Pruritus research and drug evaluation

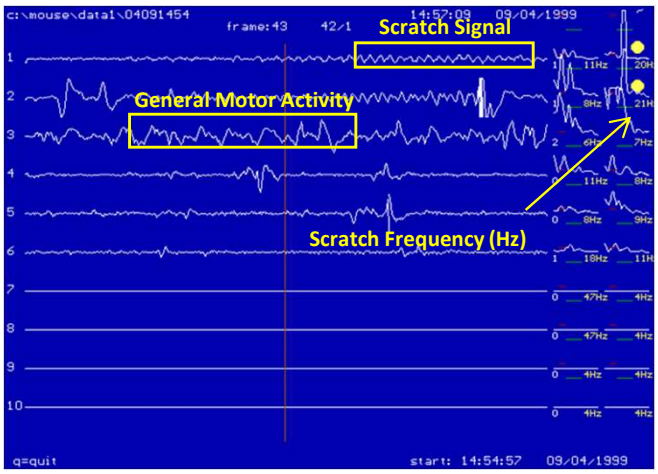
Pruritus (itching/scratching) is a symptom of various skin disorders that may occur as an idiopathic neurosis or may be symptomatic of a systemic disease. Patients commonly report that they suffer more from pruritus than other disease symptoms. As pruritus is associated with many different types of disease, a therapy that tackles the causes of the disease and alleviates pruritus will have a large commercial advantage over those products that only tackle the disease. The most commonly used species to evaluate drugs for pruritus research is the mouse. Derphartox has developed an automated method for measuring mouse scratching in real time.

Basic protocol automated scratch detection system

A metal ring is placed around the hind leg of a mouse which is placed in a cage on a Scratch Detection Unit (SDU, Figure 1). Movement of the ring in the electromagnetic field of the SDU can be transformed into a wave signal and analysed for scratch movements (Figure 2).

Figure 1. Scratch Detection Units (SDU)

Figure 2. Computer screen showing data from 10 cages simultaneously (cages 1-6 are in use).



End points

In this pruritus model the end points established include:

- Number of Scratch Events (SEs)
- General motor activity (GM)
- Scratch frequency (Hz)
- Weight/cell composition draining lymph gland
- Histological and molecular analysis of treated and control ears

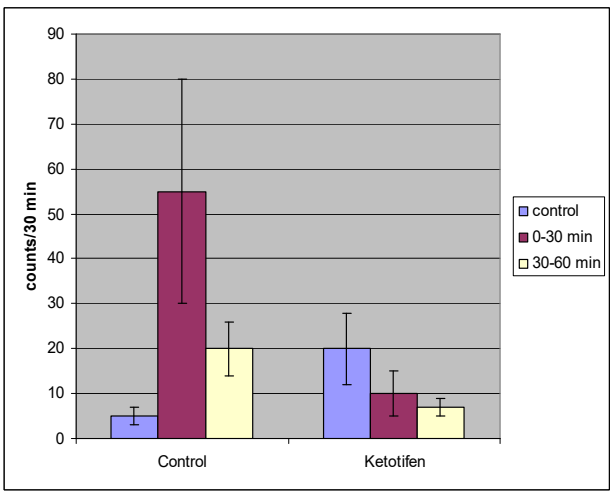
Validation

Various applications of the model have been established.

1.The inhibition of chemical induced scratching

Figure 3. Ketotifen inhibits compound 48/80 – induced scratching

Ketotifen induces mast cell degranulation and scratching during the first 30 min.

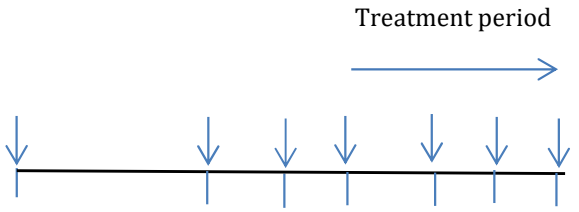


2. The oxazolone mouse ear delayed type hypersensitivity (DTH) reaction

Acute model. Mice are sensitized against oxazolone on day 0 and then challenged and treated on day 7. Scratching is normally measured for a 24 hr period. Ear thickness is measured on days 7 and 8.

Chronic model. Mice are treated chronically with oxazolone as shown in figure 4.

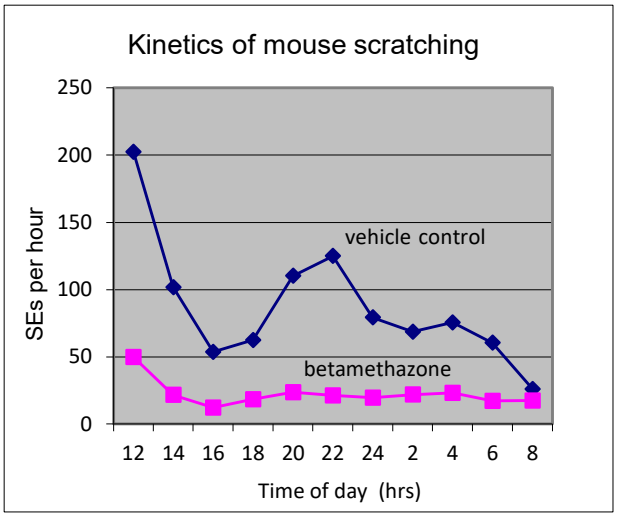
Figure 4. Time schedule basic protocol



Treat with 1% oxazolone on these days

Treatment with test compounds can begin on day 7 or later as required. Scratching is normally measured for 24 hr periods at the beginning and end of the treatment period. Ear thickness is measured daily.

Figure 5. Kinetics of oxazolone induced scratching on day 18, chronic model. Topical betamethasone treatment began on day 7.

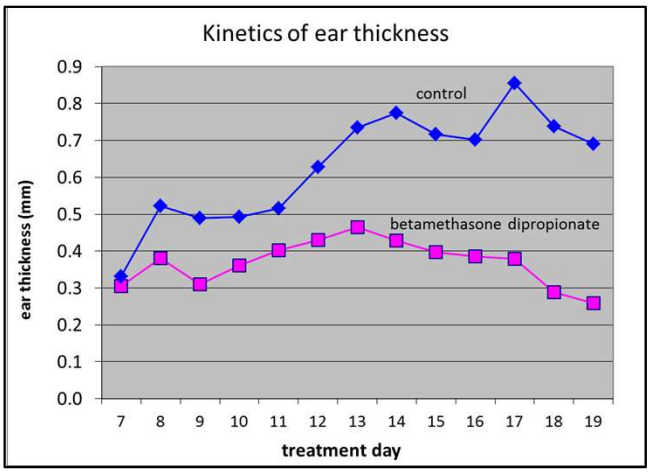


In addition to the scratching, the ear thickness parameter is also measured (Figure 6).

Timelines

These will vary depending on the protocol.

Figure 6. Kinetics of ear thickness.



Advantages of the model

This method has the following advantages:

- Unlike other automated systems, mice are housed in standard cages with food and water so that their behaviour is not modified
- Scratching can be measured continuously for 24 hr-48 hr periods
- Scratching is measured objectively
- Researchers do not have to manually count scratches (from video-film)

Associated (disease) models

- The human skin transplant model of psoriasis
- Imiquimod induced model of psoriasis
- Human skin explant culture model (normal & skin disease specific)

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References

-Elliott et al., J. Pharmacological and Toxicological Methods, 2000. 44: p. 453-59.