



# **Design and Development of Surface Modification and Synthesis Strategies to Reduce Toxicity of Nanoparticles**

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# Outline

- Determination surface modifiers and surface modification strategies
- Surface modification process and characterization of the nanoparticles
- Toxicity assesment
- Conclusions

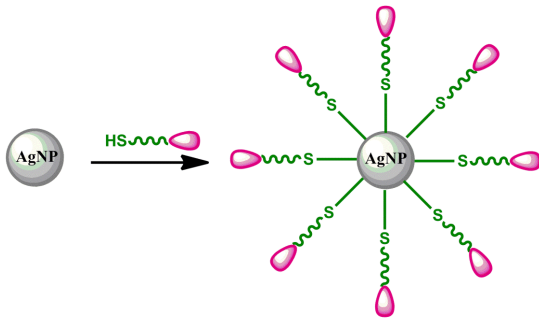
# Determination of The Best Surface Chemistry

The selection and design of the surface modifiers by considering

- Nontoxicity
- Stability
- Biocompatibility
- Cost and availability
- Compatibility with the physicochemical properties of the NMs and chemistry,

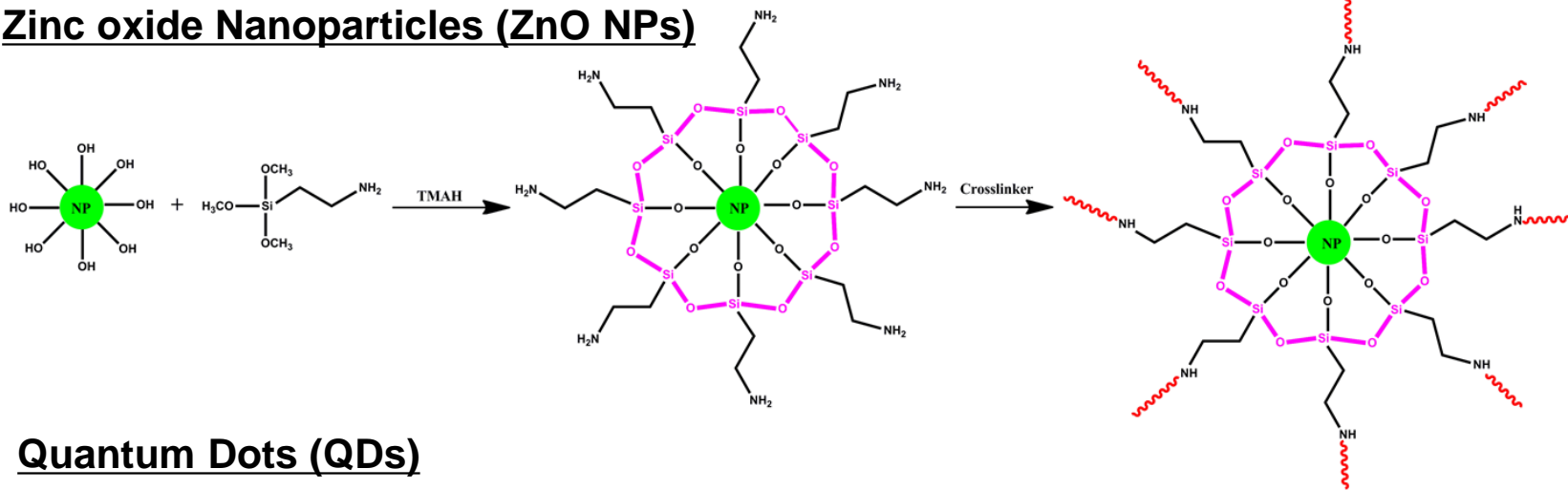
# Surface Modification Strategies

## Silver Nanoparticles (AgNPs)

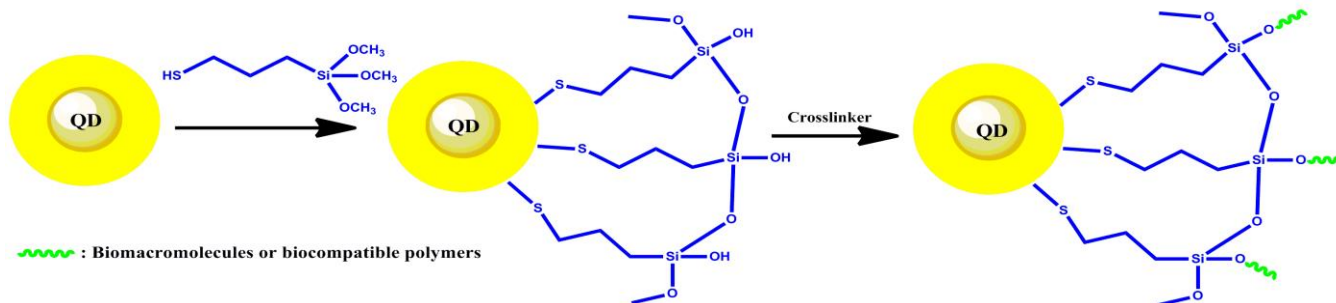


 SH : Thiolated biomolecules

## Zinc oxide Nanoparticles (ZnO NPs)

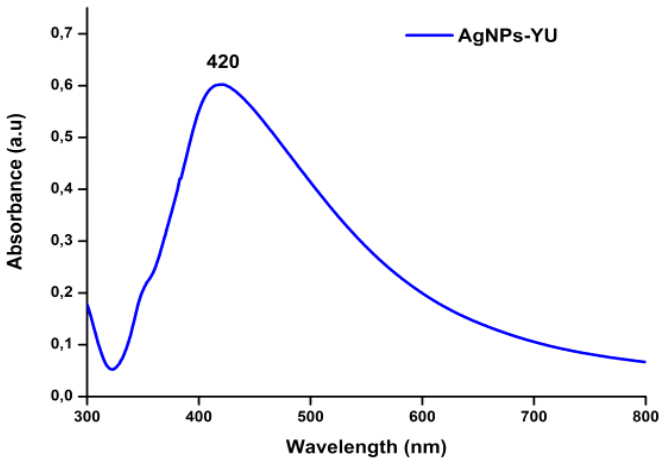


## Quantum Dots (QDs)

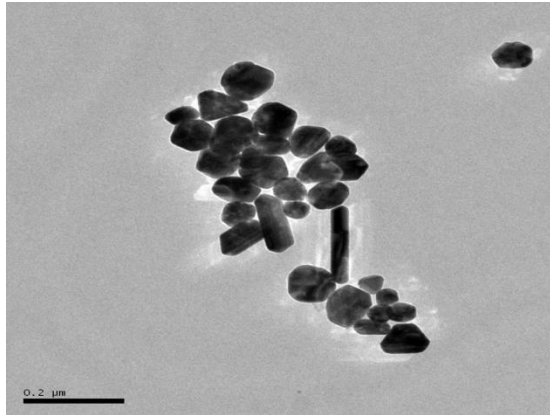


 : Biomacromolecules or biocompatible polymers

# Modification of AgNPs with thiolated carbohydrates and biomolecules

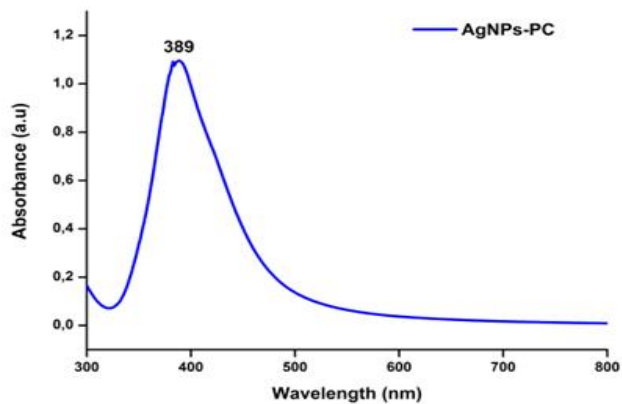


AgNPs synthesized in Yeditepe University

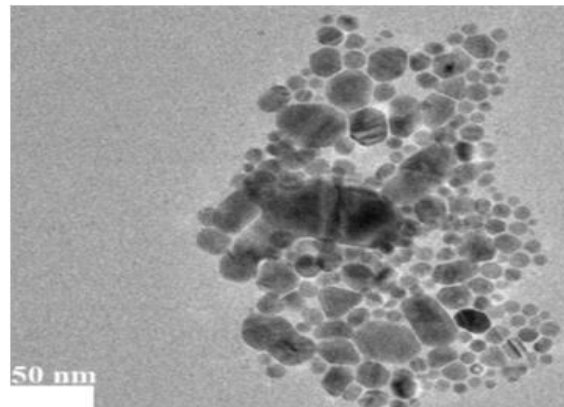


Selected Surface Modifiers;

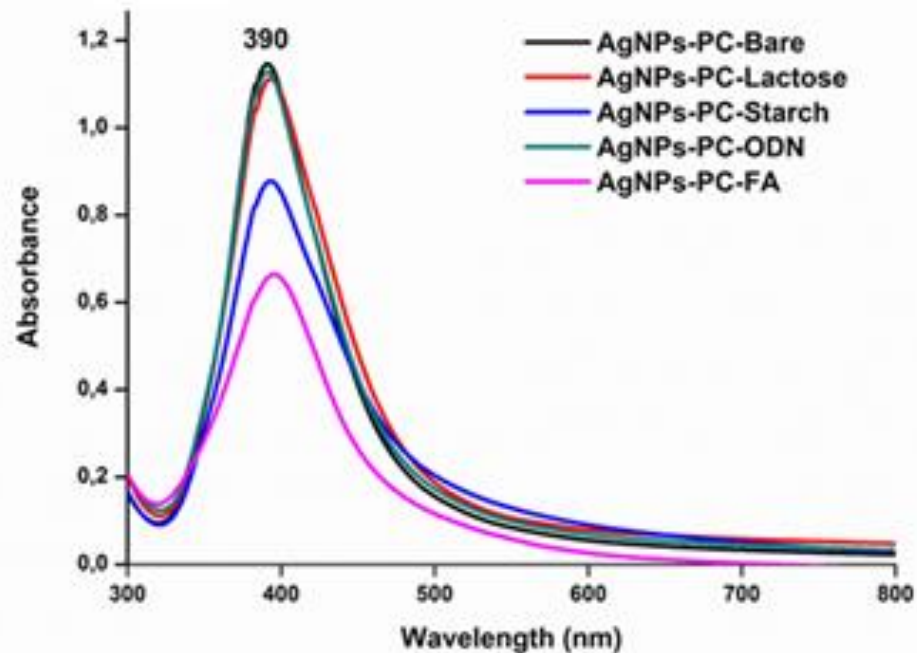
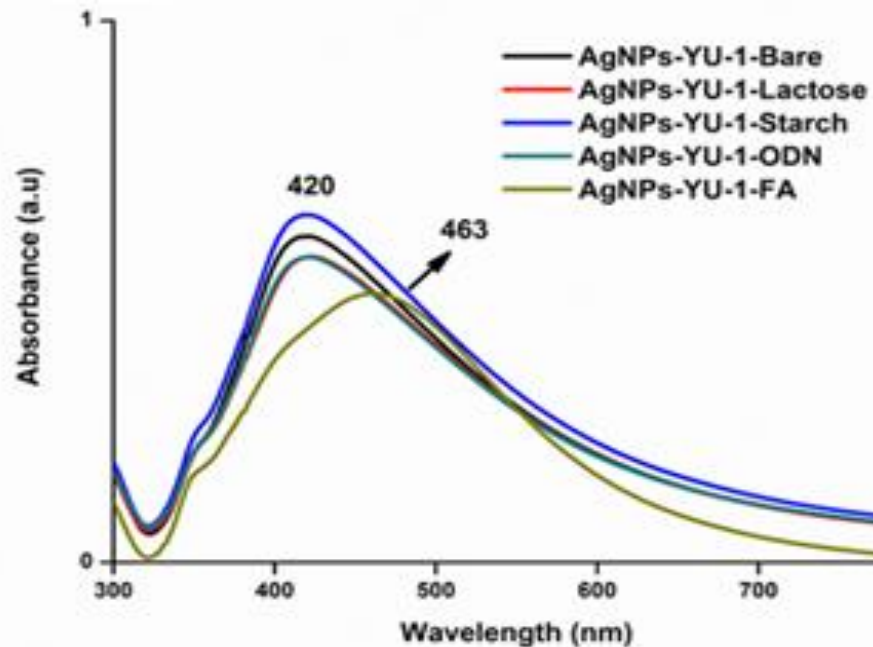
- Lactose
- Starch
- Oligonucleotide
- Folic acid



AgNPs obtained from PlasmaChem

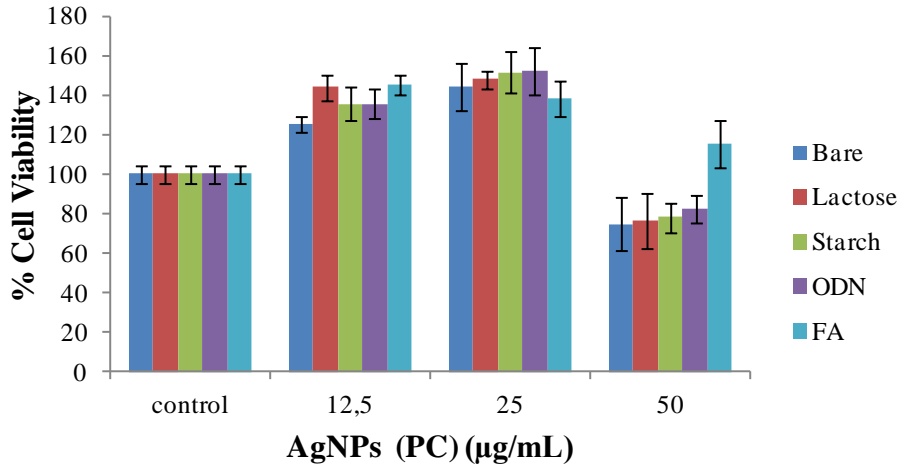


# Characterization of AgNPs with thiolated carbohydrates and biomolecules

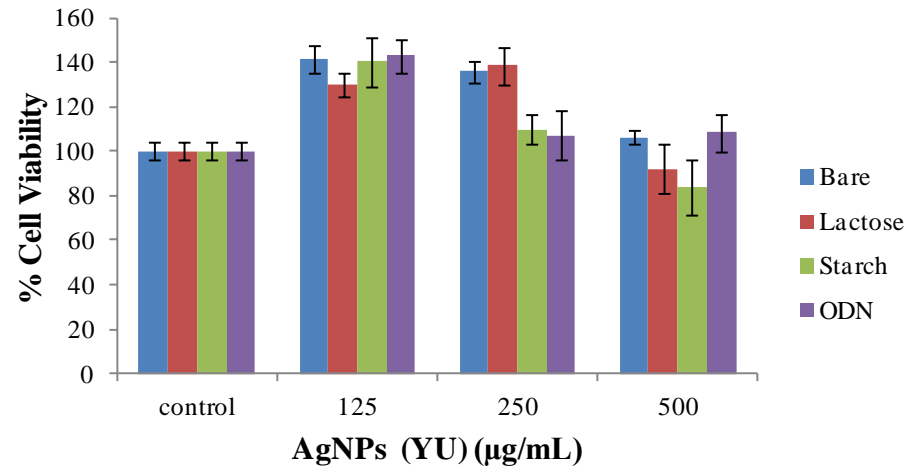


# Cytotoxicity of modified AgNPs

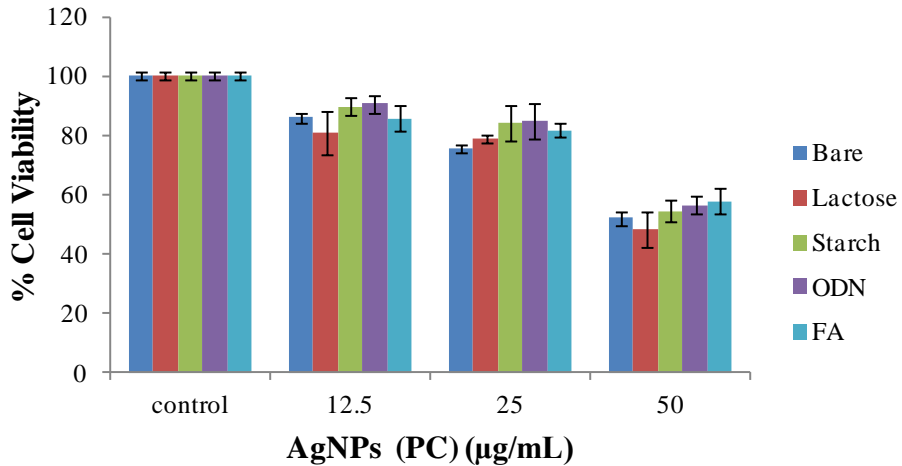
## HDF Cells



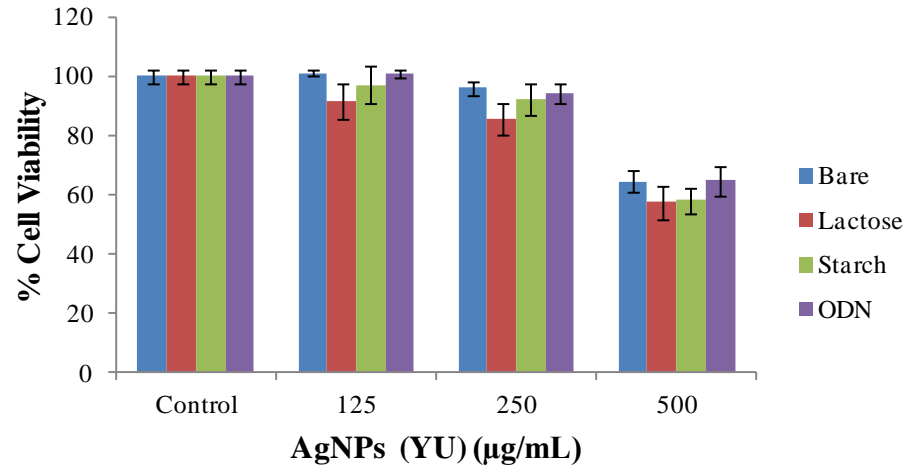
## HDF Cells



## A549 Cells



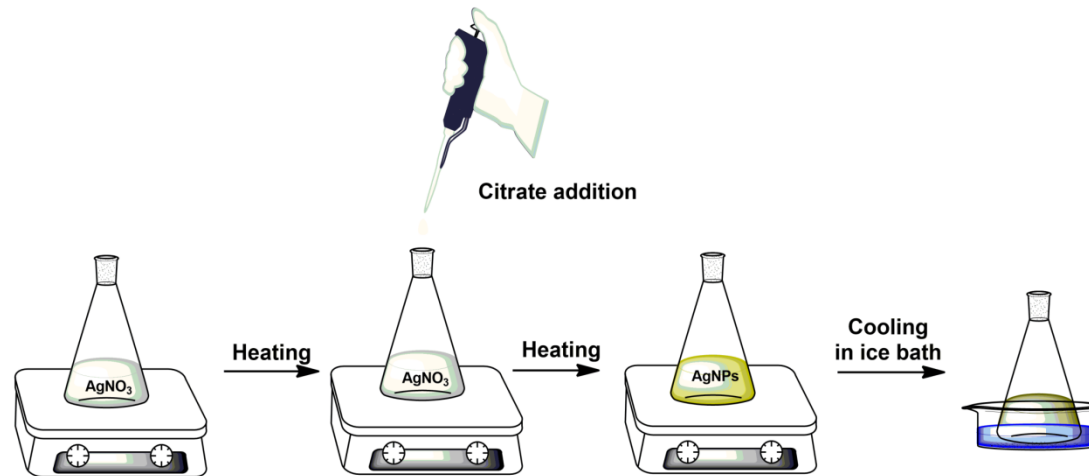
## A549 Cells



# A Safety by Design Approach for AgNPs

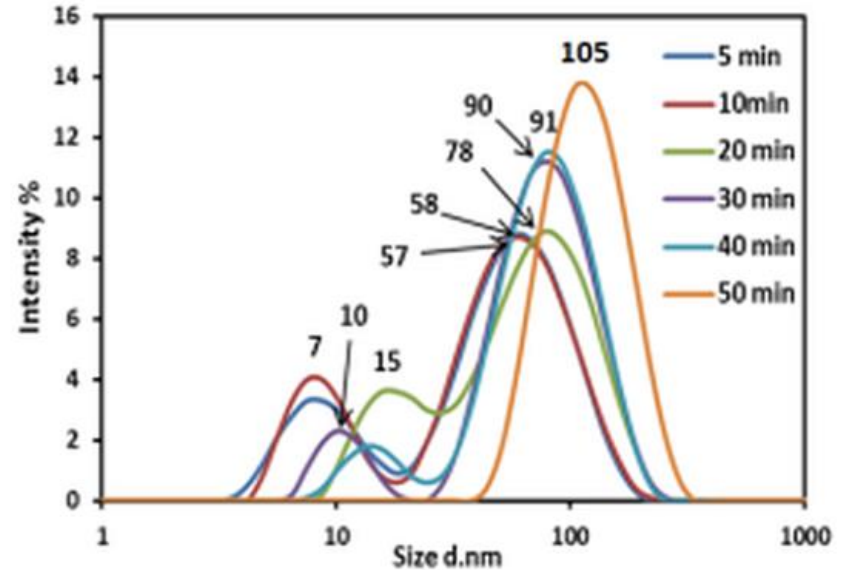
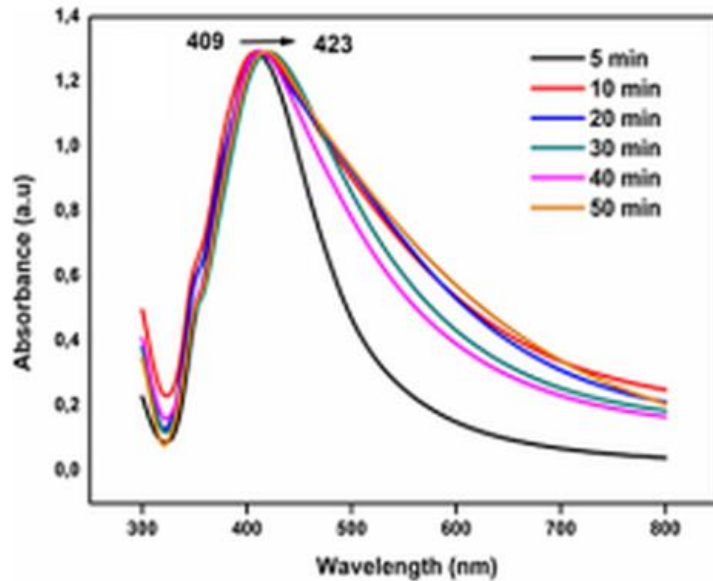
Modification the Lee and Meisel Method by varying;

- The reaction time
- The reducing agent concentration



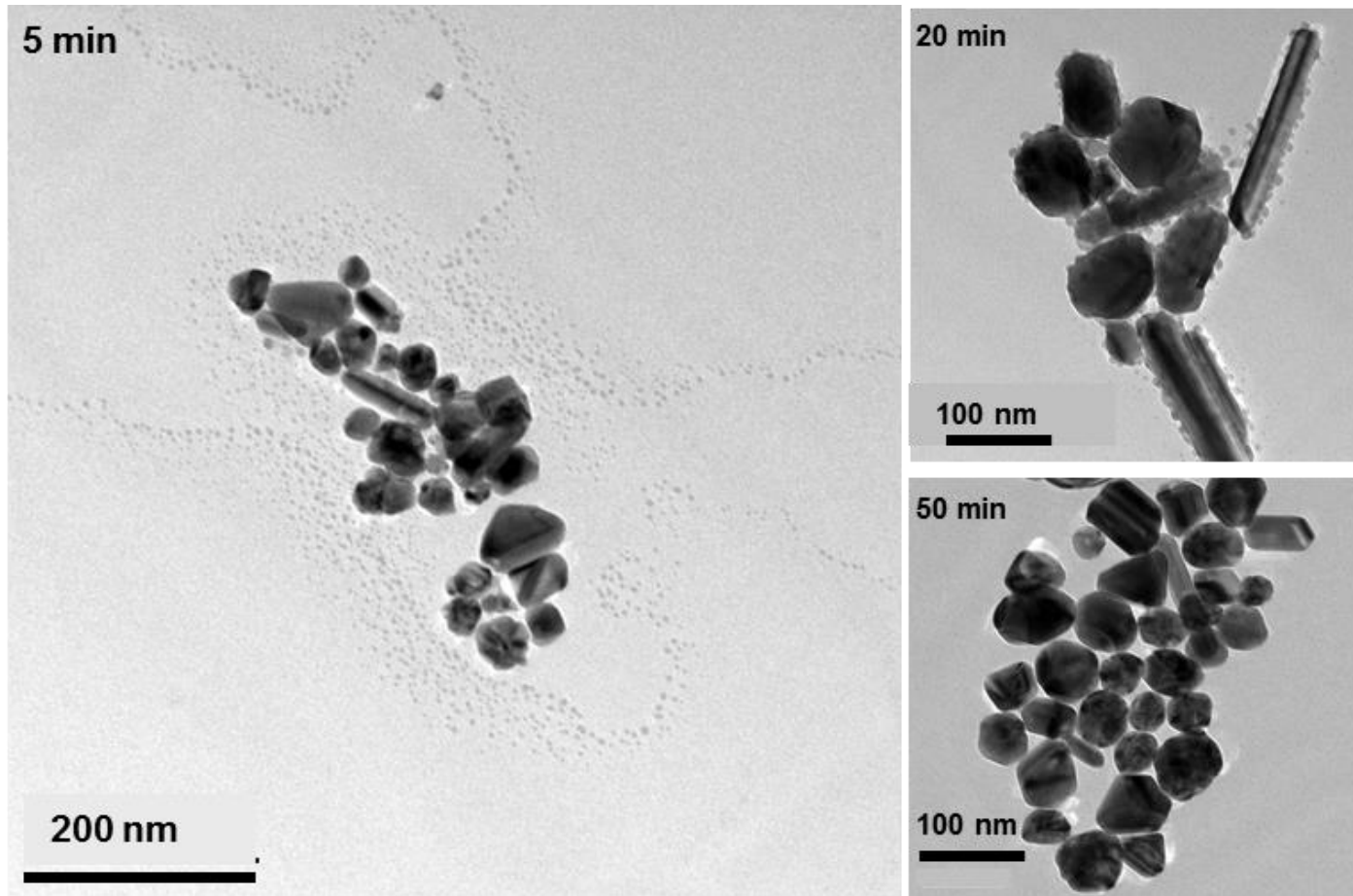


# Characterization of AgNPs synthesized by varying reaction time

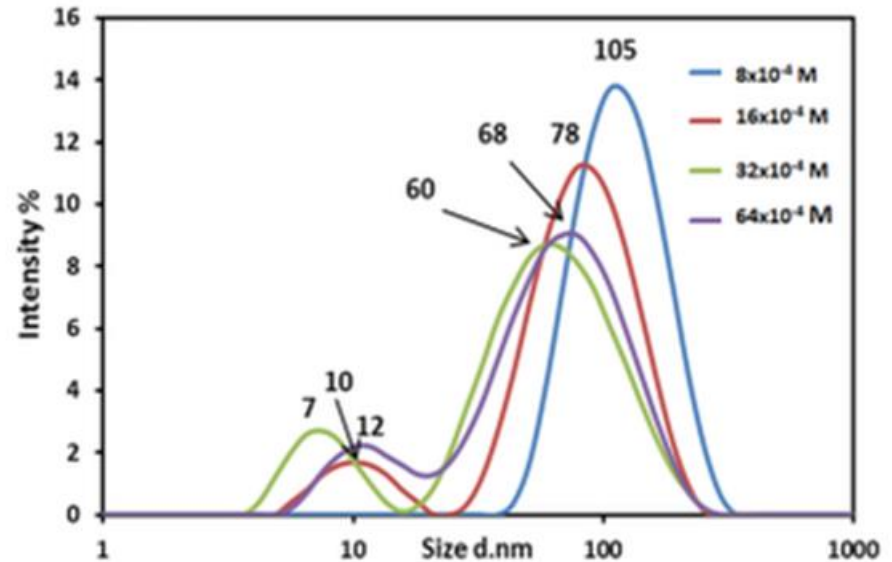
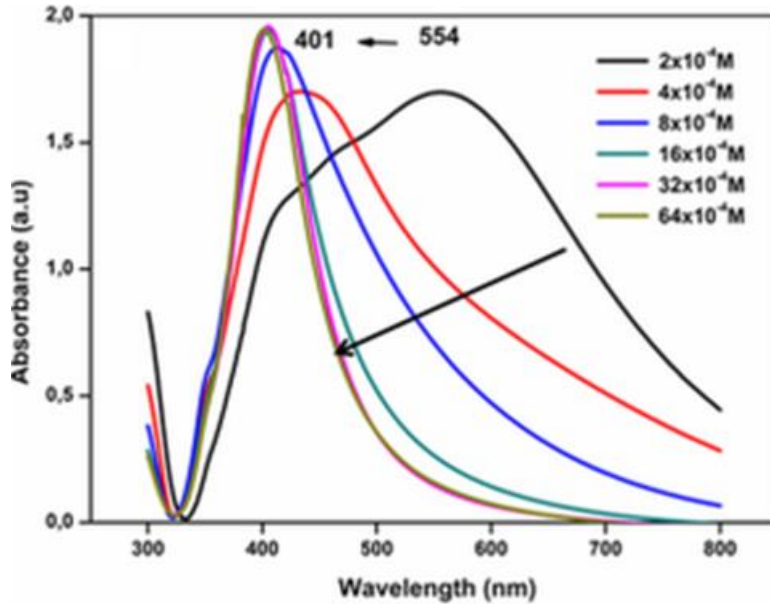


UV-Vis and DLS spectra of AgNPs prepared with increasing reaction time from 5 min to 50 min.

# Characterization of AgNPs synthesized by varying reaction time

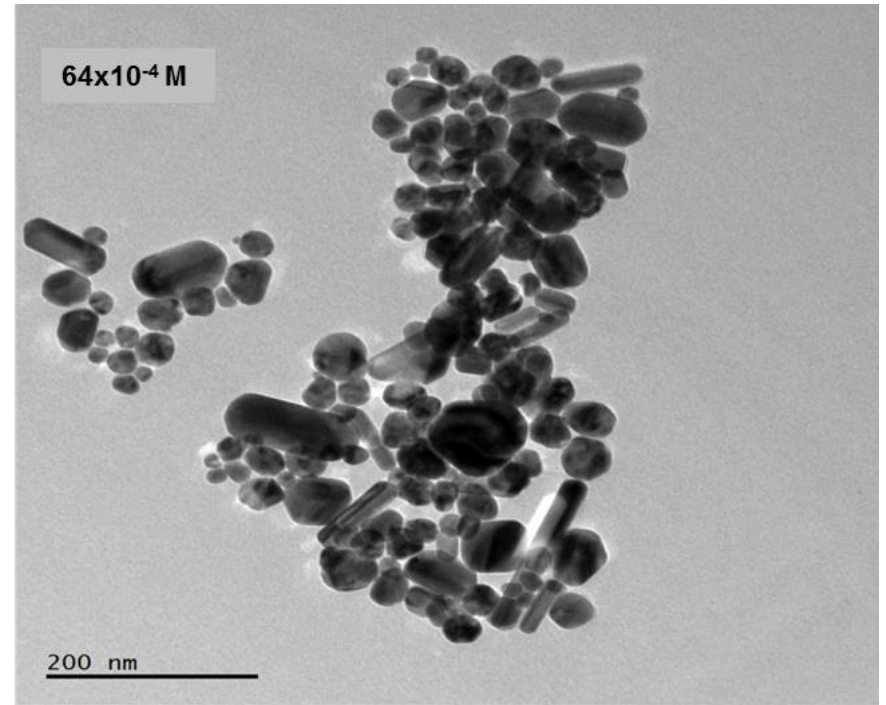
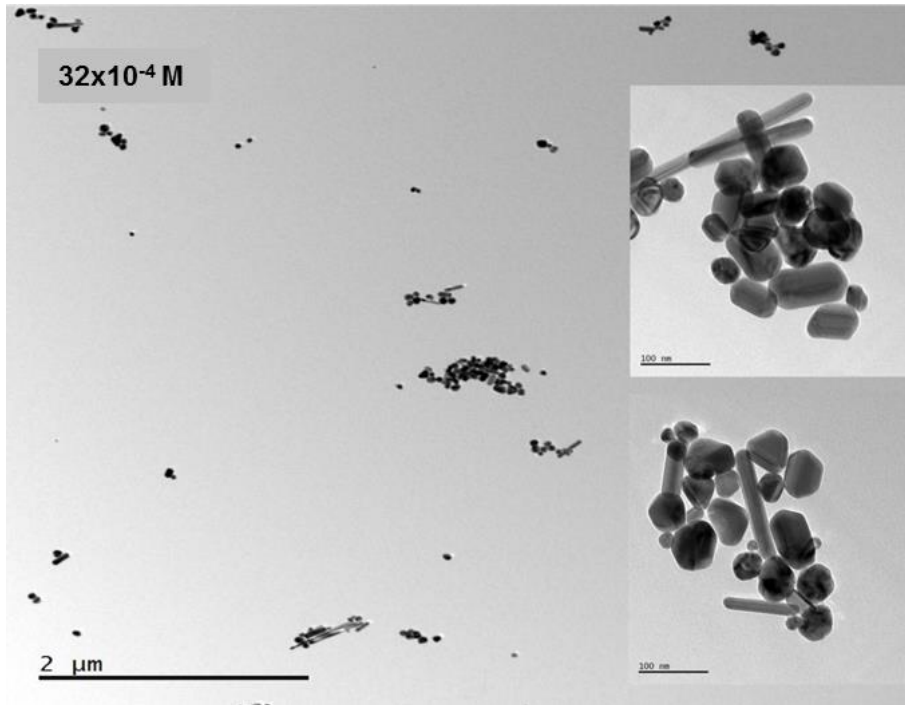


# Characterization of AgNPs synthesized by varying citrate concentration

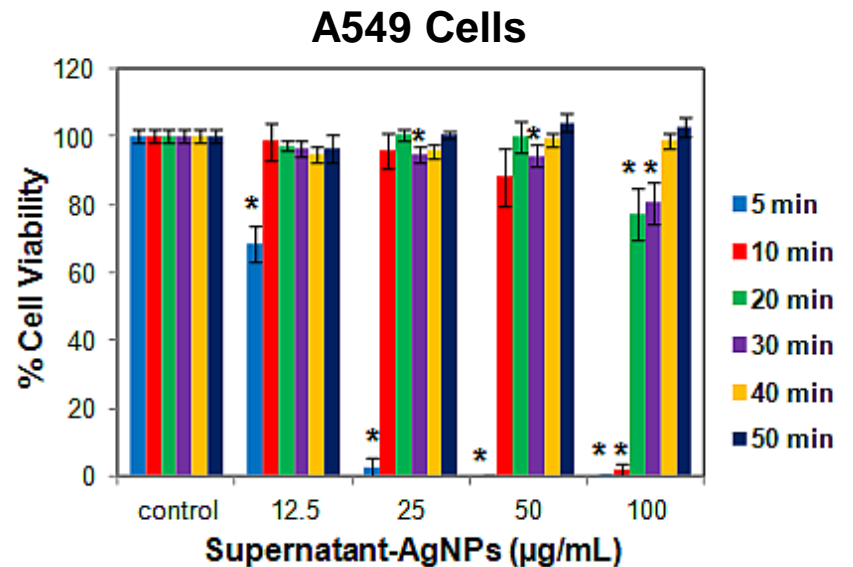
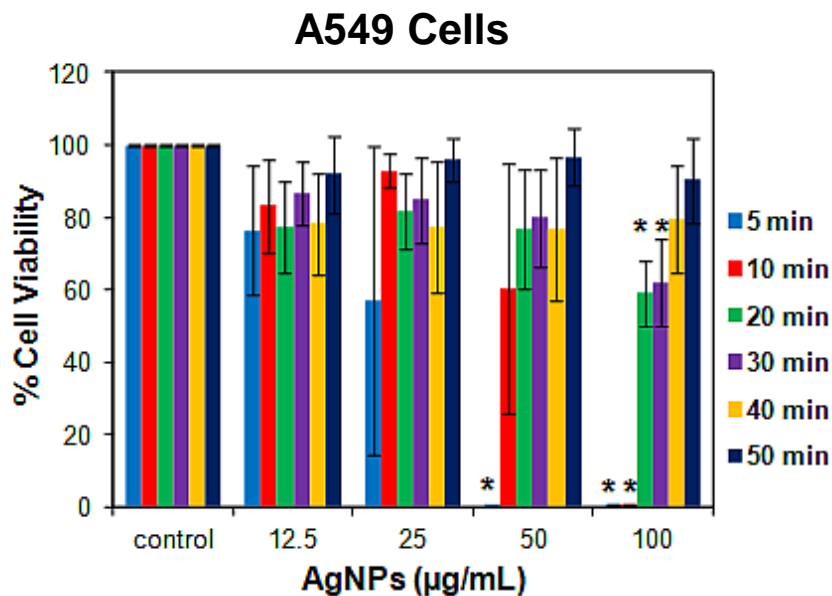
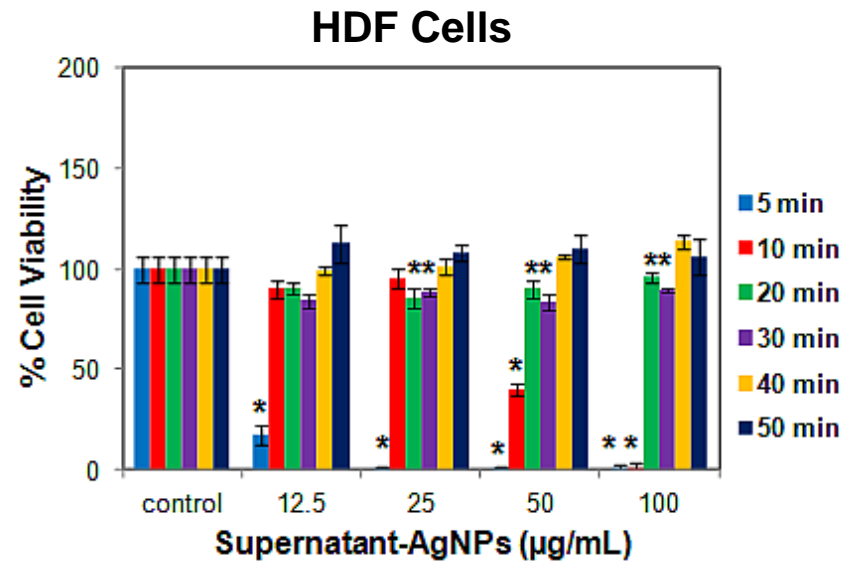
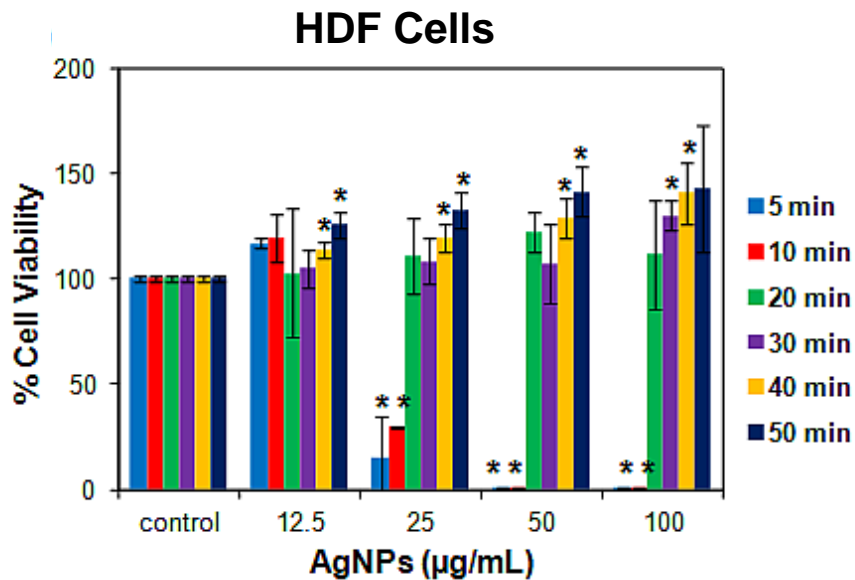


UV-Vis and DLS spectra of AgNPs prepared at different citrate concentrations.

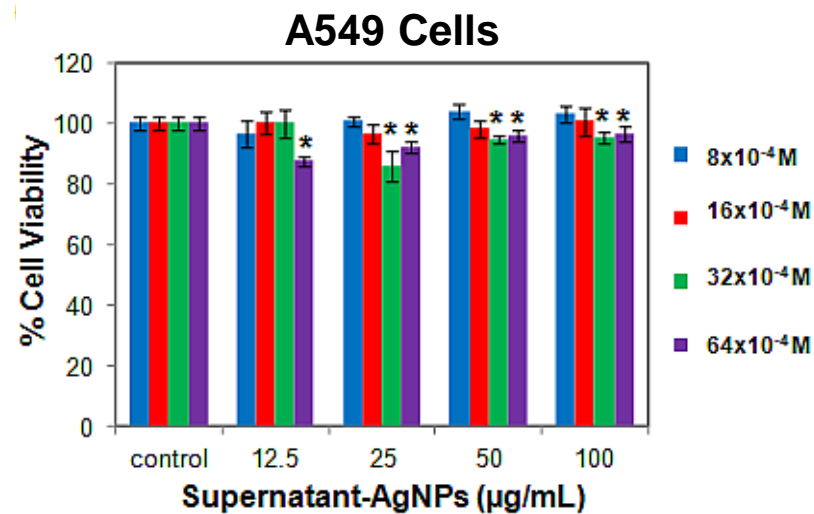
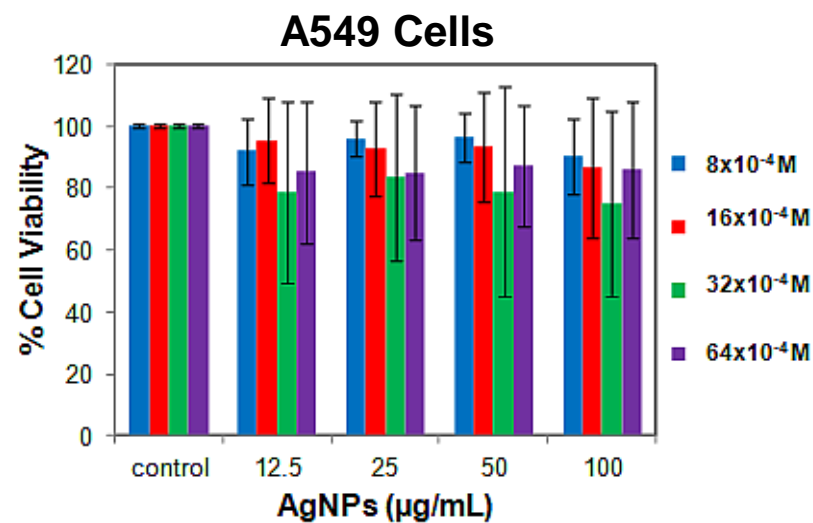
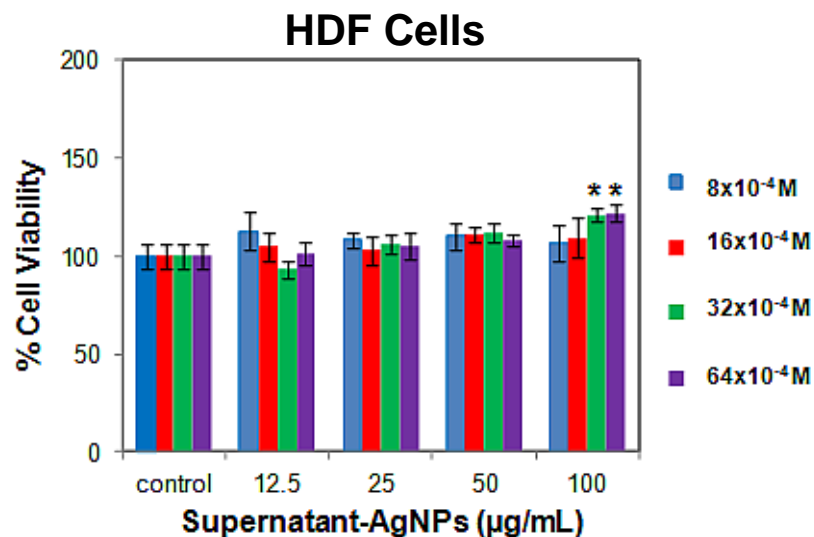
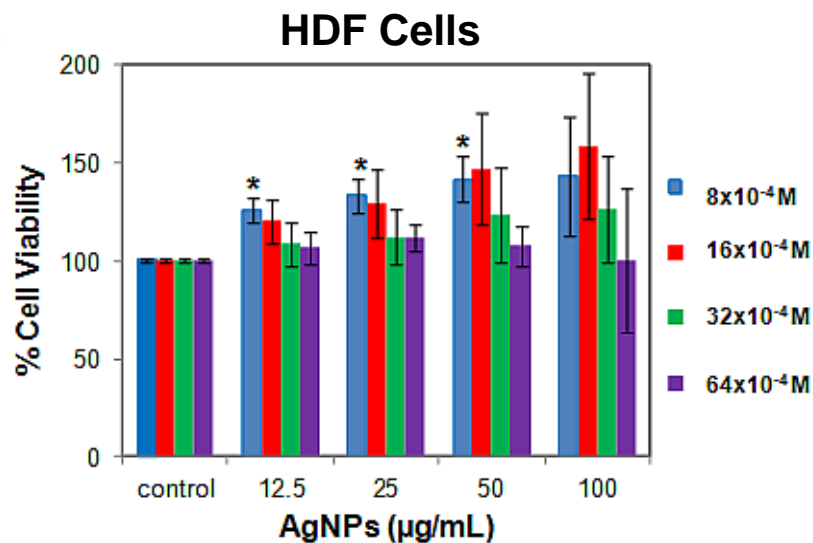
# Characterization of AgNPs synthesized by varying citrate concentration



# Cytotoxicity of AgNPs synthesized by varying reaction time and their supernatants

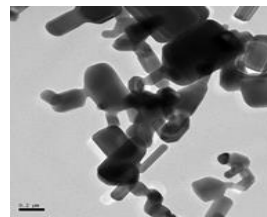
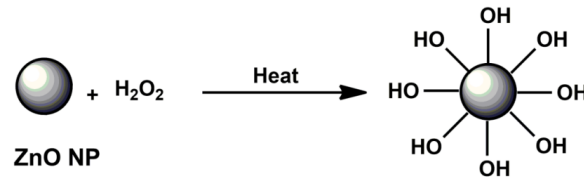


# Cytotoxicity of AgNPs synthesized by varying citrate concentration and their supernatants



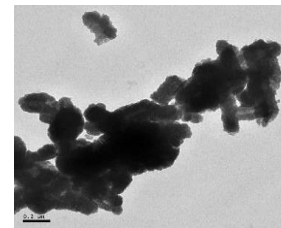
# Surface Modification Strategies for ZnO NPs

## Hydroxylation Process



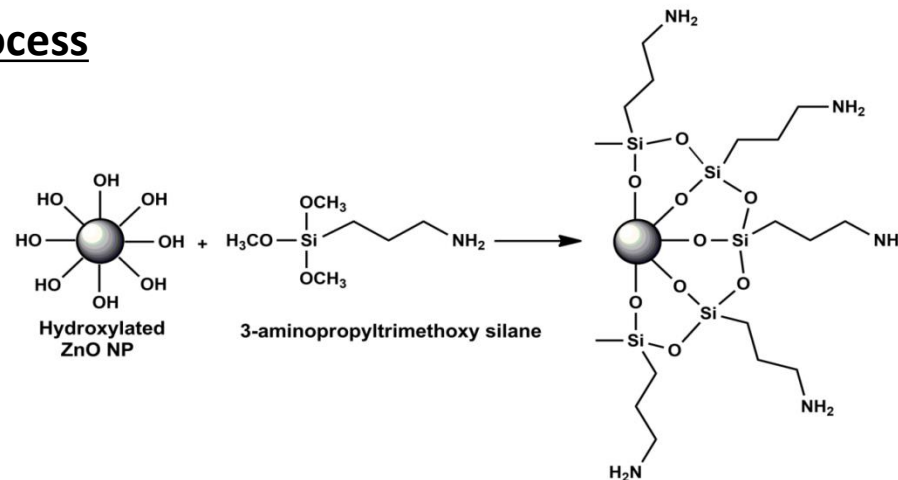
Bare ZnO

Hydroxylation

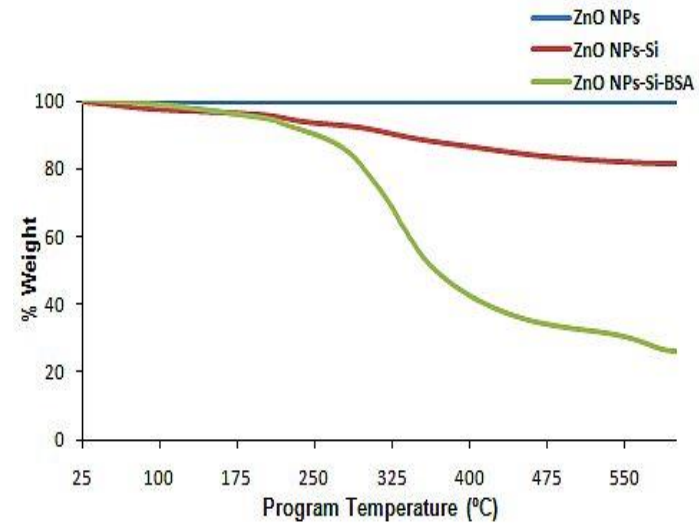
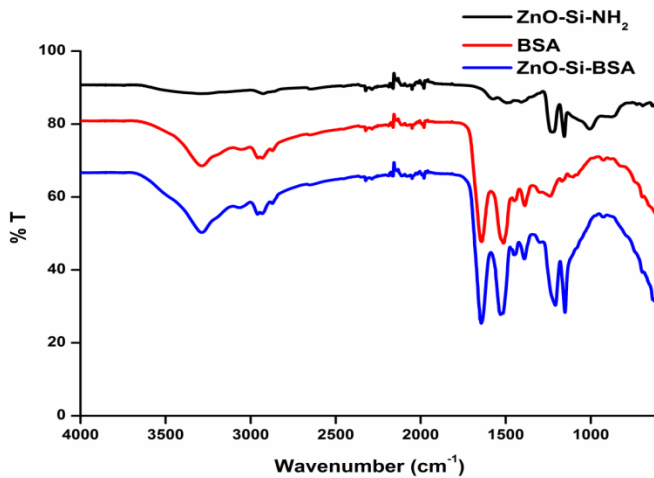
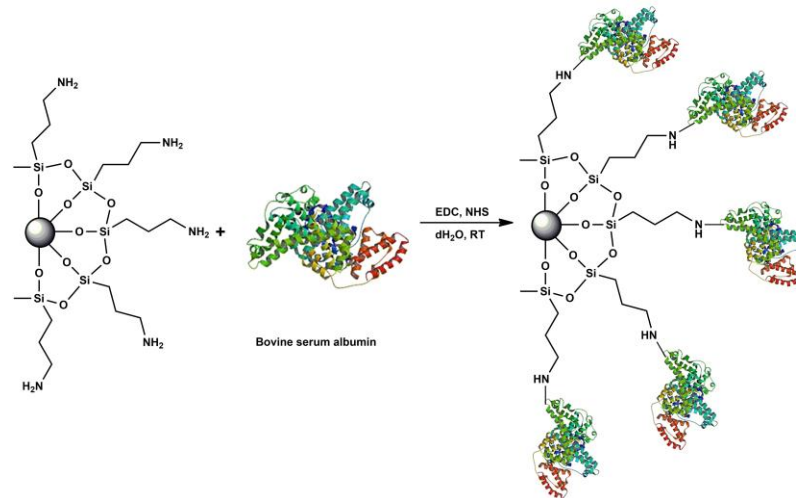


Hydroxylated ZnO

## Silica Coating Process

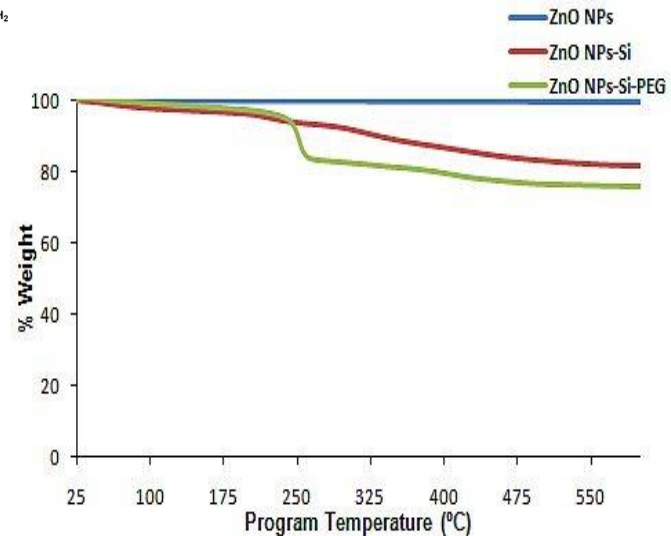
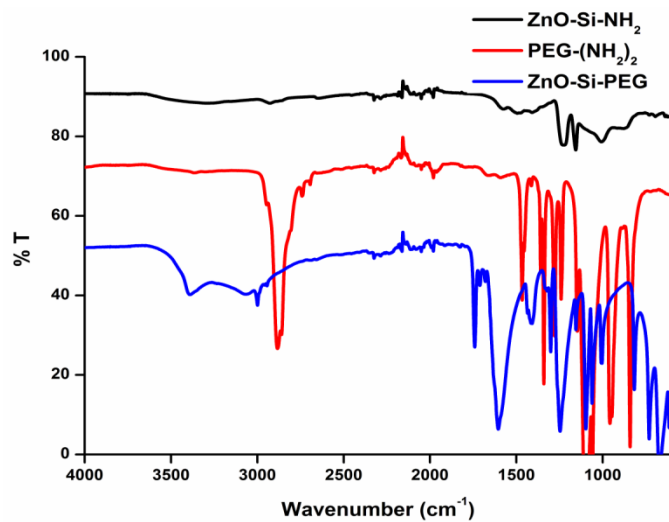
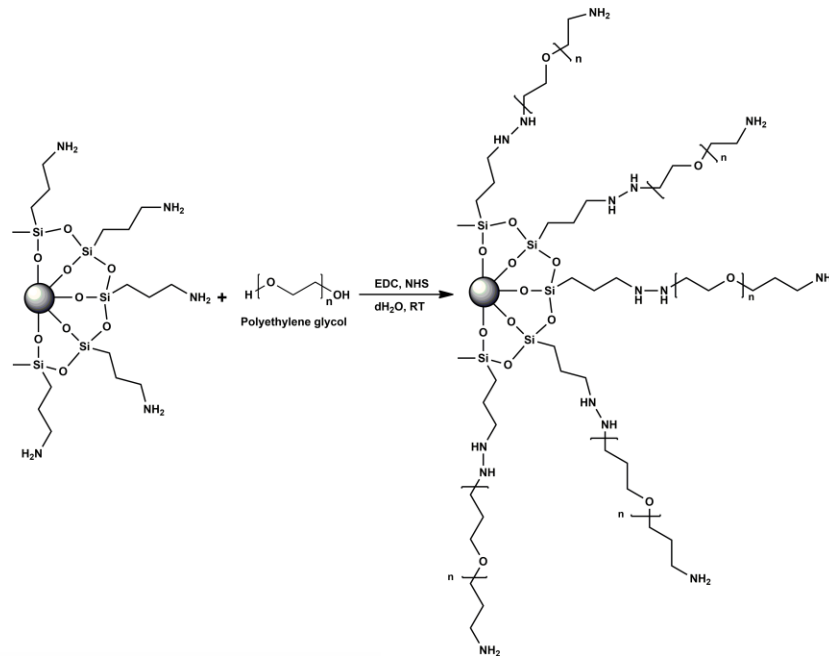


# Bovine serum albumin (BSA) attachment onto silica coated ZnO NPs



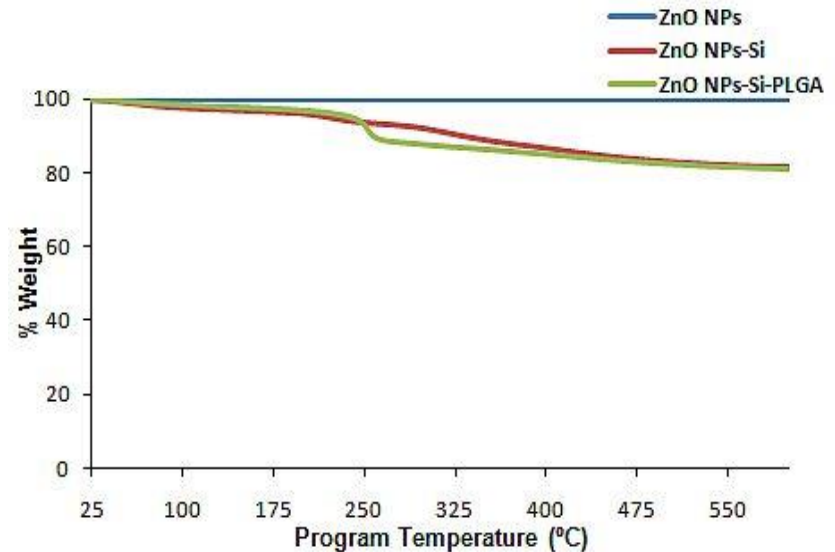
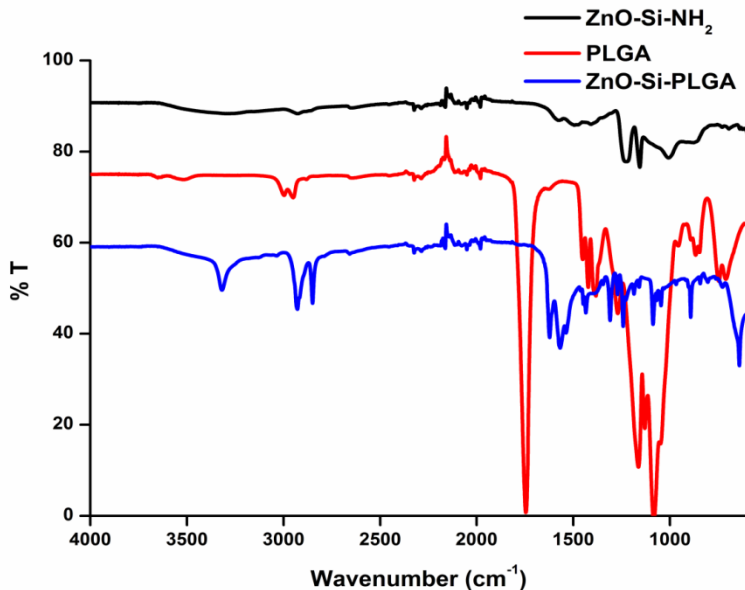
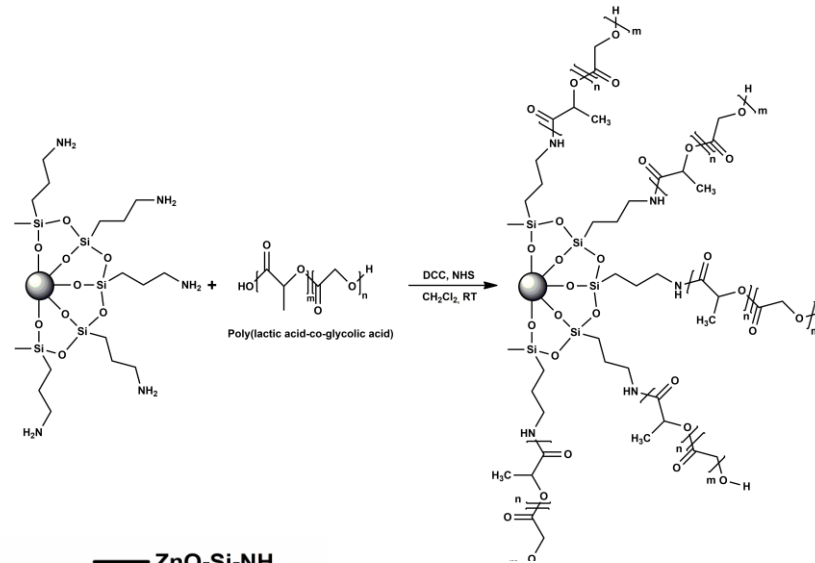


# Amine terminated poly(ethylene glycol) (PEG-NH<sub>2</sub>)<sub>2</sub> attachment onto silica coated ZnO NPs

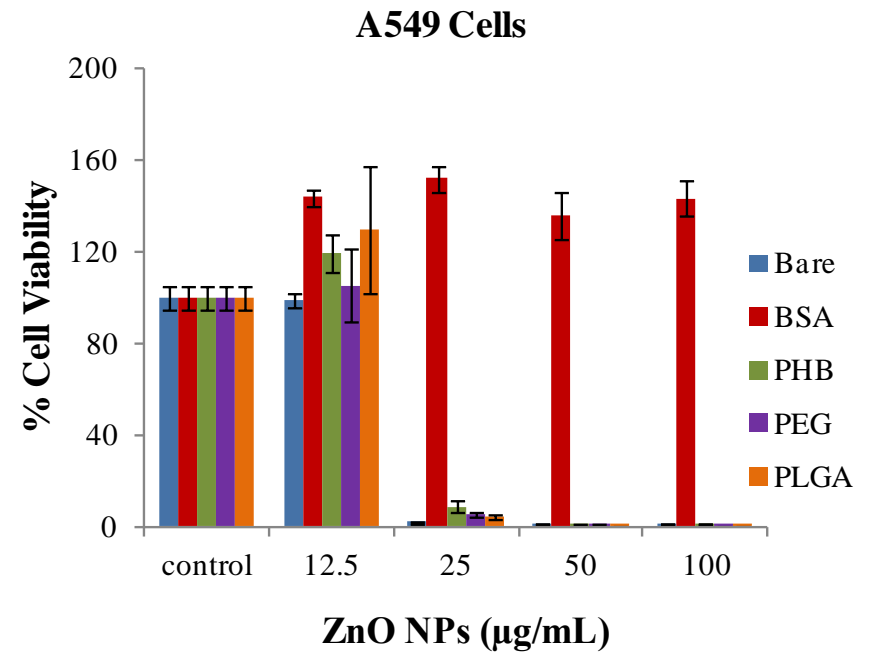
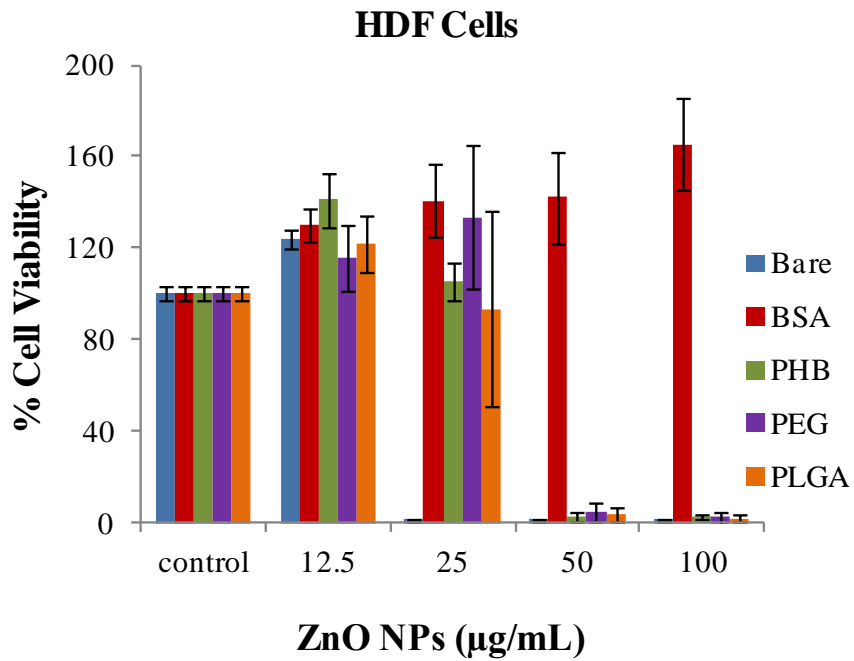




# Poly(lactide-co-glycolide) (PLGA) attachment onto silica coated ZnO NPs

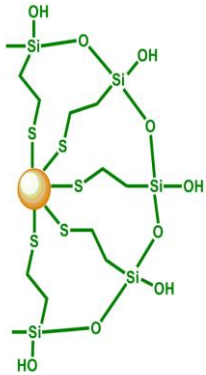


# Cytotoxicity of Modified ZnO NPs



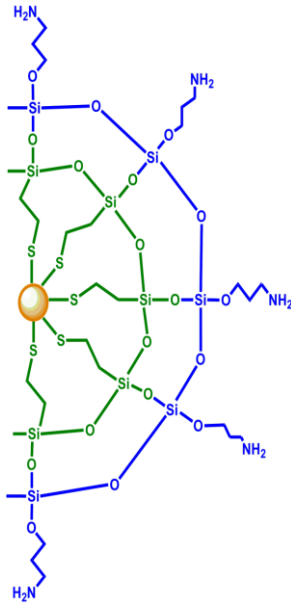
# Quantum Dots (QDs)

QD-Si-OH

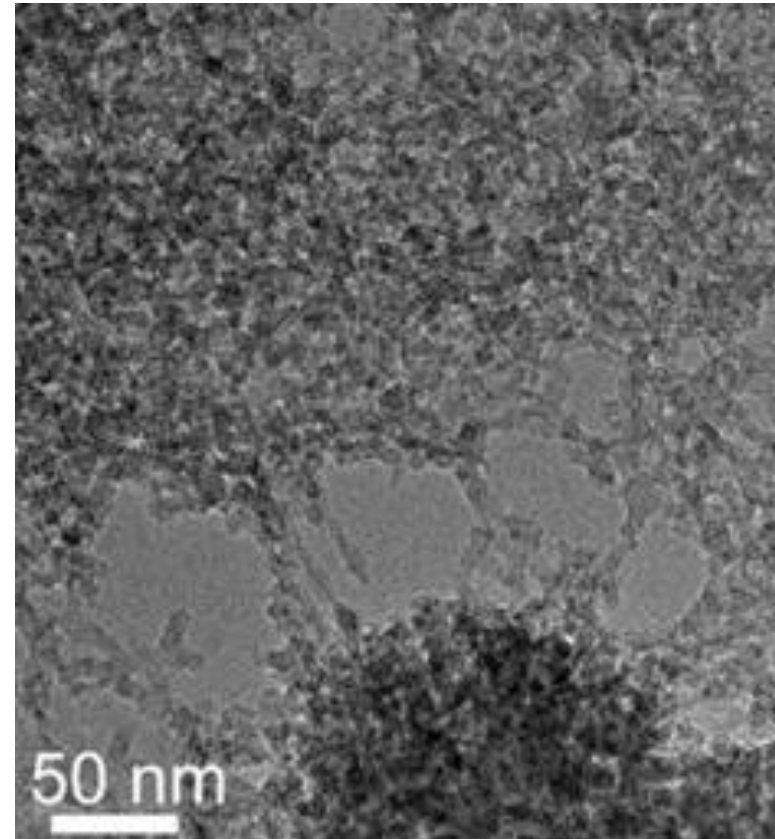
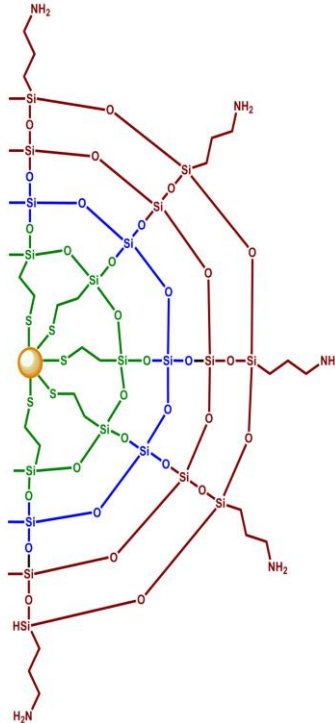


 : CdSe/ZnS

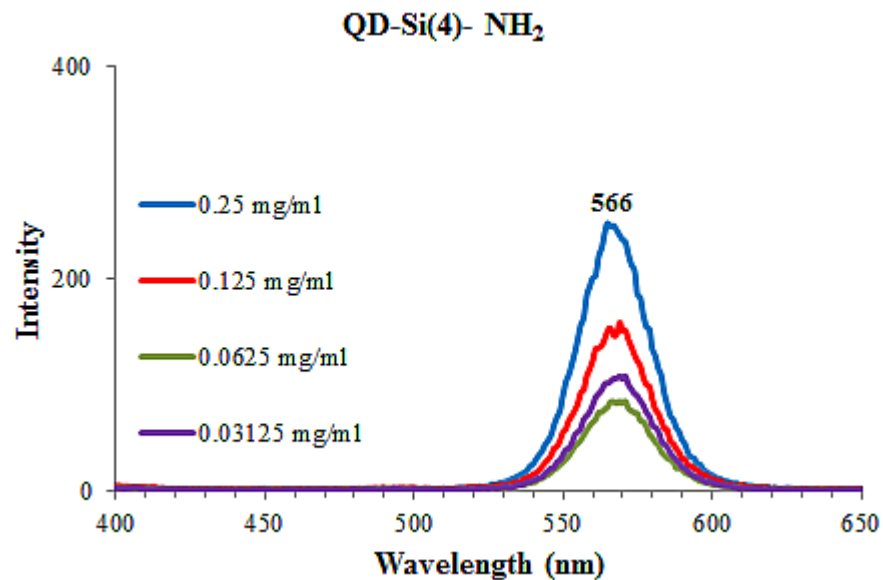
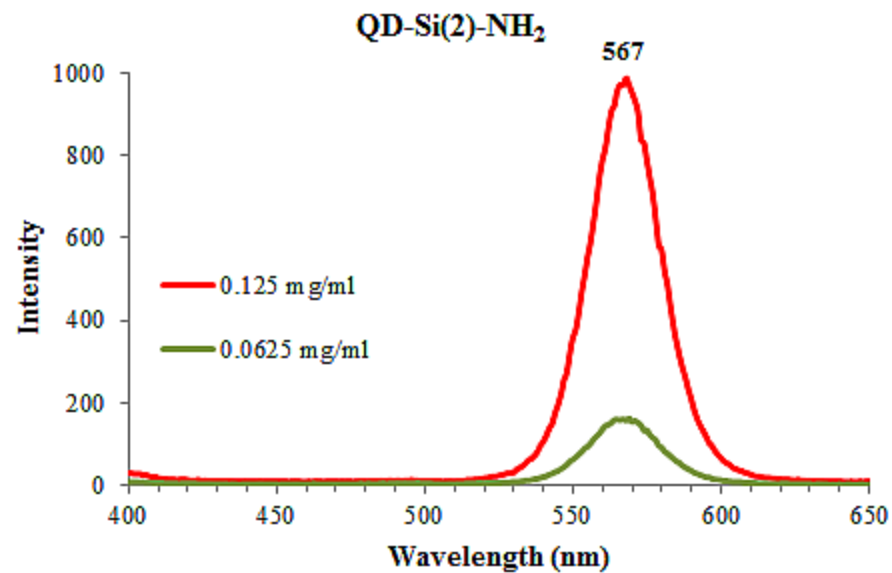
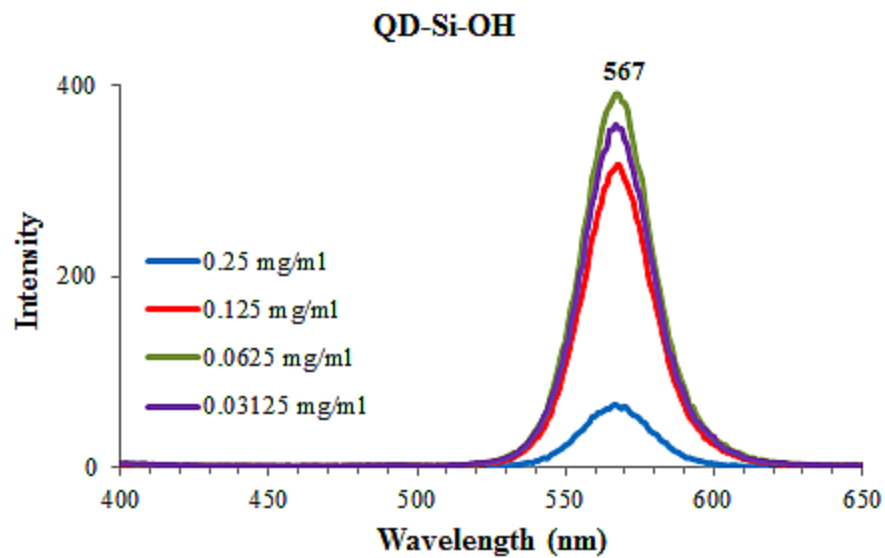
QD-Si(2)-NH<sub>2</sub>



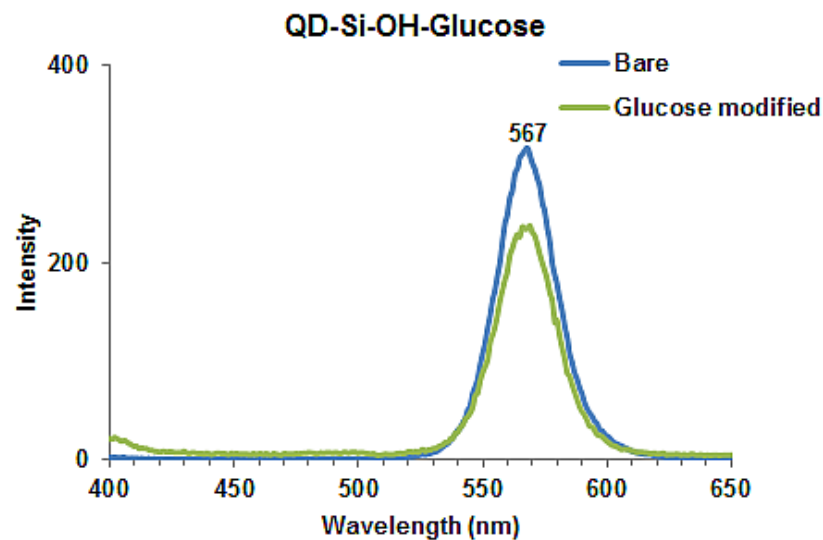
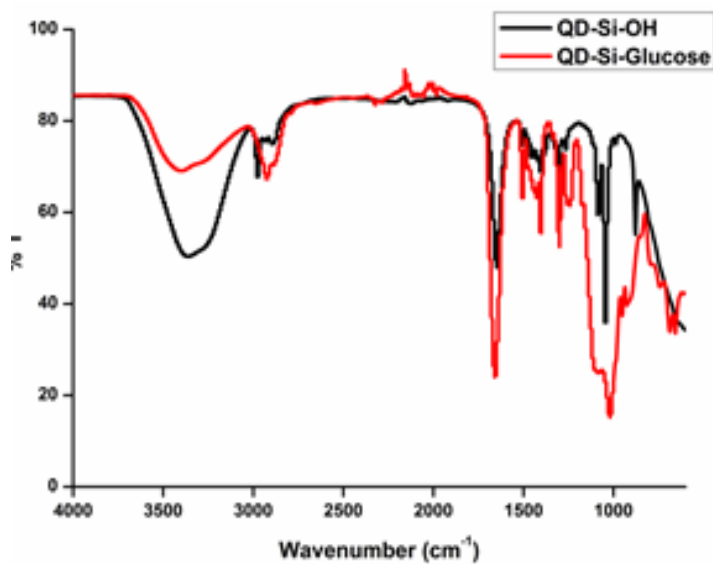
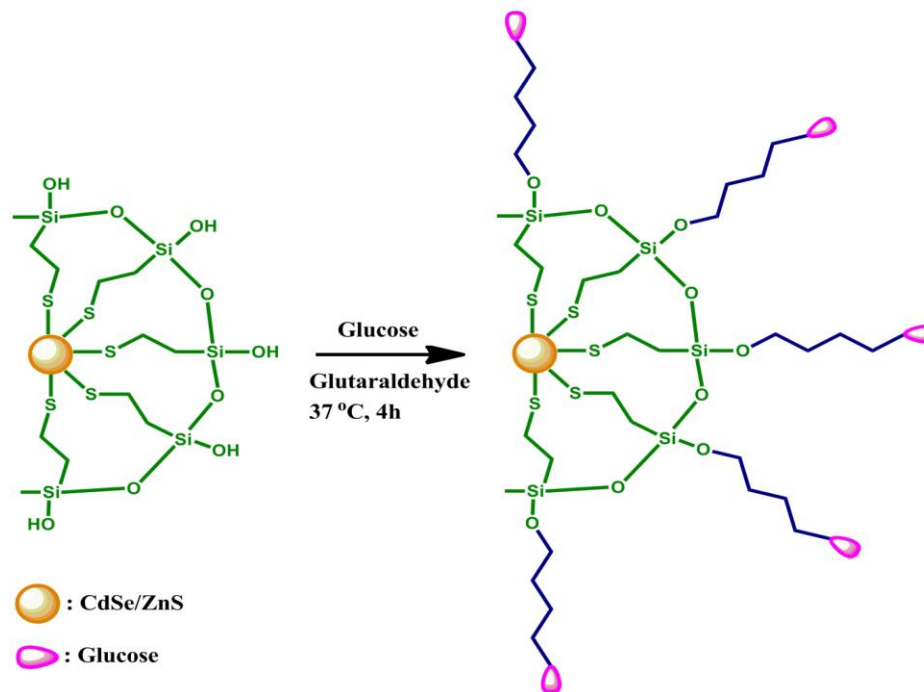
QD-Si(4)-NH<sub>2</sub>



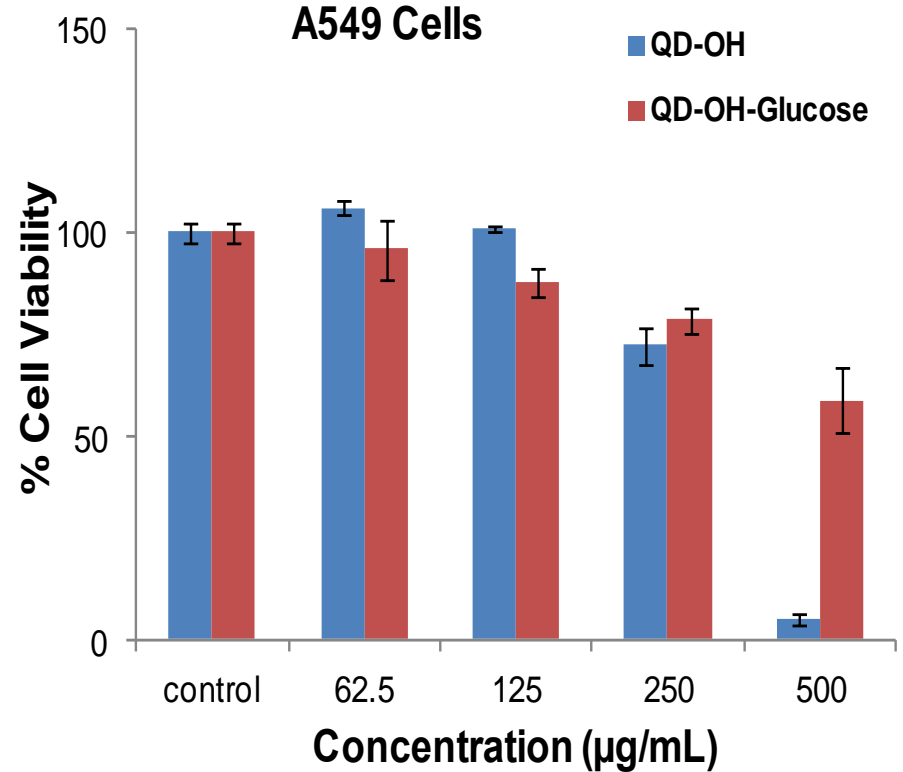
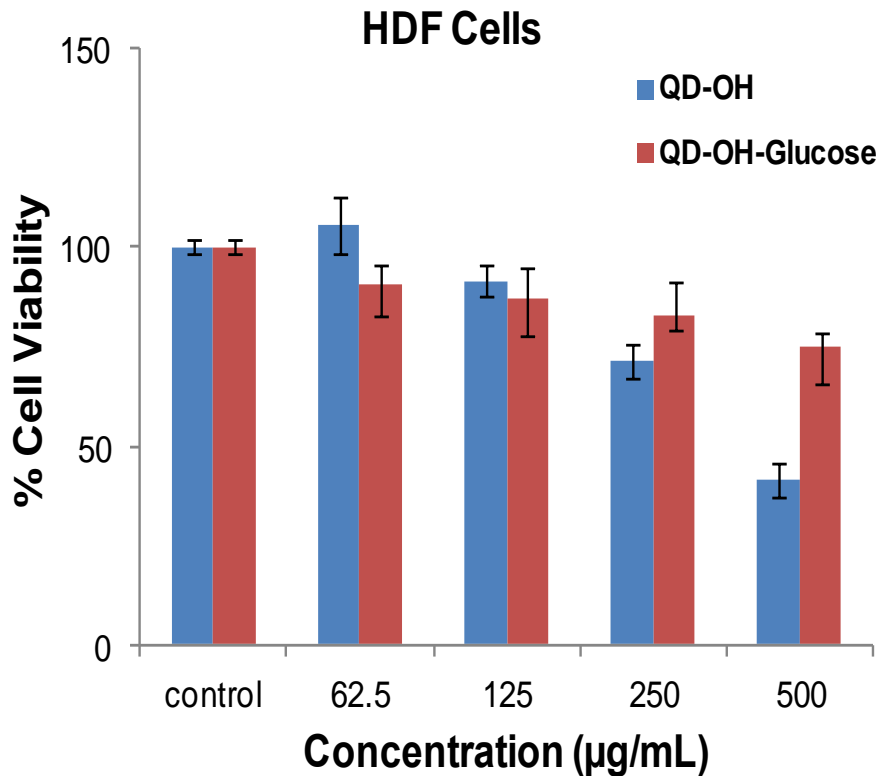
# Initial Characterization of QDs



# Glucose Modification of QDs-Si-OH



# QDs-Si-OH-Glucose Cytotoxicity Assessments





# Overall Conclusions

## AgNPs

- All attempts to reduce the toxicity with surface modifications were failed while the citrate reduced AgNPs synthesized through Lee and Meisel method were nontoxic.
- The few nanometers of AgNP seeds were the main source of toxicity in a AgNP colloidal suspension.
- Surface modification may increase lifetime of the AgNPs in the media by decreasing the dissolution of the AgNPs.

## ZnO NPs

- The initial characterization of the modified ZnO NPs suggests that all surface modifications are successful.
- Both polymers and BSA modifications helped to decrease cellular toxicity according to pristine ZnO NPs.
- The most important outcome is the surface modifications must be performed in extremely diluted suspensions by using excess amount of modifier to cover the whole surface area of ZnO NPs.

## QDs

- It is necessary to coat the surface of QDs with a silica layer to prevent the Cd ion release into the medium.
- The strategy of glucose modification helped to reduce the cytotoxicity without altering the fluorescence properties of QDs.

# NANOBIOTECHNOLOGY AND MOLECULAR ENGINEERING GROUP



***From left to right: Melis Emanet, Cansu Umran Tas, Pinar Akkus, Seda Keleştemur, Mine Altunbek, Zehra Yılmaz, Mustafa Çulha, Özlem Şen, Manolya Hatipoglu, Esen Efeoglu, Emine Kazanç, Emre Cebeci, Sevda Mert, Sinan Sabuncu, Ibrahim Can Sevim, Saban Kalay, Ertug Avcı***