〔Macromolecules, **24**, 4047-4053 (1991)〕 [Lab. of Pharm. Physical Chemistry]

A New Development of Mechanochemical Solid-State Polymerization of Vinyl Monomers: Prodrug Syntheses and Its Detailed Mechanistic Study.

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We describe the first example of mechanochemical polymerization of methacryloyl derivatives of bioactive compounds. The detailed mechanistic implications on the reaction have been clarified based on ESR kinetics on its comparison with that of the corresponding mechano-radical formation, the progressive changes in molecular weight distribution including its heterogeneity, and kinetics of the polymer conversion. The present result provides a novel and simple methodology for polymeric prodrug syntheses of low heterogeneity through a totally dry process.

〔Chem. Pharm. Bull., **39**, 3018-3022 (1991)〕 [Lab. of Pharm. Physical Chemistry]

The Nature of Hydrolysis of Novel Methacryloyl Polymeric Prodrugs Prepared by Mechanochemical Solid State Polymerization.

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The alkaline hydrolysis of several powdered methacryloyl polymeric prodrugs (1P-3P) prepared by mechanochemical polymerization, each of which contains acetaminophen (1), theophyllineacetic acid (2) and 5-fluorouracil (3) as a pendant drug group has been examined in a heterogeneous system. Since carboxyl groups are formed with the progress of hydrolysis of 1P and 3P, the rate of hydrolysis is markedly lowered. In contrast, the hydrolysis of 2P was completed within several hours and finally the suspended powders had been completely solubilized and the kinetics for hydrolysis of 2P was shown to be well correlated with the powder dissolution rate, which is known as the Hixson-Crowell cube root law.

〔Yakugaku Zasshi, **111**, 665-671 (1991)〕 [Lab. of Pharm. Physical Chemistry]

Mechanochemical Solid State Reactions of Natural Products for Medicinal Use Containing Hydroxyanthraquinone Derivatives.

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In commercial powdered natural products for medicinal use containning various combined forms of hydroxyanthraquinone derivatives such as Sennae Folium, Cassiae Semen, Rhei Rhizoma and Aroe a considerable amount of stable free radicals (ca. 10^{17}-10^{18} spin/g) was found to be contained by use of electron spin resonance (ESR) spectral measurements.

It was suggested that the mechano-radicals formed in the above natural products are metal complexs of the corresponding semiquinone anion radicals induced by solid state one electron transfer mechanism from the active metal surface, part of which is further immobilized in polymeric fibers or the like in the plant tissues.