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Preparative Chromatography: An Appropriate and Versatile Solution for the Purification of APIs from early Stage to Commercial-Scale.

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Preparative chromatography is attracting more and more interest from fine chemical and pharmaceutical industries. This attractiveness is linked to the continuous improvement of the solutions proposed to get a cheap and efficient process for the purification of the targeted molecules.

This purification technology is often recognized as an ideal choice in the early development stage of and Active Pharmaceutical Ingredient (API), where its versatility and simplicity is a clear advantage, compared to alternative purification techniques, to isolate drug candidates rapidly. This technology is now also recognized as an efficient and competitive purification process for late development stages and for the manufacture of APIs. Indeed, the development of new chromatographic processes significantly increased the efficiency of this purification technique compared to traditional batch chromatography processes.

Most of the applications are developed with liquid eluents, but chromatography can also be implemented, using supercritical carbon dioxyde. The specific properties of supercritical fluids compared to liquids (low viscosity, high diffusivity) make these solvents attractive for preparative chromatography. Supercritical Fluid Chromatography (SFC) is therefore an emerging technology, mainly for lab-scale purifications, where the flexibility and the rapidity of SFC is a clear advantage. Purification cost is reduced compared to liquid chromatography, due to higher productivities and much lower solvent consumption.

For medium-scale applications, the CYCLOJET process is an emerging solution, offering advantages compared to batch chromatography: the CYCLOJET performances are significantly higher in terms of both productivity and solvent consumption. Even if the process remains less efficient than multi-column processes used at industrial scale, the required hardware is simpler as only one column is required.

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The required hardware is very closed to what is used for an automated batch chromatography unit. This can be particularly attractive to reduce the investment costs for the purification process.

The Simulated Moving Bed (SMB) process, initially developed at very large scale for petrochemical applications, has been applied for the purification of chiral APIs at multi-ton scale. In 2005, the worldwide production capacity of multi-column chromatography processes for the purification of fine chemicals and APIs exceeded 1500 metric tons per year. This shows the competitiveness of the chromatography solutions compared to alternative purification processes like crystallization.
The VARICOL, a new multi-column continuous chromatography process, offers even better performances compared to the SMB process due to a higher flexibility in the process configuration. A higher process productivity is achieved together with a reduction of the number of columns required for the separation.

Application examples are presented to suggest the most appropriate chromatographic solutions, from early stage to large-scale production of commercial drugs.