Phosphate Binding by Calcium Salts

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BACKGROUND

Hyperphosphatemia that results from declining kidney function is a hallmark of advanced chronic kidney disease (CKD) and is associated with abnormal mineral and bone metabolism, vascular calcification, and death. Therefore, reducing serum phosphorus levels by binding dietary phosphates in the gastrointestinal tract continues to be a focus of treatment of CKD.

GOAL OF THE STUDY

This research critically examined the efficacy of phosphate binding by a new phosphate binder, calcium succinate monohydrate (CS), under three in vitro conditions designed to mimic phosphate binding in vivo. Experimental results were compared with phosphate binding by calcium acetate (PhosLo® gelcaps), under the same conditions.

DESCRIPTION OF THE EXPERIMENTS

In each experiment a quantity of calcium acetate or calcium succinate equivalent to 169 mg calcium (0.004225 mol) was incubated in 100 mL aqueous buffer solution at 37 °C either with 0.0028 mol phosphate (added as sodium hydrogen phosphate heptahydrate) or with 0.00224 mol phosphate from the same source. Three matrices (0.1 N HCl, pH 1.2; 0.1 N Acetate buffer, pH 4.5; and 0.1 N Borate buffer, pH 6.8) were studied. The solution pH was not adjusted. After sealing tightly with parafilm, the flasks were placed back in the water bath and the timer started. Aliquots (4 mL) were removed from the bulk solution in each flask at 1, 2, 4, and 6 hr and filtered. Portions of the filtrate were quantitatively diluted and analyzed for phosphate using a validated method.

SUMMARY OF FINDINGS

At pH 1 (0.1 N HCl), the pH of an empty stomach, calcium does not bind phosphate.

At pH 4.5 (0.1 N Acetate Buffer), the pH of a human stomach containing food, approximately 60-65% of the phosphate is bound by calcium succinate or calcium acetate and yields insoluble CaHPO4.

At pH 6.8 (0.1 N Borate Buffer), the pH mimicking the changes as food moves from the stomach to the upper intestine (the site of phosphate absorption), phosphate binding by ionized calcium goes to completion, and a mixture of insoluble calcium phosphates is formed.

CONCLUSIONS

PHOSVEDA® (Calcium Succinate) Capsules are oral phosphate binders that will be indicated for the reduction of serum phosphorus in patients with ESRD. The Active Pharmaceutical Ingredient is calcium (as calcium succinate), which will be provided to the patient as a dry powder formulation in HPMC capsule. We have shown that the capsules dissolve within 30 minutes to provide ionized calcium for phosphate binding. These data confirm that phosphate binding by calcium succinate is equivalent to that of the Reference Listed Drug, calcium acetate. Finally, separate studies show that PHOSVEDA® capsules are stable for years at room temperature or when exposed to elevated temperatures.