2P

INVESTIGATION OF DRUG RELEASE FROM SODIUM ALGINATE-SODIUM CALCIUM ALGINATE MATRICES

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A novel slow release solid oral dosage system based on sodium alginate (NaAlg) and sodium calcium alginate (NaCaAlg) has been described (European Patent No. 0188040). Alginates form gels by divalent cation-induced association of the polymer chains and this property is used to give matrices which prolong release. This work has investigated the influence of total alginate concentration and alginate salt cation on the release of a model compound, Acetanilide, from alginate matrices. Formulations comprising Acetanilide, NaAlg, NaCaAlg, lactose where appropriate, and "Avicel" (20% tablet weight) were dry-mixed and compressed directly to form $^1/_2$ inch flat faced tablets. In-vitro release of Acetanilide into 1 L of distilled water at 37°C, monitored by UV spectroscopy, was studied using both B.P. dissolution methods.

The release profiles shown in Fig.1 were obtained using B.P. Method I (basket 50rpm). All formulations contained equal weight ratios of NaAlg and NaCaAlg. A total alginate concentration of 4% tablet weight gave a disintegrant effect but at concentrations ranging from 8 to 70% w/w zero order drug release was observed, with a rate constant (k) 0.1% min^{-1}, after an initial period of tablet swelling and gel formation. When the total alginate concentration was maintained at 8% w/w and the NaAlg to NaCaAlg ratio varied (Fig.2), zero order release (k=0.1% min^{-1}) was observed with a weight ratio of NaCaAlg ≥50%. Release from a matrix of 4% NaAlg with 4% lactose was non-linear with time and complete in 6 hours whereas a matrix of 4% NaCaAlg with 4% lactose gave zero order release (k=0.1% min^{-1}), thus confirming NaCaAlg as the alginate salt that controlled release.

Using B.P. Method II apparatus (paddle 50rpm), in which the matrix is unconstrained, formulations containing 30, 50 and 70% w/w alginate with equal weight ratios of NaAlg and NaCaAlg gave zero order release (k=0.23, 0.16 and 0.13% min^{-1}, respectively).

Based on the study of drug release from the NaAlg-NaCaAlg matrices, it is suggested that the rate-determining step responsible for zero order release is the movement of solvent into the dry tablet core. When the swollen gel layer reaches a certain viscosity, determined by the amount of NaCa salt present, the rate of water penetration becomes constant. The B.P. Method I provides a physical restraint which prevents continuing gel swelling and associated gel dissolution. With B.P. Method II, the swollen matrix is not constrained and surface erosion of the gel occurs. Increasing alginate concentration causes a slower rate of erosion, leading to a slower rate of water penetration and decreased zero order release rate.

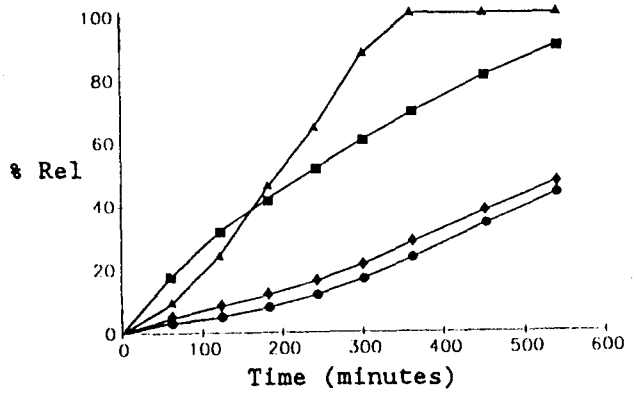

Fig.1 Release from matrices of equal NaAlg/NaCaAlg weight ratios. Total Alg concn 0% (■), 4% (▲), 8% (●), 70% (◆)

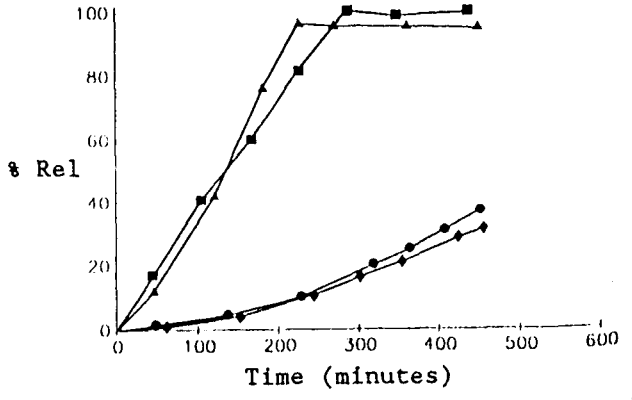

Fig.2 Release from matrices of total Alg concn 8%. NaAlg/NaCaAlg ratio 100/0 (■) 70/30 (▲), 50/50 (●), 0/100 (◆)