

# Kairomones – important substances in interspecific communication in vertebrates: a review

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**ABSTRACT:** Interspecies chemical communication is widespread among many groups of organisms, including vertebrates. Kairomones belong to a group of intensively researched substances, represent means for interspecific chemical communication in animals and bring benefit to the acceptor of the chemical signal. Important and often studied is the chemical communication between hosts and their ectoparasites such as ticks and other parasitic mite species. Uric acid is a host stimulus of the kairomone type, which is a product of bird metabolism, or secretions of blood-fed (ingested) ticks. Secretion of volatile substances with kairomone effect may depend on the health of the host organism. Another examined group is the haematophagous ectoparasite insects of the order Diptera, where in addition to the attractiveness of CO<sub>2</sub> a number of other attractants have been described. Specificity of substances in chemical communication can also be determined by their enantiomers. Detailed study of the biology of these ectoparasites is very important from a practical point of view: these parasites play an important role as vectors in a number of infectious diseases. Another area of interspecific chemical communication is the predator-prey relationship, or rather the ability to detect the proximity of predator and induce anti-predator behaviour in the prey. This relationship has been demonstrated in aquatic vertebrates (otter *Lutra lutra* – salmon *Salmo salar*) as well as in rodents and their predators. The substances produced by carnivores that induce behavioural response in mice have already been identified. The knowledge of interspecies communication (e.g., between host and parasite) is becoming a prerequisite in successful animal breeding and care.

**Keywords:** interspecific relationship; host; ectoparasite; predator; prey

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## 1. Introduction

Senses which perceive chemical stimuli are considered evolutionarily to be the oldest senses. Their importance regarding the biology of animals is likely to be considerably larger than previously thought. Pheromones are signals for intraspecific communication. Allomones are interspecies chemical signals bringing benefit to the signal-producing organism. From the groups of communication

substances kairomones are the subject of most intense research; they are interspecific chemical communication substances of animals, bringing benefit to the recipients of the chemical signal. The ability to perceive and distinguish chemical cues has been studied in various organisms. A recent study in rodents has shown that this ability involves the vomeronasal organ, a specific chemoreceptive structure of the olfactory system. Recognition of these chemosignals is important for many differ-

ent interactions: finding a mate, establishing social hierarchies, and also for initiating interspecies defensive behaviours (Chamero et al. 2012).

Detailed knowledge of interspecies communication (e.g., between host and parasite) are essential for a true understanding of farm animals and thus for successful breeding and veterinary care.

Interspecific chemical communication between different species through allelomones (i.e., kairomone, allomone and synomone) is widespread among many groups of prokaryotes, plants and invertebrates. However, it is known that allelochemically-mediated communication also exists among vertebrates including mammals (Sbarbati and Osculati 2006). This short review discusses the role of kairomones in relation to vertebrates. The very extensive area of the role of kairomones in invertebrates lies outside the scope of this article.

Our current understanding of kairomones in freshwater organisms has been presented in a review by Burks and Lodge (2002). Beside many examples of kairomones in invertebrates, the authors also mention relationships between fish and invertebrates or frog tadpoles as their prey. The authors also summarise data on the identification of the chemical composition of cues important in food interactions, investigations on how some abiotic forces impact chemical communication and a quantification of the importance of genetic variability. Kairomone communication of water animals has also been reviewed by Ferrari et al. (2010). Thus, in this review specific examples of kairomone communication in water animals are mentioned only in specific instances.

## 2. Communication between host and ectoparasite: acarids

Interspecific communication between hosts and ectoparasites is one of most studied aspects of reciprocal chemical communication between invertebrates and vertebrates. Many studies of such relationships have been undertaken on ticks and their hosts, from many different aspects. The study of Harrison et al. (2012) highlights the importance of small mammalian insectivores in the transfer of pathogens by ticks. Experiments with the species *Elephanturus myurus* and *Micaelamys namaquensis* as potential hosts of the ixodid ticks *Rhipicephalus warburtoni* and *Ixodes rubicundus* suggest that a kairomonal cue originating from the odour of *Elephanturus myurus* may stimulate the attachment

and feeding of these ticks. Further, the ixodid ticks possess immunosuppressive mechanisms specific to *E. myurus*, allowing them to feed on this host species but not on *Micaelamys namaquensis*.

Uric acid can be considered as a host cue of the kairomone type which is excreted by birds (and reptiles) and targets their ectoparasites. The lone star tick *Amblyomma americanum*, whose hosts are birds, responds to uric acid by arrestment, not by attraction. Both nymphs and adults of *Amblyomma americanum* react to uric acid, in contrast to *Dermacentor variabilis*, which prefers mammalian hosts (Yoder et al. 2003).

However, non-fed stages of this tick species (lone star tick *Amblyomma americanum* L.) have been shown to react more to filter paper discs with tick excreta than to guanine exposure or to uric acid, excretory products of birds. This suggests an ability of the tick to remain in locations with an abundance of successful (fed) ticks even when excretion levels of guanine are lower, soon after hatching and moulting of the hosts (Yoder et al. 2008).

The question of whether natural excretions contain some kairomonal cues remains to be answered. This problem was investigated using the urine of two mammal species and their ectoparasites. Urine from two principal hosts, the white-tailed deer (*Odocoileus virginianus*), which is the principal host of the adult stage of the blacklegged tick (*Ixodes scapularis*), and the White-footed mouse (*Peromyscus leucopus*), the major host for immature tick stages, did not contain any kairomonal cues for this tick (Carroll 1999a).

Results of laboratory experiments with the American dog tick *Dermacentor variabilis* (Acari: Ixodidae) suggested the distribution of host-seeking ticks. Both sexes of ticks became akinetic on residues from dog flank hair and hair from between toes; female *D. variabilis* also became akinetic on a canine paw print on a disc of filter paper (Carroll 1999b).

This tick species and two other (blacklegged ticks, *Ixodes scapularis* and lone star ticks, *Amblyomma americanum*, the principal host of both is deer) responded (became akinetic) on residues rubbed from their hosts in laboratory tests. However, the reaction also occurred using the same method of bioassay when the specific host substances were reversed. Adult exhibited responses to deer substances suggesting some use of deer as hosts. Thus, the specificity of *D. variabilis* is probably not exclusive and aspects of its host-finding strategy are still unclear (Carroll 2002).

Another investigation was concerned with factors which attract the tick *Ixodes ricinus*. Ticks with high fat content, and thus with higher energy reserves, were more likely to walk horizontally over short distances. Slightly dehydrated ticks were attracted to moisture; they moved preferentially up a humidity gradient. However, in conditions of moist air ticks walked towards the odour secreted by host skin (Crooks and Randolph 2006).

The secretion of volatile compounds with kairomonal effect can also depend on the health status of potential hosts. This was demonstrated in a study on the hedgehog (*Erinaceus europaeus*) and its ectoparasite, the *Ixodes hexagonus* tick. Healthy hedgehogs were less likely to carry ticks than sick animals; thus, the ticks preferred the faecal odour from sick hedgehogs. The faeces of sick hedgehog individuals were shown to contain raised levels of the volatile aromatic compound indole (detected in experiments using gas chromatography – mass spectrometry). Ticks were attracted by indole, but not as a unique chemical cue; there must be other undetected substances mediating the attraction, because the faeces from healthy animals with the addition of indole, were not attractive to ticks (Bunnell et al. 2011). Confirming this observation, e.g., in livestock, the health status of an animal corresponds to fewer tick attacks while a higher number of ticks could indicate a sick individual.

Kairomone-based interactions were also found in mites other than ticks. The skin and plumage of chickens (*Gallus gallus domesticus*), for instance, contain substances attractive to parasitic mites. Compounds attractive to the Poultry Red Mite (*Dermanyssus gallinae*) were soluble in benzene derivatives, amyl acetate or ethyl acetate, non-volatile, alkaline hydrolysable, susceptible to oxidation, and stable at up to 100 °C. The results of the study by Zeman (1988) demonstrated that specific diol-esters of fatty acids, prepared from the secretion of uropygial (preen) glands of hens, had comparable efficacy as a feeding stimulant for mites to the natural extract of surface lipids of birds.

### 3. Communication between host and ectoparasite: haematophagous insects

Detailed study of the biology of the mentioned ectoparasites is very important also from the practical point of view: these parasites often have prominent roles as vectors of many infectious diseases.

Individual host odour plays a key role in the host attraction for specific ectoparasites. This finding was documented in mice and the yellow-fever mosquito, *Aedes aegypti* (Diptera: Culicidae) using sticky traps. Traps baited with individual mouse odours caught more female mosquitoes than traps with volatile substances from the collection system or blind control traps (McCall et al. 1996).

An important group of ectoparasites responding to impulses of the kairomone type is haematophagous insects of the order Diptera. The Biting midge *Culicoides impunctatus* (Goetghebuer) (Diptera: Ceratopogonidae) is extremely sensitive to CO<sub>2</sub>, which is very important for host location, with release rates of 0.2–2.5 l/min. 1-octen-3-ol released at 0.06 mg/h, acetone (23 mg/h) and a mixture of six phenolic compounds (phenol, 3-ethylphenol, 4-ethylphenol, 3-methylphenol, 4-methylphenol and 4-propylphenol) at undetermined release rate have also been confirmed as strong attractants. Investigations of possible combinations of potential attractants showed synergism of CO<sub>2</sub> (0.2 l/min) and acetone, 1-octen-3-ol or cow urine with maximum effect for the triple combination of cow urine + acetone + CO<sub>2</sub> as well as cow urine + 1-octen-3-ol + CO<sub>2</sub> (22 and 24 times more effective, respectively, compared to CO<sub>2</sub> alone, using odour traps) (Bhasin et al. 2001).

In another study on potential kairomones of ornithophilic mosquitos skin from the back and the feet, and feathers from the back of White Leghorn chickens (*Gallus gallus domesticus*) were used. The hexane extracts from feathers acted as attractants to mosquitos of the genus *Culex* and contained alcohols, ketones, and diones (thus, similar substances as in the study referred to above). Analysis of hexane extracts from chicken feet, skin, and feathers showed similar levels of the compounds; quantitative differences were also only small. Ether extracts from feathers containing aldehydes (which were also present in hexane extracts) were proven to be inactive. In concentrated ether extracts of feathers aldehydes and carboxylic acids (C-6-C-9 aldehydes and acids) were found in quantitatively similar ratios (Bernier et al. 2008).

Specificity of chemical communication substances can also be determined by their enantiomers which differ only in the left or right handedness (chirality) of their orientations. Their chemical and physical properties are identical, but they can elicit different physiological and thus behavioural activity. Such enantioselective odorant receptors have been demonstrated in mammals. The study of Bohbot et al. (2009) documented for the first time

their presence in insects, namely in yellow fever mosquitos, *Aedes aegypti*, where the odorant receptor 8 (AaOR8) acts as a chiral-selective receptor for the (R)-(-)-enantiomer of 1-octen-3-ol. In the presence of other kairomones this attractant is used by blood-sucking insects to help them locate their hosts. However, the recognition process is, in fact, quite complex and is also determined by steric constraints, chain length and degree of unsaturation.

Some substances with potential biological activity are also secreted in wounds infested with the larvae of parasitic insects. Most compounds found in the wounds of sheep invaded by larvae of *Cochliomyia hominivorax* (Coquerel) were straight and methyl-branched aliphatic carboxylic acids, ranging from C2- to C5-carbon chain length. Butanoic acid, for instance, was found in an amount of approximately 0.45 mg/ml (aliphatic carboxylic acids with longer chain lengths were present in trace amounts only). Phenol and indole were the two most abundant non-acidic compounds. Twenty six electro-physiologically-active compounds were found in total using linked gas chromatography and electro-antennography; twenty five of them were characterised (Cork 1994).

Kairomones inducing arrestment, alighting and probing in male Tsetse Flies (*Glossina morsitans morsitans*) were found in the body wash of a host animal, in this case cattle. Active compounds of this matter were present in the ethyl acetate – insoluble, phenolic, acidic, neutral and basic fractions of the methanolic extract of the cattle wash. The phenolic fraction had the most pronounced effect (Saini et al. 1993).

#### 4. Kairomones in the predator-prey relationship

One of the key aspects of the predator-prey relationship is the ability of the prey to detect the proximity of predator. Predator-prey relationships also provide a classic paradigm for the study of innate animal behaviour.

The relationship can be examined in the case of a novel predator, where chemical cues can play an important role. Roberts and de Leaniz (2011) examined the role of diet-released chemical cues in facilitating predator recognition and promoting antipredator responses in predator-naive juvenile Atlantic salmon (*Salmo salar*). In these experiments blank water samples or water with diet cues from

Eurasian otter (*Lutra lutra*) spraints (a sympatric predator) fed either salmon or a non-salmon diet were used.

Antipredator behaviour was neither found among individuals tested with blank water nor on water scented with cues from an otter fed on a non-salmon diet. In contrast, strong behavioural changes – spatial avoidance, reduced activity and increasing ventilation, were observed among salmon tested on water scented with cues from an otter fed on a salmon diet. This suggests that Atlantic salmon do not innately recognise the sympatric predator *Lutra lutra* as a threat. This finding may also indicate practical recommendations: diet-released conspecific alarm cues and not predator-specific kairomones should be used for juvenile salmon, as this will teach them to recognise the predator.

There are still many open questions with regard to the role of kairomones between fish and zooplankton. The effect of fish kairomones on the acceptor (zooplankton) can be positive or negative. Samanta et al. (2011) proved by mathematical models that vertical migration of plankton can play an important role in these relationships; this factor helps zooplankton to maintain their levels by avoiding over-predation.

Single, volatile substances detected in the environment have been shown to drive an elaborate danger-associated behavioural response in mammals (Ferrero et al. 2011).

Chemical cues (or odours) from carnivores elicit fear and avoidance responses in rodents, their usual prey. The sensory mechanisms of this phenomenon are largely unknown. Ferrero et al. (2011) identified biogenic amine, 2-phenylethylamine as a substance produced by predators that activates a mouse olfactory receptor and also elicits an innate behavioural response. The predator cue used in this study was purified from bobcat urine. This substance is apparently widespread in predators; quantitative HPLC analysis in 38 mammalian species indicated enriched 2-phenylethylamine production by numerous carnivores, with some producing more than 3000-fold more than the herbivores examined.

In experiments with rats and mice an avoidance to a 2-phenylethylamine odour source was found, and together with loss-of-function studies involving enzymatic depletion of 2-phenylethylamine from a carnivore odour, this indicates that this substance seems to be required for full avoidance behaviour.

Rodent olfactory sensory neurons and chemosensory receptors have the capacity to recognise

interspecies odours. 2-phenylethylamine is a key component of a predator odour blend that triggers hard-wired aversion circuits in the rodent brain.

### 5. Other kairomonal attractants

The ability of coprophagous insects to detect a feeding source by chemical cues is well known. Aak and Knudsen (2012) investigated the attraction of the blowfly *Calliphora vicina* (Diptera: Calliphoridae) to the scent of dead mice and seven different synthetic lures made from dimethyl trisulphide, mercaptoethanol and O-cresol. The scent of dead mice yielded a significantly higher attraction and some responses even showed differences in relation to fly ovarian developmental status and to their age. The reaction to natural odours and the three-component synthetic substances depended on fly egg developmental status and induced age-dependent responses. Thus, the attractiveness of synthetic substances with kairomone activity is induced partly by the physiological status of the flies as well as by the complexity of the lure.

### 6. Examples of the practical usage of kairomones for the control of parasites and disease vectors

An important vector of sleeping sickness is the tsetse fly (*Glossina fuscipes*). Omolo et al. (2009) have studied the responses of this insect to natural host odours by odour baits. Odours of cattle, pig, human and monitor lizard (*Varanus niloticus*) were used in the experiments. Odours from cattle, pigs and humans had no significant effect on the attraction of *Glossina fuscipes fuscipes* but odour from the monitor lizard doubled the catch ( $P < 0.05$ ). Thus, lizard odour significantly increased the landing and trap entry. Pig odour had a consistent effect on *Glossina fuscipes quanzensis*, doubling the catch of females attracted to the source and increasing the landing response for fly females. Testing CO<sub>2</sub> at doses equivalent to natural hosts suggested that the response of *Glossina fuscipes fuscipes* to lizard odour was not caused by this gas. Pig odour and CO<sub>2</sub> elicited a similar response of the tsetse *Glossina fuscipes quanzensis*, but CO<sub>2</sub> had no material effect on the landing response. Thus, identifying lizard kairomones for

*Glossina fuscipes fuscipes* and pig odour for *Glossina fuscipes quanzensis* may be an important step towards control of these fly taxa.

Field studies on the response of the New World screwworm *Cochliomyia hominivorax* (Diptera: Calliphoridae) to a synthetic odour-bait composed of compounds identified from wounds infested by the larvae of this species were conducted in Mexico. The use of these substances would allow replacement of animals used as baits for female *Cochliomyia hominivorax*. Both sexes of this fly were attracted to unwounded individuals (sheep), while experiments with unwounded sheep sprayed with larval wound fluid attracted female *C. hominivorax* but not male flies. Both males and females responded to acidic components of wound fluids, while the non-acidic components alone did not induce any reaction. The most effective tested blend was comparable to the standard synthetic attractant, Swormlure-4 (which predominately attracts female flies). Further simplification of the substance blend for attracting fly females could fully replace sentinel animals, and thus contribute to finding methods of reducing the number of these parasitic insects (Cork and Hall 2007).

An example of a significant (and therefore intensively studied) kairomone relationship of aquatic animals is parasitism of the sea lice *Lepeophtheirus salmonis* towards its host – the salmon. This ectoparasite is the most prominent parasite of salmon in fish farming. In aquatic environments physical and chemical cues such as light and salinity play important sensory roles together with mechanoreception, while chemoreception has a defining role in host localisation and recognition. Semio-chemicals derived from salmon and non-host fish have been identified and can be used for protection using odour traps for monitoring the abundance of lice as well as for stimuldeterrent diversionary (push:pull) strategies in their control (Mordue (Luntz) and Birkett 2009).

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