the numbers was used for comparison (16).

Microthrombi were calculated in 10 low power microscopic fields in liver and lung and in 5 low power microscopic fields in mesentery.

Statistical analysis

All the parameters were expressed as the mean ± standard error of mean (S.E.M.). Data were checked for normal distribution using the Kolmogorov-Smirnov test.

For intragroup comparison, parametric data were analyzed by repeated measures ANOVA followed by Tukey’s multiple comparison test and non-parametric data were analyzed by Friedman test followed by Dunn’s multiple comparison test. For intergroup comparison, parametric data were analyzed by one way ANOVA followed by Tukey’s multiple comparison test and non-parametric data were analyzed by Kruskal Wallis test followed by Dunn’s multiple comparison test using GraphPad InStat (version 3.00, GraphPad Software, California USA). A p value < 0.05 was considered as statistically significant.

RESULTS

Sulfated polysaccharide was found safe up to 2000 mg/kg. Two different doses 200 and 400 mg/kg were selected for evaluation of anticoagulant activity. One animal in preventive high dose group was expired due to study related procedure. Injection of κ-carrageenan single dose in dorsal rat tail vein produced visible thrombosis maximum up to 11 cm. Figure 1 shows production of gross thrombosis in dorsal rat tail vein. As shown in Table 1, administration of SPS in high dose as a treatment and in low as well as high dose as a preventive therapy significantly reduced the gross thrombosis size in dorsal rat tail vein as compared to disease control group after 72 hour of injecting κ-carrageenan.

As shown in Table 2, κ-carrageenan significantly decreased PT at 48 h in disease control group (p < 0.05). In both the treatment groups SPS significantly restored the altered PT caused by κ-carrageenan, at 72 h (p < 0.05). Whereas in prophylaxis groups SPS significantly prevented the alteration of PT as compared to the baseline. At 72 h, PT was found higher in all the study groups as compared to disease control group. However, the statistical significant difference was found between disease control group and active control group.

International Normalised Ratio (INR) of all study groups was comparable at baseline (Table 2). INR was significantly decreased at 24 h in disease control group after injecting κ-carrageenan (p < 0.05). Altered INR was significantly restored in both the SPS treatment groups at 72 h. Whereas, in the

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group 1 (n = 8)</th>
<th>Group 2 (n = 8)</th>
<th>Group 3 (n = 8)</th>
<th>Group 4 (n = 8)</th>
<th>Group 5 (n = 8)</th>
<th>Group 6 (n = 7)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis (mm)</td>
<td>18.3 ± 8.4</td>
<td>8.4 ± 7.4</td>
<td>22.1 ± 13.4</td>
<td>7.4 ± 6.8^a</td>
<td>1.6 ± 1.5^a</td>
<td>1.4 ± 1.0^a</td>
<td>0.01</td>
</tr>
</tbody>
</table>

All values are expressed as the mean ± SEM. ^p < 0.05 as compared with DC group by Kruskal-Wallis test followed by Dunn's multiple comparison test; (DC - Disease control, AC - Active control, TLD - Treatment low dose, THD - Treatment high dose, PLD - Preventive low dose, PHD - Preventive high dose).
### Table 2. Comparison of coagulation and fibrinolytic parameters in experimental groups.

<table>
<thead>
<tr>
<th>Study groups</th>
<th>Duration (hours)</th>
<th>PT (seconds)</th>
<th>INR</th>
<th>aPTT (seconds)</th>
<th>Platelet counts (lacs/cumm)</th>
<th>Fibrinogen (ng/mL)</th>
<th>FDP (µg/mL)</th>
<th>D-Dimer (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 DC</strong> (n = 8)</td>
<td>0</td>
<td>28.91 ± 1.01</td>
<td>2.32 ± 0.09</td>
<td>60.50 ± 1.28</td>
<td>7.91 ± 0.30</td>
<td>80.49 ± 4.40</td>
<td>5.10 ± 0.85</td>
<td>1.34 ± 0.13</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>26.41 ± 0.73</td>
<td>2.06 ± 0.06</td>
<td>54.03 ± 1.72</td>
<td>9.14 ± 0.61</td>
<td>94.79 ± 18.27</td>
<td>1.29 ± 0.67</td>
<td>2.52 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>24.25 ± 0.68</td>
<td>1.87 ± 0.07</td>
<td>52.00 ± 1.66</td>
<td>9.46 ± 0.89</td>
<td>66.12 ± 4.64</td>
<td>5.77 ± 0.92</td>
<td>2.52 ± 0.12</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>24.48 ± 0.78</td>
<td>1.91 ± 0.07</td>
<td>49.63 ± 1.31</td>
<td>11.87 ± 0.96</td>
<td>114.18 ± 15.00</td>
<td>6.97 ± 0.27</td>
<td>2.44 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>28.03 ± 0.75</td>
<td>2.16 ± 0.08</td>
<td>54.00 ± 1.27</td>
<td>7.85 ± 0.26</td>
<td>103.31 ± 15.46</td>
<td>5.86 ± 0.47</td>
<td>1.10 ± 0.13</td>
</tr>
<tr>
<td><strong>Group 2 AC</strong> (n = 8)</td>
<td>24</td>
<td>27.15 ± 1.41</td>
<td>2.14 ± 0.13</td>
<td>50.53 ± 2.17</td>
<td>7.42 ± 0.39</td>
<td>99.27 ± 17.12</td>
<td>5.02 ± 0.53</td>
<td>1.87 ± 0.16</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>28.16 ± 1.09</td>
<td>2.24 ± 0.10</td>
<td>61.85 ± 2.09</td>
<td>6.24 ± 0.58</td>
<td>98.16 ± 15.84</td>
<td>4.05 ± 0.47</td>
<td>1.00 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>30.89 ± 1.36</td>
<td>2.50 ± 0.13</td>
<td>64.05 ± 2.69</td>
<td>5.05 ± 0.73</td>
<td>62.56 ± 3.84</td>
<td>2.64 ± 0.50</td>
<td>2.17 ± 0.14</td>
</tr>
<tr>
<td><strong>Group 3 TLD</strong> (n = 8)</td>
<td>0</td>
<td>25.53 ± 0.93</td>
<td>1.98 ± 0.07</td>
<td>55.09 ± 2.32</td>
<td>6.55 ± 0.24</td>
<td>118.51 ± 23.43</td>
<td>6.48 ± 0.58</td>
<td>1.15 ± 0.18</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>25.03 ± 1.22</td>
<td>1.99 ± 0.11</td>
<td>57.23 ± 2.64</td>
<td>3.51 ± 0.38</td>
<td>96.30 ± 11.15</td>
<td>6.59 ± 0.62</td>
<td>2.22 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>27.11 ± 0.97</td>
<td>2.14 ± 0.09</td>
<td>58.78 ± 3.62</td>
<td>3.79 ± 0.36</td>
<td>102.93 ± 15.03</td>
<td>6.61 ± 0.43</td>
<td>2.21 ± 0.09</td>
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<td></td>
<td>72</td>
<td>28.76 ± 0.95</td>
<td>2.30 ± 0.08</td>
<td>59.99 ± 3.01</td>
<td>4.40 ± 0.23</td>
<td>56.40 ± 9.65</td>
<td>6.56 ± 0.29</td>
<td>2.27 ± 0.11</td>
</tr>
<tr>
<td><strong>Group 4 THD</strong> (n=8)</td>
<td>0</td>
<td>26.04 ± 1.17</td>
<td>2.06 ± 0.11</td>
<td>52.68 ± 1.17</td>
<td>6.53 ± 0.38</td>
<td>141.63 ± 13.88</td>
<td>4.90 ± 0.44</td>
<td>1.19 ± 0.10</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>25.78 ± 0.87</td>
<td>2.03 ± 0.08</td>
<td>57.01 ± 1.59</td>
<td>4.31 ± 0.27</td>
<td>76.05 ± 5.53</td>
<td>5.40 ± 0.27</td>
<td>1.33 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>27.61 ± 0.91</td>
<td>2.19 ± 0.08</td>
<td>58.19 ± 0.77</td>
<td>4.56 ± 0.36</td>
<td>82.75 ± 6.18</td>
<td>5.81 ± 0.60</td>
<td>2.62 ± 0.09</td>
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<tr>
<td></td>
<td>72</td>
<td>28.65 ± 1.76</td>
<td>2.27 ± 0.16</td>
<td>60.30 ± 1.38</td>
<td>4.96 ± 0.38</td>
<td>84.75 ± 12.76</td>
<td>5.86 ± 0.35</td>
<td>2.55 ± 0.86</td>
</tr>
<tr>
<td><strong>Group 5 PLD</strong> (n=8)</td>
<td>0</td>
<td>25.55 ± 0.86</td>
<td>2.00 ± 0.08</td>
<td>52.95 ± 2.74</td>
<td>7.13 ± 0.52</td>
<td>116.04 ± 11.19</td>
<td>4.53 ± 0.66</td>
<td>1.25 ± 0.16</td>
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<td>2.11 ± 0.08</td>
<td>53.65 ± 1.63</td>
<td>6.47 ± 0.40</td>
<td>84.32 ± 5.40</td>
<td>3.65 ± 0.44</td>
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<td>26.34 ± 0.62</td>
<td>2.08 ± 0.05</td>
<td>48.96 ± 2.11</td>
<td>5.68 ± 0.38</td>
<td>101.74 ± 10.16</td>
<td>6.47 ± 0.69</td>
<td>1.36 ± 0.17</td>
</tr>
<tr>
<td><strong>Group 6 PHD</strong> (n = 7)</td>
<td>0</td>
<td>25.96 ± 0.61</td>
<td>2.00 ± 0.05</td>
<td>53.74 ± 2.80</td>
<td>6.71 ± 0.36</td>
<td>127.37 ± 19.75</td>
<td>4.73 ± 0.40</td>
<td>1.42 ± 0.26</td>
</tr>
<tr>
<td></td>
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<td>24.93 ± 1.35</td>
<td>1.86 ± 0.07</td>
<td>55.60 ± 2.75</td>
<td>6.07 ± 0.52</td>
<td>138.6 ± 16.46</td>
<td>4.45 ± 0.38</td>
<td>1.50 ± 0.31</td>
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<td>26.03 ± 1.16</td>
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<td>5.83 ± 0.37</td>
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<td>1.93 ± 0.09</td>
<td>55.54 ± 1.84</td>
<td>6.40 ± 0.59</td>
<td>109.86 ± 11.08</td>
<td>4.65 ± 0.20</td>
<td>0.87 ± 0.03</td>
</tr>
</tbody>
</table>

All values are expressed as the mean ± SEM. *p < 0.05 as compared with 0 hour value by repeated measures ANOVA followed by Dunnett multiple comparison tests; **p < 0.05 as compared with 0 hour value by Friedman test followed by Dunn’s multiple comparison tests; "p value for repeated measures ANOVA; "p value for Friedman test; "p < 0.05 as compared with DC group by one way ANOVA followed by Dunnett multiple comparison test; "p < 0.05 as compared with DC group by Kruskal-Wallis test followed by Dunn’s multiple comparison test; "p value for one way ANOVA; "p value for Kruskal-Wallis test; (DC - Disease control, AC - Active control, TLD - Treatment low dose, THD - Treatment high dose, PLD - Preventive low dose, PHD - Preventive high dose).
preventive groups, INR was not significantly altered at 72 h as compared to baseline.

After injecting κ-carrageenan intravenously, aPTT was significantly decreasing in disease control group from 24 to 72 h as compared to baseline value (p < 0.05; Table 2). At 72 h, in both doses of treatment group and high dose preventive group the altered aPTT was restored. However, statistical significance was achieved in high dose treatment with SPS (p < 0.05).

Single dose of intravenous injection of κ-carrageenan produced statistically significant increase in platelet counts at 72 h as compared to 0 h (p < 0.05; Table 2). At 72 h, two different doses of SPS as treatment and preventive therapy restored the altered platelet counts caused by κ-carrageenan.

Fibrinogen level was non-significantly increased in disease control group at 72 h after injecting κ-carrageenan in rat tail vein (Table 2). SPS and heparin administration prevented the

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**Figure 3.** Histopathological images of liver sections after hematoxylin-eosin staining under light microscope (10x): (a) disease control (b) active control (c) treatment low dose (d) treatment high dose (e) preventive- low dose (f) preventive- high dose. In a: black arrow indicates necrosis and white arrow indicates degeneration and microthrombi. Other arrows (in b-f) indicate normal hepatocyte arrangement.

**Figure 4.** Histopathological images of mesentery sections after haematoxylin-eosin staining under light microscope (x10): (a) disease control (b) active control (c) treatment low dose (d) treatment high dose (e) preventive- low dose (f) preventive- high dose. In a: black arrow indicates microthrombi and white arrow indicate capillary hemorrhage. Grey arrows indicate normal mesenteric structure.
change in fibrinogen level caused by κ-carrageenan.

κ-Carrageenan non-significantly increased the FDP and significantly increased the D-Dimer level in disease control group (Table 2). Treatment and preventive therapy of SPS did not show any effect on FDP and D-Dimer level. Effect of SPS on fibrinogen and D-Dimer levels are shown in Table 2.

As shown in Table 3, number of microthrombi in lung, liver and mesentery were significantly reduced due to SPS administration as compared to disease control group. Figures 2, 3 and 4 show the histopathological changes in lung, liver and mesentery, respectively, in various study groups.

**DISCUSSION**

The present study showed anticoagulant effect of SPS from *Codium dwarkense* Børgeesen in hypercoagulable Wistar albino rats.

Carrageenan is straight chained sulfur containing macromolecular polysaccharides composed of repeating units of D-galactose and 3, 6-anhydro-D-galactose. κ-Carrageenan is commonly used for producing tissue inflammation and tail thrombosis in experimental models. κ-Carrageenan can cause local vascular inflammation and endothelial cell injury through releasing inflammatory factors, which may lead to the formation of thrombus (17). Another mechanism for the thrombogenic activity of κ-carrageenan is an activation of Hageman factor (factor XII) that is followed by intravascular coagulation (18, 19). In present study, intravenous injection of κ-carrageenan produced significant thrombosis evidenced by gross visible thrombosis, altered coagulation parameters along with histopathological findings.

In present study, SPS significantly restored altered coagulation parameters (PT, INR, aPTT, Platelet count and Fibrinogen level) without affecting fibrinolytic parameters (FDP and D-Dimer). PT is a sensitive screening test for the extrinsic coagulation pathway while aPTT reflects the integrity of the intrinsic pathways of coagulation. Extrinsic coagulation pathway gets activated on tissue trauma that liberates tissue factor (factor III) into the blood which in turn activates factor VII. Activated factor VII ultimately activates factor X and common pathway of coagulation (20). Interference in extrinsic pathway prolongs the PT whereas, disturbances in intrinsic pathway prolongs the aPTT. When common pathway is affected, both PT and aPTT get prolonged. In our study, administration of SPS resulted into the restoration of both PT and aPTT that suggests SPS may have its anticoagulant effect through a common pathway of coagulation. During the coagulation process, activation and recruitment of platelets leads to increased platelet count. However, administration of SPS either reduced or restored the increased platelet count caused by κ-carrageenan. This finding suggests that SPS may have its effect on activation and recruitment of platelets during the coagulation process. Effect of SPS on fibrinogen level and other fibrinolytic parameters also suggests its anticoagulant effect through a common pathway of coagulation. Our *in vivo* study findings are similar to the *in vitro* findings of Shanmugam et al. (21). Administration of SPS both as a treatment and preventive therapy reduced the number of microthrombi along
with less histopathology damage in lung, liver and mesentery. Findings of histopathology parameters further support the anticoagulant effect of SPS.

We used heparin as an active control drug which is a highly sulfated mucopolysaccharide. It produce the anticoagulant effect by catalyzing antithrombin mediated inhibition of coagulation factors thrombin (factor IIa) and activated factors Xa, IXa, XIa and XIIa (22). In present study, heparin has significantly prolonged aPTT and restored PT. In low concentration, heparin prolongs aPTT without affecting PT, whereas, in high concentration it prolongs both. In present study, we used two different doses of SPS (200 mg/kg and 400 mg/kg) and we did not find significant differences of these two selected doses on coagulation parameters. It suggests that there is no dose dependent anticoagulant effect of SPS.

In present study, the extract control group was not performed due to limited amount of SPS available. Due to limited resources available, plasma levels of clotting factors were not measured.

CONCLUSION

This study shows that sulfated polysaccharides extracted from *Codium dwarkense* Borgesen in doses of 200 mg/kg and 400 mg/kg showed an anticoagulant activity in hypercoagulable Wistar albino rats. The anticoagulant activity was evidenced by restoration of altered coagulation parameters and by reduction in the number of micro-thrombi along with less structural damage in histopathology of lung, liver and mesentery. Further research is required to gain closer insights into the exact mechanism that support an anticoagulant effect of SPS and its dose dependent action before conducting researches in human beings.

Conflict of Interest: None declared.

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REFERENCES


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