The Use of Covaris Adaptive Focused Acoustics in PsychiatryCEDD DMPK

Rosemary Melarange1, Parmjit Sadra1, Andy Harris1, David Clapham2 and Jon Curtis3

GlaxoSmithKline (GSK), New Frontiers Science Park, Third Avenue Harlow, Harlow, Essex CM19 5AW
1PsychiatryCEDD DMPK (GSK)
2WW Pharmaceutical Development (GSK)
3KBioSciences, Hoddesdon, Hertfordshire

Introduction
In PsychiatryCEDD DMPK sonication and homogenisation is routinely used to aid compound dissolution and tissue sample preparation. Introduction of the Covaris using Adaptive Focused Acoustics (AFA) has enabled the formation of more consistent formulated doses for studies and fine tissue preparations for analysis. Compared to mechanical homogenisation the Covaris is a silent compact instrument which avoids contamination caused by interference of external probes.

Software
The software, SonoLAB runs the Covaris AFA. Treatment Settings with different variables can be saved.

Acoustic Treatment Setting Variables
1. Duty Cycle - % on time
2. mV or Intensity – Amplitude of the wave form
3. Cycles / Burst – No of waves applied during the on time

Preparation of Oral doses
PsychiatryCEDD DMPK studies use oral doses prepared as suspensions in 1% (w/v) methylcellulose aq. Previously these have been prepared using magnetic stirring or mechanical homogenisation and sonication. These techniques were mainly, lengthy and not reproducible.

To investigate the utility of AFA for dose preparation we used Carbamazepine, a reasonably insoluble compound was used to compare the Covaris to other preparation techniques.

Method
• 15mL doses of Carbamazepine at 1.5mg/mL in 20mL scintillation vials were prepared.
• The doses were formulated using the optimum conditions for the Covaris at 5, 15, 20 and 30min.

Duty Cycle – 20% Intensity – 10 Cycles / Burst – 500
• For comparison, Carbamazepine doses were also formulated using sonication and a magnetic stirrer (data not shown) at 15, 20 and 30min.
• The particle size of each dose pre and post formulation was measured using the “Particle Size Analyser_Lecotrac 7.01 LT100”

Results
From the graph shown, it is clearly evident that the Covaris produced a superior po dose suspension compared to sonication. The data shows that the optimum time for minimising particle size to 1um is 15mins (sonication 300um after 15mins), after which the particles begin to increase in size again.

References www.covarisinc.com