Medicilon Preclinical Inflammatory & Immune Diseases Models

Autoimmune diseases occur when our immune system attacks and destroys our own cells and tissues due to breakdown of tolerance. Immune-mediated inflammatory disease (IMID) is a group of disorders that covers a large number of disease indications thought to be related to each other through similar mechanisms of immune-system dysfunction and dysregulation. Animal models provide insights into underlying pathologies, etiologies, and specific signaling pathways of human diseases because of their physiological similarities to humans and their shorter disease progression that allows the entire disease onset and development to be studied within a relatively short amount of time.

Medicilon maintains a large in-house library of animal disease models to meet the research demands in different therapeutic areas. Medicilon provides a number of validated models of inflammatory and autoimmune diseases. Equipped with Ph.D. level scientists as well as the most innovative technology and platforms. Medicilon is committed to providing high-quality customer-oriented service support and delivering high-quality results. The Pharmacology department combines strong technical expertise with extensive experience in consulting, conducting, and evaluating efficacies of small molecule and biologic drugs, we can provide efficacy evaluation for a variety of autoimmune diseases using a wide variety of *in vitro* and *in vivo* research models.

The Models Medicilon Offer

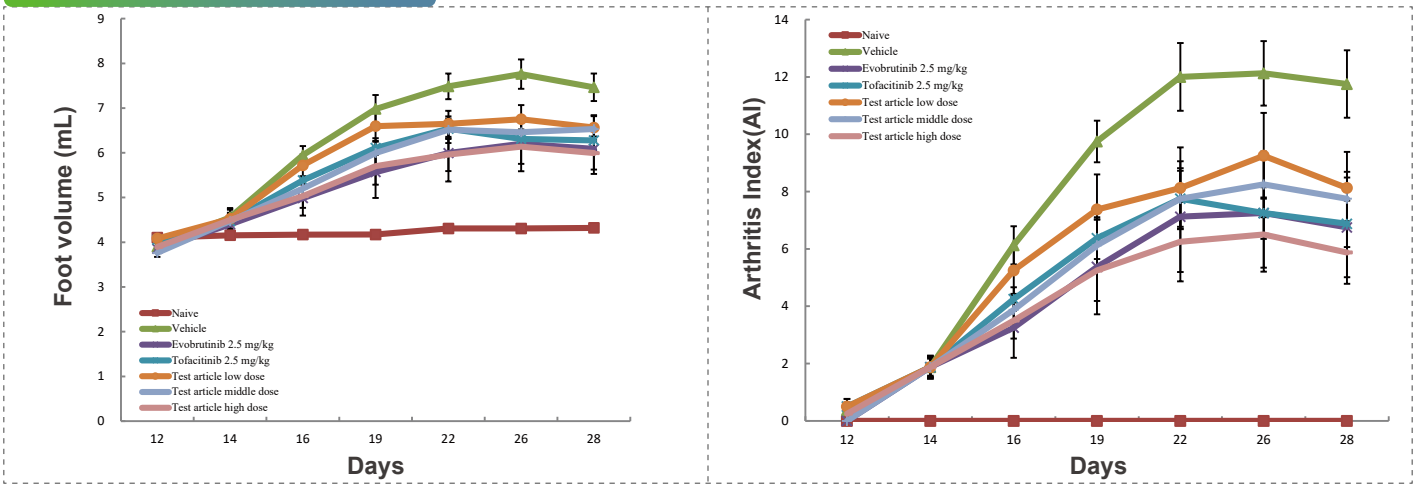
Diseases	Models
Arthritis	Rheumatoid arthritis induced by II Collagen (CIA model) Rheumatoid arthritis induced by Complete Freund's Adjuvant (AIA model) Gouty arthritis model induced by Sodium urate
Amyotrophic lateral sclerosis (ALS)	EAE allergic encephalomyelitis (EAE) model
Psoriasis	Psoriasis model induced by Imiquimod IL-23 induced auricle psoriasis model

Atopic dermatitis and eczema	Eczema-like model induced by Phorbol ester Subacute eczema-like model induced by DNFB Chronic atopic dermatitis model induced by DNFB
Inflammatory bowel disease (IBD)	TNBS induced rat ulcerative colitis model DSS induced mouse ulcerative colitis model

Collagen Induced Arthritis (CIA) Model

Animal models of rheumatoid arthritis (RA) are essential for studying the pathogenesis of RA *in vivo* and determining the efficacy of anti RA drugs. The CIA model is the most commonly studied autoimmune model of rheumatoid arthritis. CIA model can be widely used to address questions of disease pathogenesis and to validate therapeutic targets. CIA can be induced in susceptible strains of rodents and NHPs by immunization with type II collagen (CII). Following immunization, these animals develop an autoimmune-mediated polyarthritis that shares several clinical, histological, and immunological features with the human autoimmune disease rheumatoid arthritis. As with RA, susceptibility to CIA in rodents is linked to the class II molecules of the major histocompatibility complex (MHC). The immune response to CII is characterized by both the stimulation of collagen-specific T cells and the production of high titers of antibody specific for both the immunogen (heterologous CII) and the autoantigen (mouse or rat CII). Because of the important similarities between CIA and rheumatoid arthritis, this experimental model of autoimmune arthritis has been extensively used to research the mechanism of anti RA drug and evaluate the efficacy new drugs.

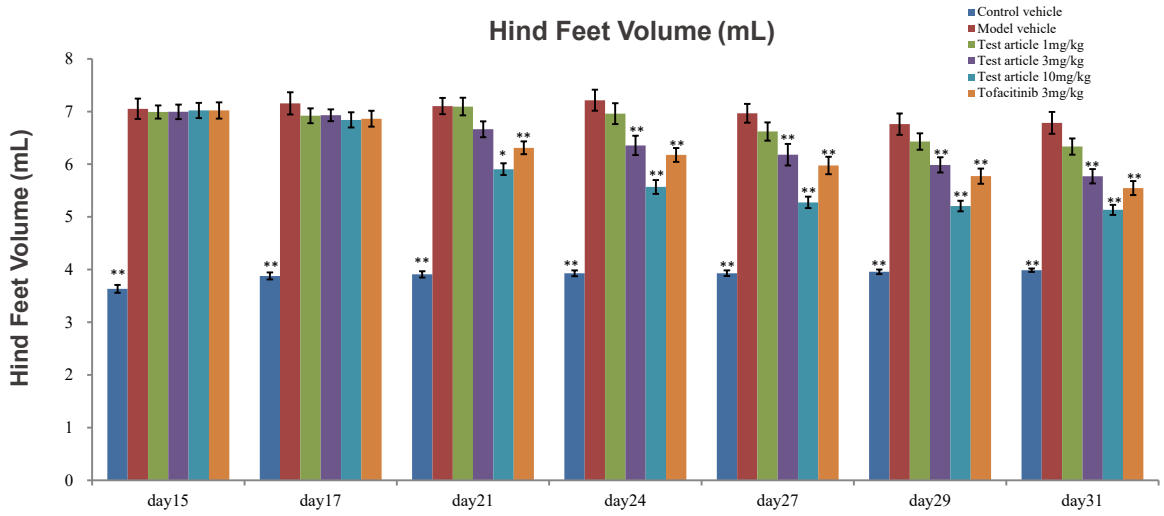
Medicilon Case: CIA model

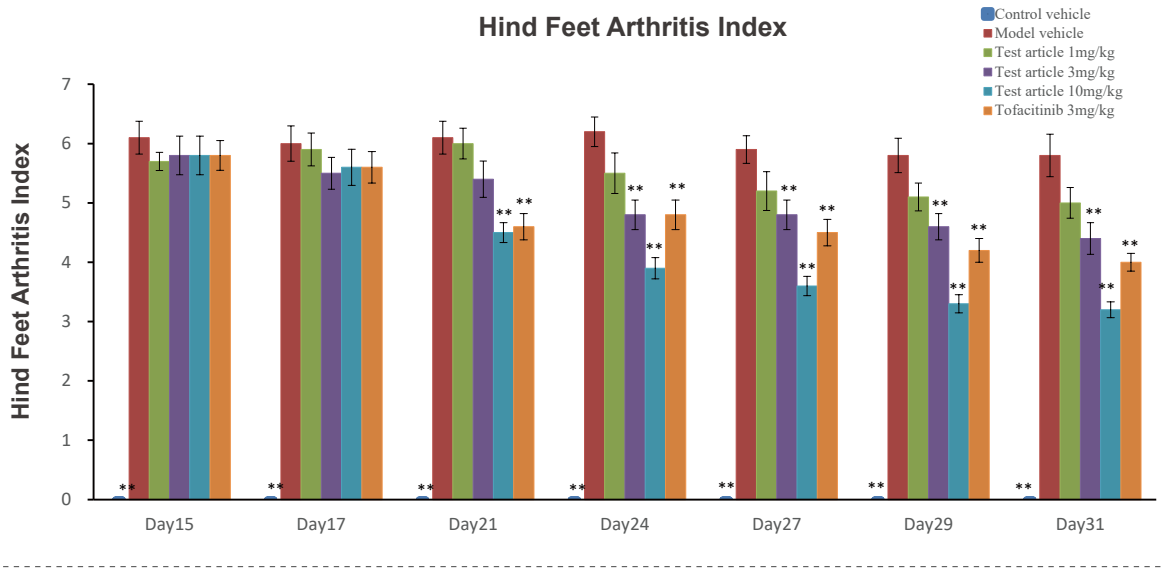


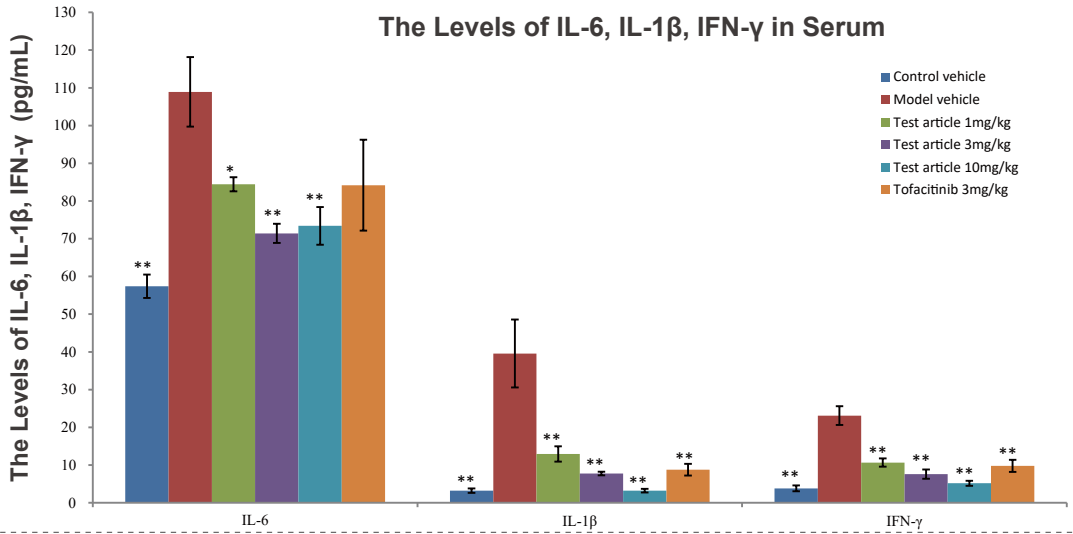
Complete Freund's Adjuvant (CFA) Induced Arthritis (AIA) Model

Rheumatoid arthritis (RA) is a chronic progressive inflammatory arthritis. Among other models of arthritis in rodents, CFA induced model displays various similarities with that of human arthritis which makes it most suitable model for inducing arthritis. CFA is a suspension of dessicated mycobacterium in paraffin oil and mannide monooleate that induces inflammation, tissue necrosis, and ulceration. CFA can be used subcutaneously in the paw, or intraperitonealy in mice and rats. CFA-induced arthritis model represents persistent inflammation with numerous systemic alterations as well as synovial hyperplasia, ear and tail "arthritis" nodules, etc. CFA-induced arthritis has been used as a model of sub-chronic or chronic inflammation in rats and is of considerable relevance for the study of pathophysiological and pharmacological control of inflammatory processes, as well as the evaluation of analgesic potential or anti-inflammatory effects of drugs.

Medicilon Case: CFA induced arthritis (AIA) model





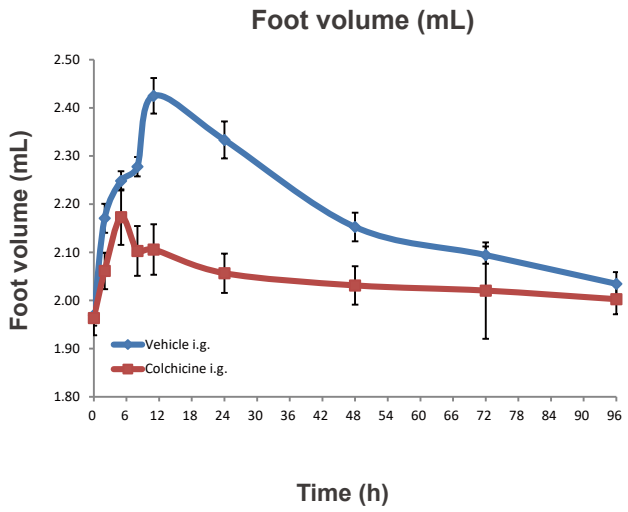


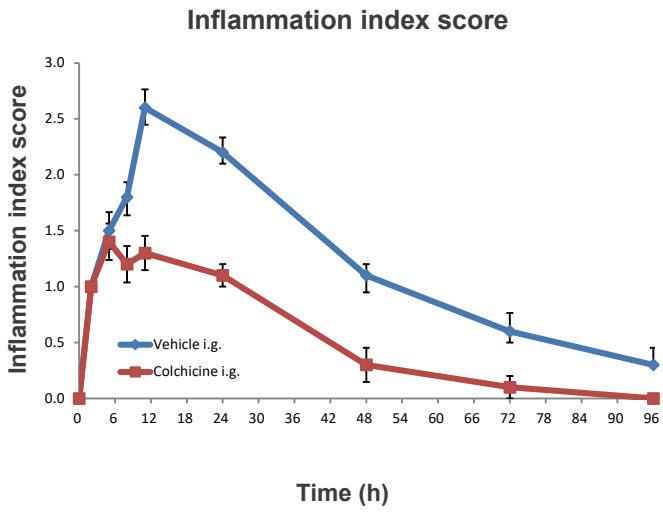
Gouty Arthritis Model Induced by Sodium Urate

Gouty arthritis is an inflammatory joint disease. The inflammatory process is initiated by the deposition of monosodium urate (MSU) crystals in the surrounding tissue. Gout is accompanied by tenderness, erythema, redness, swelling, pain, and fever in periarticular tissues or in joints. Sodium urate can be used to induce acute gouty arthritis model.

MSU crystal-induced inflammatory disorder is well-represented in the gout disease model; neutrophil infiltration into the inflamed joints is the most distinctive phenotype. MSU crystal-induced intracellular signaling generates acute joint inflammation and mediates neutrophil migration and activation. The progression of sterile inflammation in acute gouty arthritis is promoted by an auto-amplification loop of the inflammation.

Medicilon Case: Gouty arthritis model induced by Sodium urate



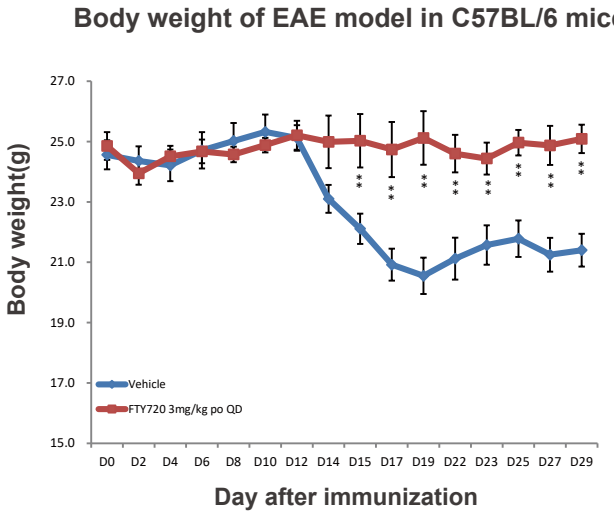


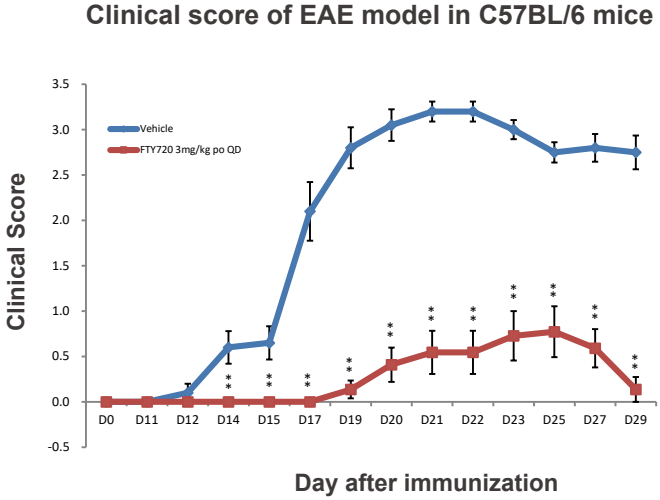
Experimental Autoimmune Encephalomyelitis (EAE) Model

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) characterized by neuroinflammation with consequent demyelination and axonal degeneration. EAE is the most widely used experimental model for MS.

EAE mice are used to model the disease progression of MS and mirror MS-like pathology. EAE mice also exhibit cognitive deficits, dyskinesia and significant disruption in the structural integrity of synapses. EAE is a complex condition in which the interaction between a variety of immunopathological and neuropathological mechanisms leads to an approximation of the key pathological features of MS: inflammation, demyelination, axonal loss and gliosis. Moreover, EAE is often used as a model of cell-mediated organ-specific autoimmune conditions in general. EAE has a complex neuropharmacology, and many of the drugs that are used in MS have been developed, tested or validated on the basis of EAE model.

Medicilon Case: EAE experimental allergic encephalomyelitis model



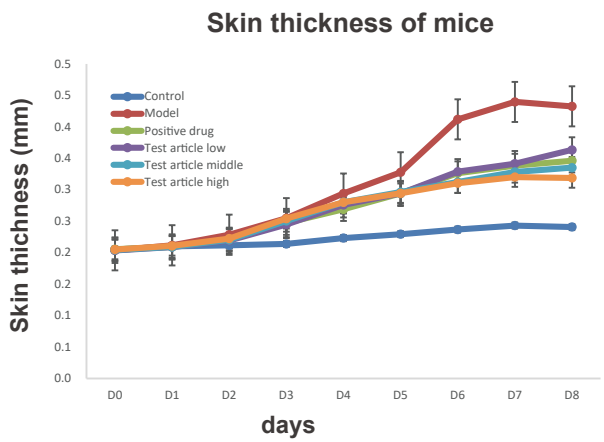


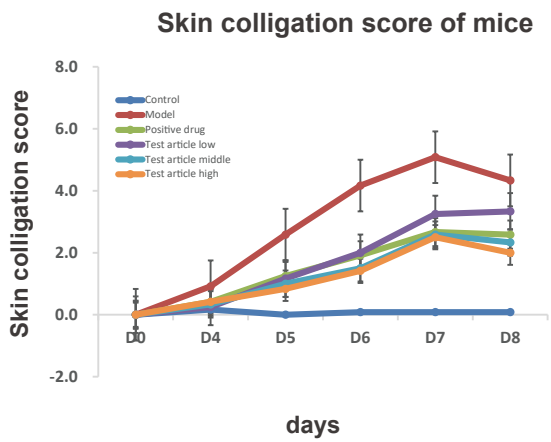
Psoriasis Model Induced by Imiquimod

Psoriasis is a chronic inflammatory skin disease associated with multiple contributing factors including autoimmune dysfunction. Psoriasis leads to the alteration of skin components which generally manifests as unwanted topical symptoms. One of the most widely approved psoriasis-like animal models is the Imiquimod (IMQ)-induced mouse model. The IMQ-induced Psoriasis model is particularly translational into the clinic as it has many of the significant markers of human disease, including histopathology of lesions and strong activation of the immune system. IMQ is a ligand for Toll-like receptors 7/8 which activates macrophages, monocytes and dendritic cells.

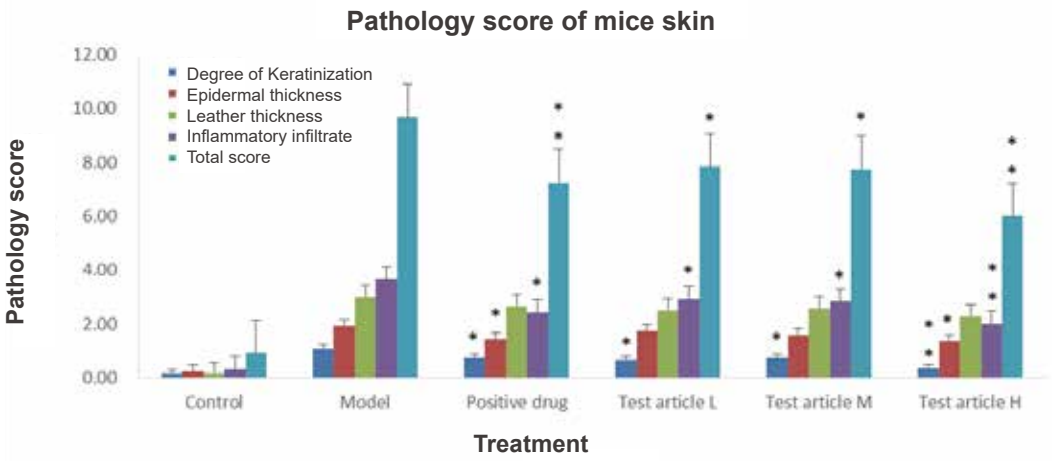
Topical application of IMQ can induce psoriasis. It is a rapid and convenient model that allows the elucidation of underlying mechanisms and the evaluation of new therapies against psoriasis.

Medicilon Case: Psoriasis model induced by Imiquimod



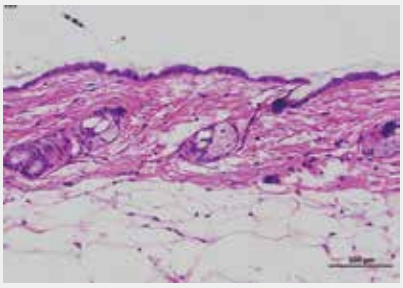


Medicilon Case: Psoriasis model induced by Imiquimod



C57BL/6 mice

BALB/C mice



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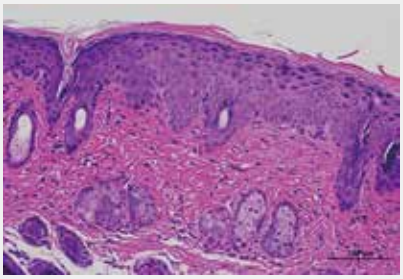


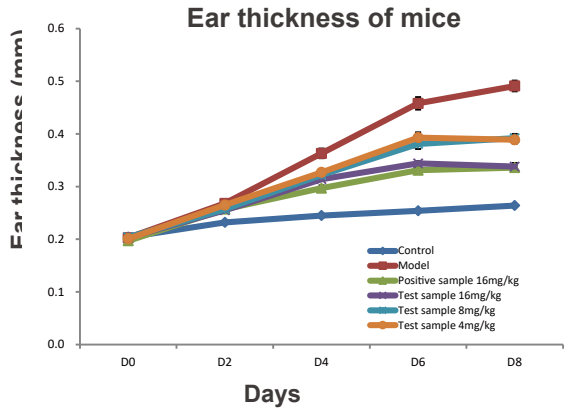
Model

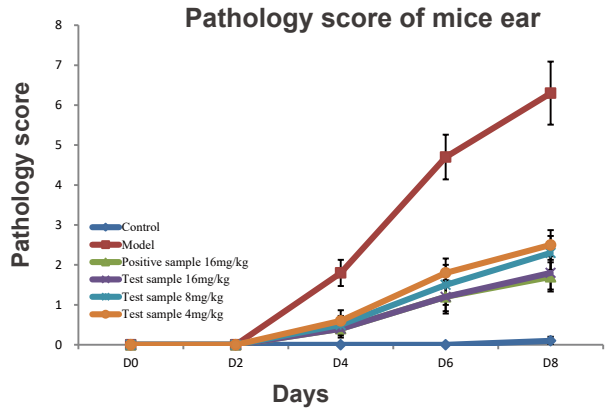
IL-23 Induced Mouse Auricle Psoriasis Model

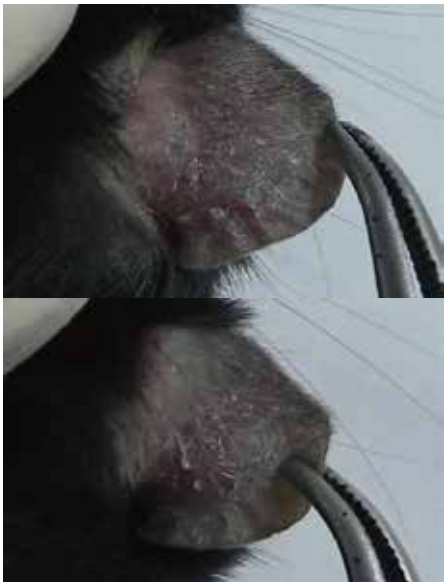
IL-23 is a heterodimeric cytokine composed of two disulfide-linked subunits, a p19 subunit that is unique to IL-23, and a p40 subunit that is shared with IL-12. IL-23 is produced by various immune cells, and stimulates the activity of Th17 cells. Th17 cells, in turn, produce cytokines that promote inflammation and recruit immune cells to the site of infection or injury. The IL-23/IL-17A pathway plays a critical role in psoriasis. IL-23 is a key cytokine produced by antigen-presenting cells that is necessary for the development of pathogenic IL-17A-secreting lymphocytes. IL-17A and other cytokines such drive the abnormal differentiation of keratinocytes and inflammation that lead to the manifestations of disease.

IL-23-induced psoriasis mouse model is the most prevalent among psoriatic mouse models due to its ease of use, convenience, and low cost. IL-23 induced psoriasis mouse mode is provoked by IL-23 intra-dermal injections produces a cutaneous phenotype in mice frequently studied as an acute model of human psoriasis. The IL-23 injection model has the advantage of using a single cytokine that is of established importance in psoriasis in initiating inflammation.

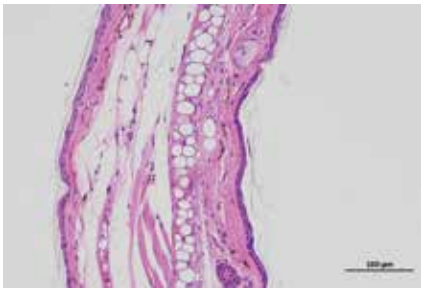
Medicilon Case: IL-23 induced mouse auricle psoriasis model







C57BL/6 mice



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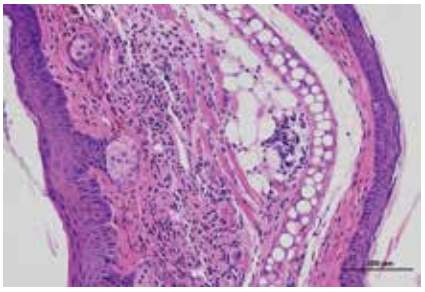


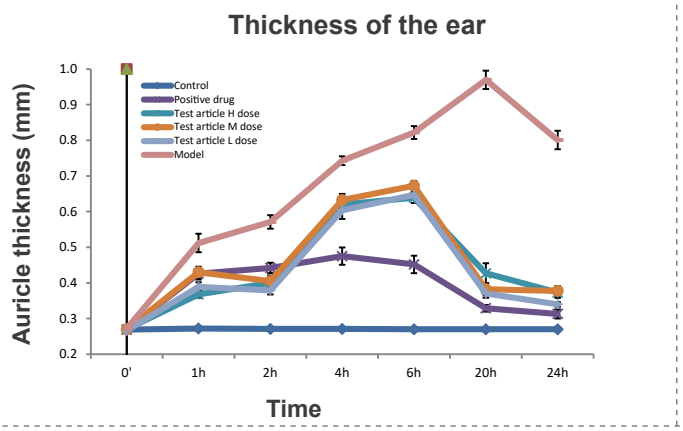
Model

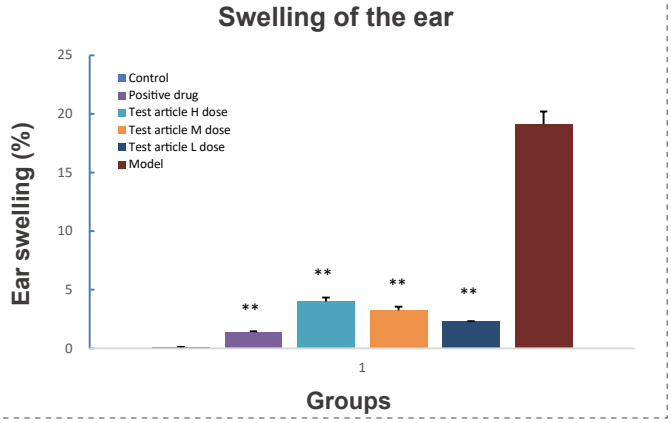
Acute Eczema-like Model Induced by Phorbol Ester

Several factors have been implicated in atopic dermatitis. Symptoms include itchiness, redness, and dryness of the skin. If left unchecked this inflammatory processes may contribute to a wide variety of human disease processes. Inappropriate inflammation is usually treated with certain steroids such as glucocorticoids or with non-steroidal anti-inflammatory drugs. Both classes of compounds can have undesirable side effects. Discovering new ways to treat inflammation is of clinical importance.

To induce an inflammatory response, a mouse model of Phorbol Ester-induced inflammation can be used. Phorbol Ester is often used as a potent inducer of sterile inflammation in screening for the relative activity of potential anti-inflammatory drugs. Phorbol Ester can be used in animal modeling to construct acute eczema-like models.

Medicilon Case: Acute eczema-like model induced by Phorbol ester



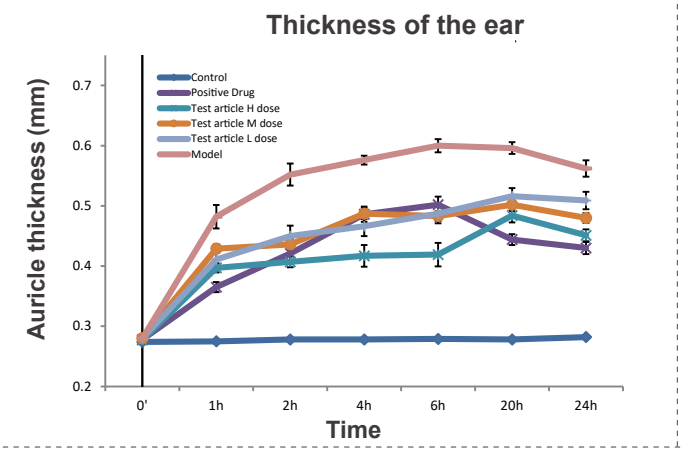


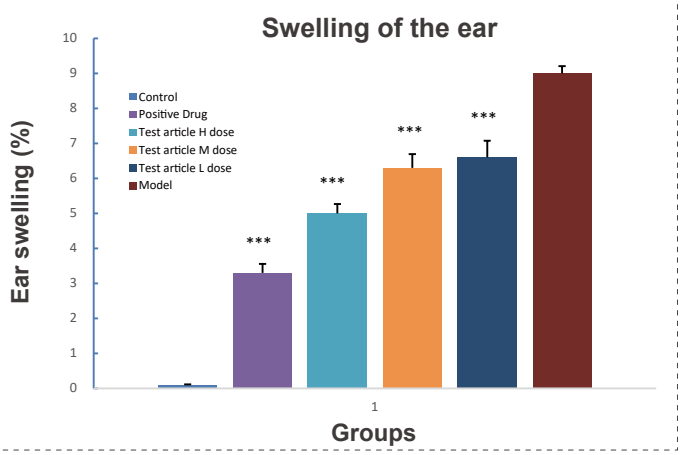
Subacute Eczema-like Model Induced by DNFB

Several studies have tried to establish mice models of atopic dermatitis (AD) through the allergen of *Dermatophagoides farinae* (Df). However, there are no typical skin lesions after epicutaneous application of an extract of Df (DfE) on BALB/c mice. Dinitrofluorobenzene (DNFB) is a common hapten that brings about contact dermatitis in mice. The integrity of mice skin gets disrupted when DNFB recruits the cytotoxic T lymphocytes to the skin, inducing keratinocyte apoptosis. Skin dysfunction induced by DNFB may be a way to enhance the effects of DfE on mice skin.

Alternating epicutaneous exposure to DNFB and DfE can produce AD-like models with typical clinical features and Th2-type immune responses in BALB/c mice. This model could be valuable for studying the pathogenesis of AD and developing novel therapeutic agents for it.

Medicilon Case: Subacute eczema-like model induced by DNFB



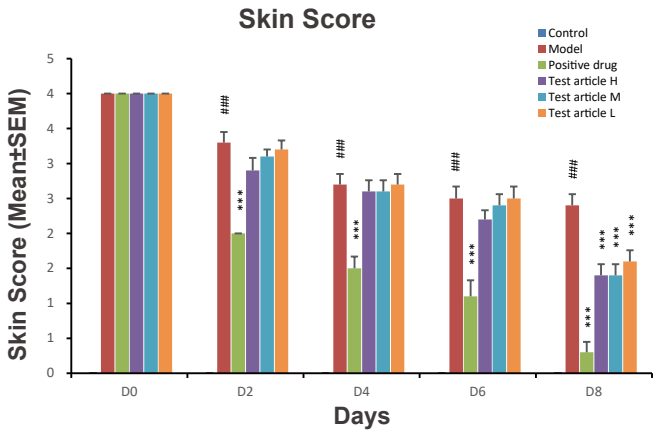


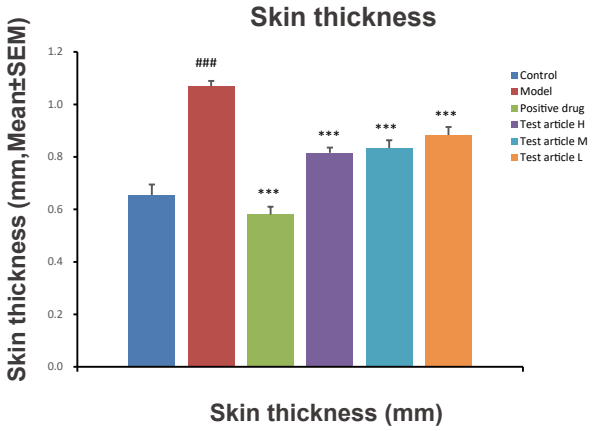
Chronic Atopic Dermatitis Model Induced by DNFB

Atopic dermatitis (AD) is a chronic and recurrent inflammatory skin disease, characterized by severe itching and recurrent skin lesions. Chronic itching is a sensation that triggers the desire to scratch. Repeated applications of 2,4-dinitrofluorobenzene (DNFB) were used to induce AD in a mouse model of annoying pruritus. Application of DNFB could be used to build chronic atopic dermatitis model. DNFB successfully induces AD-like dermatitis and histological changes as well as epidermal barrier dysfunction.

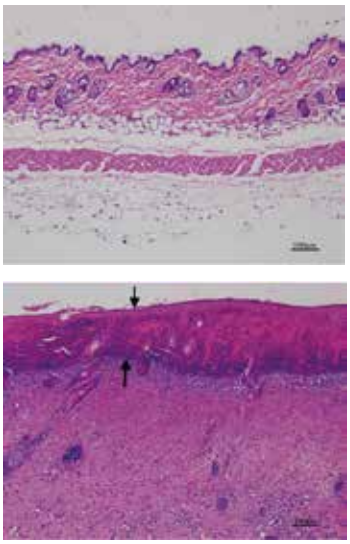
In the chronic phase of AD-like dermatitis, Th2-associated cytokines were still highly expressed, while Th1- and Th17-associated cytokines were also gradually increased. Compared with the acute phase, the JAK-STAT signaling pathway was highly expressed in the chronic phase of AD-like dermatitis. The JAK-STAT signaling pathway plays a pivotal role in the chronicity of AD.

Medicilon Case: Chronic atopic dermatitis model induced by DNFB





BALB/C mice



Control

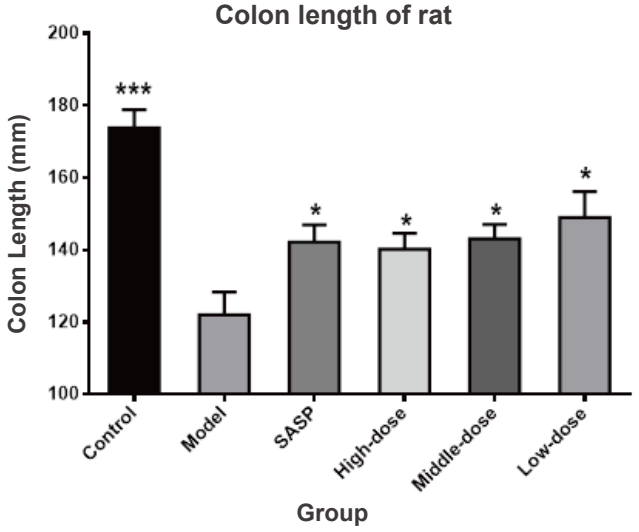
Model

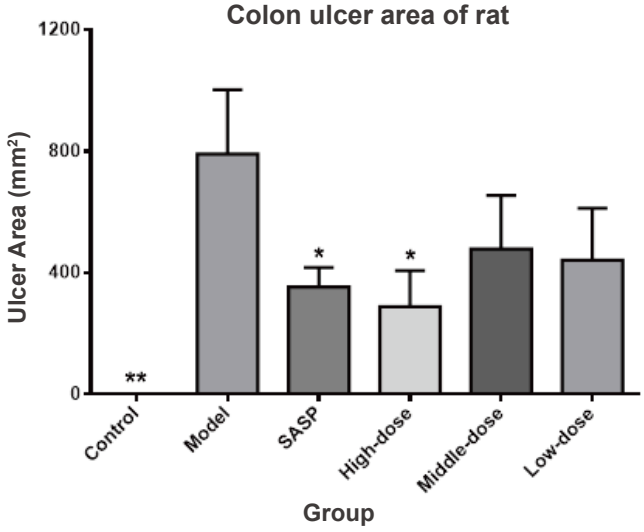
TNBS Induced Rat Ulcerative Colitis Model

Inflammatory bowel disease (IBD) including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory disorder of the intestinal tract whose etiology has not yet been fully elucidated. IBD pathogenesis is multifactorial. IBD is characterized by massive cellular infiltrates which is associated with abnormalities of the immune system including increased number of $CD4^+$ T-lymphocytes, mast cells, neutrophils, and eosinophils. These conditions give rise to inflammation, ulceration, edema, diarrhea along with blood and/or mucus, fever, and gastric dysmotility. No medical cure has been developed for IBD and the current treatment focuses on maintaining remission. IBD animal models represent certain pathophysiological features of human UC and CD involving weight loss and diarrhea accompanied by blood and/or mucus, fever, shortened colon, crypt abnormalities, gastric dysmotility and infiltration of inflammatory cells.

The 2,4,6-Trinitrobenzenesulfonic acid (TNBS) murine model of colitis is a Th1 inflammation characterized by infiltration of $CD4^+$ lymphocytes that shares features with human CD and UC. In comparison with other animal models of IBD, TNBS model is an efficient method. TNBS can mimic many of macroscopic and histological characteristics of human IBD and is widely applicable to mice and rats.

Medicilon Case: TNBS induced rat ulcerative colitis model

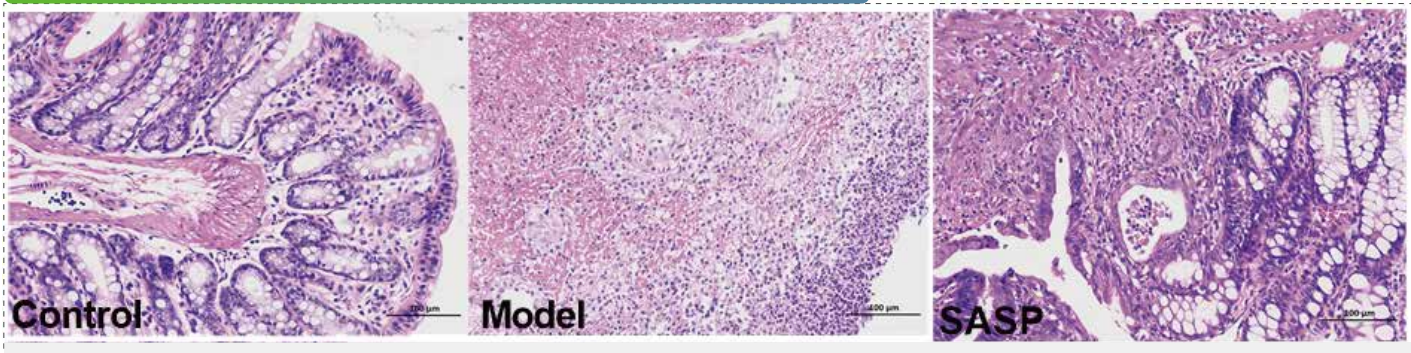




Model

Positive drug

Medicilon Case: TNBS induced rat ulcerative colitis model

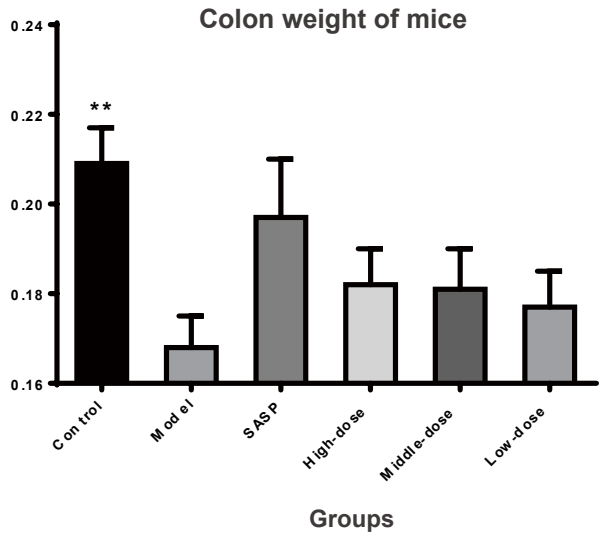


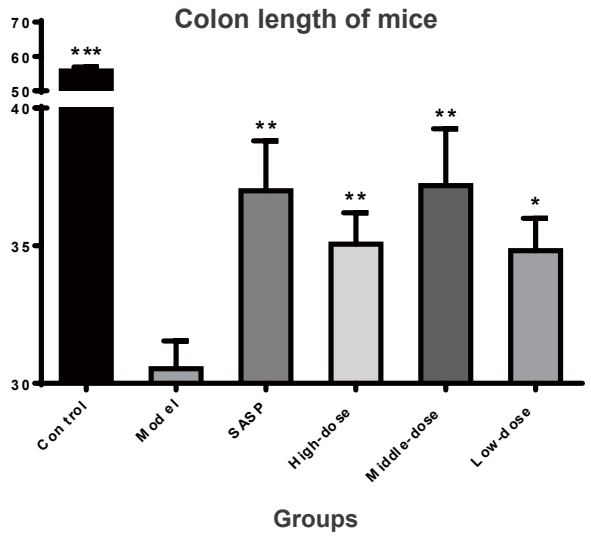
Pathology of colon of rat

DSS Induced Mouse Ulcerative Colitis Model

Inflammatory bowel diseases (IBD) mainly comprised of Ulcerative Colitis and Crohn's Disease are complex and multifactorial disease with unknown etiology. Two major IBD of the gastrointestinal tract, Crohn's Disease (CD) and Ulcerative Colitis (UC), are characterized by both acute and chronic inflammation of the intestine with multifactorial etiology. Dextran sodium sulfate (DSS) is a water-soluble, negatively charged sulfated polysaccharide with variable molecular weights. Administration of DSS in mice causes human ulcerative colitis-like pathologies due to its toxicity to colonic epithelial cells, which results in compromised mucosal barrier function. The DSS colitis model is very popular in IBD research due to its rapidity, simplicity, reproducibility and controllability. Acute, chronic and relapsing models of intestinal inflammation can be achieved by modifying the concentration of DSS and the frequency of administration.

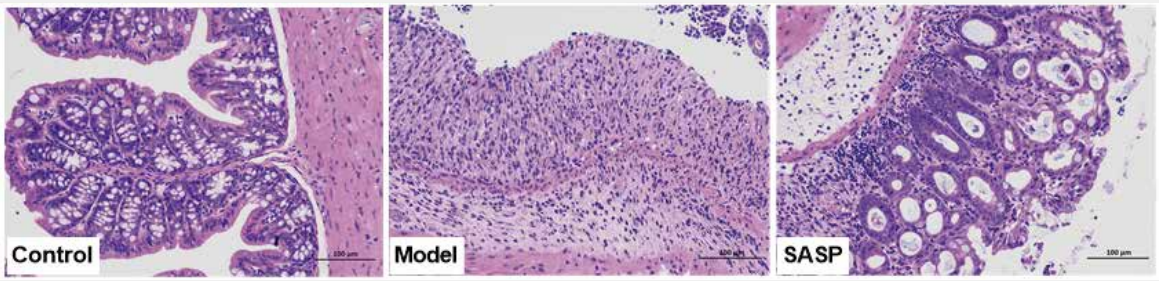
Medicilon Case: DSS induced mouse ulcerative colitis model





Medicilon Case: DSS induced mouse ulcerative colitis model

General view of colon of mice



Pathology of colon of mice

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