peptide transporters in the BBB aid in the translocation of peptide molecules into the CNS.

2.5. Nucleoside Transporters

The nucleoside transporters are a group of proteins that are important for drug disposition. The kidney and intestine possess these transport proteins, responsible for the transport of nucleoside bases and nucleoside analogs (63–66). Two types of transport systems exist: equilibrative and concentrative (21). Whereas equilibrative proteins are involved in facilitated diffusion, concentrative transport proteins are energy dependent.

The equilibrative bases, including hENT1 and hENT2, possess broad substrate specificities. These proteins are expressed in the basolateral membrane of many tissues (67). The concentrative nucleoside transporters, CNT1 and CNT2, participate in sodium-dependent transport. Substrates for nucleoside transporters consist of both endogenous and synthetic nucleosides, including many medications used to treat cancer and viral infections (33). Recent data suggests that renal equilibrative and concentrative transporters mediate active reabsorption of nucleosides by the kidney (68).

3. EXPERIMENTAL METHODS USED TO STUDY MEMBRANE DRUG TRANSPORT

Recent technological advances should be credited for producing the wealth of information that has been obtained regarding the identification and characterization of membrane transporters and assessing their impact on drug disposition and activity. Table 3 summarizes and compares the various experimental approaches available to study drug transport. Although the application of these methods in high-throughput screening of new chemical entities is discussed in Chapter 10, a summary of experimental methods that are referenced in this chapter is provided here.

3.1. Pharmaceutical Molecular Biology

Cell-culture methodology has been applied to study numerous aspects of drug transport over the past decade. Caco-2 cells, derived from human adenocarcinoma cells of the colon, have been widely used to study intestinal transport and metabolism of xenobiotics (69). A list of available cell lines used to characterize organ transport is provided in Table 4. Potential disadvantages of these isolated cell lines include diminished activity of certain enzyme systems and reduced transport activity compared with in vivo.

Gene transfection of isolated cell lines has allowed for characterization of specific membrane transporters and is particularly useful in identifying