

pH control of oxidation of the glucocorticoid hormone side-chain: the effect of arsenite*J.S.Edmonds and M.Morita**Endocrine Disrupter Research Laboratory, National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba, Ibaraki 305-8506.*

It has been known since the early 1990s that arsenite, interferes with the action of glucocorticoid hormones by binding to closely spaced thiol groups on the receptor. However, in 2001 Kaltreider et al. showed that arsenite at very low concentrations, including those found in some drinking waters, interfered with glucocorticoid action by an unknown mechanism. The experimental protocol of Kaltreider et al. appeared to leave open the possibility that steroid and arsenite could come into direct contact (this was not the case in the earlier work on the interaction of arsenite with the glucocorticoid receptor) and we have examined the effect of arsenite on pH modulated changes to the glucocorticoid steroid dihydroxy-keto side-chain. We found that aerial oxidations of the glucocorticoid side-chain in aqueous solution was under strict pH control and at pHs between 8 and 11 the presence of arsenite completely subverts the course of oxidation with a diastereoisomeric mixture of hydroxyacids being the only product instead of the etioacid as would be the case in the absence of arsenite. We hypothesize that arsenite weakly complexes with the terminal oxygen functions of the side-chain, promotes enolization and thereby facilitates conversion to the hydroxy-aldehyde form and directs the transformation of the steroid towards the inactive diastereoisomeric hydroxyacids.