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大型蛋白质色谱柱及凝胶介质的综述

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摘要　The first dedicated protein chromatography media were introduced during the 1950s and
1960s. There was an early awareness of the possibility of using these for production applications within the biopharmaceutical industry. However, the crucial limitation was the fact that those media that were most compatible with proteins lent themselves less favourably to scaling-up. The problems were primarily physical. Thus the fibrous cellulose media showed bed cracking tendencies and the bead shaped polyacrylamide, dextran, and agarose gel media, then available,were too soft to stand the hydrodynamic forces acting in large columns, leading to bed compaction and increased pressure drop. At the time, the best solution to the latter problem, after a number of intermediary solutions were tried, was the introduction of the stacked column concept in which several short column segments were connected by small bore tubing, thus reducing the force acting on the particles in each bed compartment. However, the ultimate remedy, the introduction of chromatographic matrices that combine the desired features of adequate rigidity,macroporosity, biocompatibility, chemical stability (for CIP and SIP) and derivatizability, did not occur until the middle of the 1980s when adequately cross-linked agarose gel media such as Sepharose(R) Fast Flow
were made available. The paper also recognizes the many attempts made during the past 50 years to develop continous chromatography columns. Most of the designs are based on an annular bed or on an array of annularly arranged parallel columns continuously fed with samples in a cyclic manner. The introduction of media and columns for expanded bed adsorption followed a demand for fewer purification steps and shorter process times. In recent years, columns have been introduced that allow packing and repacking without needing
to open the column. The review provides an historical account of the developments that have led to the present state-of-the-art both regarding large diameter columns and gel media intended for industrial applications of protein chromatography and also discusses the current trends that point to possible future applications.

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The Development of Gel Media and Columns for Large-Scale Chromatography of Proteins, a Historical Review

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Abstract The first dedicated protein chromatography media were introduced during the 1950s and 1960s. There was an early awareness of the possibility of using these for production applications within the biopharmaceutical industry. However, the crucial limitation was the fact that those media that were most compatible with proteins lent themselves less favourably to scaling-up. The problems were primarily physical. Thus the fibrous cellulose media showed bed cracking tendencies and the bead shaped polyacrylamide, dextran, and agarose gel media, then available,were too soft to stand the hydrodynamic forces acting in large columns, leading to bed compaction and increased pressure drop. At the time, the best solution to the latter problem, after a number of intermediary solutions were tried, was the introduction of the stacked column concept in which several short column segments were connected by small bore tubing, thus reducing the force acting on the particles in each bed compartment. However, the ultimate remedy, the introduction of chromatographic matrices that combine the desired features of adequate rigidity,macroporosity, biocompatibility,

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Key words chromatography; protein; review

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