Caffeine Concentration Simulation

- `Caffeine Concentration Simulation` https://www.edison.re.kr/web/cmed/run_simulation (https://www.edison.re.kr/web/cmed/run_simulation)
- There is also `Caffeine Concentration Predictor` shiny app. https://asan.shinyapps.io/caff (https://asan.shinyapps.io/caff)
- `Caffeine Concentration Simulation` is open to everyone. We are happy to take your input. Please fork the repo, modify the codes and submit a pull request. https://github.com/shanmdphd/CaffeineEdison (https://github.com/shanmdphd/CaffeineEdison)

Reference

This work is solely dependent on the interesting paper published in Eur J Pediatr in 2015.

- "Prediction of plasma caffeine concentrations in young adolescents following ingestion of caffeinated energy drinks: a Monte Carlo simulation." Eur J Pediatr. 2015 Dec;174(12):1671-8. doi: 10.1007/s00431-015-2581-x https://www.ncbi.nlm.nih.gov/pubmed/26113286 (https://www.ncbi.nlm.nih.gov/pubmed/26113286)
- "Clinical pharmacokinetics and pharmacodynamics: concepts and applications, 4th edition" Lippincott Williams & Wilkins. 2011. ISBN 978-0-7817-5009-7

The pharmacokinetic parameters from the paper were derived and used in the app as follows:

$$\begin{bmatrix} \eta_1 \\ \eta_2 \\ \eta_3 \end{bmatrix} \sim MVN\left(\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} 0.1599 & 6.095 \cdot 10^{-2} & 9.650 \cdot 10^{-2} \\ 6.095 \cdot 10^{-2} & 4.746 \cdot 10^{-2} & 1.359 \cdot 10^{-2} \\ 9.650 \cdot 10^{-2} & 1.359 \cdot 10^{-2} & 1.004 \end{bmatrix} \right)$$

$$\begin{aligned} CL\ (mg/L) &= 0.09792 \cdot W \cdot e^{\eta 1} \\ V\ (L) &= 0.7219 \cdot W \cdot e^{\eta 2} \\ k_a\ (1/hr) &= 4.268 \cdot e^{\eta 3} \end{aligned}$$

$$\begin{aligned} k\ (1/hr) &= \frac{CL}{V} \\ t_{1/2}\ (hr) &= \frac{0.693}{k} \\ t_{max}\ (hr) &= \frac{ln(k_a) - ln(k)}{k_a - k} \\ C_{max}\ (mg/L) &= \frac{Dose}{V} \cdot \frac{k_a}{k_a - k} \cdot (e^{-k \cdot t_{max}} - e^{-k_a \cdot t_{max}}) \\ AUC\ (mg \cdot hr/L) &= \frac{Dose}{CL} \end{aligned}$$

$$\begin{aligned} C_{av,ss} &= \frac{Dose}{CL \cdot \tau} \\ AI &= \frac{1}{1 - e^{-k_e \cdot \tau}} \end{aligned}$$

(Abbreviation: AI, accumulation index; AUC, area under the plasma drug concentration-time curve; CL, total clearance of drug from plasma; $C_{av,ss}$, average drug concentration in plasma during a dosing interval at steady state on administering a fixed dose at equal dosing intervals; C_{max}, highest drug concentration

observed in plasma; MVN, multivariate normal distribution; V, Volume of distribution (apparent) based on drug concentration in plasma; W, body weight (kg); η, interindividual random variability parameter; k, elimination rate constant; k_a, absorption rate constant; τ, dosing interval; $t_{1/2}$, elimination half-life)

R Packages

- H. Wickham. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York, 2009.
- Winston Chang, Joe Cheng, JJ Allaire, Yihui Xie and Jonathan McPherson (2016). shiny: Web Application Framework for R. R package version 0.14.2. https://CRAN.R-project.org/package=shiny (https://CRAN.R-project.org/package=shiny)
- JJ Allaire, Jeffrey Horner, Vicent Marti and Natacha Porte (2015). markdown: 'Markdown' Rendering for R. R package version 0.7.7. https://CRAN.R-project.org/package=markdown (https://CRAN.R-project.org/package=markdown)
- Hadley Wickham and Romain Francois (2016). dplyr: A Grammar of Data Manipulation. R package version 0.5.0. https://CRAN.R-project.org/package=dplyr (https://CRAN.R-project.org/package=dplyr)

Caffeine contents