

**A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL FOR
ALCOHOL METABOLISM**

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ปราधान ชิงค์: การศึกษาแบบจำลองจลเภสัชศาสตร์ทางกลไกชีวภาพสำหรับแอลกอฮอล์ (Physiologically Based Pharmacokinetics Model For Alcohol Metabolism) อ. ที่
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จุดมุ่งหมายสูงสุดของการวิจัยนี้คือการพัฒนาแบบจำลองจลเภสัชศาสตร์ทางกลไกชีวภาพสำหรับการสลายแอลกอฮอล์เพื่อช่วยในการป้องกันหรือลดเหตุการณ์เป็นพิษจากการเกิดแอลกอฮอล์แบบจำลองที่มีอยู่ทั้งหลายไม่มีความเข้ากันเองเนื่องจากแบบจำลองเหล่านั้นละเมิดกฎมาตรฐานของปฏิกิริยาถูกใจในการสลายแอลกอฮอล์งานนี้ได้ถูกพัฒนาแบบจำลองที่มีความเข้ากันเองสำหรับการสลายแอลกอฮอล์ซึ่งเป็นการรวมของจลศาสตร์ทางปฏิกิริยาเคมีชีวเคมีแบบจำลองจลเภสัชศาสตร์ทางกลไกชีวภาพแบบจำลองสามารถที่จะทำนายโครงสร้างความสัมพันธ์ระหว่างความแอทธานอดและอะเซททลดีไฮด์กับเวลาได้พร้อมกันในครั้งแรกกลไกชีวภาพของมนุษย์และสัตว์เลี้ยงลูกด้วยนมถูกจำลองโดยการรวมปริมาตรของอวัยวะเข้าด้วยกันเป็นส่วนๆซึ่งขึ้นอยู่กับอัตราการถ่ายเทของไหลผ่านอวัยวะแต่ละชิ้นและความสัมพันธ์ทางกายภาพของอวัยวะทั้งหลายรวมถึงการเอทธานอดและอะเซททลดีไฮด์เครื่องมือเพื่อหาค่าที่เหมาะสมของเมทแลปถูกใช้เพื่อหาค่าที่เหมาะสมของกลไกชีวภาพและจลศาสตร์แบบจำลองนี้ให้โครงสร้างของความสัมพันธ์ระหว่างความเข้มข้นเอทธานอดและอะเซททลดีไฮด์กับเวลาและการประมาณค่าตัวแปรซึ่งมีความสัมพันธ์อย่างดีกับค่าจากทดลอง

ABSTRACT

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Physiologically Based Pharmacokinetic (PBPK) model

The ultimate aim of this work is to develop a physiologically based pharmacokinetic model to understand alcohol metabolism to help prevent or decrease incidents of toxicity caused by alcohol poisoning. The existing models are not self consistent as they violate the stoichiometry of the series reactions in alcohol metabolism. This work has developed a robust self consistent model for alcohol metabolism which is a combination of biochemical reaction kinetics and physiologically based pharmacokinetic modeling approaches. The model can predict for the first time simultaneously the ethanol and acetaldehyde concentration time profile. Human and mammals physiology is simulated by lumping organ volumes into well mixed compartments based on the perfusion rate of fluid through each organ, the physical connectivity between organs and ethanol and acetaldehyde metabolic activity. Matlab optimization toolbox: Isqnonlin have been used to determine the optimal physiological and kinetic parameters values. The PBPK model gives simultaneously ethanol and acetaldehyde concentration time profiles and provides optimal estimates of parameter values which co-relate well with the experimental values.

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