Hyaluronic Acid

V. On the Molecular Shape of Potassium Hyaluronate *

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Corresponding values of specific viscosities of solutions containing 1 mg potassium hyaluronate in 1 ml are plotted against experimentally determined molecular weights. The graph is in agreement with Staudinger’s relation which is valid for flexible linear molecules.

It was realized rather early that a relation must exist between the symmetry of suspended macromolecules and the viscosity of a colloid solution $^1,^2$. The macromolecules are turned and twisted in Brownian motions with the consequence that the molecules appear to occupy a larger volume than they actually do. The streamlines of flow are interrupted on account of the twisting of the particles, and an additional expenditure of energy is needed to maintain a given velocity of flow, which is manifested as an increase in the viscosity.

The relation between particle symmetry and viscosity is complicated and has been treated theoretically by a number of workers $^3,^4,^5,^6,^7$. Staudinger $^8$ investigated the problem from an experimental point of view using a series of long-chain hydrocarbons dissolved in inert solvents. He found that for dilute solutions, the specific viscosity, $\eta_{sp}$

$$\left( \eta_{sp} = \frac{\eta_{sol}}{\eta_{solv}} - 1 \right)$$

is a function of the number of submolecules ("Grundmoleküle", e.g. CH$_2$ groups in a paraffin chain) contained in the chain — the degree of polymerisation. According to Staudinger the equation $\eta_{sp} = K \cdot P \cdot c$ is valid for randomly coiled flexible long-chain molecules. In this formula $K$ is a constant for a given series of compounds, $P$ is the degree of polymerisation, and $c$ is the concentration by weight.


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Fig. 1. The graph shows the relation between the specific viscosity (ordinates), and the product of molecular weight and concentration by weight (abscissae).

In the experiments to be reported here the degree of polymerisation \( P \) is replaced by the molecular weight, and the Staudinger equation is thus converted to: \( \eta_p = K \cdot M \cdot c \). The chemical characteristics of most specimens of potassium hyaluronate are given in recent papers by the author. The preparations of potassium hyaluronate are of different origin: human umbilical cords, bovine synovial fluid, human pseudomucinous ovarian cysts, and the endolymph of the labyrinths of sharks. The methods of isolation have also been varied. The relative viscosities at a concentration of 1 g/1, and at the temperature of 20.0°C are determined by a Kvorning and Dalggaard-Mikkelsen viscosimeter, and the molecular weights by an inverted microosmometer recently constructed by J. A. Christiansen and the author. As seen from Fig. 1 the experimental data fit in with the Staudinger formula, and thus it is reasonable to conclude that the molecular shape of hyaluronic acid is of the flexible long-chain type.

Attention is drawn to the fact, that opinions are still at variance as regards the validity of Staudinger's viscosity rule, but it is of special interest to the present investigation that a great number of cellulose derivatives conform closely to this empiric rule. On account of the great constitutive similarity between hyaluronic acid and various cellulose derivatives we may believe in the validity of Staudinger's rule also as regards hyaluronic acid.

Another observation which favours the assumption of a long-chain shape for the molecules of hyaluronic acid is the fact that our experimental data do not fit into the well-known expression of Einstein: \( \eta = \eta_0 \left(1 + 2.5 \Phi \right) \), which
Table 1. Relation between specific viscosity and molecular weight of different preparations of potassium hyaluronate.

<table>
<thead>
<tr>
<th>Relative viscosity</th>
<th>Specific viscosity</th>
<th>Molecular weight ( \times 10^4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.61 (^1)</td>
<td>2.61</td>
<td>3.42</td>
</tr>
<tr>
<td>4.93 (^1)</td>
<td>3.93</td>
<td>3.75</td>
</tr>
<tr>
<td>5.46 (^1)</td>
<td>4.46</td>
<td>3.16</td>
</tr>
<tr>
<td>5.75 (^2)</td>
<td>4.75</td>
<td>3.67</td>
</tr>
<tr>
<td>6.90 (^3)</td>
<td>5.99</td>
<td>4.12</td>
</tr>
<tr>
<td>6.40 (^3)</td>
<td>5.40</td>
<td>4.53</td>
</tr>
<tr>
<td>10.04 (^3)</td>
<td>9.04</td>
<td>4.61</td>
</tr>
<tr>
<td>11.80 (^1)</td>
<td>10.80</td>
<td>5.17</td>
</tr>
<tr>
<td>11.91 (^1)</td>
<td>10.91</td>
<td>5.30</td>
</tr>
<tr>
<td>12.12 (^1)</td>
<td>11.12</td>
<td>5.27</td>
</tr>
<tr>
<td>12.19 (^1)</td>
<td>11.19</td>
<td>5.16</td>
</tr>
<tr>
<td>16.10 (^3)</td>
<td>15.10</td>
<td>6.11</td>
</tr>
<tr>
<td>24.24 (^3)</td>
<td>23.24</td>
<td>7.89</td>
</tr>
<tr>
<td>42.81 (^3)</td>
<td>41.81</td>
<td>12.42</td>
</tr>
<tr>
<td>68.46 (^1)</td>
<td>67.46</td>
<td>17.50</td>
</tr>
</tbody>
</table>

1) Preparations from human umbilical cords
2) ... bovine synovial fluid
3) ... human ovarian cysts
4) ... endolymph of sharks.

is based upon the assumption of spherical rigid particles (\( \Phi \) is the volume fraction occupied by the dispersed particles). We get according to Einstein

\[
\eta/\eta_0 - 1 = K_{\text{Einstein}} \cdot c
\]

and according to Staudinger

\[
\eta/\eta_0 - 1 = K_{\text{Staudinger}} \cdot M \cdot c
\]

The fundamental difference between these expressions is evident.

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**REFERENCES**


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