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The Role of beta-blockers in lung cancer treatment: An *in vitro* approach

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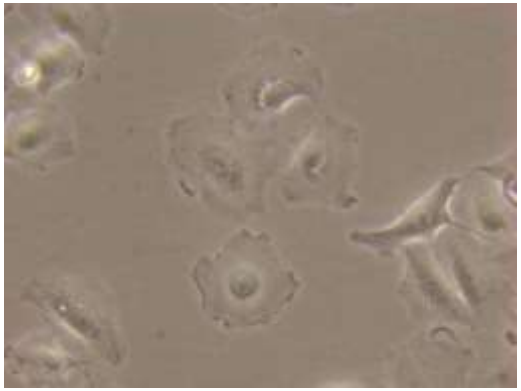
The Role of beta-blockers in lung cancer treatment: An *in vitro* approach

Singular exposure

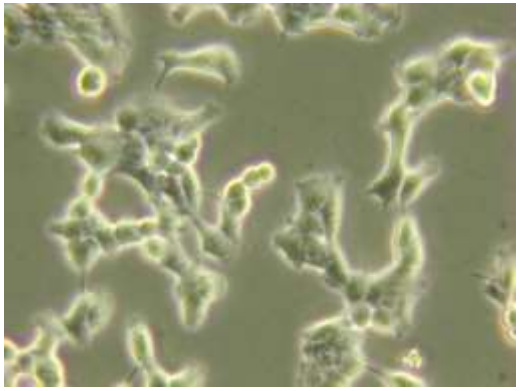
Drugs used:

- Propranolol
- Carvedilol
- Cisplatin
- Etoposide

A549



H460



Cell viability

Combined Exposures

Mixtures used:

- Propranolol + Cisplatin
- Propranolol + Etoposide
- Cisplatin + Etoposide

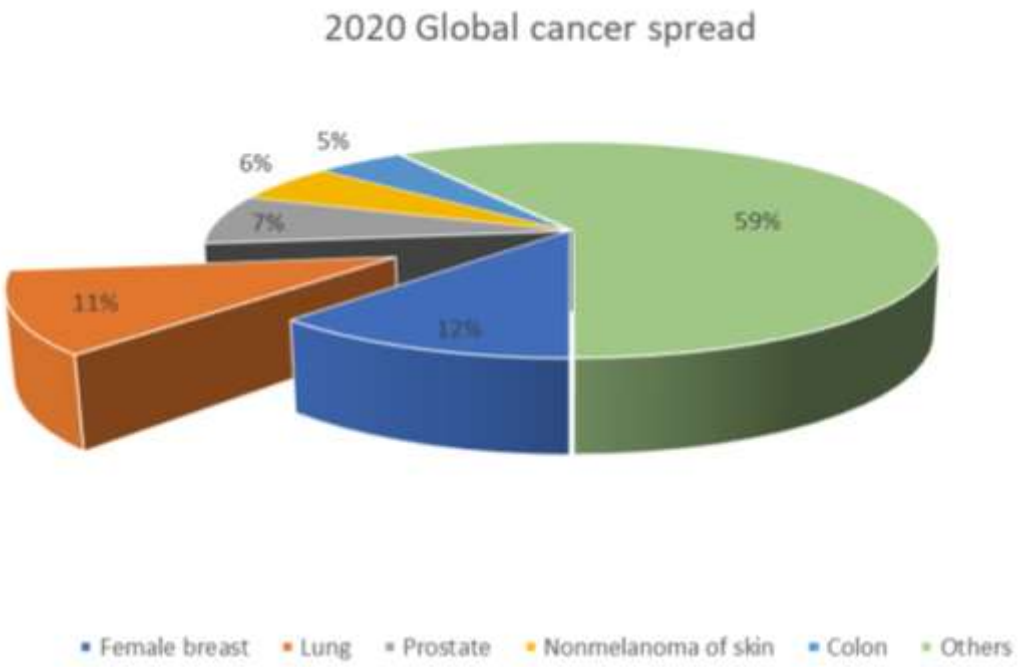
Abstract: In 2020, lung cancer was the second most common type of cancer in the world and the most lethal. Due to the high mortality rate and the low efficiency of available treatments, there is the need for more efficient approaches to fight this disease. In this regard, the use of already approved pharmaceuticals for other purposes can be valuable. Thus, the study aimed to assess the potential application of β-blockers, alone or combined with cytostatic drugs. The effects of the β-blockers propranolol (10, 25, 50, 100, 125, 150, 200 and 250 µM) and carvedilol (0.1, 1, 5, 10, 20, 60, 75 and 100 µM) and cytostatic drugs cisplatin (1, 5, 20, 50, 100, 150, 200, and 250 µM) and etoposide (0.005, 0.1, 0.5, 1, 2.5, 5, 7.5 and 10 µM) were evaluated in cancer cell lines, A549 and H460, at different time points (24, 48 and 72h), through cell viability. Overall, A549 demonstrated higher sensitivity to propranolol, cisplatin, and etoposide and H460 was more sensitive to carvedilol. The study of combined effects of β-blockers and cytostatic drugs revealed the potential value of β-blockers in the treatment of cancer.

Keywords: β-Blockers, Lung Cancer, Cell Viability, Cytostatic, Cell Lines

Introduction

Causes:
- UV radiation
- Tabaco
- Pharmacology
- Parasites
- Bacteria
- Fungi

Treatments:
- Surgery
- Chemotherapy
- Radiation therapy
- Targeted therapy

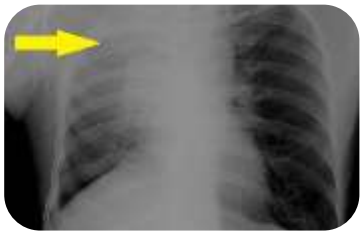


High mortality rates and low efficiency of the available treatments highlight the need for a new approaches

Introduction

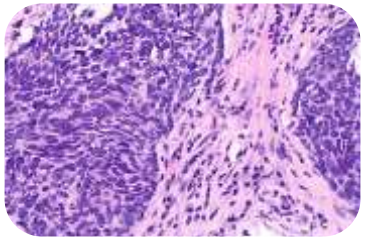
Lung Cancer

Chest Wall Tumours

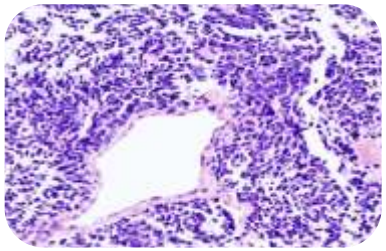


Mesothelioma

Non-Small Cell Lung Cancer



Small Cell Lung Cancer



Lung nodules

Introduction

β-Adrenergic Receptors

β1

β2

Commonly used in abnormal heart rhythms.

Tested pharmaceuticals:

Propranolol
Carvedilol

Cisplatin
Etoposide

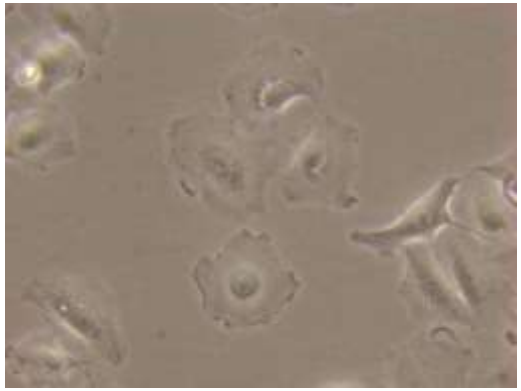
Cytostatic Drugs

Used for cancer treatment

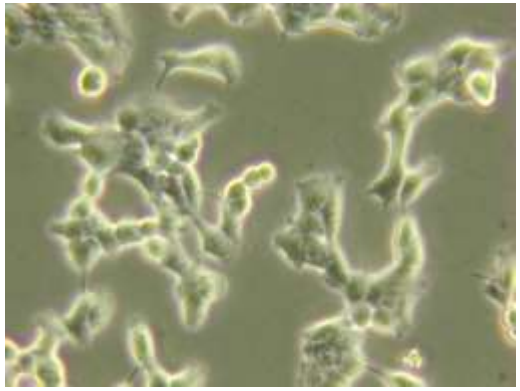
Prevent cell replication or growth.

Introduction

A549



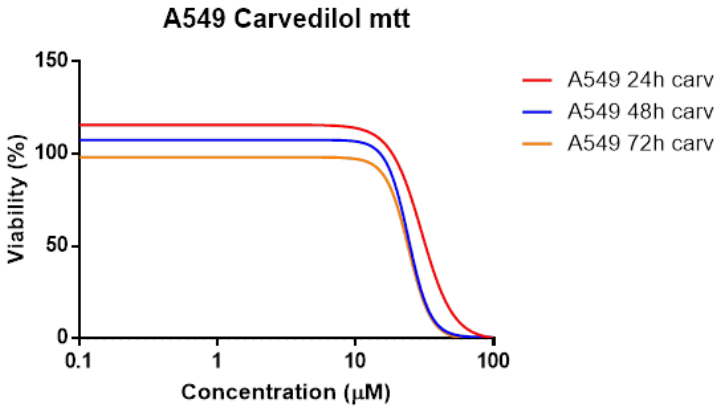
H460

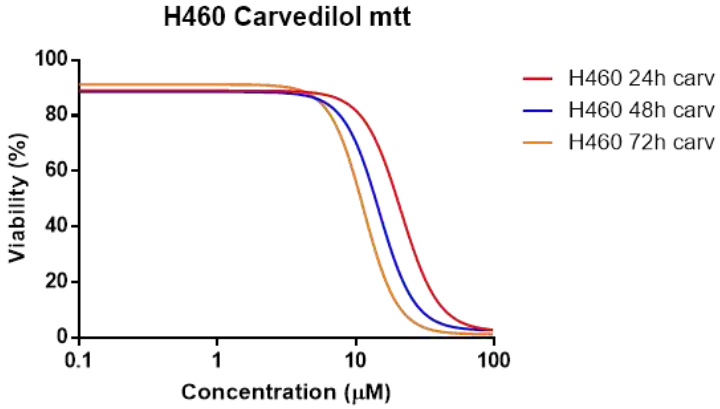


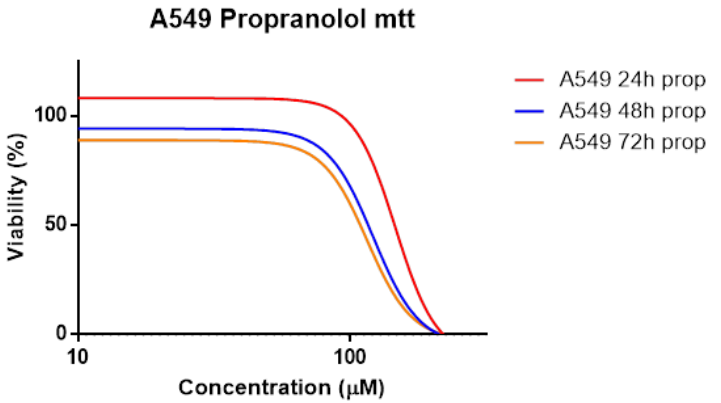
The cytotoxicity of **non-selective β-blockers** (carvedilol and propranolol), and **cytostatic drugs** (cisplatin and etoposide), was assessed **on lung cancer cell lines** A549 and H460

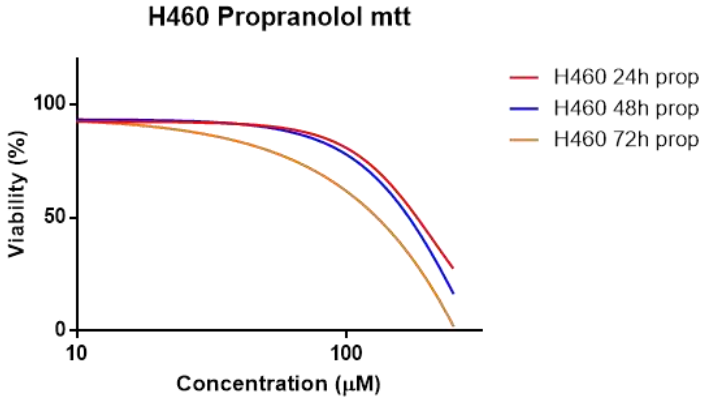
Effects of **binary combinations** of Propranolol with Cisplatin, Propranolol with Etoposide and Etoposide with Cisplatin were tested

Results: beta-blockers









Results and discussion:

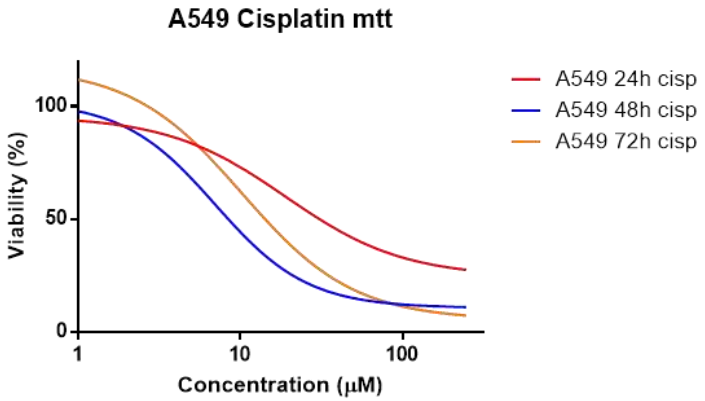
Table of LD_{50} and LD_{25}: Carvedilol

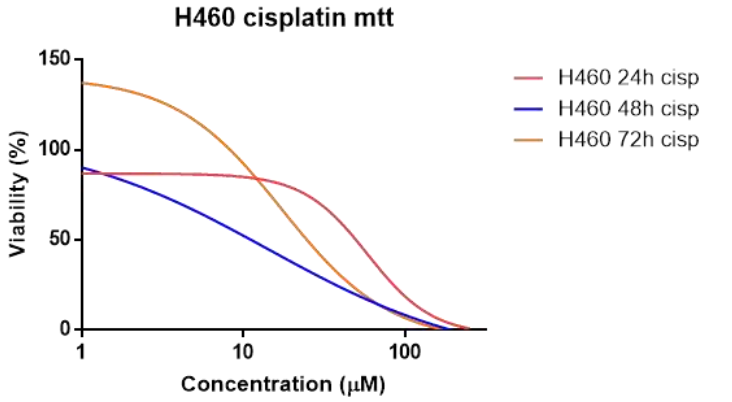
Carvedilol	µM	24 h	48 h	72 h
A459	LD_{50}	33.065	25.262	24.070
	LD_{25}	25.798	20.447	19.732
H460	LD_{50}	19.164	13.861	10.860
	LD_{25}	11.528	8.994	7.4255

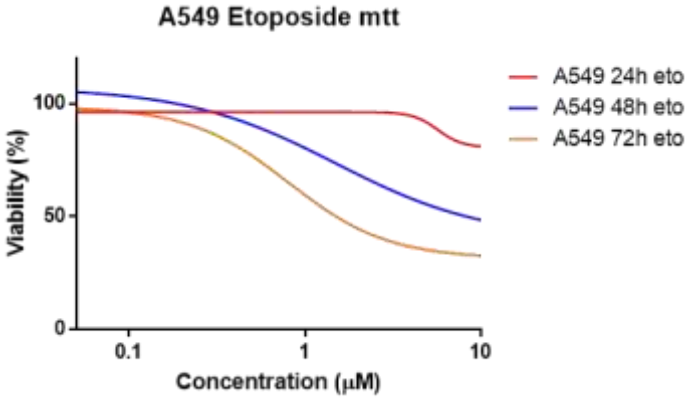
Table of LD_{50} and LD_{25}: Propranolol

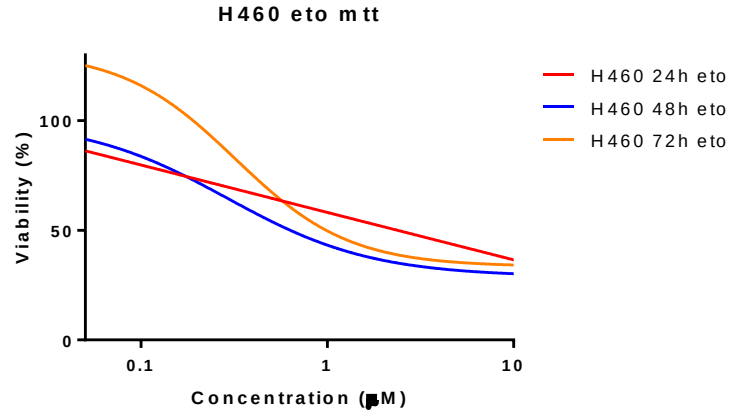
Propranolol	µM	24 h	48 h	72 h
A459	LD_{50}	145.560	116.446	108.942
	LD_{25}	124.294	92.236	83.476
H460	LD_{50}	171.623	149.218	126.553
	LD_{25}	108.645	71.647	62.901

Results: cytostatic drugs









Results and discussion:

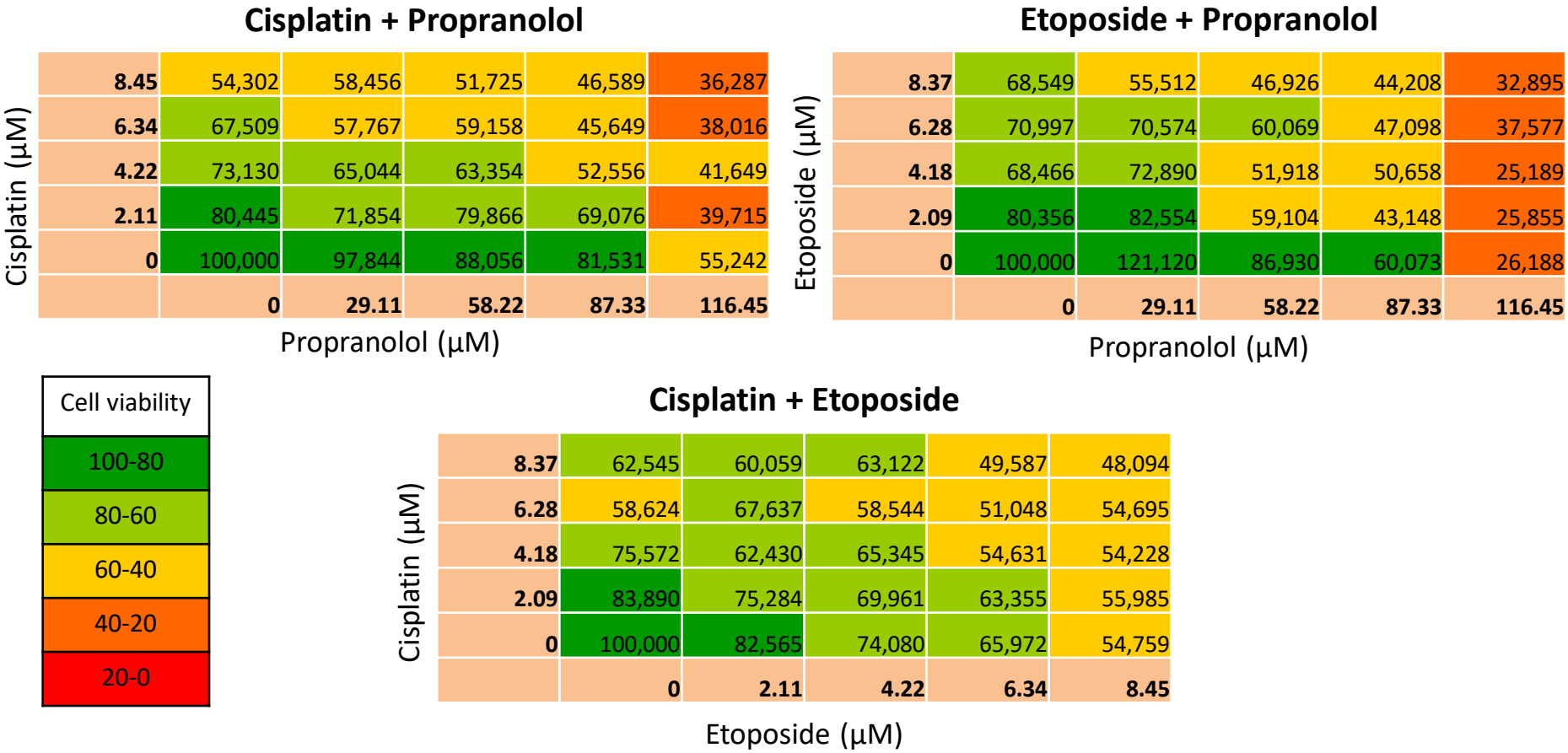
Table of LD_{50} and LD_{25}: Cisplatin

Cisplatin	µM	24 h	48 h	72 h
A459	LD_{50}	30.886	8.447	14.243
	LD_{25}	8.960	3.990	6.930
H460	LD_{50}	49.723	11.197	24.766
	LD_{25}	24.648	3.072	14.654

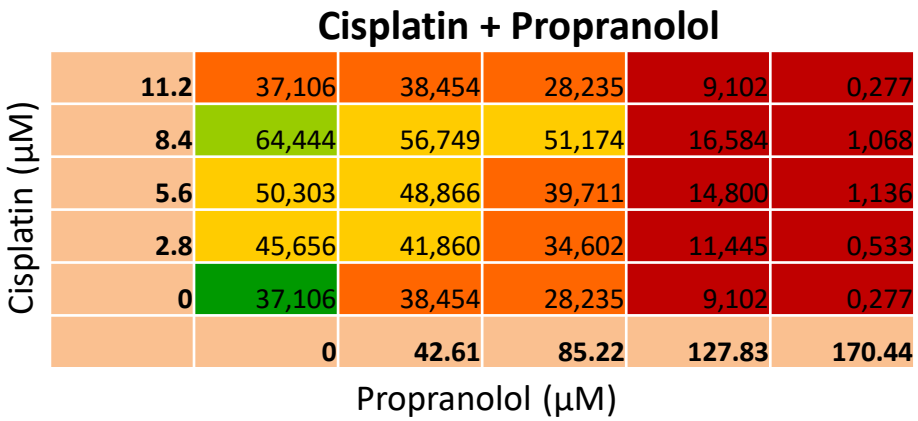
Table of LD_{50} and LD_{25}: Etoposide

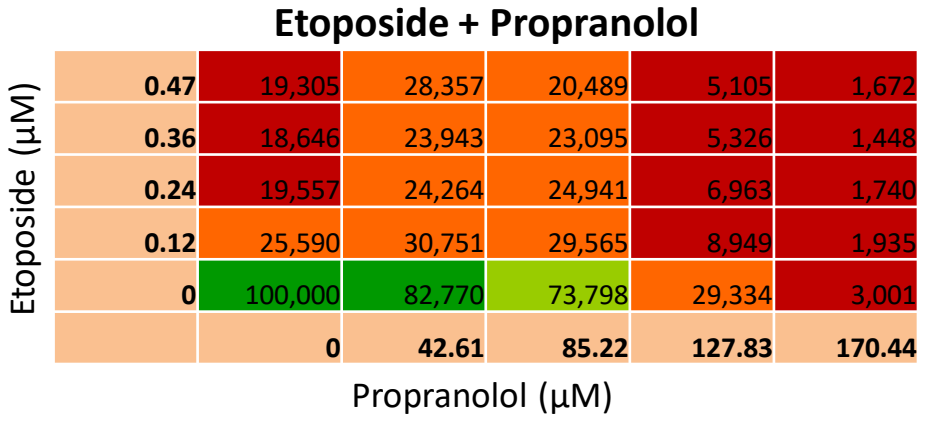
Etoposide	µM	24 h	48 h	72 h
A459	LD_{50}		8.368	1.506
	LD_{25}		1.383	0.546
H460	LD_{50}	2.252	0.474	0.747
	LD_{25}	0.168	0.116	0.313

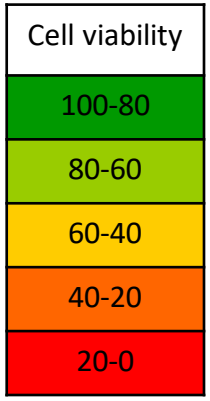
Results and discussion: Effects of Combined Exposures on A549

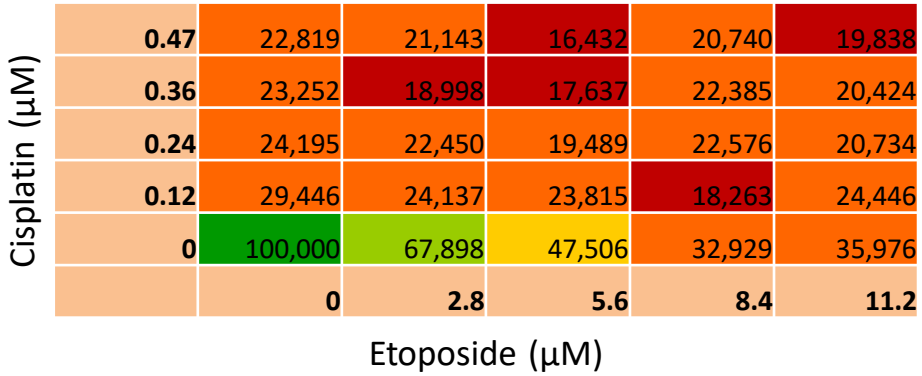


Results and discussion: Effects of Combined Exposures on H460









Conclusions

Cytostatic drugs showed higher toxicity than the β-blockers to the cell lines in study;

Propranolol, Carvedilol and Cisplatin cytotoxicity increased in a concentration dependent manner;

Etoposide cytotoxicity increased in a time dependent way in A549;

A549 was more resistant to carvedilol and etoposide while H460 to cisplatin and propranolol;

The binary mixtures showed that Propranolol combined with Etoposide and Cisplatin demonstrated a synergistic effect culminating in higher cell death;

For a future reference Human bronchial epithelial cells: HBEpC could also be used to test the effects on a non cancerous cell line.

Acknowledgments

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