aegis Therapeutics

"Novel Formulations for Non-Invasive Delivery of Peptides and Small molecule Drugs"

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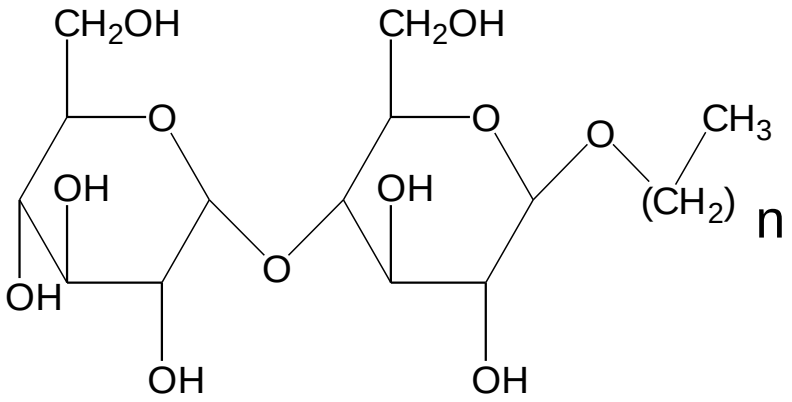
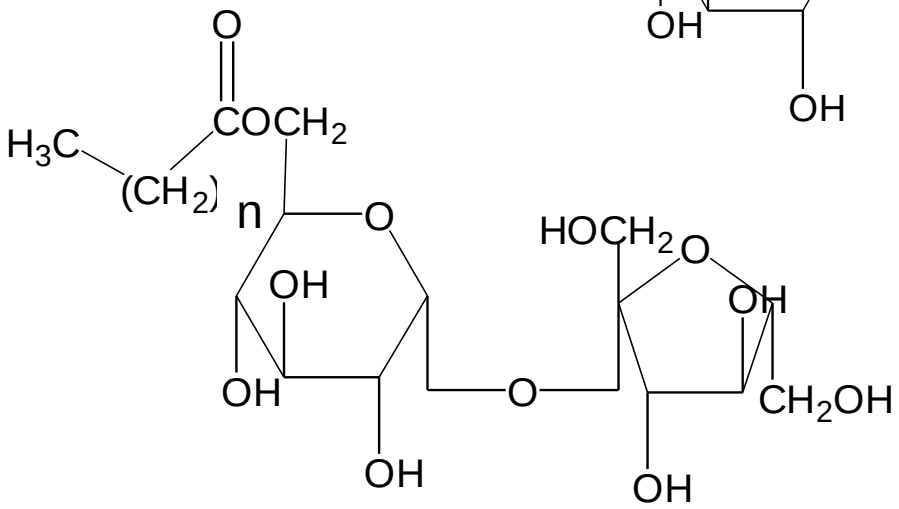
Intravail®/ProTek® Technologies - Based on Alkylsaccharides (sugar + alkyl chain - various linkages)

Typical oligosaccharides:
maltose
maltotriose
maltotetraose
sucrose
trehalose
sucrose
trehalulose
turanose
maltulose
leucrose
palatinose
isomaltose
maltitol





Typical alkyl chain lengths:
10-18 carbons

Typical linkages:
glycosidic
thioglycosidic
amide linkage
ureide
ester

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General Intravail® /ProTek® Characteristics

- Safe, odorless, tasteless, non-toxic, non-mutagenic, and non-irritating
- Synthetic pure chemical entities prepared under GMP
- Provides unmatched bioavailability - comparable to subcutaneous injection, via the intranasal and other mucosal membrane administration routes (up to ~30KDa MW)
- Allows controlled transient mucosal permeation by both paracellular (tight-junction) and transcellular routes
- Soluble in water or oils – compatible with routine liquid formulation and dispensing processes for ease of scale-up and production
- Shown to be highly effective (orally) for BCS Class III/IV small peptides and small molecules
- Shown to greatly increase oral bioavailability in tablets, oils (i.e., soft-gel compatible), and flash-dissolve oral (Zydis®-like) formats

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Multiple Modes of Transmucosal Delivery for Macromolecular Drugs

Metered spray pumps

- Nasal

Gelcaps Tablets

- Oral (gastrointestinal)

Flash dissolve

Edible films

- Oral cavity (buccal, sublingual)

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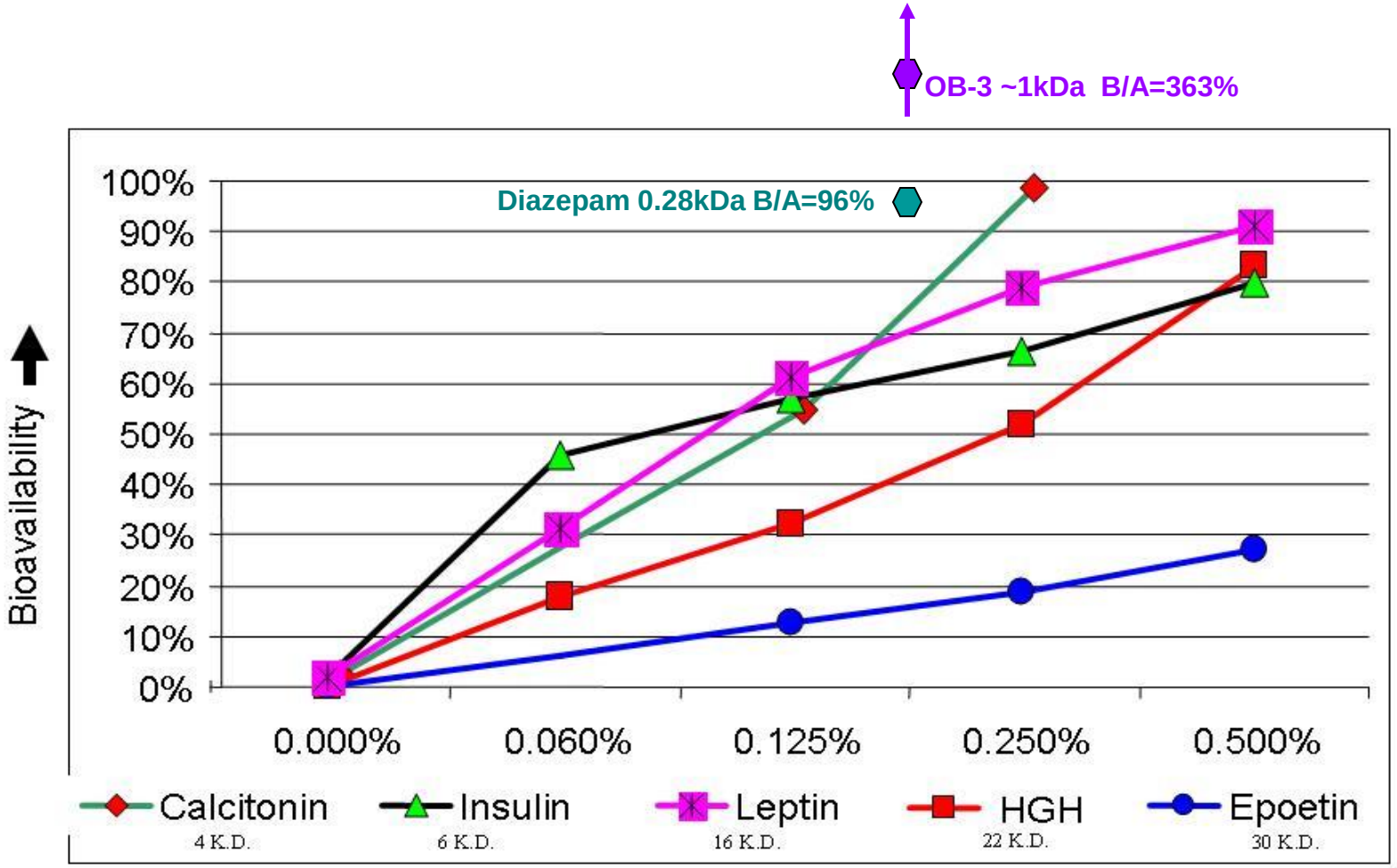
Intravail® Provides Intranasal Bioavailability Comparable to Injection



Intravail® Concentration

Sprague Dawley® rats; calcitonin i.v., all others sub-Q

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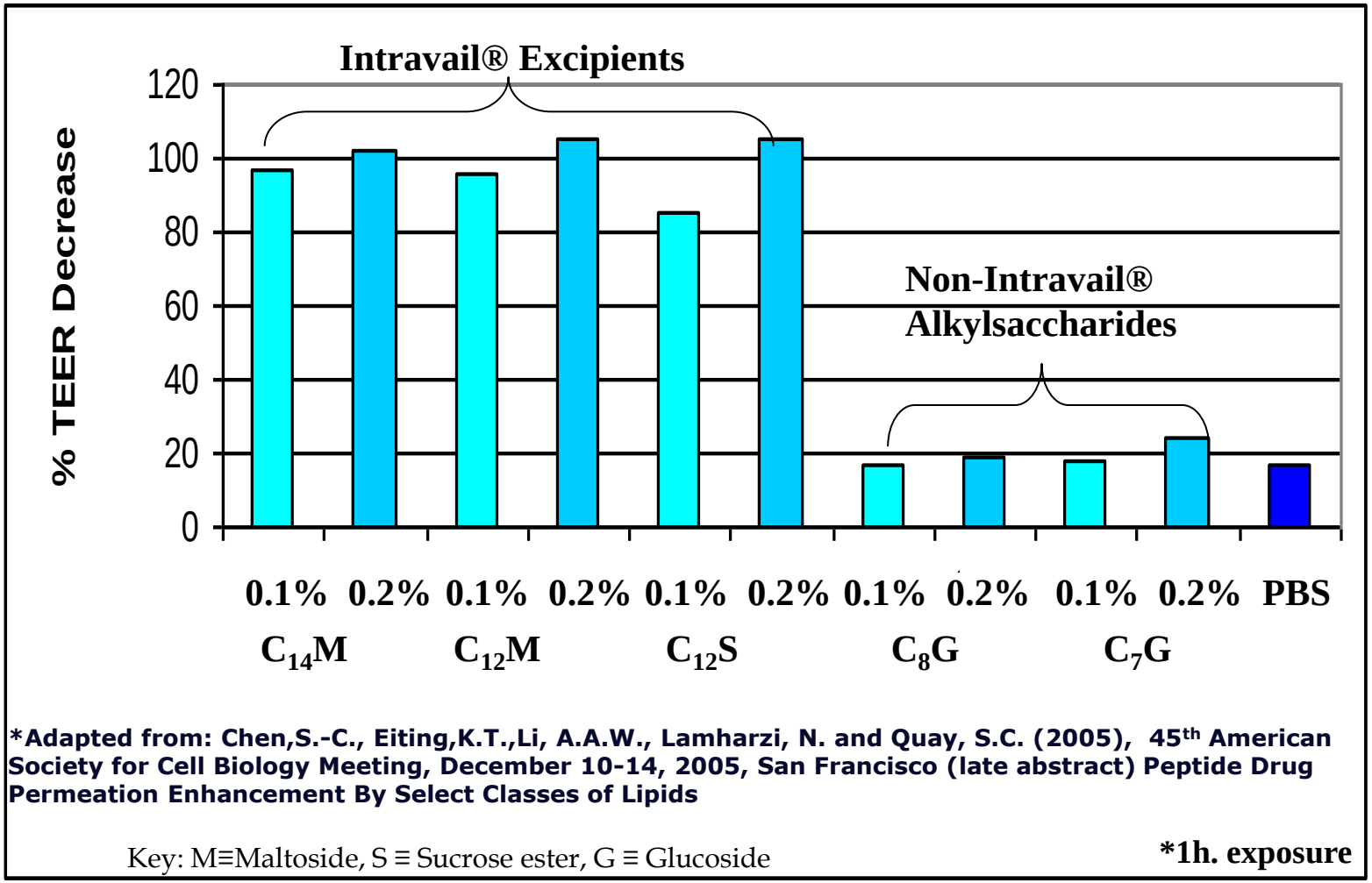
CS

Paracellular Absorption: Reduction in TEER*

(Normal Human Tracheal/Bronchial Epithelial Cell Derived Mucociliary Tissue)



*Adapted from: Chen,S.-C., Eiting,K.T.,Li, A.A.W., Lamharzi, N. and Quay, S.C. (2005), 45th American Society for Cell Biology Meeting, December 10-14, 2005, San Francisco (late abstract) Peptide Drug Permeation Enhancement By Select Classes of Lipids

Key: M≡Maltoside, S ≡ Sucrose ester, G ≡ Glucoside

*1h. exposure

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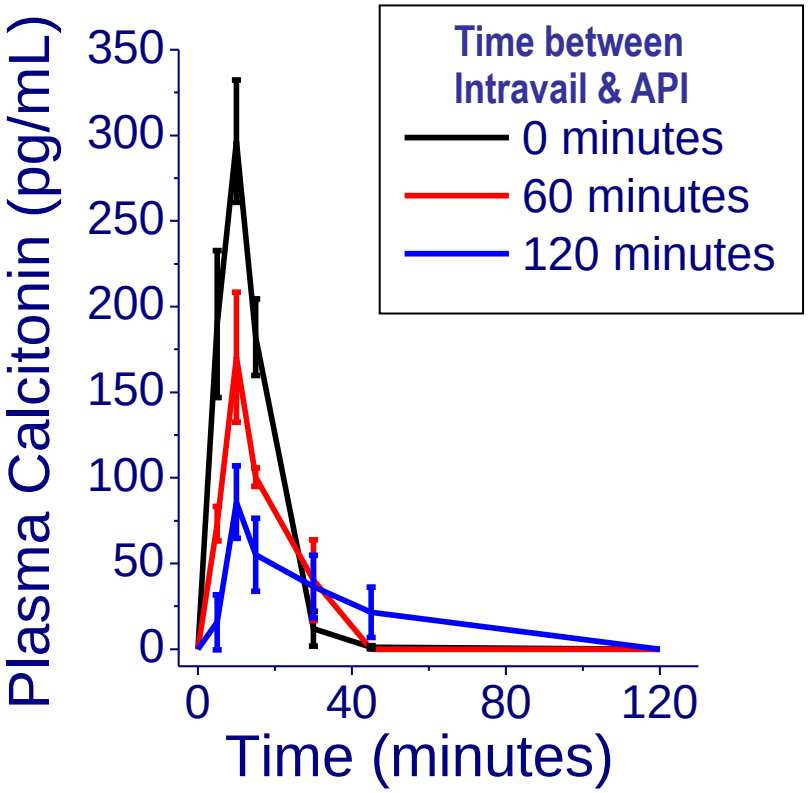
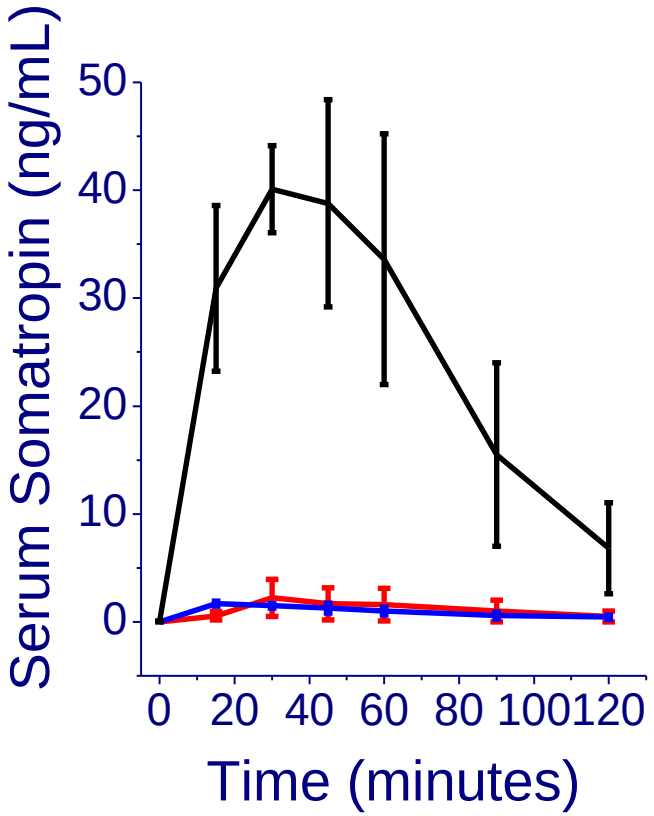
Intravail® Interacts With Nasal Mucosa – Not Drug

Rat Model Data

Calcitonin



Somatropin



Arnold, Fyrberg, Meezan, Pillion (2010) J Pharm Sci. 99(4):1912-20.

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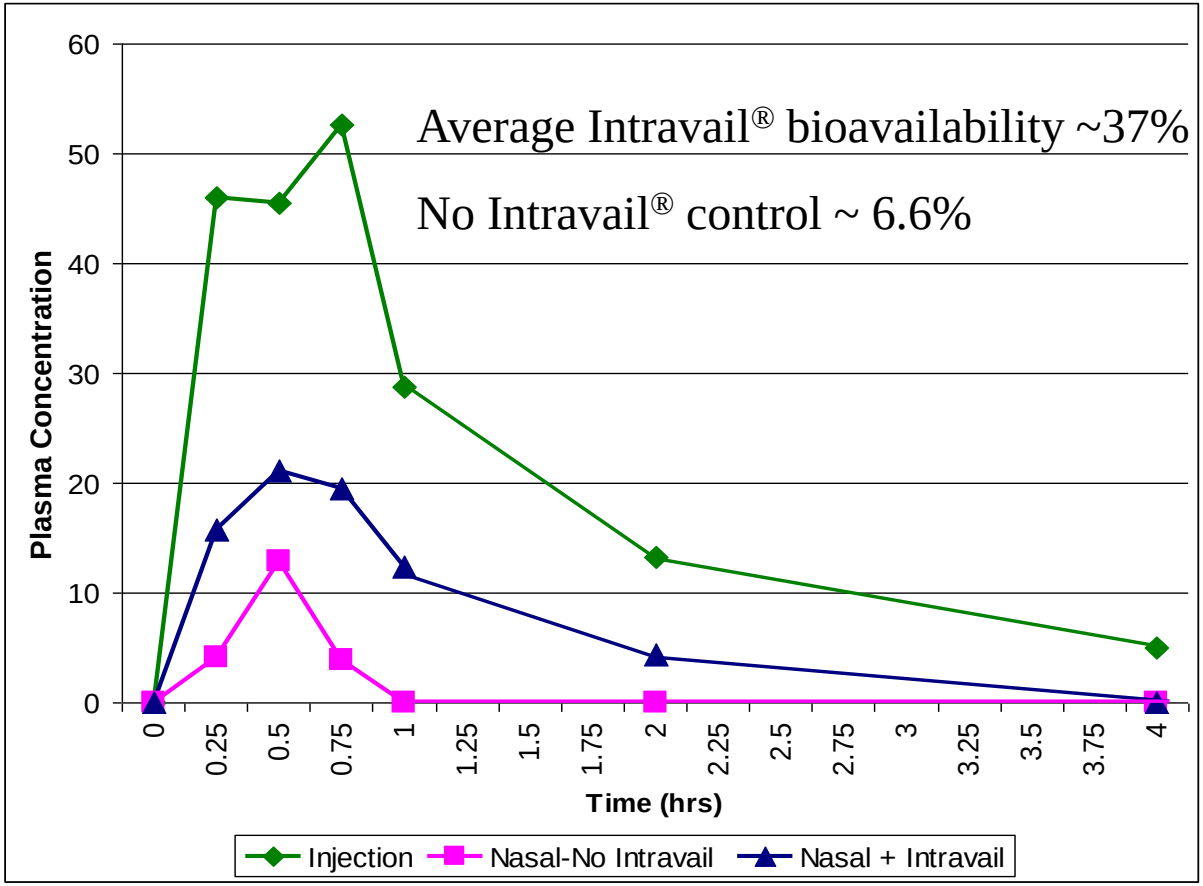
3-Way Human Crossover Study — Intravail® Increases Calcitonin Bioavailability >5-fold

Mean Plasma Drug Concentration vs. S.C. Injection in 10 Healthy Females



Maggio, Meezan, Ghambeer, and Pillion (2010) Drug Del Tech. 2010;10:58–63.

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[D-Leu-4]OB3 – First Orally Active Weight Loss & Anti-Diabetic Peptide

- Patented (7-mer peptide) leptin derived fragment
- Reduces weight gain & food intake in mouse obesity models
- Normalizes blood glucose in mouse diabetes/obesity models
- Increases osteocalcin – may prevent/reverse bone loss associated with weight loss & osteoporosis
- High oral bioavailability (56% w. Intravail®)
- High nasal bioavailability (≥100% w. Intravail®) – for rapid onset
- Multiple issued patents*

*** Dr. Patricia Grasso et al., Albany Medical College**

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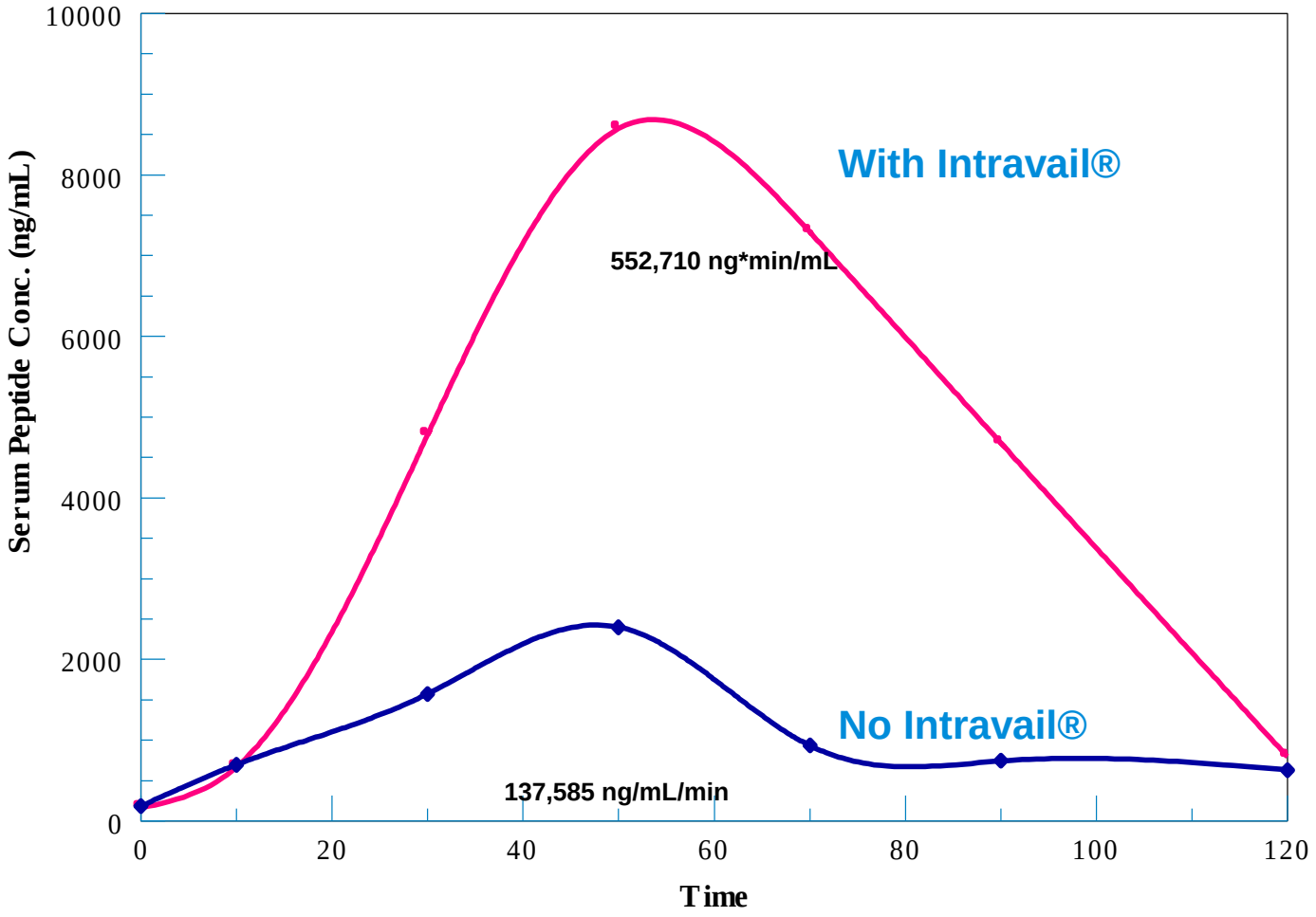
Oral Delivery of [D-leu-4]OB3 Anti-Obesity Peptide in Rodents (~1kD MW)



Lee et al. Regulatory Peptides 160 (2010) 129–132

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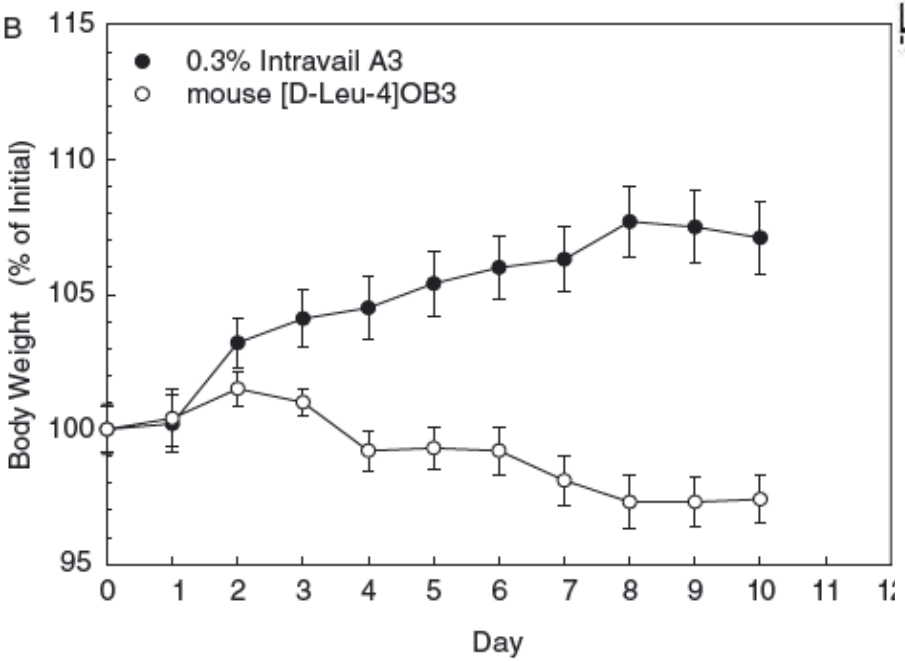
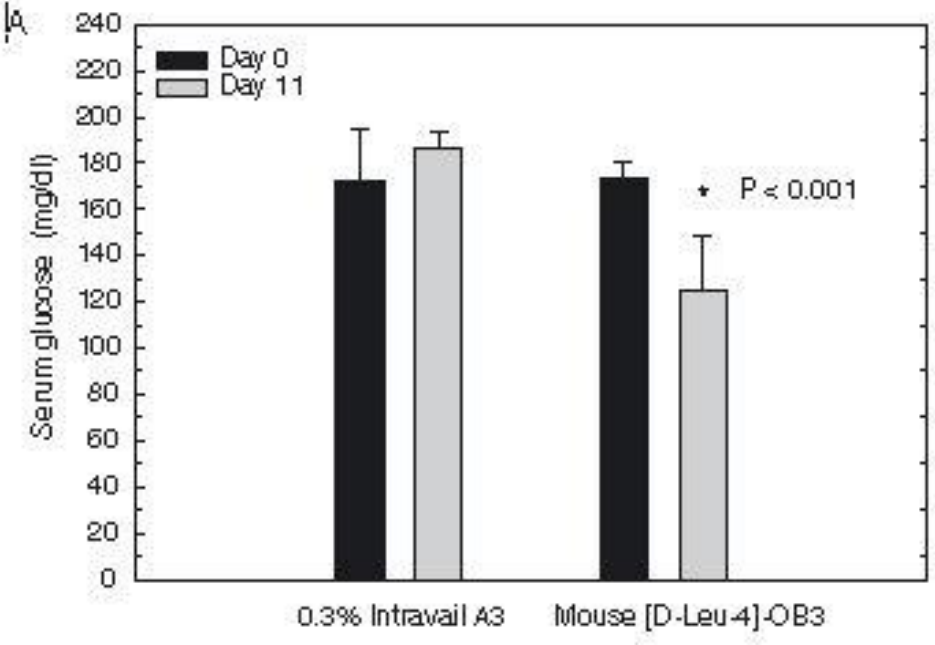
Oral OB-3 Administration - Body Weight Gain and Serum Glucose in ob/ob Mice





Novakovic, Grasso, et al. Diabetes Obes Metab. (2010) 12(6):532-9.

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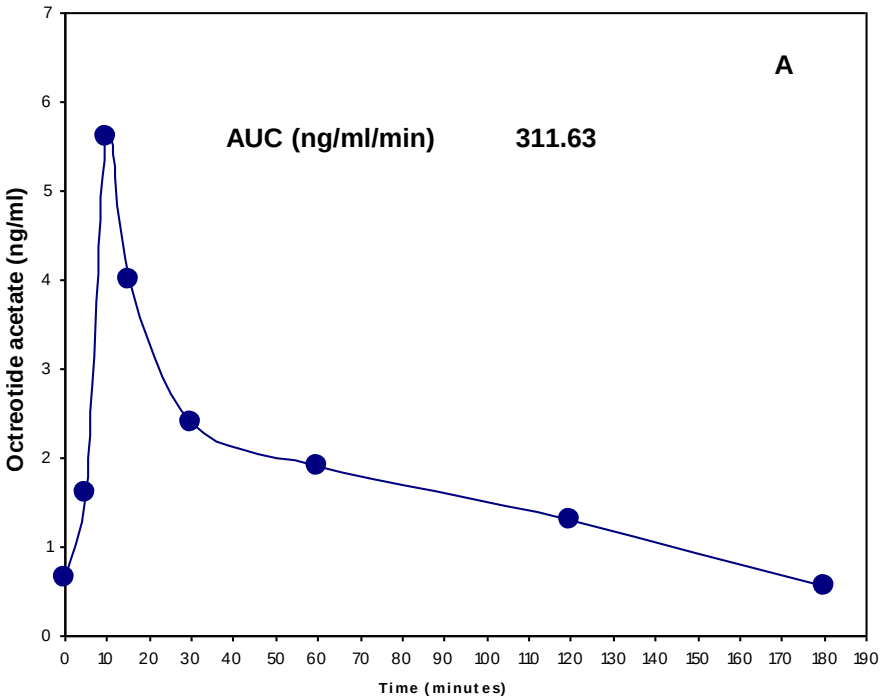
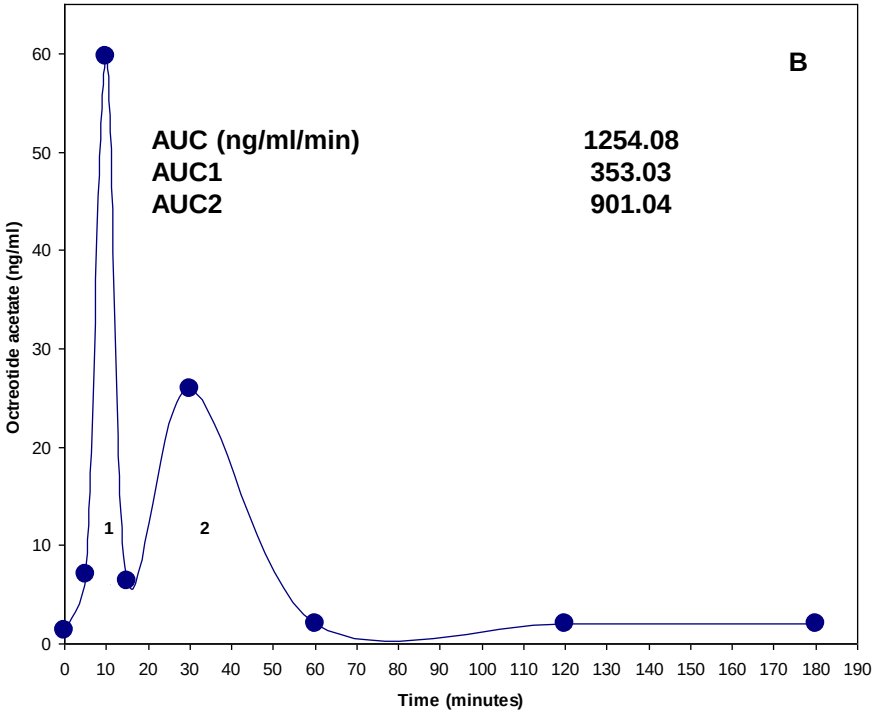
Oral Bioavailability with Intravail® Exceeds That of S.C. Injected Octreotide

Uptake of 30ug Octreotide in PBS s.c.



Oral Uptake of 30ug Octreotide in Intravail®



Maggio & Grasso Regulatory Peptides 167 (2011) 233–238

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Human Clinical Data

- Nasal sumatriptan
  - Six human trials to date
  - Tmax reduced to 8 min. from 60-120 min. for Imitrex
  - Therapeutic drug levels equivalent to Imitrex achieved in 2-3 min.. (i.e., 20X – 30X faster)
  - Licensee – a Top-10 multinational generics company
- Nasal diazepam
  - Nasal spray designed as an alternative to the Diastat rectal gel
  - Bioequivalent to Diastat
  - 96% absolute bioavailability
  - Licensee – Neurelis Inc. (San Diego)
- Nasal PTH 1-34 (~4000 Da)
  - Nasal spray
  - Three phase 1 trials completed: single dose/7 day b.i.d, and 6 weeks b.i.d.
  - Approximately 30% nasal bioavailability compared to Forteo injection
- Oral endocrine peptide (~1000 Da)
  - Formatted as a 3 sec. flash dissolve (Zydis) wafer
  - 14 patient feasibility study completed

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Intravail® Summary

- Unmatched intranasal bioavailability (up to ~30kD)
- Unmatched oral bioavailability for certain peptides
- Rapid onset of action
- Greater patient convenience and compliance
- Elimination of needle stick injuries/infections
- Avoidance of gastric hydrolysis & "first pass effect"
- Compatible with "off-the-shelf" metered nasal spray devices & oral tablet/capsule/flash-dissolve formats

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