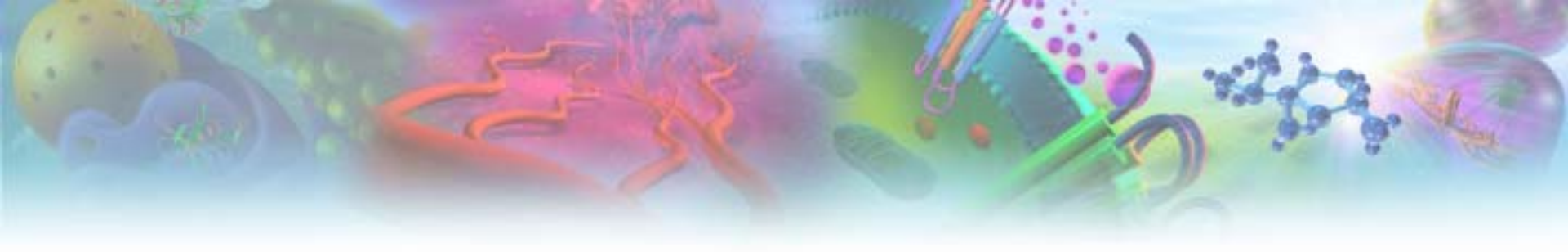

The Role and Benefits of Prepacked, Disposable Büchner Funnels in Medicinal Chemistry

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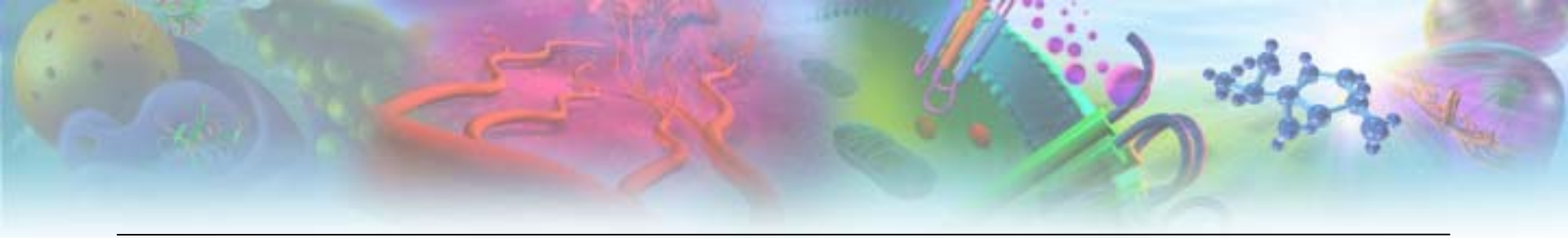
Abstract/ Introduction

Medicinal chemistry is a branch within the pharmaceutical industry that merges expertise in organic, analytical, computational chemistry, and drug metabolism to conceptualize, design, and create novel compounds for potential therapeutic use. Within this research, Flash and HPLC chromatography play a growing role in purifying and characterizing pharmaceutical candidates for further biological evaluation. Nevertheless, medicinal chemists are searching yet for simple, reliable, rapid, low-cost methods of achieving separations for a wide range of reaction scales. As a result, packed bed Büchner funnels have received mainstream commission as a simple alternative to flash and other purification techniques.



At this time, most medicinal chemists self pack reusable ceramic Büchner funnels with the desired adsorbents. Not only is this tedious and time consuming, but also poses a great safety risk for the medicinal chemist. For example, researchers are exposed to inhalable particulates during the packing process and large amounts of solvents are used to clean the Büchner funnels after use. Also, ceramic Büchner funnels can easily break during use and cleaning. In terms of performance, channeling and bed-weight inconsistency are also major problems when researchers are required to self pack Büchner funnels. In this report, we will discuss how prepacked disposable Büchner funnels address these issues as well as provide an overview of their utility within the area of medicinal chemistry research.

Experimental

Prepacked Disposable Büchner Funnel Design

- See Figure A
- 2-piece polypropylene construction
- Internal diameter: 55-11mm ID
- Bed weight ranges between 12.5-200g (Table 1)
- Lower half is the funnel
- Upper half is packed with sorbent between two 20µm polyethylene frits
- Resistant to organic solvents
- Contains a heat-sealed retaining ring to further compress sorbent-frit assembly in place
- This compression helps eliminate sorbent channeling during use

Figure A. Schematic of Prepacked Büchner Funnels

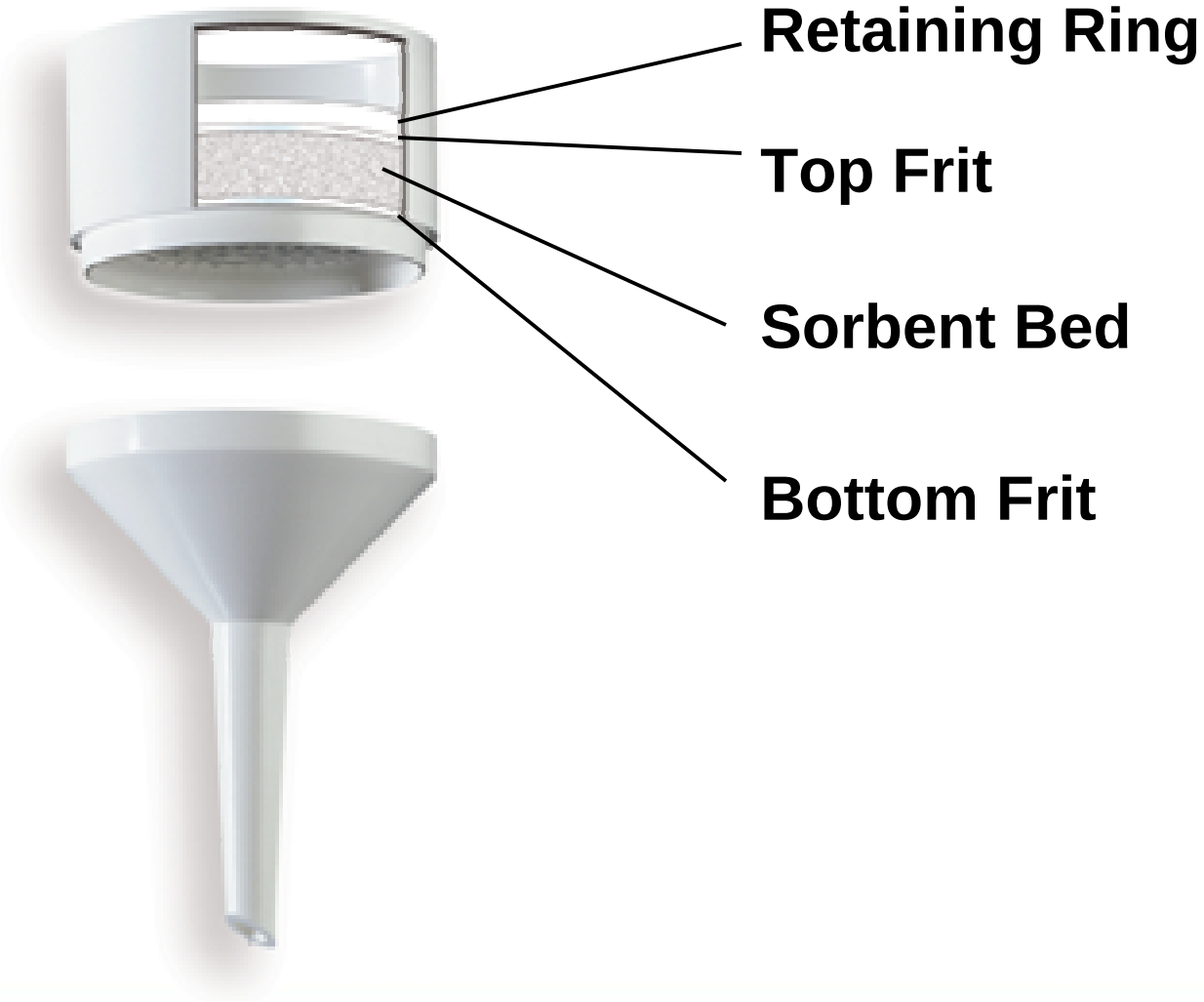


Table 1. Bed Weight Distribution vs. Funnel ID

Funnel ID	Sorbent Weight (silica)
55mm	12.5g
70mm	25g
90mm	50g
110mm	100g
190mm	200g

Common Uses for Packed Bed Büchner Funnels

- Silica sorbents often used in baseline clean-up of solution-phase synthesis reactions
  - Normal phase chromatography used to retard/retain more polar compounds via polar-polar interaction when loaded in the presence of organic sample matrix
- Polyamide phases (DPA-6S) commonly used for isolating active compounds from natural products (plant extracts)
- Other applications include dessication (solvent dehydration) and filtration (particulate removal)
- Scale-up SPE methods as tool for gross purification
- Tables 2 & 3 list common Büchner funnel sorbents and applications

Table 2. Common Büchner Funnel Sorbents

Sorbent	Composition	Particle Size
Magnesium sulfate	$MgSO_4$	
Silica (Merck)	SiO_4	choices
Silica (Discovery)	SiO_4	40-60µm
Celite 545 AW	diatomaceous earth	
Alumina A, B, or N	Al_2O_3	60/325 mesh
Florisil	Mg_2SiO_4	100/120 mesh
Charcoal	C (act. coconut)	20/40 mesh
DPA-6S	Polyamide resin	50-160µm
C18-silica	octadecyl	40-60µm

Table 3. Common Büchner Funnel Applications

Sorbent	Application
Magnesium sulfate	Dessicant
Silica	Filtration, polar compound removal, dessicant
Celite 545AW	Filtration
Alumina A, B, N	Dessicant, many specific applications
Florisil	Many specific applications
Charcoal	Removal of non-polar compounds removal, pigments, dyes
Polyamide	Isolation of tannins, chlorophyll, gallic, humic acids
C18-silica	Non-polar compound removal

Capacity Tests for Büchner Funnels

Packed bed Büchner funnels are most often used for gross purification/sample clean-up of larger scale samples. As a result, breakthrough capacity is a common concern for such applications.

1. **Representative tested compounds were loaded at increasing amounts onto 5 common sorbents packed into 55mm ID funnels preconditioned with the appropriate solvent.**

2. **The load flow through eluate was analyzed for compound breakthrough via HPLC-UV analysis.**

Results

Capacity Tests for Büchner Funnels

- On average, capacity levels of ~3.0% bed weight was observed (Table 4)
- The compression packing yielded fines in the flow-through solutions; however, fines can be adequately removed via thorough conditioning prior to addition of the sample
- Additional of a glass fiber membrane below the bottom frit may offer a potential solution for reducing fines

Table 4. Büchner Funnel Capacity and Breakthrough Values

Phase	Bed Wgt.	Analyte	Matrix	Sample Capacity (mg) 2% BKT*
DPA-6S	10g	Phloroglucinol	Water : Methanol (90:10)	240
DSC-Si	12.5g	4-Fluoro-3-nitrobenzoic acid	Methylene chloride	350
Merck Silica	12.5g	4-Fluoro-3-nitrobenzoic acid	Methylene chloride	400
Celite	12.5g	Butyl paraben	Methylene chloride	80
Charcoal	12.5g	Butyl paraben	Water : Methanol (80:20)	104

*Breakthrough is positive for the aliquot with a peak area greater than 2% that of breakthrough standard solution.

Summary

- Prepacked to eliminate exposure to inhalable particulates
- Compressed sorbent bed eliminates channeling
- Porous frit helps to spread sample across the sorbent bed
- Prepackaged design saves time in packing, cleaning and disposal