Production of small nanocrystals with radiosensitising drugs for long-acting localised treatment of glioblastoma

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QUEEN'S UNIVERSITY BELFAST
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LISBON PORTUGAL
MULTISECTOR INNOVATION *for* ADVANCING DELIVERY SCIENCE
JULY 6–9, 2026

Department for the Economy

BACKGROUND

Glioblastoma multiforme (GBM)

- Most common primary malignancy : 77-81 % [1]
- Highly aggressive
- Incidence rate : 0.6-5 every 100,000 persons [2]
- Median survival rate : 14.6 months [3]

Extensive surgical resection [4]

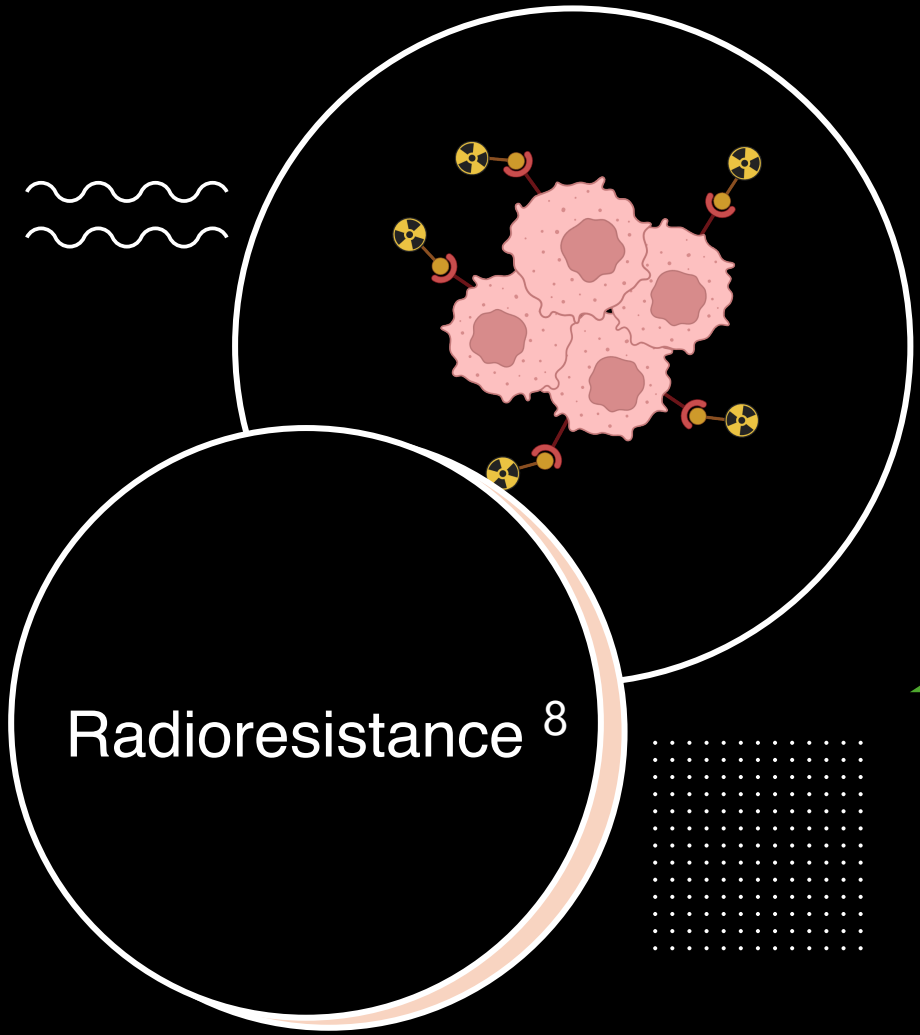
Radiation therapy [5]

EBRT total dose of 60 Gy (2 Gy daily fractions, 5 days a week)

Chemotherapy [6]

Temozolomide (TMZ) for 42 days + 6 cycles

- Surgical resection leaves microscopically progressed tumours [5]
- TMZ causes Toxicity, Lacks penetration through BBB, Development of resistant mechanisms [6]
- Repopulation surrounding the resected region
- Novel combination treatments DO NOT improve survival significantly [7]

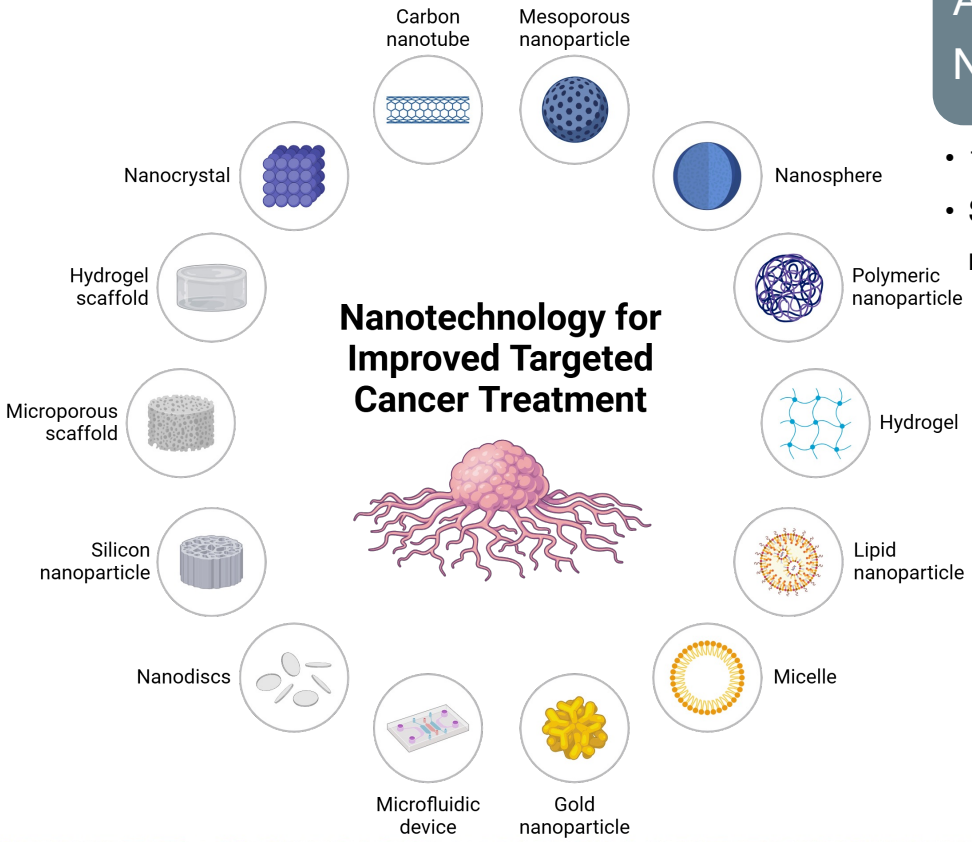


Radioresistance [8]

Factors

- Tumour hypoxia
- Metabolic alterations
- Tumour heterogeneity etc

Drugs to improve local tumour killing + enhance radiation response

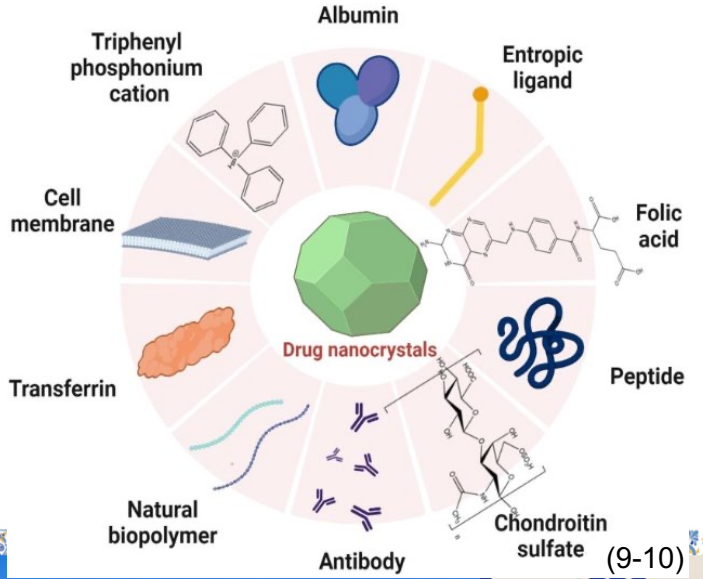


Advantages of Nanocrystals

- 100 % drug-loading
- Size and surface modifications

Application of Nanocrystals[9]

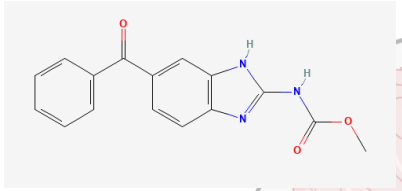
- Long-acting ability throughout cancer treatment
- Multiple administration.



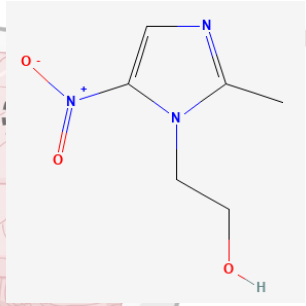
(9-10)

Drugs for screening [11]

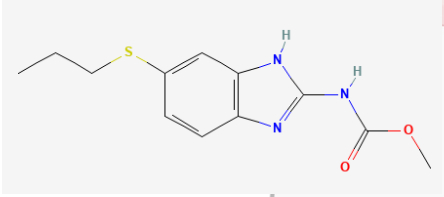
- Mebendazole (MBZ)



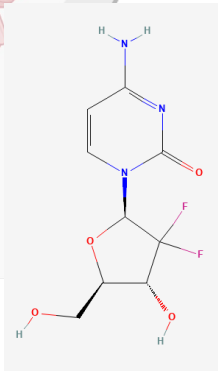
- Metronidazole (MET)



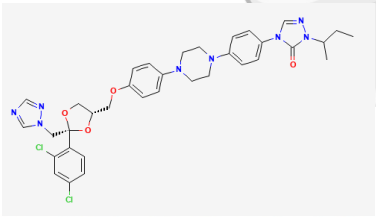
- Albendazole (ABZ)



- Gemcitabine (GEM)



- Itraconazole (ITR)



HYPOTHESIS

The drugs for screening are capable of anti-cancer effects in GBM alongside radiation, thereby, their employment as NCs will have a long-acting and superior impact

AIM

Develop novel therapeutical alternatives for the localised management of GBM, using NCs of repurposed radiosensitising drugs

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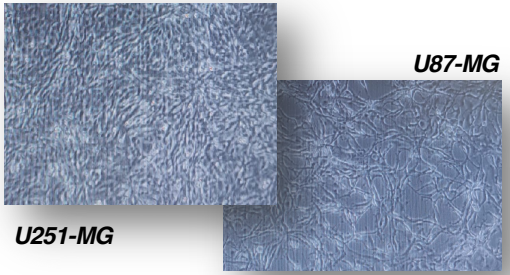
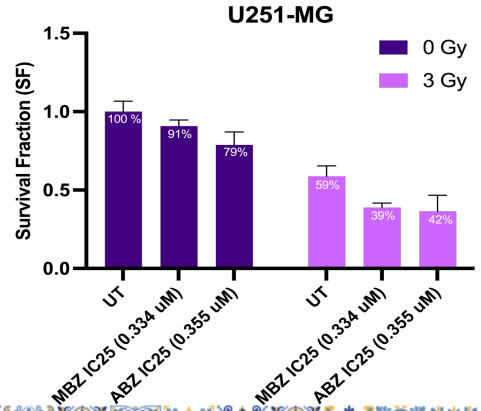
Cell Culture

Screening

Mebendazole & Albendazole selected as candidate drugs



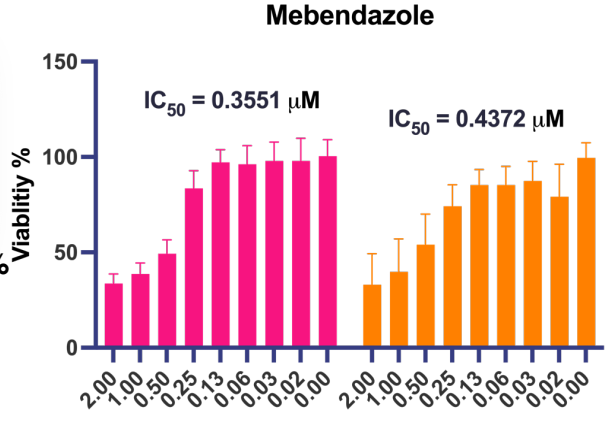
Screening clonogenic assay showed 11% radiosensitising ability by MBZ IC_{25} alongside 0 Gy & 3 Gy doses

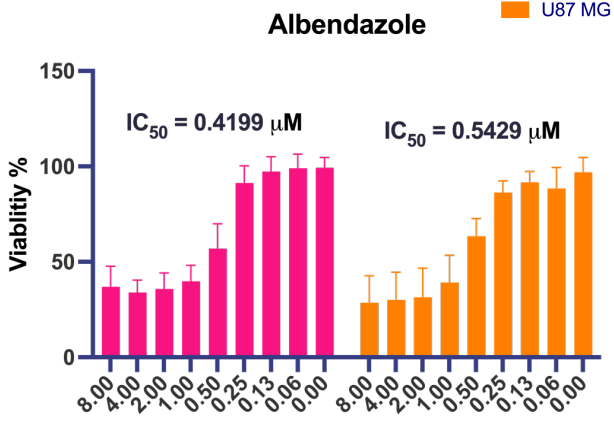


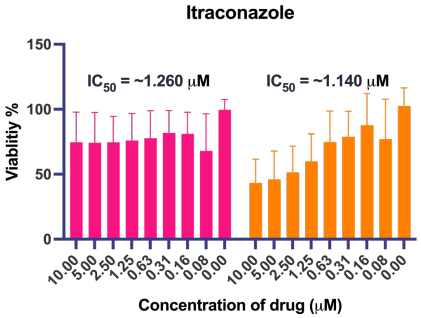
Finding IC_{50}

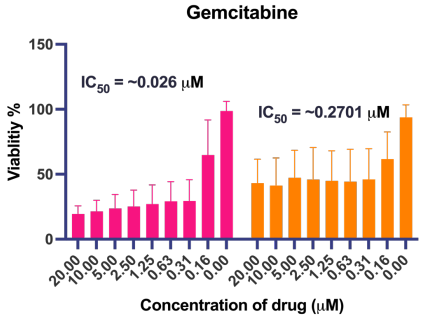
Alamar blue cell viability assay

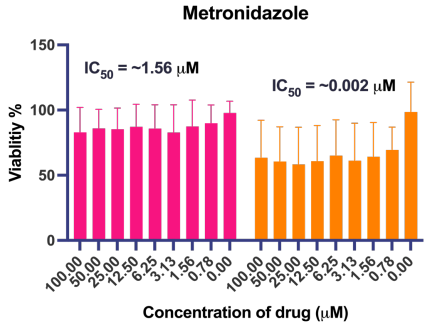
U251-MG
U87 MG







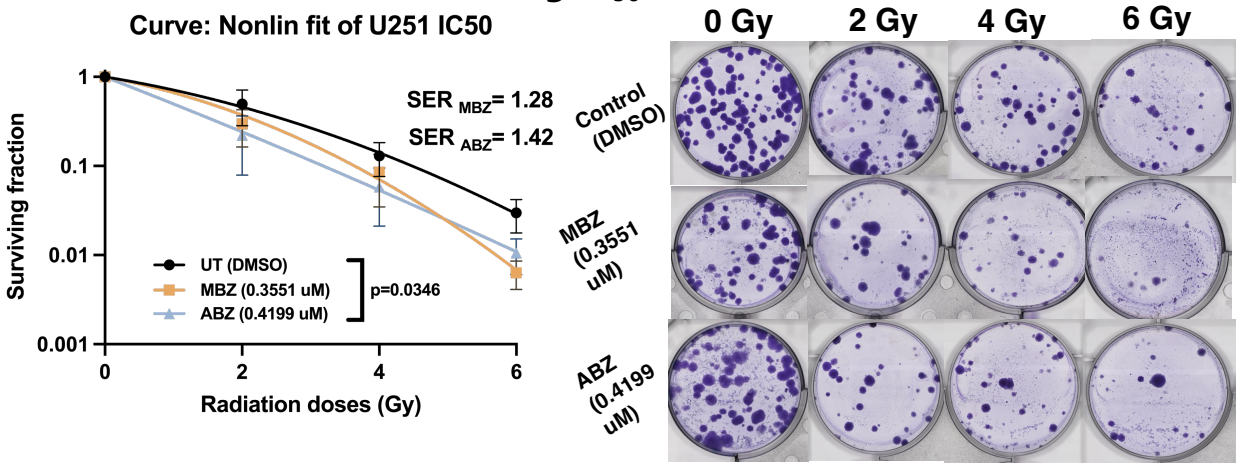




N=3

Clonogenic assay

Survival curves using IC_{50} of mebendazole & albendazole in U251-MG & U87-MG cell lines

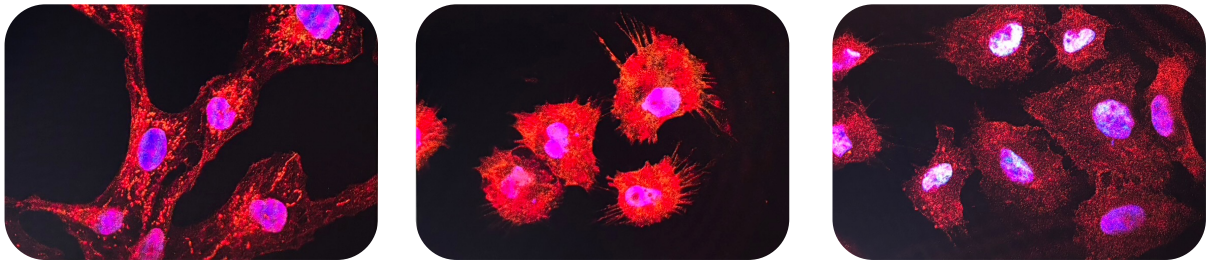


Significant **Sensitiser Enhancement Ratio** for ABZ in U251-MG

SER of MBZ not significant in U251-MG

Confocal Microscopy

disruption of microtubule formation by free drugs in U251 cells after 48 h incubation



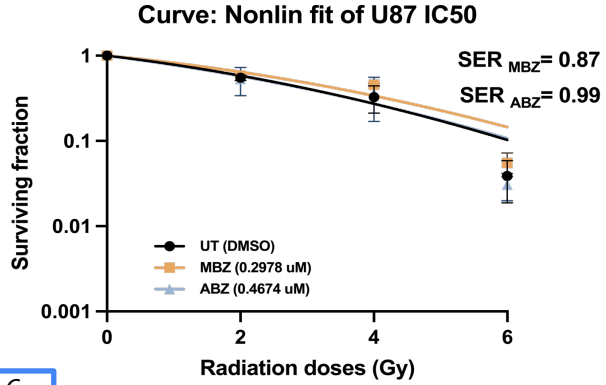
U251 cell control | U251 MBZ 0.3551 uM | U251 ABZ 0.4199 uM

N=6

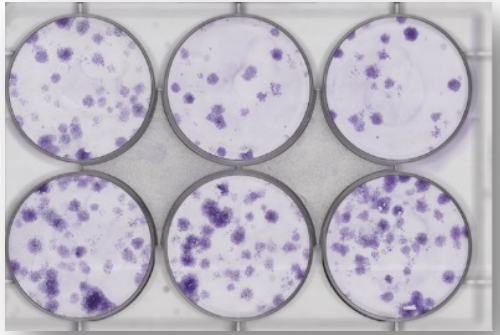
Cell Culture

Clonogenic assay

Survival curves using IC_{50} of mebendazole & albendazole in U251-MG & U87-MG cell lines



N=6

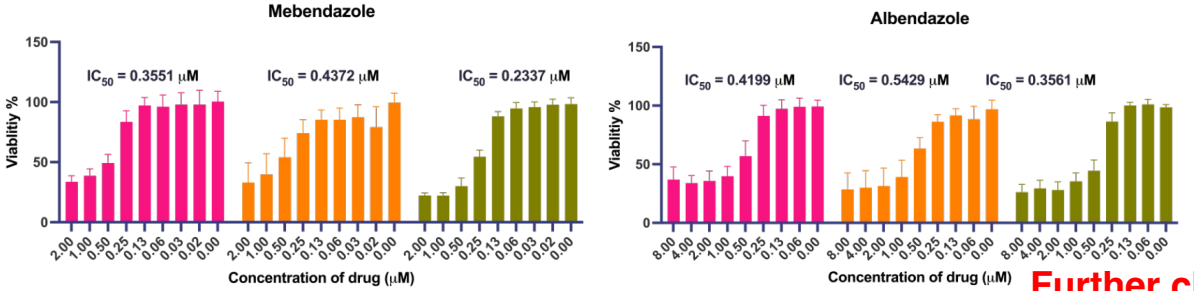


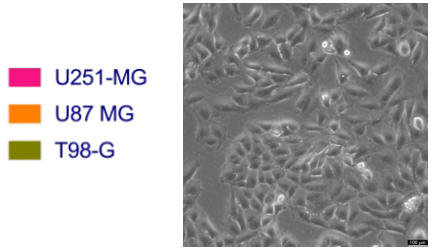
Shoulder of graph shows **radioresistance** in U87-MG.

Plating efficiency not uniform due to large diffused colonies.

Finding IC_{50}

Alamar blue cell viability assay

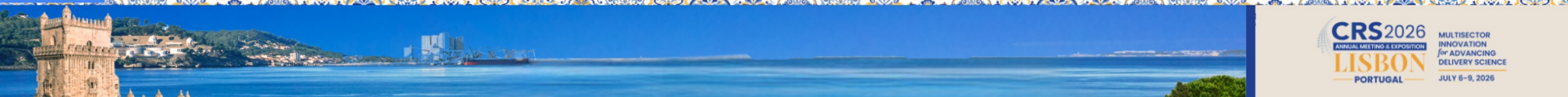


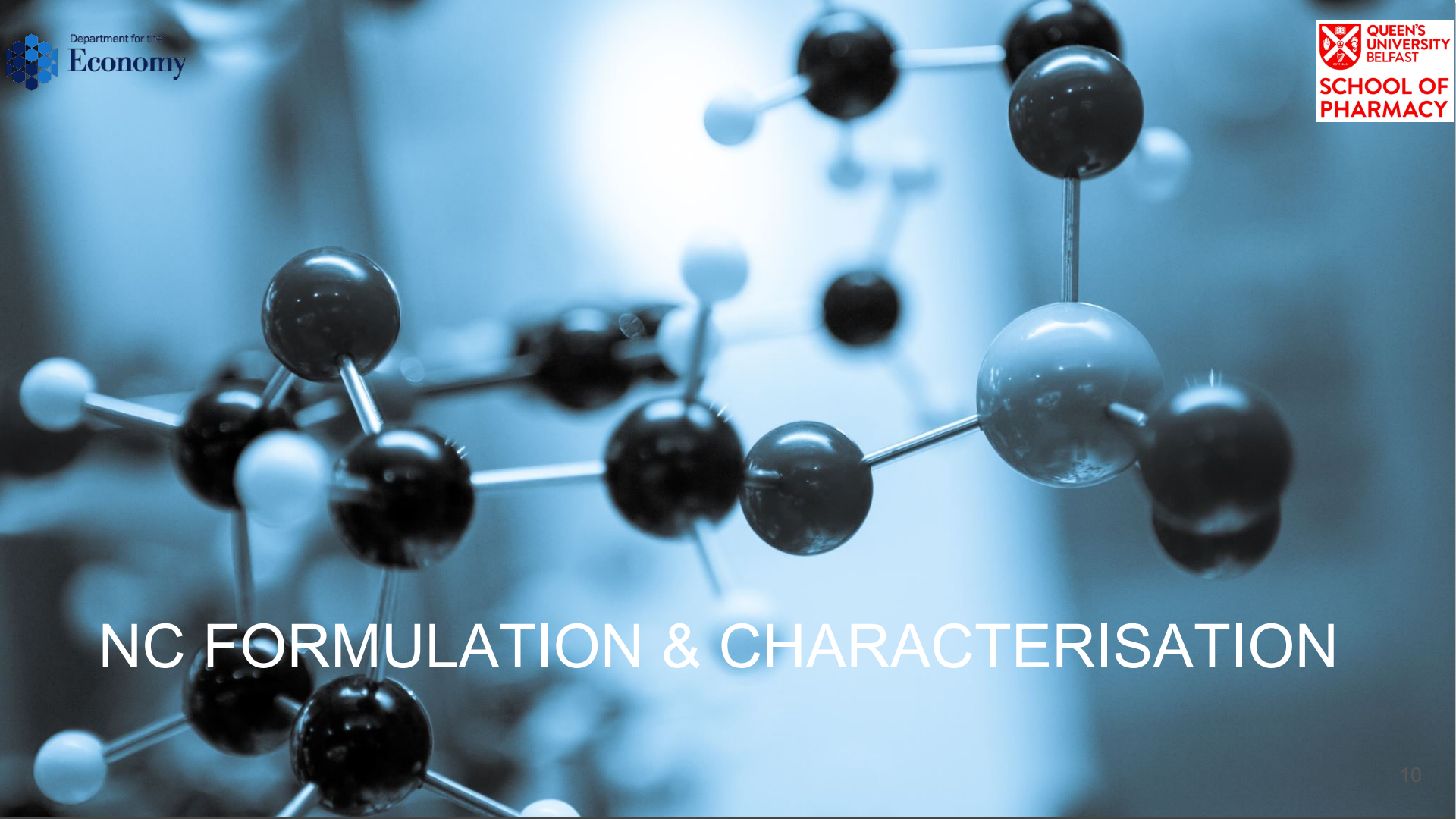


T98-G

N=3

Further clonogenic assays to support hypothesis

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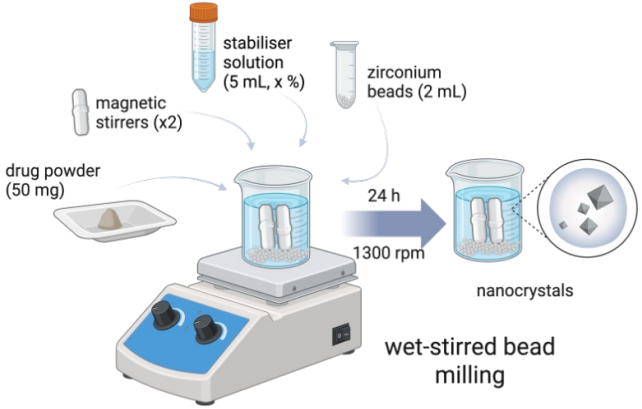
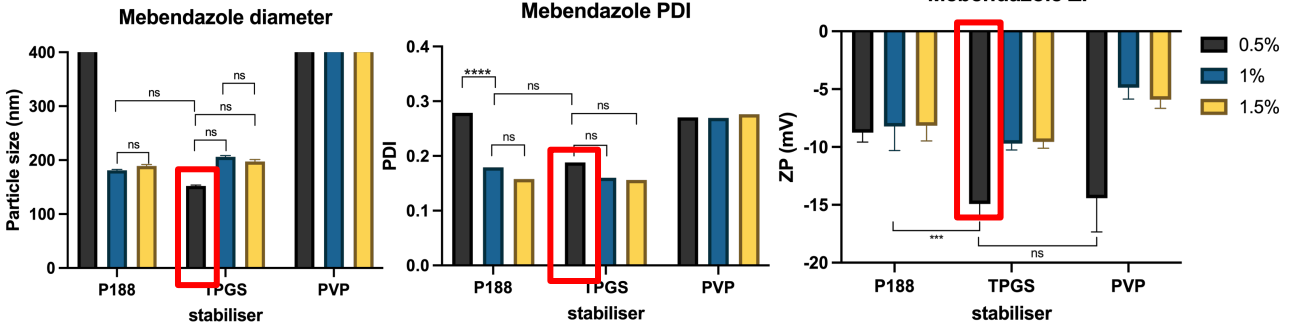
NC FORMULATION & CHARACTERISATION

NC formulation

Top-down method

Wet-stirred bead milling





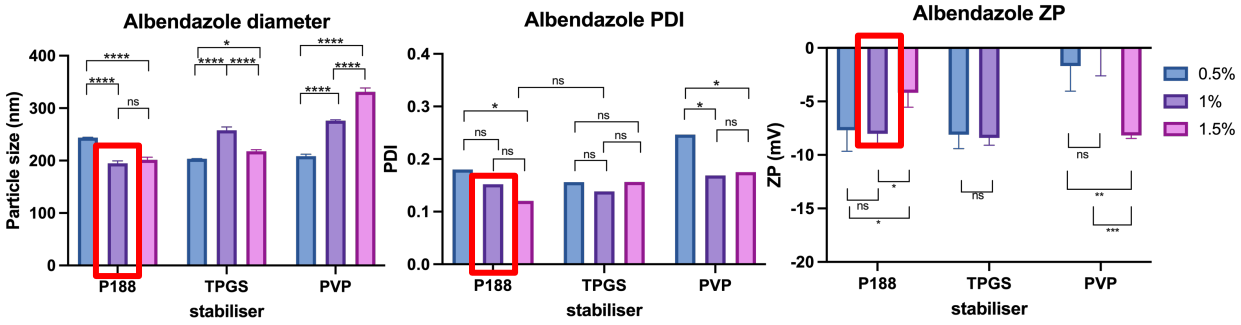
Best formulation for mebendazole

Stabiliser: 0.5 % TPGS

Polydispersity Index (PDI): 0.2

Mean hydrodynamic size: 175.96 ± 1.82 nm

Zeta Potential (ZP): -14.45 ± 3.42 mV



Best formulation for albendazole

Stabiliser: 1 % P188

Polydispersity Index (PDI): 0.15

Mean hydrodynamic size: 194.92 ± 3.23 nm

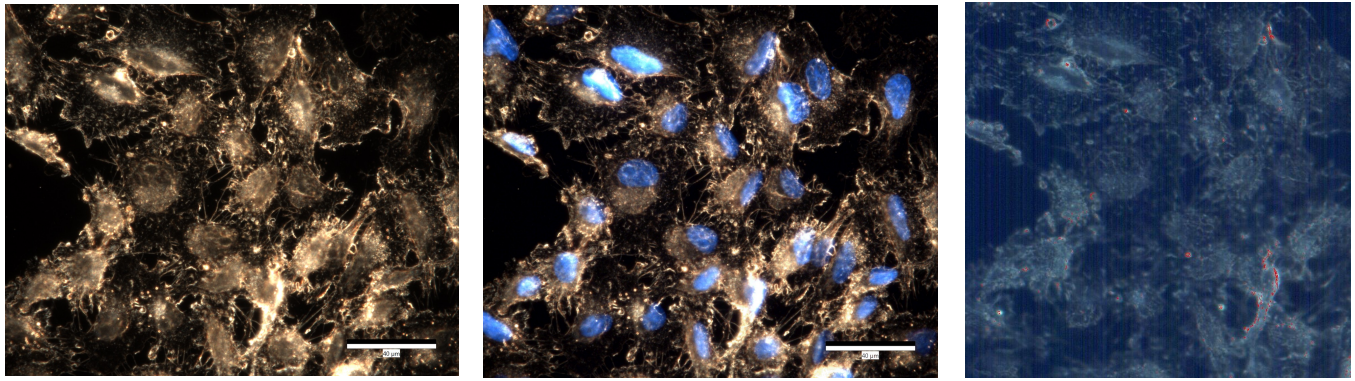
Zeta Potential (ZP): -8.294 ± 0.99 mV

N=3

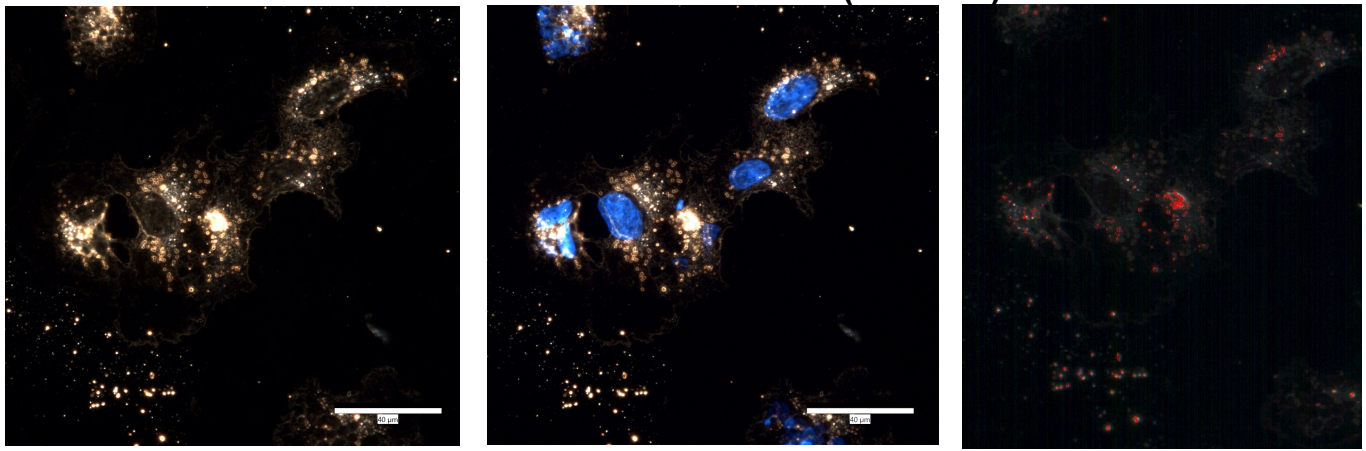
Hyperspectral microscopy

Proof-of-concept
U251-MG cells
48 h incubation
0.6 uL MBZ NS

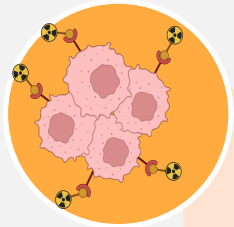
Cell control



MBZ NS 100X IC50 (35.5 uM)



Conclus



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USED AS LOCAL SPRAY AFTER SURGICAL RESECTION ALONGSIDE RADIATION

1. REPURPOSED RADIOSENSITISING DRUGS

Clinically approved drugs repurposed for enhanced radiosensitisation

- Well-characterized safety profiles
- Reduced development time and cost

2. NANOCRYSTAL FORMULATION

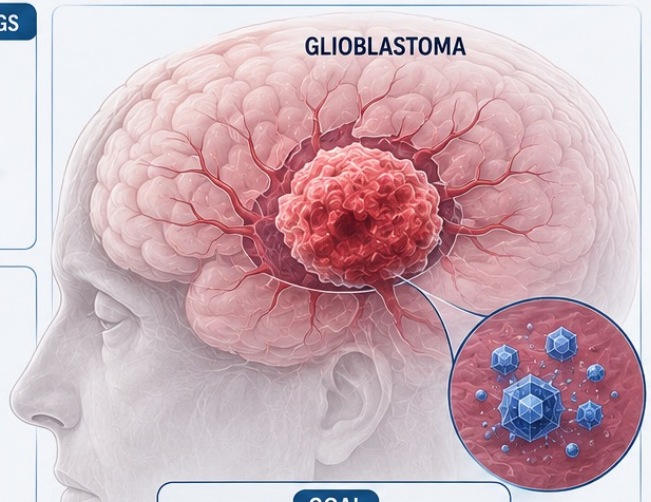
Drugs engineered into nanocrystals for sustained release and enhanced efficacy

- High drug loading
- Enhanced stability
- Sustained release
- Improved tumor penetration

3. LOCAL SPRAY APPLICATION AFTER SURGICAL RESECTION

Nanocrystal formulation is locally sprayed into the resection cavity to achieve prolonged retention and local action

- Direct application to resection cavity
- Minimizes systemic exposure
- Long-acting local drug release



GOAL

Enhance the effectiveness of radiation by delivering repurposed radiosensitising drugs as nanocrystals for sustained local release and improved outcomes in glioblastoma treatment

4. WORKING ALONGSIDE RADIATION

Nanocrystal drug enhances the effect of radiation on residual glioblastoma cells

Radiosensitising nanocrystals | Radiation | Enhanced tumor cell kill

MECHANISMS OF RADIOSENSITISATION

- Increase DNA damage
- Inhibit DNA repair
- Modify tumor microenvironment
- Induce oxidative stress
- Cell cycle modulation

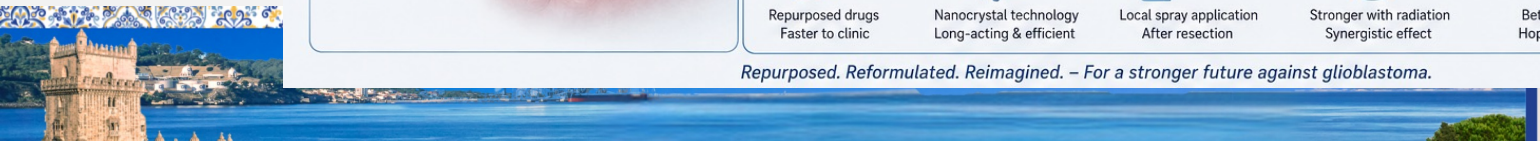
5. IMPROVED TREATMENT OUTCOMES

Greater tumor control | Prolonged progression-free survival | Improved overall survival | Better quality of life

A NOVEL STRATEGY TO TRANSFORM GLIOBLASTOMA TREATMENT

Repurposed drugs Faster to clinic → Nanocrystal technology Long-acting & efficient → Local spray application After resection → Stronger with radiation Synergistic effect → Better outcomes Hope for patients

Repurposed. Reformulated. Reimagined. – For a stronger future against glioblastoma.



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Thank you

Any questions?