Utilization of iron oxide nanoparticles coupled with nitric oxide (NO) as antibacterial treatment

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Statement of Purpose

Nowadays, nosocomial infections diseases are increasing dramatically. They are often due to pathogens resistant to common antibiotics (Raffi, 2010). Adding to this resistance, bacteria tend to form a biofilm when they are in certain environmental conditions, allowing them to survive from adverse conditions (Hetrick, 2010). Since bacteria colonize implants or invasive materials, they represent important clinical issues. The non-success of implants is not always due to the implant itself but sometimes due to the bacterial adhesion (either Gram positive or Gram negative bacteria can be found on catheters or other materials) (Subbiahdoss, 2012). The aim of this project is to develop an antibacterial treatment of implants and materials surfaces to prevent nosocomial infections. Iron oxide nanoparticles (Fe_3O_4) were chosen because they have a strong antibacterial power (Shoenfish and al). They can be easily manipulated with a magnetic field (can be guided deeply into the biofilm for example). Iron oxide will be studied to determine their antimicrobial effect. Nanoparticles will be coupled to nitric oxide (NO), to assess their effect on bacteria as. NO is well known to be a very reactive free radical, produced in inflammatory cells (like macrophages). We use a copper oxide and copper nanoparticles as positive control.

Methods

Bacteria (*S.aureus and E.coli)* were suspended in 10 m of TSB and incubated overnight at 37°C. Optic density was taken at 660nm was used to generate an inoculum of a given bacterial concentration. After 2 washes, bacteria were suspended in 10mL PBS. Bacteria suspensions were then sonicated for 1 min (to remove possible bacteria aggregation). Two suspensions of 10^6 bacteria were used (*S.aureus* was diluted in a 0.25% Proteose Peptone solution meanwhile *E.coli* was diluted in PBS). Nanoparticles suspension is also done.

Suspension A contains 10^6 of the studied bacteria (positive control). Suspension B contains 10^6 of the studied bacteria and a certain concentration of the studied nanoparticles (CuO or Cu). Serial tenfold dilutions are made (up to (10^{-4}) in PBS.. 100uL of each dilution is then plated and incubated for 24h at 37°C.

Suspension A and B are incubated for 3 hours at 37°C. After the 3 hours, another serial dilution is done and incubated for 24h at 37°C. After 24h colony forming units (viable bacteria) are counted in each plate.

Results

Copper oxide and copper nanoparticles (CuO and Cu) are extremely antibacterial, at low concentration.

Iron oxide is less effective than Cu or CuO nanoparticles but have a potential antibacterial effect. Adding NO allows an increase in the antibacterial effect for iron oxide nanoparticles without affecting their biocompatibility.

Conclusions

The utilization of iron oxide nanoparticles can allow us to have a better biocompatibility compared to copper oxide or copper nanoparticles. Coupling iron oxide nanoparticles with NO helps to increase the antibacterial effect of iron oxide nanoparticles. The release of NO was studied at 37°C (to determine the time needed to release the maximum quantity of NO). We will further increase NO release by using copper bromide to increase their toxicity effect. For NO coupling, the dose of at the iron oxide nanoparticles surface can be increased (increasing NO concentration and at the same time increasing the antibacterial effect).

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