

# Recent Advances in Drug Delivery Systems: Polymeric Prodrugs

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During the past decade, scientists have focused their attention on developing site-specific drug delivery systems, and various polymers have shown promising results in this area. Ringsdorf's model of polymeric prodrugs depicts the ideal drug delivery system — one which has all the desired physicochemical properties and delivers the drug at the desired tissue or intracellular region. This article discusses the various polymers used for site-specific drug delivery and considers the advantages and disadvantages of this type of delivery system.

In addition to bioavailability and pharmacokinetics, site-specific drug delivery has been a topic of interest to pharmaceutical scientists during the past ten years. By delivering a drug at the site of action, these "targeted" delivery systems improve the drug's therapeutic effectiveness and minimize its toxic effects on other tissues. Drug delivery systems generally are classified as carrier systems, mechanical pumps, or prodrugs. The category of carrier system is divided into three major groups: macromolecular drug delivery systems, particulate systems, and cellular drug carriers.<sup>1</sup>

Proteins such as antibodies and lipoproteins; liposomes; synthetic polymers; and polysaccharides, such as dextran and inulin, are the various types of macromolecules used as drug delivery systems.<sup>2-4</sup> Polymers have been used extensively in these systems, including systems such as nanoparticles, microcapsules, laminates, matrices, and microporous powders.<sup>5-11</sup> In all these delivery systems, the drug is merely dispersed or incorporated into the system without the formation of a covalent bond between the drug and polymer. This article will discuss only those polymeric drug delivery systems in which a drug is covalently bonded to a polymeric backbone.

Because the molecular weight of polymeric drug delivery systems is very high, such systems are often referred to as *macromolecular carrier systems*. Prodrugs, which are derivatives of

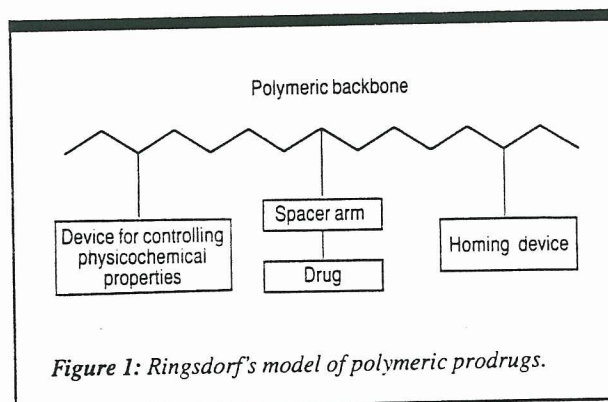


Figure 1: Ringsdorf's model of polymeric prodrugs.

drugs, undergo biotransformation to release the drug in vivo. The use of prodrugs as drug dosage forms depends on the ability of the body to release the drug in the body.<sup>12</sup> Although the majority of polymer-drug conjugate systems have no biological activity, all such systems release the conjugated drug in vivo. For this reason, these polymeric macromolecular systems have been called *polymeric prodrug systems*.

## Ringsdorf's Model

A schematic diagram of Ringsdorf's model is shown in Figure 1.<sup>13</sup> The system has a polymer backbone, which can be a homopolymer or a heteropolymer, depending on the constituents of the carrier polymer. The backbone contains three essential units; the first is a device for controlling the physicochemical properties of the entire macromolecule, which mainly involves the hydrophilic-lipophilic balance, the electric charge, and the solubility of the system.<sup>14-15</sup> The second and most important functional group is the drug itself. The drug must be covalently bonded to the polymer and must remain attached to it until the macromolecule reaches the desired site of action. The drug also must be detached from the parent polymer at the site of action. The release of drug takes place by hydrolysis or by specific enzymatic cleavage of the drug-polymer bond. In many cases, the drug is attached to the polymer through a spacer molecule, which is an amino acid or other simple molecule that can be cleaved or hydrolyzed at the desired site in the body.

The choice of drug for use in this system is based on three cri-

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