# 5. TYPES OF CONTROLLED-RELEASE DRUG DELIVERY SYSTEMS

Although there are numerous types of controlled-drug delivery systems with different release mechanisms, the two main systems based on the principle of drug release are diffusion-controlled systems and dissolution-controlled systems as presented in Table 1. Also, systems following both these principles are available, called hybrid systems or diffusion-dissolution-controlled systems. Each of these systems is further divided into matrix type and reservoir type.

## 5.1. Diffusion-Controlled Systems

Diffusion occurs from the region of higher concentration to the region of lower concentration and is described mathematically by Fick's law of diffusion as follows:

$$J = -D\frac{dc}{dx}$$

where $J$ = flux, $D$ = diffusion coefficient, and $dc/dx$ = change in concentration $c$ with distance $x$.

Hence, as the name suggests, these systems are characterized by the diffusion of the drug from the system into the surroundings, either by diffusion through the channels in the matrix or through the pores in the membrane.

### 5.1.1. Reservoir-type diffusion-controlled systems

These systems comprise of a drug core enclosed within a polymeric membrane (generally EC or PVA). Upon coming in contact with the GI fluids, the drug partitions into the membrane and diffuses out into the surrounding media as shown in Fig. 2. Such release can be mathematically be represented by the following equation:

$$\frac{dm}{dt} = ADK\frac{\Delta C}{l}$$

where $dm/dt$ = rate of drug release, $A$ = area available for diffusion, $K$ = core to membrane partition coefficient of the drug, $l$ = diffusion path length, and $\Delta C$ = concentration gradient.

In the above equation, the most important parameter is the partition coefficient of the drug between the drug core and the enclosing membrane. The more the partition coefficient, faster the drug depletes out of the core; hence, zero order is maintained for a relatively short duration of time [45].

These systems cannot be used for delivering high doses as they pose the risk of toxicity upon failure of membrane integrity. Also, the cost of dose per unit is high because additional coating operation is required to coat the polymer on active core. Nevertheless, these systems do have some potential for obtaining zero-order release with the optimization of polymer concentration and thickness of coating layer [51].

### 5.1.2. Matrix-type diffusion-controlled systems

In these systems, the drug is uniformly dispersed in an inert insoluble polymeric matrix. When the system comes in contact with GI fluid, the drug is dissolved in the fluid and diffuses out from the delivery system. The dissolved drug diffuses through the formed channels into the surrounding media as shown in Fig. 3. Here the rate-limiting step is not the dissolution but the diffusion of the drug that depends on the porosity and tortuosity in the matrix that are again dependent on the relative ratio of dispersed drug to the polymer [14].

Such release is mathematically expressed by Higuchi's equation [52] as follows:

$$Q = \frac{DE}{T} \times (2C - EC_s) \times C_s t$$

where $Q$ = drug released per unit time $t(g)$, $D$ = Diffusion coefficient, $E$ = porosity of matrix, $T$ = tortuosity of matrix, $C_s$ = drug's solubility, and $C$ = concentration of drug in system (mg/mL).

When compared with reservoir systems, these systems are easier to produce and capable of loading large amount of the drug.

## 5.2. Dissolution-controlled systems

Dissolution-controlled systems may contain drugs that show high dissolution rates, drugs with inherently slow dissolution, or drugs that form complexes in GI fluids that are slowly dissolving. All these drugs can be formulated by dispersing into an insoluble matrix or coating the granules with varying thickness of rate-controlling polymeric layers. Following the dissolution of the drug, it gets concentrated into the stagnant layer around the granules from where it diffuses into the surrounding media, and this step is the rate-limiting step [53,54].

The rate of dissolution from these systems can be mathematically be represented by

$$\frac{dm}{dt} = \frac{ADS}{h}$$

where $S$ = aqueous solubility of the drug and $h$ = thickness of the stagnant layer

### 5.2.1. Reservoir-type dissolution-controlled systems

Similar to diffusion-controlled systems, these systems also comprise of a drug core enclosed in a rate-controlling membrane. The only difference is in the principle of drug release. The release rate is dependent