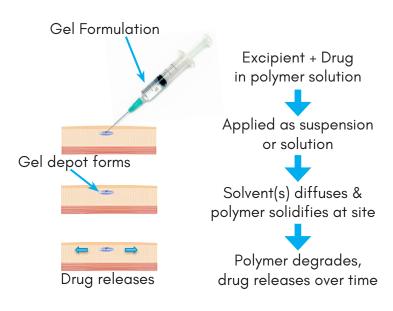
SUSTAINED RELEASE GEL FORMULATION



Release Mechanism



PLGA - poly(lactic-co-glycolic acid)

- Monomer: lactic acid (LA) and glycolic acid (GA)
- Amorphous, biocompatible andbiodegradable polymer (Tg: 40-60 C)
- Long clinical experience, favorable degradation characteristics
- Application: sustained delivery of small molecule, peptide & protein
- Degradation: hydrolysis of its ester linkages in the presence of water
- Degradation half-life: determined by molecular weight, the ratio of lactic acid to glycolic acid and end group of polymer

Gel Formulation - Dosage Form

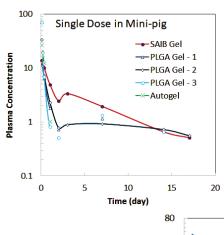


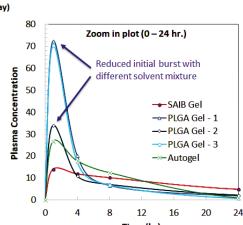


Suspension Gel Formulation

Attribute	Solution	Suspension
API Solubility	Need suitable solubilizing agent	NA
API Particle Size (PSD)	NA	Control & maintain PSD during mfg & storage
API Chemical Stability	Generally less stable in the solution	Generally more stable in the solid form
API Physical Stability	NA	Need suitable suspending agent and avoid aggregation
Dose Volume	Larger dose volume due to solubility limitation	Lower dose volume may require bigger needle
Syringeablity	Relatively smaller needle	Relatively bigger needle
Release	Relatively higher initial burst	Relatively lower initial burst
Manufacturing	Standard mfg process DP can be sterilized by filtration	Control & maintain PSD during Aseptic mfg. DP cannot be filtered

Formulation Screening Various Gel Systems for Weekly Delivery



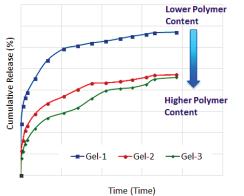


Note: Time (hr)
SAIB gel contains 6% API loading
PLGA gel contains 10% API loading with various solvent mixtures
Autogel contains 30% API loading

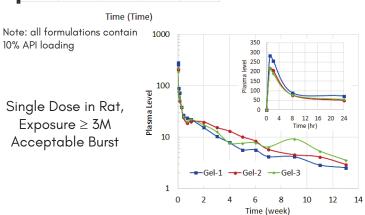
SUSTAINED RELEASE GEL FORMULATION



Formulation Screening PLGA Gel for ≥ 3M Delivery



IVR in pH 7.4 at 37°C, 50 rpm



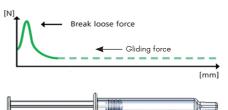
Syringeability for PLGA Gel **Acceptable Break Loose Force**

DDE Data: Break loose force for PLGA Gel Systems provide ≥ 3M Delivery

Sample	Needle Gauge	Break Loose Force (N)
PLGA Gel-1	21G 1"	5.93
	23G 1" UTW	6.12
	25G 5/8" UTW	8.85
PLGA Gel-2	21G 1"	7.96
	23G 1" UTW	13.9
	25G 5/8" UTW	21.81
PLGA Gel-3	21G 1"	21.53
	23G 1" UTW	41.71
	25G 5/8" UTW	> 60

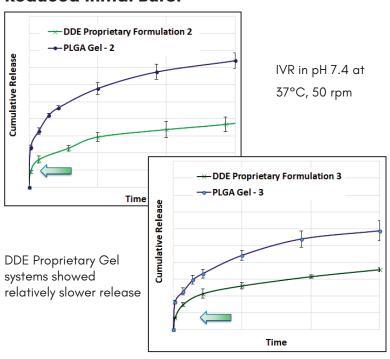
Plunger moving speed: 2 mm/sec Record force when dispensing 200 uL formulation with a 1 mL BD plastic syringe

Typical curve for empty syringes



Plunger moving direction

DDE Proprietary Formulation Reduced Initial Burst



PLGA Microsphere Various PLGA MW & Excipients

Single Dose in Rat for Weekly Delivery

