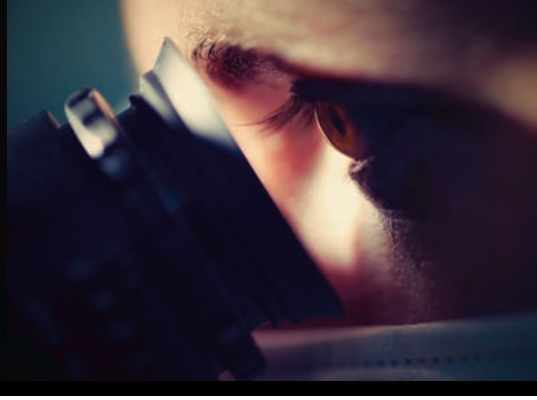


Technical Bulletin: DERMATOLOGY

Dermatology Overview

Comparative Biosciences, Inc. (CBI), a leading preclinical Contract Research Organization (CRO), has demonstrated expertise in all phases of the drug development process in preclinical contract dermatology studies. Due to CBI's unique and extensive experience in dermatology studies and state-of-the-art facilities, we have the skill and expertise to accelerate new dermatology drugs, biologics, and devices from discovery through the drug development process, to regulatory submission and studies in man.

. Dermal Toxicology Studies
. Dermal Pharmacokinetics or Bioavailability Studies
. Dermal Pharmacology and Efficacy Studies

Dermal Pharmacology and Efficacy Studies

CBI provides a wide range of established and validated dermal pharmacology and efficacy studies in all species in normal and in diseased animals, and with single, multiple or infusion/slow release dose administration with small molecules, biologics, stem cells, nanoparticles and devices. CBI also offers custom studies and custom model development.

. Dermal inflammation
. Delayed type hypersensitivity
. Dermal sensitization
. Dermal fibrosis
. Dermal scarring and wound healing
. Keloid formation
. Dermal burns
. Delivery devices
. Dermal infection
. Botulinum

COMPARATIVE BIOSCIENCES, INC.
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

Toxicology Studies

Comparative Biosciences, Inc. (CBI), a leading preclinical Contract Research Organization (CRO), has demonstrated expertise in all phases of the drug development process in preclinical contract dermal toxicology studies. Due to CBI's unique and extensive experience in preclinical studies and state-of-the-art facilities, we have the skill and expertise to accelerate new drugs, small molecules, biologics, stem cells, nanoparticles, and devices from discovery through the drug development process, to regulatory submission and studies in man.

Dermal toxicology study expertise at CBI includes:

- Skin irritation studies to intact or abraded skin
- Acute (LD50) dermal toxicity study in rats or rabbits
- Acute single or multiple dose dermal toxicity studies in rodents
- Acute single or multiple dose dermal toxicity studies in minipig or other nonrodent species
- Two week dermal toxicity studies in rodents
- Two week dermal toxicity studies in minipig or other nonrodent
- Four week dermal toxicity studies in rodents (with or without recovery period)
- Four week dermal toxicity studies in minipig or other nonrodent(with or without recovery period)
- 3, 6, or 12 month dermal toxicity studies in rodents (with or without recovery period)
- 3, 6, or 12 month dermal toxicity studies in minipig or other nonrodent(with or without recovery period)
- Two year oncogenicity dermal studies in rodents and nonrodents
- Co-carcinogenicity dermal studies in rodents and nonrodents
- Acute perivascular irritation study in rabbits
- Hypersensitization studies

Clients?

COMPARATIVE BIOSCIENCES, INC.
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

Dermal Pharmacokinetics or Bioavailability Studies

Comparative Biosciences, Inc. (CBI), a leading preclinical Contract Research Organization (CRO), offers dermal bioavailability, ADME, pharmacokinetic and toxicokinetic studies in all species in normal and in diseased animals and with single, multiple or infusion/slow release dose administration with small molecules, biologics, stem cells, nanoparticles and devices.

Dermal pharmacokinetics or bioavailability study expertise includes:

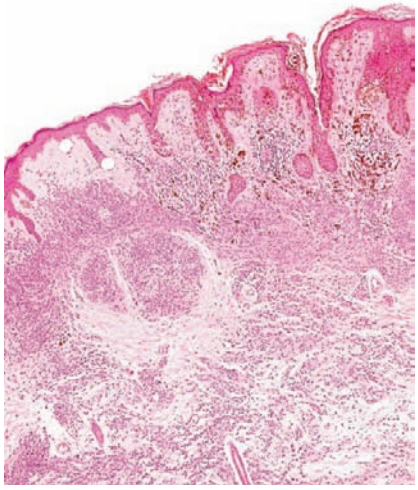
Dermal pharmacokinetics or bioavailability studies in rodents
Dermal pharmacokinetics or bioavailability studies in minipigs or other nonrodent species
Dermal pharmacokinetic and toxicokinetic studies in disease models, such as diabetes, inflammation, wound healing, or burns

Dermal Inflammation

- Assessment of retinal layers in all species
- Assessment of changes in anterior segment including cornea
- Assessment of foreign objects, materials, stem cells or tumors in the eye
- Assessment of intraocular implants

Delayed Type Hypersensitivity Studies

- STZ retinopathy in rodents
- Laser induced subretinal plaques in rodents, rabbits and pigs
- Retinopathies-either spontaneous or induced in rodents
- Ocular xenografts in rodents
- Stem cell implants
- Corneal ulceration in all species
- Anterior inflammation or lesions in all species
- Intraocular implants
- Contact lens assessments



CBI offers expertise in the following DTH studies:

In the skin, OCT may be useful in assessments of:

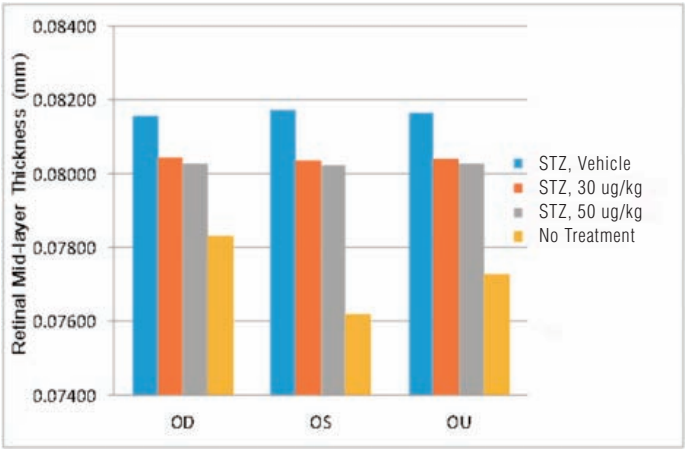
- Xenografts in rodents
- Bleomycin induced dermal fibrosis in rodents
- Dermal implants and injections in all species
- Dermal microneedles in all species
- Hypertrophic scar measurements in rabbit ears

Conclusion?

Oct is a new and powerful, sophisticated tool to support ocular and dermal investigations in rodents and larger laboratory animals. Preclinical OCT data can contribute to improved clinical trial design. It allows for non-invasive long term longitudinal assessments in animals with minimal restraint and stress. It reveals or detects subtle changes, particularly in the eye, that are not visible by other means such as with slit lamp biomicroscopy or funduscopy. OCT may be employed in a variety of modalities in GLP toxicology studies and in numerous types of research, pharmacology and efficacy studies. It has wide applications particularly in ocular work, dermatology and xenograft research.

Optimized Computer Tomography

Retinal Mid-layer Thickness, 4 weeks Test Article and Triamcinolone Treatment in STZ-treated Brown Norway Rats (triamcinolone assessment study)



Retinal Mid-layer Thickness

- Significantly increased in STZ-treated rats
- Test article has no effect on retinal thickness
- Triamcinolone administered Ivt 3 days prior to sacrafice significantly reduces the thickness of the retinal mid layer

Week		OD					OS				
4	17	0.072111	0.074831	0.076125	0.076642	**0.07493**	0.071721	0.071721	0.078455	0.075478	**0.07434**
4	67	0.075736	0.073923	0.071721	0.073534	**0.07373**	0.069909	0.075346	0.073923	0.076642	**0.07395**
4	68	0.077159	0.078971	0.079361	0.078971	**0.07862**	0.067317	0.071721	0.078971	0.080267	**0.07457**
4	1097	0.078052	0.078455	0.075346	0.075736	**0.07690**	0.075346	0.078391	0.079103	0.07483	**0.07692**
4	1098	0.079702	0.081288	0.077159	0.073923	**0.07802**	0.071594	0.072111	0.080267	0.075346	**0.07483**
4	1146	0.077159	0.078971	0.078649	0.071205	**0.07650**	0.077032	0.078455	0.084993	0.082986	**0.08087**
	Mean					**0.07645**					**0.07591**
	SD					**0.00185**					**0.00264**
6	54	0.078971	0.077548	0.073534	0.078455	**0.07713**	0.073534	0.073534	0.081173	0.082596	**0.07771**
6	65	0.073534	0.075346	0.078971	0.077159	**0.07625**	0.073534	0.073534	0.077159	0.078971	**0.07580**
6	66	0.080784	0.078971	0.077159	0.077159	**0.07852**	0.068096	0.071721	0.073534	0.075346	**0.07217**
6	1097	0.079106	0.079103	0.07483	0.07483	**0.07697**	0.073017	0.075346	0.075346	0.076642	**0.07509**
6	1145	0.075346	0.076125	0.076642	0.075346	**0.07586**	0.073017	0.07483	0.078971	0.079103	**0.07648**
6	1146	0.078455	0.079361	0.078909	0.07483	**0.07789**	0.0725	0.076642	0.081368	0.078971	**0.07737**
	Mean					**0.07710**					**0.07577**
	SD					**0.00099**					**0.00201**
7	5	0.07897	0.08117	0.07746	0.07535	**0.07824**	0.07535	0.07502	0.07716	0.07716	**0.07617**
7	6	0.07716	0.07897	0.07755	0.07353	**0.07680**	0.07172	0.07172	0.07716	0.07716	**0.07444**
7	47	0.07570	0.07936	0.07273	0.07276	**0.07514**	0.07353	0.07535	0.07703	0.07664	**0.07564**
7	48	0.08260	0.08078	0.07716	0.07535	**0.07897**	0.07353	0.07535	0.07897	0.07897	**0.07671**
7	53	0.07483	0.07483	0.07211	0.07030	**0.07302**	0.06667	0.07095	0.07936	0.07936	**0.07409**
7	1097	0.07794	0.07755	0.07794	0.07512	**0.07714**	0.07211	0.07535	0.07897	0.07703	**0.07587**
7	1151	0.07897	0.07794	0.07535	0.07366	**0.07648**	0.07431	0.07431	0.07936	0.07884	**0.07671**
7	1152	0.07250	0.07613	0.07664	0.07664	**0.07548**	0.07250	0.07522	0.07574	0.07574	**0.07480**
	Mean					**0.07641**					**0.07555**
	SD					**0.00187**					**0.00101**
8	401	0.07897	0.08117	0.07746	0.07535	**0.07824**	0.07535	0.07502	0.07716	0.07716	**0.07716**
8	402	0.07716	0.07897	0.07755	0.07353	**0.07680**	0.07172	0.07172	0.07716	0.07716	**0.07444**
8	403	0.08260	0.08078	0.07716	0.07535	**0.07897**	0.07353	0.07535	0.07897	0.07897	**0.07671**
8	404	0.078455	0.079103	0.075024	0.072111	**0.07617**	0.073665	0.072111	0.07975	0.079361	**0.07622**
8	405	0.078196	0.078455	0.073923	0.072111	**0.07567**	0.077032	0.076642	0.078455	0.079361	**0.07787**
8	406	0.080784	0.081368	0.077159	0.077159	**0.07912**	0.073923	0.076125	0.078971	0.078971	**0.07700**

OCT Measurements

Retinal Mid-layer Thickness (mm), 2 months post STZ administration with hyperglycemia and following 1 month of test article treatment

Group 1: Vehicle
Group 2: Test Article 1
Group 3: Test Article 2
Group 4-no STZ, normal rats.
There is little best article effect on increasses in retinal mid layer thickness induced by STZ-treatment.

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