Epigallocatechin-3-gallate enhances differentiation of acute promyelocytic leukemia cells via inhibition of PML-RARα and HDAC1.

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Abstract

The use of all-trans retinoic acid (ATRA) has dramatically improved the treatment and survival rate of patients with acute promyelocytic leukemia (APL). However, toxicity and resistance to this drug are major problems in the treatment of APL with ATRA. Earlier studies have suggested that the green tea polyphenol epigallocatechin gallate (EGCG) induces cell death in hematopoietic neoplasms without adversely affecting normal cells. In the present study, the potential therapeutic effect of EGCG in APL and the underlying molecular mechanisms were investigated. EGCG (100 μM) significantly inhibited proliferation and induced apoptosis in HL-60 and NB4 cells. This effect was associated with decreased expressions of multidrug resistance proteins ABCB1, and ABCC1, whereas the expressions of pro-apoptotic genes CASP3, CASP8, p21, and Bax/Bcl-2 ratio were significantly increased. EGCG, at 25 μM concentration, induced differentiation of leukemic cells towards granulocytic pattern in a similar manner to that observed for ATRA (1 μM). Furthermore, EGCG suppressed the expression of clinical marker PML/RARα in NB4 cells and reduced the expression of HDAC1 in leukemic cells. In conclusion, the results suggested that EGCG can be considered as a potential treatment for APL.

KEYWORDS:

APL; EGCG; MDR; apoptosis; differentiation