Polydopamine Nanospheres as Antimicrobial Drug Delivery Agents

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Introduction

- Antimicrobials are a group of medicines that kill microbes or stop their growth.
- However, microbes are constantly evolving to become resistant to the antimicrobials.
- Antimicrobial resistance is a growing concern and is estimated to cause 10 million deaths a year globally by 2050.[1]

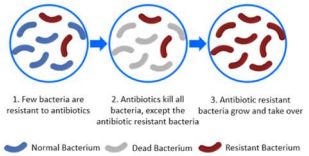


Figure 1. Development of Antibiotic Resistance

- A major contributor to the development of antimicrobial resistance is poor drug delivery efficiency to the intended target.
- Therefore, there is a need to develop more targeted and stimuli responsive approaches to deliver antimicrobials to sites of infection.
- Polydopamine nanospheres (PDNS) are bio-inspired nanomaterials, synthesized via dopamine polymerization.[5]

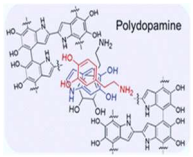
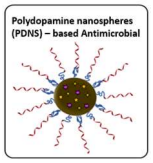
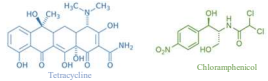


Figure 2. Polydopamine proposed molecular structure.[5]

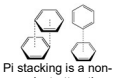
- PDNS's high biocompatibility and ability to be loaded with antimicrobials make it an ideal drug delivery agent.
- PDNS can also be readily functionalized with various molecules for specific targeting.



- Purpose: To examine how the structure of Tetracycline (TET) and Chloramphenicol (CM) affects its efficiency for drug loading and release.



- These two antibiotics differ in the number of the aromatic rings, and thus, different pi-stacking with PDNS.



Pi stacking is a non-covalent attraction between aromatic rings.[3]

Drug Loading during PDNS Synthesis

1. PDNS Synthesis and Drug Loading

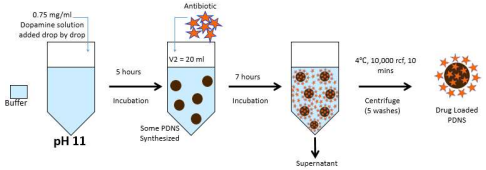


Figure 3. Schematic for PDNS Synthesis and loading antibiotic on PDNS during synthesis

2. PDNS Size – DLS, TEM, AFM

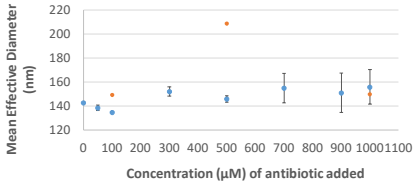
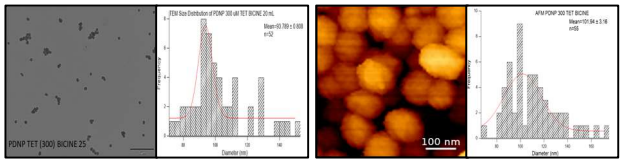


Figure 4. Dynamic Light Scattering (DLS) data for washed PDNS loaded with Tet and CM synthesized in Bicine pH 11.



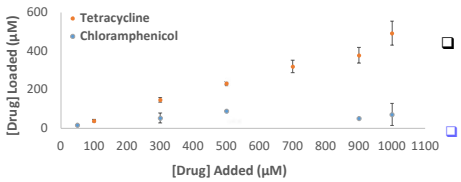
(a) (b)

Figure 5. Transmission Electron Microscopy (TEM) in (a) and Atomic Force Microscopy (AFM) in (b) for 300 µM Tet washed PDNS synthesized in Bicine pH 11. The histograms show the spread of the PDNS size.

- Synthesized PDNS of size ~100 – 150 nm as measured using DLS, TEM and AFM

3. Drug Loading Quantification

- Drug in supernatant was measured by obtaining UV/Vis spectra



- Drug loaded on PDNS = Total drug added – Drug left in supernatant
- Drug loading efficiency: Tetracycline > Chloramphenicol

Figure 6. Concentration of drug loaded on the PDNS as a function of the concentration of drug added during the PDNS synthesis

4. Passive Drug Release

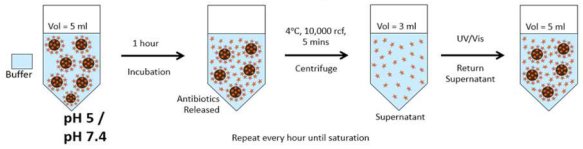
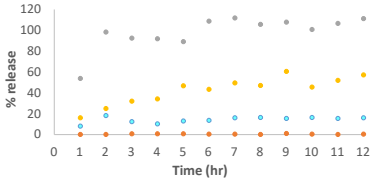


Figure 7. Schematic for passive drug release in buffer

5. Drug Release Quantification

- Drug released was measured hourly by obtaining UV/Vis spectrum of the supernatant.



- % release = [Drug] Released in buffer / [Drug] Loaded on PDNS
- Drug-release efficiency: Chloramphenicol > Tetracycline
- pH dependent drug release: pH 7.4 > pH 5 (for both drugs)

Figure 8. The amount of antibiotic released in different pH expressed as a percent of antibiotic loaded on PDNS, as a function of time (hour).

Drug Loading after PDNS Synthesis

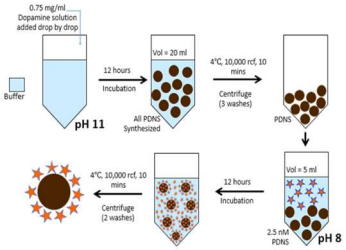


Figure 9. Schematic for PDNS Synthesis and loading antibiotic on PDNS after synthesis

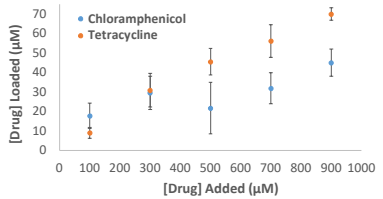


Figure 10. Concentration of Drug loaded on the PDNS as a function of the Concentration of Drug added after the PDNS synthesis

- Drug loading efficiency: Tetracycline > Chloramphenicol

Conclusion and Future Work

Summary:

- Synthesized drug loaded polydopamine nanospheres of size ~100 – 150 nm.
- TET has a higher loading efficiency than CM for drug loaded during and after PDNS synthesis
- CM seems to have a higher % release than TET
- The drug loading efficiency is higher when loaded during PDNS synthesis than loading after PDNS synthesis
- Passive release seems to be higher at pH 7.4 than pH 5

Future Directions:

- Perform more trials of passive release for drug added during and after synthesis
- Effect of drug-loaded PDNS on growth of *E. coli* in LB
- Drug loading and release efficiency of other antibiotics e.g. vancomycin

References

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Acknowledgements

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