Fortis™ Technologies Ltd.

Application Note

Pharmaceutical Metabolite Resolution

Introduction

Drug safety is paramount to all pharmaceutical companies as their products will never make it to market if they do not pass strict regulations controlling the safety of every single dose. It is often the case that the drug itself is not toxic but as the body metabolizes the drug to turn it into polar, more water soluble, metabolites that it can easily excrete it can form harmful metabolites. This is the case with paracetamol (acetaminophen), Figure 1, which has thee metabolic pathways the first 2, glucuronidation, Figure 2, and sulfation, Figure 3, form non toxic metabolites. Unfortunately the 3rd pathway results in N-acetyl-

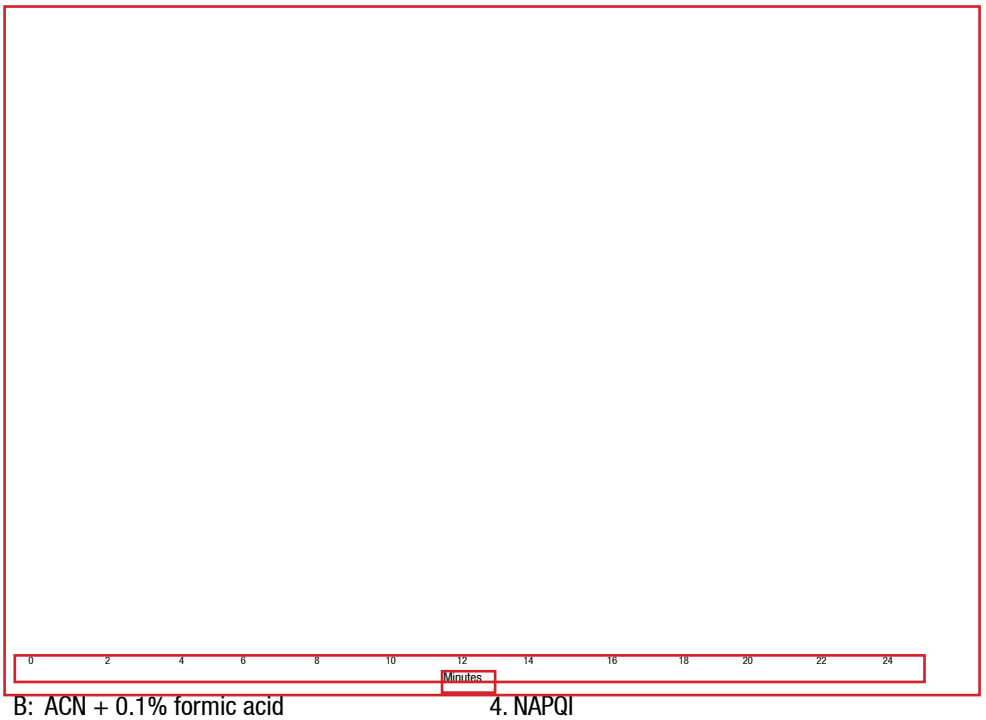
> "A drugs safety is paramount, if it doesn't pass strict regulations it will never make it to market"

p-benzo-quinone imine (NAPQI), Figure 4, which causes hepatic necrosis (death of liver cells) this is often encountered in overdose patients leading to liver failure and death. Pharmaceutical companies have to verify the safety of their drugs in the earliest stages of development in preclinical discovery and phase I development where absorption, distribution, metabolism, and excretion (ADME) testing establishes excretion routes, drug safety and tolerable dose in healthy humans. These studies include extensive investigations to identify all metabolites. HPLC is one of many techniques used to find metabolites it is often attached to mass spectrometers to allow simultaneous identification.

Experimental

Column : 1.7um Fortis Diphenyl 50x2.1mm
p/n FPH-020301

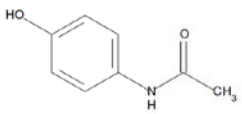
Mobile Phase:
A: H2o + 0.1% formic acid



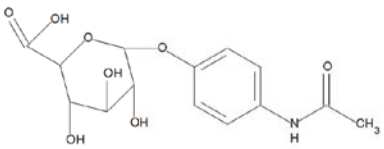
B: ACN + 0.1% formic acid

Temp : 25oC
Detection : UV 244nm

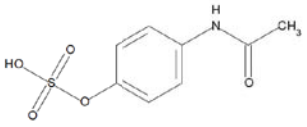
1. Paracetamol (Acetaminophen)



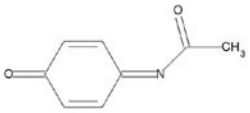
2. Paracetamol Glucuronide



3. Paracetamol Sulphate



4. NAPQI



Results

Excellent resolution of polar metabolites has been achieved on the diphenyl stationary phase.

Conclusion

Di-phenyl offers unique retention and selectivity and is a valuable stationary phase for the separation of polar metabolites.