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**17/sci03/007**

**Title : Drug delivery and revision**

**Bch306 assignment**

**Question: write explicitely on the process of metabolism of acetaminophen and how**

**It exit the body**

**Answer**:

Metabolism of acetaminophen in the body

Acetaminophen (N-acetyl-para-aminophenol, APAP or paracetamol) is the most widely used over-the- counter and prescription painkiller in the world.While safe at therapeutic doses of up to 4 grams per day for adults, acetaminophen overdoses, either accidental or intentional, are the leading cause of acute liver failure in the United States, accounting for some 56,000 emergency room visits, 2,600 hospitalizations and nearly 500 deaths annually.

**Phase1:**

Acetaminophen is metabolized by conjugation with sulfate and glucoronidate, which are inert and are excreted in the urine. Depending on dose, a fraction of APAP is converted into a highly reactive toxic intermediate, N-acetyl-p-benzoquinone imine(NAPQI) by several P450 cytochromes.

**Phase2**:

Substantial amounts of NAPQI are effectively eliminated by conjugation with glutathione (GSH). However, after a large dose of APAP, the sulfonation reaction becomes saturated and the build up of NAPQI depletes GSH in the liver, causing further accumulation of NAPQI. Unconjugated NAPQI binds to proteins and sub cellular structures and induces rapid cell death and necrosis that can lead to liver failure. Elimination occurs in the liver, where the majority of the drug is either glucuronidated or sulfated and then excreted in the urine. APAP-glucuronide accounts for 50–70% of the administered drug after a therapeutic dose in humans. Glucuronidation is catalyzed by UDP-glucuronosyl transferases (UGT) .These enzymes transfer the glucuronosyl group of uridine 5’-diphospho-glucuronic acid (UDPglucuronic acid) to target molecules, making them more water-soluble so it can exit the body .