Silver Nanoparticles Against Multi Drug Resistant Bacteria

VISION
To build a humane society through excellence in education and health care.

MISSION
To develop Nitte University as a centre of excellence, imparting quality education, generating competent, skilled manpower to face the scientific and social challenges with a high degree of credibility, integrity, ethical standards and social concern.

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From the Editor’s desk

It is said that Ptolemy may have copied sky charts in his scientific deliberations. In the present scenario it will be considered as research misconduct which according to one report is widely prevalent in the scientific world. Department of Health & Human Services defines scientific misconduct as “Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results”

Falsifying the research data, using another’s ideas without obtaining permission or giving due credit (plagiarism), Overlooking others’ use of flawed data, publishing the same data or results in two or more publications, inadequate record keeping related to research projects etc. result in loss of credibility and reliability of scientific finding.

The reasons for rampant misconduct are publish or perish pressure, desire to “get ahead”, poor supervision, lack of training and interest and desire for fame and fortune. Adopting zero tolerance and inculcating ethical behavior in researchers will certainly address the problem. Depending upon the gravity of the misconduct, retracting the publications, suspension of grants, reprimand, appointing an overseer and expulsion from the organization may be resorted to.

Research misconduct crosses all geographical borders the impact of which will be serious. All the institutions of higher studies and research must adopt vigorous monitoring of the process and sensitize the researchers about ethical conduct and practice. Addressing the reasons for research misconduct and punitive actions in some cases will be the right steps in ensuring quality research in the country.

I take this opportunity to wish all the teachers and researchers a bright and more productive academic year 2014-15.

C.S. Shastry


Dr. Saidutta M. B

Dr. Prasanna B. D

Dr. Anand Raichurkar

Faculty and students of NGSMIPS listening to the speaker
Guest lectures at NGSMIPS

Dr. Saidutta M. B., Professor of Chemical Engineering and Dean (Alumni Affairs & Institutional Relations), NITK Surathkal, Mangalore and Dr. Prasanna B.D., Asst. Professor, Dept. of Chemical Engg, NITK Surathkal, delivered a lecture on Intellectual Property Rights on May 5, 2014 at the Seminar Hall of NGSMIPS. The lecture covered important issues such as the cost involved in patenting and patentability with examples and the need for instituting a cell to handle IP related issues. The lecture was attended by the faculty, heads of sister institutions and Dr. Rajshekhar, Director of Staff Development Cell.

Dr. Anand Raichurkar, Senior Research Scientist, Astra Zeneca (India) Ltd. was invited to lecture on CADD (Computer Aided Drug Design) and its Impact on Drug Development on May 5, 2014. This lecture gave an insight to computer-assisted techniques used to discover design, and optimize new, effective and safe drugs. According to Dr. Raichurkar, recent technological developments in biochemistry, biomedical science, and nanotechnology have made computer-aided drug design and delivery systems possible on a molecular basis. Since drug discovery and development are very time and resources consuming processes, CADD may have a significant impact on the economics of drug research and reduce time periods required for bringing a new drug molecule to the marketing stage.

A lecture in the area of IR spectroscopy was arranged by the Institution for the benefit of PG students and Research scholars on June 24, 2014 at NGSMIPS. The speaker, Dr. M. Himaja, Professor, Pharmaceutical Chemistry Division, School of Advanced studies, VIT University, Vellore spoke on the topic, ‘Application of IR spectroscopy in qualitative analysis’. Dr. Himaja’s interactive lecture included the interpretation of IR spectra which was demonstrated by examples and several exercises given to the attendees.

On June 5, 2014, Mr. Umesh Baikunje, Vice President (Technical Operations), Stempeutics Research Pvt. Ltd., Bangalore was invited to speak on ‘Advances in Drug Therapy with Special Focus on Stem Cells’. In his lecture, Mr. Baikunje briefly spoke on the fundamentals of Stem Cell technology and highlighted different sources of human stem cells and its applications. He also discussed the regulatory aspects of stem cell research and therapy and the critical areas of transportation and maintenance were explained in detail. Mr. Baikunje, an alumnus of NGSMIPS concluded his talk by expressing his gratitude to the faculty members for their guidance and mentorship during his student days.

Appointments

Dr. Mudit Dixit has been appointed as Assistant Professor Grade III of the Department of Pharmaceutics with effect from May 10, 2014.

Dr. Murali B has been appointed as Professor and Deputy Director of NUCARE (Nitte University Centre for Animal Research and Experimentation) with effect from May 2014.
Nanoparticles: A Potent Weapon Against Multi Drug Resistant Bacteria

In recent decades antimicrobial therapy has been challenged by the increasing evidences of multi-drug resistant (MDR) organisms, resulting in negative clinical outcome and restricting our ability to treat common infections, thus is a cause of concern worldwide (Gemmell et al. 2006).

MRD infections have resulted in increased morbidity, mortality, length of hospital stay and cost of treatment (Gemmell et al. 2006). Therefore, research in development of new antimicrobials through natural and synthetic route, and modification of available antibiotics is essential to improve the efficacy of conventional antibiotics and to treat infectious diseases in coming days.

Nanotechnology offers a platform to modify the available agents either by reducing the agents to nano scale or by conjugating the drug to nanoparticles, as nanoparticles have been proven to be valuable in diagnosis, biological imagining, drug delivery and nano-drugs to treat various diseases (Singh and Singh 2011). Thus, there is increase in research in the area of metal nanoparticles mainly gold, silver and metal oxides such as zinc oxide.

Nanoparticles consisting metals and metal oxides, may be promising antimicrobial agents particularly against MDR strains (Gemmell et al. 2006). The bactericidal activity of nanoparticles against the MDR is associated to their high surface-area-to-volume ratio and unique physiochemical properties. Nanoparticles have been reported to exhibit antibacterial activity by causing disruption of membrane and nucleic acid through direct interactions (Kim et al. 2007).

Silver is suggested to have antimicrobial activity; the efficacy of silver has been improved by reducing the size to nano scale, resulting in change in physiochemical properties. Silver nanoparticles of 10–100 nm have been suggested to exhibit strong bactericidal activity against Gram-positive and Gram-negative bacteria, as well as against MRD strains of bacteria such as Pseudomonas aeruginosa, ampicillin-resistant Escherichia coli and methicillin-resistant Staphylococcus aureus (MRSA) (Morones et al. 2005). The antibacterial activity of silver nanoparticles is suggested to be due to formation of free radicals and disruption of the cell membrane as shown in figure 1 (Morones et al. 2005).

Gold is another metal known to possess antibacterial activity. Reports suggest that gold nanoparticles and vancomycin conjugated gold nanoparticles to be effective against vancomycin-resistant Enterococcus faecalis (VRE) and vancomycin-resistant Staphylococcus aureus. It is hypothesized that gold nanoparticles exhibit the antimicrobial activity by binding to cell-surface peptides involved in cell-wall synthesis, but no further evidence is available (Gu et al. 2003).

Metal oxide nanoparticles have been investigated for antimicrobial properties. It is suggested that metal oxide nanoparticles display antibacterial activity only when the materials are in nano scale. For example, magnesium oxide nanoparticles are reported to displayed size-dependent antibacterial activity against Escherichia coli and S. aureus (Makhluf et al. 2005). But, Dose-dependent antimicrobial activity has been observed for iron oxide nanoparticles (Taylor and Webster 2009). Furthermore, it is suggested that zinc oxide colloidal suspension with nanoparticles of size 4–7 nm inhibited 95% of MRSA and VRE, but was ineffective against Salmonella typhimurium (Raghupathi et al. 2011).

In summary, nanoparticles are effective against a range of organism, but there is need of further work to develop nanoparticles that are effective against other organism such as Salmonella typhimurium. Whilst, nanoparticles are promising as anti-infective agents, it would be remiss not to point out the toxicological concern and targeting these nanoparticles to site of infection may reduce the toxicological effects of nanoparticles and this certainly need further investigation.

![Figure 1 Silver nanoparticles showing multiple bactericidal actions](image)

### References

Gemmell CG, Edward DI, Fraimse AP: Guidelines for the prophylaxis and treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections in the UK.


DEPARTMENT OF PHARMACEUTICAL CHEMISTRY

RESEARCH PUBLICATIONS

DR. KISHWAR BHAT, Professor

MR. ABHISHEK KUMAR, Asst. Professor

DEPARTMENT OF PHARMACEUTICS

RESEARCH PUBLICATIONS

DR. R. NARAYANA CHARYULU, Professor

DR. MARINA KOLAND, Professor

Facebook: A new source of addiction

“You log off your computer, leave the house, get in car and log back on through your phone…!!!”

While reading this article, there is a good probability that you are logged into Facebook/other social networking media. Facebook, now with over 1 billion users is unarguably one of the most popular and powerful social networking media of the world. People are constantly networking, sharing, liking and commenting on this service that you start wondering how the world even still spins. How people still manage 4-5 hours/day on Facebook despite their tight busy daily schedule? There is absolutely no doubt about the efficacy of these social networking media to bring neighbors much more closer than ever thought before. But do you ever feel that spending a lot of time in a closed room, continuously hitting the refresh button is slowly making you addicted and isolated from the beautiful real world/relation? Recent studies has revealed that, dopamine, a chemical neurotransmitter associated with the motivation and reward response in the human brain is released in high quantities while consuming drugs or having sex. In the similar way, receiving and answering notifications on Facebook/social media start releasing dopamine and other neural chemicals in the brain.

Mr. Atanu Bhattacharjee
Asst. Professor
Dept. of Pharmacognosy
media result in a hit of dopamine and cause similar addictive effects. Facebook addiction is grasping the young generation rapidly and in the countries like China, Taiwan and South Korea “Internet Addiction Disorder” is already accepted as a psychological diagnosis. Hence, it’s a high time to become aware about the adverse effects of this addiction. Few of them are mentioned below

- The most severe effect is of course **time loss**. When you are busy on Facebook, you are obviously missing out every phenomena happening around you. The mental fix from Facebook seems to interest us more. Facebook or social networking in general, has a way of hogging up our brains like nothing else.
- Recent studies revealed that spending too much time online for a long period can **shrink** various parts of the brain to an extent of 10 to 20%.
- Facebook and Internet addiction can also decrease the **attention span** of users — in fact, since 2000, our collective attention span has decreased by 40%.
- Surfing for long periods is one of the most causes of **eye strain**. In past 20 years disorders relating to eye strain and use of glasses have grown from 25% to 41.6%.
- **Cyber-bullying** is very easy on Facebook. Anyone can harass any person even at any point of time as there aren’t any moderators that go around monitoring what people say to each other. Anything can be said…!
- Facebook is notorious for causing couples to break up. Spending a lot of time on Facebook reduces your time spent in sharing your emotions with others around. It leads to avoidance, un-bonding, a bit of tension and in severe situations, even divorce.
- Facebook is a cause for **insecurities** due to the fact that it makes people compare themselves with others. There is a probability that you may demoralize your self-confidence by looking into the negative tags/comments on pictures…!

This article isn’t about stopping your enjoyment of Facebook; rather, the aim here is to help you identify whether you’re using Facebook in an addictive way, and if so kindly be aware of those effects mentioned above and instead find more constructive ways to connect yourself socially.

**References:**
2. Cohen E. Five clues that you are addicted to Facebook. CNN. 2009.

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**Microneedle Technology for Transdermal Delivery of Peptide Drugs**

Dr. Marina Koland  
Professor  
Dept. of Pharmaceutics

The transdermal route of administration of drugs via patches has been considered as an important alternative to the oral delivery of those drugs which show significant bioavailability problems and to the use of painful injections. However the transdermal delivery is severely limited by the inability of the large majority of drugs to cross the skin at therapeutic rates due to the barrier characteristics of the skin’s outer stratum corneum layer. Obviously, it is extremely unlikely for large molecular size drugs such as peptides to cross the skin in sufficient concentrations into the systemic circulation that are therapeutically effective.

Although a number of different approaches have been attempted to improve skin permeability, ranging from the use of chemical/lipid enhancers to electric fields employing iontophoresis and electroporation, none of them have been successful for the transdermal delivery of peptide drugs such as Insulin. These methods share the common goal of disrupting the stratum corneum structure in order to create “holes” big enough for molecules to pass through. The size of disruptions generated by each of these methods is believed to be of nanometer dimensions, which is large enough to permit transport of small drugs, but probably small enough to prevent causing damage of clinical significance.

In recent years the emergence of a new disruptive technique known as the microneedle (MN) technology whereby larger transport pathways of microns dimensions can be created in the skin by using arrays of microscopic needles, has improved the possibility of the transdermal delivery of peptide drugs. These pathways are orders of magnitude bigger than molecular dimensions and, therefore, should readily permit transport of macromolecules, as well as possibly supramolecular complexes and microparticles. Despite their very large size relative to drug dimensions, on a clinical length scale they remain small. Although safety studies need to be performed, it is proposed that micron-scale holes in the skin are likely to be safe, given that they are smaller than holes made by hypodermic needles or minor skin abrasions.
encountered in daily life. Proper design and modulation of geometry of the microneedles and simple alteration of drug formulations can result in controlled drug deposition within targeted skin layers. MNs have been shown to penetrate the skin and cross the stratum corneum into the viable epidermis, avoiding contact with nerve fibres and blood vessels that reside primarily in the dermal layer. Therefore, the use of MNs would provide a pain-free, minimally invasive means of delivering both small and large molecular weight APIs with the prevention of bleeding at the application site.

A number of specific strategies have been employed for using microneedles in transdermal delivery. Most work has focused on making microscopic holes in the skin by inserting solid microneedles made of silicon or metal. The “poke with patch” approach uses microneedles to make holes and then apply a transdermal patch (or some prototype) to the skin surface. Transport can occur by diffusion or possibly iontophoresis if an electric field is applied. Another approach is “coat and poke,” where the needles are first coated with drug and then inserted into the skin. There is no drug reservoir on the skin surface; all the drug to be delivered is on the needle itself. A variation on this second approach is “dip and scrape,” where microneedles are first dipped into a drug solution and then scraped across the skin surface to leave behind drug within microabrasions created by the needles.

The use of hollow MNs allows the continuous delivery of a particular medication via the injection of a fluid formulation containing the medication of choice through the hollow needle bore-opening into the skin. Hollow microneedle designs and methods have also been studied using an approach more reminiscent of an injection than a patch. Although harder to make and use, hollow needles facilitate active fluid flow through the needle bore and into the skin, which can lead to much faster rates of delivery that can be modulated over time.

Another strategy is the use of patches which possess dissolvable MNs that are made of biodegradable and water-soluble polymers with the drug encapsulated in the polymer needle matrix. After application, the needle patch remains in the skin for a short time period that allows the polymer to dissolve while it releases the drug.

Among the applications of microneedle technology, the area that has gained maximum attention is in the use of biotherapeutics such as peptides, DNA, RNA etc. Microneedles can be used to deliver macromolecules such as insulin, growth hormones, immunobiologicals, proteins and peptides. The doses of these drugs are typically low which makes them suitable for MN technology since the small size of the MNs restricts quantities administered to microgram levels. Much work has been done in the transdermal delivery of Insulin through this technology using solid, hollow as well as dissolving micro needles in animal models induced with diabetes. Hollow MNs of Insulin has also progressed to human studies where human subjects with Type I diabetes were employed. The subjects found this mode of delivery less painful than the conventional injections, besides producing better control over post prandial glucose levels.

For protein vaccine delivery, “coat and poke’ method and for DNA vaccines, “dip and scrape” method were successfully used in laboratory animals.

Studies published in 2012 for a synthetic peptide coated on solid MNs used in the treatment of osteoporosis showed rapid transdermal absorption when administered. This rapid uptake was attributed to the lymphatic system. The dermis is particularly rich with lymphatic capillaries and the rate of fluid exchange in the dermis exceeds any other compartment in the body. Large molecules delivered to subcutaneous or intramuscular tissues may not be absorbed by the lymphatic capillaries as fast as they would be in the dermis.

Literature survey and patents filed revealed that microneedle-based drug delivery system can be explored as a potential tool for the delivery of a variety of macromolecules that are not effectively delivered by conventional transdermal techniques. In conclusion, MN therapy may produce enhanced therapeutic profiles of peptides and vaccines allowing for lower dose administration with wider safety margins. Moreover they may provide a useful alternative to traditional injectable therapy by improving patient compliance in chronic diseases and routine vaccination.

References:
Toppers of the year 2013-14

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