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THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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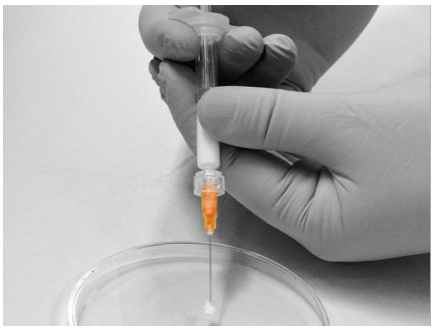


DelSiTech Silica Matrix Drug Delivery

Verified by the innovator, on Mar 2022

Developer(s)

DelSiTech

https://www.delsitech.com/

Finland

DelSiTech is the world technology leader in advanced biodegradable silica based controlled release materials

Sponsor(s)

-

-

Partnerships

Innovare r&d

http://www.innovare-rd.com.mx/

Bayer

https://www.bayer.com/

Astrazeneca

https://www.astrazeneca.com/

Visus Therapeutics

https://www.visustx.com/

The Bill & Melinda Gates Foundation

https://www.gatesfoundation.org/

UNITAID

https://unitaid.org/#en

Technology information

Type of technology

Silica microparticles; silica hydrogel; silica microparticles and silica hydrogel composite,, Biodegradable monolithic solid silica implant, Inorganic nanoparticles

Administration route

Subcutaneous, Intra-articular, intratumoral, intraocular, intrathecal and transtympanic, Intra-vitreal, Intramuscular, intratumoral, intraocular, intrathecal and transtympanic

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Entecavir (ETV)

Development Stage

Pre-clinical

Regulatory Approval

No

Description

Long-acting injectables (parenteral administration) and topical eye drops drug delivery technology where the active substance is embedded and released in controlled manner from a biodegradable silica microparticle-silica hydrogel composite material, with release period tunable from a day to several weeks, months up to a year.

Technology highlight

DelSiTech Silica Matrix long-acting drug delivery technology is adaptable to any therapeutic agents: from small molecules to peptides and complex biologics. The technology is compatible with high API loading, but also with poorly or highly soluble molecules. True controlled release that can be tuned from days up to a year, following zero-order release profile with no or limited burst release. The final dosage form is a ready to use prefilled syringe with 24 to 30G needle. Silica microparticle-silica hydrogel depot can be easily removed as one piece in case of adverse effects. With eyedrops the release can be adjusted from 24 to 48 hours with stable API concentration even overnight with a single drop.

Technology main components

The formulation contains only one main excipient silica (SiO2). in addition, WFI (water for injection), and pH controlling agents (in the hydrogel component).

Information on the raw materials sourcing, availability and anticipated price

Tetraethyl orthosilicate (TEOS) the silica precursor is widely available material used for various application.

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Not provided

Additional solubility data

Not provided

Additional stability data

APIs are stable in solid silica microparticles. There is no chemical/biological interaction with the Silica nor with external environment.

API loading: Maximum drug quantity to be loaded

30-50 wt%

API co-administration

2 different APIs : No technical limits.

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

Spray-drying process is highly scalable process and widely used.

Tentative equipment list for manufacturing

Mixer and pumping prior spray drying. Spray drying equipment. Fill and finish equipment

Manufacturing

Normal manufacturing requirements for spray drying and aseptic fill and finish.

Specific analytical instrument required for characterization of formulation

HPLC equipment, capability to perform immunoassays and the appropriate detection equipment required by the API. Dynamic light scattering (DLS) instrument for particle size distribution. Dissolution for release characteristics in water bath in shaking. Silica measurement with microwave plasma-atomic emission spectroscopy (MP-AES) or with spectrophotometric measurements. Rheometric analysis (oscillation and rotation), manual injectability and injection force measurement. SEM analysis for visualizing the particles. NMR for measuring silica condensation.

Clinical trials

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

Can be determined with a partner. Can be introduced during clinical studies.

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Single-use
- Room temperature storage
- Monolithic
- Removable
- Other(s)

  +4 to +8 degrees Celsius storage may be needed in some cases

Release properties

Release time is adjustable: as fast as one day or as slow as one year. The release is based on surface erosion mechanic.

Injectability

Silica microparticles-hydrogel depot has shear thinning properties and can be used with pain-free needles up to 30G.

Safety

Silica is inert, non-toxic and completely bio-dissolvable. The main degradation product is soluble silicic acid that is a natural component of the body. Silica is accepted for topical use and tox tolerability data available for injectables.

Stability

The APIs is homogeneously dispersed and encapsulated in inert solid silica microparticles, maintaining high chemical stability and biological activity for the APIs

Storage conditions and cold-chain related features

Room-temperature storage if encapsulated drug does not require refrigeration

Potential application(s)

Therapeutic area(s)

Diabetes
HBV
Contraception
Other(s) : "Ophthalmology (topical and parenteral delivery), infectious diseases, autoimmune disease, CNS, women´s health, hormone deficiency, vaccines, abuse deterrence & viral vectors"
Multipurpose technology : "Possible to combine multiple APIs from poorly/highly soluble small molecules to sensitive biologics like antibodies and RNA."
Malaria
HIV
Pain management
Oncology
Disease agnostic

Use case(s)

Pre-Exposure Prophylaxis (PrEP)
Treatment

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker
- To be determined
- Self-administered

Frequency of administration

Daily, Weekly, Monthly, Once every 6 months, Yearly, Once every 2 months

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults

Genders

- All
- Male
- Female
- Cisgender female
- Cisgender male
- Transgender female
- Transgender male
- Intersex
- Gender non-binary

Pregnant individuals

Yes

Lactating individuals

Yes

Healthy individuals

Yes

Comment

Those who would benefit from longer dosing intervals or for whom adherence to current treatment might be challenging.

Potential associated API(s)

Entecavir (ETV)

Class(es)

antiviral

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Hepatitis B treatment

Foreseen user group

People living with hepatitis B chronic infection

Foreseen duration between application(s)

2 months

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

No

Immunoglobulins

Class(es)

Monoclonal antibody

Development stage

Pre-clinical

Clinical trial number(s)

-

Foreseen/approved indication(s)

HIV PrEP

Foreseen user group

Individuals at risk of contracting HIV

Foreseen duration between application(s)

To be determined

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

-

Antivirals for systemic use, Cabotegravir (CAB), Dolutegravir (DTG), Islatravir (ISL)

Class(es)

Dolutegravir, cabotegravir, islatravir etc.

Development stage

Pre-clinical

Clinical trial number(s)

-

Foreseen/approved indication(s)

HIV treatment and/or prevention

Foreseen user group

To be determined

Foreseen duration between application(s)

To be determined

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

-

Genito-urinary system and sex hormones, Levonorgestrel (LNG), Etonogestrel (ENG), Oxytocin, Testosterone (T)

Class(es)

levonorgestrel, etonogestrel, testosterone, oxytocin, etc.

Development stage

Not provided

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Glucocorticoids, Dexamethasone

Class(es)

Dexamethasone etc.

Development stage

Not provided

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Analgesics, Fentanyl, hydrocodone

Class(es)

Hydrocodone, fentanyl etc.

Development stage

Not provided

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Antiparasitic products, Pyrimethamine, Antimalarials, Proguanil

Class(es)

Pyrimethamine, proguanil etc

Development stage

Pre-clinical

Clinical trial number(s)

-

Foreseen/approved indication(s)

Malaria treatment and/or prophylaxis

Foreseen user group

Not provided

Foreseen duration between application(s)

to be determined

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

-

Drugs used in diabetes, Glucagon-like peptide-1 (GLP-1) analogues (GLP-1)

Class(es)

GLP-1 receptor agonist

Development stage

Not provided

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Musculo-skeletal system, Meloxicam

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

-

Foreseen/approved indication(s)

Targets post-operative pain management in cats

Foreseen user group

Animal health

Foreseen duration between application(s)

Anticipated: release of meloxicam for 3 to 5 days after a single subcutaneous injection

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

-

Patent info

Technology patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Hydrogel composite depot formulation Expiry date: 2036-10-21 This invention relates to a depot formulation comprising a biodegradable silica hydrogel composite incorporating a nucleotide or nucleoside analogue reverse transcriptase inhibitor, wherein the silica hydrogel composite is obtainable by mixing silica particles comprising said nucleotide or nucleoside analogue reverse transcriptase inhibitor and having a maximum diameter of ≤ 1 000 µm, as such or as a suspension, with silica sol wherein the hydrogel composite is non-flowing and structurally stable when stored at rest and shear-thinning when shear stress is applied by injection. The present invention also relates to use of the depot formulation for treatment of chronic viral infections and prevention of chronic viral reinfection. The present invention further relates to a prefilled syringes comprising said depot formulation.	WO2017068245		DELSITECH OY	No	MPP search

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income

Granted	China, Türkiye, Moldova, Republic of, Mexico, South Africa, India, Brazil	Australia, Liechtenstein, Italy, Norway, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, Austria, Romania, Finland, France, Bulgaria, Poland, Latvia, Ireland, Germany, Portugal, Czechia, Lithuania, Sweden, Japan, Korea, Republic of, United States of America
Filed		Canada
Not in force	World Intellectual Property Organization (WIPO), Morocco, Albania, Serbia, Bosnia and Herzegovina, Montenegro, North Macedonia	World Intellectual Property Organization (WIPO), Malta, San Marino, Slovenia, Iceland, Cyprus, Slovakia, Estonia, Luxembourg, Monaco

MPP Licence(s)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Silica Hydrogel Composite Expiry date: 2034-06-18 This invention relates to a silica hydrogel composite obtainable by mixing silica particles, comprising an encapsulated agent, with a silica sol, wherein obtained hydrogel composite is shear-thinning. The present invention also relates to use of the silica hydrogel composite according to the invention for an injectable, flowing or extrudable formulation. The present invention further relates to a method for preparing the silica hydrogel.	WO2014207304		DELSITECH OY	No	Company

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	China, Türkiye	Australia, Canada, Liechtenstein, Italy, Norway, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, Austria, Romania, Finland, France, Bulgaria, Poland, Latvia, Ireland, Germany, Portugal, Czechia, Lithuania, Sweden, Japan, United States of America
Filed		
Not in force	World Intellectual Property Organization (WIPO), Albania, Serbia, Bosnia and Herzegovina, Montenegro, North Macedonia	World Intellectual Property Organization (WIPO), Malta, San Marino, Slovenia, Iceland, Cyprus, Slovakia, Estonia, Luxembourg, Monaco

MPP Licence(s)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Method for preparing silica compositions, silica compositions and uses thereof Expiry date: 2028-02-22 The invention relates to a method for producing a flowing silica composition comprising a sol-gel transfer, wherein redispersion is carried out. The redispersion comprises adding, after having reached gel point of said sol-gel transfer, liquid into the gel formed by the sol-gel transfer, and the adding being made within a sufficiently short time period after reaching the gel point, to result, after mixing to follow of the gel and the liquid, in a rheologically homogenous flowing silica composition, which is and remains injectable as such, or by short stirring < 30 s, through a thin 22G needle. The present invention also relates to flowing silica compositions and gels obtainable by methods of the invention. The present invention further relates to uses of flowing silica compositions	WO2008104635		DELSITECH OY	No	Company

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Serbia	Canada, Liechtenstein, Denmark, United Kingdom, Netherlands, Switzerland, Finland, France, Germany, Sweden
Filed		

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Albania, Bosnia and Herzegovina, Türkiye, North Macedonia	World Intellectual Property Organization (WIPO), Australia, Italy, Norway, Malta, Belgium, Greece, Hungary, Croatia, Spain, Slovenia, Austria, Romania, Iceland, Cyprus, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Luxembourg, Portugal, Czechia, Lithuania, Monaco, United States of America

MPP Licence(s)

Supporting material

Publications

** Silica microparticles for sustained zero-order release of an anti-CD40L antibody. Tyagi P, Koskinen M, Mikkola J, Leino L, Schwarz A. Drug Deliv Transl Res. 2018 Apr;8(2):368-374. doi: 10.1007/s13346-017-0408-1. PMID: 28752299. **

Silica microparticle hydrogel depot (HG) formulation was prepared using spray drying of silica-based sol-gels for the sustained delivery of MR1 antibody which binds to CD40 ligand (CD40L). The formulation was tested in vitro for antibody release, surface morphology, particle size, rheology, and injectability. In vivo pharmacokinetic evaluation was performed for the microparticle formulation and free MR1 antibody in BALB/c female mice. Serum samples up to day 62 were assessed using an enzyme-linked immunosorbent assay. In vitro release indicated that the MR1 antibody was uniformly encapsulated in silica microparticles, and less than 5% burst release of the antibody was observed. In vivo pharmacokinetics showed a zero-order release up to 62 days from the MR1 silica microparticle HG-controlled release composition.

Keywords: Antibody; Biologics; Silica microparticles; Sustained release.

** Sustained In-Vivo Release of Triptorelin Acetate from a Biodegradable Silica Depot: Comparison to Pamorelin® LA Nanomedicines, June 2021 Ari-Pekka Forsback, Panu Noppari, Jesse Viljanen, Jari Mikkola, Mika Jokinen, Lasse Leino, Simon Bjerregaard, Camilla Borglin and Janet Halliday **

Triptorelin acetate was encapsulated into silica microparticles by spray-drying a mixture of colloidal silica sol and triptorelin acetate solution. The resulting

microparticles were then combined with another silica sol containing silica nanoparticles, which together formed an injectable silica-triptorelin acetate depot. The particle size and surface morphology of the silica-triptorelin acetate microparticles were characterized together with the in vitro release of triptorelin, injectability and rheology of the final injectable silica-triptorelin acetate depot. In vivo pharmacokinetics and pharmacodynamics of the silica-triptorelin acetate depot and Pamorelin® were evaluated and compared in Sprague-Dawley male rats after subcutaneous administration. Serum samples up to 91 days were collected and the plasma concentrations of triptorelin and testosterone were analyzed with ultraperformance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). In vivo pharmacokinetics showed that injections of the silica-triptorelin acetate depot gave 5-fold lower Cmax values than the corresponding Pamorelin® injections. The depot also showed a comparable sustained triptorelin release and equivalent pharmacodynamic effect as the Pamorelin® injections. Detectable triptorelin plasma concentrations were seen with the depot after the 91-day study period and testosterone plasma concentrations remained below the human castration limit for the same period.

Additional documents

- Parenteral delivery of therapeutic proteins using biodegradable silica matrix - LAII2020 conference

Useful links

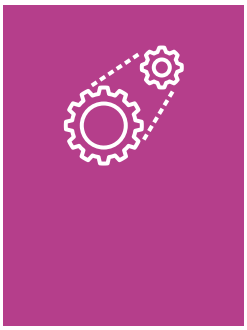
- Short Video presenting the technology

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Agree



Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Agree

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Agree

Comment & Information

More information available at https://www.delsitech.com/

Illustrations

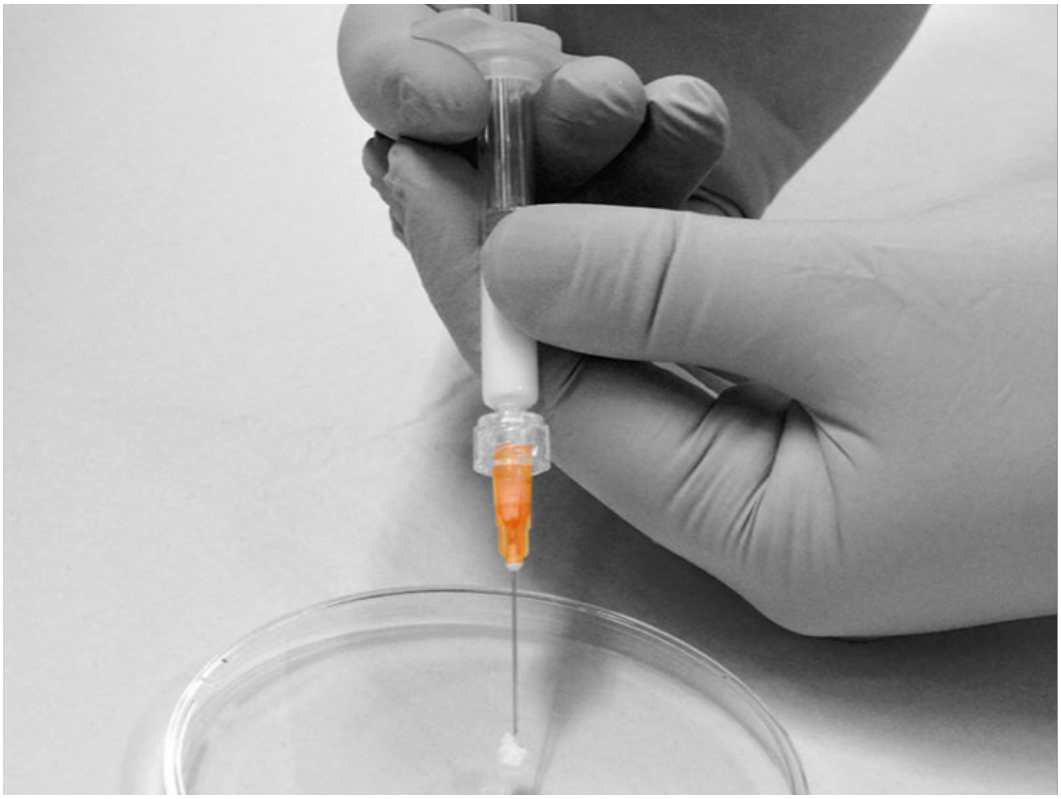
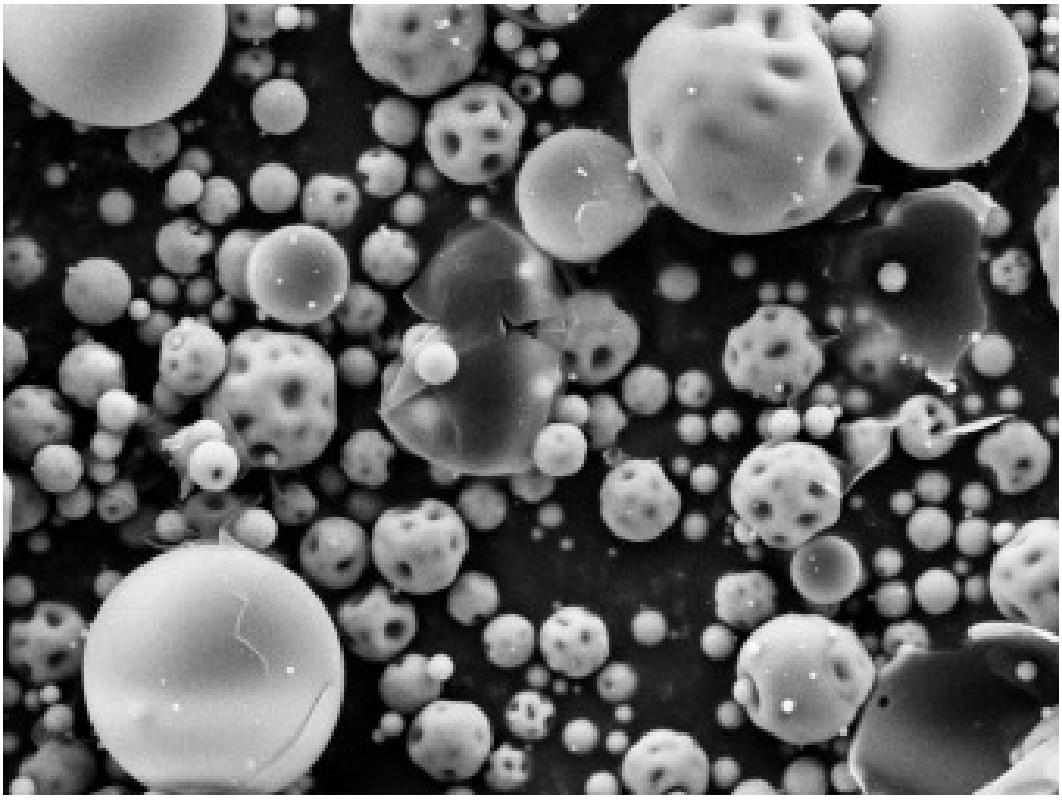


Image of the injection

DelSiTech



SEM images of silica-triptorelin acetate microparticles (magnification 5000×)