

# Technologies Available for Licensing

BIOLOGY & MEDICINE  
2010

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## TECHNOLOGIES AVAILABLE FOR LICENSING (Biology & Medicine)

### LIST OF TECHNOLOGIES

INVENTION TITLE	Tech No.	Application
• Anti-Microbial Coatings Containing Chemically Bound Biocide for Biomedical Application	RFT 282	Biomedical Coating
• Drug Delivery Vehicle for Treatment of Eye Disease: Glaucoma	RFT 263	Pharmaceutical
• Multifunctional 'Dual Action' Anti-Microbial Coatings for Implantable Catheters and Tubes	RFT 260	Biomedical Coating
• Novel Clay Based Nanocomposites for Bone Replacements and Other Biomedical Applications	RFT 244	Bone Replacement/Prosthesis
• Antibacterial Siloxane Polymer Containing Tethered Levofloxacin	RFT 232	Biomedical Coating
• Composites for Bone Tissue Engineering for Applications In Bone Replacements And Prosthetics	RFT 200	Bone Replacement/Prosthesis
• Novel Environment Friendly Coatings for Bio-Medical Applications	RFT 179	Biomedical Coating
• Novel Liposomes Designed for Controlled Release of Drugs	RFT 151	Pharmaceutical
• Drug and Pesticide Enhancers	RFT 116	Pharmaceutical, Agrochemical
• Novel Chiral Ligands that Enhance Catalytic Reactions	RFT 114	Pharmaceutical, Agrochemical
• Methods and Intermediates for Making B-Amino Acids	RFT 112	Pharmaceutical
• Unique Nanoparticles with Single Functional Groups	RFT 108	Pharmaceutical
• Novel Chemotherapeutic Agents for Anti-Tumor and Anti-Cancer Drugs	RFT 72	Pharmaceutical
• Novel Somatostatins for Diagnostic and Therapeutic Applications	RFT 51	Pharmaceutical
• Methods for Preparation of (R) and (S) Enantiomers of B-Amino Acids	RFT 28	Pharmaceutical
• DNA Vaccine Agents from Treatment of Colibacillosis Infection	RFT 21	Pharmaceutical

## Brief Descriptions

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RFT 282

### ANTI-MICROBIAL COATINGS CONTAINING CHEMICALLY BOUND BIOCIDES FOR BIOMEDICAL APPLICATION

The invention relates to novel antimicrobial environment-friendly coatings that are derived from acrylic polyols that contain chemically bound (tethered) biocide moieties.

The coatings show antimicrobial activity towards various microorganisms including gram-positive and gram-negative bacteria, diatomaceous algae and opportunistic fungal pathogens.

These paints can be suitable for application as paints and coatings in internal or external biomedical device applications.

RFT 263

### DRUG DELIVERY VEHICLE FOR TREATMENT OF EYE DISEASE: GLAUCOMA

The invention describes cerium oxide nanoparticles (nanoceria) as a potential drug delivery vehicle for treatment of the eye disease glaucoma.

While it is known that only a small amount of active medicines manage to penetrate the cornea to treat eye infections, this invention combines nanoceria with hCAII (a compound that blocks the activity of an enzyme believed to play a central role in glaucoma) to form a molecule that is exactly the right size and shape to get through and penetrate into the eye.

The disease involves abnormally high pressure of the fluid inside the eye, which, if left untreated, can result in damage to the optic nerve and vision loss. High pressure occurs, in part, because of a buildup of carbon dioxide inside the eye. This compound blocks an enzyme that produces carbon dioxide.

## MULTIFUNCTIONAL 'DUAL ACTION' ANTIMICROBIAL COATINGS FOR IMPLANTABLE CATHETERS AND TUBES

This invention pertains to 'dual action' antimicrobial polysiloxane coatings having a leachable antimicrobial agent in conjunction with a surface-bound contact active microbial agent. The composition uses silver ions and nanoparticles and quaternary ammonium salts and can be used in coating of implantable medical devices such as urinary catheters and endotracheal tubes.

The covalently bound QAS groups inhibit biofilm formation by microorganisms that come into contact with the coating, such as those present prior to insertion of the device into the body, while the leachable antimicrobial inhibits biofilm formation by microorganisms in the vicinity of the device that do not come into direct contact with the device.

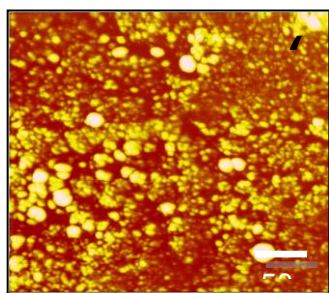
## NOVEL CLAY BASED NANOCOMPOSITES FOR BONE REPLACEMENTS AND OTHER BIOMEDICAL APPLICATION

In recent times, biopolymer based nanocomposites are replacing synthetic polymer composites for various biomedical applications, because of the biocompatible and biodegradable behavior of natural polymers.

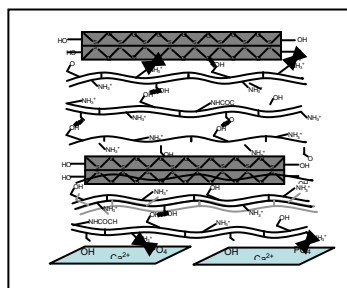
Scientists at North Dakota State University have recently synthesized a biopolymer based novel nanocomposite chitosan/montmorillonite (MMT)/hydroxyapatite (HAP) material that exhibits superior nanomechanical properties and shows promising prospects for use in tissue engineering applications. Properties include:

- Superior nano-mechanical properties
- Intercalated structure formed with an increase in d-spacing
- Well distributed nanoparticles in the chitosan matrix
- Highly biocompatible as exhibited from cell culture experiments

The composite was prepared from chitosan, unmodified MMT, and HAP precipitate in aqueous media. The properties of the composites were analyzed using X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), Atomic force microscopy (AFM), Thermogravimetric analysis (TGA) and nanoindentation. The cell culture experiments show MMT/HAP mix as highly biocompatible.



*Fig. Atomic force microscope phase images of chi/MMT/HAP composites.*



*Fig. Schematic diagram of possible interactions in chi/MMT/HAP composite*

## ANTIBACTERIAL SILOXANE POLYMER CONTAINING TETHERED LEVOFLOXACIN

This invention pertains to the development of a polymer material that exhibits superior sustained release of therapeutic levels of the active antibiotic when compared to simple physical bending or doping technologies. The material is prepared by combining a powerful, broad spectrum antibiotic (Levofloxacin), tethered to a siloxane polymer. This invention can potentially be used to coat a variety of biomedically implanted devices for prevention of microbial infection.

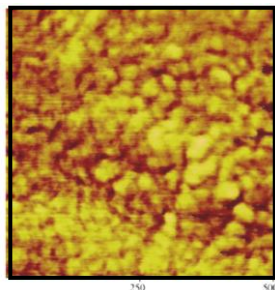
## COMPOSITES FOR BONE TISSUE ENGINEERING FOR APPLICATIONS IN BONE REPLACEMENTS AND PROSTHERICS

Bone tissue engineering represents an alternative approach to the replacement of diseased or damaged bone tissue.

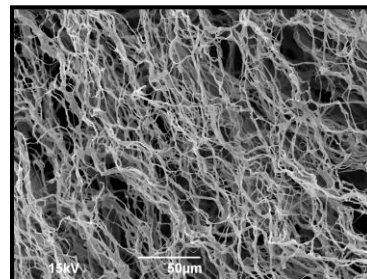
Scientists at North Dakota State University have developed a novel biocompatible composite that may have applications as a bone replacement material. This tri-molecular composite incorporates two well characterized biopolymers known to promote cellular adhesion and colonization, and are slowly degraded to non-toxic products which are absorbed by the body. The composite material is particularly attractive for use as a bone replacement scaffold that allows portions of the scaffold matrix to be replaced with natural bone tissue while maintaining sufficient mechanical strength throughout the bone formation process.

All components of the composite are currently approved by the U.S. FDA for a variety of medical applications. Properties of the material include:

- Superior mechanical properties
- Improved structural integrity under wet conditions
- Uniform distribution of hydroxyapatite nanocrystals
- Highly amenable to tailoring composite properties
- Established biocompatibility with normal proliferation, migration and differentiation of cells



*Fig. Microstructure of composite material, showing uniform distribution of Hydroxyapatite/Biopolymeric nanoparticles*



*Fig. Image of ChiPgAHAP composite showing fibrous scaffold*

## NOVEL ENVIRONMENT FRIENDLY COATINGS FOR BIO-MEDICAL APPLICATIONS

This invention pertains to the synthesis of a formulation that has biocidal activity in a single polymeric compound. The formulation is a unique environmentally friendly coating that holds promise in medical applications. It consists of biocidal moieties that are tethered to its polymer matrix, which in turn prevent them from leaching into the environment.

**APPLICATIONS:** Anti-microbial properties on medical devices.

**PROPERTIES:** The mechanical properties of these coatings are similar to silicone elastomers, yet the coating contains biocidal moieties to deter settlement of organisms. To inhibit leaching of toxic components into the water, biocide moieties are tethered to the polymer matrix.

**PREMISE:** This invention relates to coating formulations based on the modification of moisture cure siloxane elastomers with an alkoxysilane functional polymer containing ammonium salt groups.

## NOVEL LIPOSOMES DESIGNED FOR CONTROLLED RELEASE OF DRUGS

Scientists at NDSU have invented a method to release drugs and other molecules from liposomes triggered by an enzyme which is responsible for cancer cell invasion and metastasis.

The uniquely-designed liposomes release the encapsulated contents in the presence of the enzyme matrix metalloproteinase-9 (MMP-9) within an hour. Other MMPs and proteolytic enzymes do not release the contents from the liposomes. The rate and the extent of contents release are easily controlled by the amount of the active enzyme and the lipid formulations of the liposomes.

In addition, inhibitors of MMP-9 can be delivered from the liposomes with a built-in “feedback” regulation.

The unique design of a lipid-peptide conjugate makes the liposomes susceptible to releasing the encapsulated contents rapidly only in the presence of the cancer associated enzyme MMP-9. The designed lipid-peptide conjugate is not hydrolyzed by the general proteolytic enzymes found in human plasma.

The passive release of drugs and other molecules from liposomes is a slow process. The uniquely-formulated liposomes circumvent this problem by forming on the surface, triple-helical substrate peptides for MMP-9. In the presence of elevated levels of this enzyme (as found for cancer and arthritis patients), the peptides are cleaved rapidly, leading to the liposome destabilization and release of the encapsulated contents. The liposomal formulations are non-toxic to a variety of human cell lines.

## DRUGS AND PESTICIDE ENHANCERS

This invention pertains to the synthesis of molecules that have the capability of enhancing the effects of protein modulators. Its applications include pharmaceuticals and/or agrochemical (pesticide) manufacturing.

This technology provides a means by which the inhibitory effect of a chemical such as drugs or pesticides on a key enzyme in plants/animals can be improved by adding a surface binding group that will bind with the surface of the enzyme. This may result in the chemical occupying and exerting its effect in the active (allosteric) site of the enzyme, more efficiently and for longer durations.

## NOVEL CHIRAL LIGANDS THAT ENHANCES CATALYTIC REACTIONS

This invention concerns the design and synthesis of a new class of modular, chiral ligand molecules and is of value to parties involved in pharmaceuticals and agrochemical manufacturing.

These modular ligands incorporate fluxional groups to control face selectivity. A key advantage to this technology is that the fluxional groups, introduced at a later stage, allow for simple tuning of the face shielding group.

This technology obviates the need for multiple chiral sources and allows the synthesis of a family of ligands with steric groups of varying size from a single chiral source. It enables chemists to introduce a diversity of chemical modifications into a given enantiomer.

## METHODS AND INTERMEDIATES FOR MAKING BETA-AMINO ACIDS

This invention concerns certain  $\alpha$ -, $\beta$ -disubstituted  $\beta$ -amino acids, intermediate chemicals that can be useful in the synthesis of other  $\beta$ -amino acids, and a (Lewis acid-mediated, conjugate amine addition) method for making such  $\beta$ -amino acids.

$\beta$ -amino acids are important segments of bioactive molecules and are components of peptidic natural products with a wide range of biological activity. Peptides consisting of  $\beta$ -amino acids have promising pharmaceutical use as orally active drugs since they are hydrolytically stable. Given the significance of  $\beta$ -amino acids, development of new methodologies for their synthesis, especially for the stereo-selective synthesis of chiral  $\beta$ -amino acids is important.

The present invention relates to a method of making such  $\beta$ -amino acids.

## UNIQUE GOLD NANOPARTICLES WITH SINGLE FUNCTIONAL GROUPS

This invention is a novel method to prepare gold nanoparticles with a single or a limited number of functional groups in large quantities. Such gold nanoparticles are 'real' molecules and traditional synthetic chemistry can be conducted on them to make new nanoparticle materials or nanoparticle probes with predictable and reproducible properties.

This invention holds tremendous commercial value in nanotechnology and biotechnology market.

## NOVEL CHEMOTHERAPEUTIC AGENTS FOR ANTI-TUMOR AND ANTI-CANCER DRUGS

This invention relates to novel, substituted (functionalized) polysiloxane compositions (and methods for synthesis of same) that may be useful as antineoplastics (chemotherapeutics) or other therapeutic agents for cancer treatment.

Since compositions of this type can transverse cellular membranes, they may also serve as delivery vehicles for other agents with biological activities in both animals and plants (e.g., drugs, herbicides, fungicides, anti-microbials, etc.).

A thorough contextual discussion of proposed synthesis and possible drug protocol strategies are included.

## NOVEL SOMATOSTATINS FOR DIANOSTIC AND THERAPEUTIC APPLICATIONS

Somatostatins are ubiquitous polypeptides known to affect basic biological processes such as growth, development, metabolism and cell differentiation in vertebrates.

This invention, developed at North Dakota State University, provides isolated novel somatostatin polypeptides and nucleic acids, methods of making and using these polypeptides and nucleic acids, and methods of modifying mammalian somatostatin polypeptides and nucleic acids.

It also covers methods of modifying mammalian somatostatin polypeptides and nucleic acids for clinical diagnostic and therapeutic uses. Applications of this molecule include:

- Treatment of diabetes, growth disorders, and some neurological disorders.
- Provides methods of modifying mammalian somatostatin polypeptides and nucleic acids.
- New therapy possibilities with somatostatin agonists and antagonists.
- Treatment of tumors, modification of certain metabolic activities.
- Potential for somatostatin analog therapeutics.

## METHOD FOR PREPARATION OF (R) OR (S) ENANCIOMERS OF B-AMINO ACIDS

This is a new method for preparation of either the (R)- or (S)- enantiomers of  $\beta$ -amino acids in good chemical yield and high purity and has potential application for the preparation of other classes of organic compounds. Potential uses include the chiral drug market and laboratory research.

## DNA VACCINE AGENTS FOR TREATMENT OF COLIBACILLOSIS INFECTION

Scientists at North Dakota State University have cloned and sequenced the *iss* (increased serum survival) gene from virulent avian *Escherichia coli* strains and expressed its encoded ISS polypeptide sequence. This has enabled them to conduct studies in understanding the gene's potential and devise strategies to detect and control the colibacillosis infection that the gene is believed to cause.

This invention pertains to the application of this study in formulating DNA vaccines and immunogenic compositions for providing adequate prophylactic, therapeutic and diagnostic remedies against the colibacillosis infection in humans and avian organisms. Applications of this invention could be in:

- Veterinary: Avian DNA vaccine for colibacillosis (in chickens, turkeys, waterfowl) and potential diagnostics.
- Human: Potential human vaccine against urinary tract infections caused by *E. coli*.

FOR FURTHER INFORMATION

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