BIOPHARMACEUTICS AND RELEVANT PHARMACOKINETICS

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CHAPTER 23

Enteric Coatings

Definition

AN ENTERIC COATING IS ONE THAT RESISTS THE ACTION OF stomach fluids and disintegrates in the intestines.

Reasons for Enteric Coating

These are: (1) to prevent gastric digestion of a susceptible compound such as protein, or hydrogen ion catalyzed decomposition of a susceptible drug such as erythromycin; (2) to prevent nausea and vomiting caused by a drug, *e.g.*, emetine, atabrine, iron salts and diethylstilbestrol; (3) to prevent dilution of a drug before reaching its site of action in the intestine, *e.g.*, intestinal antiseptics and anthelmintics; (4) to prevent hindrance of gastric digestion of normal foodstuff by a drug, *e.g.*, alkaline medicaments; (5) to provide delayed action of a drug, *e.g.*, barbiturates, amphetamines and aspirin; (6) to deliver medication to the intestinal tract for optimum absorption in the duodenum and jejunum.

Requirements of a Good Enteric Coating

These are: (1) the coating must be nontoxic; (2) the components of the coating and their degradation products, if any, must be physiologically inactive; (3) optimally, the coating should not disintegrate or dissolve in the stomach during the time that the enteric coated dosage form remains in the stomach; (4) the enteric coated dosage form should disintegrate and release its contained medication as rapidly as possible once the dosage form empties from the stomach into the intestines.

Composition of Enteric Coatings

The patent and non-patent literature on enteric coatings is very extensive and much of it has been reviewed by Wagner (1956 and 1966); hence the reader is referred to the two chapters in *Remington's Practice of Pharmacy* for the review of early literature and references.

In general, there are two types of enteric coatings. First, those which are intended to be digestible by enzymes in the intestinal tract. These include such substances as keratin, formalized gelatin, glycerides, waxes, etc. This type of coating usually does not meet the requirements of a good enteric coating since the surface area of the "digestible substance" exposed to the enzyme is so small that the digestion is much too slow. Second, most current enteric coatings contain an ionizable polyacid and, most frequently, a long-chain polymer with ionizable carboxyl groups which is also a film-forming agent. Usually the polymeric agent is applied to the

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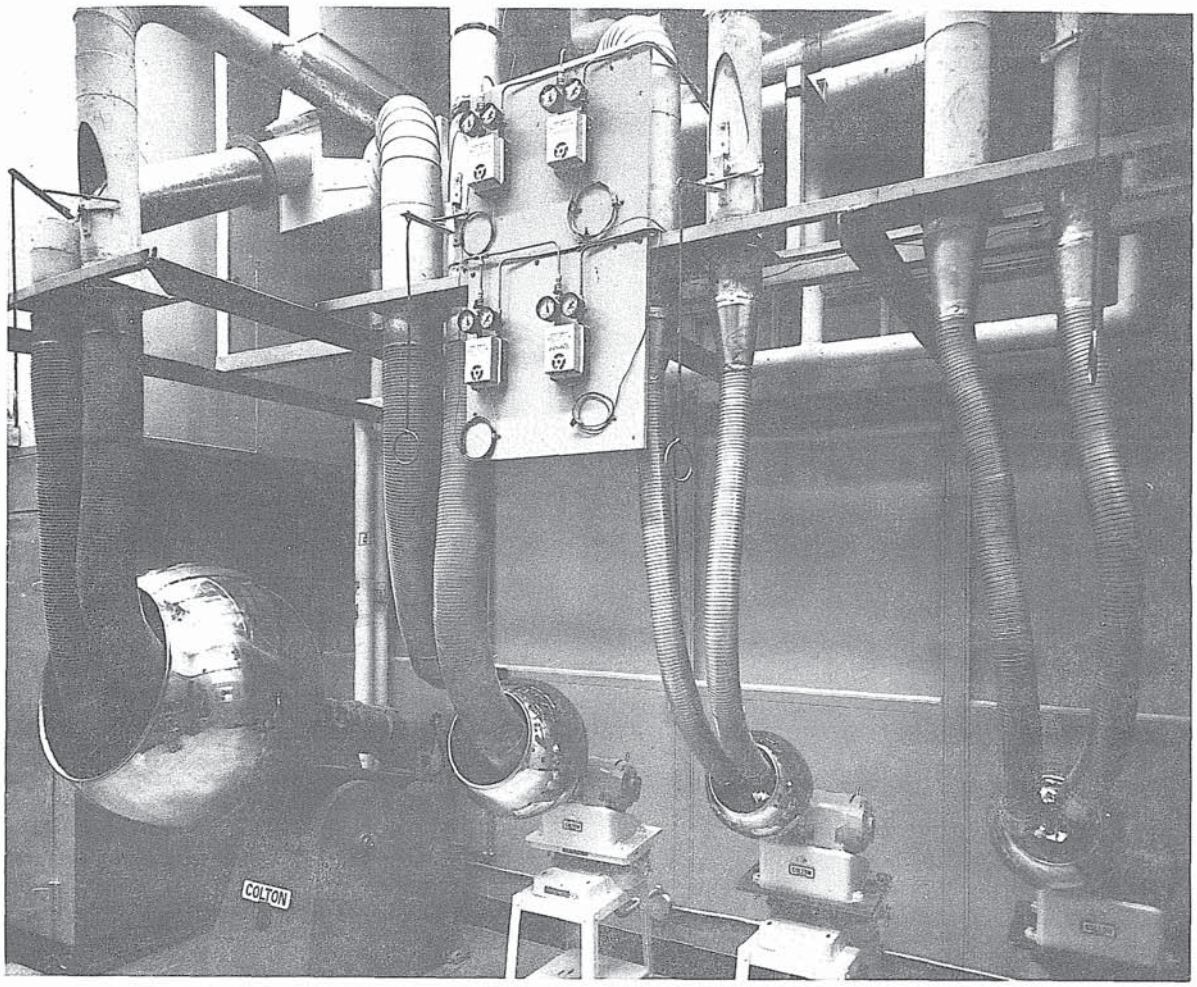

Figure 23.1. Coating pans in a Coating Development Laboratory (courtesy of The Upjohn Company)

dosage units dissolved in an organic solvent. The coating solution may also contain other substances, such as a plasticizer to aid in film formation, and a surface active agent. A dusting powder, such as talcum, is added during the coating of the dosage units to prevent the dosage units from sticking together; sometimes powder such as talcum is also suspended in the solution of the polymeric agent in the organic solvent.

Methods of Application of Enteric Coatings

There are four principal methods of applying enteric coatings to tablets. These are: (1) manual pan coating; (2) programmed pan coating; (3) fluidized-bed coating; and (4) compression coating. The oldest method, and probably the one still most widely used, is manual pan coating. Figure 23.1 shows various sizes of coating pans in a pharmaceutical development laboratory. Figure 23.2 shows a row of production-size coating pans which have a diameter of 36 inches. Larger pans are also used including some giant doughnut-shaped coating pans which handle the volume of a dozen regular commercial-size pans. In programmed pan coating most of the operations normally performed manually are done by machines but the revolving coating pan is similar to that used in manual pan coating. In fluidized-bed coating the tablets are suspended in a column by rapidly moving air introduced at the bottom of the column and the coating solution is sprayed onto the tablets while they are suspended in the air. In compression coating the components of the enteric coating are mixed in the dry state and applied by compression around the core tablet thus producing essentially a tablet-within-a tablet.

Theory of Enteric Coatings and Their Properties

In man the stomach contents are usually in the *p*H range 1 to 3.5 and *p*H 1 to 2.5 is the most common range. During the night the human stomach usually has the lowest acidity. During the day the taking of meals is the most frequent cause of changes in acidity of the stomach contents. The high acidities, near *p*H 1, are usually recovered within a short time after the meals are eaten. In man the duodenal contents are usually

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