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The cytotoxicity of alkaloids from *Alstonia macrophylla* in some cancer cell lines

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The alkaloidal fraction of the root bark of *A. macrophylla* (Apocynaceae) showed in vitro activity against human lung cancer cell lines (Keawpradub et al, 1996). Phytochemical investigation of this extract has led to the isolation of ten known and three novel indole alkaloids (Keawpradub et al, 1996; Keawpradub and Houghton, 1997).

The individual alkaloids were tested for in vitro cytotoxic activity using the SRB method against MOR-P and COR-L23 human lung cancer cell lines (Keawpradub et al, 1996) using vinblastine sulphate as a positive control. The IC_{50} value (concentration causing 50% inhibition of protein production by the cells) was calculated for each alkaloid using the Biolise statistical programme. The most active compounds after 144 hour continuous exposure are shown in Table 1.

Table 1 Cytotoxic activities of the most active alkaloids against human lung cancer cell lines
2 independent experiments, 6 replicates in each

Alkaloid	IC_{50} value (μM) mean ± s.e.m.	
	MOR-P	COR-L23
Villalstonine (VA)	2.3±0.1	2.9±0.7
Macrocarpamine (MC)	4.6±0.3	5.3±0.3
O-Acetyl-macralstonine (AM)	6.3±1.0	4.1±0.9
Vinblastine sulphate (V)	3.1±1.5*	0.9±0.2*

* values in nM

These compounds were tested, using the same method, against a normal human breast fibroblast cell line BF and four other cancer cell lines as shown in Tables 2 and 3.

Table 2 Cytotoxic activities of the most active alkaloids against breast fibroblast, melanoma and renal carcinoma cell lines, 144 hour continuous exposure.
2 independent experiments, 6 replicates in each

Alkaloid	IC_{50} value (μM) mean ± s.e.m		
	BF	StM11a	Caki-2
VA	8.5±0.5	2.4±0.1	2.9±0.2
MC	8.1±0.1	2.9±0.2	7.3±0.3
AM	21.9±2.4	3.3±0.3	4.6±0.3
V*	>100	1.7±0.1	1.9±0.2

* values in nM

StM11a = melanoma; Caki-2 = renal cell carcinoma.

Table 3 Cytotoxic activities of the most active alkaloids against breast fibroblast, breast adenocarcinoma and colon adenocarcinoma cell lines, 144 hour continuous exposure.

Alkaloid	IC_{50} value (μM) mean ± s.e.m		
	BF	MCF7	Ls174T
VA	8.5±0.5	3.4±0.3	1.9±0.1
MC	8.1±0.1	1.9±0.2	1.8±0.1
AM	21.9±2.4	2.4±0.2	2.4±0.1
V*	>100	0.5±0.1	0.8±0.1

* values in nM

MCF7 = breast adenocarcinoma; Ls174T = colon adenocarcinoma.

The most active alkaloids were about a thousand times less cytotoxic then vinblastine. O-Acetylmacralstonine is the only alkaloid which displayed selectivity for cancer cell lines and so may act as a template for drug development. Its non-acetylated analogue showed much less activity which indicates that lipophilicity may be a factor in effectiveness of this type of molecule.

Keawpradub N., Houghton P.J., Eno-Amooquaye E. and Burke P.J. (1997) Planta Medica 63:97-101.

Keawpradub N. and Houghton P.J. (1997). Phytochemistry 46:757-762.