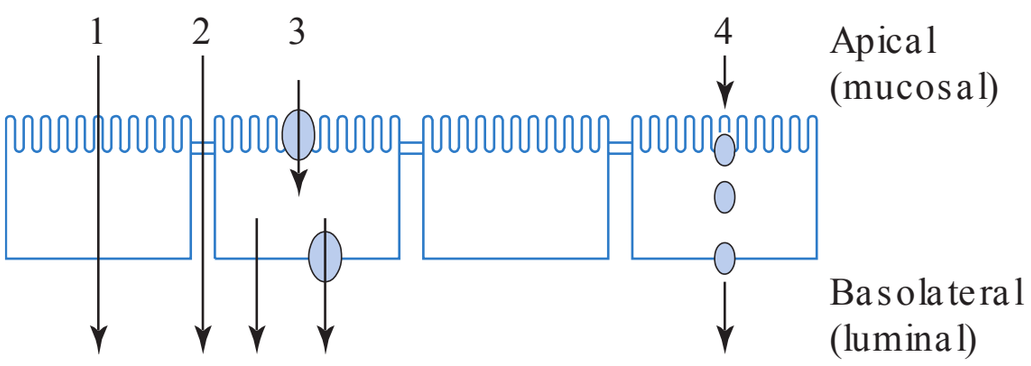
passage of others. It is permeable to amino acids, sugars, fatty acids and other nutrients and is impermeable to plasma proteins. The membrane can be viewed as a semipermeable lipoidal sieve, which allows the passage of lipid-soluble molecules across it and the passage of water and small hydrophilic molecules through its numerous aqueous pores. In addition, there are a number of transporter proteins or carrier molecules that exist in the membrane and which, with the help of energy, transport materials back and forth across it.

Mechanisms of transport across the membrane

There are two main mechanisms of drug transport across the gastrointestinal epithelium: transcellular (i.e. across the cells) and paracellular (i.e. between the cells). The transcellular pathway is further divided into simple passive diffusion, carrier-mediated transport (active transport and facilitated diffusion) and endocytosis. These pathways are illustrated in Figure 19.9.



1 – Transcellular 3 – Carrier mediated
2 – Paracellular 4 – Transcytosis

Fig. 19.9 • Mechanisms of permeability (absorptive).

Transcellular

Passive diffusion

This is the preferred route of transport for relatively small lipophilic molecules and thus many drugs. In this process, drug molecules pass across the lipoidal membrane via passive diffusion from a region of high concentration in the lumen to a region of lower concentration in the blood. This lower concentration is maintained primarily by blood flow. The rate of transport is determined by the physicochemical properties of the drug, the nature of the membrane and the concentration gradient of the drug across the membrane. The process initially involves the partitioning of the drug between the aqueous fluids within the gastrointestinal tract and the lipoidal-like membrane of the lining of the epithelium. The drug in solution in the membrane then diffuses across the epithelial cell/cells within the gastrointestinal barrier to blood in the capillary network in the lamina propria. Upon reaching the blood, the drug will be rapidly distributed, so maintaining a much lower concentration than that at the absorption site. If the cell membranes and fluid regions making up the gastrointestinal-blood barrier can be considered as a single membrane, then the stages involved in gastrointestinal absorption could be represented by the model shown in Figure 19.10.

Passive diffusion of drugs across the gastrointestinal-blood barrier can often be described mathematically by Fick's First Law of Diffusion (see Chapter 2). When considered in the context of bioavailability, this indicates that the rate of diffusion across a membrane (dC/dt) is proportional to the difference in concentration on each side of that

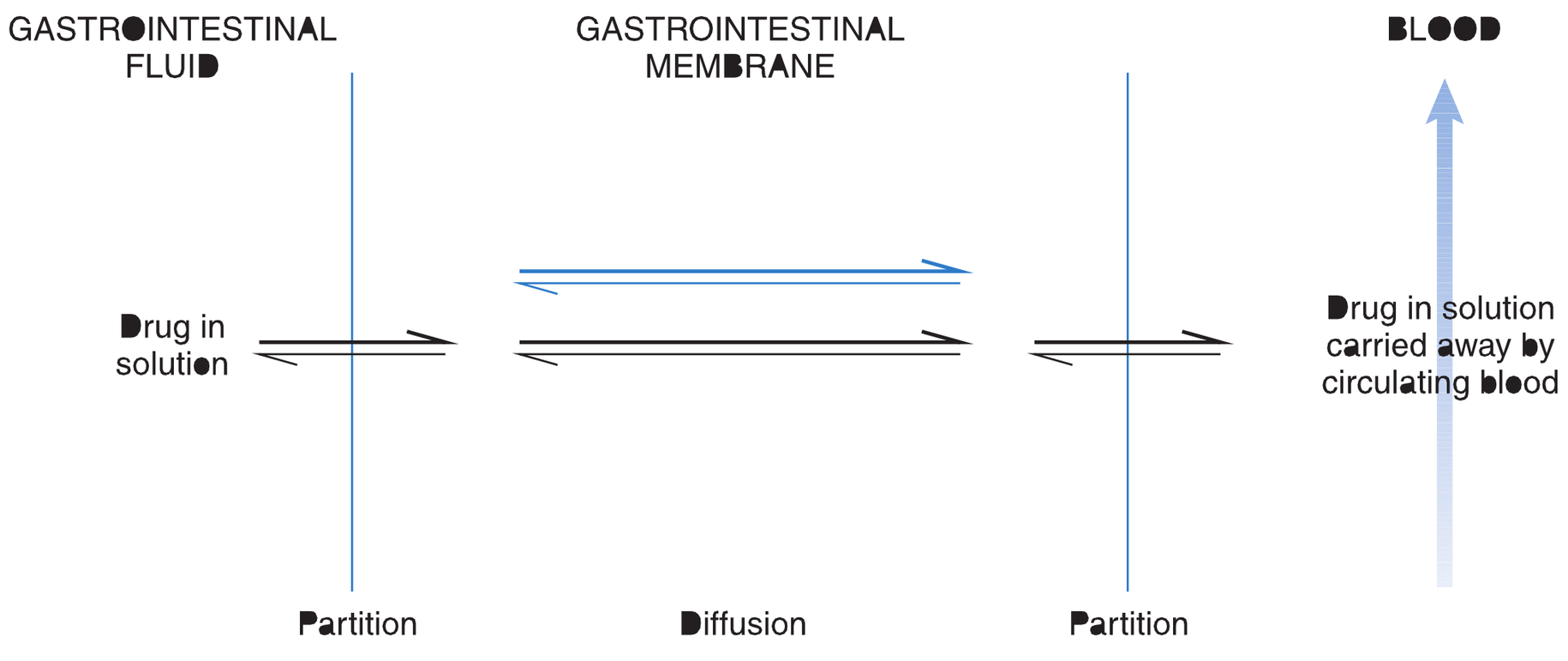


Fig. 19.10 • Diagrammatic representation of absorption via passive diffusion.