Enhancing the Efficacy of Paclitaxel with Nano-Activators: A Novel Approach to Mitigating the Chemotherapies Side-Effects

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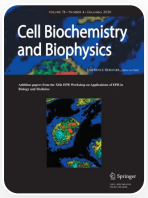

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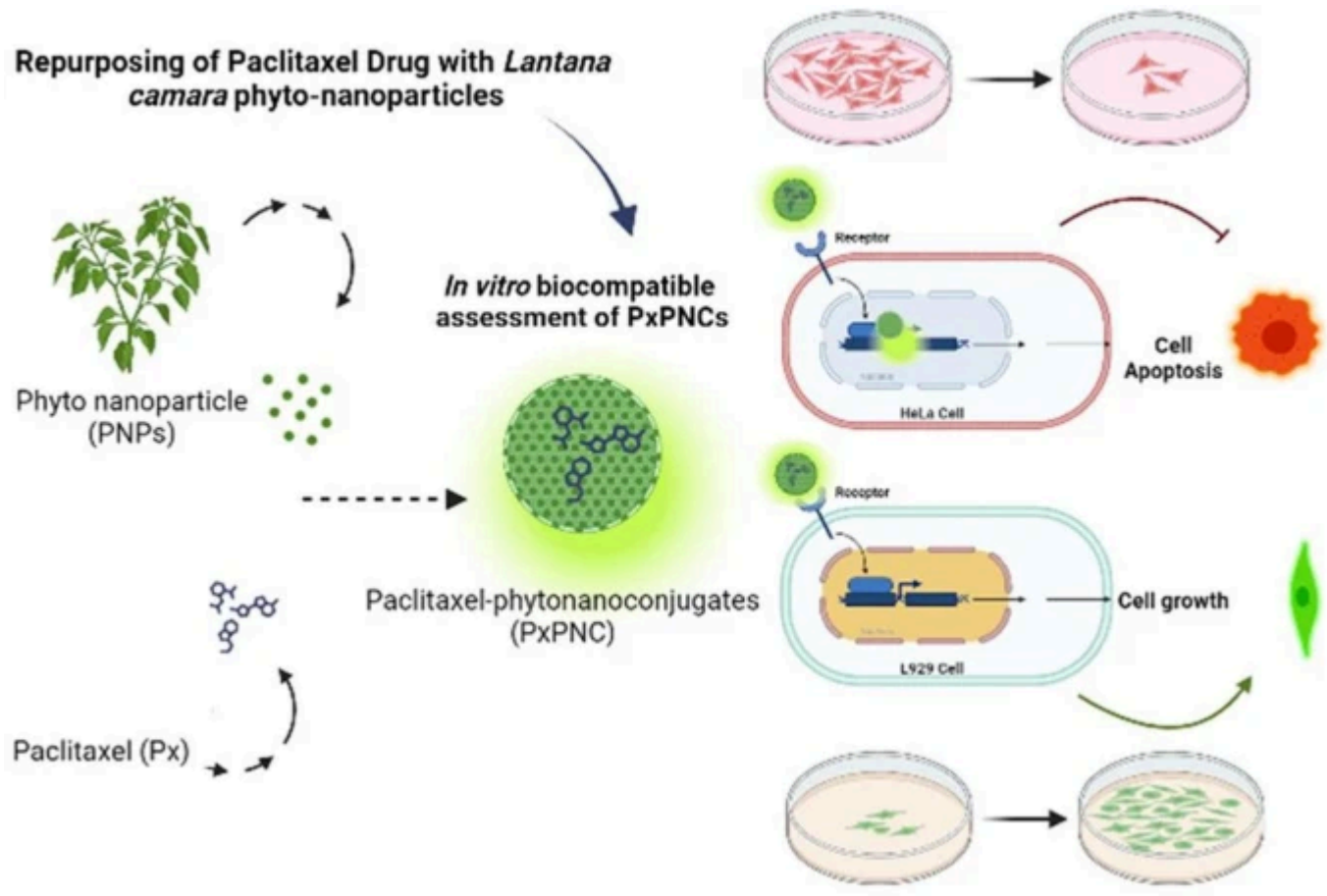
Abstract

In the modern era of medical science, nanotechnology plays a pivotal role in drug repurposing, remodelling, novel drug delivery design, and advanced diagnostics. Various nanomaterials including nanoparticles (NPs) and nanoconjugates are being explored as carriers, immune modulators, and targeted agents to selectively eliminate defective cells. However, conventional anticancer drugs like paclitaxel (Px) often exhibit limitations such as off-target cytotoxicity and immune suppression. Reformulating such drugs with naturally derived bio-enhancers may mitigate side effects and enhance therapeutic potential. In this study, we investigated the synergistic interaction between drug (Px) and phytogenic NPs derived from *Lantana camara*, a natural weed. The nanoconjugates of drug Px with phytonanoparticles (PxPNC) were synthesized using a 1 mM genipin cross-linking solution shows upto 98% drug loading efficiency and nano-crystalline nature. Physicochemical characterization confirmed the formation of NPs (198.41 ± 0.09 nm) and their conjugation with Px (PxPNC: 227 ± 0.25 nm), with stable structural integrity

maintained at pH ≥ 7 for up to 96% of drug content retention. In vitro studies demonstrated that the NPs at 0.4 µg/mL exhibited significant anti-inflammatory, antioxidant, and antiproliferative activity against cancer cell lines (HeLa cells). Importantly, concentrations < 0.5 µg/mL showed negligible cytotoxicity against fibroblast cell line (L929 cells). Notably, Half maximal Inhibitory concentration (IC_{50}) of drug Px for HeLa cells - 0.51 ± 0.02 µg/mL and L929 fibroblast cells- 0.48 ± 0.02 µg/mL significantly improved in PxPNC i.e., HeLa cells-0.34 ± 0.01 µg/mL and L929 cells-0.47 ± 0.01 µg/mL respectively. Our findings suggest that incorporating *L. camara* phyto-components enhances the therapeutic index of paclitaxel, offering a promising plant-based nanoplatform for safer, more effective anticancer treatment potentially suitable for future preclinical investigations as a generic formulation.

Graphical Abstract



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Data Availability

The data can be available from the corresponding author upon reasonable request.

Abbreviations

NPs: Nanoparticles

AgNPs: Silver Nanoparticles

AuNPs: Gold Nanoparticles

PTX / Px: Paclitaxel

PVP-b-PCL: poly(N-vinylpyrrolidone)-b-poly (epsilon-caprolactone)

PxPNCs: Paclitaxel-Phytonanoparticles conjugates

PBS: Phosphate Buffer saline

DLS: Dynamic light scattering

IC_{50} **:** Half maximal Inhibitory concentration Human Red blood cells

HRBC : Tissue culture plate

TCP: 2, 2-diphenyl-1-picrylhydrazyl

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Contributions

AD conceptualises the work, designs, supervises and performs NPs synthesis, in vitro experiments and analyses the data; SP, AS, IR and BKR performs experimental work and data analysis; ASa, IR , JB, BKR perform phytoextraction experiments and data analysis and , , NS, , SP and SM review and conclude the work.

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Ethics declarations

Conflict of Interest

The authors declare no competing interests.

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