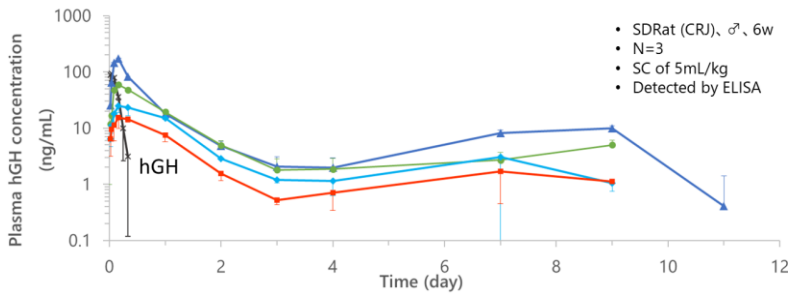
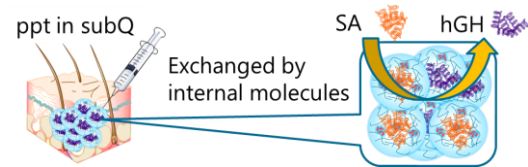
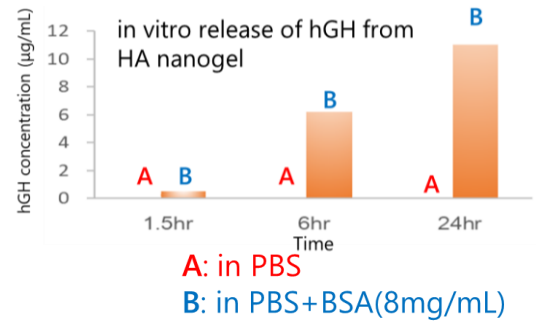


## Plasma PK of hGH after SC



Formulation	hGH	(mg/kg)	0.5	1.5	3	4.5	6
		(Loading %w/w)	-	5	10	15	20
		(mg/mL)	0.1	0.3	0.6	0.9	1.2
	HA nanogel	(mg/mL)	-	6	6	6	6
PK parameters	Cmax	(ng/mL)	99.1	16.8	27.8	58.8	173.2
	AUCinf	(ng hr/mL) <sup>†</sup>	332	562	970	1711	2963
	MRTinf	(hr)	2.6	58.4	55.7	53.1	66.3
	BA (vs SC)	(%)	-	58.2	50.3	59.1	76.8

## Speculated mechanism of sustained release from HA nanogel



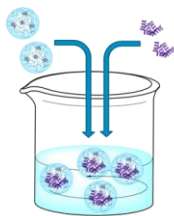
## SC injection

- hGH was dose-dependently released for 10 days.
- AUCinf increased proportionally with dose.
- hGH was released by addition of BSA.
- hGH might be released by exchange with internal molecules such as SA.

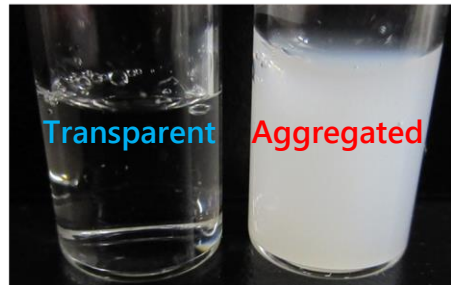
## Anti-aggregation of protein

### Protection from thermal denaturation

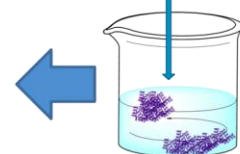
HA nanogel/ Conalbumin in water  
6mg/mL / 2mg/mL



Incubation at 58°C for 12h



Conalbumin in water  
2mg/mL



Same effect detected for both grades

- HA nanogel could protect conalbumin from aggregation caused by thermal denaturation

## Improvement of Solubility

### Solubility enhancement of drugs with poor solubility in water, by HA nanogel

Drug	Mw	Solubility (µg/mL)	Solubility with HA nanogel (µg/mL)	Enhanced solubility (times)
Paclitaxel	854	<0.3	50	> 160
Itraconazole	705	< 1	3,800	> 3,800
Cyclosporine A	1,202	30	10,000	> 300

### Comparison of solubilizing effect of HA nanogel with other solubilizers

Solubility of CyA in solubilizer (50mg/mL)	
HA nanogel:	10,000 µg/mL
Cremophor EL:	1,000 µg/mL *
TW80/TW20:	500 µg/mL *
Cyclodextrins:	100 µg/mL *

\* AAPS PharmSciTec 2001, 2(1), article 2  
(<http://www.pharmscitech.com>)

- HA nanogel can improve the solubility of poorly water-soluble drugs.