Development of dermally non-toxic material with longer retention of medicinal properties

Development of fiber material featuring thinness, high strength and comfort for medical application

Development of nonfiber which supports biocompatible material and is suitable for cultivation of cells for tissue engineering

Development of resin with high strength and high thermal conductivity through hybridization of CNF and nanoparticle

Development of gas-permeable mold material for nanoimprint and ultrafine fabrication technology

Formation of an innovative industrial cluster where the use of nanotechnology is the norm

Development of a sustainable system to create innovations through human resource development

Creation of New Value and Market

Creation of New Products and Businesses

Toyama Nanotechnology Manufacturing Cluster

Connect “Nanotechnology” with “Manufacturing” through Industry-Academia-Government-Finance Collaboration

— Practical Application and Industrialization of Cellulose Nanofiber —

Cellulose Nanofiber

Developed by Nano Size Wet Milling Technology of Toyama

Plant Fiber Based New Material

Revolutionary Nano Size Wet Milling Method using Material of Toyama

Nano Size Wet Milling Technology

(Eco-friendly and clean nano sizing technology)

Core Material

Cellulose Nanofiber

• Recyclable resource, reduces environmental burden
• Lightweight and high strength (Weighs 1/5 of iron, and is 5 times stronger than iron)
• Less thermal deformation (1/50 of glass)

High strength & High elasticity

Lightweight

Transparent

Low Thermal Expansion

High Gas-barrier Property

Distinctive Viscosity

Large Specific Surface Area

High Water Holding Property

High Aspect Ratio

Toyama Monozukuri Research and Development Center

Toyama University Faculty of Engineering

Toyama Prefectural University Faculty of Engineering

Formation of an innovative industrial cluster where the use of nanotechnology is the norm

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Toyama New Industry Organization
Improvement of Atomization Technology for Production of Nanoparticles and Nanofibers

Background and purpose of the project:
New materials with new functions by a structural change are required for functional improvement technology. In the manufacturing process, when products are molded from powder, the size of the powder greatly affects the performance of the final product. The aim of this theme is to establish the key technologies to produce nanoparticles for the next-generation manufacturing. We are developing the refinement technology of the nanoparticles and nanofibers of the materials used in electronic and cosmetic/pharmaceutical applications.

Project plans
In the current microfabrication technology, when the particle diameter is several tens of nanometers or less, the strong agglomeration of the particles occurs, making the manufacturing of the material for further refinement very difficult. In this project, we upgrade a wet jet milling technology.

(A) Monodispersion of fine particles
(B) Refinement of nanofiber

By developing these technologies, the biomass nanofibers with excellent dispensability were manufactured.

(Application field)
Electronic parts: high-performance batteries
Pharmaceuticals: highly effective products

Current Status

(A) Evaluation of aggregation/dispersion
   (Electric static potential of nanoparticles by jet milling process)

(B) Development of high-order dispersion technology for the nanoparticles by the following two methods
   ① Chemical method
   ② Physical method

(C) Evaluation methods of the nanoparticles and the nanofibers

Prospects:
Highly refined technology will lead to the innovative products
Biomass nanofiber for the skin care base material
Toyama Industrial Technology Center   Satoshi Iwatsubo, Manager
Kenji Kondoh, Researcher

Background and Purpose of the Project
It is desired to make an effective use of a cellulose and a chitin chitosan from inedible plants and crustaceans biomass. In fields of cosmetics, foods and medicines, the cellulose is widely used as an excipient for a shape preservation and a lipid absorbency base. The purpose of this study is to prepare the advanced skincare materials using the innovative biomass nanofibers.

Characteristics of the CNF
The cellulose nanofiber (CNF) "BiNFi-s" manufactured by Sugino Machine Co., Ltd. was used. The raw material is food additive cellulose. The results of safety test of the nanofibers are shown in a table.

Safety testing (an alternative to animal testing)

<table>
<thead>
<tr>
<th>Test</th>
<th>OECD TG</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial Reverse Mutation Test</td>
<td>471</td>
<td>negative</td>
</tr>
<tr>
<td>Primary skin irritation tests of three-dimensional models</td>
<td>439</td>
<td>negative</td>
</tr>
<tr>
<td>Eye mucous membrane irritation tests of three-dimensional models</td>
<td>492</td>
<td>negative</td>
</tr>
<tr>
<td>In Vitro 3T3 NRU Phototoxicity Test</td>
<td>432</td>
<td>Under consideration</td>
</tr>
<tr>
<td>human patch test</td>
<td></td>
<td>negative</td>
</tr>
</tbody>
</table>

High safety of the nanofibers

The effect of water retention of the CNF in the case of addition to cosmetics

The addition of the CNF to the cosmetics is effective in moisture retention of the stratum corneum. The water concentration of the skin increases.
Research Background

Nanofiber membrane sheets made with electrospinning are gaining attention as a material that has high filterability, moisture permeation and waterproofness. However, it has many problems with productivity and strength.

Therefore, in this research, we are working toward practical application of high performance medical nanomaterial using multi-nozzle type electrospinning machine. We are also studying new combination technology of knitting and nanofiber sheet, and CNF (cellulose nanofiber) and nanofiber sheet.

Research Progress

(a) Composite technology of nanofiber sheet and CNF.

⇒ Coating technology on nanofiber surface.
  • Reduce friction of nanofiber sheet.
  • We attach reinforcement effects on the surface of the nanofiber.
⇒ Nanofibers kneaded and dispersed with CNF.
  • Succeeded in a small sheeting.
  • We plan to develop long sheets.

(b) Laminate technology with nanofibers sheets and knitting.

⇒ Using “Heat welding process.”
  • We added strength and flexibility to nanofibers.

Prospects

Nanofiber by electrospinning method has a high function. However, it has the disadvantage of weak strength too. To overcome this drawback, we are planning to produce ultrathin and highly functional nanofiber sheets by combining cellulose nanofibers or knitting.

The composite nanofiber sheets can be used as medical supplies directly applied to the skin. Such as bandages and surgical tape.
Development of biocompatible material supported nanofibers

Makoto Nakamura, Tanveer Ahmad Mir (Invited researcher):
Graduate School of Science and Engineering (Engineering), University of Toyama

Theme: Development of nanofibers carrying biocompatible materials

Application of nanofibers and nanoparticles is expected to be applied to the fields of medical, biotechnology and medicine. In this research, we aim to do “development of nanofibers carrying biocompatible materials” by combining Toyama’s unique nanotechnology technology with the technology and know-how of Toyama University. We add and fuse biological functions and further combine it with three dimensional modeling technology, various printing technologies and micro nano processing technologies, and develop useful culture substrates and tools for cell culture and regenerative medicine, as well as next-generation pharmaceuticals etc. Aim for application to manufacturing.

1. Add cell biological function
   - Natural polymer
   - Synthetic polymer
   - Biological material
   - Hybrid material

2. Higher dimensional nanocomposites
   - Research and development of materials, equipment, equipment, etc. that contribute to basic medical research, pharmaceutical research and development and clinical medicine field

Applying cell biological function in the age of three-dimensional cell biology era

Theme: "Development of equipment for 3D cell culture"

Equipment for cell culture: call for ambitious collaborators

- 3D micro environment of cells and tissues
- 3D cell culture
- Biosensor
- Drug screening
- Toxicity test
- Animal experiment alternative method
- Regenerative medicine
- Embryology

University of Toyama

The aim of our research

- Cell behavior is transmitted and controlled by nano-sized mechanism
- Cell behavior is transmitted and controlled by nano-sized mechanism and control leads to diagnosis of disease, treatment of disease!

Nanofiber manufacturing technology in Toyama

- Inkjet type fine particle making apparatus
- Composite gel fiber making apparatus
- Electro spinning device

3D bio printing technology

Figure A: High Pressure Water Jet: Milling to Nanofiber with Ultra High Pressure Water Flow: (BINFI-s: Sugino machine)

Figure B: Electro spinning: Fabrication of nanofibers by spinning in high pressure electric field (Gelatin - Nanofiber 2011: Toyama University - Toyama Prefecture Industrial Technology Center - Tayca Pharmaceutical)

Figure C: Nanofibers of extracellular matrix (Porcine kidney nanofiber: University of Toyama, Nakamura Lab.)

Nano size in Medical and Life Sciences

- Atom
- Molecules
- Intracellular Organs
- Cells
- Intracellular Organs
- Organs / Human

Nano size in Medical and Life Sciences

- Atom
- Molecules
- Intracellular Organs
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Nanotechnology manufacturing cluster

- ① 3D Bioprinter (Ver.1 to 3)
- ② Inkjet type fine particle making apparatus
- ③ Composite gel fiber making apparatus
- ④ Electro spinning device

Three dimensional cell biology era

"Development of equipment for 3D cell culture"

- Equipment for cell culture for research in the age of 3-dimensional cell biology
- 3D cell culture equipment
- Special cell culture equipment
- Tailor-made cell culture equipment
- New biosensor and bioanalytics

Application example

- Biomaterial
- Nano material
- Bio-nano material
- Hybrid material

Call for ambitious collaborators

Contribute to the development of Medicine

- 3D cell biology
- Organ regeneration
- 3D regenerative medicine

Ministry of Education, Culture, Sports, Science and Technology
Local Innovation Strategy Support Program
Toyama Nanotechnology Connect Next Generation Manufacturing Creation Program
Development of high strength and high thermal conductivity resin by hybridization of cellulose nanofiber and nanoparticle

Department of Mechanical Systems Engineering, Faculty of engineering, Toyama Prefectural University
Professor Kazuaki Sanada
Visiting Professor Kazuya Nagata

Cellulosic Nanofibers

<table>
<thead>
<tr>
<th>Type</th>
<th>Shape of fibers</th>
<th>Water content</th>
<th>Compounding &amp; Molding Processability</th>
<th>Filler price</th>
<th>collar</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNF</td>
<td>Diameter 4 to 100 nm Length greater than a few μm</td>
<td>60 to 99wt%</td>
<td>Very difficult</td>
<td>Expensive</td>
<td>white</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Greater than ¥10,000/kg at Dry powder</td>
<td></td>
</tr>
<tr>
<td>CCNF</td>
<td>Diameter 20 to 100 nm Length 200 to 800 μm</td>
<td>50 to 3wt%</td>
<td>easy</td>
<td>low cost</td>
<td>white</td>
</tr>
<tr>
<td>LCNF</td>
<td>Diameter 50 to 100 nm Length greater than a few μm</td>
<td>60 to 90wt%</td>
<td>Difficult</td>
<td>low cost</td>
<td>Dark brown</td>
</tr>
</tbody>
</table>

Our Cellulosic Nanofibers CCNF concept

Schematic view of CCNF network structure in a polymer

CCNF composites
- High strength and rigidity
- Light weight
- Low coefficient of linear expansion
- Transparency
- Low friction coefficient
- Gas barrier
- Biomass material etc.

Dispersibility of HA coated CCNF in polymer

Nano Analysis: TEM observation

Automobile parts
Electronic parts
Packing materials etc.
Development of gas permeable template in nanoimprint process and green lithography derived from biomass
Satoshi Takei, Makoto Hanabata
Department of Pharmaceutical Engineering, Faculty of engineering, Toyama Prefectural University

Goal

Applications for green nanopatterning materials
- Biofilms
- Optical films

Nanoimprint

Green lithography

Conventional Template
Gas Permeable Template
UV cross-linkable material including volatile solvent

Void Defect No Error