Nitta Gelatin Inc.

MedGel™ II

for controlled release

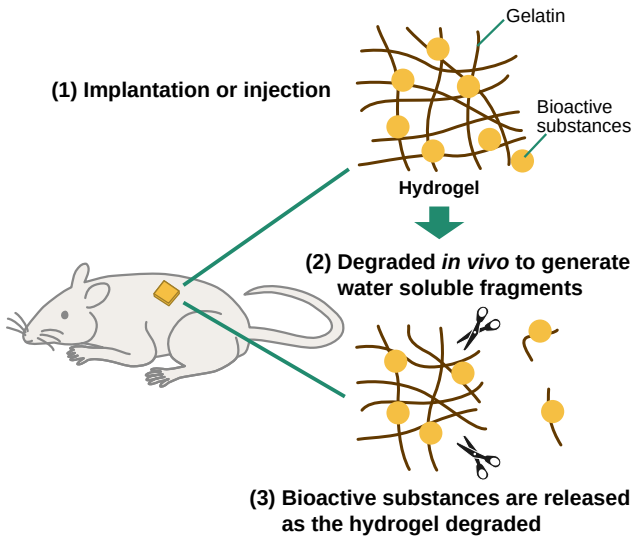
Biodegradable hydrogel for sustained release of bioactive substances

For research use only

The **MedGel™ II** is an advanced 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 few 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 physical 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

- **MedGel™ II** comes in pre sterilized packing.
- Sterility is guaranteed before opening the package.
- Best before: 2 years from manufacturing.
- Store at room temperature, away from moisture and heat.
- **For research use only.**
  Not intended for any animals or human therapeutic or diagnostic use.

How to use MedGel™ II

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.

The selection test (*in vitro*)

0 Required reagent and supplies

- Micro balance
- Incubator
- Bioactive substances detection system
- Microcentrifuge tubes (1.5ml - 2.0ml)
- Aqueous solution of bioactive substances 20µl *1
- **MedGel™ II** (PI 5, PI 9) 2mg each
- Phosphate-Buffered Saline (PBS) without Ca^{++} & Mg^{++} (10x diluted)

1 Cut and place 2mg of **MedGel™ II** into a micro centrifuge tube, and 20µl of aqueous solution of bioactive substances is dropped onto the hydrogel. (n=3 - 5) *2

2 Leave the **MedGel™ II** for 30min at 37°C or for overnight at 4°C to allow the bioactive substances sorbs into the hydrogel completely. *3

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

4 Collect the 1/10 PBS supernatant at various collection times of 30 min, 2, 4 and 8hr. Add 1ml of fresh 1/10 PBS to the tube again.

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 have a low affinity for gelatin, prolong the absorbing 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 concentration.

0 Required reagent and supplies
- Micro balance
- Incubator
- Sampling tubes
- Aqueous solution of bioactive substances
- **MedGel™ II** (sheet or particle)

1 Weigh the **MedGel™ II**. (Ex. 2mg per mouse)
2 Prepare about 10µl of aqueous solution of bioactive substances per 1mg of **MedGel™ II**.
3 Drop the aqueous solution of bioactive substances onto the hydrogel and leave it for 30min at 37°C, or for overnight at 4°C to allow the bioactive substances sorbs into the hydrogel completely.

<Sheet>

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

<Particle>

4 Add appropriate amount of saline for injection.
5 MInject bioactive substances-incorporated particle to animals following dispersion.*4

*4 Use 25G and above needle to inject.

Q&A

Q Can we decide the type of hydrogel only by the isoelectric point of protein?

A In addition to the electrostatic force, the molecular weight and the space structure of protein will affect the intermolecular interaction between the **MedGel™ II** and proteins. We recommend to conduct the selection test.

Q 100% of bioactive substances were released from the hydrogel. Why?

A Check the solvent of bioactive substances. Solution at low ionic strength is recommended.

Q Should we wait the hydrogel get transparent after the bioactive substances solution dropping?

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

Q Can we trace the degradation of **MedGel™ II** or release of bioactive substances?

A To get the precise profile, we recommend a radioisotope trace procedure.

MedGel™ II 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.

Manufactured by Nitta Gelatin Inc.
E-mail: info-bematrix@nitta-gelatin.co.jp