

# Exploring Novel Compounds for Suppressing Drug Self-Administration: A Case Study in Substance Abuse Disorder Research Utilizing HPLC-ECD Analysis

Substance abuse disorder poses a significant challenge to public health, necessitating innovative approaches for intervention and treatment. Substance abuse not only erodes physical and mental health but also strains interpersonal relationships, disrupts socioeconomic stability, and burdens healthcare systems. Recognizing the far-reaching consequences of substance abuse disorder, the team is driven by a sense of urgency to develop interventions that can alleviate the human suffering and societal burden associated with substance abuse. The Hemby Lab at High Point University focuses on understanding the neurochemical underpinnings of addiction and exploring novel compounds for mitigating drug self-administration. Employing self-administration studies as their primary investigative tool, they investigate the pharmacokinetics of experimental compounds, correlating this data with neurochemical and behavioral assessments. To facilitate these investigations, they utilize advanced analytical techniques, including High-Performance Liquid Chromatography with Electrochemical Detection (HPLC-ECD). This case study highlights their methodology, particularly focusing on how HPLC-ECD analysis enhances their understanding of substance abuse disorder and aids in the evaluation of potential therapeutic interventions. Furthermore, they integrate complementary techniques such as mass spectrometry to assess compound penetration across the blood-brain barrier, providing comprehensive insights into the efficacy of novel interventions in managing substance use disorder. In this case study, we speak with Scot McIntosh, a Lab Manager in the Hemby Lab, who works directly with HPLC-ECD to shed light on how their experimental compounds modulate drug-seeking

behavior and neurochemistry. Our interview with them has been edited for formatting.

Scot McIntosh, Lab Manager - Hemby Lab, Department of Pharmacology, High Point University.

## Research Background

**Amuza:** What is the goal of your research? What social problem do you want to tackle?

**Researcher:** We study substance use disorder, our main approach doing self-administration studies. We are currently exploring how novel compounds can suppress drug self-administration. Our approach involves doing pharmacokinetic studies with these compounds and correlating this data with neurochemistry and behavioral data. Currently, we use the HTEC for measuring amino acids and biogenic amines such as dopamine and serotonin and we also use mass spectroscopy to look at



how well the experimental compounds cross the blood brain barrier.

**Amuza:** What are some of the biggest challenges you face during your research journey?

**Researcher:** Realistically, the biggest challenge is on the self-administration side of things, since long-term studies are difficult since you need to maintain catheter patency. I find the use of the HTEC for neurotransmitter analysis is pretty straight forward.

## Prior HPLC Experience

**Amuza:** What was your experience with HPLC before the purchase of the HTEC?

**Researcher:** I had a little bit of experience and used some homemade systems in the past. Dr. Hemby had a colleague that had used the HTEC system successfully and this is the main reason behind his decision to purchase the system. His colleague reassured us that the maintenance was fairly easy and the daily use was straightforward compared to other systems.

**Amuza:** Did you have any other options to measure neurotransmitters within your samples? If yes, please let me know which and why you chose the HTEC?

**Researcher:** We had really been planning on this all along, prior to having the HTEC we were doing microdialysis and using the homemade systems to measure the analytes. The older home-made systems could be really problematic and involved lots of maintenance so we really wanted to move to a system that was more reliable and reduce the amount of down-time.

## User Experience

**Amuza:** What benefits and features stood out to you during your research experience with the HTEC?

**Researcher:** What really stands out is the ease of setting up methods since everything is streamlined. Changing the parameters on the instrument is very easy and straightforward. Again, the maintenance is much more simple than the previous system we used.

**Amuza:** What type of samples do you run and why are they important?

**Researcher:** We mostly just do dialysate, and this is something we have stuck with since we have experience doing this. We have talked about running tissue homogenates before but we can answer the same questions with microdialysate and this is less harsh on the columns and system overall.

**Amuza:** How was your experience using the HTEC different from previous methods you have used for neurotransmitter analysis?



**Researcher:** We are pretty satisfied with the sensitivity of the HTEC, the sensitivity of the other systems we have used were slightly better but the big trade-off is the

ease of use. We do not need to troubleshoot nearly as much and the HTEC has much less down time than our previous system.

**Amuza: How likely are you to recommend the HTEC to a colleague?**

**Researcher:** I would absolutely recommend the HTEC for neurotransmitter analysis, the ease of use and straightforward maintenance make this approachable even for users without extensive HPLC experience. Additionally, the application notes are very helpful which is another reason I would recommend the HTEC.

**Amuza: How has the HTEC improved your research? Has it helped you solve any difficult challenges you were facing in your research? Please let us know the details.**

**Researcher:** If anything it just made everything more streamlined, easier and it causes less issues. Data generation is much improved as the system is rarely down for maintenance issues. The old system had chart paper so the software does a lot more for us and saves us a lot of time.

**Amuza: What was your experience with the support system in place at Amuza?**

**Researcher:** You guys were a great help during the installation process. We haven't needed to lean on the support so much but when we do have issues, you guys have really come through and provided timely solutions which is great.

**Amuza: Do you have any suggestions for improvements you would like to see in the future?**

**Researcher:** One issue that comes to mind is we were buying columns and hadn't realized the method had changed. I had not paid attention to the change in mobile phase pH in the application parameters but after reaching out to Amuza, you identified and fixed the issue rather quickly. So, some form of notification on the change in application parameter would have been nice. For equipment improvements, it would be nice if you could set up a system to immediately inject microdialysate being collected in real time. Another thing that could be improved is the online storefront since some of the items can be hard to find.

### Current and Future Application

**Amuza: What was your primary application of the HTEC?**

**Researcher:** Recently, we have mostly been looking at dopamine and serotonin. But previously we have looked at both glutamate and GABA. If I remember correctly, we had a panel of somewhere around 9 amino acids we could see with that one column.

**Amuza: Do you have any planned future applications of the HTEC? If not, what do you imagine you would do with it once this project is complete?**

**Researcher:** Not that I am aware of at this point, we are really just interested in detecting DA and 5HT in order to understand how our experimental compounds are affecting neurotransmitter levels in the brain.