

# Inhibitory effects of mitotane on viability and secretory activity in mouse gonadotroph cell lines

Erica Gentilin, Daniela Molè, Teresa Gagliano, Mariella Minoia,  
Maria Rosaria Ambrosio, Ettore C. degli Uberti, Maria Chiara Zatelli

---

## A B S T R A C T

Mitotane represents the mainstay medical treatment for metastatic, inoperable or recurrent adrenocortical carcinoma. Besides the well-known adverse events, mitotane therapy is associated also with endocrinological effects, including sexual and reproductive dysfunction. The majority of male patients undergoing adjuvant mitotane therapy show a picture of hypogonadism, characterized by low free testosterone and high sex hormone binding globulin levels and unmodified LH concentrations. Since mitotane has been shown to have direct pituitary effects, we investigated whether mitotane may influence both cell viability and function of gonadotroph cells in the settings of two pituitary cell lines. We found that mitotane reduces cell viability, induces apoptosis, modifies cell cycle phase distribution and secretion of gonadotroph cells. The present data strengthen previous evidence showing a direct mitotane effect at pituitary level and represent a possible explanation of the lack of LH increase following decrease in free testosterone in patients undergoing adjuvant mitotane therapy.

---