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Perspective

Water-Soluble Steroids Produced by Hepatocytes

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DESCRIPTION

Bile Acids (BA) are a class of water-soluble steroids produced by the liver's hepatocytes during the breakdown of cholesterol. Primary bile additions are the names given to the two byproducts, cholic acid and chenodeoxycholic acid. Then, primarily to taurine or glycine, these principal bile acids are conjugated. Conjugated bile acids, which go through the gallbladder, bile duct, and duodenum to the colon, are crucial for the digestion and absorption of fats (and fat-soluble vitamins). Bile acids have a high level of cytotoxicity and can function as nuclear sensors to monitor and regulate their own amounts within the body. Additionally, some tissues' carcinogenesis is greatly influenced by bile acids (liver, gallbladder, upper and lower gastrointestinal tract). The gallbladder stores bile acids at exceptionally high concentrations (>300 mm), which are made possible by routinely removing water and electrolytes. Since cholesterol is a precursor to bile acids and is only eliminated from the body when 5% of these bile acids enter the colon for excretion in the faeces (as bile). Heavy metals like copper or iron that are in excess of what the body requires, as well as lipophilic steroids and drug metabolites that are insoluble in urine, are among the colours found in bile. Bilirubin and other hues originating from haem catabolism are also present.

Bacterial enzymes in the colon deconjugate the conjugated primary bile acids, resulting in the production of free bile acids. Additionally, the bacterial flora's enzyme activity changes the primary bile acids into secondary bile acids by removing the hydroxyl group from the molecule's seventh carbon atom. The particular enzyme at fault is 7 alpha-dehydroxylase, which creates Lithocholic Acid (LCA) from chenodeoxycholic acid and Deoxycholic Acid (DCA) from cholic acid. These secondary bile acids then travel through the portal vein to the liver, where they combine with fresh primary bile acids. The liver's canaliculi subsequently reconjugate these secondary bile acids to glycine or taurine, which is then stored in the gallbladder. The enterohepatic circulation, which can take place ten times each day, is what is known as this process of recycling bile acids. The Bile Salt Excretion Pump (BSEP) is expressed in the liver's canalicular membrane, aiding in the ATP dependent process of transport across the membrane. Conjugation makes bile acids more soluble in water and nearly impermeable to the intestine and duodenum's cell membranes, which prevents them from passing through the intestinal lumen. By doing so, bile acid concentrations in the lumen can increase until they reach sufficient levels to create micelles, which facilitate lipid emulsion and subsequent absorption. However, this chapter will concentrate on the more prevalent bile acids, including cholic and chenodeoxycholic acids (primary bile acids), deoxycholic acid and lithocholic acids, and their glycine and taurine conjugates. Many other BAs are formed at lower levels both in the colon and liver by the bacterial flora and conjugation with other biomolecules. These are the primary subcategories of bile acids, but other "minor" bile acids play important roles. One is Ursodeoxycholic Acid (UDCA), which is highly appreciated in Eastern medicine and, as its name suggests, is found in great abundance in bears. Along with other other BAs and their numerous isomers, it can also be produced by the bacterial flora of humans. Ursodeoxycholic acid is used medically to dissolve gallstones and shield cells from the damaging effects of other BAs like DCA in cholestatic disorders. It also plays a function in the regulation of human cholesterol. When used medically, UDCA is made from cholic acid, a byproduct of the slaughterhouse, rather from bears.

CYP 27A1 and cholesterol interact enzymatically in another indirect pathway, resulting in the production of both 27-hydroxycholesterol and 3-beta-hydroxy-5-cholestanoic acid (omitted from the diagram for simplification). The primary location of reaction for this route is the inner mitochondrial membranes. Steroid acute response protein in the adrenal glands transports cholesterol to the mitochondrial membrane. Star serves as a reliable source of cholesterol for these processes because it is required for steroid genesis. The brain has a second important system called the cholesterol 24-hydroxylase pathway. The plasma membranes of myelin sheaths contain about 25% of the total amount of cholesterol in the body. It is difficult for cholesterol to leave the brain in this situation because the blood-brain barrier prevents exchanges of cholesterol with circulating lipoproteins. The cytochrome P-450 enzymes (CYP 46), expressed nearly exclusively in the endoplasmic reticula of the brain, allows synthesis of 24-hydroxycholesterol.

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Due to the nature of the data, it is impossible to ascertain the relative contributions of any of these processes to overall bile-acid production. Other patients would be atypical due to illness, and many data were collected from experimental animals, which may metabolize these chemicals differently than humans. Some results were obtained from patients who had their gallbladders surgically removed. Since the intermediates could serve as substrates for multiple enzymes, the precise order of many of the events is also unknown.