MedGel

for controlled release

Biodegradable hydrogel for sustained release of drug

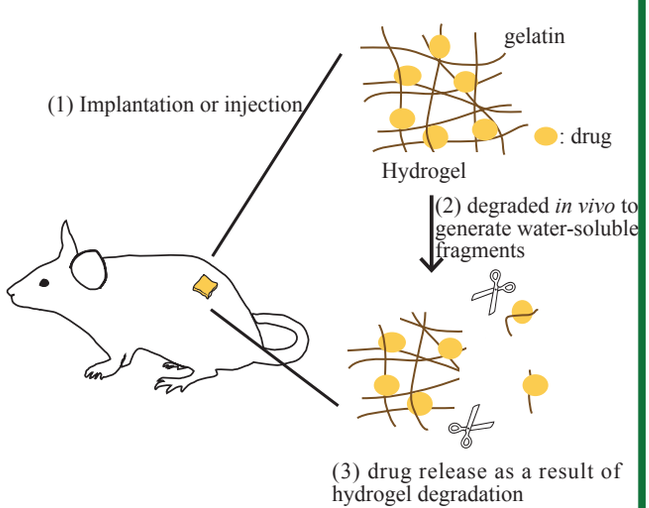
For research use only

MG0911EJ-1

The **MedGel** is a gelatin-based hydrogel for the sustained release of drug. The hydrogel material has advantages of;

- ☺ Simple use just by adding drug
- ☺ Drug release over 2 weeks
- ☺ Drug stabilization *in vivo*
- ☺ Site-specific drug release
- ☺ Easily cut to a desired size and shape

Mechanism of Drug Release



This hydrogel is prepared by chemical cross-linking of gelatin, and drug is 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)drug immobilized is released as the hydrogel is degraded.

Before use

■ **MedGel** 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 MedGel

1. Selection of an optimum hydrogel

An optimum hydrogel for the sustained release of drug is determined by the electric charge of drug (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 drug which the optimum hydrogel is known, please refer the table on the back page. If you cannot find the drug of your interest, please contact the technical support of MedGEL.

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

＊ Required drug and supplies ＊

- Micro balance
- Incubator
- Drug detection system
- Microcentrifuge tubes (1.5ml -2.0ml)
- **Drug solution** 20µl (*1)
- **MedGel** (freeze-dried hydrogel sheet) (PI5, PI9) 2mg each
- Phosphate-Buffered Saline solution(PBS) without Ca^{++} & Mg^{++}

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

1-2 Leave the **MedGel** for 30min at room temperature or for overnight at 4 °C to allow the drug 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 drug concentration of supernatants collected to evaluate the time profile of drug released.

(*1) Drug 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 drug.

(*2) Be sure to exactly drop the drug solution onto the hydrogel without spilling over.

(*3) For drug 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 drug released.

2. Preparation of drug-incorporated hydrogel

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

at high ionic concentrations.

-Required drug and supplies -

- Micro balance
- Incubator
- Sampling tubes
- **Drug solution**
- **MedGel** (sheet or microsphere)

2-1 Weigh the freeze-dried **MedGel**. (ex. 2mg per mouse)

2-2 Prepare about 10μl of drug solution per 1mg of **MedGel**.

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

<sheet>

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

<microsphere>

2-4 Add appropriate amount of saline for injection.

2-5 Inject drug-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 drugs will affect the intermolecular interaction between the MedGel and drug. We recommend to conduct the selection test.

- 100% of drugs was released from the hydrogel. Why?

  Check the solvent of drug. Solution at low ionic strengths is recommended.

- Should we wait the hydrogel get transparent after the drug solution dropping?

  Air bubbles are sometimes seen in the drug solution swollen hydrogel, but there is no influence of the hydrogel appearance on the release profiles.

- Can we trace the degradation of **MedGel** or release of drug?

  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 drugs

Hydrogel type	drugs
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

MedGel 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
PI5-9480E53	IP5	2week	sheet (approx. 25 x 25 x 3mm)	150mg
PI5-95MS		3week	microsphere	15mg x 2
PI9-9910E53	IP9	2week	sheet (approx. 25 x 25 x 3mm)	150mg
E50-MS2	E50	3week	microsphere	15mg x 2

＊ All products are EOG sterilized.

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