Ginsenoside-Gemcitabine Nanocomplex-based Delivery System for Enhanced Cancer Therapy

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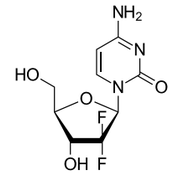
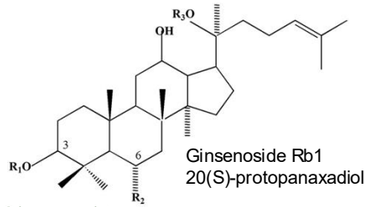
AIM : To develop and evaluate a self-assembled ginsenoside-gemcitabine nanocomplex (GGNC) as a novel bioactive drug delivery system aimed at enhancing chemotherapeutic efficacy, sustaining drug release, and minimizing toxicity in colorectal cancer therapy.

BACKGROUND

- Colorectal cancer (CRC) is the third leading cause of cancer-related mortality worldwide.
- Current chemotherapy regimens often face limitations such as drug resistance, systemic toxicity, and poor bioavailability.
- Gemcitabine, a second-line agent in CRC, is limited by rapid enzymatic degradation, short plasma half-life, and off-target toxicity[1].
- Ginsenosides, bioactive compounds from *Panax ginseng*, possess anticancer, anti-inflammatory, and antioxidant properties[2] and can self-assemble into nanoparticles.
- Ginsenosides serve as both therapeutic agents and nanocarriers, offering a promising strategy to improve drug delivery and efficacy[2].
- This study aims to develop ginsenoside-gemcitabine nanocomplexes (GGNCs) for sustained drug release, enhanced colloidal stability, and synergistic anticancer effects in vitro CRC models.



Gemcitabine



Ginsenoside

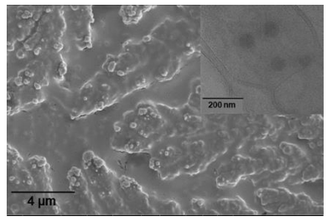
Ginsenoside Rb1 20(S)-protopanaxadiol	R1 = glu-glu R2 = -H R3 = glu-glu
Ginsenoside Rg1 20(S)-protopanaxatriol	R1 = -H R2 = O-glu R3 = glu

METHODS

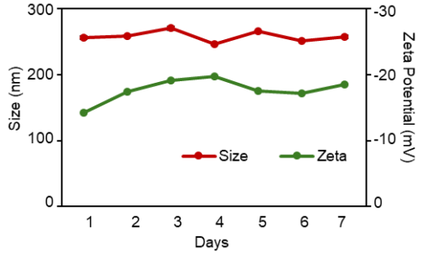
- **Preparation of GGNCs**: Ginseng dissolved in DMSO was added dropwise to gemcitabine (5:1 w/w) in water, stirred for 6 h, then filtered, washed, and lyophilized.
- **Characterization**: Particle size and morphology was analyzed by TEM; PXRD and FT-IR were used to assess crystallinity and molecular interactions.
- **Stability**: Particle size and zeta potential were monitored over 7 days in water.
- **Drug Analysis**: Drug loading and encapsulation efficiency were measured; in vitro release was assessed by HPLC.
- **Cell Viability**: Alamar Blue assay was performed on L929 and SW480 cells.

RESULTS

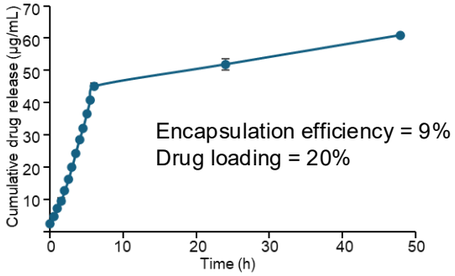
1. GNCs exhibited a uniform spherical shape as observed under SEM and TEM (inset), with a size range of ~ 200-250 nm.



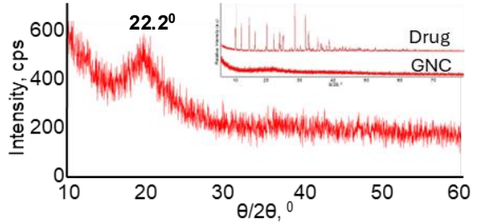
2. GGNCs showed consistent particle size (~250 - 270 nm) with no significant aggregation and stable zeta potential (-15 mV to -20 mV) over a 7-day period in aqueous conditions, indicating good short-term colloidal stability.



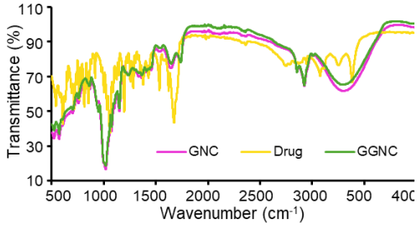
3. GGNCs showed a biphasic release profile with an initial burst followed by sustained gemcitabine release, with a cumulative release of ~61 µg/mL over 48 hours in PBS at 37 °C, confirming effective drug incorporation into the nanoparticles.



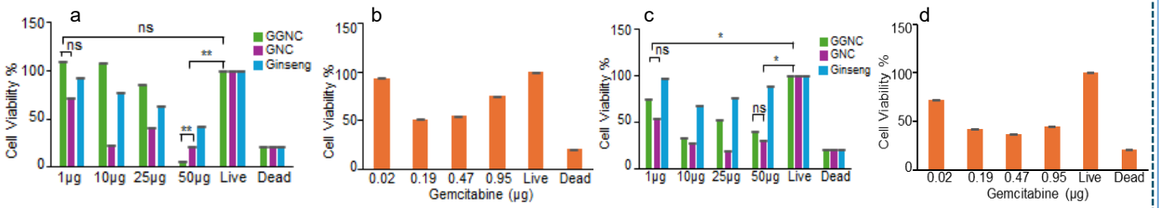
4. PXRD analysis of GGNCs exhibited a broad amorphous halo (2θ = 15°-30°), similar to GNCs, with no detectable gemcitabine peaks, confirming successful drug incorporation. Inset shows PXRD spectra of free gemcitabine and GNCs as controls.



5. FT-IR analysis showed no gemcitabine-specific peaks (N–H, C–F, C=O) in GGNCs, indicating the absence of free drug on the nanoparticle surface. Retention of ginseng-specific peaks suggests successful drug encapsulation.



6. GGNCs exhibited dose-dependent cytotoxicity in SW480 cells (a,b), reducing viability to ~10% at 50 µg. GNCs showed moderate effects, while free ginseng and gemcitabine had limited effects, indicating a synergistic response in the GGNC formulation. In L929 fibroblasts (c,d), GGNCs and GNCs caused moderate toxicity at higher concentrations (~40-30% viability), whereas free ginseng maintained >90% viability, suggesting the selective cytotoxicity of GGNCs toward cancer cells.



CONCLUSION

- ✓ This study reports the successful synthesis and characterization of ginseng-gemcitabine nanocomplexes, a self-assembled nanocarrier system utilizing ginsenosides for dual therapeutic and delivery functions.
- ✓ GGNCs demonstrated sustained drug release, maintained colloidal stability over 7 days, and cytotoxicity against colorectal cancer cells suggesting synergistic therapeutic effect.
- ✓ These findings highlight GGNCs as a promising, safe, and effective strategy for cancer therapy.

REFERENCES

1. Zeng, X., et al. Front. Endocrinol. 14, 1170526 (2023).
2. Zuo, S., et al. Front. Bioeng. Biotechnol. 10, 945472 (2022).

ACKNOWLEDGMENT

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