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# Enhanced cytotoxic effect of chemically conjugated polymeric sirolimus against ht-29 colon cancer and a-549 lung cancer cell lines

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**Background/ Aim:** Sirolimus (SR) is highly protein binding drug (92%) and lipophilic (log P=4.917) in nature. It has half life of 57-63 hrs and oral bioavailability is 20% even less when after eating food rich in fat. In our objective of the study, SR is chemically conjugated with biodegradable polymers like Methoxy-polyethylene glycolic acid (mPEG COOH) and Poly(Lactic-co glycolic acid)(PLGA) .It was ensured that there is a structurally correlation among the chemical structures of SR, mPEG COOH-SR conjugate, PLGA-SR conjugate, PLGA and m-PEG COOH polymers.

**Methods/Materials:** The cytotoxicity assay of both conjugates was carried out on specific A-549 lung cancer and HT-29 colon cancer cell lines using vincristine sulfate, tamoxifen and cisplatin as controls separately.

**Results:** All results were showing the positive effects of PLGA-SR and cisplatin with IC50 values of 2.88 µg/ml and 9 µg/ml indicatively more active than cisplatin *in vitro*. Whereas mPEG-SR conjugate was similar activity of cisplatin with IC50 value of 8.88 µg/ml on A-549 lung cancer cell line. Both conjugates were not shown any cytotoxicity activity on 3T3 fibroblast normal cell lines. On the other hand, PLGA-SR conjugate was nine times more active than vincristine sulfate with IC50 value of 7 µg/ml, where as MPEG-SR conjugate is more active than other controls and SR alone on HT-29 colon cancer cell line. These results are indicated that both conjugates with potent cytotoxicity activity against specific lung cancer and colon cancer types than SR alone.

**Conclusion:** Polymeric conjugation is a useful approach in a novel drug delivery system. These conjugates are basic precursors to formulate into novel drug delivery systems especially in as nanocarriers for better release with surface modification to enter the tumor cells with significant increase in the bioavailability.

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