ABM-FD

TOXICITY STUDY BY

ORAL GAVAGE ADMINISTRATION TO

CD RATS FOR 13 WEEKS

(Volume 1 of 2)

Report

ABM-FD

TOXICITY STUDY BY

ORAL GAVAGE ADMINISTRATION TO

CD RATS FOR 13 WEEKS

(Volume 1 of 2)

Sponsor

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Final: 11 October 2005

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COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

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The study described in this report was conducted in compliance with the following Good Laboratory Practice standards and I consider the data generated to be valid:

The UK Good Laboratory Practice Regulations (Statutory Instrument 1999 No. 3106, as amended by Statutory Instrument 2004 No. 994).

OECD Principles of Good Laboratory Practice (as revised 1997), ENV/MC/CHEM(98)17.

EC Commission Directive 2004/10/EC of 11 February 2004 (Official Journal No. L 50/44).

These principles of Good Laboratory Practice are accepted by the regulatory authorities of the United States of America and Japan on the basis of intergovernmental agreements.

C. Horne ..... 11 October 2005

C. Horne, B.Sc. (Hons.)
Study Director
Huntingdon Life Sciences Ltd.

Date

QUALITY ASSURANCE STATEMENT

ABM-FD

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The following inspections and audits have been carried out in relation to this study:

Study Phase	Date(s) of Inspection	Date of Reporting to Study Director and Management
Protocol Audit	11 October 2004	11 October 2004
Study Based Inspections		
Dose Formulation	4 November 2004	4 November 2004
Dosing, post dose observations and study preparation	4 November 2004	4 November 2004
Clinical signs	14 December 2004	14 December 2004
Necropsy	3 February 2005	3 February 2005
Report Audit	8 April 2005 to 5 May 2005 10 October 2005	 5 May 2005 10 October 2005

In addition, process based inspections were conducted of other routine and repetitive procedures employed on this type of study at or about the time this study was in progress. Similarly an inspection of the facility where this study was conducted was carried out on an annual basis. These inspections were reported to Company Management.

N Jolly ..... 11 OCTOBER 2005 .....

N. Jolly, B.Sc., M.R.Q.A.
Group Manager
Department of Quality Assurance
Huntingdon Life Sciences Ltd.

Date

CONTRIBUTING SCIENTISTS

ABM-FD

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CD RATS FOR 13 WEEKS

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SUMMARY

The systemic toxic potential of ABM-FD, an extract of the mushroom Himematsutake, to Crl:CD® (SD)IGS BR rats, when given orally, was assessed over a period of 13 weeks. Three groups of 20 male and 20 female rats were treated by gavage at dosages of 500, 1000 or 2000 mg/kg/day. A similarly constituted Control group received the vehicle (water for irrigation) and the same volume-dosage (10 mL/kg bodyweight).

During the study, clinical condition, arena observations, sensory reactivity and grip strength, motor activity, bodyweight, food consumption, ophthalmoscopy, haematology, blood chemistry, urinalysis, organ weight, macroscopic and microscopic pathology investigations were undertaken.

Results

There were no treatment-related signs. Three deaths incidental to treatment occurred during the treatment period.

There were no treatment-related findings at the Week 12 detailed physical examination, arena observations, sensory reactivity and grip strength. Motor activity assessment in Week 12 indicated a high number of high beam (rearing) breaks throughout the 60 minute observation period in females receiving 2000 mg/kg/day.

Bodyweight, food consumption and food conversion efficiency were not affected by treatment.

There were no treatment-related ocular changes.

Haematological changes related to treatment comprised low haematocrit, haemoglobin concentration and erythrocyte count in Week 13 in males receiving 2000 mg/kg/day, with erythrocyte counts being slightly low in these animals in Week 7, a slight, but consistently high mean cell volume in males receiving 2000 mg/kg/day, low lymphocyte and large unstained cell counts in females receiving 1000 or 2000 mg/kg/day, with a similar trend being present in Week 2 in females receiving 500 mg/kg/day.

Plasma urea concentrations were high in Week 13 in males receiving 1000 mg/kg/day and in males and females receiving 2000 mg/kg/day which, at 2000 mg/kg/day, was associated with high plasma creatinine concentration. Plasma urea and creatinine concentrations were also slightly high in Week 7 in females receiving 2000 mg/kg/day. Plasma glucose concentrations were consistently high in males receiving 2000 mg/kg/day. Changes in plasma electrolytes comprised consistently high potassium concentrations at all dosages in males, and was also high in Week 2 and 7 in females receiving 1000 or 2000 mg/kg/day and in Week 7 in those receiving 500 mg/kg/day; slightly reduced calcium and phosphorus concentrations in Week 13 at all dosages in females.

The composition of the urine was not affected by treatment.

Spleen weights were low after 13 weeks in females given 2000 mg/kg/day.

Macrosopic examination after 13 weeks of treatment revealed a high incidence of dark areas on the thymus in males given 2000 mg/kg/day.

There were no treatment-related histopathological findings.

Conclusion

It is concluded that the oral administration of ABM-FD, an extract of the mushroom Himematsutake, to CD rats for 13 weeks at dosages up to 2000 mg/kg/day was well-tolerated, with no evidence of any toxicologically significant change and no treatment-related histopathological finding. Consequently, the no-observed- adverse-effect level (NOAEL) of ABM-FD in this study was considered to be 2000 mg/kg/day.

INTRODUCTION

Objective

The objective of this study was to assess the systemic toxic potential of ABM-FD (an extract from the mushroom Himematsutake), when administered orally by gavage to rats for 13 weeks.

Regulatory compliance

The study was designed to meet the requirements of the following guideline:

> The Office of Food Additive Safety (Redbook 2000) guidelines of the US Food and Drug Administration.

The study was conducted in accordance with the requirements of current, internationally recognised Good Laboratory Practice Standards, and the applicable sections of the United Kingdom Animals (Scientific Procedures) Act 1986.

Test system

The rat was chosen as the test species because of its acceptance as a predictor of toxic change in man and the requirement for a rodent species by regulatory agencies. The Crl:CD® (SD)IGS BR strain was used because of the historical control data available in this laboratory.

Route of administration

The oral gavage route of administration was chosen to simulate the conditions of human exposure since the text material is a dietary supplement.

Treatment groups and dosages

The dosages used in this study (0, 500, 1000 and 2000 mg/kg/day) were selected in conjunction with the Sponsor with reference to previous work with similar extracts from Himematsutake, which have been shown to be of low toxicity. The highest dosage (2000 mg/kg/day) was the maximum practical dosage in a study of this duration. The low (500 mg/kg/day) and intermediate (1000 mg/kg/day) dosages were selected using a factor of 0.5 or 0.25 of the high dosage.

Study location

The test system was maintained at the following laboratory:

Huntingdon Life Sciences Ltd.,
Eye Research Centre,
Eye,
Suffolk,
IP23 7PX,
England.

The analyses described in the test material/formulation analysis, blood chemistry and urinalysis sections of this report were performed by:

Huntingdon Life Sciences Ltd.,
Huntingdon Research Centre,
Woolley Road,
Alconbury,
Huntingdon,
Cambridgeshire,
PE28 4HS,
England.

EXPERIMENTAL PROCEDURE

STUDY SCHEDULE AND STRUCTURE

Duration of treatment

The test substance, ABM-FD, was administered over a period of 13 consecutive weeks. The necropsy procedures were completed in four days, during which time treatment continued, and serial observations were recorded at appropriate intervals. The duration of treatment is reported as 13 weeks.

Time schedule

Study initiation: (Protocol signed by Study Director)	5 October 2004
Experimental start date: (Pre-treatment chemistry assays)	20 October 2004
Animal arrival:	20 October 2004
Treatment commenced:	4 November 2004
Necropsy completed:	8 February 2005
Experimental completion date: (Pathology)	26 April 2005
Study completion:	11 October 2005

Identity of treatment groups

The study consisted of one Control and three treated groups of rats, identified as follows:

Group	Treatment	Dosage# (mg/kg/day)	No. of animals		Cage/Animal numbers	
			Male	Female	Male	Female
1	Control	0	20	20	21-40	81-100
2	ABM-FD	500	20	20	61-80	121-140
3	ABM-FD	1000	20	20	41-60	141-160
4	ABM-FD	2000	20	20	1-20	101-120

Expressed in terms of test material as supplied.

Some serial observations needed to be performed without the knowledge of the treatment group, therefore the animal numbering system was such that it was not easy to identify a treatment group from the animal number.

TEST SUBSTANCE AND FORMULATION

Test substance

Information supplied by the Sponsor regarding the test substance is contained in the test substance data sheet, which is retained in study records, and the Certificate of Analysis, which is presented in Annex 2.

The following information is given in summary:

Identification:	ABM-FD	
Description:	Brown Solid	
Storage conditions:	Room temperature and protected from light	
Supplier:	Sponsor	
Batch number:	EX 200408	EX 200408
Date of receipt:	27 August 2004	31 August 2004
Quantity received:	Approximately 1584 bottles	660 bottles
Expiry date:	July 2006	
Purity:	2.9g/100g	

The Sponsor was responsible for the characterisation of the test substance and the documentation of the methods of synthesis, fabrication or derivation and stability.

Before the consignments of the test substance was used one bottle containing the test-material was taken as a representative sample. This sample was stored in the archives at -20°C in the dark.

Vehicle

Water for formulation.

Formulation

The test substance, ABM-FD, was prepared for administration as a series of graded concentrations in the vehicle, by selecting the required number of test-material vials and adding 15 mL of vehicle to each followed by hand swirling to ensure dissolution. These vial contents were then pooled to obtain sufficient volume of the highest concentration (200 mg/mL) for administration to high dosage animals and for the serial dilution of the low and intermediate dosage preparations. This was then placed on a magnetic stirrer for a minimum of five minutes.

The intermediate (100 mg/mL) and low (50 mg/mL) concentration was obtained by serial dilution. The intermediate concentration was obtained by measuring the required volume of high concentration formulation and diluting this to the required volume using the vehicle. This formulation was again stirred using a magnetic stirrer to ensure dissolution. The final low concentration was obtained by measuring out the required volume of intermediate concentration formulation and diluting this to the required volume using the vehicle. This formulation was again stirred using a magnetic stirrer to ensure dissolution.

Group	Treatment	Dosage (mg/kg/day)	Concentration (mg/mL)	Volume dosage (mL/kg)
1	Control	0	0	10
2	ABM-FD	500	50	10
3	ABM-FD	1000	100	10
4	ABM-FD	2000	200	10

The test substance was used as supplied. All formulations were prepared freshly each day for the first five weeks of treatment and each week for all subsequent weeks (6 to 13).

Detailed records of compound usage were maintained. The amount of test substance necessary to prepare the formulations and the amount actually used were determined on each occasion. The difference between these amounts was checked before the formulations were dispensed.

Formulation analysis

The suitability of the proposed mixing procedure was determined and specimen formulations were analysed to assess the stability of the test substance in the liquid matrix. Samples of each formulation prepared for administration in Weeks 1 and 12 of treatment were analysed for achieved concentration of the test substance.

The method of analysis was an adaptation of a method supplied by the Sponsor; further details on test procedures and results are presented in the Formulation Chemistry Report (Annex 1).

ANIMAL MANAGEMENT

Animal supply, acclimatisation and allocation

A total of 85 male and 84 female Crl:CD® (SD)IGS BR rats were received from Charles River (UK) Ltd, Margate, Kent, England. The rats were ordered at 33 to 37 days of age and within a weight range of 15 g for each sex.

On arrival, the animals were removed from the transit boxes and allocated to study cages. Using the sequence of cages in the battery, one animal was placed in each cage. Each sex was allocated separately.

The cages constituting each group were blocked together by sex and the groups were dispersed in batteries so that possible environmental influences arising from their spatial distribution were equilibrated, as far as was practicable. Additionally, batteries of cages were rotated around the room at weekly intervals to further minimise possible spatial variations.

Each animal was assigned a number and identified uniquely within the study by a tail tattoo. Each cage label was colour-coded according to group and was numbered uniquely with cage and study number, as well as the identity of the occupant.

Before the start of treatment, two males and three females with non-resolving ophthalmic lesions and one male and one female with bodyweights at the extreme of the weight range were replaced with spare animals of suitable weight from the same batch. Four males and two females already allocated to groups were swapped within groups to equalise group mean bodyweights.

The animals were allowed to acclimatise to the conditions described below for 15 days before treatment commenced. For those animals selected for this study, their age at the start of treatment was 48 to 52 days and their bodyweights were in the range of 221 to 270 g for males and 157 to 203 g for females.

The spare animals were removed from the study room eight or nine days after treatment commenced.

Animal housing, diet and water supply

Animals were housed inside a barriered rodent facility (Building 8, Room 09). Animals were transferred to Room 01 or 13 (within the same building) during neurobehavioural screening Sensory reactivity and grip strength assessments were performed in Room 09 and the motor activity was performed in Room 01 for pre-treatment and Room 13 for Week 12. The facility was designed and operated to minimise the entry of external biological and chemical agents and to minimise the transference of such agents between rooms. Before the study the room was cleaned and disinfected with a bactericide.

Each animal room was kept at positive pressure with respect to the outside by its own supply of filtered fresh air, which was passed to atmosphere and not re-circulated. The temperature and relative humidity controls were maintained within the range of 19 to 23°C and 40 to 70% respectively. Artificial lighting was controlled to give a cycle of 12 hours continuous light and 12 hours continuous dark per 24 hours.

Periodic checks were made on the number of air changes in the animal rooms. Temperature and humidity were monitored daily. Since these data show that there were no deviations from target ranges they are not presented.

Alarms were activated if there was any failure of the ventilation system, or temperature limits were exceeded. A stand-by electricity supply was available to be automatically brought into operation should the public supply fail.

The animals were housed individually. The cages were made of a polycarbonate body with a stainless steel mesh lid. The cages had wood shavings as bedding (lignocel type 3/4 wood flakes). Cages, food hoppers and water bottles were changed at appropriate intervals.

The animals were allowed free access to a standard rodent diet (Rat and Mouse No. 1 Maintenance Diet from Special Diets Services Ltd., Witham, Essex, England), except when urine was being collected and overnight before routine blood sampling. This diet contained no added antibiotic or other chemotherapeutic or prophylactic agent.

Potable water taken from the public supply was freely available via polycarbonate bottles fitted with sipper tubes, except when urine was being collected.

Each animal was provided with an Aspen chew block by Datesand, Manchester, England for environmental enrichment. Chew blocks were provided throughout the study but removed during periods of food deprivation, and were replaced when necessary, but at a minimum frequency of every two weeks.

Each batch of diet was analysed routinely by the supplier for various nutritional components and chemical and microbiological contaminants. Supplier's analytical certificates were scrutinised and approved before any batch of diet was released for use. The quality of the water supply is governed by regulations published by the Department for Environment, Food and Rural Affairs. Certificates of analysis were received routinely from the water supplier. Certificates of analysis were received routinely from the supplier of the aspen chew blocks and wood flakes. Since the results of these various analyses did not provide evidence of contamination that might have prejudiced the study, they are not presented.

No other specific contaminants that were likely to have been present in the diet or water were analysed, as none that may have interfered with or prejudiced the outcome of the study was known.

Administration

Animals received the test substance or vehicle control formulations orally at a volume-dosage of 10 mL/kg bodyweight, using a suitably graduated syringe and a rubber catheter (Ch 8 or Ch 10) inserted via the mouth into the stomach.

All animals were dosed in sequence of cage-number within each group, once each day at approximately the same time each day, seven days per week. The volume administered to each animal was calculated from the most recently recorded scheduled bodyweight.

A daily record of the weight of each formulation dispensed and the amount remaining after dosing was made. The balance of these two weights was compared with the predicted usage as a check that the doses had been administered correctly. No significant discrepancy was found.

Formulations were stirred using a magnetic stirrer before and throughout the dosing procedure.

SERIAL OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit as well as to the group observations and examinations outlined in this experimental procedure were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

All observations described below were performed in sequence of cage-number within each group except where otherwise indicated.

Clinical observations

Animals were inspected visually at least twice daily for evidence of ill-health or reaction to treatment. Cages were inspected daily for evidence of ill-health amongst the occupant. Any deviation from normal was recorded at the time in respect of nature and severity, date and time of onset, duration and progress of the observed condition, as appropriate.

Daily during the first week of treatment, twice weekly during Weeks 2 to 4 (middle and end of each week) and weekly thereafter, detailed observations were recorded at the following times in relation to dose administration:

Immediately before dosing
Immediately after dosing on return of the animal to its cage
On completion of dosing of each group
Between one and two hours after completion of dosing of all groups
As late as possible in the working day.

In addition, a more detailed weekly physical examination was performed on each animal to monitor general health.

During the acclimatisation period, observations of the animals and their cages were recorded at least once per day.

Detailed physical examination and arena observations

Before treatment commenced detailed physical examination and arena observations were performed on each animal. During Week 12 of treatment detailed physical examination and arena observations were performed on 10 males and 10 females with the lowest animal numbers from each group (see Deviations from Protocol section). On each occasion, the examinations were performed at approximately the same time of day (before dosing during the treatment period), by an observer unaware of the experimental group to which the animal belonged.

After removal from the home cage, animals were assessed for physical condition and behaviour during handling and after being placed in a standard arena. Any deviation from normal was recorded with respect to the nature and, where appropriate, degree of severity. Particular attention was paid to possible signs of neurotoxicity, such as convulsions, tremor and abnormalities of gait or behaviour.

Findings were either reported as "present" or assigned a severity grade - slight, moderate or marked.

Sensory reactivity and grip strength

Before commencement of treatment and during Week 12 of treatment (before dosing) sensory reactivity and grip strength assessment was performed by an observer unaware of the experimental group to which each animal belonged. Animals were not necessarily all tested on the same day, but the number of animals was balanced across the groups on each day of testing. These observations were performed before any laboratory investigations.

The following measurements, reflexes and responses were recorded:

Approach response - A blunt probe was brought towards the animal's head until it was close to the animal's nose (but not touching the vibrissae). The animals reaction was recorded as:

1 - no reaction or ignores probe;
2 - normal awareness and reaction (approaches and/or sniffs probe);
3 - abnormally fearful or aggressive reaction.

Grip strength - Forelimb and hindlimb grip strength was measured using Mecmesin Portable Force Indicators. Three trials were performed for each animal.

Auditory startle reflex - The animal's response to a sudden loud noise was assessed. The animal was stationary and the source of sound was not visible. The response was scored as:

1 - no response;
2 - weak response (ear twitch only);
3 - normal response (obvious flinch or startle);
4 - exaggerated response (all feet off the floor).

Tail pinch response - The animal's tail was pinched sharply with forceps approximately one third from the tip. The response was graded as:

1 - no response;
2 - weak response (e.g. turns round slowly or weak vocalisation without moving away);
3 - normal response (e.g. jumps forward or turns around sharply, usually with vocalisation);
4 - exaggerated response (e.g. excessive vocalisation, body movement or aggression).

Touch response - The nape of the animal's neck was stroked gently with a blunt probe and the reaction recorded as:

1 - no reaction or ignores probe;
2 - normal awareness and reaction;
3 - abnormally fearful or aggressive reaction.

Motor activity

Before commencement of treatment and during Week 12 of treatment (before dosing) the motor activity of each animal was measured using a Rodent Activity Monitoring System, with hardware supplied by Pearson Technical Services (Saxmundham, Suffolk, England) and software developed and maintained by Huntingdon Life Sciences.

Animals were tested individually in clear polycarbonate cages and motor activity was measured by counting infra-red beam breaks over ten 6-minute intervals (one hour total). Ten beams were set at two height levels (five low and five high) to detect cage floor and rearing activity. All animals were not necessarily tested on the same day, but the number of animals was balanced across the

groups on each day of testing. These observations were performed before any laboratory investigations.

Mortality

Debilitated animals were observed carefully and, where necessary. Animals judged *in extremis* were killed. Animals were also killed to prevent unnecessary or prolonged suffering. Where possible, blood samples were taken *ante mortem* and analysed for the characteristics specified in the haematology and blood chemistry sections below. A complete necropsy was performed in all cases as described below.

Bodyweight

The weight of each rat was recorded on the day that treatment commenced (Week 0), weekly throughout the treatment period, and before necropsy.

More frequent weighings were instituted, when appropriate, for animals displaying ill-health, so that the progress of the observed condition could be monitored. These data are not reported here.

Food consumption

The weight of food supplied to each animal, that remaining and an estimate of any spilled was recorded each week throughout the treatment period. From these records the mean weekly consumption per animal (g/rat/week) was calculated.

Ophthalmic examination

Before treatment commenced, the eyes of all animals allocated to the study (including spare animals) were examined by means of a binocular indirect ophthalmoscope. Rejected animals were replaced with animals with no adverse ocular abnormality, selected from the spare animals for the study. During Week 13 of treatment the eyes of all animals of Groups 1 (Control) and 4 (2000 mg/kg/day) were similarly examined.

Prior to each examination, the pupils of each animal were dilated using 0.5% tropicamide ophthalmic solution (Mydriacyl, Alcon Laboratories Ltd.). The adnexae, conjunctiva, cornea, sclera, anterior chamber, iris (pupil dilated), lens, vitreous and fundus were examined.

As no treatment-related changes were observed, the examination was not extended to animals of Groups 2 or 3 (500 or 1000 mg/kg/day).

Haematology, peripheral blood

During Weeks 2, 7 and 13 of treatment (before dosing on each occasion), blood samples were obtained from 10 males and 10 females with the highest surviving animal identity numbers after overnight starvation. Animals were held under light general anaesthesia induced by isoflurane and blood samples were withdrawn from the sublingual vein.

Blood samples (nominally 0.5 mL) were collected into tubes containing EDTA as anticoagulant and examined for the following characteristics using a Technicon H·1 haematology analyser:

- Haematocrit (Hct)
- Haemoglobin concentration (Hb)
- Erythrocyte count (RBC)
- Mean cell haemoglobin (MCH)
- Mean cell haemoglobin concentration (MCHC)
- Mean cell volume (MCV)
- Total leucocyte count (WBC)
- Differential leucocyte count
  - Neutrophils (N)
  - Lymphocytes (L)
  - Eosinophils (E)
  - Basophils (B)
  - Monocytes (M)
  - Large unstained cells (LUC)
- Platelet count (Plt)

Abnormal morphology was flagged by the Technicon analyser. The most common morphological changes, anisocytosis, micro/macrocytosis and hypo/hyperchromasia were recorded as follows:

-	=	no abnormalities detected
+	=	slight
++	=	moderate
+++	=	marked

Blood film (prepared for all samples flagged by the Technicon analyser) - stained using Romanowsky stain and examined for abnormalities by light microscopy. Confirmation or a written description from the blood film was made where appropriate.

Reticulocyte count (Retic) - stain reagent containing brilliant cresyl blue and basic blue 24, examined by light microscopy for reticulocytes and abnormalities, including Heinz bodies.

Additional blood samples (nominally 0.5 mL) were taken into tubes containing citrate anticoagulant and examined in respect of:

Prothrombin time (PT) - using an ACL 3000 Plus analyser and IL PT-Fibrinogen reagent

Activated partial thromboplastin time (APTT) - using an ACL 3000 Plus Analyser and IL APTT reagent.

Haematology, bone marrow

Bone marrow samples were obtained from the femur (see Deviations from Protocol section) during necropsy of all animals killed. Smears prepared from these samples were air-dried, fixed in methanol and stained using a Romanowsky procedure.

The smears from all animals are retained pending any possible future examination.

Blood chemistry

At the same time and using the same animals as for peripheral haematology, further blood samples (nominally 0.7 mL) were collected into tubes containing lithium heparin as anticoagulant. All tubes were mechanically agitated for at least two minutes and the sample subsequently centrifuged at 3000 rpm for 10 minutes in order to separate the plasma. After separation, the plasma was examined for the following characteristics using a Hitachi 917 Clinical Chemistry Analyser:

Alkaline phosphatase (ALP)
Alanine aminotransferase (ALT)
Aspartate aminotransferase (AST)
Gamma-glutamyl transpeptidase (gGT)
Total bilirubin (Bili)
Urea
Creatinine (Creat)
Glucose (Gluc)
Total cholesterol (Chol)
Triglycerides (Trig)
Sodium (Na)
Potassium (K)
Chloride (Cl)
Calcium (Ca)
Inorganic phosphorus (Phos)
Total protein (Total Prot)

Electrophoretic protein fractions; albumin (Alb), α1 globulin (a1), α2 globulin (a2), β globulin (Beta) and γ globulin (Gamma) were analysed with agarose gel, using a Beckman test kit, staining with Paragon blue and scanning with a suitable densitometer.

Albumin/globulin ratio (A/G Ratio) was calculated from total protein concentration and analysed albumin concentration.

Urinalysis

During Weeks 2, 7 and 13 of treatment, overnight urine samples were collected from all animals. Animals were placed in an individual metabolism cage without food or water at approximately 16:00 hours; urine was collected until approximately 07:00 hours the following day.

The individual samples were examined for the following characteristics:

Appearance (App) - by visual assessment using the following abbreviations:

PY	Pale yellow appearance	CMY	Cloudy, medium yellow appearance
CPY	Cloudy, pale yellow appearance	MY	Medium yellow appearance

Volume (Vol)
pH - using a Radiometer PHM 92 pH meter
Specific gravity (SG) - using Atago UR-1 digital refractometer
Protein (Prot) - using Hitachi 917 Clinical Chemistry Analyser

Glucose (Gluc), ketones (Keto), bile pigments (Bili), haem pigments (Blood) by Multistix. Multistix are diagnostic reagents obtained from Bayer plc, Newbury, England and were used as qualitative indicators of analyte concentration. Results for haem pigments are reported as positive or negative only whilst results for glucose, ketones and bile pigments are reported according to the following convention:

0	=	negative
TR	=	trace
+	=	'small amount' of analyte
++	=	'moderate amount' of analyte
+++	=	'large amount' of analyte
++++	=	'very large amount' of analyte

A microscopic examination of the urine sediment was performed. An aliquot of the urine sample was centrifuged, stained with Kova stain and the resulting deposit spread on a microscope slide. The deposit was examined for the presence of the following:

Crystals (Cryst)
Epithelial cells(Epi)
Leucocytes (Leuc)
Erythrocytes (RBC)
Casts
Spermatozoa and precursors (Sperm)
Other abnormal components (Abn)

The grading of cell frequency in the centrifuged deposit is as follows:

0	=	None found in any field examined
1	=	A few found in some fields examined
2	=	A few found in all fields examined
3	=	Many found in all fields examined

NECROPSY AND HISTOLOGY

Method of kill

The animals that were killed during the study and those surviving until the end of the scheduled treatment period were killed by carbon dioxide asphyxiation. The sequence in which the animals were killed after completion of treatment was selected to allow satisfactory inter-group comparison.

Macroscopic pathology

All animals were subject to a detailed necropsy.

After a review of the history of each animal, a full macroscopic examination of the tissues was performed. All external features and orifices were examined visually. The cranial roof was removed to allow observation of the brain, pituitary gland and cranial nerves. After ventral mid-line incision, the neck and associated tissues and the thoracic, abdominal and pelvic cavities and their viscera were exposed and examined *in situ*. Any abnormal position, morphology or interaction was recorded.

The requisite organs were weighed and external and cut surfaces of the organs and tissues were examined as appropriate. Any abnormality in the appearance or size of any organ and tissue was recorded and the required tissue samples preserved in appropriate fixative.

The retained tissues were checked before disposal of the carcass.

Organ weights

The following organs, taken from each animal killed after 13 weeks of treatment, were dissected free of adjacent fat and other contiguous tissue and the weights recorded:

Adrenals
Brain
Epididymides
Heart
Kidneys
Liver
Lymph node - axillary (largest node on left side)
- mesenteric (closest node to caecum)
Ovaries
Pituitary
Prostate
Spleen
Testes
Thymus
Thyroid with parathyroids *
Uterus with cervix

* Weighed after partial fixation.

Bilateral organs were weighed together. Organ weights were also adjusted for terminal bodyweight, using the weight recorded immediately before necropsy.

Fixation

Testes and epididymides were fixed in Bouin's solution prior to transfer to 70% industrial methylated spirit and eyes were fixed in Davidson's fluid. Samples (or the whole) of the other tissues listed below from all animals were preserved in 10% neutral buffered formalin:

Adrenals
Aorta - thoracic
Brain
Caecum
Colon
Duodenum
Epididymides
Eyes
Femurs+
Harderian glands
Head#
Heart
Ileum
Jejunum
Kidneys
Liver
Lungs
Lymph nodes - axillary
- mesenteric
Mammary area - caudal
Nasal turbinates
Oesophagus
Optic nerves
Ovaries
Pancreas
Pituitary
Prostate
Rectum
Salivary glands - submandibular+
Sciatic nerves+
Seminal vesicles
Skeletal muscle - thighs+
Skin
Spinal cord
Spleen
Sternum
Stomach
Testes
Thymus
Thyroid with parathyroids
Tongue
Trachea
Ureters
Urinary bladder
Uterus and cervix
Vagina

+ Only one processed for examination
# Not processed for examination

Femoral bone marrow smears, taken from all animals killed, were processed and examined as described in the haematology, bone marrow section.

Samples of any abnormal tissues were also retained and processed for examination. In those cases where a lesion was not clearly delineated, contiguous tissue was fixed with the grossly affected region and sectioned as appropriate.

Samples of the head (including paranasal sinuses and nasopharynx) and the remaining femur, salivary gland, sciatic nerve and skeletal muscle (thigh) were not examined histologically, but are retained against any future requirement for microscopic examination.

Histology

For those animals specified in the Pathology section, the relevant tissues were subject to histological processing.

Tissue samples were dehydrated, embedded in paraffin wax, sectioned at approximately four to five micron thickness and stained with haematoxylin and eosin.

Those tissues subject to histological processing included the following regions:

Adrenals	-	cortex and medulla
Brain	-	cerebellum, cerebrum and midbrain
Femur with joint	-	longitudinal section including articular surface, epiphysial plate and bone marrow
Heart	-	included auricular and ventricular regions
Ileum	-	included Peyer's patches
Kidneys	-	included cortex, medulla and papilla regions
Liver	-	section from all main lobes
Lungs	-	section from two major lobes, to include bronchi
Spinal cord	-	transverse and longitudinal section at the cervical, lumbar and thoracic levels
Sternum	-	included bone marrow
Stomach	-	included keratinised, glandular and antrum in sections
Thyroid	-	included parathyroids in section where possible
Uterus	-	uterus section separate from cervix section

For bilateral organs, sections of both organs were prepared. A single section was prepared from each of the remaining tissues required for microscopic pathology.

PATHOLOGY

Light microscopy

Microscopic examination was performed as follows:

All tissues preserved for examination (as specified above) were examined for all animals of Groups 1 (Control) and 4 (2000 mg/kg/day) sacrificed on completion of the scheduled treatment period and for all animals killed or dying during the study.

Axillary and mesenteric lymph nodes, spleen, thymus and bone marrow (femur and sternum only) were examined for all animals of Group 2 (500 mg/kg/day) and Group 3 (1000 mg/kg/day) sacrificed on completion of the scheduled treatment period.

Tissues reported at macroscopic examination as being grossly abnormal were examined for all Main animals.

Findings were either reported as "present" or assigned a severity grade. In the latter case one of the following five grades was used - minimal, slight, moderate, marked or severe. A reviewing pathologist undertook a peer review of the microscopic findings.

DATA TREATMENT

This report contains serial observations pertaining to all weeks of treatment completed, together with signs data collected during the necropsy period. The only serial observations relating to the acclimatisation period included in this report relate to the detailed physical examination and arena observations, sensory reactivity and grip strength, motor activity and ophthalmic examination.

Summary statistics (e.g. means and standard deviations) presented in this report were calculated from computer-stored individual raw data. The summary statistics and the individual data were stored in the computer to a certain number of decimal places, different for each parameter. For presentation purposes, however, they were usually rounded to fewer places. It is, therefore, not generally possible to reproduce the presented means and standard deviations exactly using the presented individual data.

The death codes in the appendices have the following meaning:

7	Terminal kill
F	Found dead
K	Killed *in extremis*

Throughout the report the following abbreviations are used:

N [or n]	Number of animals examined
SD [or sd]	Standard deviation

Definition of "Week"

The first week of treatment started at midnight prior to treatment commencing and ended at midnight on the seventh day following. Subsequent experimental weeks of treatment were of the same duration.

Signs

A detailed history of individual animals that showed signs is presented in Appendix 1, as the weeks in which the specified sign was observed.

There were no clinical signs observed that were associated with the time of dosing and consequently no data are presented in this report.

Bodyweight

Group mean weight changes were calculated from the weight changes of individual animals surviving the specified period.

Food consumption

Overall mean food consumption values were calculated from the weekly group mean values presented.

Food conversion efficiency

Food conversion efficiency is the efficiency of conversion of food to new body tissue.

Group mean food conversion efficiencies were calculated for each week of treatment, and were derived from unrounded cage values.

The weekly group mean values presented were calculated by first deriving the weekly cage values. These were calculated from the bodyweight gain of animals alive at the end of the week and the total weight of food consumed in the cage.

$$\text{Food conversion efficiency} = \frac{\text{Bodyweight gain (g)}}{\text{Total food consumed (g/animal)}} \times 100$$

Overall group mean values were calculated as the overall group mean bodyweight gain (Table 3), divided by the total food consumption, expressed as a percentage.

Ophthalmic examination

All observations made at ophthalmoscopic examination are recorded in the raw data. This report only contains those that were considered to be unusual, abnormal, and those which may correlate with findings recorded elsewhere in this report, for example those observed at veterinary examination or at micropathology. Observations were bilateral unless otherwise indicated.

Haematology

The abbreviation used in Appendix 8 has the following meaning:

CTD Clotted sample

Group mean values for reticulocyte counts are not presented as the distribution of these data is not normal

Blood chemistry

The abbreviation used in Appendix 9 has the following meaning:

NVR No Valid result - Group 3 Male No. 60, lithium heparin sample taken during Week 7 of treatment was not separated and stored at the incorrect temperature overnight. This error resulted in the sample being unsuitable for analysis and is recorded in the appendix as NVR.

Albumin to globulin (A/G) ratios were calculated as:

$$A/G = \frac{\text{Albumin concentration}}{\text{Total protein} - \text{albumin concentration}}$$

Urinalysis

The abbreviation used in Appendix 10 has the following meaning:

TR Trace detected

Group means and standard deviations are presented for volume, pH, specific gravity and protein only.

Pathology

Tissues which could not be examined are specified in Appendix 12. The absence of a comment for a tissue scheduled for examination therefore indicates that the tissue was examined and found to be normal. Tissues recorded as abnormal macroscopically but found to be normal microscopically are described as 'No significant lesion' in the microscopic pathology appendix. In all tabular presentations of data the tissues specified in the protocol for histopathological examination precede other tissues.

Statistical analysis

All statistical analyses were carried out separately for males and females.

All analyses were carried out using the individual animal as the basic experimental unit.

The following data types were analysed at each timepoint separately:

Grip strength and motor activity
Bodyweight, using gains over appropriate study periods
Blood chemistry, haematology and urinalysis
Organ weights, both absolute and adjusted for terminal bodyweight
Pathological findings, for the number of animals with and without each finding

For categorical data, including pathological findings, the proportion of animals was analysed using Fisher's Exact test (Fisher 1973) for each treated group versus the control.

For continuous data, Bartlett's test (Bartlett 1937) was first applied to test the homogeneity of variance between the groups. Using tests dependent on the outcome of Bartlett's test, treated groups were then compared with the Control group, incorporating adjustment for multiple comparisons where necessary.

For bodyweight gains and organ weights, whenever Bartlett's test was found to be statistically significant, a Behrens-Fisher test (Cochran and Cox 1957) was used to perform pairwise comparisons, otherwise a Dunnett's test was used.

The following sequence of statistical tests was used for grip strength and motor activity, bodyweight, food consumption, organ weight and clinical pathology data:

If 75% of the data (across all groups) were the same value, for example c, then a frequency analysis was applied. Treatment groups were compared using a Mantel test for a trend in proportions (Mantel 1963) and also pairwise Fisher's Exact tests (Fisher 1973) for each dose group against the control both for i) values <c versus values >=c, and for ii) values <=c versus values >c, as applicable.

If Bartlett's test for variance homogeneity (Bartlett 1937) was not significant at the 1% level, then parametric analysis was applied. If the F1 test for monotonicity of dose-response (Healey 1999) was not significant at the 1% level, Williams' test for a monotonic trend (Williams 1971, 1972) was applied. If the F1 test was significant, suggesting that the dose-response was not monotone, Dunnett's test (Dunnett 1955, 1964) was performed instead.

If Bartlett's test was significant at the 1% level, then logarithmic and square-root transformations were tried. If Bartlett's test was still significant, then non-parametric tests were applied. If the H1 test for monotonicity of dose-response (Healey 1999) was not significant at the 1% level, Shirley's test for a monotonic trend (Shirley 1977) was applied. If the H1 test was significant, suggesting that the dose-response was not monotone, Steel's test (Steel 1959) was performed instead.

Significant differences between Control and treated groups were expressed at the 5% ($p<0.05$) or 1% ($p<0.01$) level. The following statistical cyphers were used throughout the report:

a - $p<0.05$; b - $p<0.01$ - using categorical or parametric tests
A - $p<0.05$; B - $p<0.01$ - using non-parametric tests

QUALITY ASSURANCE AND ARCHIVING PROCEDURES

Quality Assurance

Details of the Quality Assurance inspections and audits are presented on the Quality Assurance Statement.

Archives

Following completion of this study all raw data, specimens and samples, except those generated or used during any Sponsor's or supplier's analysis, were stored in the archives of Huntingdon Life Sciences. Types of sample and specimen which are unsuitable, by reason of instability, for long term retention and archiving may be disposed of after the periods stated in Huntingdon Life Sciences Standard Operating Procedures.

A copy of the final report and all Quality Assurance inspection records will be retained indefinitely. All other appropriate specimens and records will be retained for a minimum period of ten years from the date of issue of the final report. At the end of the ten year retention period the Sponsor will be contacted and advice sought on the above requirements. Under no circumstances will any item be discarded without the Sponsor's knowledge.

DEVIATIONS FROM PROTOCOL

The following deviations from protocol occurred:

Bone marrow smears were taken from the femur in line with Eye Research Centre procedures and not the tibia as stated in the Protocol.

Due to three premature deaths, only nine Control males and eight females in Group 4 (2000 mg/kg/day) were tested during the Week 12 sensory reactivity, grip strength and motor activity, in error.

These deviations were considered to have not affected the integrity or validity of the study.

RESULTS

Formulation chemistry (Annex 1)

The glucose content of ABM-FD in aqueous formulations was confirmed as consistent at nominal concentrations of 50 and 200 mg/mL during storage at ambient temperature for one day and refrigerated storage for eight days. The storage times represented the maximum time from preparation to completion of administration.

The mean concentrations of ABM-FD, analysed with respect to glucose content, in Weeks 1 and 12 in test formulations were between 92 and 120% of nominal concentrations confirming accuracy of formulation.

Signs and mortality (Appendix 1 and 12)

There were no signs of reaction to treatment at either the post-dosing observations or weekly physical examination.

There were no treatment-related deaths. There were, however three deaths that were not considered related to the test material. Female No. 109 receiving 2000 mg/kg/day died in Week 8. Macroscopic examination revealed oesophageal trauma, abnormal thoracic contents, congested lungs and thickened pericardium. Female No. 110 receiving 2000 mg/kg/day was killed *in extremis* in Week 8 after showing slow breathing, râles, gasping, pallor and reduced body temperature. Macroscopic examination revealed oesophageal trauma, abnormal thoracic and gastrointestinal contents, congested lungs, thickened pericardium and pleura, pallid extremities and oedematous thymus. Both deaths were considered accidental, related to dose administration. Control male No. 23 died in Week 10. Macroscopic examination revealed an enlarge heart with thickened pericardium and dark pericardial fluid surrounding due to marked pericarditis, enlarged mandibular lymph node and numerous adhesions between the lungs, pericardium, rib cage and diaphragm. This death was considered fortuitous.

Detailed physical examination and arena observations (Appendix 1)

There were no signs related to treatment at the Week 12 physical examination and arena observations.

Sensory reactivity and grip strength (Table 1; Appendix 2)

There was no effect of treatment upon sensory reactivity and grip strength.

During Week 12, males receiving 500 or 2000 mg/kg/day showed slightly low grip strength in the hindlimbs, when compared with Controls. In the absence of dosage-relationship and any effect upon forelimb grip strength, these variations of hindlimb grip strength were considered unrelated to treatment.

Motor activity (Figure 1; Table 2; Appendix 3)

During Week 12 increased motor activity, as demonstrated by an increased number of high beam (rearing) breaks, was apparent throughout the 60 minute observation period in females receiving 2000 mg/kg/day. A similar trend was observed in females receiving 1000 mg/kg/day but as the difference from Control was only slight it was not attributed to treatment. Males were unaffected.

Bodyweight (Figure 2; Table 3; Appendix 4)

Bodyweight gains during the 13-week treatment period were unaffected by treatment.

Food consumption (Table 4; Appendix 5)

Food consumption was not affected by treatment with ABM-FD.

Food conversion efficiency (Table 5; Appendix 6)

Food conversion efficiency was unaffected by treatment.

Ophthalmic examination (Appendix 7)

Ophthalmic examination after 13 weeks of treatment revealed no findings related to treatment with ABM-FD.

Haematology (Table 6; Appendix 8)

In males receiving 2000 mg/kg/day there was a reduction of haematocrit, haemoglobin concentration and erythrocyte count in Week 13 when compared with the Controls, and the erythrocyte count was also slightly low in Week 7. At all investigations, there was a slight, but consistently high mean cell volume in males receiving 2000 mg/kg/day. Erythrocyte counts were also low in Week 13 in males receiving 500 or 1000 mg/kg/day but there was no dosage-relationship and no effect upon any of the other erythrocytic characteristics and, consequently, these changes were not attributed to treatment. Variations of erythrocytic parameters in females were minor and transient and were attributed to normal biological variation.

At 2000 mg/kg/day, females showed a consistent reduction of lymphocyte and large unstained cell counts, when compared with the Controls, though this was statistically significant only in Week 7 and 13. There was also a trend towards low lymphocyte count in females receiving 1000 mg/kg/day, with those receiving 500 mg/kg/day showing a similar trend in Week 2 only; these differences did not attain statistical significance. As a consequence of these changes, total leucocyte counts were slightly low in females receiving 1000 or 2000 mg/kg/day, and in Week 2 in females receiving 500 mg/kg/day, though statistical significance was attained only in Week 7 and 13 in high dosage females.

Other differences from the Controls were minor, lacked dosage-relationship or were confined to a single investigation and were, therefore, not attributed to treatment. Such changes included the variations of basophil and monocyte counts in females and the transiently increased neutrophil count in Week 7 in males.

Blood chemistry (Table 7; Appendix 9)

In females receiving 2000 mg/kg/day there was a small, but consistently low plasma alanine amino-transferase activity compared with the Controls. This trend was not present in males. Such reductions of transaminase activity are not considered toxicologically significant.

In Week 13 there was an increased plasma urea concentration in males receiving 1000 mg/kg/day and in males and females receiving 2000 mg/kg/day. At 2000 mg/kg/day this was associated with an increased of plasma creatinine. Plasma urea and creatinine concentrations were also slightly increased, compared with the Controls, in Week 7 in females receiving 2000 mg/kg/day.

Plasma glucose concentrations were consistently higher than the Controls in males receiving 2000 mg/kg/day, though the difference lacked statistical significance in Week 7. Females were not affected. The increase of plasma glucose concentration in Week 2 in females receiving 2000 mg/kg/day was, because of its transient nature, less clearly attributable to treatment.

There was a number of variations of plasma electrolytes at each investigation. Potassium concentrations were consistently high at all dosages in males and were also high in Week 2 and 7 in females receiving 1000 or 2000 mg/kg/day and in Week 7 in those receiving 500 mg/kg/day. The difference from controls was not always dose-related. In Week 13 there was a slight reduction of calcium concentration at all dosages, in a broadly dose-related manner. A similar change occurred in Week 2 in treated females. In females in Week 13 there was also a slight reduction of phosphorus concentration but this was not dose-related.

All other differences from the Controls were minor, lacked dosage-relationship or were confined to a single investigation and were, therefore, not attributed to treatment. Such changes included the variations of sodium concentration in both sexes and the variations of plasma protein concentrations, predominantly in the males.

Urinalysis (Table 8; Appendix 10)

There were no consistent changes in the composition of the urine that could be attributed to treatment with ABM-FD. A few minor variations of urinary pH and specific gravity occurred but these were confined to one investigation and were therefore considered chance occurrences.

Organ weights (Table 9; Appendix 11)

After 13 weeks of treatment, when compared with Controls, absolute and bodyweight relative spleen weights were low for females given 2000 mg/kg/day. Males were not affected.

Other variations from Controls were either minor or lacked dosage relationship and were therefore attributed to normal biological variation. Such changes included the low thymus weights for males

given 1000 mg/kg/day, the high absolute and bodyweight-relative thyroid weights in females given 1000 or 2000 mg/kg/day and high axillary lymph node weights in these animals. The high mean axillary lymph node weights in males given 2000 mg/kg/day was attributable to a very high value in one animal.

Macropathology (Table 10; Appendix 12)

Macrosopic examination after 13 weeks of treatment revealed when compared to Controls a high incidence of dark area of the thymus in males given 2000 mg/kg/day.

Histopathology (Table 11; Appendix 12)

There were no changes that were considered related to treatment with ABM-FD.

A range of findings were seen which were considered to be within normal limits for CD rats of this age.

DISCUSSION

The daily oral gavage administration of ABM-FD, an extract of the mushroom Himematsutake, to CD rats for 13 weeks, at dosages up to 2000 mg/kg/day was well tolerated, with no evidence of any toxicologically significant change. The dosage of 2000 mg/kg/day is the maximum dosage required by the guidelines and treatment up to this did not cause any treatment-related signs or any effect upon bodyweight and food consumption.

Many of the minor changes observed on this study may be consequences of the composition of ABM-FD as they could not be correlated with any other findings. Such changes included the consistently high glucose concentrations in males and variations of plasma electrolytes.

The reason for the low lymphocyte and large unstained cell counts reported in females receiving 1000 or 2000 mg/kg/day and transiently in those given 500 mg/kg/day is unknown. The differences from Controls were generally small and not of a toxicologically significant magnitude as the individual values were still within the normal background range.

The cause of the low haematocrit, haemoglobin concentration and erythrocyte count in males receiving 2000 mg/kg/day in Week 13 was unknown. For the high mean cell volume there was no evidence for any change in erythrocyte turnover (such as increased reticulocytes or high plasma bilirubin) or other cause of blood loss. Since the differences from controls were generally minor they are not considered toxicologically significant.

High plasma creatinine and urea concentrations, when observed together, are indicative of an effect upon the kidney, and in particular upon glomerular filtration. There was, however, no alteration of urinary composition or any histopathological finding in the kidney. Consequently, any effect upon the kidney is considered an adaptive response to treatment which is of no toxicological importance.

In the absence of any histopathological correlate the low spleen weights in females given 2000 mg/kg/day and the dark areas on the thymus of males given 2000 mg/kg/day are of doubtful toxicological significance.

The cause of the increased motor activity in Week 12, as demonstrated by high beam breaks, in females receiving 2000 mg/kg/day is unclear. No increase in activity was observed at the routine investigations, though these investigations would not identify subtle changes in activity.

In the absence of any histopathological change or any toxicologically significant finding during the course of the 13-weeks of treatment, the no-observed-adverse-effect level (NOAEL) of ABM-FD in this study was considered to be 2000 mg/kg/day.

CONCLUSION

It is concluded that the oral administration of ABM-FD, an extract of the mushroom Himematsutake, to CD rats for 13 weeks at dosages up to 2000 mg/kg/day was well-tolerated, with no evidence of any toxicologically significant change and no treatment-related histopathological finding. Consequently, the no-observed- adverse-effect level (NOAEL) of ABM-FD in this study was considered to be 2000 mg/kg/day.

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FIGURE 1

Motor activity - group mean scores (beam breaks) for males before commencement of treatment

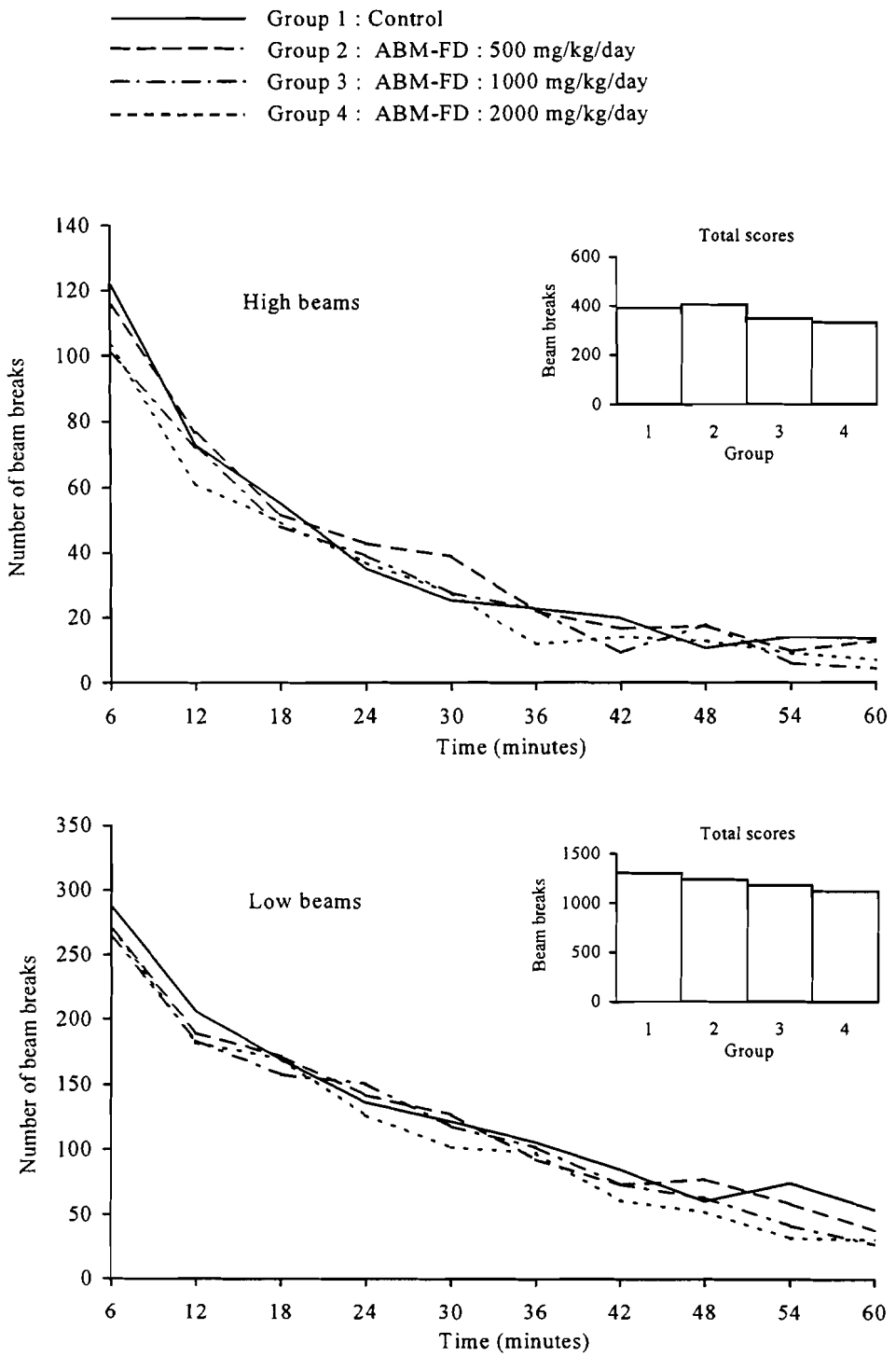


FIGURE 1 - continued

Motor activity - group mean scores (beam breaks) for females before commencement of treatment

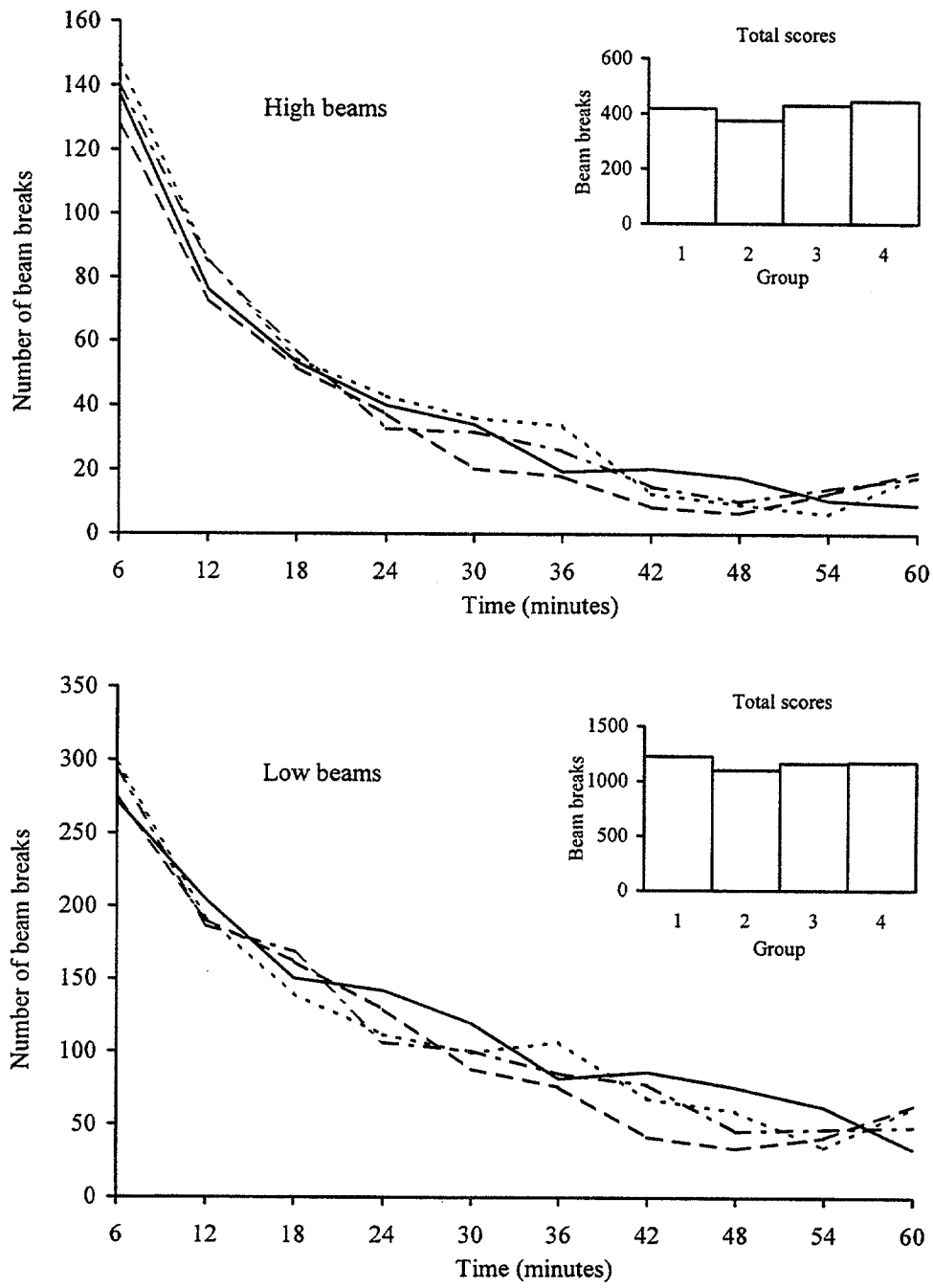
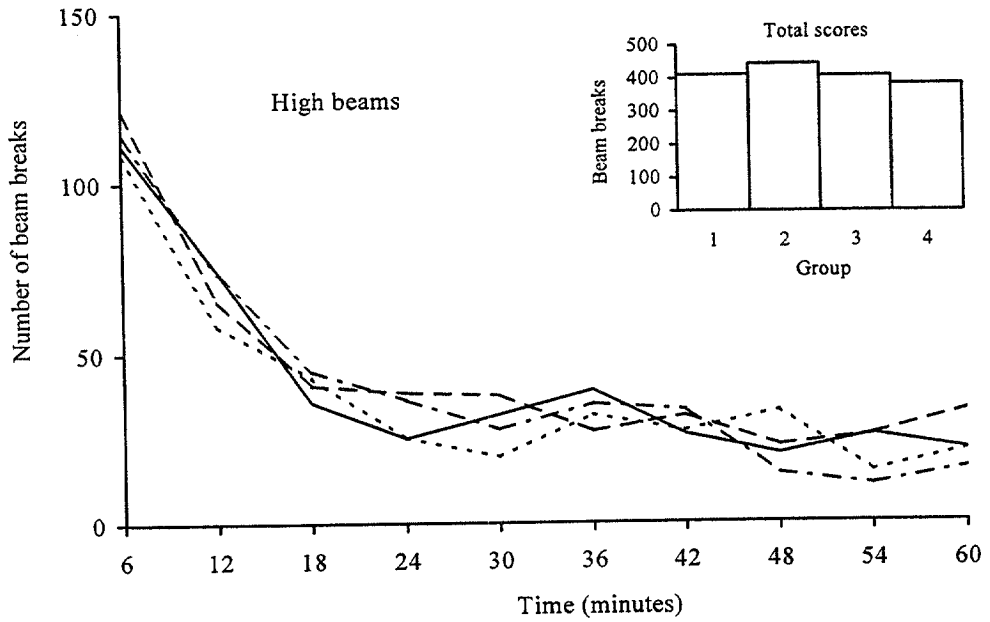


FIGURE 1 - continued

Motor activity - group mean scores (beam breaks) for males during Week 12 of treatment



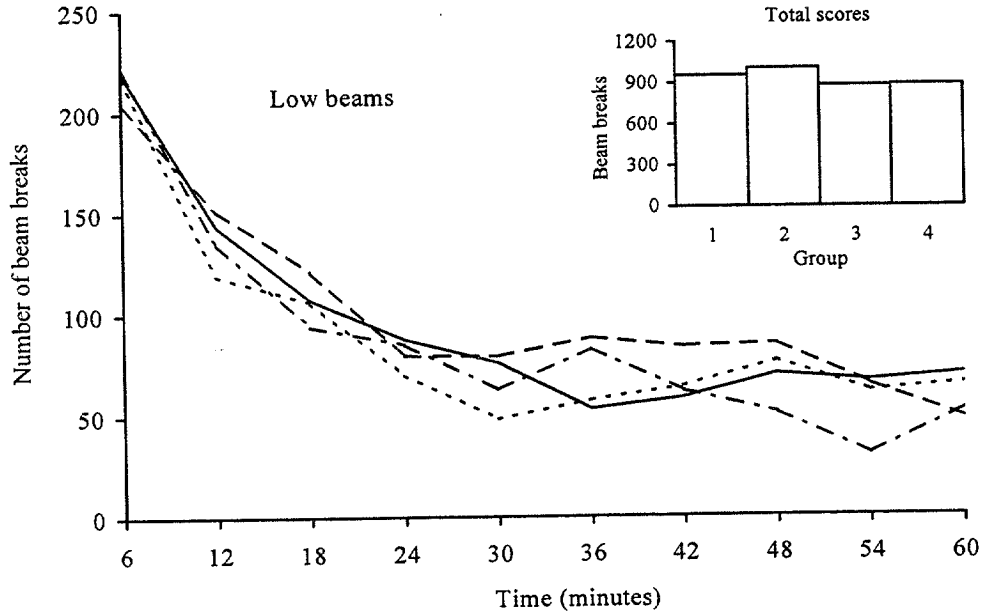


FIGURE 1 - continued

Motor activity - group mean scores (beam breaks) for females during Week 12 of treatment

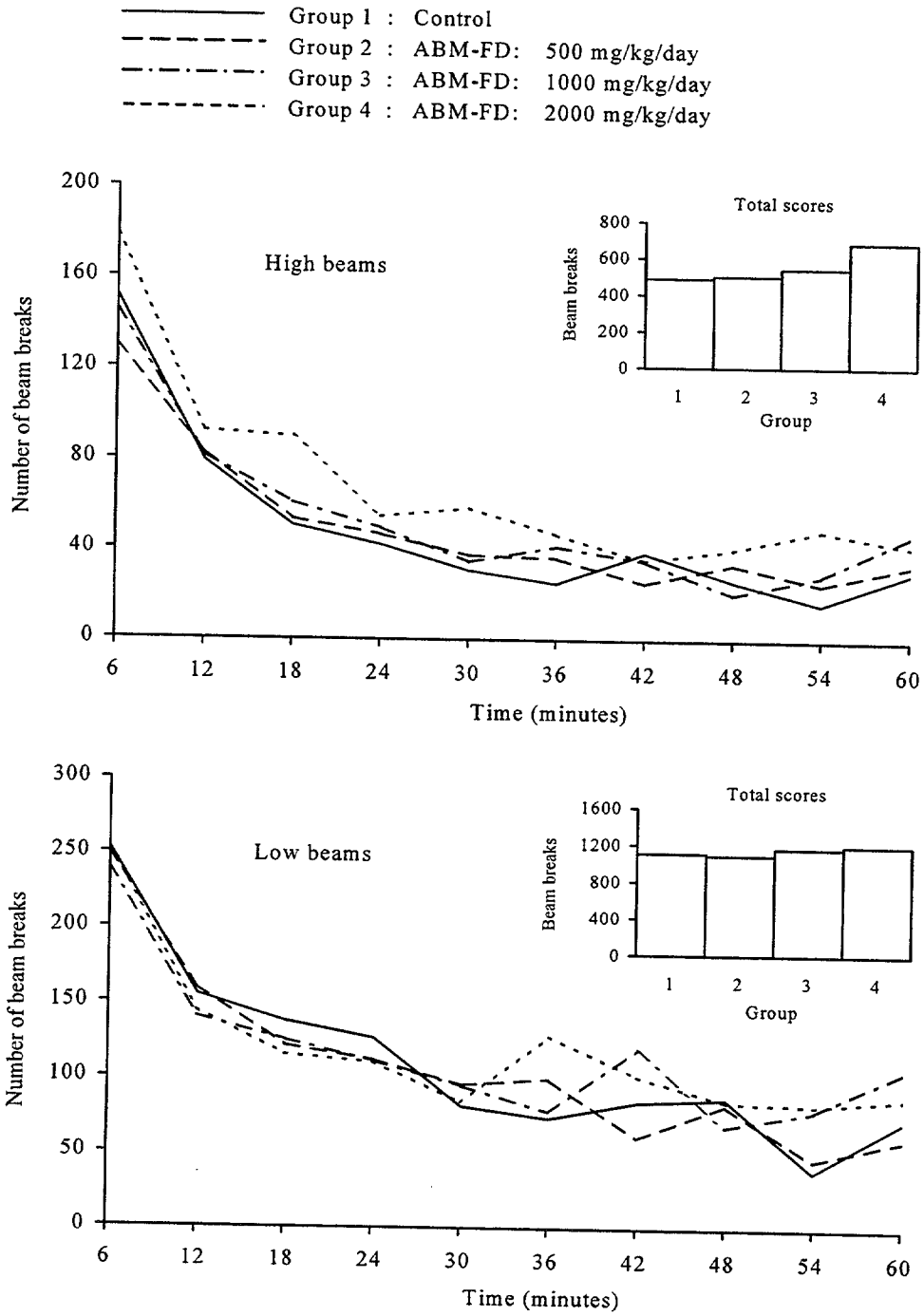


FIGURE 2

Bodyweight - group mean values (g) for males

Group	:	1	2	3	4
Compound	:	Control	----------	AMB-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

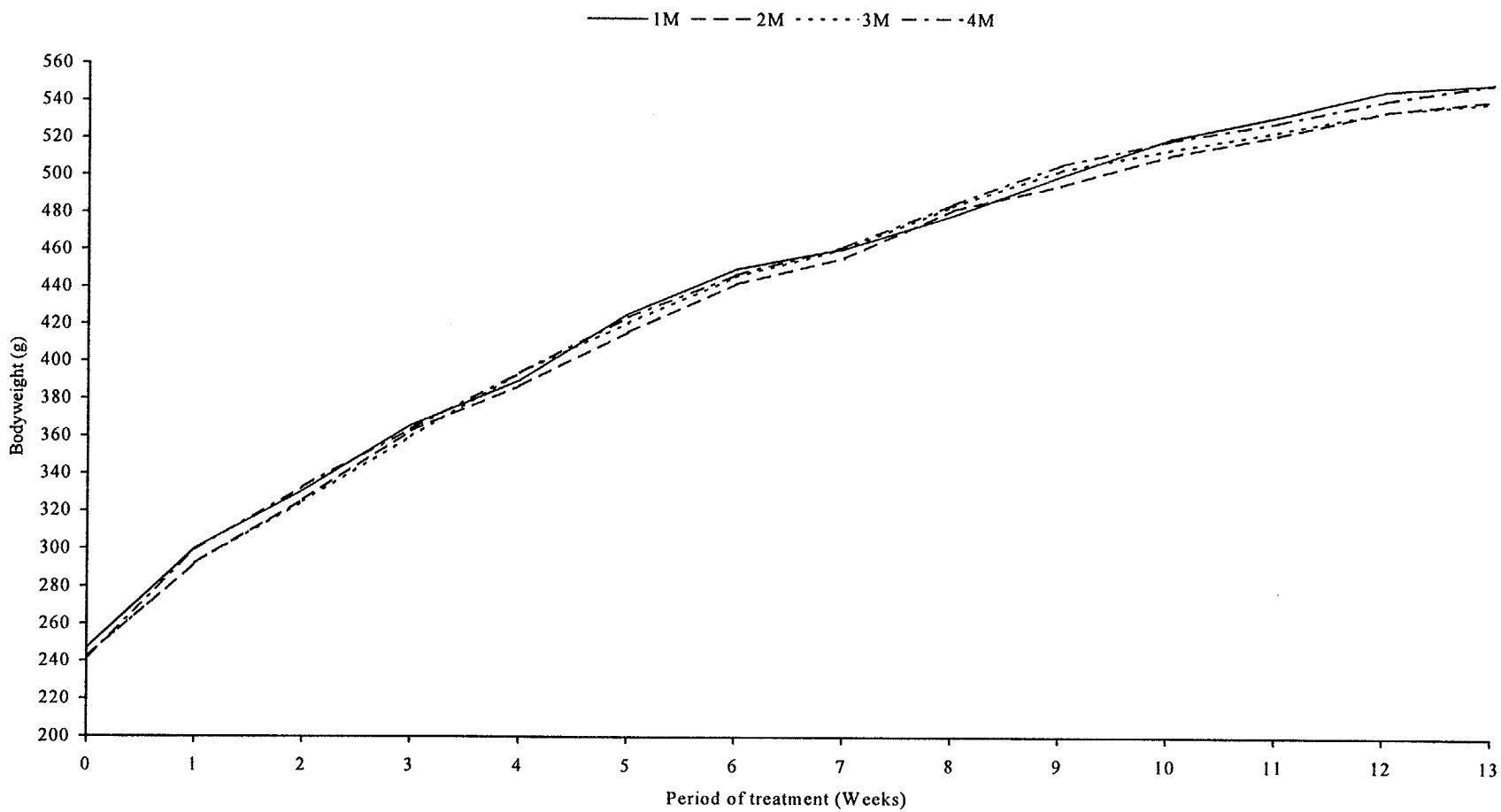


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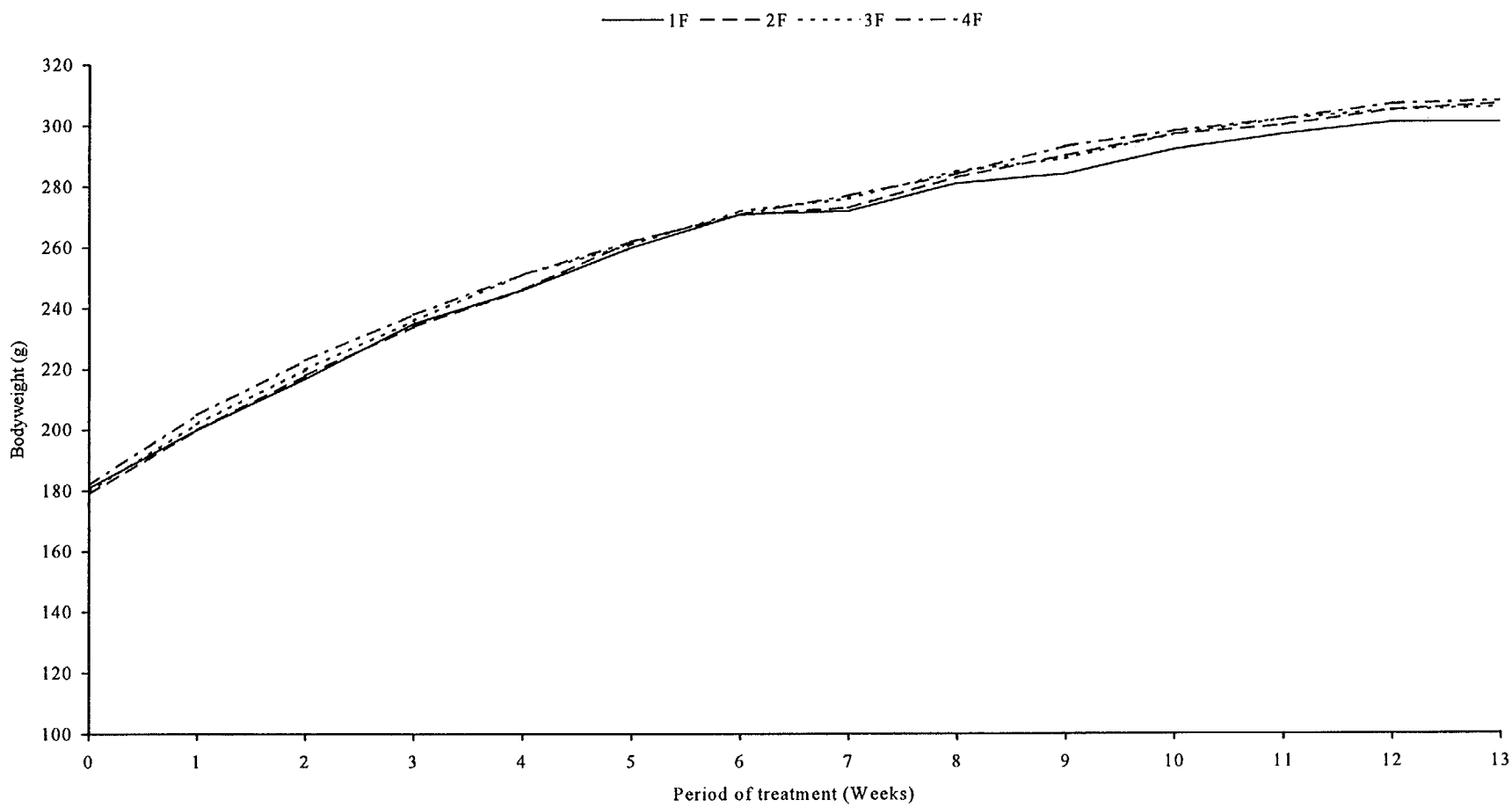
FIGURE 2 - continued

Bodyweight - group mean values (g) for females

Group	:	1	2	3	4
Compound	:	Control	----------	AMB-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000



IKI 001/052114

TABLE 1

Sensory reactivity and grip strength - summary of findings before commencement of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

		Group and sex							
		1M	2M	3M	4M	1F	2F	3F	4F
Number of animals:		20	20	20	20	20	20	20	20
Parameter	Grade								
Approach response (1-3)	1	1	1	0	0	1	2	3	0
	2	19	19	20	20	19	18	17	20
Touch response (1-3)	1	1	1	2	1	0	0	1	0
	2	19	19	18	19	20	20	19	20
Auditory startle reflex (1-4)	3	20	20	20	20	20	20	20	20
Tail pinch response (1-4)	3	20	20	18	20	20	20	20	20
	4	0	0	2	0	0	0	0	0
Forelimb grip strength (kg)	Mean	0.52	0.52	0.53	0.54	0.51	0.48	0.51	0.51
	SD	0.04	0.05	0.04	0.05	0.05	0.04	0.04	0.06
Hindlimb grip strength (kg)	Mean	0.26	0.26	0.25	0.26	0.23	0.23	0.22	0.23
	SD	0.02	0.02	0.02	0.03	0.03	0.03	0.02	0.02
Additional observations*									
Moderate vocalisation during grip strength		0	0	2	0	1	0	1	0

* Each animal may have more than one observation
$p \geq 0.05$, no statistical significance

TABLE 1 - continued

Sensory reactivity and grip strength – summary of findings during Week 12 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

		Group and sex							
		1M	2M	3M	4M	1F	2F	3F	4F
Number of animals:		9	10	10	10	10	10	10	8
Parameter	Grade								
Approach response	1	2	0	1	1	1	2	0	1
(1-3)	2	7	10	9	9	9	8	10	7
Touch response	1	1	0	0	1	0	0	1	0
(1-3)	2	8	10	10	9	10	10	9	8
Auditory startle reflex (1-4)	3	9	10	10	10	10	10	10	8
Tail pinch response	3	7	8	10	10	10	9	9	8
(1-4)	4	2	2	0	0	0	1	1	0
Forelimb grip strength (kg)	Mean	0.84	0.83	0.90	0.86	0.68	0.75	0.74	0.70
	SD	0.07	0.09	0.12	0.12	0.08	0.06	0.07	0.07
Hindlimb grip strength (kg)	Mean	0.52	0.44 b	0.53	0.47 a	0.35	0.38	0.37	0.37
	SD	0.04	0.05	0.05	0.04	0.03	0.06	0.04	0.02

Significant when compared with Control: a - $p<0.05$; p -b<0.01

TABLE 2

Motor activity - group mean scores (beam breaks) before commencement of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex	Number of animals	Beam level	Time (minutes) 6	12	18	24	30	36	42	48	54	60	Total
1M	20	High	122.3	72.9	55.3	35.0	25.3	22.7	19.8	10.6	14.0	13.4	391.0
		SD	23.5	20.5	19.6	16.6	17.4	25.8	21.7	14.9	21.0	21.0	110.0
2M	20	High	115.9	76.7	51.8	42.8	38.9	22.0	16.6	17.4	9.7	12.7	404.3
		SD	25.6	16.5	18.5	27.1	30.4	23.6	23.7	28.1	14.2	20.6	96.3
3M	20	High	100.9 a	72.3	48.3	39.1	27.6	22.5	9.1	17.8	6.0	4.2	347.6
		SD	27.3	27.7	21.7	18.9	23.0	22.2	9.7	29.0	15.7	10.8	100.1
4M	20	High	103.4 a	61.1	49.5	36.9	27.6	11.7	14.0	12.8	9.0	7.0	332.8
		SD	23.6	20.8	21.6	24.2	21.7	13.3	20.3	22.1	19.2	11.6	118.7
1M	20	Low	288.3	205.9	169.3	136.2	121.4	105.5	84.5	60.6	74.6	54.0	1300.0
		SD	44.3	53.9	49.4	63.4	49.2	64.1	55.5	71.9	94.5	84.6	363.2
2M	20	Low	270.2	189.4	171.9	141.8	127.0	92.8	73.1	77.5	58.8	38.1	1240.5
		SD	46.3	42.5	46.0	70.0	68.3	69.2	60.9	74.9	74.8	57.4	358.7
3M	20	Low	264.0	183.8	157.4	150.8	117.7	101.9	73.3	63.2	41.9	26.9	1180.8
		SD	60.8	52.3	67.9	41.6	63.5	64.7	62.9	75.3	55.8	45.5	331.0
4M	20	Low	270.2	181.9	169.7	126.3	102.0	97.5	61.0	52.5	32.2	30.4	1123.5
		SD	59.5	55.1	59.7	62.7	58.4	76.1	72.7	67.8	49.9	44.6	334.3

Significant when compared with Control: a – $p<0.05$

IKI 001/052114

TABLE 2 - continued

Motor activity - group mean scores (beam breaks) before commencement of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex	Number of animals	Beam level	Time (minutes) 6	12	18	24	30	36	42	48	54	60	Total
1F	20	High	137.2	76.2	53.4	40.1	34.2	19.5	20.5	17.8	10.6	9.2	418.5
		SD	24.3	18.5	32.1	24.3	27.4	27.0	20.4	22.8	13.5	17.9	116.7
2F	20	High	127.8	72.8	51.7	37.4	20.4	18.1	8.5	6.6	12.9	19.5	375.4
		SD	25.4	31.0	22.1	28.0	18.0	21.8	22.6	15.0	20.0	22.5	120.1
3F	20	High	139.6	84.5	57.2	32.8	31.9	26.1	15.0	10.2	14.3	17.9	429.3
		SD	27.5	28.6	22.5	22.5	33.7	30.5	21.2	15.6	27.0	25.2	133.9
4F	20	High	146.7	85.0	54.3	42.9	36.1	34.0	12.7	9.4	6.4	18.5	445.7
		SD	36.6	29.5	38.1	37.1	37.7	32.6	19.3	15.7	12.3	21.2	172.9
1F	20	Low	271.8	204.5	150.6	142.0	119.5	81.6	86.3	75.8	62.1	33.2	1227.1
		SD	49.2	59.6	62.9	73.2	78.4	71.0	64.8	71.8	75.1	45.3	398.2
2F	20	Low	273.9	190.2	161.8	129.2	88.0	76.1	41.7	33.5	41.2	63.5	1098.9
		SD	44.6	50.8	68.0	44.1	71.7	66.3	45.0	56.7	47.7	70.3	270.0
3F	20	Low	293.1	186.5	168.7	106.1	100.8	85.0	77.7	45.5	47.0	48.4	1158.7
		SD	32.6	49.5	58.7	65.8	80.0	68.9	79.3	60.4	70.7	62.7	316.3
4F	20	Low	297.3	192.4	139.5	111.7	99.3	106.7	67.7	59.2	34.1	61.9	1169.6
		SD	69.3	52.6	59.9	61.1	70.0	72.1	65.9	74.8	40.5	69.5	338.0

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 2 - continued

Motor activity - group mean scores (beam breaks) during Week 12 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex	Number of animals	Beam level	Time (minutes) 6	12	18	24	30	36	42	48	54	60	Total
1M	9	High	111.3	74.3	35.6	25.1	32.0	39.2	25.9	20.1	25.7	21.3	410.6
		SD	24.9	23.9	18.9	16.3	38.8	64.5	19.6	9.5	27.7	18.9	198.1
2M	10	High	121.2	65.7	40.8	38.5	37.7	26.9	31.5	22.5	25.6	33.0	443.4
		SD	22.1	21.9	21.7	23.5	26.3	14.3	21.4	13.6	31.1	52.5	162.1
3M	10	High	114.0	73.7	45.0	36.4	27.6	35.1	33.2	14.3	10.9	15.9	406.1
		SD	12.4	21.4	25.2	28.7	23.9	16.0	28.8	15.2	16.7	15.3	129.8
4M	10	High	108.1	58.4	43.1	25.2	19.6	31.8	26.9	32.9	14.8	21.2	382.0
		SD	30.2	29.2	28.6	29.2	26.6	22.8	18.0	20.8	14.3	20.2	138.4
1M	9	Low	220.0	143.6	107.4	87.8	76.1	53.3	58.7	70.1	66.7	70.0	953.7
		SD	58.3	39.2	49.1	39.5	55.9	46.7	47.5	44.1	47.2	42.6	306.2
2M	10	Low	203.7	151.9	121.6	79.9	79.4	88.2	83.7	85.0	64.9	48.1	1006.4
		SD	50.8	55.2	30.3	47.8	44.0	48.1	39.0	45.6	40.5	39.5	248.4
3M	10	Low	221.6	135.2	94.1	85.4	63.0	82.7	61.9	51.0	30.4	52.2	877.5
		SD	30.9	34.9	41.6	45.8	39.6	28.8	42.1	35.1	26.4	42.6	204.2
4M	10	Low	217.3	119.4	106.2	70.2	48.5	57.6	64.2	76.6	61.5	65.2	886.7
		SD	27.2	17.7	49.6	37.4	37.5	25.6	35.6	56.6	53.0	50.0	132.0

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 2 - continued

Motor activity - group mean scores (beam breaks) during Week 12 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex	Number of animals	Beam level	Time (minutes) 6	12	18	24	30	36	42	48	54	60	Total
1F	10	High	151.5	78.9	50.6	42.1	30.7	25.2	38.7	26.4	16.2	30.0	490.3
		SD	25.9	27.3	26.5	26.0	16.5	15.9	30.2	26.8	20.1	29.3	153.2
2F	10	High	129.4	82.7	53.4	46.7	37.5	36.4	25.3	33.9	24.9	33.5	503.7
		SD	31.4	19.9	20.9	24.1	19.1	16.1	26.1	28.1	36.5	27.1	135.0
3F	10	High	144.9	81.4	60.7	49.5	34.6	41.6	35.2	20.4	28.9	47.1	544.3
		SD	37.5	24.9	44.3	24.5	34.9	26.9	19.2	19.1	28.7	27.2	195.1
4F	8	High	178.1	92.1	89.9	54.6	58.3	46.9	35.5	40.6	49.1 a	42.1	687.3 a
		SD	43.5	57.6	74.3	29.3	68.8	30.4	30.9	35.8	35.8	34.5	286.6
1F	10	Low	253.2	155.2	137.7	126.6	81.4	73.5	84.3	87.1	38.6	72.0	1109.6
		SD	66.1	41.6	44.2	62.6	46.0	41.1	62.9	69.1	37.3	48.5	353.1
2F	10	Low	248.9	159.6	121.6	112.2	95.8	99.8	60.8	83.1	46.2	60.1	1088.1
		SD	48.4	38.8	38.3	31.0	27.8	38.4	35.8	49.0	36.4	45.1	188.9
3F	10	Low	239.3	140.5	125.2	111.4	95.1	78.0	120.3	68.7	79.1	105.9	1163.5
		SD	52.7	35.5	47.5	29.8	40.3	56.2	97.6	44.8	57.5	41.2	315.8
4F	8	Low	252.6	144.5	115.4	110.5	84.1	128.6	101.8	85.1	83.0 a	87.4	1193.0
		SD	51.6	68.8	44.4	27.3	54.3	103.9	90.0	64.9	40.4	44.8	365.3
Historical control data (3 studies)													
High beams		Mean	153.4	90.4	51.1	44.2	33.2	25.3	19.7	29.1	16.6	25.2	488.3
		Minimum	130.1	84.7	42.0	38.8	30.7	20.5	13.9	13.2	14.4	18.4	464.3
		Maximum	175.2	93.4	64.3	46.9	37.5	33.4	26.3	45.5	19.2	32.1	504.5

Significant when compared with Control: a – $p<0.05$

IKI 001/052114

TABLE 3

Print No: 0001

Bodyweight - group mean values (g)

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Protocol Number: IKI 001

Group :	1	2	3	4
Compound :	Control	------ ABM-FD ------		
Dosage (mg/kg/day) :	0	500	1000	2000

SEX:		MALE				FEMALE			
	GROUP:	1	2	3	4	1	2	3	4
WEEK									
0	N	20	20	20	20	20	20	20	20
	MEAN	247	242	242	242	181	179	180	182
	S.D.	11.1	13.1	13.0	14.7	11.2	13.0	13.0	10.4
1	N	20	20	20	20	20	20	20	20
	MEAN	300	292	292	299	200	200	202	205
	S.D.	16.0	19.6	19.6	23.5	13.6	16.8	15.5	11.1
2	N	20	20	20	20	20	20	20	20
	MEAN	331	326	325	333	217	218	220	223
	S.D.	18.7	28.5	27.8	28.6	15.4	17.0	18.2	14.5
3	N	20	20	20	20	20	20	20	20
	MEAN	366	363	360	364	235	234	236	238
	S.D.	25.4	32.0	34.0	36.1	17.7	18.3	20.5	15.7
4	N	20	20	20	20	20	20	20	20
	MEAN	390	387	394	394	246	246	251	251
	S.D.	25.6	36.3	36.3	37.4	19.8	21.3	20.8	18.9
5	N	20	20	20	20	20	20	20	20
	MEAN	426	416	421	424	260	262	261	262
	S.D.	31.3	37.6	38.4	40.8	19.4	24.1	22.3	17.0
6	N	20	20	20	20	20	20	20	20
	MEAN	450	442	446	447	271	271	272	271
	S.D.	36.5	39.1	41.9	41.9	21.9	25.0	24.0	18.8
7	N	20	20	20	20	20	20	20	20
	MEAN	461	456	461	462	272	273	276	277
	S.D.	40.6	39.8	47.7	39.7	21.6	25.1	25.9	20.4
8	N	20	20	20	20	20	20	20	18
	MEAN	479	482	484	485	281	283	285	284
	S.D.	47.2	42.0	51.4	43.5	23.7	27.7	25.6	20.9
9	N	20	20	20	20	20	20	20	18
	MEAN	500	495	503	506	284	290	289	293
	S.D.	49.6	45.1	53.3	46.5	23.2	29.2	25.4	20.2

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TABLE 3 - continued.

Print No: 0001

Bodyweight - group mean values (g)

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Page: 2

Protocol Number: IKI 001

Group	1	2	3	4
Compound	Control	ABM-FD		
Dosage (mg/kg/day)	0	500	1000	2000

SEX:		MALE				FEMALE			
WEEK	GROUP:	1	2	3	4	1	2	3	4
10	N	19	20	20	20	20	20	20	18
	MEAN	520	511	514	519	292	297	297	298
	S.D.	48.6	46.2	55.9	50.1	24.7	28.4	28.2	21.9
11	N	19	20	20	20	20	20	20	18
	MEAN	532	522	524	529	297	300	302	302
	S.D.	51.5	47.3	59.1	50.6	26.0	28.9	28.2	22.3
12	N	19	20	20	20	20	20	20	18
	MEAN	546	535	535	541	301	305	305	307
	S.D.	54.5	47.9	61.3	54.1	26.9	29.7	28.0	23.7
13	N	19	20	20	20	20	20	20	18
	MEAN	550	541	540	550	301	307	306	308
	S.D.	53.6	50.2	63.5	51.0	27.9	31.0	29.6	23.7
Gain 0-13	N	19	20	20	20	20	20	20	18
	MEAN	303	299	298	308	120	129	127	126
	S.D.	48.3	41.3	55.1	41.6	20.9	24.4	21.3	16.7
As % of Control		-	99	98	102	-	108	106	105

TABLE 4

Food consumption - group mean values (g/animal)

Protocol Number: IKI 001

Group	1	2	3	4
Compound	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	0	500	1000	2000

	SEX:	MALE				FEMALE			
WEEK	GROUP:	1	2	3	4	1	2	3	4
1	N	20	20	20	20	20	20	20	20
	MEAN	203	197	197	204	140	134	137	141
	S.D.	14.3	13.2	16.4	19.4	12.5	11.1	15.2	11.9
2	N	20	20	20	20	20	20	20	20
	MEAN	189	189	182	185	138	135	133	132
	S.D.	13.7	22.6	24.3	18.8	12.9	10.6	16.1	11.5
3	N	20	20	20	20	20	20	20	20
	MEAN	201	204	194	194	145	146	146	141
	S.D.	16.8	18.7	18.5	18.6	11.4	13.1	14.8	13.2
4	N	20	20	20	20	20	20	20	20
	MEAN	208	206	204	199	146	146	147	148
	S.D.	14.0	21.0	22.0	15.9	10.9	12.2	11.6	12.0
5	N	20	20	20	20	20	20	20	20
	MEAN	204	191	196	196	149	145	145	147
	S.D.	13.7	32.6	17.3	15.5	16.9	12.7	14.0	13.4
6	N	20	20	20	20	20	20	20	20
	MEAN	203	194	197	193	141	141	143	139
	S.D.	13.9	19.6	18.3	16.3	13.6	11.8	13.9	11.3
7	N	20	20	20	20	20	20	20	20
	MEAN	188	187	185	184	135	134	135	134
	S.D.	13.5	22.4	22.3	13.7	11.8	12.6	18.1	12.0
8	N	20	20	20	20	20	20	20	18
	MEAN	196	203	194	192	138	142	143	142
	S.D.	36.7	18.3	18.6	16.7	10.7	13.8	13.2	12.8
9	N	20	20	20	20	20	20	20	18
	MEAN	200	198	202	195	140	140	141	138
	S.D.	23.5	26.7	16.5	25.5	10.2	11.5	13.3	11.3
10	N	19	20	20	20	20	20	20	18
	MEAN	200	196	196	198	135	141	140	138
	S.D.	18.7	16.6	20.8	16.3	17.2	11.5	14.1	12.8

TABLE 4 - continued

Print No: 0002

Food consumption - group mean values (g/animal)

Group :	1	2	3	4
Compound :	Control	------	ABM-FD	------
Dosage (mg/kg/day) :	0	500	1000	2000

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Protocol Number: IKI 001

WEEK	SEX: GROUP:	MALE 1	MALE 2	MALE 3	MALE 4	FEMALE 1	FEMALE 2	FEMALE 3	FEMALE 4
11	N	19	20	20	20	20	20	20	18
	MEAN	200	194	196	195	141	140	140	136
	S.D.	18.2	18.3	21.4	15.8	14.4	11.9	13.8	10.6
12	N	19	20	20	20	20	20	20	18
	MEAN	202	196	193	193	135	138	136	135
	S.D.	16.3	16.8	19.3	19.4	15.8	13.8	15.5	13.6
13	N	19	20	20	20	20	20	20	18
	MEAN	195	190	187	191	137	133	135	130
	S.D.	15.9	18.2	21.4	16.6	14.9	12.8	16.0	18.4
MEAN 1-13		199	196	194	194	140	140	140	139
as % of CONTROL		-	98	97	97	-	100	100	99

TABLE 5

Print No: 0003

Food conversion efficiency - group mean values (%)

Printed: 31-MAR-05
Page: 1

Protocol Number: IKI 001

Group :	1	2	3	4
Compound :	Control	------ ABM-FD ------		
Dosage (mg/kg/day) :	0	500	1000	2000

SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
WEEK								
1	26.1	25.4	25.1	27.5	13.9	15.8	16.2	16.7
2	15.8	17.5	17.7	18.5	11.7	13.2	13.4	13.5
3	17.3	17.9	18.0	15.6	12.8	10.8	10.8	10.3
4	12.0	11.6	16.7	15.1	7.2	8.3	10.1	8.4
5	17.3	11.9	14.0	15.5	9.7	10.9	7.1	8.1
6	11.9	14.0	12.6	11.5	7.2	6.5	7.5	6.3
7	5.7	6.8	7.6	8.2	0.9	1.1	2.9	4.1
8	6.3	12.9	12.0	11.7	6.9	6.7	6.1	4.1
9	10.4	5.4	9.5	11.0	1.8	5.1	3.3	6.0
10	7.5	8.4	5.1	6.6	5.8	4.9	5.3	4.1
11	6.0	5.4	5.1	5.0	3.7	2.6	3.7	2.6
12	7.0	6.6	5.8	6.1	3.1	2.9	2.0	3.8
13	1.7	3.2	2.6	4.6	*	1.8	0.8	0.2
Overall 1-13	11.7	11.7	11.8	12.2	6.6	7.1	7.0	7.0

* Bodyweight stasis or loss, food conversion efficiency not calculable.

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TABLE 6

Haematology - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1M	Mean	0.438	15.2	7.38	20.6	34.7	59.4
	SD	0.0190	0.74	0.368	0.46	0.58	1.55
	n	10	10	10	10	10	10
2M	Mean	0.444	15.4	7.38	20.9	34.8	60.2
	SD	0.0093	0.35	0.229	0.59	0.39	1.80
	n	10	10	10	10	10	10
3M	Mean	0.444	15.4	7.45	20.7	34.7	59.6
	SD	0.0152	0.55	0.165	0.46	0.30	1.58
	n	10	10	10	10	10	10
4M	Mean	0.437	15.0	7.14	21.1	34.4	61.3 a
	SD	0.0137	0.50	0.402	0.76	0.47	2.10
	n	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC $x10^9/L$	N $x10^9/L$	L $x10^9/L$	E $x10^9/L$	B $x10^9/L$	M $x10^9/L$	LUC $x10^9/L$	Plt $x10^9/L$	PT sec	APTT sec
1M	Mean	11.09	1.61	8.82	0.08	0.03	0.31	0.23	1169	13.5	21.7
	SD	2.696	0.677	2.311	0.030	0.020	0.115	0.089	104.6	0.23	1.20
	n	10	10	10	10	10	10	10	10	10	10
2M	Mean	12.90	1.50	10.54	0.08	0.05	0.41	0.31	1195	13.4	21.8
	SD	2.238	0.297	1.950	0.042	0.030	0.113	0.101	104.9	0.43	1.66
	n	10	10	10	10	10	10	10	10	10	10
3M	Mean	12.14	1.31	10.08	0.07	0.05	0.34	0.29	1177	13.6	22.5
	SD	3.102	0.651	2.493	0.037	0.031	0.078	0.151	126.4	0.46	2.31
	n	10	10	10	10	10	10	10	10	10	10
4M	Mean	11.41	1.63	9.07	0.08	0.03	0.34	0.25	1178	13.6	22.9
	SD	1.660	0.797	1.326	0.029	0.014	0.121	0.099	95.1	0.48	1.05
	n	10	10	10	10	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 6 - continued

Haematology - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1F	Mean	0.432	15.3	7.36	20.8	35.4	58.7
	SD	0.0115	0.42	0.211	0.33	0.35	1.00
	n	10	10	10	10	10	10
2F	Mean	0.419	14.7 A	7.16	20.5	35.1	58.5
	SD	0.0130	0.47	0.224	0.37	0.46	1.03
	n	10	10	10	10	10	10
3F	Mean	0.417	14.6 A	7.17	20.3	35.0	58.2
	SD	0.0301	1.22	0.476	0.66	0.55	1.52
	n	10	10	10	10	10	10
4F	Mean	0.419	14.7 A	7.16	20.5	35.1	58.5
	SD	0.0124	0.46	0.376	0.73	0.55	1.75
	n	10	10	10	10	10	10

Significant when compared with Group 1: A - $p<0.05$; B - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC x10^9/L	N x10^9/L	L x10^9/L	E x10^9/L	B x10^9/L	M x10^9/L	LUC x10^9/L	Plt x10^9/L	PT sec	APTT sec
1F	Mean	10.99	1.15	9.15	0.12	0.03	0.35	0.20	1187	13.6	17.4
	SD	2.028	0.321	1.725	0.043	0.008	0.100	0.055	154.4	0.48	1.32
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	9.78	1.36	7.92	0.08	0.02	0.23 a	0.17	1132	13.6	17.1
	SD	1.743	0.544	1.402	0.018	0.009	0.051	0.042	156.9	0.39	2.06
	n	10	10	10	10	10	10	10	10	9	9
3F	Mean	9.58	1.32	7.69	0.09	0.02	0.25 a	0.21	1212	13.8	17.2
	SD	5.108	1.299	3.642	0.038	0.016	0.074	0.196	333.9	0.32	1.37
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	8.72	1.14	7.06	0.09	0.02 a	0.27 a	0.14	1156	13.6	16.6
	SD	2.020	0.347	1.662	0.036	0.011	0.109	0.064	102.5	0.48	1.36
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1M	Mean	0.456	15.4	8.13	19.0	33.8	56.1
	SD	0.0171	0.47	0.372	0.61	0.50	1.66
	n	10	10	10	10	10	10
2M	Mean	0.449	15.3	7.87	19.5	34.2	57.1
	SD	0.0097	0.47	0.173	0.53	0.44	1.34
	n	10	10	10	10	10	10
3M	Mean	0.449	15.4	7.89	19.4	34.2	56.8
	SD	0.0156	0.51	0.282	0.38	0.33	0.88
	n	10	10	10	10	10	10
4M	Mean	0.444	15.1	7.72 a	19.6 a	33.9	57.7 a
	SD	0.0128	0.49	0.467	0.73	0.42	2.53
	n	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC $x10^9/L$	N $x10^9/L$	L $x10^9/L$	E $x10^9/L$	B $x10^9/L$	M $x10^9/L$	LUC $x10^9/L$	Plt $x10^9/L$	PT sec	APTT sec
1M	Mean	11.31	1.41	9.19	0.10	0.03	0.26	0.31	1029	14.6	19.9
	SD	2.910	0.601	2.325	0.040	0.013	0.098	0.147	63.8	0.42	1.92
	n	10	10	10	10	10	10	10	10	10	10
2M	Mean	15.09	2.56	11.56	0.11	0.06 b	0.40	0.40	1024	14.5	19.6
	SD	2.869	1.781	1.914	0.040	0.038	0.170	0.122	107.4	0.47	2.76
	n	10	10	10	10	10	10	10	10	9	9
3M	Mean	13.63	2.05	10.60	0.15	0.04 b	0.36	0.42	1046	14.4	18.8
	SD	4.069	1.016	3.543	0.159	0.020	0.176	0.172	106.5	0.30	2.26
	n	10	10	10	10	10	10	10	10	10	10
4M	Mean	13.70	2.96 a	9.91	0.13	0.05 b	0.32	0.34	1084	14.7	19.3
	SD	3.027	2.150	1.694	0.056	0.017	0.131	0.157	169.2	0.63	1.96
	n	10	10	10	10	10	10	10	10	8	8

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1F	Mean	0.440	15.2	7.63	19.9	34.6	57.7
	SD	0.0100	0.36	0.162	0.38	0.39	1.07
	n	10	10	10	10	10	10
2F	Mean	0.440	15.2	7.68	19.9	34.6	57.4
	SD	0.0119	0.44	0.256	0.42	0.36	0.88
	n	10	10	10	10	10	10
3F	Mean	0.449	15.6	7.90	19.7	34.6	56.9
	SD	0.0233	0.65	0.401	0.57	0.47	1.77
	n	10	10	10	10	10	10
4F	Mean	0.442	15.3	7.79	19.7	34.6	56.9
	SD	0.0119	0.44	0.396	0.60	0.36	1.57
	n	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 6 - continued

Haematology - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC $x10^9/L$	N $x10^9/L$	L $x10^9/L$	E $x10^9/L$	B $x10^9/L$	M $x10^9/L$	LUC $x10^9/L$	Plt $x10^9/L$	PT sec	APTT sec
1F	Mean	9.96	1.11	8.26	0.11	0.02	0.23	0.23	977	14.7	14.7
	SD	1.737	0.239	1.565	0.060	0.006	0.038	0.068	140.6	0.62	2.27
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	10.24	1.35	8.34	0.10	0.03	0.19	0.23	1058	14.8	14.3
	SD	1.471	0.529	1.444	0.032	0.009	0.050	0.059	145.5	0.57	2.91
	n	10	10	10	10	10	10	10	10	9	9
3F	Mean	8.54	1.22	6.84	0.09	0.02	0.18	0.19	971	15.1	15.8
	SD	2.736	1.107	2.294	0.023	0.011	0.071	0.090	84.5	0.48	1.64
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	7.56 a	1.26	5.85 b	0.10	0.02	0.19	0.15 a	1034	15.2	14.9
	SD	1.888	0.507	1.450	0.035	0.008	0.054	0.064	108.0	0.37	1.50
	n	10	10	10	10	10	10	10	10	9	9

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1M	Mean	0.453	15.7	8.70	18.0	34.6	52.1
	SD	0.0204	0.63	0.387	0.54	0.41	1.40
	n	10	10	10	10	10	10
2M	Mean	0.441	15.4	8.28 a	18.6	34.9	53.4
	SD	0.0147	0.58	0.286	0.55	0.35	1.63
	n	10	10	10	10	10	10
3M	Mean	0.440	15.3	8.32 a	18.4	34.7	52.9
	SD	0.0151	0.54	0.279	0.32	0.32	0.95
	n	10	10	10	10	10	10
4M	Mean	0.436 a	15.0 a	8.14 b	18.4	34.4	53.6 a
	SD	0.0184	0.63	0.512	0.68	0.67	1.74
	n	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 6 - continued

Haematology - group mean values during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC $x10^9/L$	N $x10^9/L$	L $x10^9/L$	E $x10^9/L$	B $x10^9/L$	M $x10^9/L$	LUC $x10^9/L$	Plt $x10^9/L$	PT sec	APTT sec
1M	Mean	13.20	2.21	9.97	0.17	0.04	0.43	0.37	1072	14.6	20.6
	SD	4.366	1.267	3.004	0.055	0.041	0.133	0.154	85.1	0.85	2.75
	n	10	10	10	10	10	10	10	10	9	9
2M	Mean	16.11	2.94	12.10	0.16	0.07	0.48	0.37	1098	14.8	20.4
	SD	2.352	1.340	1.518	0.053	0.035	0.122	0.116	141.3	0.39	2.08
	n	10	10	10	10	10	10	10	10	10	10
3M	Mean	14.64	2.37	11.36	0.14	0.06	0.38	0.33	1061	14.9	21.7
	SD	3.795	1.401	2.973	0.058	0.039	0.115	0.087	126.8	0.61	2.37
	n	10	10	10	10	10	10	10	10	10	10
4M	Mean	12.49	1.76	9.97	0.14	0.03	0.32	0.27	1056	14.7	19.5
	SD	2.214	0.444	1.846	0.044	0.017	0.109	0.094	139.1	0.77	2.51
	n	10	10	10	10	10	10	10	10	8	8

$p \geq 0.05$, no statistical significance

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TABLE 6 - continued

Haematology - group mean values during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Hct L/L	Hb g/dL	RBC $x10^{12}/L$	MCH pg	MCHC g/dL	MCV fL
1F	Mean	0.430	15.2	7.72	19.7	35.3	55.7
	SD	0.0155	0.53	0.334	0.56	0.55	1.21
	n	10	10	10	10	10	10
2F	Mean	0.418	14.8	7.55	19.6	35.4	55.4
	SD	0.0126	0.46	0.318	0.46	0.29	1.33
	n	10	10	10	10	10	10
3F	Mean	0.428	15.1	7.81	19.4	35.3	54.8
	SD	0.0202	0.71	0.330	0.63	0.26	1.95
	n	10	10	10	10	10	10
4F	Mean	0.426	15.0	7.79	19.3	35.3	54.8
	SD	0.0151	0.44	0.472	0.74	0.64	1.76
	n	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 6 - continued

Haematology - group mean values during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		WBC $x10^9/L$	N $x10^9/L$	L $x10^9/L$	E $x10^9/L$	B $x10^9/L$	M $x10^9/L$	LUC $x10^9/L$	Plt $x10^9/L$	PT sec	APTT sec
1F	Mean	9.63	1.08	7.91	0.12	0.03	0.27	0.23	1040	14.7	15.8
	SD	1.599	0.477	1.777	0.044	0.018	0.054	0.081	145.2	0.83	1.82
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	9.58	1.10	7.98	0.08	0.02	0.21	0.18	1052	15.0	15.4
	SD	1.537	0.363	1.268	0.015	0.007	0.076	0.044	120.9	0.69	2.08
	n	10	10	10	10	10	10	10	10	10	10
3F	Mean	8.25	0.94	6.82	0.09	0.02	0.21	0.17	981	14.7	15.1
	SD	1.725	0.429	1.502	0.031	0.012	0.050	0.034	110.4	0.72	2.00
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	7.35 a	1.20	5.70 b	0.10	0.02	0.20 a	0.14 b	1040	14.9	15.7
	SD	2.649	0.733	1.861	0.035	0.010	0.136	0.100	109.3	0.67	2.31
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1M	Mean	252	33	78	1	2	4.38	44	4.90	1.98	0.68
	SD	33.5	3.8	5.6	1.5	0.5	0.692	3.8	0.698	0.478	0.177
	n	10	10	10	10	10	10	10	10	10	10
2M	Mean	240	35	74	2	2	4.55	42	4.74	2.09	0.87
	SD	50.6	7.2	6.9	1.1	0.5	0.701	2.8	0.363	0.475	0.297
	n	10	10	10	10	10	10	10	10	10	10
3M	Mean	224	37	80	2	1	5.02	47	5.28	2.01	0.85
	SD	41.1	9.7	5.5	1.2	0.5	0.557	5.8	0.596	0.360	0.228
	n	10	10	10	10	10	10	10	10	10	10
4M	Mean	221	35	79	2	2	4.59	43	5.53 a	2.11	0.73
	SD	42.8	4.8	3.7	1.3	0.5	0.713	4.4	0.413	0.407	0.404
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1M	Mean	146	4.3	101	2.65	3.36
	SD	0.8	0.27	1.6	0.080	0.237
	n	10	10	10	10	10
2M	Mean	145	4.8 a	102	2.69	3.30
	SD	0.6	0.34	0.8	0.072	0.225
	n	10	10	10	10	10
3M	Mean	146	4.6 a	102	2.63	3.29
	SD	0.8	0.38	1.2	0.081	0.198
	n	10	10	10	10	10
4M	Mean	144 b	4.9 b	102	2.66	3.02 b
	SD	1.2	0.42	1.4	0.037	0.242
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1M	Mean	63	30	14	3	14	2	0.89
	SD	3.2	1.3	1.0	0.0	0.5	1.0	0.053
	n	10	10	10	10	10	10	10
2M	Mean	63	29	15	3 A	14	1	0.89
	SD	2.4	1.5	1.1	0.7	1.4	0.0	0.102
	n	10	10	10	10	10	10	10
3M	Mean	61	29	14	3	14	1	0.90
	SD	2.1	1.6	1.2	0.4	1.1	0.0	0.095
	n	10	10	10	10	10	10	10
4M	Mean	61	29	14	3	14	1	0.90
	SD	1.3	1.2	1.0	0.3	0.8	0.7	0.073
	n	10	10	10	10	10	10	10

Significant when compared with Group 1: A - $p<0.05$; B - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1F	Mean	131	40	76	1	2	5.63	44	5.48	2.47	0.43
	SD	19.1	31.9	13.0	0.5	0.5	0.586	2.2	0.818	0.456	0.125
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	144	28	72	0	2	5.45	43	5.50	2.22	0.42
	SD	28.0	5.0	6.8	0.3	0.0	0.645	2.3	0.243	0.470	0.140
	n	10	10	10	10	10	10	10	10	10	10
3F	Mean	143	27	79	1	2 b	5.73	44	5.44	1.98 a	0.41
	SD	28.4	2.4	13.7	0.8	0.4	0.815	3.0	0.408	0.384	0.092
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	124	23 B	68	0	2	5.38	42	6.06 A	2.21 a	0.46
	SD	16.0	2.9	7.9	0.5	0.5	0.742	2.7	0.566	0.190	0.163
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$
Significant when compared with Group 1: A - $p<0.05$; B - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1F	Mean	143	3.9	101	2.70	2.46
	SD	0.7	0.18	0.9	0.093	0.226
	n	10	10	10	10	10
2F	Mean	143	4.1	102	2.62 a	2.34
	SD	0.9	0.24	1.0	0.052	0.147
	n	10	10	10	10	10
3F	Mean	142	4.2 b	102	2.62 b	2.48
	SD	1.2	0.26	1.2	0.054	0.200
	n	10	10	10	10	10
4F	Mean	142	4.3 b	102	2.61 b	2.32
	SD	1.2	0.20	1.4	0.074	0.150
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1F	Mean	64	31	13	4	15	2	0.92
	SD	3.1	2.1	0.8	0.5	1.0	0.6	0.048
	n	10	10	10	10	10	10	10
2F	Mean	62	31	13	3	14	2	0.96
	SD	1.9	1.4	0.9	0.0	1.2	0.8	0.066
	n	10	10	10	10	10	10	10
3F	Mean	61	30	12	3	14	2	0.98
	SD	1.6	2.7	1.1	0.3	1.9	0.6	0.157
	n	10	10	10	10	10	10	10
4F	Mean	62	29	13	3	15	2	0.89
	SD	2.2	2.1	1.6	0.5	1.5	0.5	0.082
	n	10	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1M	Mean	127	36	70	3	2	4.34	51	5.99	1.64	0.76
	SD	21.0	5.9	5.7	1.9	0.6	0.704	9.2	0.752	0.421	0.541
	n	10	10	10	10	10	10	10	10	10	10
2M	Mean	132	38	70	3	2	4.11	51	5.87	1.67	0.85
	SD	26.3	11.4	8.7	0.8	0.6	0.358	4.6	0.760	0.365	0.347
	n	10	10	10	10	10	10	10	10	10	10
3M	Mean	128	36	71	4	2	4.49	53	5.71	1.65	0.81
	SD	24.0	6.4	5.4	1.1	0.6	0.283	5.4	0.724	0.320	0.269
	n	9	9	9	9	9	9	9	9	9	9
4M	Mean	123	37	75	4	2	4.67	54	6.78	1.77	1.07
	SD	24.1	5.2	6.8	1.0	0.8	0.812	6.9	1.306	0.318	0.603
	n	10	10	10	10	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1M	Mean	144	4.3	101	2.77	2.35
	SD	0.8	0.24	0.9	0.042	0.109
	n	10	10	10	10	10
2M	Mean	142 a	5.0 B	101	2.76	2.34
	SD	1.0	0.40	1.0	0.060	0.149
	n	10	10	10	10	10
3M	Mean	142 a	5.1 B	101	2.73	2.31
	SD	1.1	0.96	1.1	0.040	0.083
	n	9	9	9	9	9
4M	Mean	142 a	4.9 B	101	2.75	2.38
	SD	1.3	0.31	0.9	0.062	0.115
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$
Significant when compared with Group 1: A - $p<0.05$; B - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1M	Mean	66	31	17	3	14	2	0.86
	SD	2.5	2.2	0.7	0.5	1.9	1.2	0.129
	n	10	10	10	10	10	10	10
2M	Mean	67	29	16	3	16 a	3	0.78
	SD	2.9	0.9	1.9	0.4	1.4	1.7	0.071
	n	10	10	10	10	10	10	10
3M	Mean	66	29 a	16	3	16 b	3	0.78
	SD	2.6	0.8	1.0	0.5	1.0	0.9	0.058
	n	9	9	9	9	9	9	9
4M	Mean	67	29 a	16	3	17 b	2	0.78
	SD	2.2	1.2	0.9	0.5	1.4	1.3	0.089
	n	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1F	Mean	65	38	70	3	2	5.79	54	6.06	2.13	0.49
	SD	11.1	11.1	3.9	0.8	0.8	0.683	4.0	0.657	0.295	0.092
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	76	35	72	3	2	5.70	53	5.99	2.02	0.45
	SD	20.1	8.5	7.2	0.8	0.5	0.592	4.1	0.956	0.357	0.087
	n	10	10	10	10	10	10	10	10	10	10
3F	Mean	73	31	73	3	2	6.22	57	5.76	1.93	0.46
	SD	15.2	5.9	7.6	0.7	0.7	1.008	5.8	0.555	0.283	0.081
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	65	30 a	69	3	1 b	6.58 a	59	6.56	1.95	0.45
	SD	6.9	5.1	5.3	1.3	0.5	0.905	7.9	0.684	0.317	0.083
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1F	Mean	143	4.0	102	2.79	1.94
	SD	1.1	0.28	1.7	0.120	0.136
	n	10	10	10	10	10
2F	Mean	141 a	4.4 b	100	2.80	1.95
	SD	1.0	0.34	1.5	0.063	0.220
	n	10	10	10	10	10
3F	Mean	142 a	4.3 b	101	2.78	1.95
	SD	1.1	0.28	1.5	0.038	0.234
	n	10	10	10	10	10
4F	Mean	142 a	4.5 b	101	2.75	2.00
	SD	0.9	0.16	1.3	0.052	0.182
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD ----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1F	Mean	70	35	14	3	16	3	1.00
	SD	4.1	2.2	1.7	0.3	1.4	1.0	0.093
	n	10	10	10	10	10	10	10
2F	Mean	71	34	14	3	16	3	0.94
	SD	3.2	2.2	1.4	0.7	0.7	0.6	0.075
	n	10	10	10	10	10	10	10
3F	Mean	71	35	14	3	15	3	1.00
	SD	3.1	2.5	0.9	0.3	1.6	1.3	0.125
	n	10	10	10	10	10	10	10
4F	Mean	70	35	14	3	16	3	1.00
	SD	3.0	2.0	1.7	1.2	1.9	1.4	0.100
	n	10	10	10	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1M	Mean	88	36	73	1	2	4.74	53	7.91	1.90	1.17
	SD	10.7	8.5	11.1	1.3	0.6	0.646	6.1	1.565	0.518	0.752
	n	10	10	10	10	10	10	10	10	10	10
2M	Mean	89	42	77	3 a	2	5.15	58	7.54	1.89	1.06
	SD	16.1	17.3	25.6	1.0	0.3	0.357	3.4	0.509	0.433	0.375
	n	10	10	10	10	10	10	10	10	10	10
3M	Mean	91	38	73	3 a	2	5.69 b	60	7.61	1.90	1.04
	SD	14.2	7.9	10.6	1.7	0.6	0.674	7.3	0.513	0.383	0.431
	n	10	10	10	10	10	10	10	10	10	10
4M	Mean	82	37	76	5 b	2	6.07 b	69 b	9.43 A	2.02	1.01
	SD	17.7	5.4	7.7	1.5	0.7	0.760	9.6	1.160	0.247	0.428
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$
Significant when compared with Group 1: A - <0.05; B - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1M	Mean	143	4.8	100	2.88	2.24
	SD	1.1	0.51	0.9	0.051	0.120
	n	10	10	10	10	10
2M	Mean	142	5.3 a	101	2.81 a	2.26
	SD	1.1	0.30	1.2	0.066	0.119
	n	10	10	10	10	10
3M	Mean	143	5.3 a	102	2.76 b	2.25
	SD	1.5	0.99	1.1	0.076	0.170
	n	10	10	10	10	10
4M	Mean	142 a	5.8 b	101	2.76 b	2.32
	SD	0.8	0.49	1.3	0.057	0.164
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1M	Mean	71	33	16	3	16	2	0.89
	SD	2.7	1.7	1.5	0.5	1.0	1.3	0.084
	n	10	10	10	10	10	10	10
2M	Mean	69	32 b	14	3	17	3	0.83
	SD	3.3	1.2	1.1	0.6	1.8	1.0	0.054
	n	10	10	10	10	10	10	10
3M	Mean	69	31 b	16	3	17	3	0.82 a
	SD	3.2	0.9	1.3	0.6	1.2	1.4	0.056
	n	10	10	10	10	10	10	10
4M	Mean	69	31 b	16	3	17	3	0.81 a
	SD	1.8	1.3	1.1	0.6	0.8	0.8	0.077
	n	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		ALP u/L	ALT u/L	AST u/L	gGT u/L	Bili µmol/L	Urea mmol/L	Creat µmol/L	Gluc mmol/L	Chol mmol/L	Trig mmol/L
1F	Mean	42	39	73	2	3	6.25	59	7.80	2.36	0.70
	SD	9.3	13.1	8.2	0.5	0.5	0.626	2.5	0.856	0.438	0.173
	n	10	10	10	10	10	10	10	10	10	10
2F	Mean	46	38	76	2	2	6.78	60	7.46	2.28	0.61
	SD	15.3	26.6	20.1	1.6	0.6	0.889	4.2	0.763	0.586	0.142
	n	10	10	10	10	10	10	10	10	10	10
3F	Mean	42	31	72	1	2	6.30	61	7.42	2.27	0.68
	SD	9.1	10.0	9.5	0.5	0.6	0.460	3.8	0.404	0.334	0.255
	n	10	10	10	10	10	10	10	10	10	10
4F	Mean	41	27 a	69	2	2 a	7.20 b	71 b	7.73	2.11	0.70
	SD	6.6	4.7	9.8	0.9	0.8	0.858	8.2	0.786	0.246	0.212
	n	10	10	10	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L	Phos mmol/L
1F	Mean	142	4.5	101	2.92	1.89
	SD	1.5	0.39	1.3	0.117	0.281
	n	10	10	10	10	10
2F	Mean	141 a	4.7	102	2.83 a	1.57 a
	SD	1.4	0.98	1.5	0.081	0.262
	n	10	10	10	10	10
3F	Mean	141 a	4.5	102	2.81 a	1.69 a
	SD	0.6	0.34	0.8	0.059	0.253
	n	10	10	10	10	10
4F	Mean	141 a	4.7	103	2.80 b	1.72 a
	SD	0.9	0.36	1.5	0.082	0.136
	n	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 7 - continued

Blood chemistry - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Total Prot g/L	Alb g/L	a1 g/L	a2 g/L	Beta g/L	Gamma g/L	A/G Ratio
1F	Mean	73	37	12	4	17	4	1.05
	SD	5.3	4.5	1.6	0.5	1.1	0.7	0.141
	n	10	10	10	10	10	10	10
2F	Mean	74	35	13	4	18	4	0.91
	SD	4.5	3.2	2.7	1.1	1.2	1.3	0.125
	n	10	10	10	10	10	10	10
3F	Mean	72	34	12	4	18	4	0.89
	SD	3.9	2.6	1.6	0.5	1.3	1.0	0.092
	n	10	10	10	10	10	10	10
4F	Mean	72	36	12	3 a	17	4	1.04
	SD	2.8	2.8	1.1	0.6	2.0	1.2	0.152
	n	10	10	10	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 8

Urinalysis - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1M	Mean	6.4	7.0	1032	0.59
	SD	2.37	0.44	11.3	0.204
	n	10	10	10	10
2M	Mean	6.4	7.1	1029	0.64
	SD	1.59	0.32	6.0	0.198
	n	10	10	10	10
3M	Mean	6.3	7.0	1031	0.69
	SD	3.05	0.31	7.9	0.219
	n	10	10	10	10
4M	Mean	6.9	6.6 b	1027	0.68
	SD	1.76	0.23	2.6	0.189
	n	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 8 - continued

Urinalysis - group mean values during Week 2 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1F	Mean	3.8	6.4	1039	0.07
	SD	1.86	0.36	14.1	0.036
	n	10	10	10	10
2F	Mean	4.0	6.2	1036	0.12
	SD	1.50	0.41	8.6	0.076
	n	10	10	10	10
3F	Mean	5.1	6.5	1032	0.10
	SD	2.41	0.35	9.1	0.043
	n	10	10	10	10
4F	Mean	3.2	6.2	1035	0.11
	SD	1.52	0.30	5.9	0.051
	n	10	10	10	10

$p \geq 0.05$, no statistical significance

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TABLE 8 - continued

Urinalysis - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	---------- ABM-FD	----------	
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1M	Mean	8.6	6.6	1030	0.72
	SD	3.43	0.43	6.6	0.222
	n	10	10	10	10
2M	Mean	8.4	6.8	1027	0.72
	SD	1.70	0.39	2.8	0.184
	n	10	10	10	10
3M	Mean	8.2	6.9	1025 a	0.68
	SD	1.95	0.19	3.3	0.136
	n	10	10	10	10
4M	Mean	10.3	6.7	1024 b	0.57
	SD	1.47	0.21	2.6	0.145
	n	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 8 - continued

Urinalysis - group mean values during Week 7 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------	ABM-FD	----------
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1F	Mean	5.8	6.7	1027	0.08
	SD	1.54	0.36	3.8	0.037
	n	10	10	10	10
2F	Mean	6.1	6.4	1030	0.11
	SD	2.93	0.28	6.6	0.061
	n	10	10	10	10
3F	Mean	5.7	6.5	1029	0.08
	SD	1.86	0.18	4.9	0.040
	n	10	10	10	10
4F	Mean	6.0	6.3 b	1029	0.07
	SD	2.32	0.21	6.1	0.024
	n	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 8 - continued

Urinalysis - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1M	Mean	8.9	6.9	1030	0.76
	SD	3.05	0.23	6.5	0.295
	n	10	10	10	10
2M	Mean	8.3	7.0	1028	0.72
	SD	1.47	0.30	2.1	0.136
	n	10	10	10	10
3M	Mean	9.3	7.3 b	1026	0.65
	SD	2.62	0.34	2.6	0.178
	n	10	10	10	10
4M	Mean	11.1	6.8	1026	0.61
	SD	1.67	0.17	3.9	0.089
	n	10	10	10	10

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

IKI 001/052114

TABLE 8 - continued

Urinalysis - group means during Week 13 of treatment

Group	:	1	2	3	4
Compound	:	Control	----------ABM-FD----------		
Dosage (mg/kg/day)	:	0	500	1000	2000

Group / sex		Vol ml	pH	SG g/L	Prot g/L
1F	Mean	4.7	6.7	1032	0.04
	SD	1.61	0.56	7.0	0.029
	n	10	10	10	10
2F	Mean	6.0	6.5	1030	0.08
	SD	1.77	0.29	4.1	0.033
	n	10	10	10	10
3F	Mean	5.5	6.5	1029	0.06
	SD	2.03	0.27	4.5	0.024
	n	10	10	10	10
4F	Mean	5.5	6.3	1031	0.16
	SD	2.16	0.25	5.9	0.366
	n	10	10	10	10

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 9

Print No: 0016

Organ weights - group mean absolute values (g) for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
TERMINAL BODY WEIGHT (g)								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	544.9	538.4	537.6	545.8	300.6	307.4	304.8	308.7
sd :	52.8	49.1	63.5	50.5	29.5	30.1	28.9	25.5
ADRENALS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.057	0.053	0.052	0.057	0.063	0.063	0.061	0.067
sd :	0.007	0.006	0.007	0.008	0.011	0.012	0.011	0.009
BRAIN								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	2.17	2.11	2.12	2.14	1.94	1.97	1.94	1.97
sd :	0.07	0.07	0.11	0.11	0.09	0.09	0.07	0.09
PITUITARY								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	19	20	20	18
MEAN :	0.013	0.012	0.012	0.013	0.013	0.015	0.014	0.014
sd :	0.002	0.002	0.002	0.002	0.003	0.004	0.003	0.004
EPIDIDYMIDES								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	1.314	1.342	1.308	1.318				
sd :	0.138	0.087	0.083	0.111				

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 9 - continued.

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Organ weights - group mean absolute values (g) for animals killed after 13 weeks of treatment

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Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
HEART								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	1.616	1.614	1.596	1.629	1.040	1.048	1.067	1.051
sd :	0.113	0.137	0.165	0.164	0.107	0.109	0.133	0.104
KIDNEYS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	3.54	3.36	3.45	3.74	1.95	2.00	1.97	2.05
sd :	0.30	0.33	0.40	0.47	0.19	0.22	0.20	0.17
LIVER								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	20.63	19.69	19.92	22.03	11.37	11.41	11.14	11.56
sd :	3.24	2.23	3.03	3.13	1.77	2.01	1.62	1.13
LN AXILLARY								
	BEHREN'S - FISHER'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0231	0.0290	0.0311a	0.0356	0.0213	0.0214	0.0195	0.0197
sd :	0.0094	0.0146	0.0136	0.0296	0.0100	0.0105	0.0078	0.0136
LN MESENTERIC								
	DUNNETT'S TEST				BEHREN'S - FISHER'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0108	0.0106	0.0110	0.0128	0.0117	0.0106	0.0105	0.0086
sd :	0.0058	0.0054	0.0067	0.0056	0.0079	0.0055	0.0048	0.0043

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 9 - continued.

Print No: 0016

Organ weights - group mean absolute values (g) for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------	ABM-FD	------
Dosage (mg/kg/day)	:	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
PROSTATE								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	0.718	0.723	0.686	0.702				
sd :	0.162	0.138	0.143	0.167				
SPLEEN								
	DUNNETT'S TEST				BEHREN'S - FISHER'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.844	0.857	0.839	0.792	0.601	0.647	0.570	0.534 a
sd :	0.147	0.155	0.109	0.141	0.092	0.453	0.129	0.086
TESTES								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	3.56	3.66	3.53	3.61				
sd :	0.39	0.24	0.24	0.24				
THYMUS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.292	0.281	0.229 a	0.273	0.253	0.269	0.245	0.273
sd :	0.083	0.081	0.057	0.049	0.077	0.084	0.091	0.058
THYROIDS+PARAS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.018	0.020	0.020	0.018	0.011	0.012	0.014 b	0.013 a
sd :	0.003	0.004	0.004	0.004	0.003	0.002	0.002	0.002

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

TABLE 9 - continued.

Print No: 0016

Organ weights - group mean absolute values (g) for animals killed after 13 weeks of treatment

Group :	1	2	3	4
Compound :	Control	------	ABM-FD	------
Dosage (mg/kg/day) :	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
UTERUS & CERVIX								
					DUNNETT'S TEST			
N :					20	20	20	18
MEAN :					0.737	0.700	0.846	0.772
sd :					0.314	0.258	0.386	0.337
OVARIES+OVIDUCTS								
					DUNNETT'S TEST			
N :					20	20	20	18
MEAN :					0.116	0.116	0.116	0.121
sd :					0.020	0.015	0.016	0.018

p≥0.05, no statistical significance

IKI 001/052114

TABLE 9 - continued

Print No: 0015

Organ weights - group mean bodyweight relative values (%) for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
TERMINAL BODY WEIGHT (g)								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	544.9	538.4	537.6	545.8	300.6	307.4	304.8	308.7
sd :	52.8	49.1	63.5	50.5	29.5	30.1	28.9	25.5
ADRENALS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0105	0.0099	0.0098	0.0105	0.0212	0.0208	0.0200	0.0218
sd :	0.0013	0.0014	0.0015	0.0018	0.0040	0.0043	0.0027	0.0028
BRAIN								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.401	0.394	0.399	0.395	0.651	0.646	0.639	0.640
sd :	0.036	0.033	0.036	0.031	0.061	0.054	0.049	0.043
PITUITARY								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	19	20	20	18
MEAN :	0.0023	0.0023	0.0023	0.0023	0.0045	0.0049	0.0045	0.0044
sd :	0.0004	0.0003	0.0003	0.0003	0.0009	0.0012	0.0009	0.0011
EPIDIDYMIDES								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	0.2423	0.2511	0.2466	0.2431				
sd :	0.0272	0.0263	0.0334	0.0273				

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 9 - continued

Print No: 0015

Organ weights - group mean bodyweight relative values (%) for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
HEART								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.2983	0.3009	0.2982	0.2985	0.3467	0.3422	0.3512	0.3408
sd :	0.0268	0.0235	0.0247	0.0153	0.0267	0.0317	0.0424	0.0251
KIDNEYS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.652	0.624	0.644	0.686	0.652	0.653	0.649	0.665
sd :	0.058	0.037	0.047	0.054	0.044	0.066	0.059	0.043
LIVER								
	BEHREN'S - FISHER'S TEST				BEHREN'S - FISHER'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	3.787	3.654	3.701	4.038	3.774	3.711	3.650	3.749
sd :	0.489	0.188	0.285	0.441	0.345	0.568	0.365	0.261
LN AXILLARY								
	BEHREN'S - FISHER'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0043	0.0053	0.0057a	0.0066	0.0071	0.0070	0.0064	0.0063
sd :	0.0018	0.0026	0.0024	0.0058	0.0034	0.0034	0.0023	0.0042
LN MESENTERIC								
	DUNNETT'S TEST				BEHREN'S - FISHER'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0020	0.0020	0.0021	0.0024	0.0039	0.0035	0.0034	0.0028
sd :	0.0011	0.0009	0.0012	0.0010	0.0026	0.0019	0.0017	0.0013

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 9 - continued

Print No: 0015

Organ weights - group mean bodyweight relative values (%) for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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Protocol Number: IKI 001

SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
PROSTATE								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	0.1328	0.1345	0.1298	0.1281				
sd :	0.0315	0.0235	0.0343	0.0273				
SPLEEN								
	DUNNETT'S TEST				BEHREN'S - FISHER'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.1550	0.1589	0.1574	0.1455	0.2000	0.2119	0.1862	0.1721b
sd :	0.0238	0.0228	0.0222	0.0248	0.0233	0.1533	0.0331	0.0170
TESTES								
	DUNNETT'S TEST							
N :	19	20	20	20				
MEAN :	0.656	0.684	0.665	0.668				
sd :	0.072	0.075	0.081	0.077				
THYMUS								
	DUNNETT'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0537	0.0520	0.0429a	0.0503	0.0838	0.0877	0.0796	0.0883
sd :	0.0152	0.0132	0.0107	0.0093	0.0235	0.0251	0.0228	0.0171
THYROIDS+PARAS								
	BEHREN'S - FISHER'S TEST				DUNNETT'S TEST			
N :	19	20	20	20	20	20	20	18
MEAN :	0.0033	0.0037	0.0036	0.0033	0.0038	0.0040	0.0045a	0.0043
sd :	0.0005	0.0009	0.0005	0.0007	0.0010	0.0009	0.0006	0.0007

Significant when compared with Group 1: a - $p<0.05$; b - $p<0.01$

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TABLE 9 - continued

Print No: 0015

Organ weights - group mean bodyweight relative values (%) for animals killed after 13 weeks of treatment

Group :	1	2	3	4
Compound :	Control	------	ABM-FD	------
Dosage (mg/kg/day) :	0	500	1000	2000

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SEX:	MALE				FEMALE			
GROUP:	1	2	3	4	1	2	3	4
NUMBER:	19	20	20	20	20	20	20	18
UTERUS & CERVIX								
					DUNNETT'S TEST			
N :					20	20	20	18
MEAN :					0.2511	0.2284	0.2776	0.2521
sd :					0.1216	0.0822	0.1219	0.1115
OVARIES+OVIDUCTS								
					DUNNETT'S TEST			
N :					20	20	20	18
MEAN :					0.0386	0.0378	0.0383	0.0393
sd :					0.0065	0.0045	0.0051	0.0050

$p \geq 0.05$, no statistical significance

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TABLE 10

Print No: 0006

Macropathology - group distribution of findings for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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	--- NUMBER-OF-ANIMALS-AFFECTED ---							
SEX:	-------MALE-------				------FEMALE------			
GROUP:	-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-
ORGAN AND KEYWORD(S) OR PHRASE / NUMBER:	19	20	20	20	20	20	20	18
** TOP OF LIST **								
ADRENALS ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
PALE AREA(S)	1	1	0	0	0	0	0	0
DARK	0	0	0	1	0	0	0	0
CAECUM ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
THICKENED	0	1	0	0	0	0	0	0
COLON ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
DISTENDED	0	1	0	0	0	0	0	0
DUODENUM ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
PALE AREA(S)	0	0	0	0	0	0	0	1
KIDNEYS ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
PELVIC DILATION	0	0	1	0	0	0	1	0
DEPRESSION(S)	0	0	0	0	0	0	1	1
DARK AREA(S)	0	0	0	0	0	0	0	1
LIVER ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
MASS(ES)	0	0	0	1	0	0	0	0
MISSHAPEN	0	0	0	1	0	0	0	0
LOBE(S) SMALL	0	0	0	1	0	0	0	0
LOBE(S) SWOLLEN	0	0	0	0	0	1	0	0
MEDIAN CLEFT PALE AREA(S)	0	0	0	0	0	0	1	0
LN AXILLARY ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
ENLARGED	0	0	0	1	0	0	0	0
REGIONAL TO MASS	0	0	0	0	0	0	0	1
LUNGS & BRONCHI ..... NUMBER EXAMINED:	19	20	20	20	20	20	20	18
CONGESTED	0	0	3	1	0	0	2	2

$p \geq 0.05$, no statistical significance

IKI 001/052114

TABLE 10 - continued

Print No: 0006

Macropathology - group distribution of findings for animals killed after 13 weeks of treatment

Group	:	1	2	3	4
Compound	:	Control	------ ABM-FD ------		
Dosage (mg/kg/day)	:	0	500	1000	2000

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		--- NUMBER-OF-ANIMALS-AFFECTED ---							
	SEX:	-------MALE-------				------FEMALE------			
	GROUP:	-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	19	20	20	20	20	20	20	18
** FROM PREVIOUS PAGE **									
LUNGS & BRONCHI	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
MASS(ES)		1	0	0	0	2	0	0	0
DARK AREA(S)		0	1	0	0	0	0	0	0
INCOMPLETE COLLAPSE		0	0	2	0	0	0	0	0
PALE AREA(S)		0	0	0	0	0	1	0	1
SEMINAL VESICLES	NUMBER EXAMINED:	19	20	20	20				
SMALL		0	1	0	0				
SPLEEN	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
MISSHAPEN		0	1	0	0	0	0	0	0
ENLARGED		0	0	0	0	0	1	0	0
SWOLLEN		0	0	0	0	0	1	0	0
PALE AREA(S)		0	0	0	0	0	1	0	0
STOMACH	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
ANTRUM WHITE NODULE(S)		0	0	0	0	2	1	1	1
PALE AREA(S)		0	0	0	0	1	0	0	0
DEPRESSION(S)		0	0	0	0	0	1	0	0
THYMUS	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
DARK		0	0	1	1	0	0	0	0
DARK AREA(S)		5	4	4	14 a	1	0	2	1
THYROIDS	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
UNILATERALLY SMALL		1	1	1	0	0	0	0	0
SMALL		0	0	0	1	1	0	0	0
TRACHEA	NUMBER EXAMINED:	19	20	20	20	20	20	20	18
ABNORMAL CONTENTS		0	0	0	0	0	0	1	0

Significant when compared with Group 1: a - p<0.05; b - p<0.01

IKI 001/052114