Rethinking peptones as first-line optimization tools

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In the biopharmaceutical space, peptones are often not viewed as first-line solutions for underperforming CHO-based bioprocesses. Peptones are protein hydrolysates derived from yeast, plant, or animal sources. They can improve the yields of workflows that have plateaued, so they have high potential value for a wide range of applications from the outset of development. Peptones can also improve potency and lot-to-lot consistency.

Leveraging peptones during early screening or medium development can go a long way toward optimizing protein titers and culture longevity, enabling quick titer gains without meaningful process adjustments further along in development. Although the use of chemically defined (CD) processes has become a dominant trend for many applications, this can create limitations for the optimization process. This is where peptones can offer functional benefits that CD media and/or feeds alone may not provide. When manufacturers encounter growth plateaus, declining viability, or suboptimal titers despite optimizing their feed strategies, peptones can enhance viable cell density, extend high viability windows, and improve productivity with minimal process change.

Whether addressing a drop in viability or a stalled yield curve, peptones provide a flexible, nutrient-rich boost to complement CD media. As such, incorporating the right peptones at the right concentrations is a valuable approach to unlocking process improvements that would otherwise require significant redevelopment. Peptones can be powerful tools to help developers accelerate timelines, reduce risk, and achieve robust performance earlier in the product lifecycle.

Nutritional diversity supports robust scale-up

Scaling up bioprocesses often introduces unexpected challenges, and identifying quick, low-risk interventions is critical for keeping development on track. Peptones can be valuable solutions for mitigating scale-up risks like batch failure, costly rework, and delay during tech transfer. These benefits can contribute to reducing the cost of goods (COGs) and accelerate speed to clinic, enabling a rapid, low-effort solution for restoring key performance metrics without requiring a complete medium redesign or costly process redevelopment. For developers, the potential benefit of peptone supplementation is better performance with less time and effort. For process development teams trying to improve performance without significant process changes, peptones can be "rescue" solutions that can help them avoid rework and keep development on track.

The broad utility of peptones stems from their complex nutritional compositions, which include peptides, free amino acids, trace metals, and other micronutrients. This diversity supports a range of cellular functions across multiple cell types and applications. Long praised for their wide-ranging benefits, peptones offer multifunctional advantages without many of the regulatory and consistency challenges associated with serum. Different peptones have distinct nutritional profiles, making screening with a diverse panel critical to any potential process improvements.
A high-performing CHO system may not require peptone supplementation, but some bioprocesses can benefit from thoughtful integration of the right peptones in the right process steps to achieve peak performance. A key to successful implementation is identifying the optimal working concentration. Like over-feeding, excess supplementation can stress cells and negatively impact performance. Titration studies are thus critical to determine the ideal concentration to maximize benefit without adverse effects. When the right composition is introduced at the right time in the right quantity, a peptone can significantly improve growth, viability, and yield, ultimately unlocking more robust and scalable biomanufacturing processes.

Why peptone diversity and concentration matter

No two cell lines will respond the same way to a given nutritional input. That is why an effective peptone strategy begins with evaluating a broad panel of peptone bases, such as soy, yeast, and cotton. Developers can identify which sources align best with the metabolic needs of their specific CHO lineages or other host systems based on their initial screening results. This initial screening phase provides insight into how each peptone interacts with the base medium and feeding regimen, as well as how it influences key metrics like viable cell density (VCD) and protein titer.

Likewise, when it comes to incorporating a peptone or peptones into an optimal feeding strategy, excessive concentration(s) may result in osmotic stress or nutrient imbalance, ultimately harming cell health and productivity. This is why titration studies are essential. Beginning with a cautious 1 g/L dose on day 0 allows for early assessment of performance. If the system benefits from the supplement, the concentration can be incrementally raised or added on multiple days, particularly in high-VCD cultures with greater metabolic demands and broader tolerance.

Once individual peptone bases have been screened, blending can be explored as a possible path to further performance gains. A simple 50:50 blend of two high-performing peptones may deliver unique nutritional synergies not seen with either component alone. While blending success is highly dependent on the cell line and medium, it remains an important step in the development workflow. Early experimentation can reveal unexpected enhancements in titer, protein quality, or growth kinetics—opportunities that would be missed with a single-source strategy.

Case study: comparison of peptones in simple fed-batch cultures

While some processes mandate the use of CD media, others may see a trade-off between the control offered by a completely CD system and performance gains through strategic supplementation. Peptones can bridge this gap by enhancing yield and viability without compromising process consistency. Many users remain open to performance-driven optimization, particularly in early- and mid-phase programs. In these cases, peptones can be powerful tools. Ultimately, a structured, data-informed approach to screening, titration, and blending will allow teams to evaluate the full potential of peptones without compromising process control or product consistency.

In a recent case study, Gibco™ Difco™ Phytone™ Supplement, Gibco™ Difco™ Soytone, and Gibco™ Soy 100 peptone were evaluated against other commercially available soy products to explore their consistency and utility for CHO-based processes. Gibco peptones are designed specifically for manufacturing biologics. Our dedicated R&D, production, and quality control teams focus solely on delivering consistent, high-performing solutions for cell culture applications.

The experimental data showed that peptone supplementation increased IgG production by CHO-K1 cells cultured in Gibco™ CD OptiCHO™ Medium (Table 1). Supplementation with Soy 100 peptone at 6 g/L on day 0 resulted in the highest IgG titer of 661.23 mg/L, which was 103% higher than the no-peptone control (325.28 mg/L). The results of the case study illustrate how peptone source, design, and application strategy can influence key performance metrics like VCD and IgG titer. The study highlights the ability of Soy 100 to enhance cell productivity under these conditions, offering a clear opportunity to accelerate development timelines and reduce the cost per gram of product.

Table 1. Comparison of terminal IgG titers measured on day 13 after supplementation with Gibco™ soy peptones or soy peptones from other suppliers.

		Terminal IgG titer			Difference	
Peptone	Peptone concentration	Mean titer (mg/L)	Standard deviation (SD)	Coefficient of variation (%)	No peptone	6 g/L Soy 100
None	0 g/L	325.28	–	–	0%	–51%
Difco Phytone Supplement	1 g/L	385.14	5.11	1.33	18%	–42%
	3 g/L	461.74	26.88	5.82	42%	–30%
	6 g/L	449.85	27.03	6.01	38%	–32%
Difco Soytone	1 g/L	382.07	18.53	4.85	17%	–42%
	3 g/L	496.78	8.20	1.65	53%	–25%
	6 g/L	477.05	1.10	0.23	47%	–28%
Soy 100	3 g/L	555.54	5.35	0.96	71%	–16%
	6 g/L	661.23	1.90	0.29	103%	0%
Supplier 1 peptone 1	1 g/L	362.94	20.63	5.68	12%	–45%
	3 g/L	470.84	78.10	16.59	45%	–29%
	6 g/L	550.74	10.51	1.91	69%	–17%
Supplier 1 peptone 2	1 g/L	360.69	14.58	4.04	11%	–45%
	3 g/L	441.62	16.79	3.80	36%	–33%
	6 g/L	368.79	24.86	6.74	13%	–44%
Supplier 2 peptone 1	1 g/L	364.93	7.20	1.97	12%	–45%
	3 g/L	521.60	62.18	11.92	60%	–21%
	6 g/L	602.31	1.40	0.23	85%	–9%
Supplier 2 peptone 2	1 g/L	411.83	17.04	4.14	27%	–38%
	3 g/L	531.01	12.74	2.40	63%	–20%
	6 g/L	604.23	54.45	9.01	86%	–9%
Supplier 3 peptone 1	1 g/L	347.66	8.38	2.41	7%	–47%
	3 g/L	524.40	7.38	1.41	61%	–21%
	6 g/L	521.86	7.79	1.49	60%	–21%

The analysis also reveals that the optimal peptone concentration can vary in CD OptiCHO Medium. Peak IgG titers with Difco Phytone Supplement, Difco Soytone, and Supplier 1 peptone 2 were observed with 3 g/L supplementation, suggesting potential saturation at higher concentrations (Figure 1). Conversely, improvements with Soy 100 peptone continued with supplementation up to 6 g/L.

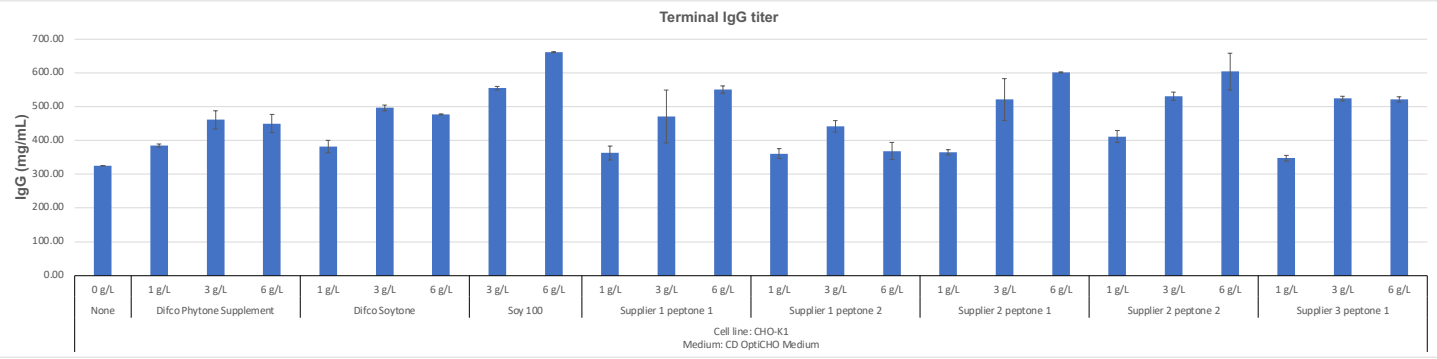

Figure 1. Terminal IgG titers across soy peptones tested at different concentrations.

Gibco peptones performed as well as or better than products from other suppliers across VCDs (Table 2 and Figure 2). Although some variability was observed, Gibco peptones generally supported higher titers and healthier VCD profiles. These findings emphasize the importance of choosing a high-quality peptone supplier and working with the supplier to identify the optimal fit for each process. We offer specifically tailored starter packs for a variety of applications, simplifying the process of identifying the most appropriate peptone for your processes.

Table 2. Peak viable cell densities observed after supplementation with Gibco soy peptones or soy peptones from other suppliers.

		Peak viable cell density				Change	
Peptone	Peptone concentration	Mean (x 10^6 cells/mL)	Day	SD	CV (%)	No peptone	6 g/L Soy 100
None	0 g/L	14.14	7	–	–	0%	–12%
Difco Phytone Supplement	1 g/L	12.99	5	2.94	22.64	–8%	–19%
	3 g/L	13.35	5	0.18	1.37	–6%	–17%
	6 g/L	14.24	5	0.45	3.18	1%	–11%
Difco Soytone	1 g/L	14.54	5	1.73	11.91	3%	–9%
	3 g/L	14.32	7	0.77	5.38	1%	–11%
	6 g/L	12.57	7	0.18	1.41	–11%	–22%
Soy 100	3 g/L	18.42	7	4.43	24.03	30%	15%
	6 g/L	16.03	7	1.68	10.50	13%	0%
Supplier 1 peptone 1	1 g/L	14.04	5	0.25	1.81	–1%	–12%
	3 g/L	14.99	5	0.75	4.98	6%	–7%
	6 g/L	14.57	5	0.15	1.00	3%	–9%
Supplier 1 peptone 2	1 g/L	15.01	5	0.63	4.17	6%	–6%
	3 g/L	14.76	7	2.34	15.86	4%	–8%
	6 g/L	8.68	7	0.20	2.28	–39%	–46%
Supplier 2 peptone 1	1 g/L	13.78	5	2.93	21.27	–3%	–14%
	3 g/L	11.72	7	0.71	6.10	–17%	–27%
	6 g/L	13.84	5	0.12	0.90	–2%	–14%
Supplier 2 peptone 2	1 g/L	12.99	7	0.54	4.19	–8%	–19%
	3 g/L	13.12	5	0.28	2.17	–7%	–18%
	6 g/L	12.98	5	0.38	2.91	–8%	–19%
Supplier 3 peptone 1	1 g/L	11.50	10	2.93	25.53	–19%	–28%
	3 g/L	16.02	7	1.54	9.62	13%	0%
	6 g/L	11.84	7	0.18	1.55	–16%	–26%

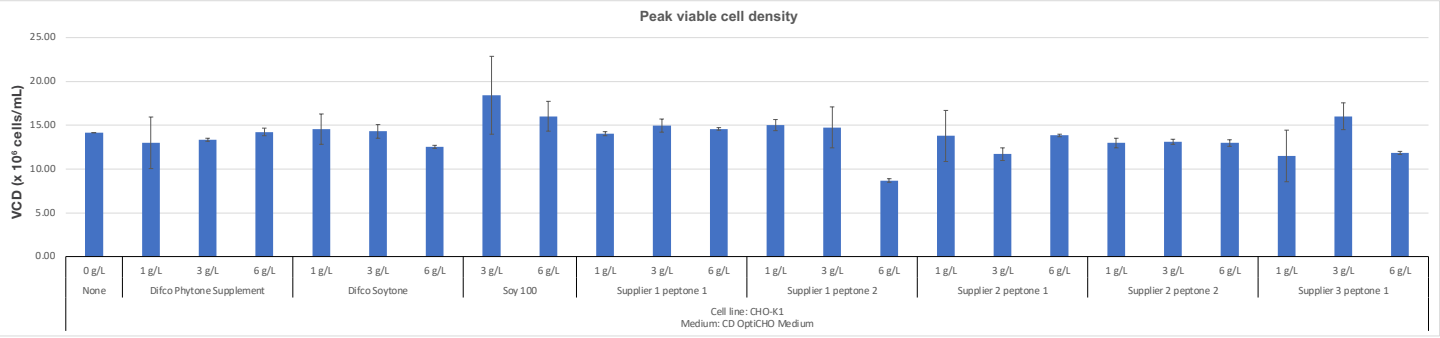

Figure 2. Peak viable cell densities observed after supplementation with Gibco soy peptones or soy peptones from other suppliers.

Conclusion

The improvements in IgG titer and VCD observed in the case study demonstrate the potential benefits of Gibco soy peptones for upstream bioprocess performance. By combining purposeful formulation, robust quality controls, and a deep understanding of bioproduction needs, we deliver soy peptones that can outperform or match peptones from other suppliers.

By delivering complex nutritional inputs that support cellular metabolism and protein expression, peptones can serve as crucial complements to CD media by potentially improving productivity, buffering against scale-related stress, and enabling more robust process performance across diverse conditions. Unlike many peptones developed for use in food or microbial applications, Gibco peptones are designed exclusively for biomanufacturing. This singular focus has enabled us to refine our manufacturing processes while minimizing lot-to-lot variability.

As bioproduction grows more complex, our evolving services, including test-and-hold programs and key driver identification (KDI) services, help reduce potential risk through several support layers. Test-and-hold programs allow customers to reserve specific peptone lots for validation, supporting consistency in future runs. KDI services can provide early insight into how individual components drive cell performance, enabling formulation adjustments tailored to each bioprocess.

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