Talanta 306 (2026) 129677

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Conical columns for liquid chromatography: A narrative review of design principles, performance benefits and renewed opportunities enabled by contemporary technologies

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ARTICLE INFO

Keywords:
3d-printing
Custom column design
Non-cylindrical geometry
Preparative separations
Tapered columns
Zone focusing

ABSTRACT

The geometry of a chromatographic column plays a central role in determining separation efficiency, speed, and practical usability. Although cylindrical columns dominate modern chromatography, alternative geometries have been proposed to address specific limitations of uniform-diameter designs. Among these, conical columns, characterised by a continuously changing internal diameter, offer a fundamentally different flow environment that directly influences solute transport and band dispersion. This article reviews the development of conical chromatographic columns and discusses the theoretical considerations required to describe separations in systems where mobile-phase velocity varies along the column axis. Experimental evidence indicates that conical columns are generally disadvantaged under simple isocratic conditions, but can provide tangible benefits in gradient elution and preparative-scale applications. Representative case examples demonstrate improved solute focusing, reduced peak tailing, higher sample loadability, and reduced consumption of stationary phase and solvents. The limited adoption of conical columns is discussed in the context of theoretical complexity and historical manufacturing constraints. Recent advances in additive manufacturing and digital design are identified as key factors that enable a revisit to non-cylindrical and hybrid column geometries, opening new possibilities for cost-efficient, high-load chromatographic separations.

1. Introduction

The chromatographic column is central to any chromatographic separation and ultimately determines analytical efficiency, resolution, throughput, and overall separation speed. Over the past few decades, substantial advances in column technology – including the development of novel stationary phase chemistries, innovations in particle design, and major breakthroughs in column manufacturing – have dramatically enhanced chromatographic performance. Consequently, the chromatographic column has remained a central focus of continuous innovation, particularly as demands for sustainability, sensitivity, loadability, robustness, and faster analytical and preparative separation methods continue to intensify [1–3].

Chromatographic columns can be subdivided based on geometry (cylindrical, conical, capillary, etc.), scale (analytical, preparative, microfluidic), and type of column bed (monolithic, packed). The topic of chromatographic columns with unconventional geometries has been explored on several occasions, with both experimental and theoretical studies consistently highlighting the potential advantages these designs may offer over traditional cylindrical columns. This review specifically focuses on conical columns, characterised by a continuously varying diameter that directly influences mobile phase linear velocity and, consequently, chromatographic performance. The review traces the historical development of column design, briefly addresses the theoretical foundations related to column efficiency, synthesises current knowledge regarding the performance benefits of conical columns, and highlights selected case studies involving novel approaches to column shape design [4–6].

In addition, we discuss current knowledge gaps, limitations, and practical challenges that have hindered the widespread adoption of conical columns. At present, these column geometries remain largely of academic interest within niche areas of separation science, in contrast to cylindrical columns, which continue to dominate chromatographic practice. Nevertheless, conical columns represent a largely untapped

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https://doi.org/10.1016/j.talanta.2026.129677
Received 16 January 2026; Received in revised form 6 March 2026; Accepted 16 March 2026
Available online 18 March 2026

potential in modern chromatographic separations. In light of recent technological advances, especially the rapid evolution of additive manufacturing technologies, non-standard and custom column housings can now be produced affordably and rapidly. Both the scientific community and the chromatography industry can benefit from these new possibilities.

2. Historical background and evolution of conical columns

The origins of liquid chromatography date back to the early 1900s, with Mikhail S. Tswett's pioneering experiments in 1906 providing the conceptual and practical foundation for modern chromatographic techniques. In gravity-driven classical column chromatography, a vertical glass cylinder was used to contain various solid sorbents, onto which the sample mixture was carefully applied at the top. Depending on the relative types and strengths of analyte interactions with the stationary phase and the mobile phase, individual sample components were gradually eluted from the column using an appropriate solvent or solvent mixture [2,7].

A simpler and more accessible form, paper chromatography, emerged in the 1940s. In this technique, a sample was spotted near the lower edge of a paper strip and then developed in a closed chamber containing a solvent. As the solvent front rose by capillary action, analytes partitioned differently between the paper, acting as the stationary phase, and the solvent, serving as the mobile phase, and thus migrated to different heights along the strip. Notably, some advantages of conical or non-uniform geometries were already explored in early paper chromatography formats [7,8].

The introduction of pressure-driven chromatographic systems is commonly attributed to a 1966 publication by Piel, in which solid sorbent was slurry-packed into glass columns with internal diameters of 1 or 2 mm, and the mobile phase was then forced through the column using centrifugal force [6,9]. Shortly afterwards, compressed air pressure was adopted by Still, Kahn, and Mitra, who introduced flash chromatography in 1978. The development of pressure-driven chromatography enabled significantly faster separations, while also shifting attention to critical operational parameters such as flow rate control and sorbent packing quality [2,9].

One of the first commercially available high-pressure liquid chromatography (HPLC) columns was developed in the 1960s by Csaba Horvath and Sandy Lipsky, specifically for nucleic acid analyses. This column consisted of a coiled steel tube approximately 3 m in length and 1 mm in internal diameter, filled with glass beads coated with a very thin porous layer on their surface, known as pellicular particles. Silica-based pellicular sorbents soon followed, further expanding the applicability of high-pressure separations. In the 1970s, the now-standard column internal diameter of 4.6 mm was selected largely for economic and practical reasons, as stainless steel tubing of this dimension was widely available. Consequently, research and development in HPLC accelerated rapidly, with separation times decreasing by several orders of magnitude over the half-century time period, from the 1960s to the 2010s [2,7].

One of the earliest reported practical applications of a non-cylindrical column geometry included a polymer-based column housing with variable inner diameter designed by Stahr in 1966 (Fig. 1-A), with the primary objective of minimizing the band volume of collected chromatographic fractions [10,11]. Subsequent theoretical calculations by Said in 1979 demonstrated that a single conical column could be more efficient than coupled cylindrical columns containing an equivalent amount of stationary phase and sharing the same total length [12]. Giddings' theory of non-uniform columns later established that, under isocratic conditions, conical columns are inherently less efficient than cylindrical columns because they induce variations in the average linear velocity along the column length [5,13]. However, later theoretical work by Blumberg in 1992 predicted that conical columns could outperform cylindrical columns, but only under gradient elution conditions, with optimal performance achieved when the mobile phase flow is directed from the wider toward the narrower end of the column [5,14].

Conical precolumns, as described by Ruijten in 1987 (Fig. 1-B), were demonstrated to significantly enhance sample preconcentration in HPLC, thereby addressing several inherent limitations associated with conventional cylindrical precolumns [15]. By gradually reducing the

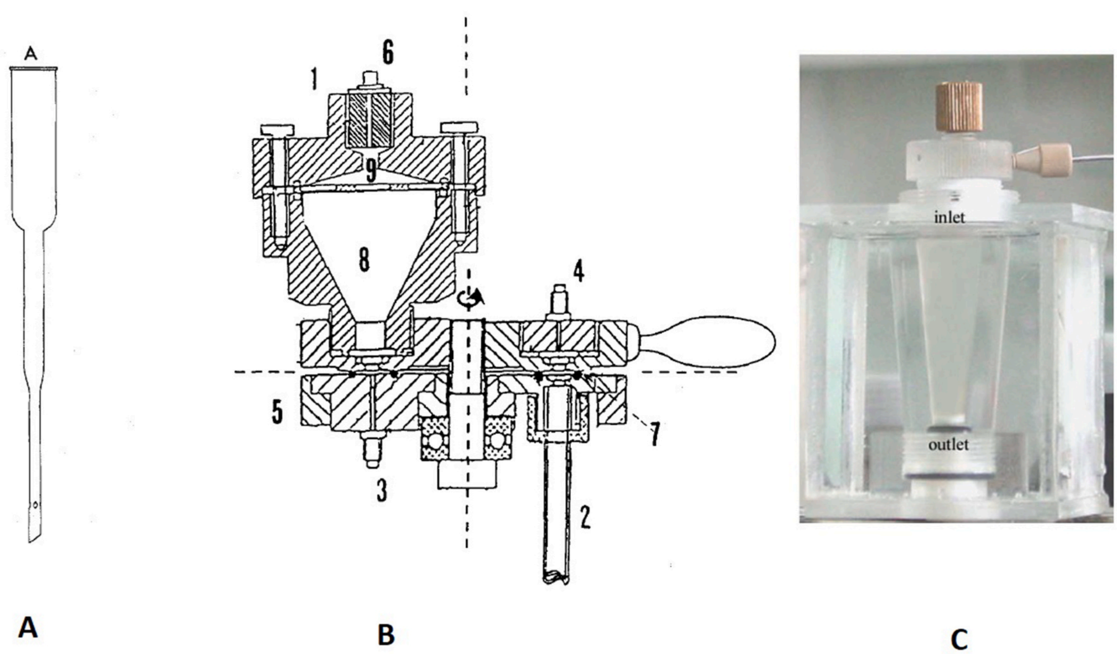

Fig. 1. Historical examples of conical columns. A – a schematic representation of the earliest known non-uniform diameter column, as proposed by Stahr, 1966 [10]; B - conical precolumn setup by Ruijten, 1987 [15] (1 = precolumn, 2 = separation column, 3 = waste exit, 4 = capillary connection, 5 = valve, 6 = inserter for capillary tubing connection, 7 = gliding gasket, 8 = packed section, 9 = distribution part); C - semi-preparative conical column by Ma et al., 2004 [6]. The figures are reproduced with permission from publishers.

column diameter, these conical precolumns enabled more effective focusing of analytes before analytical separation, resulting in improved sensitivity and peak shapes.

Further practical investigations by Pečavar et al., published in 1997 and 1999, reported the development and evaluation of a conically shaped analytical column with a total length of 150 mm and an internal diameter that continuously decreased from 4.0 mm at the inlet to 2.5 mm at the outlet. In parallel, preparative-scale conical columns featuring taper angles ranging from 7° to 15° were fabricated and experimentally tested by several research groups in the early 2000s (Fig. 1-C). These designs were specifically intended to compensate for distorted flow profiles, a phenomenon commonly observed in large-diameter columns [5,6,16–18].

3. Theoretical foundations

Most chromatographic theory has traditionally been developed for columns with a constant inner diameter, in which flow conditions and separation behavior are assumed to remain uniform along the entire column length under ideal operating conditions. Within this framework, separation efficiency is most commonly described using plate theory and expressed through the van Deemter equation, which accounts for peak broadening as the combined contribution of multiple flow paths through the packed bed, longitudinal molecular diffusion along the column, and finite mass transfer between the mobile phase and the stationary phase [19]. In this case, plate height H is constant and the plate number is given by Eq. (1):

$$N = \frac{L}{H} \tag{1}$$

In this expression, N is the total number of theoretical plates and L is the length of the column.

Subsequent theoretical developments moved beyond the concept of discrete theoretical plates and instead described solute transport as a continuous process, placing greater emphasis on how diffusion and mass-transfer limitations control peak width and band dispersion [13,20]. Nevertheless, these models retain the assumption of spatially invariant flow velocity and retention behavior. In a conical column, the cross-sectional area $A(z)$ varies continuously along the length L. Since the volumetric flow rate F is constant, the local linear velocity $u(z)$ becomes Eq. (2):

$$u(z) = \frac{F}{A(z)\,\varepsilon} \tag{2}$$

where ε is the interstitial porosity. Thus, the velocity increases toward the narrower end of the column. Consequently, residence time, mass transfer, and dispersion become functions of axial position. For a non-uniform column, variance σ accumulates locally according to Eq. (3):

$$d\sigma^2 = 2\frac{D_{eff(z)}}{u(z)^2}dz \tag{3}$$

where $D_{eff}(z)$ is the effective axial dispersion coefficient. Integration along the column length therefore gives Eq. (4):

$$\sigma^2 = 2\int_0^L \frac{D_{eff(z)}}{u(z)^2}dz \tag{4}$$

The cumulative, apparent plate number N_a is therefore Eq. (5):

$$N_a = \int_0^L \frac{dz}{H(z)} \tag{5}$$

For non-uniform columns, $N_e/N_a < 1$, and additivity of plate numbers applies only when cross-sectional area and plate height are constant [5,14]. Numerical analysis has shown that, for equal total length and stationary-phase volume, a conical column can exhibit higher effective efficiency than an equivalent composite cylindrical column [5]. The lengthwise increase in velocity toward the narrower end reduces retention times, while upstream wider regions provide greater loadability. Because local velocity affects equilibration time, the mass-transfer term of the van Deemter equation becomes position-dependent [19]. Consequently, peak width and resolution may deviate from predictions based on constant-diameter models [13,20].

Therefore, separations in conical columns must be described using a position-dependent transport model in which efficiency results from the overall balance of local dispersion and velocity gradients along the column. However, given the limited experimental data so far and the current lack of more appropriate theoretical models, numerical predictions on the chromatographic performance of conical columns are rather hard, if not impossible, to make.

4. Performance evaluation and case studies of applications

To provide a clear comparison between conical and cylindrical chromatographic columns, Table 1 summarises available data on key performance metrics including column efficiency, separation impedance, loadability, and peak shape, highlighting the practical advantages of conical designs. Values represent approximate ranges derived from multiple literature sources and vary with column design, mobile phase, and experimental conditions.

The performance of conical columns depends greatly on the direction of flow. Both theoretical analysis and practical experiments confirm the intuitive assumption that these columns should be operated with the mobile phase moving from the wide end towards the narrow end to

Table 1
Summary of available data on conical columns' performance, including an illustrative RAPI-style assessment of conical versus cylindrical columns. Each metric shows the performance of the conical column relative to the cylindrical column, with colored dots indicating scores (Red●: disadvantage, Amber○: minor loss, Green●: advantage). RAPI (Red–Amber–Green Analytical Procedure Index) is a semi-quantitative tool for evaluating method efficiency, solvent use, sample loadability, and other performance metrics, allowing a quick visual comparison of alternative column designs.

Metric	Performance of conical column, compared to baseline (cylindrical)	References
Separation impedance (resistance to flow and band dispersion)	● Lower (less resistance)	[5,6,18]
Efficiency under constant mobile phase composition	○ 85-89% of cylindrical	[5,6,18,23]
Number of resolved peaks achievable under gradient elution	○ 8.5-11% loss vs cylindrical	[5,18]
Efficiency under semi-preparative conditions	● 22–45% higher than cylindrical	[6,11]
Peak width at half height	● 4–14% narrower than cylindrical	[5,6,11]
Peak height	● 11–27% higher than cylindrical	[5,6]
Loadability (injection volume)	● 30-40% higher	[11,18]
Loadability (sample mass)	● 50-60% higher	[11,18]
Reduced plate height	● ~12% lower (= better efficiency)	[5,6,18,23]
Analysis time under constant flow	● Generally longer	[6]
Peak tailing	● Improved peak shape	[5,6]
Solvent consumption	● Lower; depends on flow rate	[5,6,11]
Stationary phase consumption	● Lower; depends on geometry	[5,6]

achieve higher sample loadability, optimal resolution and separation efficiency [5].

Conical liquid chromatographic columns have shown superior performance compared with traditional cylindrical columns in terms of sample loading capacity and separation efficiency. The main advantage of a conical column arises from its larger inlet cross-sectional area relative to a cylindrical column of the same overall length and volume, allowing it to accommodate a higher sample load (both volume and mass) without compromising performance, compared to a cylindrical column of equivalent volume. Conical columns with a 10° taper could improve sample loadability by approximately 30–40% in injection volume and 50–60% in total sample mass, compared to standard constant-diameter columns of the same length [18].

The internal flow profile within a chromatographic column significantly influences overall efficiency. Cylindrical columns generally exhibit a parabolic flow profile, with the mobile phase flowing more rapidly in the centre of the column than near the walls, where friction slows the solvent. In contrast, conical columns can achieve a flatter, more 'plug-like' flow profile, minimizing velocity gradients across the column cross-section and thereby improving column efficiency [6,18].

Non-cylindrical chromatographic columns have been studied in a range of practical analytical and preparative applications. The following case studies demonstrate their versatility and show how performance depends on specific column geometry, taper angle, and operational conditions.

- For example, a conical analytical column with a length of 150 mm and a diameter tapering from 4.0 mm at the inlet to 2.5 mm at the outlet was used to separate a standard mixture of esters of p-hydroxybenzoic and p-nitrobenzoic acid under isocratic conditions. Compared with a conventional analytical column of the same length, the conical column achieved shorter retention times and reduced solvent consumption, demonstrating both efficiency and economy [17].
- In another study, a mixture of five alkanophenones – acetophenone, propiophenone, butyrophenone, valerophenone, and hexanophenone – was separated using a conical column measuring 150 mm in length, with inlet and outlet diameters of 4.2 mm and 2.1 mm, respectively. While isocratic elution in this setup resulted in a small loss of efficiency compared to a cylindrical column, the conical column showed noticeably reduced peak tailing, highlighting one of the advantages of its tapered geometry [5].
- Early applications of conical geometries also demonstrated practical benefits. Filter papers folded into conical shapes were used for chromatographic scanning of natural oils and bacteriostatic extracts from rock samples. The narrowing cone shape concentrated the separated compounds into sharply focused zones, which proved particularly useful for isolating antibacterial substances from coal and other mineral sources [8].
- The effect of conical angle has been investigated as well. In semi-preparative liquid chromatography, conical columns with angles of 7°, 10°, and 15° were studied using iodine for flow visualization and a mixture of carmine and brilliant blue to test separation performance. All columns were equal in length and total volume, with differences in angle achieved by varying the ratio of inlet to outlet diameter. These experiments revealed that the 15° column produced a 'reverse parabolic' flow profile, whereas the 10° column produced the desired flat profile and also gave the best separation performance, yielding the highest resolution, even surpassing the standard cylindrical column (Fig. 2). This demonstrated the potential to optimize column geometry in order to improve efficiency, particularly for preparative-scale separations [6,11].
- Contemporary non-cylindrical column designs enabled by three-dimensional printing have begun to demonstrate practical advances in analytical separations. In one example, a 3D-printed array helical monolithic column chip with integrated serial microchannels was used for high-throughput sample pretreatment and analysis of trace rare-earth elements, achieving enhanced extraction throughput and improved separation performance compared with simple straight channels due to the expanded surface interaction of the hierarchical structure; this application highlights how non-uniform geometry can facilitate efficient, parallelised processing in complex analyses [21].
- Additive manufacturing has also enabled columns capable of direct coupling with mass spectrometry for biomolecule separation: a 3D-printed serpentine size-exclusion chromatography column with post-print surface coating tolerated pressures up to 110 bar and delivered baseline separation of ubiquitin–angiotensin mixtures and myoglobin–insulin pairs with high reproducibility and minimal peak tailing, demonstrating robustness of custom geometries in high-pressure applications [22].

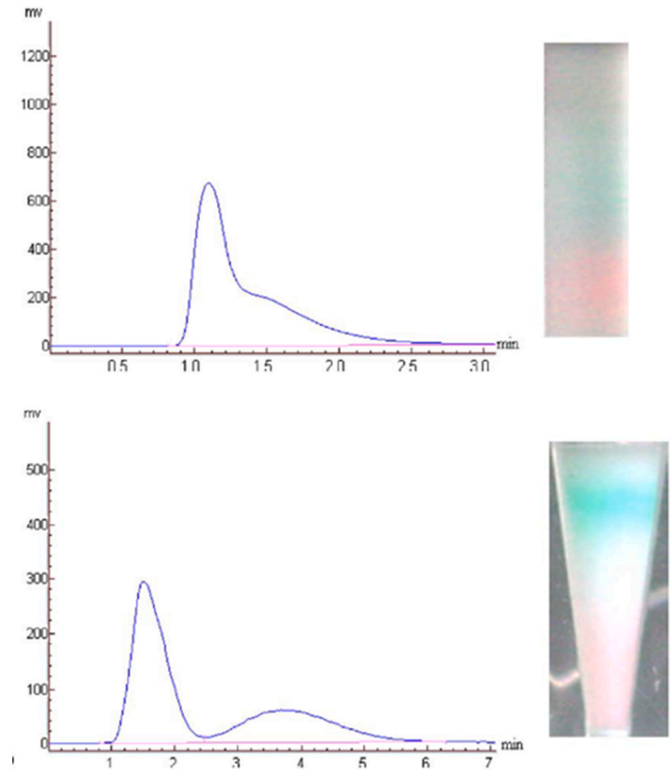

Fig. 2. A comparison of flow profile and chromatogram of two pigments in a cylindrical (top) and conical column (bottom; angle = 10°), other conditions being the same (Ma et al., 2004) [6]; reproduced with permission from publisher.

Taken together, these case studies show that although conical and other non-cylindrical columns may not always surpass cylindrical columns in raw efficiency under simple isocratic conditions, their unique geometry offers important advantages. These include reduced peak tailing, increased analyte concentration in the eluate, and the ability to optimize flow profiles for enhanced resolution in gradient and preparative applications. Additional benefits of conical columns include cost savings, as the tapered geometry allows reduced consumption of stationary phase and solvents, making them especially attractive for semi-preparative and preparative chromatography.

5. Limitations, challenges, and practical considerations

While offering certain notable advantages, conical columns also present several inherent performance limitations when compared with standard cylindrical columns. Under isocratic conditions, in which the mobile phase composition remains constant throughout the separation, the performance of a conical column generally cannot match that of a conventional cylindrical column [5]. This limitation arises from the fact that variations in column diameter create changes in local linear velocity along the column, leading to uneven band broadening that cannot be fully compensated under constant mobile phase flow and elution strength conditions.

Under gradient elution conditions, theoretical studies suggest that conical columns can, in some cases, slightly outperform cylindrical columns, particularly for separating peptide mixtures and small organic molecules. However, the maximum relative gain in peak capacity is modest and typically does not exceed a few percent, indicating that the advantages of the conical geometry may be limited to specific conditions and applications. A similar conclusion was reached when evaluating cylindrical columns packed with particles of gradually decreasing size (from larger to smaller diameters along the column). In this scenario, no improved performance was observed under isocratic conditions, and only limited improvement was seen under gradient elution [5,23].

Although improvements under gradient elution conditions have been both observed and predicted, a fully satisfactory explanation for this phenomenon is still lacking. One possible explanation is the combined positive effect of analyte band focusing and the substantially greater variation in analyte linear velocity (compared with isocratic conditions) during gradient elution in a conical column configuration. However, more systematic experimental data are needed to confirm or negate this hypothesis. From a theoretical perspective, as mentioned, chromatographic modeling of conical columns is inherently more complex than that of cylindrical columns. Because the linear velocity of the mobile phase is not constant along the column axis, standard equations and models developed for uniform-diameter columns are no longer valid. More sophisticated theoretical approaches are required to accurately describe solute transport, peak broadening, and mass-transfer behavior in these non-uniform geometries [6,24,25].

There are certainly many other aspects yet to be uncovered, both experimentally and theoretically, regarding the chromatographic behavior of conical columns. For example, as mentioned in the study by Ma et al. [6], an optimum taper angle of 10° was established, but their studies were all conducted on columns of the same length. Further studies by Guan et al. [18] on various columns using the same taper angle of 10° and the same cross-sectional area ratio found marked differences in performance depending on the overall column geometry; a longer and wider column provided greater efficiency, indicated by a lower reduced plate height. This finding implies that many other parameters also affect performance, most likely by influencing the flow profile of solutes in a yet unknown and probably interconnected manner. Another experimental aspect that certainly affects the flow profile is the viscosity of the mobile phase, which depends on chemical composition and temperature. Since the available experimental data is currently scarce and unsystematic, the topic of conical columns remains an understudied field. Further research should ideally continue using well-defined parameters, such as stationary phase chemistry and particle size, mobile phase composition, a defined set of analytes (solutes), and column temperature. Another important (and rarely studied) aspect of conical columns could be flow-gradient programming, which can help partially optimize the mobile phase linear velocity as the analyte passes through the column, thereby maintaining chromatographic performance within optimal limits. Based on the data obtained from a large set of column geometries and experimental setups, an empirical theoretical model could likely be developed.

Historically, the fabrication of non-cylindrical columns has been challenging due to limitations in available manufacturing technologies and precision control. Traditional (subtractive) production methods often rely on time- and labor-intensive, multi-step procedures. In addition, inconsistent material properties, inadequate machining or packing tools, and the high cost of producing custom components represent significant technical bottlenecks that have hindered the broader adoption of conical column designs, which remained mainly a niche area of research for several decades [26–28]. Advances in modern manufacturing technologies, such as additive manufacturing and precision milling, may help overcome most of these obstacles. It is therefore very probable that conical columns will regain interest both as a research topic and within certain application areas.

6. Additive manufacturing as a tool for custom column housing design

3D printing has found its most immediate and practical application in chromatography in the production of customized column housings. This is particularly true for preparative and semi-preparative chromatography, where column diameters are larger and pressure requirements are moderate. Conventional preparative column housings are typically machined from stainless steel or engineered polymers, which limits rapid iteration and customization. Additive manufacturing enables rapid prototyping of housings with non-standard geometries, including conical profiles, tapered inlets, integrated distributors, and custom port configurations, all of which can be digitally optimized before fabrication [29].

Among additive manufacturing techniques, fused deposition modeling has become the most widely used approach for preparative column housings due to its compatibility with chemically resistant thermoplastics. Materials such as polypropylene, polyether ether ketone, and polyetherimide have been successfully printed into column shells capable of holding packed beds or monoliths for preparative separations. Although fused deposition modeling lacks the resolution required for stationary phase fabrication, its layer-by-layer extrusion process is well suited for producing thick-walled housings that can tolerate moderate pressures when properly designed. Studies have shown that printed polypropylene and reinforced polymer housings can withstand typical preparative chromatography pressures when wall thickness, print orientation, and infill density are optimized [30].

Stereolithography and digital light processing are also used for column housings when smoother internal surfaces and tighter dimensional tolerances are required. While photopolymer resins generally exhibit lower mechanical strength than thermoplastics or metals, the use of chemically resistant, highly cross-linked resins combined with thick housing walls has been shown to produce column shells suitable for moderate-pressure applications [31].

Metal additive manufacturing, particularly selective laser melting, represents the most robust option for 3D-printed column housings and is especially relevant for preparative and pilot-scale chromatography. Stainless steel and titanium alloy housings produced by laser melting exhibit excellent mechanical stability, high pressure tolerance, and broad chemical compatibility. These properties make them suitable for repeated use, aggressive cleaning protocols, and scale-up scenarios. Metal printing also allows the integration of complex internal features such as flow distributors, support grids, and tapered bed retainers directly into the housing, eliminating the need for separate frits or distributor plates. Spiral and non-cylindrical housings printed in titanium have been demonstrated to withstand liquid chromatography operating pressures while maintaining consistent flow behavior [32].

Additively manufactured housings typically require design compensation for shrinkage, layer anisotropy, and surface roughness. For polymer prints, internal surfaces can be smoothed through chemical treatment or coating, while metal housings may undergo abrasive flow machining or chemical polishing to reduce roughness and improve cleanability [33].

The use of 3D-printed housings in combination with conventional packed beds or monolithic stationary phases has been shown to yield reproducible chromatographic performance when bed packing procedures are carefully controlled. Multiple studies report consistent pressure–flow relationships and retention behavior across replicate housings printed from the same digital design, supporting the feasibility of additive manufacturing for reproducible preparative hardware. Chemical compatibility remains material-dependent, with metal housings offering the broadest solvent tolerance, while polymer housings require validation against swelling, solvent uptake, and long-term mechanical stability [29].

The main industrial application barriers for 3D-printed preparative chromatography column housings center on scalability, regulatory compliance, mechanical robustness, and systems integration. While academic studies demonstrate feasibility at lab scale, scaling additive manufacturing to produce large-diameter, high-pressure prep columns with tight dimensional tolerances and long-term mechanical stability remains challenging. Poor layer adhesion and surface finish can limit pressure ratings and reproducibility compared to conventionally machined housings. Material compatibility is another concern: many common photopolymers or thermoplastics exhibit solvent swelling, leaching, or insufficient chemical resistance for aggressive mobile phases, raising regulatory and GMP compliance issues. Integration with existing HPLC/preparative systems also presents barriers: standardized fittings, pressure limits, reliable sealing, validation requirements, etc. Potential solutions include hybrid manufacturing approaches (for example printed outer shells with metal liners), adoption of high-performance polymers such as PEEK, PEKK, or carbon-fiber–reinforced composites, and post-processing techniques (annealing, solvent smoothing, internal coating) to improve strength and chemical resistance. Standardization of designed 3D files aligned with industrial column geometries, along with rigorous testing, can help make the connection from academic prototypes to validated industrial tools.

From an industrial perspective, the strongest case for 3D printing currently lies in preparative-scale column housings, where customization, rapid iteration, and integration of complex flow features outweigh the need for extreme dimensional precision. As additive manufacturing technologies mature and material options expand, 3D-printed housings are likely to play an increasingly important role in process development and niche production environments where flexibility and speed are critical.

7. Cross-field connections and potential directions for future research

Studies confirm that while conical columns are less efficient than cylindrical ones under isocratic conditions, they offer distinct advantages in gradient elution and preparative-scale applications. Their most tangible benefits, however, must not be overlooked: savings in solvents and stationary phase, which are far more significant in preparative than in analytical separations.

Future theoretical work is likely to focus on developing a more comprehensive and predictive numerical model that fully accounts for the variable velocity and mass-transfer effects inherent to conical columns, enabling their more systematic design and use in ultra-fast separations and high-load preparative chromatography. Because linear velocity is not uniform along the length of a conical column, conventional chromatographic theory must be significantly extended to accurately describe solute transport, band broadening, and retention behavior. A more sophisticated understanding of these dynamics is essential for optimizing column performance, particularly for complex separations or applications that push the limits of sample capacity.

Recent advances in digital manufacturing and precision engineering are expected to facilitate the fabrication of non-traditional column geometries, which have historically been difficult and costly to produce. In particular, additive manufacturing offers the ability to construct complex and custom column shapes that are virtually impossible (or too expensive) to achieve with conventional machining, while AI-assisted design optimization could accelerate development, improve reproducibility, and reduce prototyping and production times. Contemporary 3D-printing technology, even on consumer level, already enables the production of mechanical parts with dimensional tolerances on a par with, or even below, 0.1 mm. It is therefore to be expected that more systematic studies on this topic in the near future will also lead to a better theoretical understanding.

Non-cylindrical columns could also be potentially linked to ultrahigh-performance liquid chromatography (UHPLC) and two-dimensional liquid chromatography (2D-LC). Microfluidic and 3D-printed designs, including serpentine and tapered geometries, provide precise control over flow velocities and mass transfer, enabling high-resolution separations under UHPLC conditions while reducing solvent and stationary phase consumption [34]. AI-assisted designing could be used to optimize column geometry, mobile phase composition, and gradient programming, facilitating integration of non-traditional column shapes into complex workflows. These tools are particularly valuable for 2D-LC, where orthogonally coupled separations require careful tuning [35].

Looking forward, the integration of non-cylindrical column geometries with advanced manufacturing and AI-assisted design holds significant potential to transform chromatographic practice. Future research will likely focus on optimizing column geometry to fully exploit the unique advantages of non-traditional column shapes, opening new opportunities for environmentally conscious separation science.

8. A proposed design for a combined, semi-conical column

Taking into account the positive aspects regarding the conical column design, namely greater sample loadability, reduced stationary phase and solvent consumption, reduced peak tailing, and potentially better band focusing, we propose a hybrid design, combining the benefits of both the conical and the cylindrical geometry within a single column housing (Fig. 3). The upstream, conical part should preferably be filled with a coarser stationary phase, having primarily a pre-concentration function, similar to the design of Ruijten et al. [15], but in a more simplified setup. This conical part can be seamlessly integrated with a cylindical column downstream (without any additional fittings etc.), this one having a finer stationary phase of the same type

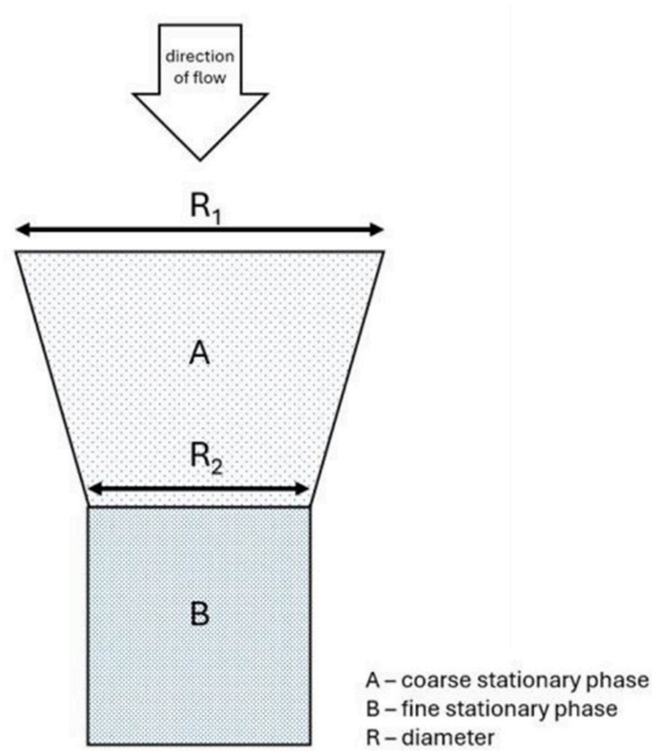

Fig. 3. Proposed schematical design of a semi-conical column.

(chemistry), where the most critical part of separation should take place. The flow rate should then be preferably adjusted to the linear velocity optimal for the finer stationary phase in the cylindrical part. In such a way, for the separation within the conical part, having proportionally lower mobile phase linear velocities, a coarser stationary phase should be more appropriate in order to reach the optimal separation conditions.

Since the majority of the stationary phase would be of the coarser grade, which is usually more economical, such column designs have a lot of practical potential in preparative separations, at least hypothetically. Such a design would probably be best suitable for separations under isocratic conditions with a constant flow rate. The exact geometrical proportions and individual stationary phase gradations (mesh sizes) of such a column design have yet to be established empirically and based on specific applications. While the manufacturing of such a semi-conical column housing might have been challenging or at least quite costly (due to custom production) even a decade ago, nowadays with afforrdable table-top 3D-printing of high performance plastics at low cost, the production cost of such custom column housing prototypes has become low, and it can be designed and produced within a few hours.

9. Conclusions

Conical chromatographic columns have been investigated mainly in the context of analytical separations and primarily with respect to chromatographic performance. Most studies have focused on efficiency, resolution, and flow behavior, while their potential for reducing solvent and stationary phase consumption has received comparatively little attention. Yet these practical and economic aspects may represent some of their most important advantages. Although conical columns generally do not surpass cylindrical columns under simple isocratic conditions, they can provide clear benefits in gradient elution and, in particular, in semi-preparative and preparative separations. Their tapered geometry allows higher sample loadability, improved peak symmetry, enhanced solute focusing, and reduced solvent use. In preparative chromatography, where material consumption and operating costs are critical, their potential for cost savings has not yet been systematically evaluated.

Historically, limited adoption of conical columns has been linked to theoretical complexity and manufacturing constraints. Today, however, the widespread availability and affordability of additive manufacturing, especially table-top 3D printing, make the production of custom or small-series conical column housings a practical reality. Rapid prototyping enables systematic testing of non-cylindrical and hybrid geometries that were previously difficult or too expensive to fabricate. Our proposed combined semi-conical column aims to integrate the advantages of both conical and cylindrical geometries within a single housing, combining preconcentration and high-resolution separation zones while simultaneously reducing stationary phase and solvent consumption. Due to the affordability of 3D printing, a renewed interest in conical columns is to be expected, along with a better understanding of their behavior as research in this area progresses. Conical columns, however, should not be viewed as some universal replacements for conventional cylindrical columns, but as complementary tools with particular relevance in high-load and cost-sensitive separations. With modern manufacturing technologies removing some previous technical barriers, conical column shapes deserve renewed attention, especially in preparative-scale applications.

CRediT authorship contribution statement

Sonja Mavri: Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Alen Albreht:** Writing – review & editing, Conceptualization. **Mitja Križman:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Data curation, Conceptualization.

Declaration of use of generative AI

During the preparation of this work, the authors used SciSpace, InstaText and ChatGPT as supportive tools to assist with identifying and summarizing relevant literature, as well as grammar checking. We support the responsible use of generative AI in literature searches and review, as it can help optimize time management and facilitate rapid familiarization with emerging research and novel writing approaches. The tasks given to AI in this case were formulated along the lines of: "Are there additional recent articles or books that confirm X?", "What recent publications address Y in the context of Z?", or "Using this list of sources, summarize the following bullet points in a concise paragraph suitable for a scientific manuscript." AI-generated outputs were used as drafts or starting points only. All suggested references were independently verified, and all summaries were carefully reviewed, edited, and rewritten where necessary. The authors take full responsibility for the final content of the publication and emphasize that AI tools were used solely to support, not replace, critical evaluation and scientific judgment.

Funding

This work was supported by the research core funding No. P1-0005 (Slovenian Research and Innovation Agency, former Slovenian Research Agency).

Declaration of competing interest

There is no competing interest for any of the authors.

Acknowledgement

The authors want to acknowledge their deepest gratitude to prof. dr. Janez Mavri for his precious help and expertise in the elaboration of theoretical aspects of this manuscript.

Data availability

Data will be made available on request.

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