

Table II. Components explaining more than 4% of the total variance (for explanation see text)

Total							
P 1	Affinitive	Play	Aggressive	Submissive	Show	Excitement	Infantile
78%	23.7%	13.8%	11.5%	9.1%	8.2%	6.2%	5.6%
P 2	Affinitive	Play	Aggressive	Submissive	Excitement	♂ sex	♀ sex
75%	19.8%	15.3%	13.4%	11.8%	6.2%	4.5%	4.4%
P 3	Aggressive	Affinitive	Play	Submissive	Excitement	Groom	♂ sex
69%	13.7%	13.5%	13.4%	8.2%	8.1%	7.6%	4.8%
T	Affinitive	Play	Aggressive	Submissive	Excitement	Show	
79%	25.8%	20.0%	12.7%	9.9%	6.3%	4.6%	

> 0.35 regarded as significant). A component can be identified by considering the behaviour elements that have high loadings on it.

Results and discussion. The results, of which the general nature rather than the details interests us here, are presented in Table I. The loadings of the behaviour elements on the 7 most 'important' components (i.e. together explaining more than 80% of the total variance) are given. The first 4 components can easily be characterized as the 'affinitive' (= social positive) system, the 'play' system, the 'aggressive' system and the 'submissive' system respectively. Component V combines a number of elements with a rather agitated appearance and has, therefore, been called the 'excitement' system. Number VI, combining a few 'conspicuous' patterns, is termed the 'show' system, though most of the loadings on which the identification is based hardly surpass the significance level. The latter is also true for component VII which is termed the 'groom' system. The other components remain insignificant, do not permit a meaningful interpretation and have therefore not been presented here.

Inspection of Table I shows that all behaviour elements have loadings > 0.35 on 1 of the first 5 components; all but 1 have their greatest loadings (in all cases > 0.40) on 1 of the first 5. Apparently the repertoire of social behaviour patterns of this group of chimpanzees is satisfactorily categorized in terms of these 5 components. This is confirmed by the following.

In order to get an insight into the stability of the material, the total amount of observations (T) was split up in 3 parts (P1, P2, P3), for each of which the same analysis was done. As Table II shows, T's first 4 components also appear as the first in P1, P2 and P3. The 'excitement' component occupies the fifth place in 3 cases and the sixth in 1 case. Besides, practically all behaviour elements have significant loadings on these 5 com-

ponents. There are considerable differences only with respect to the following components, that may occasionally manifest themselves, depending on the relative frequency of occurrence of their 'typical' elements.

Thus the picture emerges of an hierarchical motivational structure with 5 (or at least 4) main motivational systems and a certain number of more specific motivational (sub)systems whose influence does not manifest itself consistently. A similar structure of the social behaviour has also been revealed by a different method, namely hierarchical cluster analysis¹⁰.

The categorization thus obtained is not based on any a priori postulated reference classes but is determined by the material itself. It can serve as an objective starting point for further, more detailed research. It would be valuable to perform this type of study on other groups of chimpanzees in order to find out whether the motivational categories found are indeed representative.

Zusammenfassung. Mittels Komponentenanalyse wurde die Struktur des sozialen Verhaltens einer in Halb-Gefangenschaft lebenden Gruppe von Schimpansen untersucht. Das Repertoire der 53 allgemeinsten sozialen Verhaltensmuster konnte als Funktion von 5 unabhängigen motivationellen Komponenten beschrieben werden.

J. A. R. A. M. VAN HOOFF

*Laboratorium voor Vergelijkende Fysiologie,
Utrecht (The Netherlands), 20 November 1969.*

¹⁰ L. L. McQuitty, *Educ. psychol. Measur.* 26, 825 (1966).

A New Broad-Spectrum Anthelmintic: 2-(4-Thiazolyl)-5-isopropoxycarbonylamino-benzimidazole

Discovery of the anthelmintic effectiveness of thiazobenzazole [2-(4-thiazolyl)benzimidazole, I] was reported by H. D. BROWN et al.¹ in 1961. It was subsequently found safe and effective against a wide spectrum of parasitic nematodes in ruminants, horses, swine, poultry, and other animals, as well as man²⁻⁵. An extensive program of structural modification was continued in this laboratory,

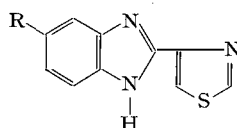
with the aim of finding new thiabendazole relatives with unique properties.


We now wish to report the finding that a number of derivatives (e.g., III-VI) of 5-aminothiabendazole (II) demonstrated the same breadth of anthelmintic activity as thiabendazole, and with an enhanced degree of potency. Of some 300 such compounds synthesized for anthelmintic

evaluation, 2-(4-thiazolyl)-5-isopropoxycarbonylamino-benzimidazole (III) was selected for further development on the basis of overall safety and effectiveness.

Nitration of thiabendazole (I) in sulfuric acid/nitric acid at room temperature afforded 5-nitrothiabendazole (VII), which was then catalytically reduced to the amine II. Amide derivatives III–VI were provided by reaction of II with the appropriate acid halide in the presence of base. Properties of the new compounds and an estimate

thiabendazole. This potency increase is attributed tentatively to an alteration in its mode of metabolism relative to that of thiabendazole. The latter compound is known to be rapidly inactivated in, for example, sheep⁶ via metabolic hydroxylation in the 5-position. Introduction of the acylamino group at C-5 as in III appears to inhibit this and other modes of rapid metabolism, allowing expression of more of the intrinsic efficacy of this class of anthelmintics.



Compound	R	Melting point (recrystallizing solvent)	Relative anthelmintic Potency ^a
I	-H (thiabendazole)		1.0
II	-NH ₂	232–233° (ethanol/hexane)	0.8
III	-NHCO ₂ CH(CH ₃) ₂	240–242° (isopropanol/water)	6
IV	-NHCO- 	260–261° (methanol)	4
V	-NHCOC ₆ H ₅	118–120° (methanol/water)	4
VI	-NHCOC ₆ H ₄ -F-(<i>p</i>)	155–156° (methanol)	4
VII	-NO ₂	240–241° (dimethylformamide)	0.2

^a Based on efficacy against a trichostrongyle nematode in laboratory animals.

of their relative anthelmintic potency in the laboratory animal model assays are given in the Table:

Biological results and discussion. Studies in sheep demonstrated that the new anthelmintic (III), at dosages of 5–15 mg/kg per os, was highly effective against mature and immature worms of the genera *Haemonchus*, *Ostertagia*, *Trichostrongylus*, *Cooperia*, *Nematodirus*, *Strongyloides*, *Chabertia* and *Oesophagostomum*. In cattle, compound III, at a dosage of 10–30 mg/kg per os, was highly effective against mature and immature worms of the genera *Haemonchus*, *Ostertagia*, *Trichostrongylus*, *Cooperia*, *Nematodirus*, *Strongyloides*, *Bunostomum* and *Oesophagostomum*. The compound was also highly effective against lungworm (*Dictyocaulus viviparus*) in cattle at 22–44 mg/kg (D. B. Ross, personal communication). For removal of immature worms from sheep or cattle, the required dosage generally tended toward the upper limit of the ranges cited.

The new anthelmintic has also proved to be highly potent in suppressing the development of *Ascaris suum* in swine, when fed in the diet at a concentration of 0.03%. It thus seems to be 3 times more potent than thiabendazole, and at least as potent as parbendazole, against the migratory phase of *Ascaris*. In the therapy of patent *Strongyloides ransomi* infections in swine, the compound was fully effective as a single oral dose at 7.5 mg/kg.

Other studies have shown that compound III, like certain other benzimidazoles, is extremely potent in preventing the development of helminth eggs or larvae. It also shares with other benzimidazole anthelmintics a high degree of efficacy against the early enteral and parenteral stages of *Trichinella spiralis* in mice.

The above studies indicate that the anthelmintic spectrum of III is similar to that of thiabendazole, and that the new compound is several times more potent than

Preliminary studies indicate that this new anthelmintic has relatively low toxicity in mammals; its therapeutic index in ruminants is tentatively estimated as at least 10.

Zusammenfassung. Es werden die Synthese sowie die biologischen Eigenschaften des neuen Anthelminticums 2-(4-Thiazolyl)-5-isopropoxycarbonylamino-benzimidazols beschreiben.

D. R. HOFF, M. H. FISHER, R. J. BOCHIS,
A. LUSI, F. WAKSMUNSKI, J. R. EGERTON,
J. J. YAKSTIS, A. C. CUCKLER and
W. C. CAMPBELL

Merck Sharp and Dohme Research Laboratories,
Rahway (New Jersey 07065, USA), and
Merck Institute for Therapeutic Research,
Rahway (New Jersey, USA), 16 October 1969.

- H. D. BROWN, A. R. MATZUK, I. R. ILVES, L. H. PETERSON, S. A. HARRIS, L. H. SARETT, J. R. EGERTON, J. J. YAKSTIS, W. C. CAMPBELL and A. C. CUCKLER, J. Am. chem. Soc. 83, 176 (1961). – H. D. BROWN, Texas Rep. Biol. Med., in press.
- J. E. GIBSON, *Veterinary Anthelmintic Medication*, 2nd Edn. (Commonwealth Agricultural Bureaux, Farnham Royal, Bucks, England 1965).
- A. C. CUCKLER and K. C. MEZEY, *Arzneimittelforsch.* 16, 411 (1966).
- W. C. CAMPBELL and A. C. CUCKLER, Texas Rep. Biol. Med., in press.
- L. G. EATON, O. H. SIEGMUND, A. D. RANKIN and R. G. BRAMEL, Texas Rep. Biol. Med., in press.
- D. J. TOCCO, R. P. BUHS, H. D. BROWN, A. R. MATZUK, H. E. MERTEL, R. E. HARMAN and N. R. TRENNER, J. med. Chem. 7, 399 (1964).