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Letter to the editors

Bridget T. Hill and Richard D. H. Whelan

Laboratory of Cellular Chemotherapy, Imperial Cancer Research Fund, Lincoln's Inn Fields, London WC2A 3PX, England

Dear Sir,

West and Stratford have recently reported on the comparative in vitro cytotoxicities of adriamycin (ADM) and 4'[(9-acridinyl)-amino] methane sulphon-*m*-anisidide (mAMSA) [5]. They showed that both drugs were highly cytotoxic towards Chinese hamster V79 cells but proved less active against human tumor cell suspensions derived from either a small-cell lung carcinoma (ME/MAR) or a melanoma xenograft (HX117): ADM was more effective than mAMSA against both human tumor cell lines. We have carried out a similar comparative study, briefly reported previously [6] and have since extended this evaluation.

Our data summarized in Table 1 illustrate the following points: (a) the cytotoxic effects of ADM and mAMSA were independent of both the cell proliferation rate, as judged by population doubling times, and the colony-forming efficiencies in this range of cell lines; (b) mAMSA exhibited the greatest cytotoxicity toward the murine L5178Y lymphoma and proved more cytotoxic than ADM against both these murine cells and the Syrian hamster NIL 8 cells by factors of 2.7 and 1.3, respectively; (c) in contrast, mAMSA was less effective than ADM in killing the range of human tumor cell lines tested, with one exception – namely, the DU145 cells. However, there was a very large range of responses recorded since, for example,

Table 1. Cell line characteristics and comparative in vitro sensitivities to adriamycin and mAMSA

Cell line [ref]: origin	Media and sera used	Population doubling time (h)	Colony-forming efficiency	IC_{50} values (μmol dm^{-3}) for 24-h drug exposures[e]	
				Adriamycin	mAMSA
L5178Y [2]: murine lymphoma	Fischer's + 10% HS[a]	22	65%[b]	0.016	0.006
NIL 8 [3]: Syrian hamster	Eagle's + 10% CS[a]	14	55%[c]	0.055	0.043
CHP100 [1]: human neuroblastoma	RPMI1640 + 10% FCS[a]	22	30%[d]	0.013	0.018
CHP212 [1]: human neuroblastoma	RPMI1640 + 10% FCS	26	20%[d]	0.011	0.152
LAN-1 [1]: human neuroblastoma	Ham's F12 + 10% FCS	31	15%[d]	0.015	0.158
DU145 [4]: human prostatic carcinoma	RPMI + 10% FCS	24	15%[d]	0.046	0.033
LNCaP [4]: human prostatic carcinoma	RPMI + 10% FCS	36	12%[d]	0.011	0.033
PC3mA2 [4]; human prostatic carcinoma	RPMI + 10% FCS	24	25%[d]	0.028	0.058
LoVo [3]: human colonic carcinoma	Ham's F12 + 10% FCS	34	26%[c]	0.011	0.064
COLO 205 [3]: human colonic carcinoma	RPMI + 10% FCS	22	30%[d]	0.017	0.064

[a] CS, calf serum; HS, horse serum; FCS, fetal calf serum
[b] Cloning in 0.2% agar
[c] Cloning on plastic
[d] Cloning in 0.17% agarose
[e] Drug concentration required to reduce colony formation by 50%

whereas mAMSA proved only approximately 1.4-fold more cytotoxic than ADM against the CHP100 human neuroblastoma cells, there was a 14-fold difference favoring mAMSA in one of the other neuroblastoma lines tested (CHP212). This serves to emphasize the need for evaluating panels of cell lines of the same tumor type before attempting any generalizations about tumor-specific drug sensitivities. (d) This demonstration that mAMSA is less effective against cell lines in vitro derived from human "solid" tumors than against a murine leukemia would appear consistent with clinical experience, as pointed out by West and Stratford [5]. Although the data in Table 1 are not strictly comparable with the cytotoxicity data presented by West and Stratford [5] since we used a 24-h rather than 1-h drug treatment, we have now tested NIL 8 cells using a 1-h drug exposure and the IC_{50} values are 0.64 μmol dm^{-3} for ADM and 0.24 μmol dm^{-3} for mAMSA; these values are in line with our 24-h data.

Therefore, our results using this range of mammalian tumor cell lines support and extend the conclusion made by West and Stratford [5] that there are inherent differences between cell types, which reflect differences in the cellular pharmacokinetics and modes of action of these two clinically useful antitumor drugs. We further endorse their statement pointing out the importance of using a range of cell lines when assessing the effectiveness of antitumor drugs or attempting to identify new, more selective agents.

References

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