TaBaTa gel
for controlled release

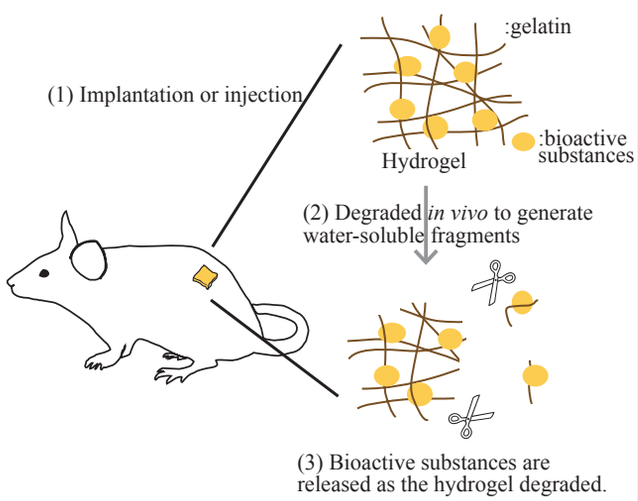
Biodegradable hydrogel for sustained release of bioactive substances

For research use only

The **TaBaTa Gel** is a gelatin-based hydrogel for the sustained release of bioactive substances. The hydrogel material has advantages of;

- ☺ Simple use just by dropping aqueous solution
- ☺ Sustained release over 2-3 weeks
- ☺ Hold and stabilize bioactive substances *in vivo*
- ☺ Site-specific release of bioactive substances
- ☺ Easily cut to a desired size and shape

Product outline



This hydrogel is prepared by chemical cross-linking of gelatin, and bioactive substances are immobilized in the hydrogel through the intermolecular interaction forces with gelatin. (1)upon administration into the body,(2)the hydrogel is degraded by enzymes, such as collagenase secreted from the surrounding tissue, and (3)bioactive substances immobilized are released as the hydrogel is degraded.

Before use

■ **TaBaTa gel** is supplied in a freeze-dried state. Store at room temperature and avoid humidity.

■ EOG (Ethylene oxide gas) sterilization is recommended.

■ Sterility is guaranteed before opening the package.

■ **For research use only.**

Not intended for any animals or human therapeutic or diagnostic use.

How to use TaBaTa gel

1. Selection of an optimum hydrogel

An optimum hydrogel for the sustained release of bioactive substances is determined by the electric charge of bioactive substances (isoelectric point of protein) and the molecular weight. To maximize the release effect of hydrogel, please conduct a selection test before the *in vivo* use.

For the bioactive substances which the optimum hydrogel is known, please refer the table on the back page. If you cannot find the bioactive substances of your interest, please contact the technical support of MedGEL.

-The selection test (***in vitro***)-

＊Required reagent and supplies ＊

- Micro balance
- Incubator
- Bioactive substances detection system
- Microcentrifuge tubes (1.5ml -2.0ml)
- Aqueous solution of bioactive substances 20µl (*1)
- **TaBaTa gel** (freeze-dried hydrogel sheet) (IP5, IP9) 2mg each
- Phosphate-Buffered Saline (PBS) without Ca^{++} & Mg^{++}

1-1 Cut and place 2mg of **TaBaTa gel** into a microcentrifuge tube, and 20µl of aqueous solution of bioactive substances is dropped onto the hydrogel. (n=3-5) (*2)

1-2 Leave the **TaBaTa gel** for 30min at room temperature or for overnight at 4 °C to allow the bioactive substances to sorbs into the hydrogel completely. (*3)

1-3 Add 1ml of 1/10 PBS into the tube, followed by gentle shaking.

1-4 Collect the PBS supernatant 30 min or 2, 4 and 8hr later. Add 1ml of fresh PBS to the tube again.

1-5 Measure the concentration of supernatants collected to evaluate the time profile of bioactive substances released.

(*1) Bioactive substances should be dissolved with double distilled water or 1/10 PBS. Solution containing carrier proteins or chelate compounds often suppresses the intermolecular interaction between the hydrogel and bioactive substances.

(*2) Be sure to exactly drop the aqueous solution of bioactive substances onto the hydrogel without spilling over.

(*3) For bioactive substances which has a low affinity for gelatin, prolong the sorbing time up to 3 hr at 37°C.

For optimization, it is necessary to select the hydrogel which shows less cumulative amount of bioactive substances released.

2. Preparation of bioactive substances-incorporated hydrogel

For the purpose of implantation and injection, please use the sterilized hydrogel. Bioactive substances should be dissolved with double distilled water, PBS or normal saline. Do not use the solution containing carrier

protein or at high ionic concentrations.

-Required reagent and supplies -

- Micro balance
- Incubator
- Sampling tubes
- **Aqueous solution of bioactive substances**
- **TaBaTa gel** (sheet or microsphere)

2-1 Weigh the freeze-dried **TaBaTa gel**. (Ex. 2mg per mouse)

2-2 Prepare about 10μl of aqueous solution of bioactive substances per 1mg of **TaBaTa gel**.

2-3 Drop the a aqueous solution of bioactive substances onto the freeze-dried hydrogel and leave it for 30min at room temperature, or for overnight at 4°C to allow the bioactive substances sorbs into the hydrogel completely.

<sheet>

2-4 Implant the bioactive substances-incorporated hydrogel to animals by surgical treatment.

<microsphere>

2-4 Add appropriate amount of saline for injection.

2-5 Inject bioactive substances-incorporated microsphere to animals following dispersion. (*1)

(*1) Use 25G and above needle to inject.

Q&A

- Can we decide the type of hydrogel only by the isoelectric point of protein?
  In addition to the electrostatic force, the molecular weight and the space structure of protein will affect the intermolecular interaction between the MedGel and proteins. We recommend to conduct the selection test.
- 100% of bioactive substances were released from the hydrogel. Why?
  Check the solvent of bioactive substances. Solution at low ionic strengths is recommended.
- Should we wait the hydrogel get transparent after the bioactive substances solution dropping?
  Air bubbles are sometimes seen in the swollen hydrogel, but there is no influence of the hydrogel appearance on the release profiles.
- Can we trace the degradation of **TaBaTa gel** or release of bioactive substances?
  To get the precise profile, we recommend a radioisotope trace procedure.

For further information, please contact the technical support of MedGEL.

Optimal hydrogel for different bioactive substances

Hydrogel type	bioactive substances
IP5	bFGF (Basic Fibroblast Growth Factor) TGF-β1 (Transforming Growth Factor) HGF (Hepatocyte Growth Factor) PDGF-BB (Platelet-Derived Growth Factor) NGF (Nerve Growth Factor) BDNF (Brain-derived neurorophic factor) GDNF (Glial cell line -derived neurorophic factor) PRP (Platelet-Rich Plasma)、cisplatin
IP9	BMP-2 (Bone Morphogenic Protein 2) HB-EGF (Heparin-Binding EGF-like Growth Factor) KGF (Keratinocyte Growth Factor) FGF10 (Fibroblast Growth Factor) EPO (Erythropoietin)
E50	EGF (Epidermal Growth Factor) G-CSF (Granulocyte Colony Stimulating Factor) CTGF (Connective Tissue Growth Factor) Plasmid DNA、siRNA

TaBaTa gel is also available for the sustained release of peptide and antibody

References

Review

Tabata Y. Significance of release technology in tissue engineering. Drug Discov Today. 2005 10(23-24):1639-46.

Yamamoto M, Tabata Y. Tissue engineering by modulated gene delivery. Adv Drug Deliv Rev. 2006 58(4):535-54.

Original paper

Yamamoto M, Takahashi Y, Tabata Y. Controlled release by biodegradable hydrogels enhances the ectopic bone formation of bone morphogenetic protein. Biomaterials. 2003 24(24):4375-83.

Tabata Y, Nagano A, Ikada Y. Biodegradation of hydrogel carrier incorporating fibroblast growth factor. Tissue Eng. 1999 (2):127-38.

Code	Hydrogel type	Release period	Shape	package
IP5-MG	IP5	2week	sheet (approx. 25 x 25 x 3mm)	hydrogel 150mg saline 1.5ml×2
IP5-MGMS		3week	microsphere	hydrogel 15mg×2 saline 1.5ml×2
IP9-MG	IP9	2week	sheet (approx. 25 x 25 x 3mm)	hydrogel 150mg saline 1.5ml×2
E50-MG	E50	3week	microsphere	hydrogel 15mg×2 saline 1.5ml×2

Manufacturing by MedGEL

For research use only. Not for clinical diagnosis.

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