

A NEW TREATMENT APPROACH TO LYSOSOMAL STORAGE DISEASE: EXPLORING POTENTIAL BIOMEDICAL APPLICATIONS OF SIMPLE METAL ION SALTS. Kathryn B. Grant and Dominique Williams, Department of Chemistry, Georgia State University, P.O. Box 4098, Atlanta, Georgia 30302-4098

Niemann-Pick disease and drug-induced phospholipidosis are examples of lysosomal storage disorders caused by the pathogenic accumulation of phospholipids in cellular lysosomes. Here we have explored the possibility of developing metal-based therapeutic agents to reverse phospholipid build-up through phosphate ester bond hydrolysis. It would be ideal for a small-molecule, hydrolytic agent to have optimal activity at lysosomal pH (~ 4.8), with considerably less reactivity at cytoplasmic pH (~ 7.2). Towards this end, we have utilized mass spectrometry in combination with malachite green/molybdate- and Amplex® Red-based colorimetric assays in order to rapidly evaluate phospholipid hydrolysis by twelve simple, d- and f-block metal ion salts. In reactions conducted at 60 °C and 37 °C, the yields produced by the cerium(IV) salt were found to be overwhelmingly superior. Significantly more phospholipid hydrolysis occurred at lysosomal pH compared to near neutral pH.