The effect of an ethanol extract of catnip *(Nepeta cataria)* on the behavior of the young chick

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Summary. The alcohol extract of catnip has a biphasic effect on the behavior of young chicks. Low and moderate dose levels (25–1800 mg/kg) cause increasing numbers of chicks to sleep, while high dose levels (i.e. above 2 g/kg) cause a decreasing number of chicks to sleep.

Catnip *(Nepeta cataria)*, a member of the mint family, is widely distributed in both the United States and Europe. It is widely known that catnip is a potent behavior altering drug and/or hallucinogen in domestic cats[1] and large wild cats[2].

In addition to its wide distribution in the wild, catnip is available from a wide variety of commercial sources (i.e. pet stores, supermarkets, herb stores, seed supply stores, etc.) for use in making catnip toys for cats or for use as a herbal remedy for humans. Catnip tea (i.e. the water extract), and to a lesser extent, catnip tincture (i.e. the alcohol extract), are among the most common herbal or folk remedies prescribed by naturopaths, herbalists, folk doctors, etc. in both the United States and Europe[3,4]. Catnip tea is commonly prescribed for nervous, stomach, and respiratory problems[3–5]. According to a commonly used recipe, 1 pint (i.e. approximately 473 ml) of boiling water is poured over 1 ounce (i.e. approximately 28 g) of dried catnip and the mixture is allowed to steep in a closed container for 1 h and then filtered. The dose of this 'catnip tea' is approximately 1 cup/day, administered in 1–3-tablespoon lots at periodic intervals[6]. When catnip tea is prepared in this manner, an average dose of 3 tablespoons contains 144 mg of a solid residue upon evaporation of the water. When catnip is smoked, it provides a cannabis-like effect, with hallucinations, but somewhat less intense than cannabis. Although catnip is commonly administered by herbalists and due to its widespread availability, its potential for abuse as a hallucinogen is great, and relatively little is known about the pharmacology of catnip. Since the young chick has a fairly limited behavioral repertoire and since it is known to respond to other hallucinogens in a relatively stereotyped manner[7–9], we decided, as a first step in determining the mechanism of action of this drug, to determine what effect it would have on the young chick.

Methods. Male White Leghorn chickens were obtained at 1 day of age from the Kazmeier Hatchery (Bryan, Tx.) and housed in temperature controlled brooders, with food and water available ad libitum. A commercial ethanol extract of catnip was used in these experiments (Meer Corp., solid extract of catnip herb, 1-4, Lot No. 46-00770). Weighed samples (100, 400, 600, 1000 mg) of the extract were dissolved in 0.1 ml of ethanol (95%) and then slowly added to distilled water which contained 0.05 ml of Triton X-100 (Sigma Chemical Co., St. Louis, Mo.) and the volume adjusted to 10 ml. This allowed a dose level of 0.01 ml/g b.wt. All drugs were administered i.p. The control chicks received the same volume of the alcohol-detergent solution. Groups of 12 chicks were injected at each dose level and immediately after injection, each chick was placed in a standard galvanized steel mouse cage, 1 animal per cage, and closely observed for 45 min. During this time period, at 1-min intervals, each chick was observed and placed in 1 of the following categories which best described the behavior of the chick: a) Light sleep (i.e. the chick sat or stood quietly, without peeping, with eyes closed and head up); b) deep sleep (the chick sat down without moving or peeping, with eyes closed, and head down or lost posture and lay on side); c) quiet wakefulness (the chick stood or sat quietly, without peeping, with eyes open); d) normal wakefulness (the chick moved about and peeped).

In addition, in order to evaluate the effects of lower (25, 50, 75 mg) and higher (1200, 1400, 1600, 1800 mg) dose levels, additional groups of 12 chicks each were injected with these dose levels and observed for 20 min to determine how many chicks would show 2 consecutive 1-min sleep periods. When it was noted that these dose levels were not toxic (i.e. no animals died), and in an effort to find a dose level that caused sleep in 12 out of 12 subjects, additional groups of 12 chicks each were injected with 2000 and 2200 mg of catnip extract.

Results. At dose levels of 100 and 400 mg/kg, there was no significant change in the average total duration of light or deep sleep when compared to the control animals. However, at 600 and 1000 mg/kg, the average total duration of both light and deep sleep was significantly increased when compared to the controls, as determined by the Kruskal-Wallis 1-way analysis of variance and Nemenyi's test (confidence level = 0.05)[10]. The following is a list of dose levels and the number of chicks that displayed 2 sequential 1-min sleep periods during the first 20 min of observation: 25 mg/kg (0/12); 50 (1/12); 75 (1/11); 1000 (5/12); 1200 (7/11); 1400 (9/12); 1600 (11/12); 1800 (11/12); 2000 (5/11); 2200 (6/12). It was clear that in the young chick,

The effect of an ethanol extract of catnip on the behavior of young chicks. The 1st number in each pair represents the average number of 1-min intervals that the chick engaged in the behavior. The number immediately below it is the SD

	Average total duration Light sleep	Deep sleep	Quiet wakefulness	Drug effect
Control	9.27	0	5.55	27.45
	(9.77)	(0)	(5.54)	(9.75)
100 mg/kg catnip extract	8.00	0	24.50	49.20
	(5.60)	(0)	(16.35)	(21.92)
400 mg/kg catnip extract	5.60	0	43.90	61.30
	(4.39)	(0)	(10.95)	(16.91)
600 mg/kg catnip extract	61.17	6.00	87.17	165.67
	(60.74)	(3.61)	(42.12)	(37.59)
1000 mg/kg catnip extract	61.45	33.14	48.64	150.91
	(47.55)	(24.05)	(20.36)	(60.06)

catnip had a biphasic effect. At levels up to 1800 mg/kg, increasing dose levels caused an increase in the number of chicks that displayed 2 sequential 1-min sleep periods during the first 20 min of observation. Higher dose levels (i.e. 2000 and 2200 mg/kg) showed a decrease in the number of chicks that were affected in this way. There was no increase in mortality at any dose level, so the lethal dose 50% must be higher than 2200 mg/kg.

Discussion. Since catnip is widely used in herbal medicine and a potential drug of abuse, it is important to gain greater insight into its mechanism and site of action. It is clear that the alcohol extract of catnip causes biphasic effects in young chicks. Low and moderate dose levels cause an increase in the number of animals that sleep, while high levels cause a decrease in this number. It will be important to isolate that active agent (or agents), identify it, and elucidate its pharmacology. In an attempt to achieve this goal, we are currently screening other solvent extracts of catnip for pharmacological activity and determining how the ethanol extract of catnip interacts with other psychopharmacological agents.

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Anticonvulsant activity of farnesylacetone epoxide – a novel marine natural product

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Summary. A marine natural product, farnesylacetone epoxide, which is chemically related to juvenile hormone, has anticonvulsant properties at nonsedative doses in mice.

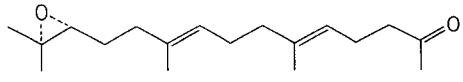
A dichlormethane extract of a brown alga, *Cystophora moniliformis,* was found to have anticonvulsant activity in mice. The active constituent farnesylacetone epoxide (**I**) (figure 1) was isolated and found to be an analogue of juvenile hormone[1]. The pharmacological activity of farnesylacetone epoxide has been studied and the anticonvulsant properties compared with phenytoin.

Farnesylacetone epoxide could protect mice against all phases of the convulsive response to electroshock but only after an i.p. dose of 600 mg/kg (table). Phenytoin at this dose level could not prevent the clonic convulsive response after electroshock, although doses as low as 30 mg/kg i.p. did prevent the tonic limb flexion and tonic extensor phases.

The effect of farnesylacetone epoxide and phenytoin on convulsions induced by electroshock (30 mA, 160 V, 0.2 sec via corneal electrodes) or metrazol (110 mg/kg i.p.) in mice

	Farnesylacetone epoxide	Phenytoin
Protection against electroshock (ED_{50} mg/kg i.p.)		
Tonic limb flexion	550	20
Tonic extensor	370	20
Clonic convulsion	460	> 300
Protection against metrazol (ED_{50} mg/kg i.p.)		
Tonic limb flexion	320	25
Tonic extensor	190	20
Clonic convulsion	> 600	> 300
LD_{50} (mg/kg i.p.)	> 900	190

Fig. 1.



Farnesylacetone epoxide at 300 mg/kg i.p. did prevent the tonic extensor phase of metrazol (110 mg/kg i.p.) induced convulsions. However a dose of 600 mg/kg i.p. was necessary for full protection of tonic limb flexion, tonic extensor and the lethal consequence of the convulsion induced by metrazol. Both farnesylacetone epoxide and phenytoin could not prevent the clonic convulsive response to metrazol at any dose level. As with electroshock, phenytoin did prevent the tonic limb flexion and tonic extensor phases of the metrazol response at doses as low as 30 mg/kg i.p. After oral administration farnesylacetone epoxide was inactive against all phases of electroshock or metrazol induced convulsions.

For electromyographic studies mice were anaesthetized with pentobarbitone (80 mg/kg i.p.) and recording electrodes (fine stainless steel pins) were implanted in the interdigital muscles of the ipsilateral foot and in the anterior tibialis muscle of the contralateral hind limb. Stimulating electrodes were placed close to the sciatic nerve.

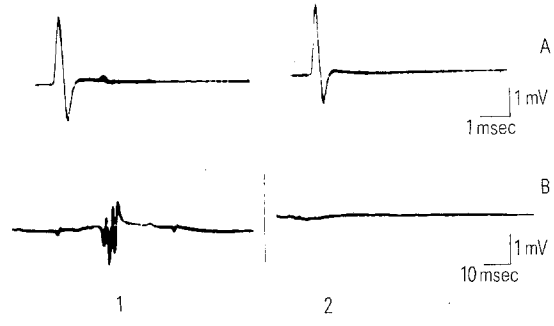


Fig. 2. The effect of farnesylacetone epoxide on peripheral neuromuscular transmission (A) and polysynaptic reflex discharge (B) in an anaesthetized mouse. 1. Control responses; 2. responses 15 min after the injection of farnesylacetone epoxide (300 mg/kg i.p.).