Alpha-santalol, a major component of sandalwood oil inhibits growth of cultured prostate cancer cells in vitro by causing apoptosis. The present study was undertaken to determine the in vivo efficacy of α-santalol using TRAMP (Transgenic Adenocarcinoma of Mouse Prostate) mice as a model. Administration of α-santalol (100 mg/kg) significantly decreased the incidence of prostate tumors, average wet weights of urogenital organs and prostate weight compared to control mice. Furthermore, the dorsolateral sections of prostate from α-santalol-treated mice exhibited decreased cell proliferation (Ki-67 staining) in association with induction of apoptosis (TUNEL-positive cells). In agreement with immunohistochemical analysis, Western blotting analysis of prostate/tumor samples from α-santalol-treated group revealed a decrease in survivin, XIAP, PCNA, cyclin D and CDC2 levels compared to control-treated samples. c-RAF, a proto-oncogene was also downregulated in alpha-santalol treated group compared to the control group. In conclusion, the present study indicates that α-santalol administration inhibits the development of prostate cancer in TRAMP mice by decreasing cell proliferation, and inducing apoptosis and warrants future studies for its clinical development. This study was supported by Wilkes University’s Provost Research grant and mentoring grant.