

Aptamer and Nanotechnology- based Approaches for Active Targeted Delivery of Anti-Tuberculosis Drugs

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Outline

- Background: Challenges in the current TB treatment
- Proposed Solution: Nanomedicine
- Experimental Design
- Results
- Conclusions
- Acknowledgements

Background

TB epidemic presents a real threat to human kind!!!



- Infecting over 2M a year globally
- 2 billion people have latent TB
- 1 TB patient is dying every 20 seconds



TB patient

Aggravated by patient non-compliance

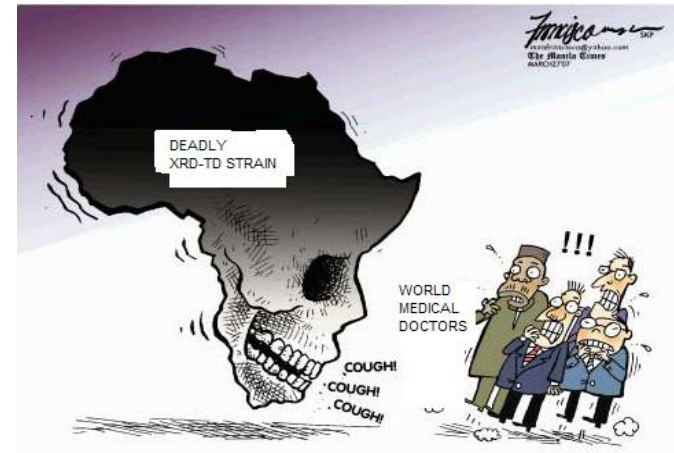
- *Lengthy Treatment*
- *Handful daily dose*
- *Toxic side effect*

HIV co-infection:

- *75% of TB patients are HIV positive in sub-Saharan Africa*



MDR/XDR-TB

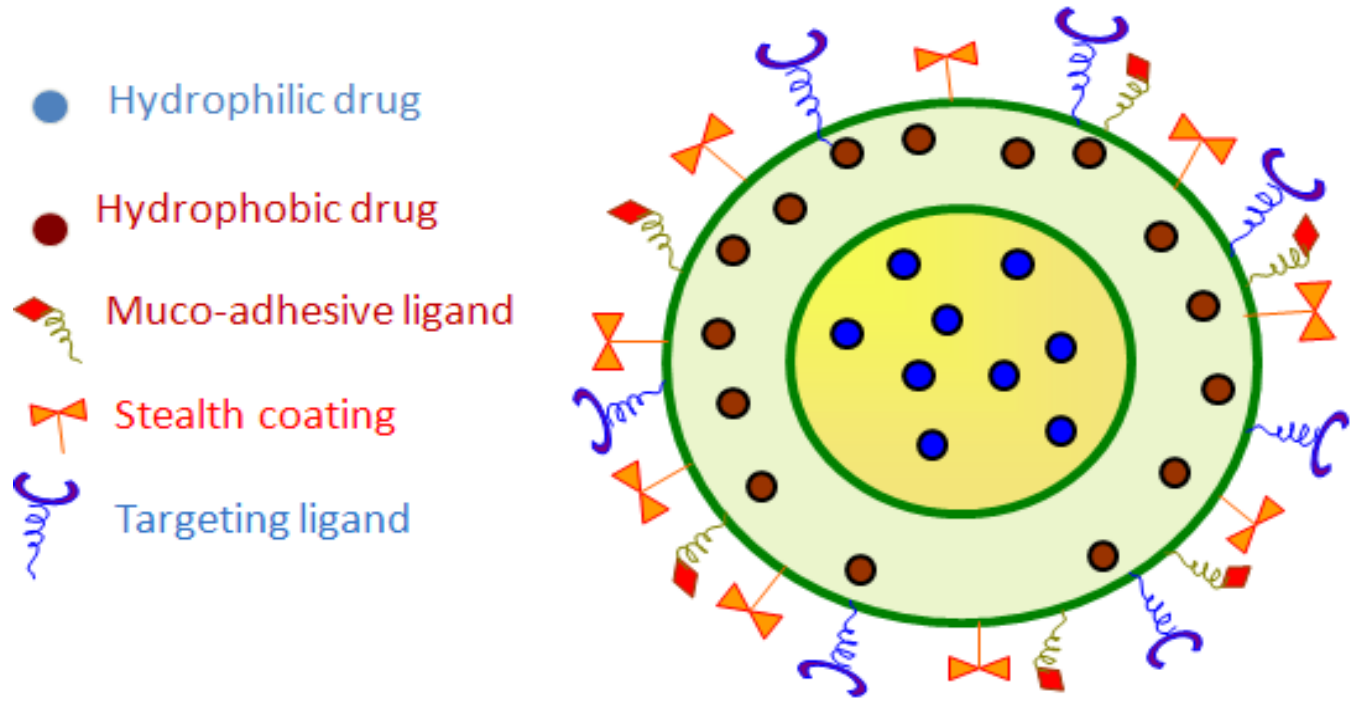


Strategy for improving TB therapy

- *Improvement of bioavailability*
 - By minimising the premature degradation of drug in the GIT
 - By releasing the drug in the blood stream in controlled and steady fashion
- *Enhance patients compliance*
 - By reducing dose and dose frequency (i.e. once a week dose)
 - By reducing treatment time
 - By reducing unpleasant side effects
- *Targeted Delivery*
 - Delivering the drug to the site of infection
- *All this may be achieved using Nanomedicine*

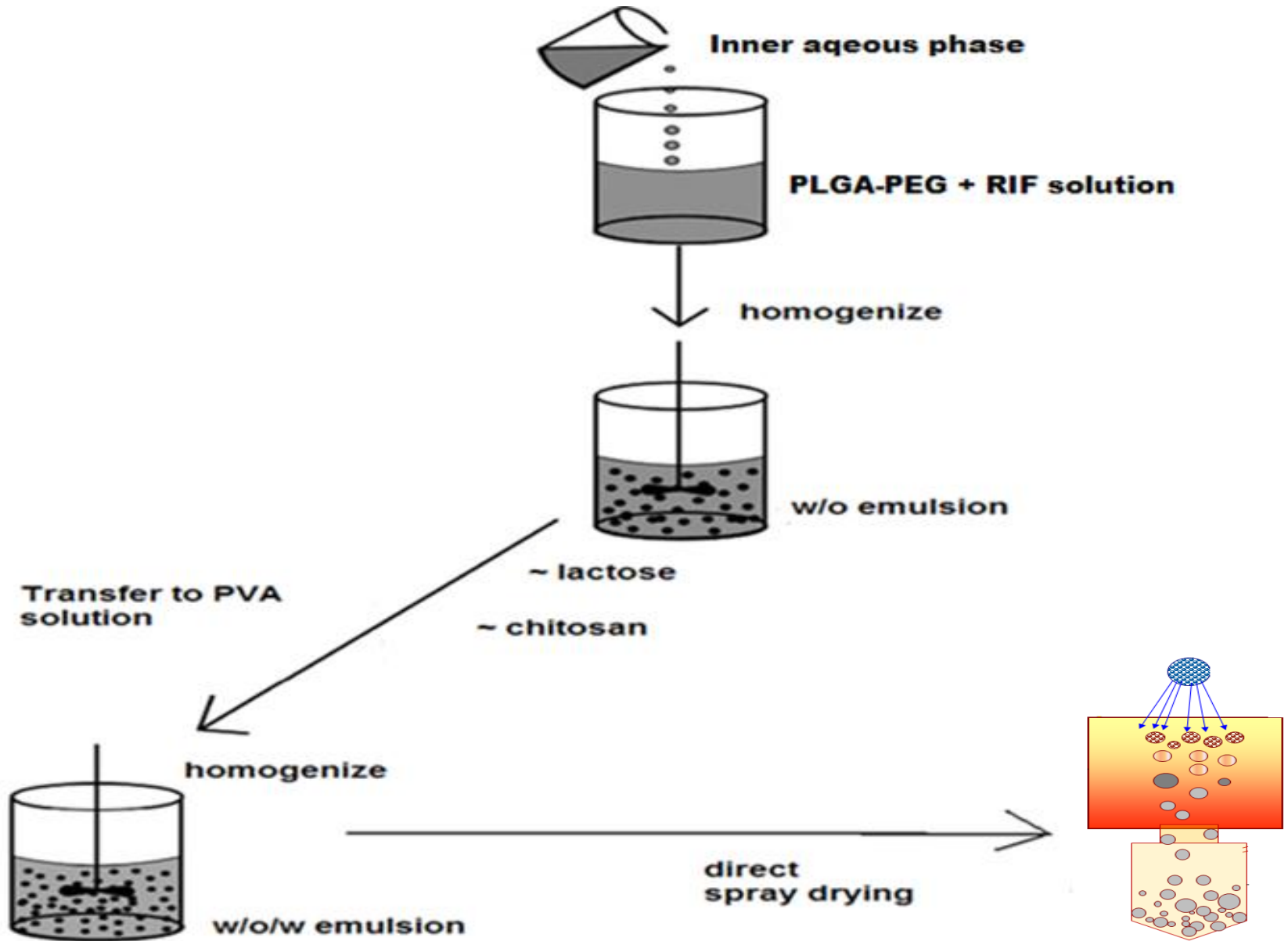
Proposed Solution

Encapsulation of ATD's into multifunctional polymeric nanoparticles

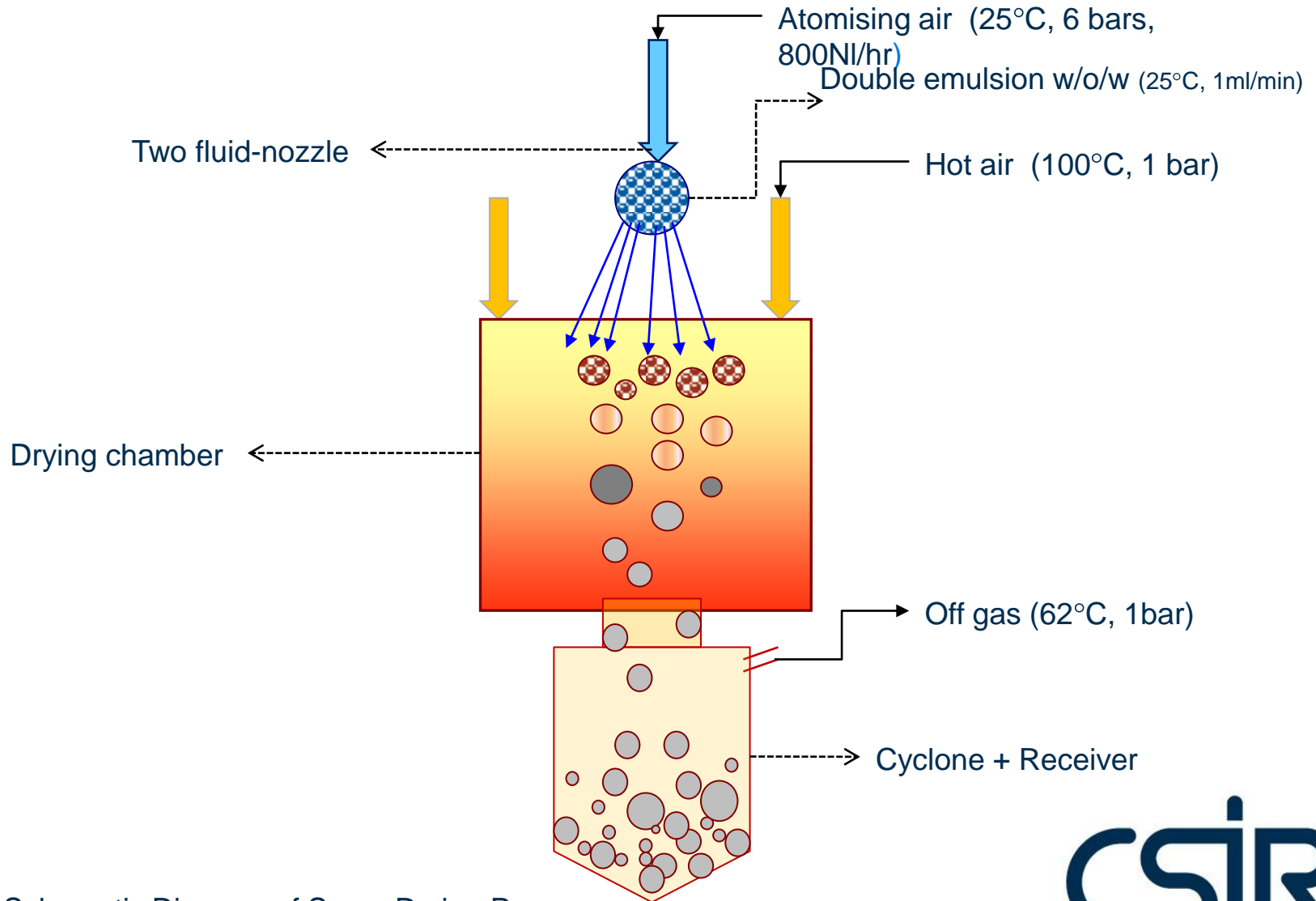


Schematic Diagram of Multifunctional Polymeric Nanocarrier

Manufacturing of nanoparticles

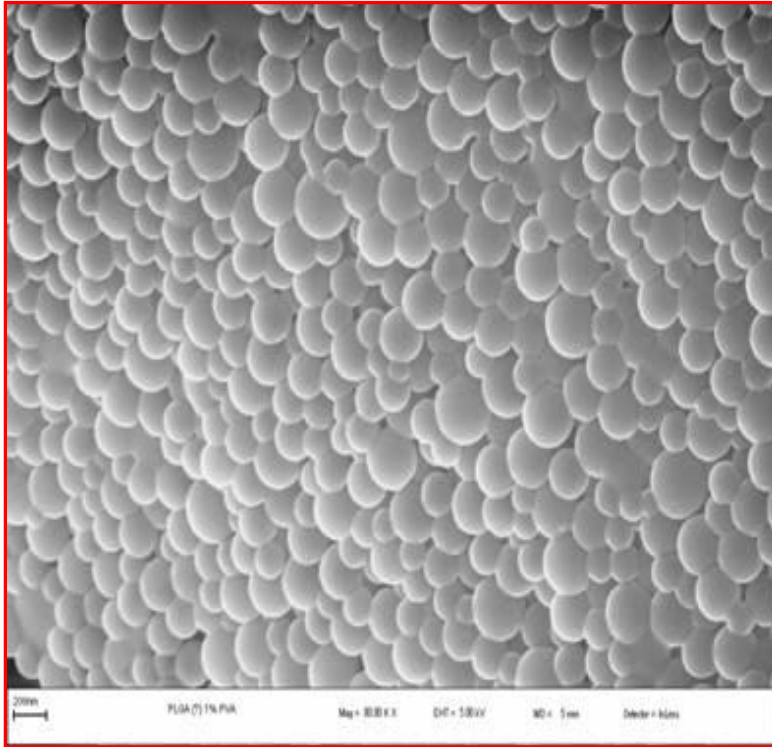


Spray Drying of Nanoparticles



Schematic Diagram of Spray Drying Process

Results: Characterisation of nanoparticles

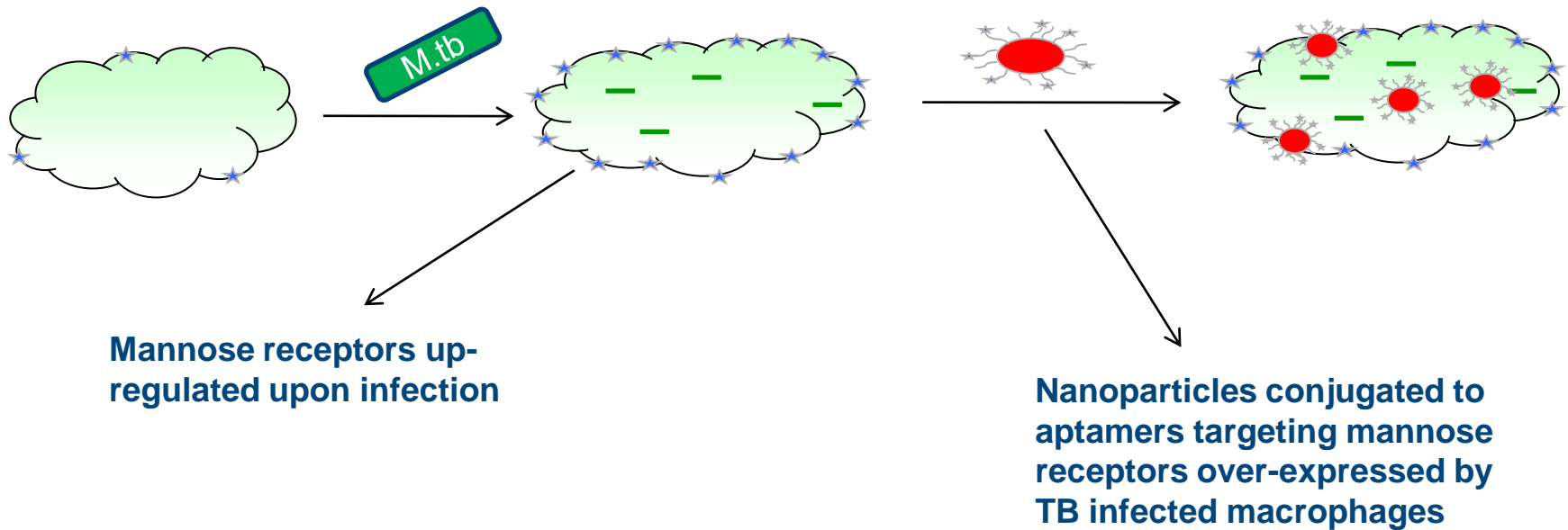


Characteristics	Values
Particle Size (nm)	241 ± 22
Size Distribution (PDI)	0.15 ± 0.05
Zeta Potential (Surface Charge) (mV)	20 ± 3
Encapsulation Efficiency (%)	70 ± 5
Drug Loading (%)	20 ± 3

SEM Image of PLGA NPs

Table of Results

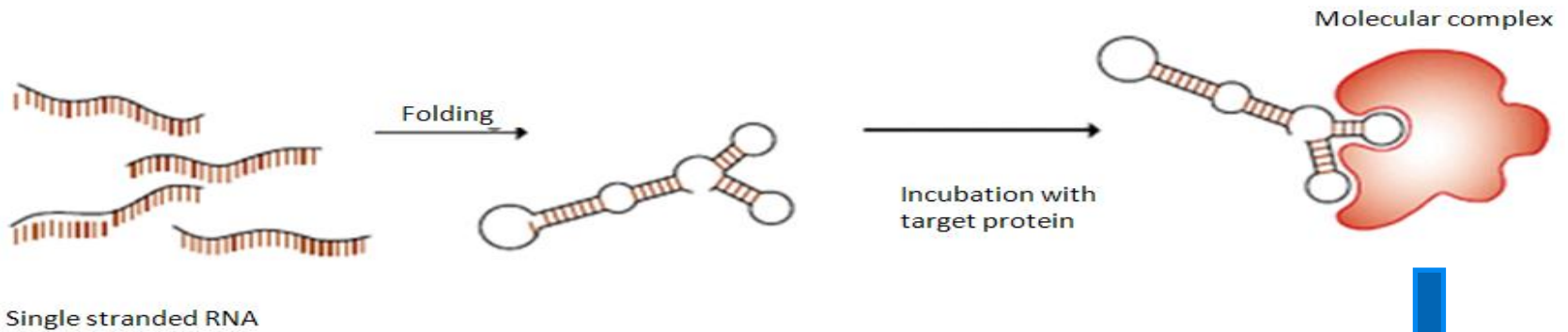
Targeting nanoencapsulated anti-TB drugs to sites of infection



Aptamers: RNA/DNA that bind to a specific target molecule

- Enhance drug efficiency at site of infection
- Reduce systemic toxicity

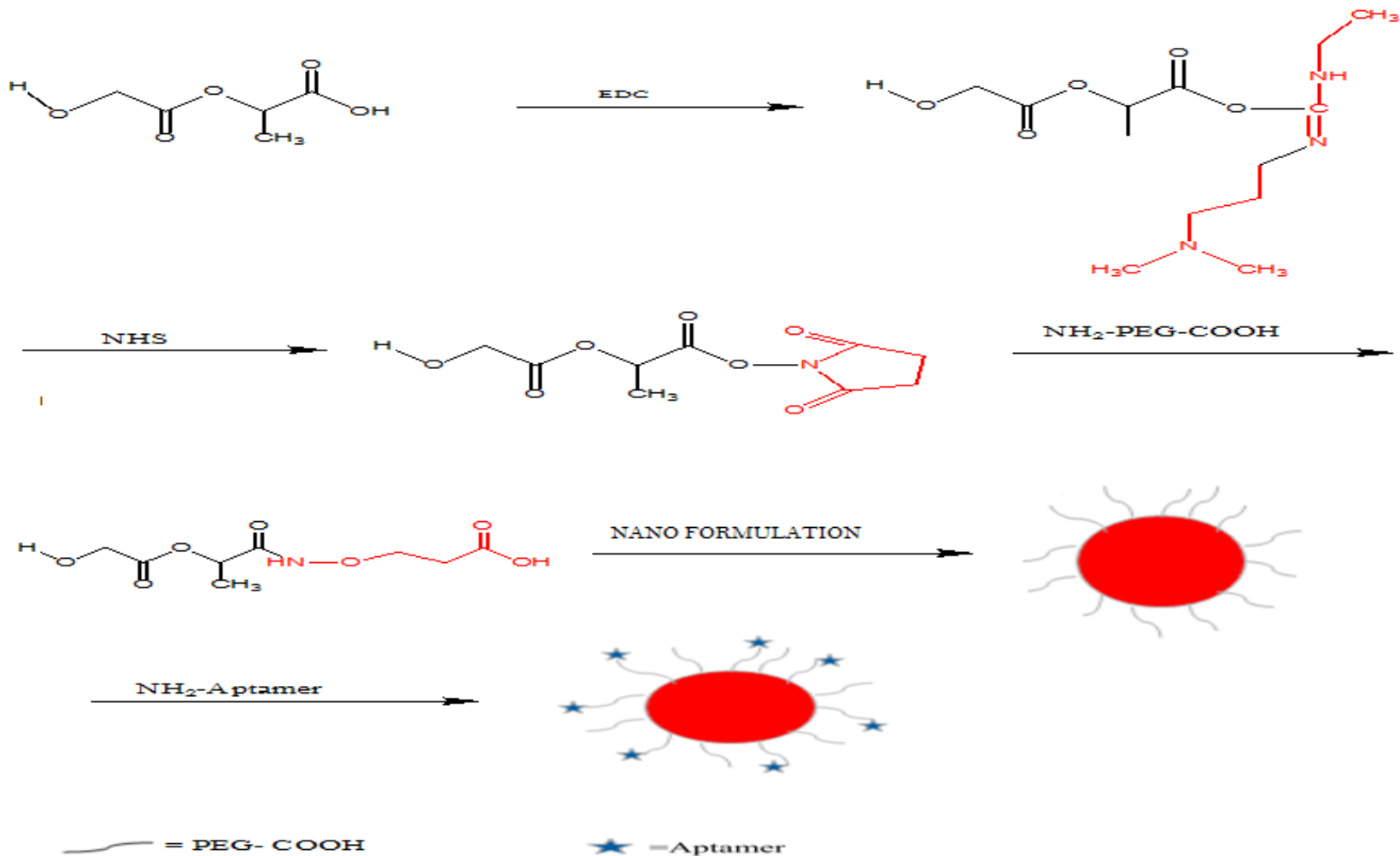
Aptamer Synthesis: SELEX Method



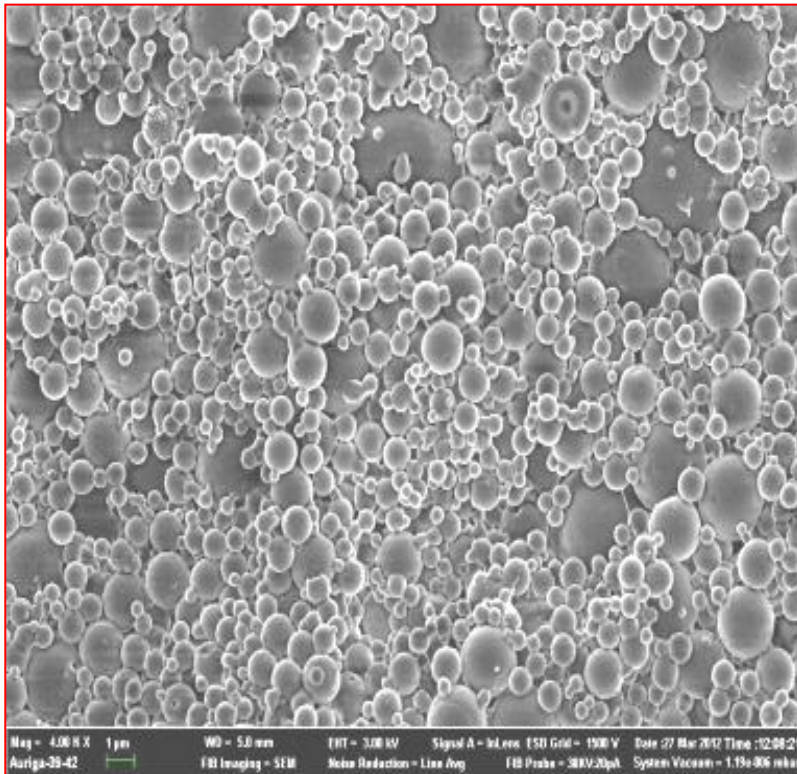
Partitioning with NanoSep
100kDa MWCO,
Selection of aptamers against
target receptor using size
exclusion

Test aptamer clones for
binding affinity on Biacore
biosensor

Conjugation of aptamers to nanoparticles



Results: Characterisation of aptamer-conjugated nanoparticles



SEM Image of PLGA-Apt NPs

Characteristics	Values
Particle Size (nm)	262 ± 28
Size Distribution (PDI)	0.12 ± 0.08
Zeta Potential (Surface Charge) (mV)	18 ± 2
Encapsulation Efficiency (%)	68 ± 4
Drug Loading (%)	20 ± 3

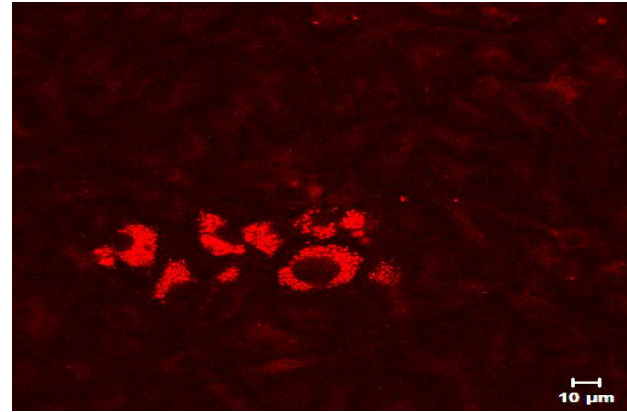
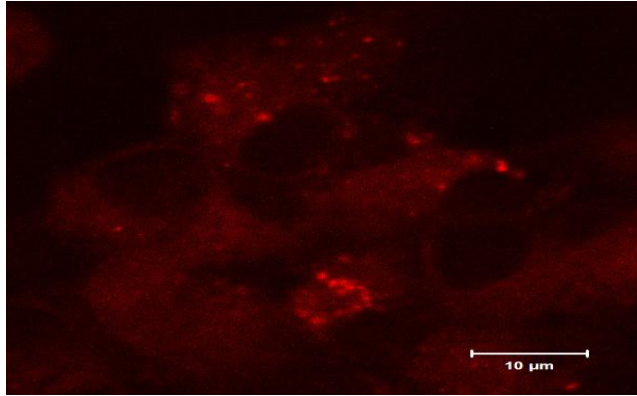
Table of results

Particle uptake: Confocal Microscopy

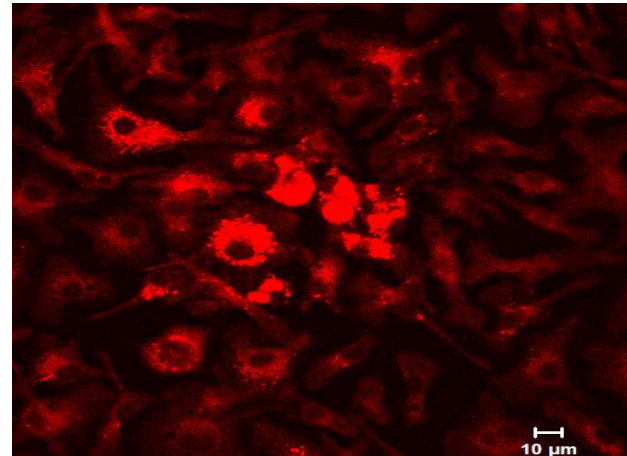
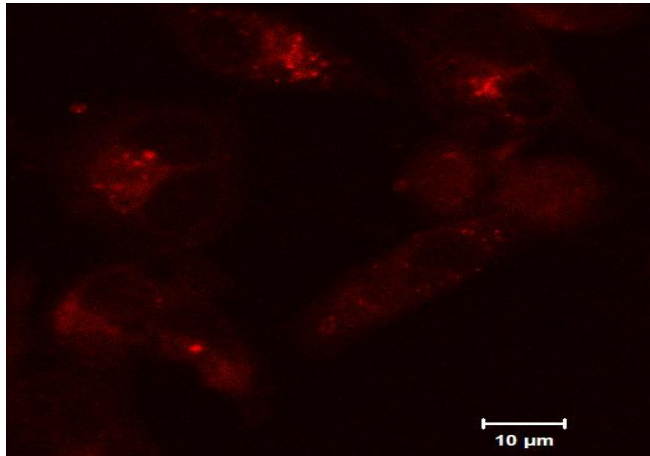
THP-1 cells

BM cells

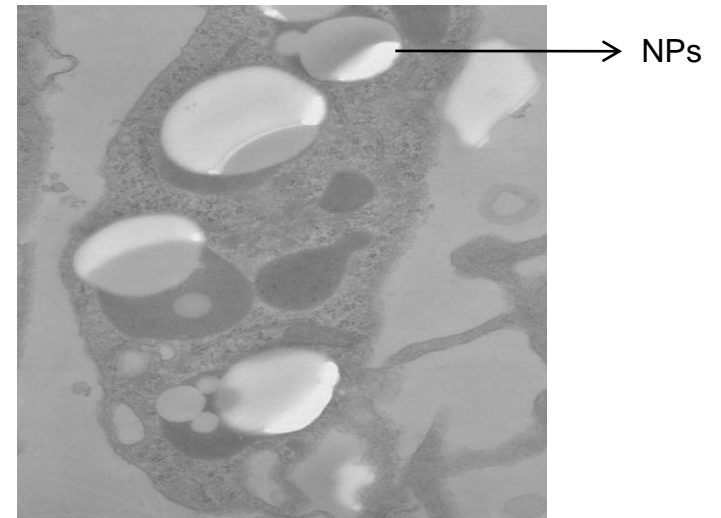
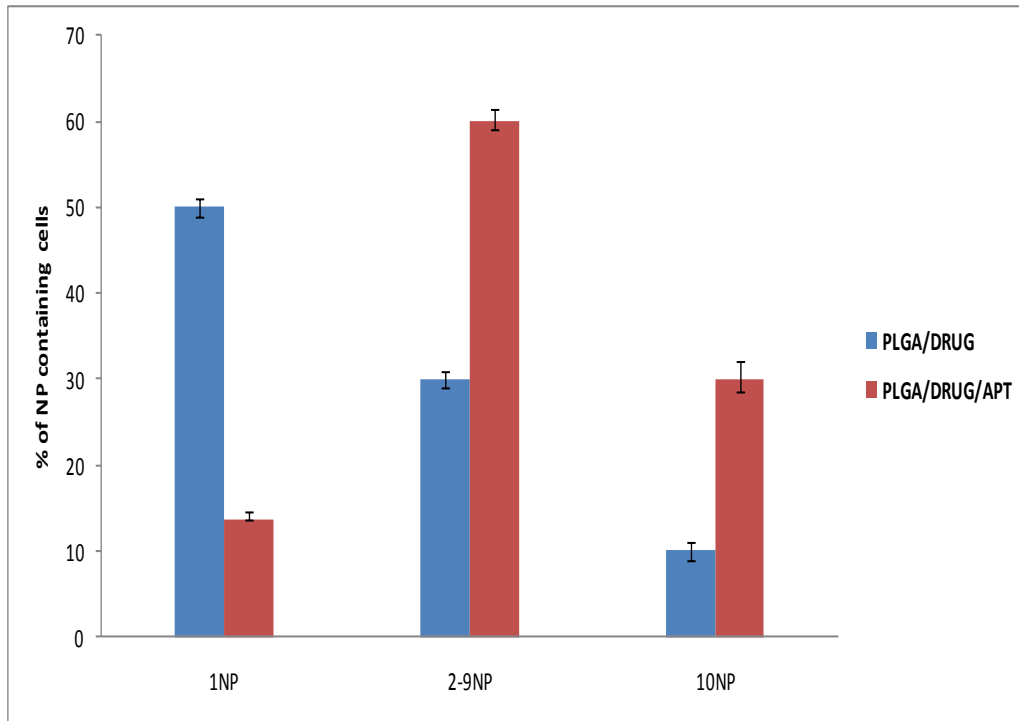
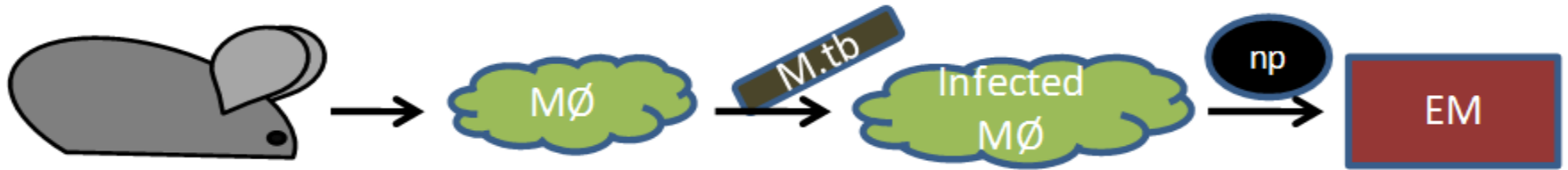
Rh-NPs



Rh-NPs-Apt



Particle Uptake: BM cells (Electron Microscopy)



TEM image of BM cells with NPs

Conclusions

- Formulation of multifunctional polymeric nanoparticles for encapsulation of ATDs with optimum physico-chemical properties has been achieved
- Aptamers (against mannose receptors) can assist uptake of nanoparticles in TB infected cells
- Delivery of nanoparticles to site of infection can be achieved via active targeting without compromising properties of nanoparticles

Acknowledgements

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- CSIR for the financial support and the infrastructure
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Thank you!