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The Value of Partial Racemates in Intraspecific Communication

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Abstract: Compounds which are not enantiomerically-pure will enable animals to communicate most effectively.

The scientific literature contains increasing numbers of reports of biologically-active compounds which are partially-racemic (optically-impure; <100% enantiomerically pure; <100% enantiomeric excess). It is the purpose of this communication to indicate that partially-racemic compounds may have considerable pheromonal advantages to the host animal.

Recent discussion and tabulations of the relationship between stereochemistry and pheromonal activity have demonstrated the necessity in some cases for the presence of both enantiomers in order to achieve biological activity, but there appears to be no discussion of the advantages of partial racemates for animal communication. Silverstein[1] in a review of chiral semiochemicals has discussed the pheromonal activity of racemates *v* the natural or unnatural enantiomer, and insect responses have been tabulated for situations when both enantiomers of the bioactive agent are present. Tumlinson[2] has similarly reviewed chirality *v* pheromonal activity and reported insect species where both enantiomers have activity. Mori,[3] in his review of synthetic methodologies, discusses the significance of chirality in pheromone perception and identifies a number of relationships between stereochemistry and pheromonal activity. In some insect examples one enantiomer may be bioactive while the other antipode inhibits pheromonal action, but in other examples both enantiomers are required.

While mammalian pheromones are chemically less-well investigated, recent work with urinary metabolites of the brushtail possum[4] shows a number of volatile components which are again partially racemic.

A single pure compound (either achiral or as a single enantiomer) can presumably carry only one useful bit of pheromonal information; namely the presence or absence of that material above a certain threshold. The concentration of the chemical may provide additional information, but this will be so dependant upon distance, time and other factors that it may not be pheromonally-useful. A single pure compound would then be useful only when a single message is required, e.g. fly upwind until a mate is found.

More complex mixtures of compounds can obviously carry more complex messages, and it seems likely that animals with complex intraspecific social relationships will necessarily need complex chemical mixtures as pheromones. However this complexity comes at a price. Each component of the mixture will have a different volatility, a different evaporation rate, and a different rate for chemical removal or destruction. Thus the relative concentrations of the components will vary with time. While this could be useful in some time-related message; e.g. a 60:40 ratio of two components could indicate an animal had passed one hour previously, when it had then laid a 50:50 trail with one component more volatile than the other; in other messages there is obviously a disadvantage in having variability with time. In these cases the pheromonal message may simply be a sum of the presence or absence of the individual components, with little or no contribution from their relative concentrations. A multi-component mixture will then be able to carry only 2^n-1 distinctive messages, where n = the number of components; and a two component mixture can carry a maximum of only three independent messages.

A partial-racemate does not suffer this same time-based variability. Provided intermolecular association between the enantiomers is unimportant, the evaporation rates of two enantiomers from an achiral surface will be essentially identical. Thus a 60:40 mixture of enantiomers may remain at that ratio over a period of time. The human nose (and taste) can distinguish some enantiomers from their antipodes[3,4] and clearly animals can do likewise. Perhaps a male animal could distinguish a 60:40 female from a 58:42 female, even if the pheromonal marker had been laid some variable time previously. Thus a mixture of just two enantiomers could carry perhaps 50 different messages, all invariant with time.

Individual scent recognition among mammals, reviewed by Albone[5] and Halpin,[6] continues to be an area of active research,[7,8] with recent work[8] aimed at exploring individually distinctive odours and their role in mate recognition. The chemicals responsible for these effects have not yet been identified, but there would appear to be considerable elegance and simplicity in the use of partial racemates in overcoming the inherent problems of individual recognition by chemical means, and it would be surprising if animals did not make use of such methodology. We predict that as these materials are further chemically investigated, more will be found to be partially racemic.

Obviously animals which use preformed complex chiral molecules (e.g. steroids) as pheromones may have problems in obtaining these materials as a mixture of enantiomers. However in those cases where a *de novo* synthesis from achiral precursors is utilised, or where the generation of functionality is from a prochiral centre, then both enantiomers may be readily and advantageously available to the animal as a pheromone.

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