- **first-pass metabolism:-** a process in which a drug administered by mouth is absorbed from the gastrointestinal tract and transported via the portal vein to the liver, where it is metabolized. As a result, in some cases only a small proportion of the active drug reaches the systemic circulation and its intended target tissue. First-pass metabolism can be bypassed by giving the drug via sublingual or buccal routes.

- The first-pass effect (also known as first-pass metabolism or pre systemic metabolism) is a phenomenon of drug metabolism whereby the concentration of a drug is greatly reduced before it reaches the systemic circulation. It is the fraction of drug lost during the process of absorption which is generally related to the liver and gut wall. Notable drugs that experience a significant first-pass effect are imipramine, morphine, propranolol, buprenorphine, diazepam, midazolam, demerol, cimetidine, and lidocaine.

- After a drug is swallowed, it is absorbed by the digestive system and enters the hepatic portal system. It is carried through the portal vein into the liver before it reaches the rest of the body. The liver metabolizes many drugs, sometimes to such an extent that only a small amount of active drug emerges from the liver to the rest of the circulatory system. This first pass through the liver thus greatly reduces the bioavailability of the drug.

- The four primary systems that affect the first pass effect of a drug are the enzymes of the gastrointestinal lumen, gut wall enzymes, bacterial enzymes, and hepatic enzymes.
- In drug design, drug candidates may have good drug likeness but fail on first-pass metabolism, because it is biochemically selective.

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- Alternative routes of administration like suppository, intravenous, intramuscular, inhalational aerosol, transdermal and sublingual avoid the first-pass effect because they allow drugs to be absorbed directly into the systemic circulation. Note that the intravenous route also avoids the absorption phase.

- Drugs with high first pass effect have a considerably higher oral dose than sublingual or parenteral dose. There is marked individual variation in the oral dose due to differences in the extent of first pass metabolism. Oral bioavailability is apparently increased in patients with severe liver diseases like Cirrhosis. It is increased if another drug competing with it in first pass metabolism given concurrently. Eg. propranolol and chlorpromazine

First pass Metabolism

- Metabolism of a drug during its passage from the site of absorption into the systemic circulation.
- Extent of first pass metabolism differs in different drugs

Extent of first pass metabolism of important drugs

Low	Intermediate	High – not given orally	High oral dose
Phenobarbitone	Aspirin	Isoprenaline	propranolol
Phenylbutazone	Quinidine	Lignocaine	Alprenolol
Tolbutamide	Desipramine	Hydrocortisone	Verapamil
Pindolol	Nortriptyline	Testosterone	Salbutamol