# Simulación PKPD-VK

Ivermectina en el tratamiento de infección por SARS-CoV-2

Daniel S. Parra G.

Universidad Nacional de Colombia

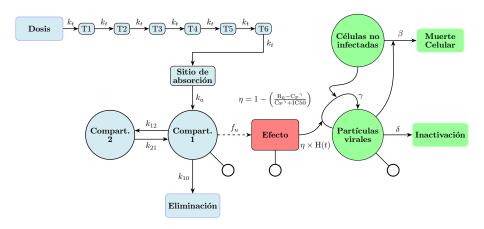
10 de julio de 2020

# Conteni<u>do</u>

Introducción

Cinética viral

## Modelo combinado



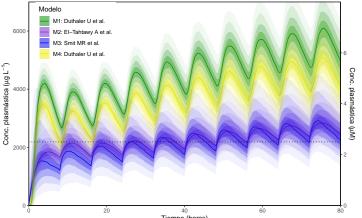
Modelo PK: Duthaler U, Suenderhauf C, Karlsson MO, et al. Population pharmacokinetics of oral ivermectin in venous plasma and dried blood spots in healthy volunteers. Br J Clin Pharmacol 2019; 85: 626–633.

Modelo PD: Caly L, Druce JD, Catton MG, et al. The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res 2020; 104787.

## Simulación PK de ivermectina

#### Simulación farmacocinética Ivermectina

Ivermectina PO Dosis inicial 800 mg + 400mg q8h



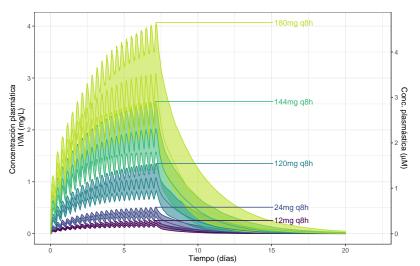
Tiempo (horas)

Marc Lavielle (2019). mlxR: Simulation of Longitudinal Data. R package version 4.1.0. https://CRAN.R-project.org/package=mlxR

[M1] Dutaler I., et al. Population pharmacokinetics of oral ivermectin in venous plasma and dried blood spots in healthy volunteers. Br J Clin Pharmacol. 2019; 56(3):562–33 (M2) El-Tahlathy A et al. The effect of azithromycin on the writerion pharmacokinetic model analysis. PLoS Negl Trop Dis. 2008; 2(5) [M3] Smit MR, Ochrom EO, Waterhous D. Kwamba III. Alborgo BO, Boussmar I. et al. Pharmacokinetics—Pharmacokinetics—Does wermechine with Dityrionatemismin—Piperaquine on Meyoliucotidal Activity and OT-Prolongation (VERNAL). Clin Pharmacokinetic oral pharmacokinetics—Alboracokine

## Farmacocinética

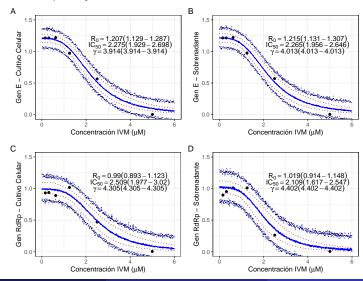
#### Farmacocinética de ivermectina; tratamiento por 7 días



PK: Duthaler U, Suenderhauf C, Karlsson MO, Hussner J, Meyer zu Schwabedissen H, Krähenbühl S, et al. Population pharmacokinetics of oral ivermectin in venous plasma and dried blood spots in health volunteers Br. J Clin Pharmacol. 2019;95(3):628–33.

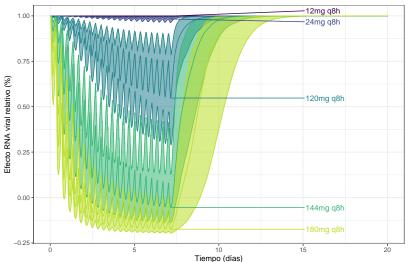
### Modelamiento PD ivermectina

Inhibición replicación SARS-II COVID-19 Estimación bayesiana algoritmo NUTS - Ivermectina



# Farmacodinámica

Reducción relativa viral vs dosis de ivermectina RNA Gen E - Cultivo Celular

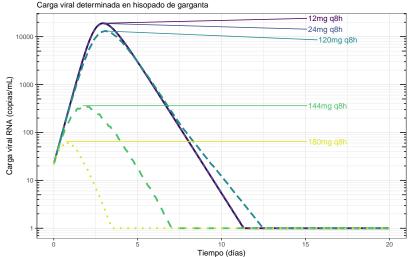


Simulación PKPD-VK

PD: Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved Drug Ivermectin

# Cinética viral (1)

### Curso de la infección SARS-COV-2 vs dosis de ivermectina

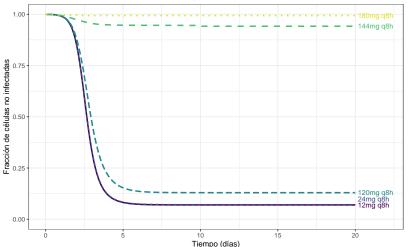


Farmacodinamia: Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved Drug Ivermeditin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res. 2020:10477. Cinética viral: Kim KS, Ejima K, Ito Y, Iwanami S, Ohashi H, Koizumi Y, et al. Modelling SARS-CoV-2 Dynamics: Implications for Therapy medity. 2020:2020.03 23 2004.045.

# Cinética viral (2)

#### Curso de la infección SARS-COV-2 vs dosis de ivermectina

Fracción: células no infectadas vs células susceptibles iniciales



Farmacodinamia: Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA–approved Drug Ivermectin inhibits the replication of SARS–COV-2 in vitro. Antiviral Res. 2020;104787. Cinética viral: Kim KS, Ejima K, Ito Y, Iwanami S, Ohashi H, Kolzumi Y, et al. Modelling SARS–COV-2. Drumanies: Implications for Therany medRev. 2020;2020;103:23.2004.0493.

# Treemap Ivermectina

Treemap of Adverse Drug Reactions (ADR) with Ivermectin

ADR total count: 8613; The area of each square represents the number of reported cases.

Vascular Asthenia disorders General disorders and urinary administration site Eve disorders disorder Pyrexia Gastrointestinal infestation disorders Rosacea Skin and Blister subcutaneous tissue Nervous Injury, poisoning and Dsystem procedural

Adapted from: Uppsala Monitoring Center. Vigiaccess. Available at: http://www.vigiaccess.org/ [Accessed: July 2020]

Made by DSPG