Tech Session 3: Local Chapters 2

THASHREE MARIMUTHU

CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

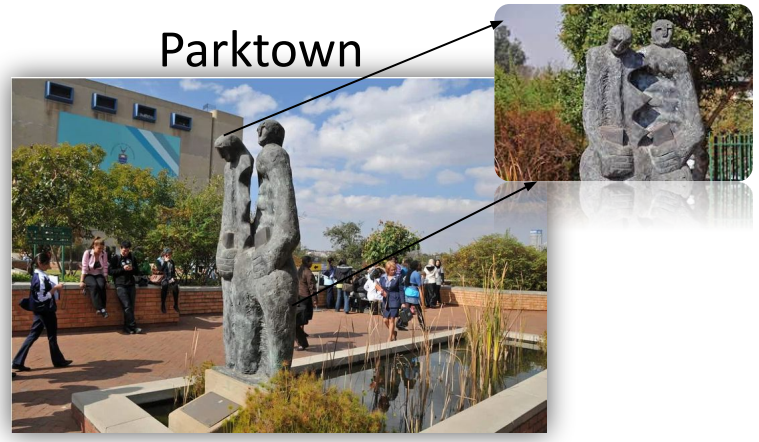
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG 100 1922 2022 | FACULTY OF HEALTH SCIEN

WADDP
WITS Advanced Drug Delivery Platform

Braamfontein

Metal oxide Nanosystems for Targeted Chemotherapy

Parktown



Thashree Marimuthu and Yahya E. Choonara

Wits Advanced Drug Delivery Platform Research Unit, Department of Pharmacy and Pharmacology,
School of Therapeutic Science, Faculty of Health Sciences, University of the Witwatersrand,
7 York Road, Parktown, Johannesburg, 2193, South Africa

THERAPEUTIC Sciences

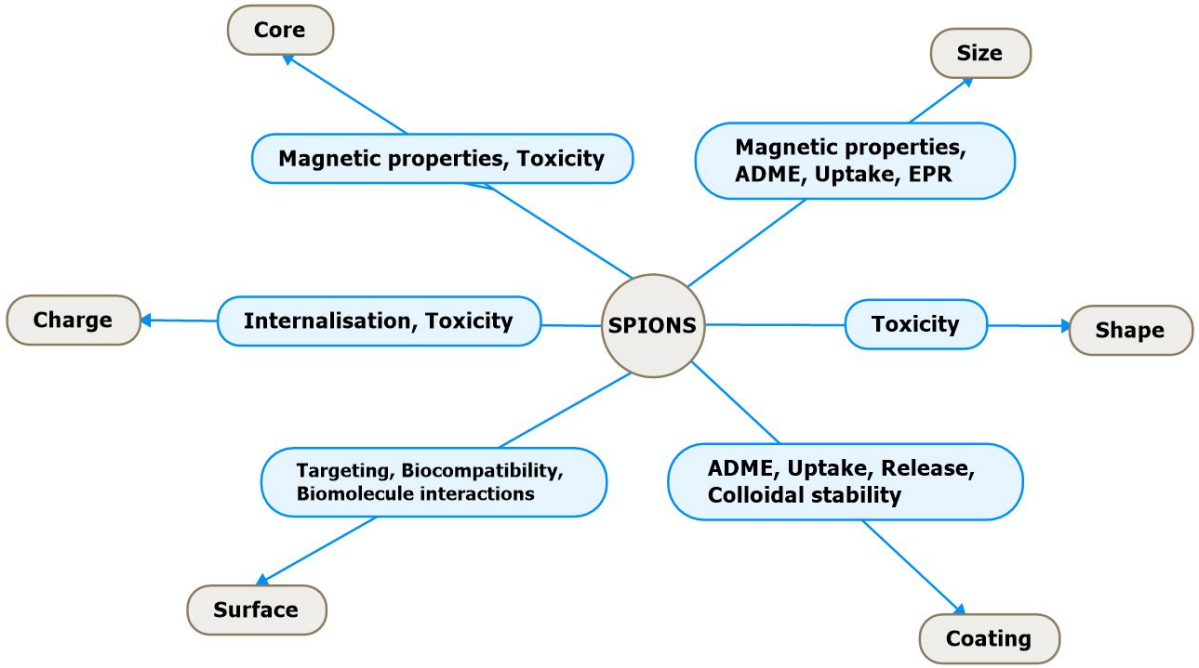
WITS PHARMACY

Introduction

- Chemotherapy involves intravenous or oral administration where drugs are systemically distributed but the distribution presents with side effects.
- The targeted delivery of drugs to the tumour employing functionalized nanoparticles like iron oxide nanosystems are good candidates to overcome these challenges.
- Rational design of iron oxide nanosystems can result in multifunctional nanoplatforms[1].

1. Tran H-V, Ngo N M et al. Materials (Basel). 2022;15(2):503.

What do we know about iron oxide Nanosystems?

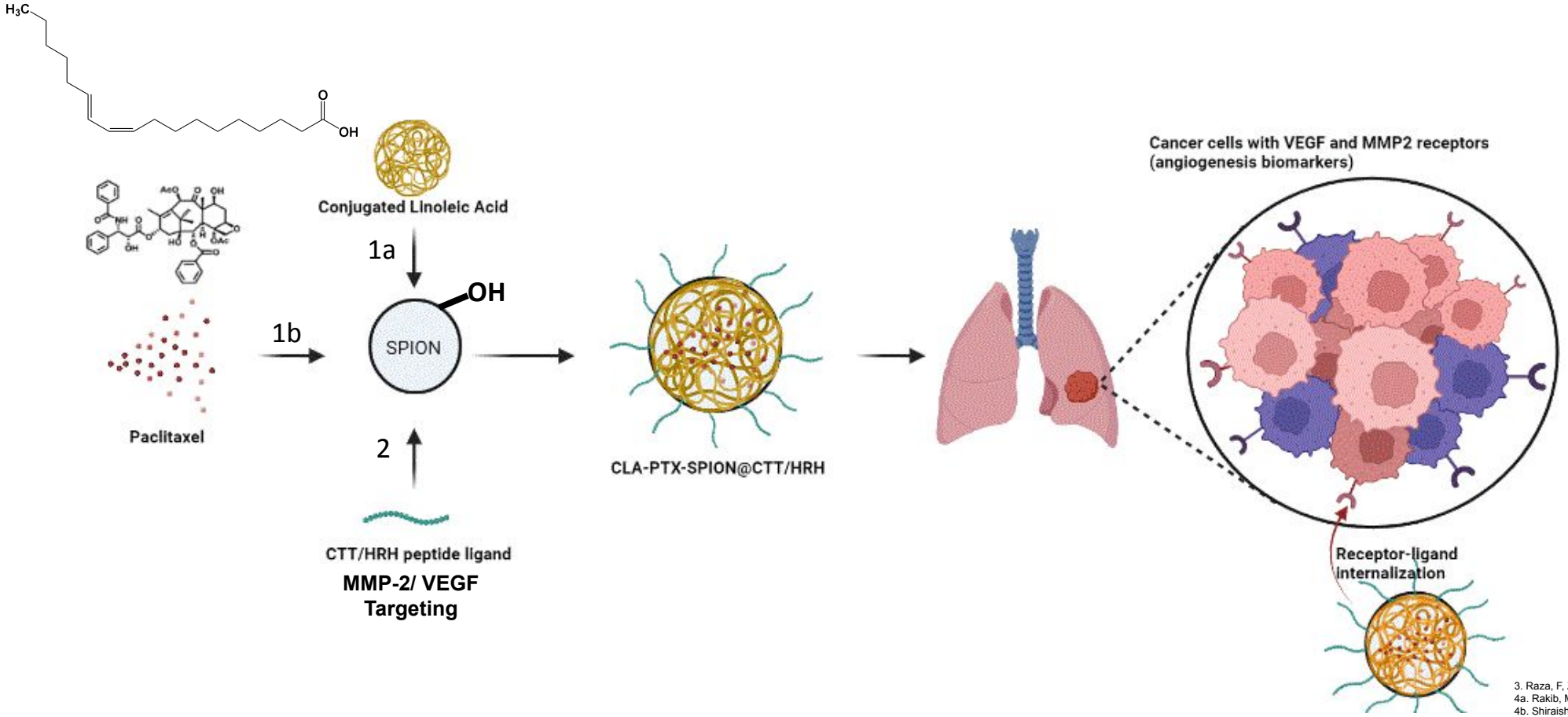


Relationship between physicochemical properties of superparamagnetic iron oxide nanoparticles (SPIONs) with bio- nano interactions and pharmacokinetic descriptors[2].

2. *Laurent S, Saei A, et al. 2014. Expert Opinion on Drug Delivery 29(9):1-22*

How have we exploited these properties to design novel Nanosystem A?

- Four primary components will be used for the design and development of these nanosystems, viz.
- (a) an approved chemotherapy drug for NSCLC with rationale for nanoformulation[3]
- (b) naturally derived biomolecules with evidenced based anti-cancer activity[4a-e]
- (c) established Vascular endothelial growth factor (VEGF) or matrix metalloproteinase (MMP2) targeting short peptides and
- (d) superparamagnetic iron oxide nanoparticles (SPIONS) with established biocompatibility and methods that modulate size, morphology and surface chemistry.

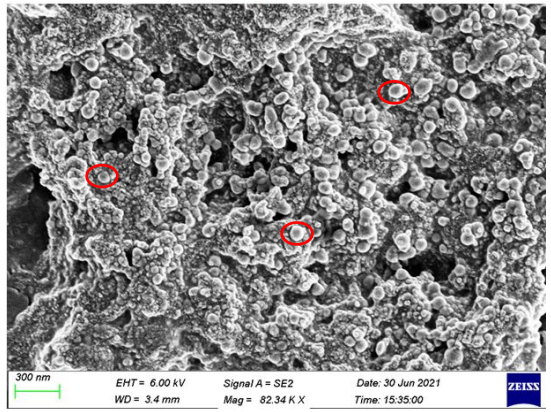


3. Raza, F, Zafar, H et al. Mater. Adv., 2022, 3, 2268–2290
4a. Rakib, M.A.; Lee, W.S.; et al. Med. 2013, 2013, 429393.
4b. Shiraishi, R.; Iwakiri, R.; et al. Gastroenterol. 2010, 45, 625–635.
4c. Ha, Y.L.; Storkson, J.; Pariza, M.W. Cancer Res. 1990, 50, 1097–1101.
4d. Moreira, T.G.; Horta, L.S.; et al. Mucosal Immunol. 2019, 12, 188–199
4e. Ochoa, J.J.; Farquharson, et al. Carcinogenesis 2004, 25,1185–1191.

Novel drug-loaded conjugated linoleic acid (CLA) targeted therapeutic nanosystems for Non-Small Cell Lung Carcinoma

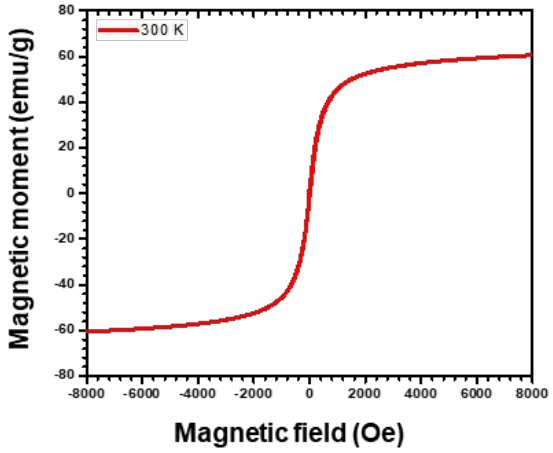
- Synthesis, physicochemical characterization, and *in vitro* evaluation of paclitaxel-loaded, CLA-coated SPIONs.

SEM: CLA-coated PTX-SPIONs

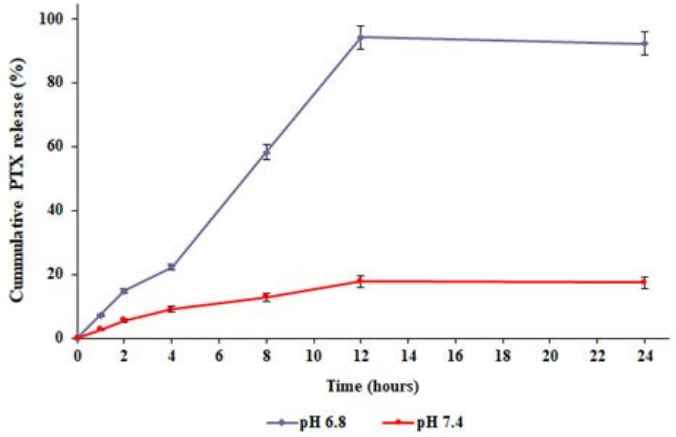


- Average particle size: 96.5 ± 0.6 nm
- Zeta potential: -27.3 ± 1.9 mV.
- PTX adsorption efficiency: 98.5%; drug loading capacity: 9.8%.

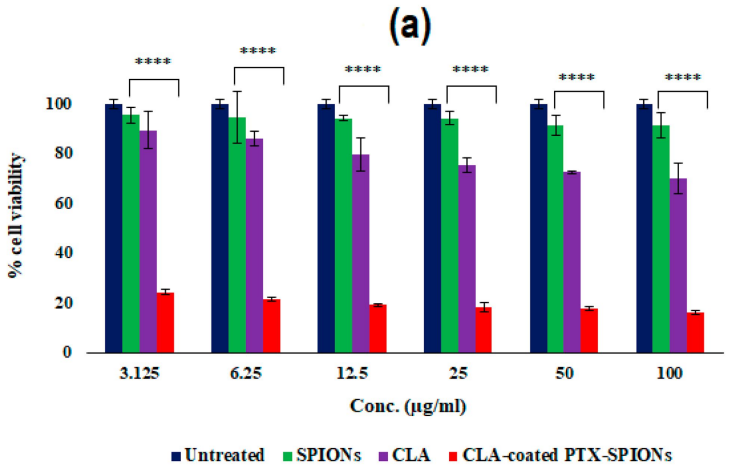
Magnetic properties

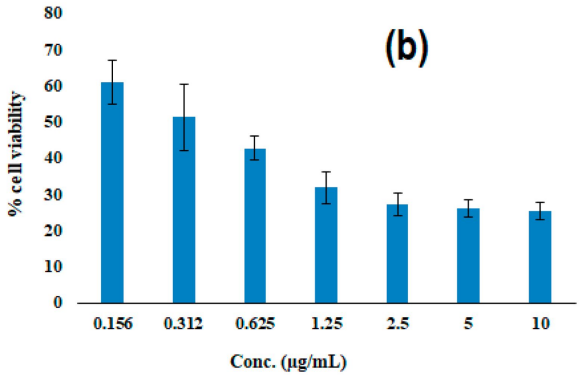


***In vitro* PTX release profiles**



% Cell viability of lung adenocarcinoma cell line (A549)

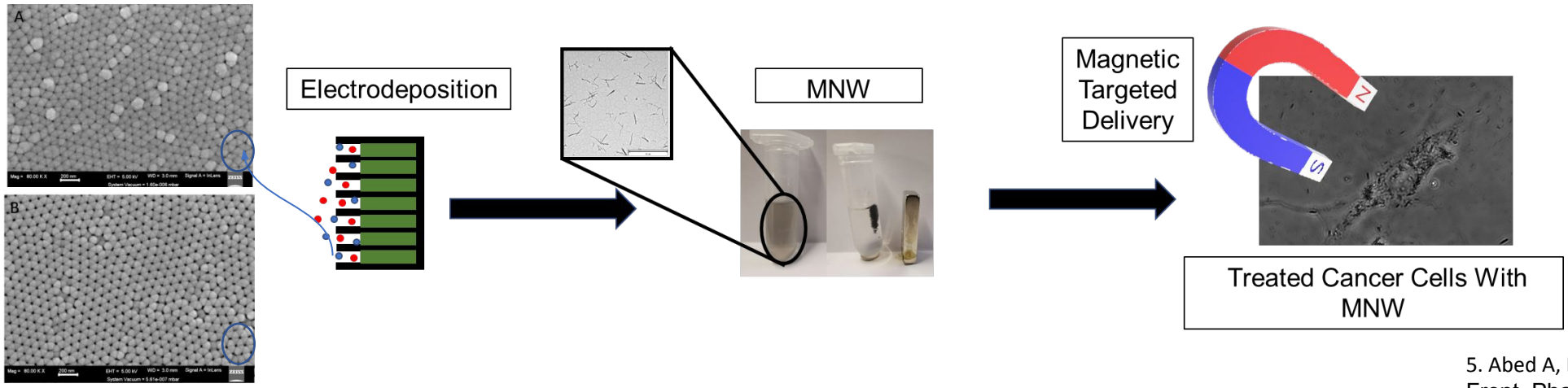




Ngema et al. Pharmaceutics. 2022;14(4):829.

How have we utilised similar physio-chemical properties to design Nanosystem B?

- Aim: To develop a magnetically targeted delivery platform composed of iron (Fe)/platinum (Pt) composite nanowires (NWs), combining the ferromagnetic behaviour of Fe with the cytotoxic activity of Pt against Testicular Cancer (TC) cells
- Fe NW have good magnetic properties and Pt NPs have known cytotoxic activity against many types of cancerous cells[5].

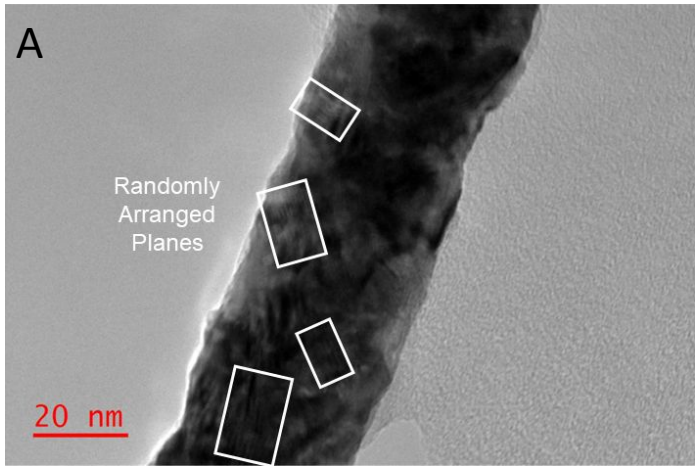


5. Abed A, Derakhshan M, et al. Front. Pharmacol. 2022;13

Design, synthesis, and *in vitro* study of magnetic nanowires in testicular cancer treatment

Preliminary

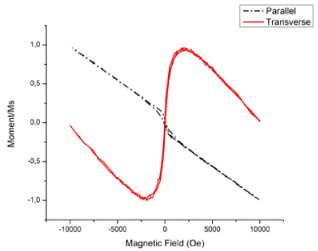
Pt NWs (polycrystalline)

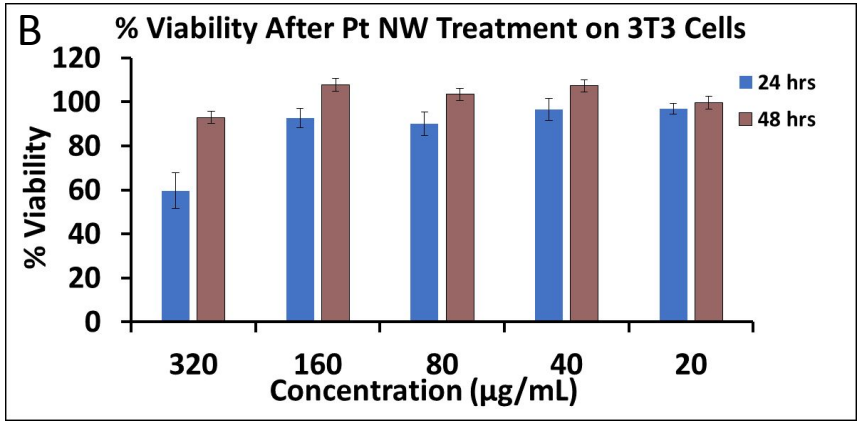


HRTEM image

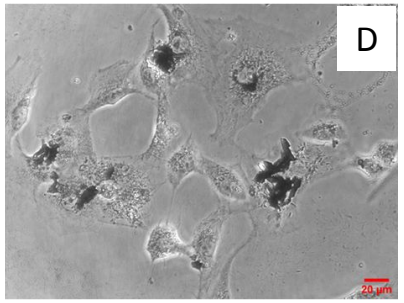
- Zeta potential: -22.3 ± 1.1 mV
- Average length: 2.2 ± 1.2 µm.
- Average diameter: 39 ± 2.0 nm

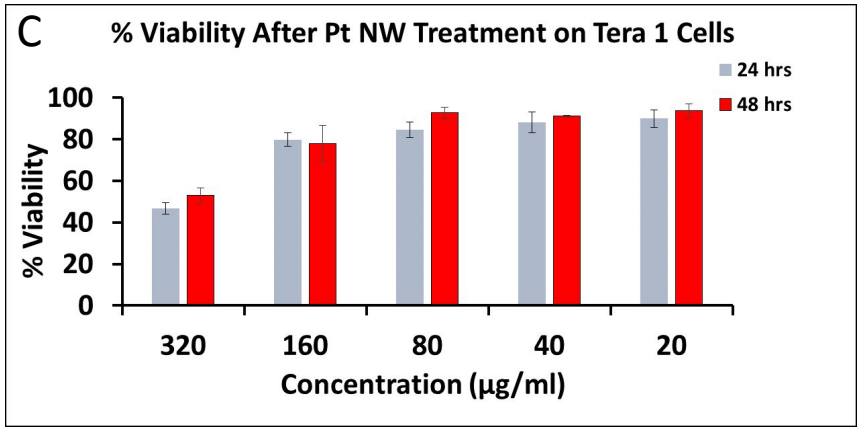
Magnetic properties



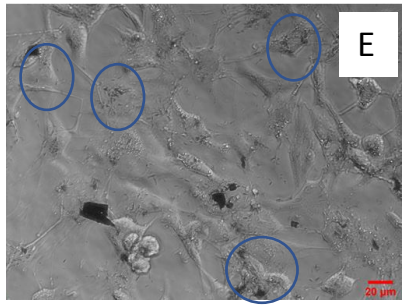


Phase contrast image 3T3 48hr





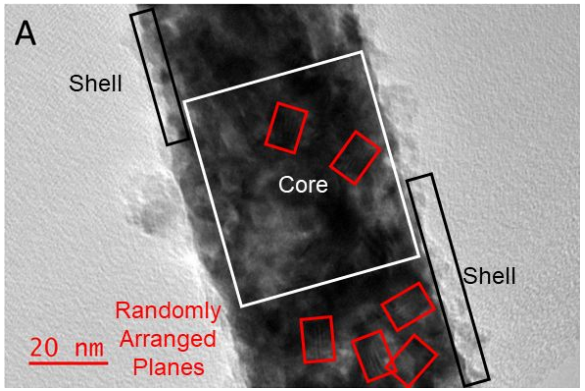
Phase contrast image Tera-1 48hr

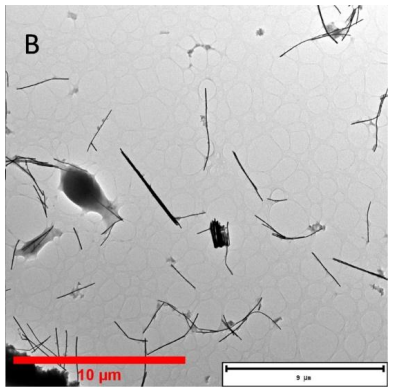


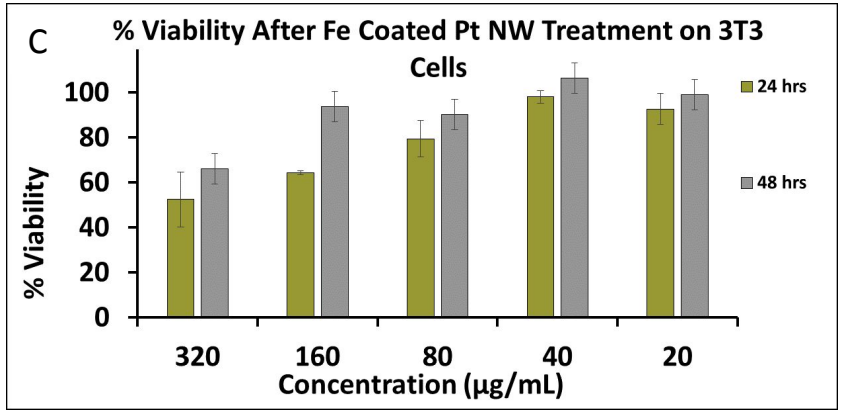
Development of Fe/Pt composite NWs to enable multifunctionality

Preliminary

Fe coated Pt NWs (polycrystalline)

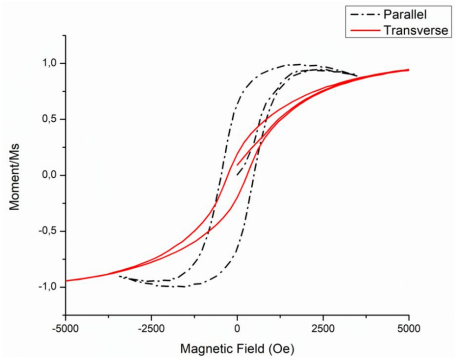


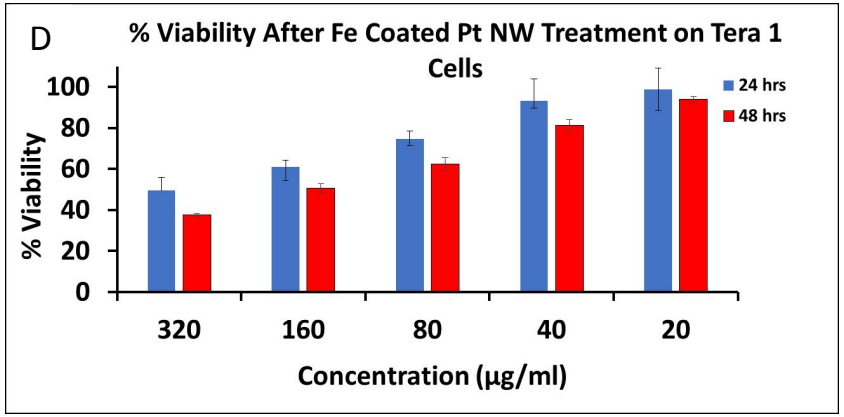




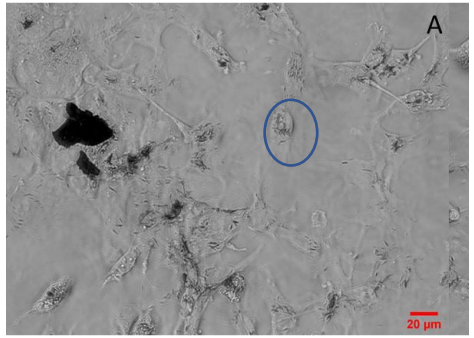
- Zeta potential: -34.6 ± 1.1 mV
- Average length: 2.2 µm.
- Average diameter: 54 ± 4.0 nm

Magnetic properties





Phase contrast image (Tera-1 48 hrs)



Conclusions and future perspectives

Parameter	Nanosystem A	Nanosystem B: Fe coated Pt NWs
Size	Clode to desired size (<100 nm).	Fitted within desired dimensions (2.2 μm (L) 54 nm (d).
Charge	Displayed zeta potential of -31.8±0.5 and -30.4±2.3 for minimal toxicity to cells.	Displayed zeta potential of -34.6±1.1 mV for good colloidal stability.
Shape	Spherical; non coated particles where cytocompatibile.	Elongated, good aspect ratio (d:l) for cellular uptake.
Coating	Improved overall surface charge- biocompatibility and allowed for drug loading..	PtNWs coated with Fe enable magnetic properties towards Magnetic Targeted Delivery.
Surface	Enabled coating and will bestow future functionalisation with homing peptides.	-
Core	Magnetic properties confirmed but future work to study its impact and or application.	Developed **Fe coated Pt NWs** Nanocomposite platform for potential increased cytotoxicity.

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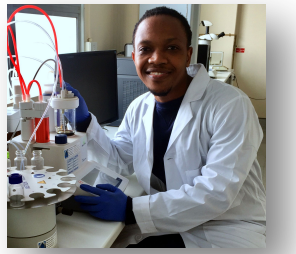
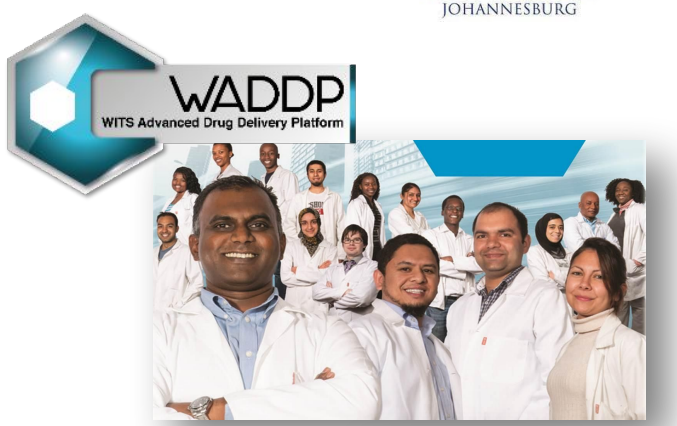
  - **Postdoctoral fellows**
    - Dr Samson Adeyemi
    - Dr Phil Ubanako
  - **Postgraduate Candidates**
    - Mr Lindokuhle Ngema
    - Mr Abu Bakr Nana





Late Mr T Marimuthu

THANK YO

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