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This Week's Citation Classic™

Flodin P & Killander J. Fractionation of human-serum proteins by gel filtration.
Biochim. Biophys. Acta 63:403-10, 1962.
[Research Laboratory, AB Pharmacia, and Department of Clinical Chemistry, University of Uppsala, Sweden]

In this paper, the preparative separation of human serum proteins according to molecular size is reported. A new type of dextran gel, Sephadex G-200, was used and the separated fractions analyzed by paper electrophoresis, immunoelectrophoresis, gel diffusion, serological titration, and density gradient ultracentrifugation. [The *SCI*® indicates that this paper has been cited in over 625 publications since 1962.]

Per Flodin
Department of Polymer Technology
Chalmers University of Technology
S-412 96 Göteborg
Sweden

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"The first Sephadex types developed separated only low molecular weight proteins and not those of a size corresponding to the blood serum proteins. It was a disappointment since our interests were pretty much focused on preparative separation of biological macromolecules and primarily of proteins. The reason was that the first gels were made in blocks which were subsequently ground to a size suitable for column packing. The irregular form caused high resistance to flow and compression of the softer gels with low cross-linking density. This limited the use of the gels to a relatively low molecular weight region.

"In 1960, a method to make gels in spherical bead form was developed in my laboratory.[1,2] The beads made it possible to push the limit of separation upward to include, e.g., the blood proteins. At that time, Johan Killander and I decided to look into the possibility of fractionating and identifying serum protein components with the new G-200 gel type. His background in clinical chemistry matched my separation experience and very soon interesting results began to appear.

"Early in 1962, I accepted a job in another company. Before leaving Uppsala, I wanted to obtain a PhD and was therefore in a hurry to write a thesis. It was finished during the spring and the present paper was part of it. Parenthetically, it may be worth mentioning that the summary of the thesis was a monograph,[2] 12,000 copies of which were sent on request to interested scientists during the following year.

"The method we described provided a way to make preparative fractionations of serum proteins with simple equipment and essentially without denaturation. The latter was shown by the immunological tests we applied. Since a vast number of scientists, for obvious reasons, study blood serum proteins, we expected a considerable interest. To judge from the number of reprints I still have in my possession, other papers in the gel filtration series were more popular. However, the number of citations seems to confirm our earlier belief.

"The paper has no doubt contributed to the awards I have received for the gel filtration method and the Sephadex gels. In 1963, I received, together with Jerker Porath, the Arrhenius medal of the Swedish Chemical Society; in 1968, the gold medal of the Swedish Academy of Engineering Sciences; and in 1979, the Tswett medal in chromatography.

"A recent comprehensive review of the subject can be found in *Gel Chromatography*."[3]

1. **Flodin P.** *Process for preparing hydrophilic copolymerization and product obtained thereby.* U.S. patent 3,208,994, 28 September 1965.
2. ----------. *Dextran gels and their applications in gel filtration.* Uppsala, Sweden: Pharmacia AB, 1962. 85 p.
3. **Kremmer T & Boross L.** *Gel chromatography: theory, methodology, applications.* London: Wiley, 1979. 298 p.