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Investigating the Cytotoxic Effects of Aminoglycosides on A549 Lung Cancer Cell Line

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ABSTRACT

Objective: The current study was carried out to evaluate the cytotoxicity activity of aminoglycosides, specifically amikacin and gentamicin, on human lung cancer cell lines.

Methods: Cytotoxicity activity was evaluated on human cancer cell lines such as lung cancer (A549) using the MTT assay method.

Results: The selected aminoglycosides showed dose-dependent cytotoxicity activity on the tested cell lines. Variations in cytotoxicity were observed on different cell lines for the tested aminoglycosides. The cytotoxicity of the aminoglycosides increased as their concentration increased. Among the tested aminoglycosides, gentamicin showed better cytotoxicity activity on the tested cell lines.

Conclusion: The results of the present study suggest that amikacin and gentamicin have bioactive constituents with cytotoxic properties and their isolation can be useful for developing new anticancer drugs.

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INTRODUCTION

Cancer is one of the major diseases causing mortality worldwide. It is characterized by the uncontrolled proliferation of cells in any part of the body, leading to organ enlargement or tumor formation, which are detrimental to the body's function. Commonly affected parts of the body include the lungs, liver, cervix, breast, stomach, and oral regions [1]. Cancer can spread through metastasis from the initially affected area to other parts of the body.

Lung cancer is particularly prevalent and is mainly caused by factors such as smoking, secondhand smoke, and exposure to toxins [2]. Currently, chemotherapy is the most commonly used treatment for cancer, which includes alkylating agents, antimetabolites, antitumor antibiotics, and platinum analogs. However, these treatments often lead to significant side effects, including the potential to cause secondary cancers such as skin or lung cancer over long-term use.

There is a pressing need to identify new, cost-effective, highly efficient, and low side-effect treatments for cancer. Aminoglycosides such as amikacin and gentamicin, which are antibiotics used to treat serious infections caused by gram-negative bacteria, have shown potential in cancer treatment. However, the scientific evidence supporting their biological activities in cancer treatment remains limited [3,4, 5].

With this in mind, our study aims to evaluate the in vitro cytotoxicity activity of selected aminoglycosides, specifically amikacin and gentamicin, on lung cancer cell lines.

MATERIALS AND METHODS

Drugs

Gentamicin was purchased from Chetana Pharmaceutical, Perinthalmanna, Malappuram Kerala and Amikacin was purchased from Yarrow Chem products,Mumbai

Cell lines

A549 cell line for lung cancer is used for the present study. A549 cell line was Procured from NCCS Pune.

Cytotoxic assay

The MTT assay is a colorimetric, non-radioactive, rapid, and cost-effective method widely utilized to measure cell viability and proliferation in mammalian cells. This assay was used to evaluate the cytotoxicity of aminoglycosides, specifically amikacin and gentamicin. The yellow tetrazolium salt, MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide), is reduced by metabolically active cells via dehydrogenase enzymes, producing reducing equivalents such as NADH and NADPH. This process generates intracellular purple formazan, which can be solubilized and measured spectrophotometrically. Lower absorbance values compared to control cells indicate a decrease in cell proliferation, while higher absorbance values suggest an increase. Morphological changes can provide evidence of cell death [6,7].

Samples	Concentrations	OD values (triplicate) - 24hrs					IC50 Value
		1	2	3	Average	% of viability	
Control cells (without treatment)		1.538	1.546	1.542	1.542	100%	-
Etoposide (standard drug)	50 µg	0.948	0.945	0.939	0.944	38.78	205 mcg/ml
AMIKACIN	50µg	0.216	0.211	0.218	0.215	86.06	
	100 µg	0.299	0.307	0.303	0.303	80.35	
	150µg	0.387	0.398	0.407	0.397	74.25	
	200 µg	0.503	0.497	0.508	0.503	67.38	
	250µg	0.612	0.593	0.604	0.603	60.89	
GENTAMICIN	50µg	0.202	0.213	0.218	0.211	86.32	216 mcg/ml
	100 µg	0.318	0.322	0.327	0.322	79.12	
	150µg	0.426	0.431	0.429	0.429	72.18	
	200 µg	0.541	0.536	0.531	0.536	65.24	
	250µg	0.656	0.641	0.649	0.649	57.91	

Result and discussion

Aminoglycosides such as amikacin and gentamicin have been used in the treatment of various diseases before the advent of modern medicine. Synthetic drugs used in modern medicine for treatment have their roots in naturally isolated compounds [7,8]. However, the long-term use of synthetic drugs can cause unwanted side effects and decrease immunity toward normal diseases. Natural products, including aminoglycosides, have shown potential for the discovery of new bioactive molecules with high efficiency and fewer side effects [9]. This study was conducted to identify the cytotoxicity (anticancer) activity of amikacin and gentamicin on A549 cell lines for lung cancer.

The selected aminoglycosides showed dose-dependent cytotoxicity activity on the tested cell lines (Fig. 1). Cytotoxicity variations were observed in different cell lines for the selected aminoglycosides. The IC50 values are shown in Table 1. The cytotoxicity of the aminoglycosides increased as their concentration increased. Amikacin and gentamicin have been used in various regions for treating diseases[10.11].

Amikacin showed more cytotoxic activity on A549 cell lines compared to gentamicin. The IC50 values for amikacin and gentamicin on A549 cell lines were 205 mcg/ml and 216 mcg/ml, respectively. These variations in activity may be due to the response of chemical compounds present in them.

Cancer involves the uncontrolled growth of cells in the affected area. To mitigate the effects of cancer, the uncontrolled growth of cell numbers must be reduced. Although there is no accurate treatment for cancer yet, the uncontrolled increase in cell number due to cancer can be decreased by affecting the cell's metabolic pathways to kill them[12]. The cytotoxic effect of the selected aminoglycosides may be due to the killing of abnormally growing cells due to cancer and the elimination of those cells through apoptosis or necrosis[13,14] .

Apoptosis involves the activation of endonucleases that cause double-strand breaks in DNA between nucleosomes, leading to DNA fragmentation and cell death. Necrotic cell death is an unregulated process resulting from severe damage, such as ATP depletion, hypoxia, various toxins, and hyperthermia, characterized by cell swelling, lysis, and the release of intracellular contents associated with pathological tissue injury[15,16]. Aminoglycosides have diverse chemical constituents for their metabolic activities, as well as defense from their predators. These compounds may be responsible for increasing the mortality of cancer cells. Additional studies are required to isolate the pure compounds and their derivatives from the chosen aminoglycosides responsible for cytotoxicity[17] .

Table 1 Effect of Aminoglycosides on A459 Cell viability

Conclusion

The present study showed that the selected aminoglycoside like Amikacin and Gentamicin Process the cytotoxic activity on A459 lung cancer cell lines. This drug could be added drug for treatment of cancer. Furhter studies are required to prove the mechanism and efficacy at target protein,

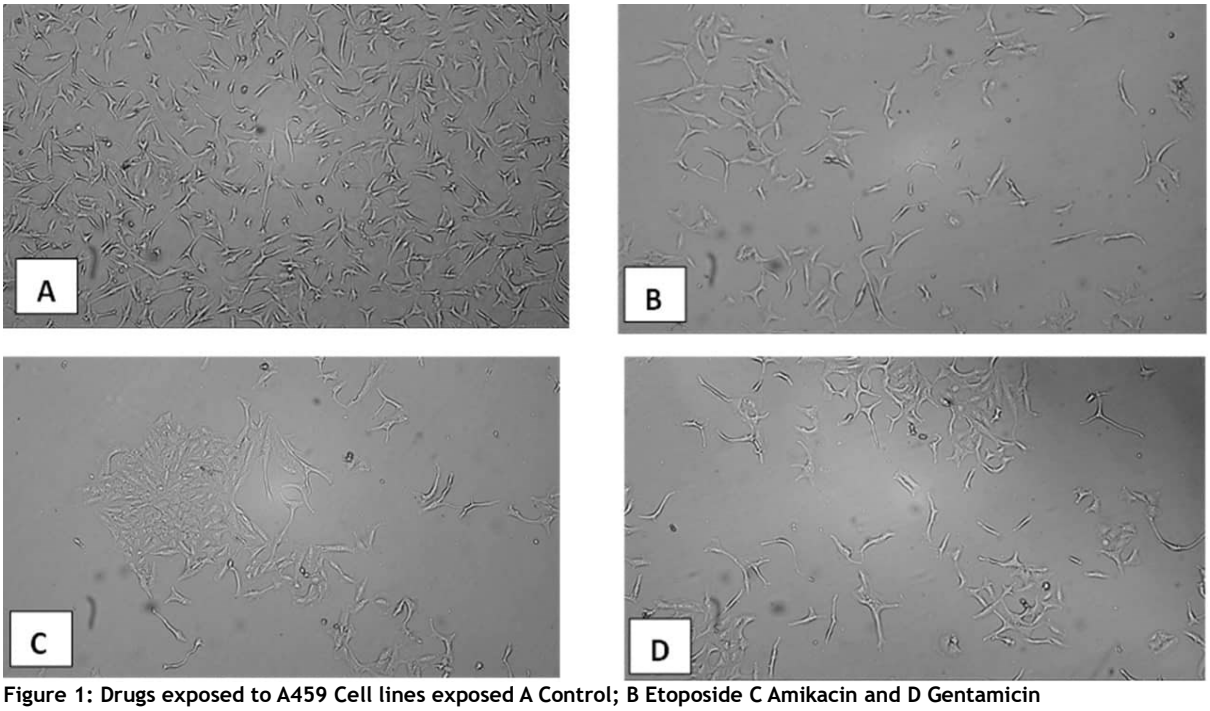

Figure 1: Drugs exposed to A459 Cell lines exposed A Control; B Etoposide C Amikacin and D Gentamicin

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