Communications

Synthetic Polymers as Potential Enteric and Sustained-Release Coatings

Sir:

We wish to report pharmaceutical applications of various copolymers as potential enteric and sustained-release coatings. These coatings are based on a series of partial esters (ethyl through decyl) of water-soluble copolymers of maleic anhydride with ethylenic compounds, *e.g.*, ethylene or vinyl methyl ether (1). Preliminary results indicate that films of these polymeric derivatives are brilliantly clear, chemically and physically stable, and nontoxic. Variations in ester chain length and degree of esterification effect a gradation in dissolution pH.

An increase in ester chain length for the essentially one-half ester produces a corresponding increase in dissolution pH. This highly significant property permits the design of pharmaceuticals which release their medicament only upon reaching a specific intestinal pH. Thus, specific coatings may be selected in order to obtain maximum therapeutic effect from those drugs which are absorbed in various areas of the intestinal tract. This effect on absorption by the gradation in dissolution pH is illustrated in Table I by the plasma salicylate levels from enteric coated acetylsalicylic acid tablets. Complete physiological availability (relative to a control) was obtained.

TABLE I.—PLASMA SALICYLATE LEVELS[a]

Coating Polymer	2 hr. Level, mcg./ml.	Peak Level, mcg./ml.	Peak Time,[b] hr.
Uncoated	38	38	2
1/2 Ethyl PVM/MA[c]	11	38	4
1/2 Isopropyl PVM/MA[c]	6	34	5
1/2 *n*-Butyl PVM/MA[c]	1	26	8

[a] Following administration of 652 mg. of acetylsalicylic acid to fasting patients. [b] Time of maximum plasma level. [c] Copolymer of vinyl methyl ether and maleic anhydride.

Sustained release may be obtained in two ways for those drugs which are well absorbed throughout the gastrointestinal tract. First, a series of polymer coatings dissolving at different pH may be used to coat small portions of the dose. Second, the rate of solubility of a coating based on a single polymeric ester can be decreased as desired by the addition of suitable extenders. In both instances, initial levels may be obtained by the administration of uncoated drug.

A comprehensive report on the characterization, coating techniques, and clinical evaluation will be forthcoming.

(1) Voss, A., and Dickhauser, E., U. S. pat. 2,047,398, July 14, 1936.

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Book Notices

The Actinomycetes. Vol. 3. Antibiotics of Actinomycetes. By SELMAN A. WAKSMAN and HUBERT A. LECHEVALIER. The Williams & Wilkins Co., 428 East Preston St., Baltimore 2, Md., 1962. viii + 430 pp. 17 × 25.5 cm. Price $18.

More than 400 substances and preparations isolated from cultures of actinomycetes are covered in this volume. More than 30 of these products have found practical application in chemotherapy. Part A covers the nature, formation, and activities of antibiotics; and Part B includes descriptions of the antibiotics produced by actinomycetes. A general index and an index of organisms are appended.

Actualités Pharmacologiques. 14th Series. Edited by RENE HAZARD and JEAN CHEYMOL. Masson et Cie., 120, boulevard SaintGermain, Paris VI[e], France, 1961. 250 pp. 16 × 24 cm. Paperbound. Price 45 NF.

Subjects covered in this book (in French) are: Vitamin E and its therapeutic utilization; Pharmacologic aspects of cardiac and striated muscles; Bradykinine and its antagonists; Barbiturates and hypnosedatives; Cardiotonic alkaloids; Hydrazide derivatives and hydrazine inhibitors of monoamine oxidase (mechanisms); Neurohumoral activity of the hypothalamic centers; Rational study of new synthetic drugs; Norsteroid structure.