Amsacrine is an anticancer chemotherapeutic acridine derivative that is clinically used to treat acute myelogenous leukemia (AML). Amsacrine acts as a DNA intercalator, binding AT base pairs; this inhibits the activity of topoisomerase II, preventing DNA repair. In leukemia cells, amsacrine decreases expression of matrix metalloproteinases 2 and 9 (MMP2/9), inhibiting cell invasion. This modulation of MMP2/9 expression is caused by increases in ROS and activation of p38 MAPK and JNK, which increases levels of protein phosphatase 2A (PP2A), a negative regulator of MMP activity. In vitro, amsacrine inhibits human Ether-a-go-go-Related Gene (hERG) K+ channels, causing potential prolongation of the QT interval.

References

