Editorial

In defence of dependability and reliability: LC–UV/DAD

In this edition of *Pharmaceutical Methods*, I am impressed by the number of articles that use as their means of analysis Liquid Chromatography with UV/Diode Array Detection (DAD). Five or more years ago, the predictions were that all such UV/DAD would be by now replaced by Liquid Chromatography–Mass Spectrometry (LC–MS) technologies. LC–MS technologies were heralded as infallible as they are highly sensitive and selective even in the presence of multiple compounds within very complex matrices, are capable of finding related analogues and isomers, are high mass accuracy technologies that could discern between isobaric compounds or between co-eluting compounds, and their ability is seemingly endless.

One could be factious and say the main reason is the very high price point of MS and associated software, and this is a very considerable factor for most laboratories and industries. I believe that there are other reasons as well for the persistence and prevalence of UV/DAD. Firstly the use of derivative UV/Vis spectroscopy facilitates the determination of one or more wavelengths where the compound of interest absorbs. Thus, the compound can be analyzed with negligible absorption from excipients/matrix. In one of the articles in this journal, I see the use of isobestic point in a bi-component sample analysis. Also, the widespread replacement of conventional (and very limited) UV/Vis detectors with DAD allows for simultaneous multi-component analysis, once certified or reference standards are available. DAD detectors are equipped with the software to perform peak purity assessment, thus providing an extra level of quality control to the LC–UV/DAD analysis. Unknown components in a sample are unlikely to be a problem in the pharmaceutical industry as they may be in, for example, the field of natural products chemistry. Even in the event that a drug preparation contains an alien component, there are many consultancy laboratories that will provide analyte identification quickly and economically, thus negating the need for an organization to invest in very elaborate and costly technologies. LC–UV/DAD does, however, require that three conditions are met:

1. The molecule must possess a chromophore or be tagged with a UV absorbing group.
2. There has to be reasonable resolution between the target analyte and co-eluting impurities.
3. The target compound and co-elutant must absorb at different wavelengths.

Once these criteria are fulfilled, the LC–UV/DAD technology is more than capable of fulfilling the requirement of the regulatory authorities.

There is also, I think personally, a growing awareness that MS technology is not the panacea that it once seemed; for example, it is prone to ion suppression/enhancement effects which can compromise its quantitative ability. Many published papers fail to investigate whether or not their method is susceptible to this phenomenon. Ion suppression results in the presence of low volatile interferences (salts, ion pairing agents, and drug components amongst others have been identified as culprits) in the sample matrix that hinders droplet formation and evaporation at the ionization interface. This then affects the amount of charged ion in the gas that reaches the detector. In fact, ion suppression may not be evident during method development and emerges only in the sample analysis stage. There are also many published papers which emphasize that LC–MS requires little or no sample clean up. There are papers that have even gone so far as to say that chromatographic resolution of co-elutants is unnecessary. This may be the case for qualitative analysis where, for example, multiple reaction monitoring (MRM) may be deployed but is a gravely insufficient and misleading strategy for

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method validation. As stated before, mobile phase additives and interfering compounds can diminish (or in rare cases enhance) ion signal;[1] also, large compounds may suppress the ionization of smaller components[2] and more polar components can experience a higher degree of suppression than moderately or non-polar species.[3]

However, there are strategies ensuring that ion suppression can be identified and ameliorated (the real risk is lack of awareness that a problem exists and exaggerated claims by users).

Another difficulty that I have found in my own laboratory with LC–MS, especially when using an electrospray ionization (ESI) interface, is that after a few days of intense sample analysis, a fall off is observed in the sensitivity of the method. The problem is that the ESI needle gets dirty; cleaning of the needle and skimmer region rectifies the problem. Again, this is a shortcoming of LC–MS that is not, I find, discussed broadly. I also feel that the complexity of the MS detector (especially when things go wrong) can lead to protracted down time when compared with the UV/DAD.

Do not misunderstand me, I am an advocate of LC–MS in the pharmaceutical industry, and as a research tool, I find it indispensable but I predict that we will see the persistence of LC–UV/VIS and DAD methodologies for many years to come. As sometimes what is adequate and simple is completely fit for purpose.

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