Paracetamol ADME

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references


Reactome database release: 79

This document contains 1 pathway and 13 reactions (see Table of Contents)
Paracetamol ADME

Stable identifier: R-HSA-9753281

Paracetamol (APAP, aka acetaminophen or N-acetyl-p-aminophenol) is an analgesic drug used for to treat mild to moderate pain and as an antipyretic agent. It is one of the most widely used drugs in the world and is available alone or in combination with other drugs for pain relief, fever and allergy. It is thought to act through the inhibition of cyclooxygenases 1 and 2 (Graham et al. 2013, Esh et al. 2021). Paracetamol is generally safe at therapeutic doses but in overdose cases, it causes mitochondrial dysfunction and centrilobular necrosis in the liver which can lead to death.

APAP has a high oral bioavailability (~88%), is well absorbed and reaches peak blood concentrations after 90 minutes after ingestion. APAP binds plasma proteins to a small extent and has a plasma half-life of 1.5-3 hours. Most of the drug is eliminated by glucuronidate and sulfate conjugation (~55% and ~30% respectively) in the liver or as unchanged drug (~5%) (Forrest et al. 1982). A small amount (5-15%) is oxidised to the reactive metabolite N-acetyl-para-benzoquinone imine (NAPQI). NAPQI is usually detoxified by binding to liver glutathione but in overdose cases, glutathione is depleted and NAPQI instead, binds to sulfhydryl groups on proteins, leading to liver damage. ABCC2, ABCC3, ABCC4 and ABCG2 transporters mediate the efflux of APAP metabolites out of cells (McGill & Jaeschke 2013).

Literature references


Editions

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APAP translocates from extracellular region to cytosol

**Location:** Paracetamol ADME

**Stable identifier:** R-HSA-9754180