Ashwagandha is a common shrub used in Indian Ayurvedic medicine. A variety of health-promoting effects have been claimed, but the molecular mechanisms of its action remain largely unexplored. Here we used cultured human normal and cancer cells and identified that the leaf extract from Ashwagandha (Lash) has growth arresting activity selective for human cancer cells. We found that this selectivity of Lash for tumor cells is due, in part, to its (i) wild type p53-activating function (ii) restoration of tumor suppressor function to mutant p53 (Ref) and (iii) inhibitory activity for telomerase. By multiple integrative approaches including purification of the lash components, target hunting by shRNA library mediated gene silencing and molecular analysis of cancer markers we have identified the active anti-cancer component. Taken together, for the first time, by the coherent use of human normal and cancerous cells in culture, we have identified selective cancer cell killing activity, its molecular targets and mechanism of action. We provide the first molecular evidence for the anticancer component in Ashwagandha and open the new era of Ayurveda-derived safe anti-cancer medicine.