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2-ペンチルアントラキノンの  
ラットを用いる28日間反復経口投与毒性試験  
(回復14日間)

厚生労働省医薬食品局審査管理課

化学物質安全対策室 委託

財団法人食品薬品

秦野研究



試験の表題： 2-ペンチルアントラキノンのラットを用いる 28 日間反復経口投与  
毒性試験（回復 14 日間）

試験委託者： 厚生労働省医薬食品局審査管理課化学物質安全対策室  
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試験施設： 財団法人食品薬品安全センター秦野研究所  
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[REDACTED] 2005年12月21日

試験の表題： 2-ペンチルアントラキノンのラットを用いる 28 日間反復経口投与  
毒性試験（回復 14 日間）

試験責任者：

試験担当主任者：

試験担当者（○試験主担当者）

投与・観察：

尿 検 査：

血液学検査：

血液生化学検査：

病理学検査：  
(採血を含む)

動物飼育管理：  
(検疫を含む)

検体調製：

被験物質管理：

化 学 分 析：

本試験は、OECD 化学物質試験法ガイドライン「[407]げっ歯類における 28 日間反復経口投与毒性試験」(1995 年 7 月 27 日採択)に準拠し、「化学物質 GLP」(平成 12 年 3 月 1 日改正、環保安第 41 号、生衛発第 268 号、平成 12・02・14 基局第 1 号)を遵守して実施したものである。

2005 年 12 月 21 日

試験責任者：

## 信頼性保証証明書

試験の表題： 2-ペンチルアントラキノンのラットを用いる 28 日間反復経口投与毒性試験  
(回復 14 日間)

試験計画番号： C-03-036

本試験に関する信頼性保証部門による査察および監査状況等は下記のとおりであった。

査察・監査項目	査察・監査年月日	運営管理者および試験責任者への報告年月日
試験計画書	2004年 3月16日	2004年 3月16日
試験計画書修正書 C-03-036～修①	2005年 4月 1日	2005年 4月 1日
動物の受入れおよび検疫	2004年 3月22日	2004年 3月22日
検体調製・含量試験	2004年 3月29日	2004年 3月29日
投与・一般状態の観察	2004年 3月30日	2004年 3月30日
体重測定・摂餌量(給餌量)測定	2004年 3月31日	2004年 3月31日
尿検査	2004年 4月21日	2004年 4月22日
詳細な症状観察・機能検査	2004年 4月22日	2004年 4月22日
採血・剖検・器官重量測定・血液学検査・ 血液生化学検査	2004年 4月27日	2004年 4月27日
病理学検査	2004年 6月17日	2004年 6月17日
報告書案(第一次)・生データ	2005年 3月16～22日	2005年 3月23日
報告書案(第二次)	2005年12月15日	2005年12月15日
最終報告書	2005年12月21日	2005年12月21日

本試験は、「新規化学物質に係る試験及び指定化学物質に係る有害性の調査の項目等を定める省令第4条に規定する試験施設について(化学物質GLP)」(平成12年3月1日改正、環保安第41号、生衛発第268号、平成12・02・14基局第1号)を遵守して実施され、また、この報告書は試験に使用された方法および手順を正確に記載し、記載された結果は試験の生データを正確に反映していることを証明する。

2005年12月21日

財団法人食品薬品安全センター  
秦野研究所 信頼性保証責任者  


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## 【要 約】

2-ペンチルアントラキノン (PAQ) の 28 日間反復経口投与毒性試験 (回復 14 日間) を雌雄の Sprague-Dawley 系ラットを用いて実施した。雌雄とも 3.75、15 および 60 mg/kg の用量の被験物質投与群ならびに媒体 (コーン油) を投与する対照群の計 4 群を設定し、28 日間の反復強制経口投与を行った。試験には雌雄とも各群 5 匹の他、対照群および 60 mg/kg 投与群には回復試験として各 5 匹を加え、計 60 匹の動物を使用した。

その結果、一般状態の変化として、投与直後の一過性の流涎が 60 mg/kg 投与群の雌雄で散見された。

投与期間終了時の血液学検査では、プロトロンビン時間の有意な延長が 15 および 60 mg/kg 投与群の雄で観察された。また、投与期間終了時の剖検では前胃粘膜の肥厚が 60 mg/kg 投与群の雄で認められ、同群の雄では、肝臓の実重量および相対重量が有意に増加し、組織学検査では軽微な小葉中心性の肝細胞肥大が観察された。

回復試験期間終了時では、投与期間終了時にみられた変化は観察されず、被験物質投与の影響は 14 日間の休薬により回復することが示唆された。

その他、体重、摂餌量、尿検査および血液生化学検査に被験物質投与の影響は認められなかった。また、詳細な症状観察および機能検査に異常は認められず、神経毒性を示唆する所見はみられなかった。

以上の結果から、本試験条件下における PAQ の無作用量は雄では 3.75 mg/kg/day、雌では 15 mg/kg/day であると考えられた。

### 【試験目的】

2-ペンチルアントラキノン（別名 2-アミルアントラキノン）は、アントラキノン類の1つで、光重合用増感剤、アントラキノン法過酸化水素製造用水素キャリアーなどに使用されている化学物質である。

今回、OECD既存化学物質安全性点検等に係る毒性調査の一環として、ラットを用いる28日間反復経口投与毒性試験を実施したのでその結果を報告する。なお、本試験は、OECD化学物質試験法ガイドライン「[407]げっ歯類における28日間反復経口投与毒性試験」（1995年7月27日採択）に準拠し、「化学物質GLP」（平成12年3月1日改正、環保安第41号、生衛発第268号、平成12・02・14基局第1号）、「動物の愛護および管理に関する法律」（平成11年12月22日改正、法律第221号）および「実験動物の飼養及び保管等に関する基準」（昭和55年3月27日、平成14年5月28日一部改正、総理府告示第6号）を遵守して実施した。

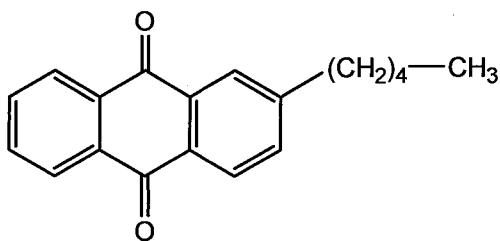
## 【試験方法】

### 1. 被験物質

2-ペンチルアントラキノン（英名 2-Pentylanthraquinone、略称 PAQ）は、別名 2-アミルアントラキノン、CAS No. 13936-21-5、分子量 278.35、分子式  $C_{19}H_{18}O_2$ 、沸点 227°C/667 Pa (5 mmHg)、密度 1.14 g/cm<sup>3</sup> (30°C、固体)、分配係数 Log Pow > 3.0 (オクタノール／水) の淡黄色固化固体である(構造式を下図に示す)。本試験には、山本化成株式会社のロット番号 01-13001-50、含量 98.6%、不純物としてアントラキノン 0.5%、他ピーク合計 (10 ピーク以上) 0.9% を含む PAQ を被験物質として使用した。受領した被験物質(被験入手日 2003 年 11 月 19 日)は、密閉容器に入れ冷所(冷蔵)で保管した(実測値 2~8°C)。

また、被験物質提供先である山本化成株式会社において、動物試験前後に本被験物質の品質試験を実施し (Appendix A)、試験期間中の被験物質の安定性を確認した。

<構造式>



### 2. 使用動物および飼育方法

4 週齢の Sprague-Dawley (SD) 系 [Crj:CD (SD) IGS, SPF] の雌雄ラット(日本チャールス・リバー、厚木飼育センター)を購入し、検疫と飼育環境への馴化を兼ねて、入荷日を含め 8 日間予備飼育した。検疫・馴化期間中は毎日の一般状態観察、1 回の詳細な症状観察ならびに入荷日および検疫終了日の体重測定を実施した。その結果、異常が認められた動物はいなかった。試験には雌雄各 30 匹を使用し、検疫終了時の体重をもとに、体重別に順位化し、体重のばらつきが可能な限り少なくなるように、順位の上位ないし下位の動物を棄却して、体重別層化無作為抽出法により群分けした。投与開始時の週齢は 5 週齢であった。入荷時および投与開始時の匹数および体重を以下に示した。

日付	匹数	体重範囲
動物入荷日 2004 年 3 月 22 日	雄 34 匹 雌 34 匹	85.4~96.2g (平均 90.4g) 70.9~84.2g (平均 78.6g)
投与開始日 2004 年 3 月 30 日	雄 30 匹 雌 30 匹	156.0~176.2g (平均 164.8g) 128.5~150.4g (平均 138.5g)

群分け後の棄却動物は、供試動物と同室で回復試験終了日まで飼育した。このうち、雄4例雌1例は微生物モニタリング用として感染症の疑いが生じた場合の血清検査用に採血した後剖検し、その他の動物は安樂死させた。なお、感染症を疑う事態が発生しなかったため、血清検査は行わなかった。

群分け後の個体識別は耳パンチにより動物番号を標識した。また、識別の補助として、群ごとに色彩の異なる動物カードに、試験計画番号、性別、群（投与量）および動物番号を記入し、飼育ケージに掛けた。なお、検疫・馴化期間中の個体識別は試験計画番号および仮動物番号を記載した動物カードを、飼育ケージに掛けて行った。

動物は、許容温度 21.0～25.0°C、許容湿度 40.0～75.0%、換気回数約 15 回/時間、照明 12 時間（7 時～19 時点灯）に制御された飼育室内で、金属製金網床ケージ（220w×270d×190h mm）に 1 匹ずつ収容し、固型飼料（CE-2、日本クレア）と水道水（秦野市水道局給水）を自由に摂取させて飼育した（ただし、解剖前 18～21 時間は絶食）。なお、飼育期間中の温度は 22.5～24.5°C、湿度は 47.0～61.5% であり、いずれも許容範囲内にあった。また、供給した飼料および水道水の分析結果からは、試験に支障を来す可能性のある混入物は検出されなかった。

### 3. 投与検体の調製

被験物質を秤量し、メスシリンダーを用いて媒体であるコーン油（英語表記 Corn oil、ロット番号 V2P1825、製造発売元 ナカライトスク）を加えて、1.2 w/v% 溶液を調製した。この 1.2 w/v% 溶液を段階希釈して 0.3 および 0.075 w/v% 溶液を作製した。調製後の投与検体はガラス瓶に分取し、冷蔵庫内（温度実測値 5～7°C）に保管した。また、投与に先立ち、0.05 および 5 w/v% の調製検体について安定性試験を実施した結果（Appendix B）、冷蔵条件下における 8 日間の安定性が確認されたため、投与検体の調製は投与前 8 日以内に行った。

また、初回調製時の投与検体について含量測定を実施した結果（Appendix C）、被験物質の平均含量は所定濃度の 92.8～98.5% であり、許容範囲内（90.0～110%）であることが確認された。

調製検体中の被験物質濃度の測定は、各調製検体の 0.5 mL を採取し、ヘキサンで一定量とした後、ヘキサンで適宜希釈して試料溶液を調製した。別に、被験物質を必要量秤取し、ヘキサンに溶解して標準溶液（1、2、5 µg/mL）を調製した。試料溶液および標準溶液を高

速液体クロマトグラフ (HPLC) 法により測定し、標準溶液から作成する検量線を用いて濃度を求めた。HPLC 条件を以下に示した。

分析カラム : Inertsil SIL-100A  
(内径 4.6 mm、長さ 250 mm、粒子径 5 µm、ジーエルサイエンス)  
移動相 : ヘキサン／酢酸エチル (19:1 v/v)  
流速 : 1.0 mL/min  
カラム温度 : 25°C  
検出波長 : 330 nm  
試料注入量 : 20 µL

#### 4. 投与量の設定および投与方法

投与用量は、本試験に先立って実施した予備試験（試験計画番号 C-03-035）の結果を基に決定した。即ち、PAQ を 62.5、250 および 1000 mg/kg 体重の用量で、雌雄各群 3 匹のラットに 7 日間反復投与した結果、1000 mg/kg 投与群では雌雄各 1 例が死亡し、体重減少、軟便、被毛の汚れ、皮膚蒼白、自発運動の低下、褐色尿等が認められた。また、同投与群の雌雄では血液学検査で赤血球数、血色素量およびヘマトクリット値の減少が認められ、剖検所見では肝臓および腎臓の大型化、前胃粘膜の肥厚、剥離および潰瘍が認められた。250 mg/kg 投与群では投与初期に軽度の体重増加抑制がみられ、62.5 および 250 mg/kg 投与群では肝臓、腎臓および脾臓の大型化、前胃粘膜の肥厚が観察され、低用量群でも被験物質投与の影響が認められた。以上の結果から、60 mg/kg の PAQ を 28 日間反復投与した場合でも被験物質投与の影響が認められると予想されたことから、60 mg/kg を本試験の高用量とし、以下公比 4 で除して、中用量および低用量をそれぞれ 15 および 3.75 mg/kg に設定した。

投与は 1 日 1 回の頻度で、28 日間、毎日 9~12 時の間に行い、ラット用胃管を用いて強制的に経口投与した。投与液量は各投与時の最近時の体重を基に個体別に算出した。対照群および高用量群の動物番号の若い方から雌雄各 5 匹は投与期間終了後、回復試験に用いた。

各群の投与量および動物番号を含めた設定を以下に示した。

群	投与物質	投与用量 (mg/kg)	濃度 (w/v%)	投与容量 (mL/kg)	動物番号		剖検時期
					雄	雌	
対照	コーン油	0	0	5	1~5	31~35	回復
					6~10	36~40	投与
低用量	PAQ	3.75	0.075	5	11~15	41~45	投与
中用量	PAQ	15	0.3	5	16~20	46~50	投与
高用量	PAQ	60	1.2	5	21~25	51~55	回復
					26~30	56~60	投与

回復：投与期間終了後、回復試験に用い、回復試験終了日翌日に定期解剖を行った。

投与：投与期間終了日翌日に定期解剖を行った。

なお、投与期間中の日数および週の表記は、投与開始日および投与開始週をそれぞれ投与第1日および投与第1週とし、回復試験期間中の日数および週の表記法もこれに準じて回復第1日および回復第1週とした。

## 5. 観察および検査

### 1) 一般状態の観察

毎日（投与期間中は投与前および投与後1回以上、回復試験期間中は1日1回）、全例について生死を含む一般状態を観察した。

### 2) 詳細な症状観察

検疫期間中に1回、投与期間および回復試験期間中は1週間に1回の頻度で、毎回13時～16時に全例の詳細な症状観察を、スコアリング法を用いて行った。まず、ケージ越しでの観察（姿勢・体位、自発運動、発声、振戦、痙攣）を行った後、動物をケージから取り出して外表を観察し（取り出し易さ、扱い易さ、心拍動、体温、被毛、皮膚色、可視粘膜、流涙、眼球突出、瞳孔径、流涎）、作業台上での観察（体位・姿勢、探索行動、身づくろい、発声、拳尾反応、歩行、常同行動、奇妙な行動、振戦、痙攣、呼吸数、立毛、眼裂、排尿回数、排便回数、接触に対する反応、撤去反応、耳介反射）を行った。投与量および動物番号の情報はブラインドにして実施した。

### 3) 機能検査

投与第4週および回復第2週の詳細な症状観察時に全例の検査を行った。機能検査は聴覚刺激に対する反応（驚愕反応）、視覚刺激に対する反応（視覚定位、瞳孔反射）、固有感覚刺激に対する反応（正向反射）を観察した。

### 4) 体重測定

投与第1週は投与第1、2および4日、第2週以降回復第2週までは毎週2回の頻度でそれぞれの週の第1日と第4日のいずれも投与前に全例の体重を測定した。また、投与期間終了日（投与第28日）、回復試験期間終了日（回復第14日）および剖検日にも体重を測定した。

### 5) 摂餌量測定

全例について、投与第1週では、投与第1日から2日にかけて1日あたりの摂餌量を測定し、以後回復第2週まで毎週1回の頻度で、それぞれの週の第1日から第2日にかけて1日あたりの摂餌量を測定した。

### 6) 尿検査

投与第4週（投与後）および回復第2週に全例を代謝ケージに収容し、採尿開始後4時間の時点で尿を採取して以下の項目について検査した。

項目	測定法	使用機器
色調・濁度	視診	
pH・潜血・蛋白・ブドウ糖・ケトン体・ウロビリノゲン・ ビリルビン	試験紙法	クリニテック 200+ (バイエル・三共)
沈渣	鏡検	光学顕微鏡

### 7) 採血

全例を、採血前（屠殺剖検前）に18～21時間絶食させた。その後、ペントバルビタールナトリウム麻酔下で、腹部後大静脈から以下の順序で採血した。採血は可能な限り対照群から低、中、高用量群の順に各群1匹ずつ、動物番号の若いほうから選抜して行った。

- ① 血液学検査用採血（抗凝固剤：クエン酸ナトリウム）
- ② 血液学検査用採血（抗凝固剤：EDTA-2K）
- ③ 血液生化学検査用採血（抗凝固剤：ヘパリン）

### 8) 血液学検査

全例について、上記7)採血の項②で採取した血液を用い、以下の項目について検査した。ただし、プロトロンビン時間および活性部分トロンボプラスチン時間は、7)項①で採取した血液から血漿を分離して測定に用いた。また、赤血球系の検査で被験物質投与の影響が疑われたことから、全例の網状赤血球比率を算出した。なお、白血球分類は、血液自動分析装置により自動的に行い、検査の補助として作製した静脈血塗抹標本(Wright-Giemsa染色)の観察は行わなかった。

項目	測定法	使用機器
赤血球数 (RBC)	電気抵抗法	血液自動分析装置 CELL-DYN3500 (ダ付ボット)
白血球数 (WBC)	フローサイトメトリー・ レーザー光散乱法/電気抵抗法	同上
白血球分類	フローサイトメトリー・ レーザー光散乱法	同上
血色素量 (Hb)	吸光度法	同上
平均赤血球容積 (MCV)	電気抵抗法	同上
血小板数	同上	同上
ヘマトクリット値 (Ht)	計算 (RBC × MCV × 0.001)	
平均赤血球血色素量 (MCH)	計算 (Hb × 1000/RBC)	
平均赤血球血色素濃度 (MCHC)	計算 (Hb × 100/Ht)	
網状赤血球比率	Brecher 法	光学顕微鏡
プロトロンビン時間 (PT)	光散乱検出法	全自動血液凝固測定装置 CA-1000 (東亜医用電子)
活性部分トロンボーフラスチン時間 (APTT)	同上	同上

## 9) 血液生化学検査

全例について、上記 7) 採血の項③で採取した血液から血漿を分離し、以下の項目について検査した。

項目	測定法	使用機器
総蛋白濃度	ピカレット法	生化学自動分析装置 COBAS MIRA plus (ロシュ・ダイアグノスティックス)
アルブミン濃度	BCG 法	同上
総コレステロール濃度	コレステロールキシダーゼ・HDAOS 法	同上
トリグリセライド濃度	GPO・HDAOS (グリセリン消去) 法	同上
ケルコース濃度	ヘキソキナーゼ・G-6-PDH 法	同上
尿素窒素濃度	ウレアーゼ・G1DH 法	同上
クレアチニン濃度	Jaffé 法	同上
総ビリルビン濃度	アゾビリルビン法	同上
アルカリ fosfターゼ (ALP) 活性	GSCC 法	同上
アスパラギン酸アミトランスフェラーゼ (AST (GOT)) 活性	IFCC 法	同上
アラニンアミトランスフェラーゼ (ALT (GPT)) 活性	同上	同上
γ-グルタミルトランスペプチダーゼ (γ-GTP) 活性	同上	同上
カルシウム濃度	OCPC 法	同上
無機リン濃度	モリブデン酸直接法	同上
A/G 比	計算	

項目	測定法	使用機器
ナトリウムイオン濃度	イオン電極法	全自動電解質分析装置 EA05 (エイアンドティー)
カリウムイオン濃度	同上	同上
塩素イオン濃度	同上	同上

#### 10) 病理学検査

全例について、7) 項の採血後、必要に応じて腋窩動脈を切断して放血屠殺し、器官および組織の肉眼的観察を実施した。また、各動物の肝臓、腎臓、副腎、精巣、精巣上体、卵巣、胸腺、脾臓、脳、心臓および甲状腺の重量（実重量）を測定したほか、各器官の重量を剖検日の体重で除して比体重値（相対重量）を算出した。

肉眼的観察に引き続き、全例の肉眼的病変部\*、脳\*、脊髄\*、胃\*、小腸（十二指腸、空腸、回腸\*）、大腸（結腸\*、直腸）、肝臓\*、腎臓\*、副腎\*、脾臓\*、心臓\*、胸腺\*、甲状腺\*、気管\*、肺\*（気管支\*を含む）、生殖腺（精巣\*、卵巣\*）、副生殖器（精巣上体\*、前立腺\*、子宮\*、精嚢、腫）、膀胱\*、リンパ節（腸間膜リンパ節\*、下頸リンパ節\*）、坐骨神経\*（腓腹筋\*を含む）、大腿骨および骨髓\*、大動脈、舌、食道、脾臓\*、顎下腺\*、舌下腺\*、下垂体\*、上皮小体および眼球\*を固定保存した。精巣および精巣上体はブアン液に固定し、その他の器官・組織の固定ならびに全ての器官・組織の長期保存には 0.1M リン酸緩衝 10% ホルマリン溶液を使用した。また、肺は、固定液を気管より注入して膨らませてから浸漬した。さらに、投与期間終了時の対照群および高用量群全例の\*印を付した器官・組織をパラフィン包埋して薄切り、ヘマトキシリソ・エオジン染色標本を作製した後、光学顕微鏡を用いて病理組織学的に検査した。この検査の結果、肝臓に被験物質投与に起因した可能性のある変化が認められたため、回復試験群を含む全例の肝臓の組織学的検査を実施した。

#### 6. データの解析

各検査値の解析は、以下の手順で行った。いずれの場合も有意水準は 5% とした。

##### 1) 定量的検査値

体重、摂餌量、血液学検査および血液生化学検査値ならびに器官重量の各測定値については、群ごとに平均値および標準偏差を求めた。次に試験群の構成により手法を選択し、対照群と被験物質投与群との間の平均値の差を検定した。

投与期間および投与期間終了時の各値（対照群を含めて 4 群）については、まず、Bartlett

の方法により分散の一様性について検定を行った。次いで、分散が一様であった場合には一元配置型の分散分析を行い、群間に有意性が認められた場合は、Dunnett 法により多重比較を行った。一方、分散が一様でなかった場合は Kruskal-Wallis の順位検定を行い、群間に有意性が認められた場合には、Dunnett 型の検定法で多重比較を行った。ただし、いずれかの群で分散が 0 となった場合には、Bartlett の検定は行わずに Kruskal-Wallis の順位検定を行い、同様に多重比較を行った。

回復試験期間および回復試験期間終了時の各値（対照群を含めて 2 群）については、F 検定を行い、等分散の場合は Student の t 検定、不等分散の場合には Aspin-Welch の t 検定を行った。ただし、どちらかの群で分散が 0 となった場合、t 検定は実施しなかった。

なお、15 mg/kg 投与群の雌 1 例（No. 46）では解剖当日に爪剥がれによる出血が認められ、血液学検査で貧血が認められたことから、同例のデータを血液学検査および血液生化学検査の検定対象から除外した。その結果、同群の例数が 1 例減ったものの統計解析は実施可能で、毒性評価の上で問題ないと判断した。

## 2) 半定量的検査成績

尿の試験紙による検査成績、尿の色調および濁度については、試験群の構成により手法を選択し、対照群と被験物質投与群との間のグレードの差を検定した。ただし、全群を通して分散が 0 となった項目は検定を実施しなかった。

投与第 4 週に得られた各検査値は、下表に示す列の累積または分割表を用いる  $\chi^2$  検定を行い（pH、雄の尿蛋白については実施せず）、有意性が認められた場合には、Dunnett 型の検定法により多重比較を行った。また、 $2 \times 2$  の分割表の場合、対照群および被験物質投与群、陰性（-）および陽性（±～++）で二分した。回復第 2 週に得られた各検査値は、下表に示す Wilcoxon の順位和検定を行った。

項 目	検 定 方 法			
	3 群以上あるとき		2 群間	
	$\chi^2$	順位化 Dunnett	Wilcoxon 順位和	
色調	分割表 $m \times n$	両側	両側	
濁度	列の累積	片側	片側	
試験紙				
pH	(実施せず)	両側	両側	
蛋白	雄 (実施せず)	両側	両側	
	雌 列の累積	片側	片側	
ブドウ糖	分割表 $2 \times 2$	片側	片側	
ケトン体	列の累積	片側	片側	

項 目	検 定 方 法		
	3 群以上あるとき		2 群間
	$\chi^2$	順位化 Dunnett	Wilcoxon 順位和
試験紙			
ビリルビン	分割表 2×2	片側	片側
潜血	分割表 2×2	片側	片側
ウロビリノーゲン	列の累積	片側	片側
沈渣	検定実施せず		

### 3) 病理組織所見

グレード分けしたデータは Mann-Whitney の U 検定により、また陽性グレードの合計値は Fisher の直接確率の片側検定により、対照群と各被験物質投与群との間の有意差検定を行った。

【予見することができなかつた試験の信頼性に影響を及ぼす疑いのある事態及び試験  
計画書に従わなかつたこと】

被験物質を保管していた冷蔵庫付属の自記記録温度計のチャート紙交換ミスにより、温度記録が行われなかつた時間が発生した（2004年1月16日11時から同日16時30分）。しかし、許容温度範囲（2~8°C）を外れた時点で鳴る設定にしていた警報が鳴らなかつたことから、この期間の温度は許容温度範囲であったことが確認された。従つて、本事態が試験に及ぼす影響はないと判断した。

その他、本試験期間中に、「予見することができなかつた試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかつたこと」はなかつた。

## 【試験結果】

### 1. 死亡例

死亡例および切迫屠殺例はいずれの群にもみられなかった。

### 2. 一般状態 (Table 1、Appendix 1)

投与期間中、60 mg/kg 投与群の雄 3 例、雌 4 例で、投与直後の一過性の流涎が投与第 3 週以降に散見された。その他、15 mg/kg 投与群の雌 1 例 (No. 46) では解剖当日に爪をケージ等に引っかけたためと思われる爪剥がれによる出血が認められた。

回復試験期間中には、いずれの群にも一般状態の変化は認められなかった。

### 3. 詳細な症状観察 (Table 2、Appendix 2)

投与期間中および回復試験期間中ともに、いずれの群にも特記すべき変化は認められず、神経毒性を示唆する所見は観察されなかった。

### 4. 機能検査 (Table 3、Appendix 3)

投与第 4 週および回復第 2 週の検査とともに、いずれの群においても異常は認められなかつた。

### 5. 体重 (Fig. 1、Table 4~5、Appendix 4~5)

投与期間中および回復試験期間中ともに、各被験物質投与群の体重および体重増加量は対照群との間に差は認められなかった。

### 6. 摂餌量 (Fig. 2、Table 6、Appendix 6)

投与期間中および回復試験期間中ともに、各被験物質投与群の摂餌量は対照群との間に差は認められなかった。

### 7. 尿検査 (Table 7、Appendix 7)

投与第 4 週および回復第 2 週の検査とともに、いずれの群においても異常は認められず、対照群と各被験物質投与群との間に差は認められなかった。

## 8. 血液学検査(Table 8、Appendix 8、Appendix D)

投与期間終了時の検査では、プロトロンビン時間の有意な延長が 15 および 60 mg/kg 投与群の雄でみられた。また、60 mg/kg 投与群の雄では赤血球数が低い傾向がみられた。その他、好中球比率の減少およびリンパ球比率の増加が 15 mg/kg 投与群の雄で、単球比率の増加が 15 mg/kg 投与群の雌でそれぞれ有意に認められた。白血球百分比を絶対数に換算して比較すると (Appendix D)、各被験物質投与群の各白血球数は対照群との間に差は認められなかつたことから、白血球百分比の変化は被験物質投与による影響ではないと判断した。

回復試験期間終了時の検査では、赤血球数および血色素量の有意な減少が 60 mg/kg 投与群の雄でみられた。

## 9. 血液生化学検査(Table 9、Appendix 9)

投与期間終了時の検査では、アルカリリフォスファターゼ活性の有意な低下が 60 mg/kg 投与群の雄でみられた。また、総蛋白濃度の有意な減少が 15 mg/kg 投与群の雄で認められたが、アルブミン濃度や A/G 比に変化はみられず、60 mg/kg 投与群では有意差が認められなかつたことから、被験物質投与による影響ではないと判断した。

回復試験期間終了時の検査では、グルコース濃度の有意な減少が 60 mg/kg 投与群の雌で認められた。

## 10. 病理学検査

### 1) 器官重量 (Table 10～11、Appendix 10～11)

投与期間終了時剖検例では、肝臓の実重量および相対重量の有意な増加が 60 mg/kg 投与群の雄でみられた。また、甲状腺の実重量の有意な増加が 60 mg/kg 投与群の雄で、甲状腺の相対重量の有意な増加が 15 mg/kg 投与群の雄で認められた。

回復試験期間終了時剖検例では、精巣上体の実重量の有意な減少が 60 mg/kg 投与群の雄でみられたが、相対重量に変化は認められなかつたこと、投与期間終了時剖検例の精巣上体重量や組織学的变化はみられなかつたことから、被験物質投与による影響ではないと判断した。

### 2) 剖検所見 (Table 12、Appendix 12)

投与期間終了時剖検例において、前胃粘膜の肥厚が 60 mg/kg 投与群の雄 1 例で観察され

た。回復試験期間終了時剖検例では、肉眼的異常所見は認められなかった。

### 3) 組織学検査所見(Table 13, Appendix 13)

#### ① 投与期間終了時剖検例

肝臓では、軽微な小葉中心性の肝細胞肥大が 60 mg/kg 投与群の雄 4 例でみられ、この所見の発現頻度は対照群と比較して有意に高かった。また、軽微な単細胞壊死が 3.75 および 60 mg/kg 投与群の各雄 1 例で、軽微あるいは軽度の門脈周囲性の肝細胞脂肪化が対照群を含む雌雄の各群で認められたが、いずれの変化も対照群に比較して差はなかった。

腎臓では、軽微な好塩基性尿細管およびリンパ球浸潤が対照群および 60 mg/kg 投与群の雌雄で、軽微あるいは軽度の硝子滴が対照群および 60 mg/kg 投与群の雄で認められたが、いずれの変化も対照群に比較して差はなかった。

脾臓では、軽微から中等度の髓外造血が対照群および 60 mg/kg 投与群の雌雄全例で認められたが、対照群に比較して差はなかった。

前立腺では、軽度あるいは中等度のリンパ球浸潤が対照群および 60 mg/kg 投与群の各雄 1 例で認められたが、対照群に比較して差はなかった。

心臓では、軽微な心筋の変性／線維化が対照群の雄 1 例で観察された。

剖検で前胃粘膜の肥厚が観察された 60 mg/kg 投与群を含め、胃には組織学的異常所見は認められなかった。

病理組織学検査を実施したその他の器官には、組織学的異常所見は認められなかった。

#### ②回復試験期間終了時剖検例

肝臓では、軽微な門脈周囲性の肝細胞脂肪化が対照群および 60 mg/kg 投与群の雌雄で認められたが、対照群に比較して差はなかった。

## 【考 察】

2-ペンチルアントラキノン (PAQ) を 3.75、15 および 60 mg/kg の用量で雌雄の Sprague-Dawley 系ラットに 28 日間反復経口投与し、その後 14 日間の回復試験を実施した。

その結果、高用量群の雄では、投与期間終了時に肝臓の実重量および相対重量が有意に増加し、組織学検査では軽微な小葉中心性の肝細胞肥大が認められた。本被験物質と同じアントラキノン類である 2-エチルアントラキノン<sup>1)</sup>やアントラキノン<sup>2)</sup>の 28 日間経口投与試験あるいは 1-アミノ-2,4-ジブロモアントラキノンの 13 週間混餌投与試験<sup>3)</sup>でも、肝臓に同様の変化が観察されていることから、本試験でみられた肝臓の変化は PAQ 投与の影響であると考えられた。

また、高用量群の雄 1 例では投与期間終了時に前胃粘膜の肥厚が観察された。予備試験でも PAQ 1000 mg/kg 投与群で前胃粘膜の肥厚、剥離および潰瘍がみられ、62.5 および 250 mg/kg 投与群でも前胃粘膜の肥厚が観察されたことから、PAQ が刺激性物質であり、前胃粘膜に軽度の傷害を生じたものと考えられた<sup>4)</sup>。また、高用量群の雌雄で投与期間中に散見された投与直後の一過性の流涎も、PAQ の刺激によって生じたと考えられた。

血液学検査では、投与期間終了時に 15 および 60 mg/kg 投与群の雄で用量依存的なプロトロンビン時間の延長がみられた。アントラキノン類である PAQ と p-ナフトキノンの誘導体であるビタミン K は同じキノン化合物であることから、肝臓でプロトロンビン生成や血液凝固因子形成促進の役割を果たしているビタミン K の作用に被験物質が影響を及ぼしている可能性は十分にある。よって、プロトロンビン時間の延長は被験物質投与による影響であると考えられた。また、高用量群の雄で、投与期間終了時に赤血球数の減少傾向が、回復試験期間終了時に赤血球数および血色素量の有意な減少がみられた。予備試験の血液学検査でも貧血所見がみられたほか、脾臓の大型化が認められた。また、前述したアントラキノン類<sup>1-3)</sup>のほか 1-アミノアントラキノンの反復経口投与毒性・生殖発生毒性併合試験<sup>5)</sup>でも貧血所見が認められており、溶血性貧血の可能性が示唆されている。一方、本試験では網状赤血球の増加や骨髄の造血亢進像、脾臓の髓外造血増強は認められておらず、尿検査および血液生化学検査でも溶血を示唆する所見はみられていない。また、出血所見もみられず血液生化学検査から血液希釈の可能性も考えられない。従って、赤血球数および血色素量の減少と PAQ 投与との関連も疑われたが、その原因を明らかにすることはできなかった。

その他、血液生化学検査では、アルカリフオスファターゼ活性の有意な低下が投与期間終了時に高用量群の雄でみられたが、用量依存的な変化ではなく、血中カルシウム濃度に変動はみられないことから、被験物質投与による影響ではないと判断した。また、回復試験期間終了時にグルコース濃度の有意な減少が高用量群の雌で認められたが、投与期間終了時ではグルコースに変動はみられず、胰臓、副腎および甲状腺に器質的変化は認められなかったことから、被験物質との関連はないと考えられた。さらに、投与期間終了時に甲状腺の実重量の有意な増加が 60 mg/kg 投与群の雄で、甲状腺の相対重量の有意な増加が 15 mg/kg 投与群の雄で認められたが、いずれも用量依存的な変化ではなく、甲状腺に組織学的な変化も認められなかった。また、これらの甲状腺重量の変化と背景データ (Appendix E) を比較すると大きな差は認められなかったことから、被験物質投与による影響ではないと判断した。

体重、摂餌量および尿検査に被験物質投与の影響は認められなかった。詳細な症状観察および機能検査でも異常は認められず、PAQ の神経毒性を示唆する所見は観察されなかった。

以上の結果から、PAQ 投与によりプロトロンビン時間の延長、肝重量の増加および肝細胞肥大が認められ、また、PAQ の刺激による流涎や前胃粘膜の肥厚が観察された。これらの変化は 14 日間の休薬により回復することが示唆された。従って、本試験条件下における PAQ の無作用量は雄では 3.75 mg/kg/day、雌では 15 mg/kg/day であると考えられた。

## 【参考文献】

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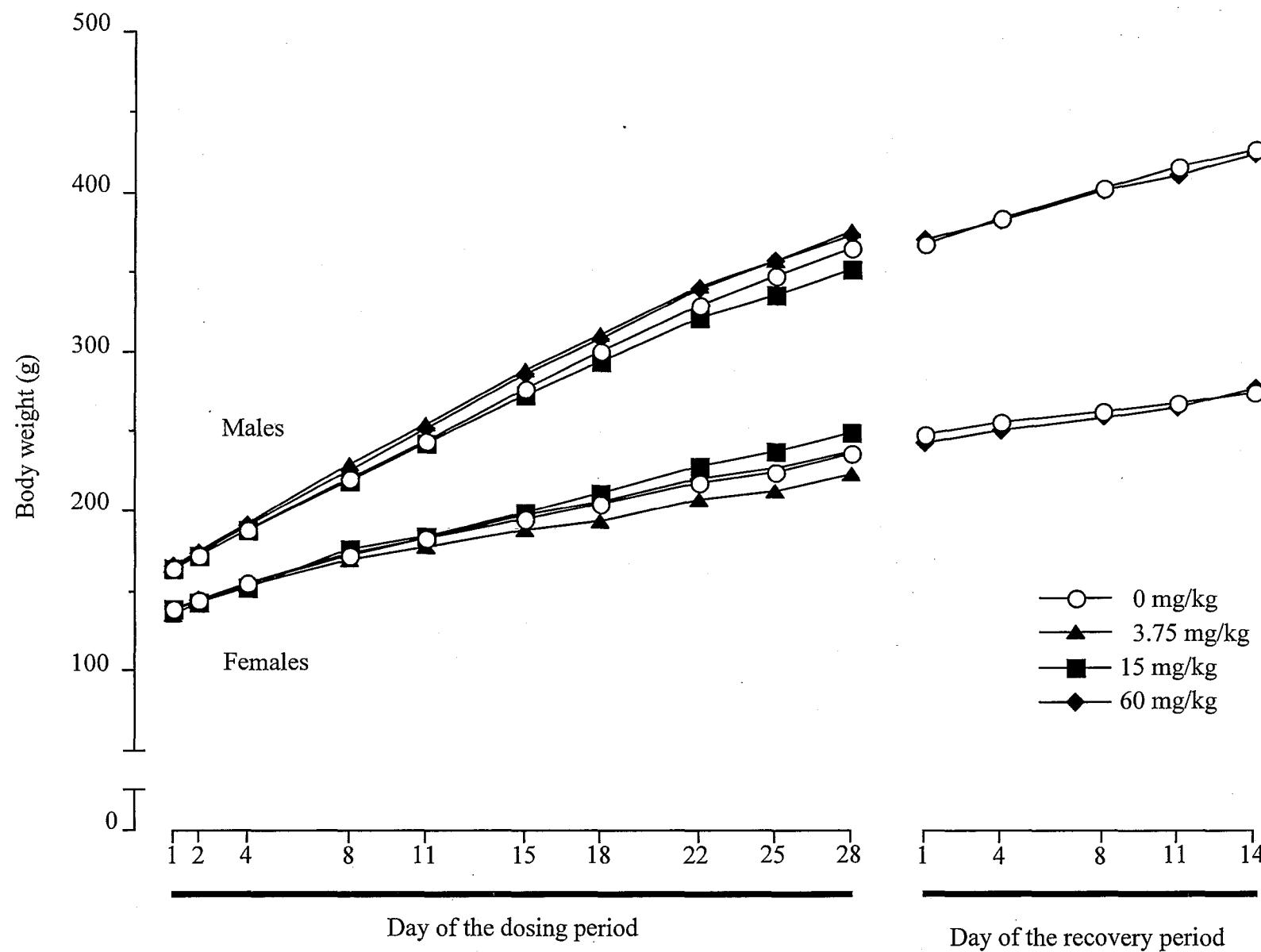


Fig. 1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Body weight changes in males and females

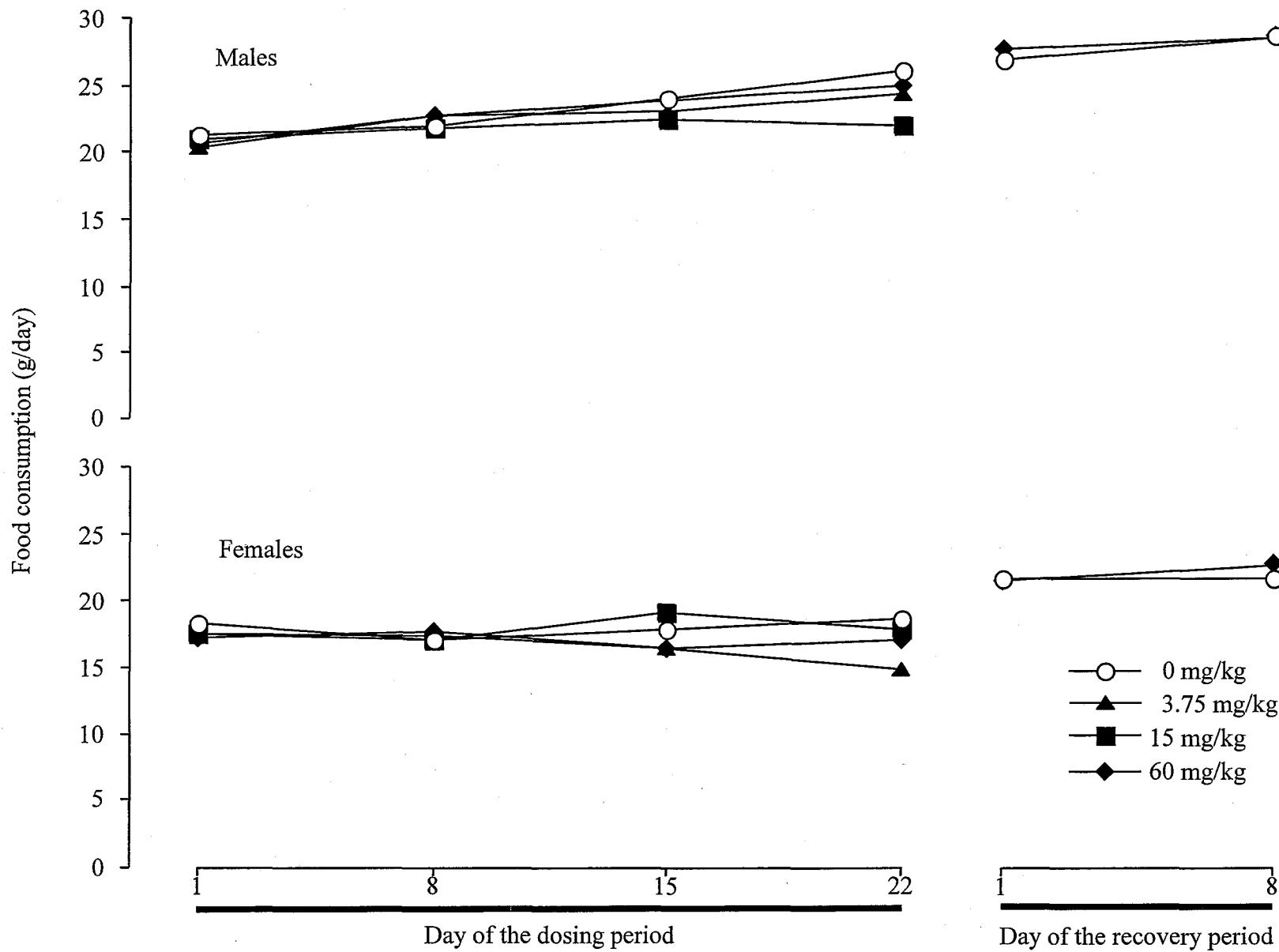


Fig. 2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Food consumption in males and females

Table 1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Clinical signs in males

Dose (mg/kg)	Clinical signs	Day of the dosing period																											Day of the recovery		Total			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14			
	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	10		
0	No abnormality in general condition																																	
	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
3.75	No abnormality in general condition																																	5
	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
15	No abnormality in general condition																																	5
	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	10	
60	Salivation immediately after administration	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	1	0	0	0	1	1	1

## Clinical signs in females

Dose (mg/kg)	Clinical signs	Day of the dosing period																											Day of the recovery		Total			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14			
	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	10		
0	No abnormality in general condition																																	
	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
3.75	No abnormality in general condition																																	5
	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
15	No abnormality in general condition																																	5
	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	10	
60	Salivation immediately after administration	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Parameter, number of animals with clinical signs

Table 2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Detailed clinical observations in males

Observations	Score /code	Dose Period	0 mg/kg					3.75 mg/kg				15 mg/kg				60 mg/kg										
			Pre. <sup>a</sup>	D1 <sup>b</sup>	D2	D3	D4	R1 <sup>c</sup>	R2	Pre.	D1	D2	D3	D4	Pre.	D1	D2	D3	D4	Pre.	D1	D2	D3	D4	R1	R2
Number of animals examined			10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	10	10	10	10	5	5	
Home cage observations																										
Posture	O		10	10	8	10	10	5	5	4	5	3	5	5	5	5	3	5	4	10	9	10	10	10	5	5
	R		0	0	2	0	0	0	0	1	0	2	0	0	0	0	2	0	1	0	1	0	0	0	0	0
Locomotor	-		1	0	0	5	9	3	0	0	0	0	3	1	0	0	0	2	2	2	0	2	6	9	4	0
	4		9	10	10	5	1	2	5	5	5	5	2	4	5	5	5	3	3	8	10	8	4	1	1	5
Responses to handling																										
Behavior while removing from cage	0		0	8	10	9	10	4	5	0	5	4	5	5	0	4	5	5	5	1	9	10	10	10	5	5
	2		0	2	0	1	0	1	0	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0	0
	4		10	0	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	9	0	0	0	0	0	0
Handling behavior	0		1	8	10	9	9	5	5	1	4	4	4	5	0	4	5	4	5	4	9	9	9	10	5	5
	2		0	1	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
	4		9	1	0	1	0	0	0	4	0	1	1	0	5	0	0	1	0	6	0	1	1	0	0	0
Observed at the outside of home cage																										
Posture	O		10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	10	10	10	10	10	5	5
Urination (frequency/30sec.)	0		9	9	9	9	9	4	4	3	4	3	5	5	5	5	5	5	5	10	9	8	10	10	4	2
	1		1	1	1	0	1	1	1	2	1	2	0	0	0	0	0	0	0	0	1	2	0	0	1	2
	2		0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Defecation (frequency/30sec.)	0		9	9	9	9	10	5	5	3	3	4	4	5	5	4	5	5	5	10	10	10	10	10	5	5
	1		1	0	1	0	0	0	0	1	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	2		0	1	0	1	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

a, pre-treatment (the acclimatizing period)

Parameter, number of animals showed the signs

b, 1st week of the dosing period

c, 1st week of the recovery period

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

Table 2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Detailed clinical observations in females

Observations	Score /code	Dose Period	0 mg/kg					3.75 mg/kg				15 mg/kg				60 mg/kg											
			Pre. <sup>a</sup>	D1 <sup>b</sup>	D2	D3	D4	R1 <sup>c</sup>	R2	Pre.	D1	D2	D3	D4	Pre.	D1	D2	D3	D4	Pre.	D1	D2	D3	D4	R1	R2	
Number of animals examined			10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	10	10	10	10	5	5		
<b>Home cage observations</b>																											
Posture	O		10	10	9	8	7	5	4	4	5	3	4	3	5	5	3	4	5	9	10	9	9	10	5	5	
	R		0	0	1	2	3	0	1	1	0	2	1	2	0	0	2	1	0	1	0	1	1	0	0	0	
Locomotor	-		4	4	0	1	2	3	0	1	0	0	0	0	0	0	0	0	0	1	2	2	0	0	3	4	0
	4		6	6	10	9	8	2	5	4	5	5	5	5	5	5	5	5	4	8	8	10	10	7	1	5	
<b>Responses to handling</b>																											
Behavior while removing from cage	0		2	9	9	9	10	5	5	0	4	3	4	5	1	5	5	5	5	0	10	10	10	10	5	5	
	2		2	1	1	1	0	0	0	0	1	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4		6	0	0	0	0	0	0	5	0	0	0	0	4	0	0	0	0	0	10	0	0	0	0	0	
Handling behavior	0		2	6	10	9	10	5	4	0	2	4	5	4	1	4	4	5	5	0	8	9	10	10	4	4	
	2		0	1	0	1	0	0	1	0	0	1	0	1	0	0	1	0	0	1	1	1	0	0	0	1	
	4		8	3	0	0	0	0	0	5	3	0	0	0	4	1	0	0	0	9	1	0	0	0	1	0	
<b>Observed at the outside of home cage</b>																											
Posture	O		10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	10	10	10	10	10	5	5	
Urination (frequency/30sec.)	0		9	8	10	10	10	5	5	4	5	5	5	5	4	5	5	5	5	8	8	9	10	10	5	5	
	1		1	2	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	2	2	1	0	0	0	0	
	2		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Defecation (frequency/30sec.)	0		10	10	10	10	10	5	5	5	5	5	5	5	5	4	5	5	5	10	9	9	10	10	5	5	
	1		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	
	2		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	

a, pre-treatment (the acclimatizing period)

Parameter, number of animals showed the signs

b, 1st week of the dosing period

c, 1st week of the recovery period

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

Table 3

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Functional observations in males and females (sensory reactivity to stimuli)

	Score	Period	Sex		Male				Female			
			Dose (mg/kg)		0	3.75	15	60	0	3.75	15	60
			D4	R2	D4	D4	D4	R2	D4	R2	D4	D4
Number of animals examined			10	5	5	5	10	5	10	5	5	5
Auditory												
Startle response	4		10	5	5	5	10	5	10	5	5	5
Visual												
Visual placing	4		10	5	5	5	10	5	10	5	5	5
Pupillary reflex	4		10	5	5	5	10	5	10	5	5	5
Proprioceptive stimuli												
Righting reflex	4		10	5	5	5	10	5	10	5	5	5

a, 4th week of the dosing period

b, 2nd week of the recovery period

Parameter, number of animals showed the signs

Score 4, normal score

Table 4-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Body weight changes in males

Compound	2-Pentylanthraquinone										
	Dose (mg/kg)	0 <sup>a)</sup>			3.75			15			60
<b>Day of the dosing period</b>											
1	163.9 ± 4.4 (10)	165.8 ± 6.4 (5)	164.6 ± 6.7 (5)	165.4 ± 5.5 (10)							
2	172.2 ± 4.2 (10)	174.2 ± 5.8 (5)	172.0 ± 7.4 (5)	173.5 ± 6.1 (10)							
4	188.5 ± 4.5 (10)	192.2 ± 7.6 (5)	187.3 ± 8.6 (5)	190.6 ± 7.9 (10)							
8	220.0 ± 6.2 (10)	228.9 ± 10.3 (5)	218.5 ± 13.2 (5)	225.5 ± 9.0 (10)							
11	243.6 ± 6.9 (10)	254.1 ± 10.6 (5)	242.0 ± 13.4 (5)	250.8 ± 10.4 (10)							
15	276.9 ± 12.0 (10)	288.3 ± 12.4 (5)	272.1 ± 13.6 (5)	285.4 ± 13.2 (10)							
18	300.8 ± 15.8 (10)	310.4 ± 14.1 (5)	293.5 ± 15.6 (5)	307.9 ± 15.8 (10)							
22	329.4 ± 20.8 (10)	341.4 ± 16.4 (5)	320.9 ± 15.5 (5)	339.8 ± 17.7 (10)							
25	347.4 ± 24.1 (10)	357.0 ± 15.2 (5)	336.5 ± 16.9 (5)	357.0 ± 19.3 (10)							
28	365.3 ± 25.8 (10)	375.7 ± 21.7 (5)	352.6 ± 14.8 (5)	373.3 ± 20.6 (10)							
<b>Day of the recovery period</b>											
1	367.6 ± 23.4 (5)							371.1 ± 13.6 (5)			
4	383.6 ± 24.4 (5)							382.6 ± 14.6 (5)			
8	401.6 ± 22.7 (5)							400.7 ± 18.5 (5)			
11	414.9 ± 24.2 (5)							409.8 ± 19.0 (5)			
14	426.5 ± 25.7 (5)							423.9 ± 21.3 (5)			

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 4-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Body weight changes in females

Compound	2-Pentylanthraquinone									
	Dose (mg/kg)	0 <sup>a)</sup>	3.75	15	60					
<b>Day of the dosing period</b>										
1		138.7 ± 5.8 (10)	135.6 ± 7.1 (5)	138.6 ± 5.6 (5)	139.6 ± 7.8 (10)					
2		144.7 ± 5.7 (10)	142.4 ± 8.3 (5)	143.6 ± 4.7 (5)	144.5 ± 7.3 (10)					
4		155.3 ± 7.1 (10)	153.4 ± 10.6 (5)	152.7 ± 8.1 (5)	154.8 ± 8.0 (10)					
8		171.9 ± 7.9 (10)	168.9 ± 13.0 (5)	175.8 ± 13.1 (5)	172.8 ± 12.6 (10)					
11		182.1 ± 11.0 (10)	177.0 ± 15.9 (5)	183.9 ± 13.8 (5)	182.6 ± 13.8 (10)					
15		194.3 ± 13.5 (10)	187.5 ± 15.4 (5)	198.9 ± 18.0 (5)	196.9 ± 15.8 (10)					
18		204.1 ± 17.4 (10)	193.7 ± 19.5 (5)	210.3 ± 21.2 (5)	205.4 ± 16.1 (10)					
22		216.7 ± 19.8 (10)	206.4 ± 23.4 (5)	227.4 ± 26.4 (5)	220.3 ± 18.7 (10)					
25		224.1 ± 23.0 (10)	212.2 ± 21.4 (5)	236.3 ± 30.0 (5)	226.8 ± 19.4 (10)					
28		234.9 ± 25.6 (10)	221.7 ± 23.0 (5)	248.9 ± 31.1 (5)	236.5 ± 20.1 (10)					
<b>Day of the recovery period</b>										
1		247.1 ± 27.3 (5)				242.8 ± 22.1 (5)				
4		255.4 ± 29.0 (5)				249.5 ± 19.6 (5)				
8		262.3 ± 32.3 (5)				258.6 ± 21.5 (5)				
11		267.8 ± 30.4 (5)				264.8 ± 25.0 (5)				
14		274.3 ± 33.2 (5)				276.4 ± 24.7 (5)				

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 5-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in males

Compound	2-Pentylanthraquinone										
	Dose (mg/kg)	0 <sup>a)</sup>			3.75			15			60
<b>Day of the dosing period</b>											
1- 2	8.3 ± 1.6 (10)	8.4 ± 1.8 ( 5)	7.4 ± 1.6 ( 5)	8.1 ± 0.8 (10)							
2- 4	16.3 ± 2.4 (10)	18.0 ± 2.6 ( 5)	15.2 ± 1.8 ( 5)	17.2 ± 2.6 (10)							
4- 8	31.5 ± 4.5 (10)	36.7 ± 4.5 ( 5)	31.2 ± 5.1 ( 5)	34.9 ± 4.2 (10)							
8-11	23.6 ± 2.1 (10)	25.2 ± 2.0 ( 5)	23.5 ± 1.1 ( 5)	25.3 ± 2.6 (10)							
11-15	33.3 ± 6.3 (10)	34.2 ± 4.6 ( 5)	30.1 ± 4.0 ( 5)	34.7 ± 5.2 (10)							
15-18	23.9 ± 5.0 (10)	22.1 ± 3.9 ( 5)	21.4 ± 4.5 ( 5)	22.4 ± 4.0 (10)							
18-22	28.7 ± 5.9 (10)	31.0 ± 3.6 ( 5)	27.5 ± 4.2 ( 5)	32.0 ± 3.7 (10)							
22-25	18.0 ± 4.3 (10)	15.6 ± 2.3 ( 5)	15.5 ± 2.3 ( 5)	17.2 ± 3.3 (10)							
25-28	17.9 ± 4.2 (10)	18.8 ± 6.7 ( 5)	16.2 ± 3.3 ( 5)	16.3 ± 1.8 (10)							
<b>Day of the recovery period</b>											
1- 4	16.1 ± 4.0 ( 5)							11.5 ± 4.1 ( 5)			
4- 8	17.9 ± 7.2 ( 5)							18.1 ± 4.0 ( 5)			
8-11	13.4 ± 3.1 ( 5)							9.2 ± 3.9 ( 5)			
11-14	11.6 ± 4.3 ( 5)							14.1 ± 3.3 ( 5)			

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 5-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in females

Compound	2-Pentylanthraquinone									
	Dose (mg/kg)	0 <sup>a)</sup>	3.75	15	60					
<b>Day of the dosing period</b>										
1- 2	6.0 ± 2.3 (10)	6.7 ± 1.3 (5)	5.0 ± 1.1 (5)	4.9 ± 2.4 (10)						
2- 4	10.6 ± 2.1 (10)	11.0 ± 3.0 (5)	9.1 ± 4.3 (5)	10.3 ± 1.7 (10)						
4- 8	16.6 ± 3.9 (10)	15.5 ± 4.2 (5)	23.1 ± 6.0 (5)	18.0 ± 5.1 (10)						
8-11	10.2 ± 4.3 (10)	8.1 ± 5.4 (5)	8.1 ± 2.9 (5)	9.8 ± 4.6 (10)						
11-15	12.2 ± 3.2 (10)	10.5 ± 2.4 (5)	15.0 ± 4.6 (5)	14.3 ± 3.4 (10)						
15-18	9.9 ± 4.8 (10)	6.2 ± 5.2 (5)	11.3 ± 3.4 (5)	8.5 ± 6.6 (10)						
18-22	12.6 ± 3.4 (10)	12.7 ± 5.5 (5)	17.1 ± 5.3 (5)	15.0 ± 4.0 (10)						
22-25	7.4 ± 4.0 (10)	5.8 ± 3.7 (5)	9.0 ± 5.3 (5)	6.4 ± 3.6 (10)						
25-28	10.8 ± 4.7 (10)	9.5 ± 4.3 (5)	12.6 ± 5.3 (5)	9.8 ± 5.6 (10)						
<b>Day of the recovery period</b>										
1- 4	8.4 ± 4.4 (5)				6.7 ± 7.6 (5)					
4- 8	6.8 ± 4.4 (5)				9.1 ± 2.9 (5)					
8-11	5.6 ± 5.9 (5)				6.2 ± 5.1 (5)					
11-14	6.5 ± 4.0 (5)				11.6 ± 5.9 (5)					

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 6-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Food consumption in males

Compound	2-Pentylanthraquinone									
	Dose (mg/kg)	0 <sup>a)</sup>			3.75			15		
<b>Day of the dosing period</b>										
1- 2	21.4 ± 1.6 (10)	20.4 ± 1.8 ( 5)	21.0 ± 1.6 ( 5)	20.7 ± 2.0 (10)						
8- 9	22.0 ± 1.5 (10)	22.8 ± 2.2 ( 5)	21.8 ± 1.3 ( 5)	22.8 ± 1.3 (10)						
15-16	24.0 ± 2.4 (10)	23.1 ± 2.3 ( 5)	22.5 ± 2.6 ( 5)	23.8 ± 2.1 (10)						
22-23	26.0 ± 2.4 (10)	24.4 ± 4.1 ( 5)	21.9 ± 0.6 ( 5)	24.9 ± 3.0 (10)						
<b>Day of the recovery period</b>										
1- 2	26.8 ± 2.0 ( 5)							27.6 ± 2.1 ( 5)		
8- 9	28.6 ± 2.6 ( 5)							28.6 ± 1.2 ( 5)		

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 6-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Food consumption in females

Compound	2-Pentylanthraquinone											
	Dose (mg/kg)	0 <sup>a)</sup>	3.75			15			60			
<b>Day of the dosing period</b>												
1- 2	18.3	± 1.0	(10)	17.6	± 1.8	( 5)	17.6	± 0.9	( 5)	17.3	± 1.1	(10)
8- 9	17.0	± 2.4	(10)	17.4	± 1.9	( 5)	17.1	± 3.2	( 5)	17.7	± 1.3	(10)
15-16	17.9	± 2.3	(10)	16.4	± 2.0	( 5)	19.1	± 1.8	( 5)	16.5	± 1.9	(10)
22-23	18.6	± 3.2	(10)	14.8	± 1.1	( 5)	17.9	± 3.1	( 5)	17.0	± 2.1	(10)
<b>Day of the recovery period</b>												
1- 2	21.7	± 2.7	( 5)						21.5	± 1.1	( 5)	
8- 9	21.6	± 3.8	( 5)						22.8	± 1.5	( 5)	

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D. in grams

Parentheses indicate the number of animals

Table 7-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in males and females on day 23 of the dosing period

Sex Compound Dose (mg/kg)	Males				Females			
	2-Pentylanthraquinone				2-Pentylanthraquinone			
	0 <sup>a)</sup>	3.75	15	60	0 <sup>a)</sup>	3.75	15	60
Number of animals examined	10	5	5	10	10	5	5	10
Quality								
Color	ly	10	4	5	7	10	5	5
	y	0	1	0	3	0	0	2
Turbidity	-	10	5	5	10	10	5	10
pH	5.5	0	0	0	0	1	1	0
	6.0	0	0	0	0	0	0	2
	6.5	1	0	0	0	1	1	2
	7.0	2	1	4	4	4	2	1
	7.5	1	1	1	5	2	1	4
	8.0	2	0	0	0	1	0	1
	8.5	3	2	0	1	1	0	0
	≥9.0	1	1	0	0	0	0	1
Protein	-	0	0	0	0	4	1	0
	±	0	0	0	0	0	1	2
	+	4	3	2	4	6	2	1
	++	6	2	3	6	0	1	2
Glucose	-	10	5	5	10	10	5	5
Ketone	-	1	1	1	2	7	2	2
	±	5	3	1	5	3	3	4
	+	3	1	3	3	0	0	0
	++	1	0	0	0	0	0	0
Bilirubin	-	10	4	5	8	10	5	5
	+	0	1	0	2	0	0	3
Occult blood	-	10	5	5	10	10	5	5
Urobilinogen	±	5	4	3	6	5	2	2
	+	5	1	2	4	5	3	5
Microscopic examination of urinary sediment								
Red blood cells	-	10	5	5	10	10	5	5
Crystal	-	1	0	0	0	2	1	1
	±	9	5	5	10	8	4	4
Cast	-	10	5	5	10	10	5	5
White blood cells	-	10	5	5	10	10	5	5
Epithelial cells	-	10	5	5	10	10	5	10

a), vehicle control (corn oil, 5mL/kg)

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Table 7-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in males and females on day 11 of the recovery period

Sex Compound Dose (mg/kg)	Males		Females	
	0 <sup>a)</sup>	60	0 <sup>a)</sup>	60
Number of animals examined	5	5	5	5
Quality				
Color	ly	5	5	5
Turbidity	-	5	5	5
pH	6.5	0	0	1
	7.0	5	3	0
	7.5	0	1	2
	8.0	0	0	1
	8.5	0	1	0
Protein	-	0	0	5
	±	0	0	0
	+	3	3	0
	++	2	2	0
Glucose	-	5	5	5
Ketone	-	1	1	5
	±	0	2	0
	+	4	2	0
Bilirubin	-	5	5	5
Occult blood	-	5	5	5
Urobilinogen	±	3	1	5
	+	2	4	0
Microscopic examination of urinary sediment				
Red blood cells	-	5	5	5
Crystal	-	0	0	2
	±	5	5	3
Cast	-	5	5	5
White blood cells	-	5	5	5
Epithelial cells	-	4	4	5
	±	1	1	0

a), vehicle control (corn oil, 5mL/kg)

Color: ly, light yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Table 8-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Hematological findings in males and females at the end of the dosing period

Compound	2-Pentylanthraquinone				
	Dose (mg/kg)	0 <sup>a)</sup>	3.75	15	60
<b>Males</b>					
RBC ( $\times 10^4/\mu\text{L}$ )	729 ± 43 (5)	744 ± 40 (5)	710 ± 33 (5)	691 ± 33 (5)	
Hemoglobin (g/dL)	14.7 ± 0.7 (5)	15.1 ± 0.7 (5)	14.1 ± 0.5 (5)	14.1 ± 0.4 (5)	
Hematocrit (%)	44.0 ± 2.2 (5)	45.1 ± 1.9 (5)	42.2 ± 1.6 (5)	42.2 ± 1.3 (5)	
MCV (fL)	60.3 ± 1.5 (5)	60.6 ± 1.5 (5)	59.5 ± 2.1 (5)	61.0 ± 1.1 (5)	
MCH (pg)	20.2 ± 0.5 (5)	20.4 ± 0.4 (5)	19.9 ± 0.8 (5)	20.5 ± 0.5 (5)	
MCHC (g/dL)	33.4 ± 0.2 (5)	33.7 ± 0.4 (5)	33.4 ± 0.3 (5)	33.6 ± 0.3 (5)	
Reticulocyte (%)	1.8 ± 0.4 (5)	2.5 ± 0.7 (5)	2.3 ± 0.6 (5)	2.5 ± 0.8 (5)	
Platelet ( $\times 10^4/\mu\text{L}$ )	110.7 ± 11.4 (5)	109.5 ± 8.1 (5)	114.2 ± 9.4 (5)	117.3 ± 8.3 (5)	
PT (sec)	17.9 ± 3.7 (5)	20.3 ± 3.1 (5)	23.7 ± 2.5 * (5)	25.1 ± 3.6 ** (5)	
APTT (sec)	23.2 ± 2.6 (5)	25.1 ± 2.4 (5)	25.4 ± 2.0 (5)	26.3 ± 2.4 (5)	
WBC ( $\times 10^2/\mu\text{L}$ )	84.2 ± 18.6 (5)	86.0 ± 15.6 (5)	90.2 ± 22.0 (5)	82.9 ± 31.0 (5)	
Neutrophil (%)	16 ± 5 (5)	12 ± 4 (5)	9 ± 2 * (5)	15 ± 3 (5)	
Eosinophil (%)	1 ± 0 (5)	1 ± 0 (5)	1 ± 0 (5)	1 ± 0 (5)	
Basophil (%)	0 ± 0 (5)	0 ± 0 (5)	0 ± 0 (5)	0 ± 0 (5)	
Monocyte (%)	4 ± 3 (5)	4 ± 1 (5)	2 ± 0 (5)	3 ± 2 (5)	
Lymphocyte (%)	78 ± 4 (5)	84 ± 4 (5)	88 ± 2 ** (5)	81 ± 4 (5)	
<b>Females</b>					
RBC ( $\times 10^4/\mu\text{L}$ )	710 ± 21 (5)	700 ± 42 (5)	709 ± 18 (4)	694 ± 56 (5)	
Hemoglobin (g/dL)	14.2 ± 0.3 (5)	14.2 ± 0.6 (5)	14.3 ± 0.3 (4)	14.1 ± 0.8 (5)	
Hematocrit (%)	42.1 ± 1.0 (5)	41.9 ± 2.2 (5)	42.6 ± 1.0 (4)	42.0 ± 2.3 (5)	
MCV (fL)	59.2 ± 1.6 (5)	59.9 ± 2.0 (5)	60.0 ± 0.5 (4)	60.6 ± 2.0 (5)	
MCH (pg)	20.0 ± 0.5 (5)	20.2 ± 0.9 (5)	20.1 ± 0.1 (4)	20.3 ± 0.7 (5)	
MCHC (g/dL)	33.7 ± 0.1 (5)	33.8 ± 0.8 (5)	33.5 ± 0.2 (4)	33.5 ± 0.2 (5)	
Reticulocyte (%)	1.5 ± 0.5 (5)	1.4 ± 1.0 (5)	1.2 ± 0.4 (4)	1.4 ± 0.2 (5)	
Platelet ( $\times 10^4/\mu\text{L}$ )	111.8 ± 9.2 (5)	114.4 ± 10.1 (5)	113.3 ± 8.9 (4)	106.6 ± 12.7 (5)	
PT (sec)	12.6 ± 0.4 (5)	12.7 ± 1.6 (5)	12.3 ± 0.5 (4)	13.2 ± 1.0 (5)	
APTT (sec)	21.2 ± 2.5 (5)	21.3 ± 2.8 (5)	21.1 ± 0.6 (4)	24.1 ± 1.8 (5)	
WBC ( $\times 10^2/\mu\text{L}$ )	59.9 ± 27.9 (5)	61.2 ± 9.6 (5)	60.9 ± 21.2 (4)	64.0 ± 11.1 (5)	
Neutrophil (%)	11 ± 6 (5)	18 ± 12 (5)	24 ± 10 (4)	9 ± 3 (5)	
Eosinophil (%)	1 ± 0 (5)	1 ± 0 (5)	2 ± 1 (4)	1 ± 0 (5)	
Basophil (%)	0 ± 0 (5)	0 ± 0 (5)	0 ± 0 (4)	0 ± 0 (5)	
Monocyte (%)	3 ± 1 (5)	3 ± 1 (5)	6 ± 2 * (4)	2 ± 1 (5)	
Lymphocyte (%)	85 ± 6 (5)	77 ± 14 (5)	69 ± 10 (4)	88 ± 3 (5)	

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

Table 8-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Hematological findings in males and females at the end of the recovery period

Compound	2-Pentylanthraquinone				
	Dose (mg/kg)	0 <sup>a)</sup>	60		
<b>Males</b>					
RBC ( $\times 10^4/\mu\text{L}$ )	806 ± 12	(5)	765 ± 31*	(5)	
Hemoglobin (g/dL)	15.3 ± 0.3	(5)	14.6 ± 0.5*	(5)	
Hematocrit (%)	45.3 ± 0.9	(5)	43.7 ± 2.0	(5)	
MCV (fL)	56.2 ± 0.5	(5)	57.1 ± 2.4	(5)	
MCH (pg)	18.9 ± 0.3	(5)	19.0 ± 0.8	(5)	
MCHC (g/dL)	33.6 ± 0.6	(5)	33.3 ± 0.3	(5)	
Reticulocyte (%)	2.8 ± 0.6	(5)	3.3 ± 1.2	(5)	
Platelet ( $\times 10^4/\mu\text{L}$ )	120.8 ± 10.3	(5)	105.3 ± 16.0	(5)	
PT (sec)	23.4 ± 11.6	(5)	22.8 ± 6.0	(5)	
APTT (sec)	24.8 ± 3.9	(5)	25.1 ± 1.4	(5)	
WBC ( $\times 10^2/\mu\text{L}$ )	118.8 ± 18.5	(5)	124.9 ± 31.1	(5)	
Neutrophil (%)	9 ± 3	(5)	11 ± 5	(5)	
Eosinophil (%)	1 ± 0	(5)	1 ± 0	(5)	
Basophil (%)	0 ± 0	(5)	0 ± 0	(5)	
Monocyte (%)	4 ± 2	(5)	4 ± 2	(5)	
Lymphocyte (%)	86 ± 4	(5)	84 ± 5	(5)	
<b>Females</b>					
RBC ( $\times 10^4/\mu\text{L}$ )	745 ± 14	(5)	715 ± 26	(5)	
Hemoglobin (g/dL)	14.4 ± 0.4	(5)	13.9 ± 0.6	(5)	
Hematocrit (%)	42.8 ± 1.0	(5)	41.1 ± 2.1	(5)	
MCV (fL)	57.5 ± 0.7	(5)	57.5 ± 2.4	(5)	
MCH (pg)	19.3 ± 0.4	(5)	19.4 ± 0.7	(5)	
MCHC (g/dL)	33.6 ± 0.4	(5)	33.9 ± 0.4	(5)	
Reticulocyte (%)	1.4 ± 0.4	(5)	1.9 ± 0.5	(5)	
Platelet ( $\times 10^4/\mu\text{L}$ )	107.6 ± 10.0	(5)	112.3 ± 8.3	(5)	
PT (sec)	12.3 ± 0.4	(5)	12.3 ± 0.5	(5)	
APTT (sec)	19.7 ± 1.0	(5)	19.2 ± 1.2	(5)	
WBC ( $\times 10^2/\mu\text{L}$ )	68.6 ± 13.7	(5)	70.8 ± 12.5	(5)	
Neutrophil (%)	10 ± 5	(5)	10 ± 4	(5)	
Eosinophil (%)	1 ± 0	(5)	1 ± 0	(5)	
Basophil (%)	0 ± 0	(5)	0 ± 0	(5)	
Monocyte (%)	4 ± 2	(5)	3 ± 1	(5)	
Lymphocyte (%)	85 ± 7	(5)	86 ± 6	(5)	

a), vehicle control (corn oil, 5 mL/kg)

\*, significant difference from control, p&lt;0.05

Values represent at mean ± S.D.

Parentheses indicate the number of animals

Table 9-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Biochemical findings in males and females at the end of the dosing period

Compound Dose (mg/kg)	2-Pentylanthraquinone				
	0 <sup>a)</sup>	3.75	15	60	
<b>Males</b>					
Total protein (g/dL)	5.5 ± 0.1 (5)	5.5 ± 0.2 (5)	5.3 ± 0.2* (5)	5.3 ± 0.1 (5)	
Albumin (g/dL)	3.6 ± 0.1 (5)	3.7 ± 0.3 (5)	3.6 ± 0.2 (5)	3.5 ± 0.1 (5)	
A/G	1.90 ± 0.19 (5)	2.00 ± 0.34 (5)	2.15 ± 0.26 (5)	1.94 ± 0.25 (5)	
BUN (mg/dL)	16 ± 3 (5)	14 ± 2 (5)	13 ± 2 (5)	15 ± 2 (5)	
Creatinine (mg/dL)	0.6 ± 0.1 (5)	0.6 ± 0.1 (5)	0.6 ± 0.0 (5)	0.7 ± 0.0 (5)	
Glucose (mg/dL)	159 ± 14 (5)	162 ± 9 (5)	149 ± 6 (5)	161 ± 5 (5)	
Total cholesterol (mg/dL)	44 ± 10 (5)	46 ± 5 (5)	40 ± 10 (5)	44 ± 10 (5)	
Triglyceride (mg/dL)	23 ± 8 (5)	28 ± 12 (5)	25 ± 12 (5)	17 ± 6 (5)	
Total bilirubin (mg/dL)	0.02 ± 0.01 (5)	0.02 ± 0.00 (5)	0.02 ± 0.00 (5)	0.02 ± 0.01 (5)	
Inorganic phosphorus (mg/dL)	7.0 ± 0.5 (5)	6.9 ± 0.3 (5)	7.2 ± 0.5 (5)	7.1 ± 0.9 (5)	
Ca (mg/dL)	9.4 ± 0.2 (5)	9.5 ± 0.3 (5)	9.2 ± 0.1 (5)	9.3 ± 0.3 (5)	
Na (mEq/L)	142.9 ± 0.7 (5)	141.9 ± 0.9 (5)	142.4 ± 0.7 (5)	142.3 ± 1.1 (5)	
K (mEq/L)	3.87 ± 0.19 (5)	3.88 ± 0.33 (5)	3.82 ± 0.17 (5)	3.90 ± 0.33 (5)	
Cl (mEq/L)	105.9 ± 0.8 (5)	105.4 ± 1.7 (5)	106.3 ± 0.8 (5)	105.2 ± 0.9 (5)	
ALP (U/L)	354 ± 68 (5)	286 ± 62 (5)	413 ± 21 (5)	268 ± 45* (5)	
ALT (U/L)	24 ± 6 (5)	27 ± 8 (5)	23 ± 3 (5)	24 ± 3 (5)	
AST (U/L)	56 ± 7 (5)	60 ± 15 (5)	59 ± 6 (5)	56 ± 5 (5)	
γ-GTP (U/L)	1 ± 1 (5)	1 ± 1 (5)	1 ± 1 (5)	1 ± 1 (5)	
<b>Females</b>					
Total protein (g/dL)	5.8 ± 0.3 (5)	5.5 ± 0.3 (5)	5.9 ± 0.2 (4)	5.8 ± 0.2 (5)	
Albumin (g/dL)	3.9 ± 0.2 (5)	3.8 ± 0.2 (5)	3.7 ± 0.3 (4)	3.9 ± 0.2 (5)	
A/G	2.15 ± 0.31 (5)	2.14 ± 0.30 (5)	1.75 ± 0.32 (4)	2.03 ± 0.25 (5)	
BUN (mg/dL)	21 ± 3 (5)	19 ± 3 (5)	20 ± 2 (4)	19 ± 2 (5)	
Creatinine (mg/dL)	0.7 ± 0.1 (5)	0.7 ± 0.0 (5)	0.7 ± 0.1 (4)	0.7 ± 0.1 (5)	
Glucose (mg/dL)	130 ± 8 (5)	136 ± 23 (5)	132 ± 24 (4)	129 ± 10 (5)	
Total cholesterol (mg/dL)	52 ± 14 (5)	46 ± 9 (5)	56 ± 14 (4)	53 ± 9 (5)	
Triglyceride (mg/dL)	19 ± 14 (5)	11 ± 5 (5)	22 ± 16 (4)	12 ± 4 (5)	
Total bilirubin (mg/dL)	0.05 ± 0.02 (5)	0.05 ± 0.02 (5)	0.04 ± 0.01 (4)	0.04 ± 0.01 (5)	
Inorganic phosphorus (mg/dL)	6.3 ± 0.6 (5)	6.5 ± 0.4 (5)	6.5 ± 0.8 (4)	6.8 ± 0.5 (5)	
Ca (mg/dL)	9.2 ± 0.5 (5)	9.3 ± 0.3 (5)	9.6 ± 0.2 (4)	9.5 ± 0.2 (5)	
Na (mEq/L)	141.0 ± 0.8 (5)	141.7 ± 1.4 (5)	140.6 ± 1.3 (4)	141.2 ± 0.9 (5)	
K (mEq/L)	3.76 ± 0.35 (5)	3.74 ± 0.32 (5)	3.61 ± 0.22 (4)	3.74 ± 0.26 (5)	
Cl (mEq/L)	107.1 ± 1.2 (5)	107.9 ± 1.7 (5)	106.4 ± 1.1 (4)	107.1 ± 1.2 (5)	
ALP (U/L)	222 ± 59 (5)	207 ± 54 (5)	207 ± 17 (4)	185 ± 44 (5)	
ALT (U/L)	21 ± 2 (5)	21 ± 4 (5)	23 ± 2 (4)	24 ± 5 (5)	
AST (U/L)	60 ± 6 (5)	58 ± 7 (5)	56 ± 5 (4)	59 ± 8 (5)	
γ-GTP (U/L)	1 ± 1 (5)	1 ± 1 (5)	1 ± 1 (4)	1 ± 1 (5)	

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

\*, significant difference from control, p&lt;0.05

Table 9-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
Biochemical findings in males and females at the end of the recovery period

Compound	2-Pentylanthraquinone			
	Dose (mg/kg)	0 <sup>a)</sup>	60	
<b>Males</b>				
Total protein (g/dL)	5.8 ± 0.1	(5)	5.6 ± 0.4	(5)
Albumin (g/dL)	3.7 ± 0.2	(5)	3.5 ± 0.2	(5)
A/G	1.74 ± 0.22	(5)	1.67 ± 0.15	(5)
BUN (mg/dL)	16 ± 1	(5)	17 ± 2	(5)
Creatinine (mg/dL)	0.7 ± 0.1	(5)	0.7 ± 0.1	(5)
Glucose (mg/dL)	160 ± 16	(5)	163 ± 20	(5)
Total cholesterol (mg/dL)	52 ± 9	(5)	46 ± 3	(5)
Triglyceride (mg/dL)	29 ± 6	(5)	32 ± 15	(5)
Total bilirubin (mg/dL)	0.05 ± 0.02	(5)	0.05 ± 0.01	(5)
Inorganic phosphorus (mg/dL)	7.1 ± 0.5	(5)	7.4 ± 0.7	(5)
Ca (mg/dL)	9.1 ± 0.3	(5)	9.0 ± 0.2	(5)
Na (mEq/L)	143.1 ± 1.0	(5)	142.3 ± 0.9	(5)
K (mEq/L)	4.02 ± 0.28	(5)	4.05 ± 0.20	(5)
Cl (mEq/L)	105.7 ± 1.0	(5)	104.6 ± 1.2	(5)
ALP (U/L)	245 ± 38	(5)	252 ± 43	(5)
ALT (U/L)	26 ± 6	(5)	25 ± 6	(5)
AST (U/L)	62 ± 8	(5)	58 ± 9	(5)
γ-GTP (U/L)	2 ± 1	(5)	1 ± 0	(5)
<b>Females</b>				
Total protein (g/dL)	6.0 ± 0.2	(5)	6.0 ± 0.3	(5)
Albumin (g/dL)	4.1 ± 0.4	(5)	3.9 ± 0.2	(5)
A/G	2.13 ± 0.40	(5)	1.91 ± 0.17	(5)
BUN (mg/dL)	21 ± 3	(5)	19 ± 1	(5)
Creatinine (mg/dL)	0.7 ± 0.1	(5)	0.7 ± 0.0	(5)
Glucose (mg/dL)	163 ± 13	(5)	142 ± 12*	(5)
Total cholesterol (mg/dL)	69 ± 13	(5)	60 ± 8	(5)
Triglyceride (mg/dL)	31 ± 18	(5)	21 ± 6	(5)
Total bilirubin (mg/dL)	0.06 ± 0.02	(5)	0.07 ± 0.01	(5)
Inorganic phosphorus (mg/dL)	5.4 ± 0.9	(5)	6.1 ± 0.7	(5)
Ca (mg/dL)	9.1 ± 0.3	(5)	9.3 ± 0.2	(5)
Na (mEq/L)	142.2 ± 1.2	(5)	141.7 ± 0.3	(5)
K (mEq/L)	3.93 ± 0.28	(5)	4.10 ± 0.38	(5)
Cl (mEq/L)	107.0 ± 1.2	(5)	106.7 ± 0.9	(5)
ALP (U/L)	121 ± 19	(5)	141 ± 19	(5)
ALT (U/L)	15 ± 3	(5)	15 ± 2	(5)
AST (U/L)	56 ± 13	(5)	53 ± 7	(5)
γ-GTP (U/L)	2 ± 1	(5)	2 ± 1	(5)

a), vehicle control (corn oil, 5 mL/kg)

\*, significant difference from control, p&lt;0.05

Values represent at mean ± S.D.

Parentheses indicate the number of animals

Table 10-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in males and females at the end of the dosing period

Compound Dose (mg/kg)	2-Pentylanthraquinone			
	0 <sup>a)</sup>	3.75	15	60
<b>Males</b>				
Terminal body weight (g)	340.3 ± 30.4 (5)	346.3 ± 18.7 (5)	328.1 ± 13.7 (5)	350.6 ± 21.1 (5)
Brain (mg)	1869.7 ± 18.0 (5)	1955.8 ± 29.3 (5)	1947.5 ± 156.4 (5)	1915.4 ± 96.7 (5)
Thymus (mg)	505.1 ± 109.3 (5)	513.0 ± 125.7 (5)	519.4 ± 65.8 (5)	536.0 ± 108.5 (5)
Heart (mg)	1170.4 ± 117.0 (5)	1202.0 ± 131.1 (5)	1138.5 ± 151.1 (5)	1145.3 ± 122.1 (5)
Liver (mg)	11725.9 ± 1375.6 (5)	12016.7 ± 683.5 (5)	11025.2 ± 515.8 (5)	13687.2 ± 1158.5* (5)
Kidneys (mg)	2618.3 ± 285.6 (5)	2810.8 ± 386.0 (5)	2668.0 ± 113.2 (5)	2839.9 ± 157.5 (5)
Spleen (mg)	721.4 ± 81.1 (5)	759.8 ± 97.3 (5)	763.1 ± 120.6 (5)	881.8 ± 210.3 (5)
Thyroid gland (mg)	13.3 ± 2.6 (5)	18.9 ± 5.3 (5)	18.0 ± 0.9 (5)	17.8 ± 1.9* (5)
Adrenal glands (mg)	52.1 ± 8.0 (5)	55.5 ± 8.6 (5)	46.1 ± 7.7 (5)	50.8 ± 7.2 (5)
Testes (mg)	2939.5 ± 268.1 (5)	3194.9 ± 424.9 (5)	2920.1 ± 250.3 (5)	3054.1 ± 161.8 (5)
Epididymides (mg)	738.0 ± 62.3 (5)	737.0 ± 88.1 (5)	712.3 ± 37.9 (5)	727.8 ± 54.3 (5)
<b>Females</b>				
Terminal body weight (g)	205.4 ± 19.4 (5)	204.9 ± 22.2 (5)	227.4 ± 30.3 (5)	211.9 ± 15.4 (5)
Brain (mg)	1759.2 ± 78.4 (5)	1770.8 ± 57.4 (5)	1815.2 ± 101.7 (5)	1745.5 ± 43.7 (5)
Thymus (mg)	441.1 ± 38.2 (5)	412.0 ± 101.4 (5)	428.5 ± 81.8 (5)	536.5 ± 71.8 (5)
Heart (mg)	756.8 ± 86.4 (5)	736.8 ± 90.6 (5)	829.9 ± 150.5 (5)	747.8 ± 54.1 (5)
Liver (mg)	6711.1 ± 890.2 (5)	6695.9 ± 1035.4 (5)	8097.3 ± 1438.9 (5)	7545.7 ± 856.5 (5)
Kidneys (mg)	1683.7 ± 74.4 (5)	1706.8 ± 216.4 (5)	1900.3 ± 195.8 (5)	1776.6 ± 99.0 (5)
Spleen (mg)	453.3 ± 49.9 (5)	524.5 ± 81.5 (5)	500.5 ± 144.6 (5)	485.3 ± 61.3 (5)
Thyroid gland (mg)	13.3 ± 3.4 (5)	15.2 ± 0.5 (5)	13.8 ± 3.6 (5)	14.6 ± 3.3 (5)
Adrenal glands (mg)	66.8 ± 10.0 (5)	61.2 ± 7.0 (5)	69.7 ± 10.6 (5)	57.5 ± 7.2 (5)
Ovaries (mg)	81.0 ± 8.3 (5)	84.4 ± 7.6 (5)	79.5 ± 10.2 (5)	89.8 ± 7.7 (5)

a), vehicle control (corn oil, 5 mL/kg)

\*, significant difference from control, p&lt;0.05

Values represent at mean ± S.D.

Parentheses indicate the number of animals

Table 10-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats  
 Absolute organ weights in males and females at the end of the recovery period

Compound	2-Pentylanthraquinone	
	0 <sup>a)</sup>	60
<b>Males</b>		
Terminal body weight (g)	391.4 ± 22.5 (5)	391.4 ± 18.5 (5)
Brain (mg)	1929.8 ± 97.7 (5)	1920.4 ± 59.4 (5)
Thymus (mg)	368.8 ± 83.5 (5)	416.5 ± 119.5 (5)
Heart (mg)	1231.2 ± 119.0 (5)	1273.8 ± 95.4 (5)
Liver (mg)	12134.8 ± 1083.4 (5)	12209.8 ± 890.4 (5)
Kidneys (mg)	2921.4 ± 64.8 (5)	3093.6 ± 191.1 (5)
Spleen (mg)	744.1 ± 55.8 (5)	835.3 ± 73.0 (5)
Thyroid gland (mg)	15.1 ± 3.5 (5)	18.5 ± 2.8 (5)
Adrenal glands (mg)	54.4 ± 4.4 (5)	55.9 ± 5.3 (5)
Testes (mg)	2989.8 ± 168.7 (5)	3185.1 ± 259.2 (5)
Epididymides (mg)	961.3 ± 36.1 (5)	891.9 ± 24.9** (5)
<b>Females</b>		
Terminal body weight (g)	252.1 ± 30.5 (5)	250.3 ± 21.8 (5)
Brain (mg)	1829.0 ± 58.1 (5)	1842.0 ± 57.8 (5)
Thymus (mg)	437.5 ± 64.7 (5)	457.8 ± 173.9 (5)
Heart (mg)	838.4 ± 109.2 (5)	859.0 ± 66.8 (5)
Liver (mg)	8003.8 ± 1433.4 (5)	8029.0 ± 944.6 (5)
Kidneys (mg)	1867.3 ± 139.2 (5)	2054.5 ± 250.4 (5)
Spleen (mg)	523.9 ± 151.4 (5)	590.3 ± 44.7 (5)
Thyroid gland (mg)	16.1 ± 2.0 (5)	16.2 ± 3.5 (5)
Adrenal glands (mg)	69.5 ± 13.2 (5)	69.1 ± 7.7 (5)
Ovaries (mg)	82.3 ± 16.8 (5)	95.9 ± 18.2 (5)

a), vehicle control (corn oil, 5 mL/kg)

\*, significant difference from control, p&lt;0.05

Values represent at mean ± S.D.

\*\*, significant difference from control, p&lt;0.01

Parentheses indicate the number of animals

Table 11-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in males and females at the end of the dosing period

Compound Dose (mg/kg)	2-Pentylanthraquinone			
	0 <sup>a)</sup>	3.75	15	60
<b>Males</b>				
Terminal body weight (g)	340.3 ± 30.4 (5)	346.3 ± 18.7 (5)	328.1 ± 13.7 (5)	350.6 ± 21.1 (5)
Brain (mg/g)	5.530 ± 0.500 (5)	5.660 ± 0.303 (5)	5.947 ± 0.576 (5)	5.481 ± 0.453 (5)
Thymus (mg/g)	1.490 ± 0.345 (5)	1.483 ± 0.363 (5)	1.582 ± 0.170 (5)	1.539 ± 0.359 (5)
Heart (mg/g)	3.438 ± 0.089 (5)	3.468 ± 0.289 (5)	3.471 ± 0.438 (5)	3.267 ± 0.274 (5)
Liver (mg/g)	34.458 ± 2.562 (5)	34.751 ± 2.184 (5)	33.611 ± 1.148 (5)	38.993 ± 1.096** (5)
Kidneys (mg/g)	7.699 ± 0.559 (5)	8.093 ± 0.684 (5)	8.137 ± 0.333 (5)	8.113 ± 0.446 (5)
Spleen (mg/g)	2.122 ± 0.164 (5)	2.188 ± 0.184 (5)	2.338 ± 0.453 (5)	2.516 ± 0.577 (5)
Thyroid gland (mg/g)	0.039 ± 0.006 (5)	0.055 ± 0.015 (5)	0.055 ± 0.002** (5)	0.051 ± 0.005 (5)
Adrenal glands (mg/g)	0.154 ± 0.026 (5)	0.161 ± 0.030 (5)	0.141 ± 0.025 (5)	0.144 ± 0.015 (5)
Testes (mg/g)	8.656 ± 0.617 (5)	9.199 ± 0.759 (5)	8.910 ± 0.803 (5)	8.736 ± 0.680 (5)
Epididymides (mg/g)	2.173 ± 0.146 (5)	2.123 ± 0.157 (5)	2.177 ± 0.187 (5)	2.080 ± 0.163 (5)
<b>Females</b>				
Terminal body weight (g)	205.4 ± 19.4 (5)	204.9 ± 22.2 (5)	227.4 ± 30.3 (5)	211.9 ± 15.4 (5)
Brain (mg/g)	8.611 ± 0.678 (5)	8.718 ± 0.947 (5)	8.062 ± 0.790 (5)	8.275 ± 0.651 (5)
Thymus (mg/g)	2.161 ± 0.240 (5)	2.019 ± 0.465 (5)	1.883 ± 0.244 (5)	2.542 ± 0.379 (5)
Heart (mg/g)	3.683 ± 0.199 (5)	3.598 ± 0.245 (5)	3.650 ± 0.463 (5)	3.533 ± 0.163 (5)
Liver (mg/g)	32.652 ± 2.721 (5)	32.575 ± 2.218 (5)	35.567 ± 4.354 (5)	35.550 ± 1.867 (5)
Kidneys (mg/g)	8.240 ± 0.627 (5)	8.325 ± 0.406 (5)	8.393 ± 0.503 (5)	8.418 ± 0.705 (5)
Spleen (mg/g)	2.217 ± 0.266 (5)	2.562 ± 0.317 (5)	2.170 ± 0.352 (5)	2.286 ± 0.167 (5)
Thyroid gland (mg/g)	0.065 ± 0.020 (5)	0.075 ± 0.009 (5)	0.062 ± 0.018 (5)	0.069 ± 0.015 (5)
Adrenal glands (mg/g)	0.328 ± 0.066 (5)	0.300 ± 0.029 (5)	0.309 ± 0.048 (5)	0.272 ± 0.030 (5)
Ovaries (mg/g)	0.397 ± 0.056 (5)	0.417 ± 0.070 (5)	0.354 ± 0.060 (5)	0.425 ± 0.034 (5)

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

Table 11-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in males and females at the end of the recovery period

Compound Dose (mg/kg)	2-Pentylanthraquinone	
	0 <sup>a)</sup>	60
<b>Males</b>		
Terminal body weight (g)	391.4 ± 22.5 (5)	391.4 ± 18.5 (5)
Brain (mg/g)	4.934 ± 0.186 (5)	4.914 ± 0.241 (5)
Thymus (mg/g)	0.951 ± 0.252 (5)	1.055 ± 0.265 (5)
Heart (mg/g)	3.149 ± 0.311 (5)	3.253 ± 0.162 (5)
Liver (mg/g)	30.999 ± 2.186 (5)	31.171 ± 1.100 (5)
Kidneys (mg/g)	7.479 ± 0.382 (5)	7.921 ± 0.658 (5)
Spleen (mg/g)	1.910 ± 0.231 (5)	2.141 ± 0.244 (5)
Thyroid gland (mg/g)	0.039 ± 0.011 (5)	0.047 ± 0.006 (5)
Adrenal glands (mg/g)	0.139 ± 0.015 (5)	0.144 ± 0.020 (5)
Testes (mg/g)	7.678 ± 0.872 (5)	8.152 ± 0.750 (5)
Epididymides (mg/g)	2.462 ± 0.168 (5)	2.282 ± 0.100 (5)
<b>Females</b>		
Terminal body weight (g)	252.1 ± 30.5 (5)	250.3 ± 21.8 (5)
Brain (mg/g)	7.329 ± 0.788 (5)	7.388 ± 0.460 (5)
Thymus (mg/g)	1.748 ± 0.259 (5)	1.810 ± 0.591 (5)
Heart (mg/g)	3.336 ± 0.354 (5)	3.446 ± 0.336 (5)
Liver (mg/g)	31.648 ± 2.856 (5)	32.076 ± 2.714 (5)
Kidneys (mg/g)	7.474 ± 0.881 (5)	8.204 ± 0.702 (5)
Spleen (mg/g)	2.067 ± 0.464 (5)	2.363 ± 0.135 (5)
Thyroid gland (mg/g)	0.064 ± 0.005 (5)	0.064 ± 0.012 (5)
Adrenal glands (mg/g)	0.276 ± 0.041 (5)	0.277 ± 0.030 (5)
Ovaries (mg/g)	0.324 ± 0.029 (5)	0.381 ± 0.051 (5)

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

Table 12-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Macroscopical findings in males at the end of the dosing period

Dose	0 mg/kg		3.75 mg/kg		15 mg/kg		60 mg/kg	
Grade	-	+	-	+	-	+	-	+
(Forestomach)	[ 5 ]		[ 5 ]		[ 5 ]		[ 5 ]	
Increase thickness, mucosa	5	0	5	0	5	0	4	1

-, negative; +, positive.

[ ], number of animals examined.

No significant changes were observed in organs unless otherwise described above.

## Macroscopical findings in females at the end of the dosing period

Dose	0 mg/kg		3.75 mg/kg		15 mg/kg		60 mg/kg	
Grade	-	+	-	+	-	+	-	+
(All organs)	[ 5 ]		[ 5 ]		[ 5 ]		[ 5 ]	

No remarkable change

-, negative; +, positive.

[ ], number of animals examined.

Table 12-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Macroscopical findings in males at the end of the recovery period

Dose	0 mg/kg		60 mg/kg	
Grade	-	+	-	+
(All organs)	[ 5 ]		[ 5 ]	

No remarkable change

-, negative; +, positive.

[ ], number of animals examined.

## Macroscopical findings in females at the end of the recovery period

Dose	0 mg/kg		60 mg/kg	
Grade	-	+	-	+
(All organs)	[ 5 ]		[ 5 ]	

No remarkable change

-, negative; +, positive.

[ ], number of animals examined.

Table 13-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Histological findings in males at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg								
Grade	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.				
(Liver)	[ 5 ]					[ 5 ]					[ 5 ]					[ 5 ]								
Hypertrophy, hepatocyte, centrilobular	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	1	4	0	0	0	4 #
Single cell necrosis	5	0	0	0	0	0	4	1	0	0	0	1	5	0	0	0	0	0	4	1	0	0	0	1
Fatty change, periportal	2	3	0	0	0	3	3	1	1	0	0	2	3	2	0	0	0	2	4	1	0	0	0	1
(Kidney)	[ 5 ]															[ 5 ]								
Basophilic tubule	3	2	0	0	0	2										3	2	0	0	0	2			
Hyaline droplet	0	5	0	0	0	5										1	3	1	0	0	4			
Cellular infiltration, lymphocyte	4	1	0	0	0	1										4	1	0	0	0	1			
(Spleen)	[ 5 ]															[ 5 ]								
Hematopoiesis, extramedullary	0	1	3	1	0	5										0	0	4	1	0	5			
(Heart)	[ 5 ]															[ 5 ]								
Myocardial degeneration/fibrosis	4	1	0	0	0	1										5	0	0	0	0	0			
(Prostate)	[ 5 ]															[ 5 ]								
Cellular infiltration, lymphocyte	4	0	1	0	0	1										4	0	0	1	0	1			
(Thymus)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Stomach)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Brain)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Spinal cord)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Ileum)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Colon)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Adrenal gland)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Thyroid gland)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Trachea)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								
(Lung & Bronchus)	[ 5 ]															[ 5 ]								
No remarkable change																[ 5 ]								

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

#, p&lt;0.05 by Fisher's exact test.

Table 13-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in males at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
Grade	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.
(Testis)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Epididymis)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Urinary bladder)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Submandibular lymphnode)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Mesenteric lymphnode)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Sciatic nerve & Gastrocnemial muscle)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Bone marrow of femur)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Pancreas)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Submandibular & sublingual gland)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Pituitary gland)	[ 5 ]															[ 5 ]				
No remarkable change																				
(Eye)	[ 5 ]															[ 5 ]				
No remarkable change																				

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

#, p&lt;0.05 by Fisher's exact test.

Table 13-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Histological findings in females at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg								
Grade	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.	-	±	+	++++	Pos.				
(Liver)	[ 5 ]					[ 5 ]					[ 5 ]					[ 5 ]								
Fatty change, periportal	2	3	0	0	0	3	0	2	3	0	0	5	2	2	1	0	0	3	1	2	2	0	0	4
(Kidney)	[ 5 ]															[ 5 ]								
Basophilic tubule	4	1	0	0	0	1										2	3	0	0	0	3			
Cellular infiltration, lymphocyte	3	2	0	0	0	2										3	2	0	0	0	2			
(Spleen)	[ 5 ]															[ 5 ]								
Hematopoiesis, extramedullary	0	5	0	0	0	5										0	5	0	0	0	5			
(Brain)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Spinal cord)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Stomach)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Ileum)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Colon)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Adrenal gland)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Heart)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Thymus)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Thyroid gland)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Trachea)	[ 5 ]															[ 5 ]								
No remarkable change																								
(Lung & Bronchus)	[ 5 ]															[ 5 ]								
No remarkable change																								

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

Table 13-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in females at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg									
Grade	-	±	+	++	+++	Pos.	-	±	+	++	+++	Pos.	-	±	+	++	+++	Pos.	-	±	+	++	+++	Pos.	
(Ovary)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Uterus)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Urinary bladder)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Submandibular lymphnode)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Mesenteric lymphnode)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Sciatic nerve & Gastrocnemial muscle)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Bone marrow of femur)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Pancreas)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Submandibular & sublingual gland)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Pituitary gland)	[ 5 ]																								[ 5 ]
No remarkable change																									
(Eye)	[ 5 ]																								[ 5 ]
No remarkable change																									

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

Table 13-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in males at the end of the dosing period

Dose	0 mg/kg						60 mg/kg					
	-	±	+	++	+++	Pos.	-	±	+	++	+++	Pos.
(Liver)	[ 5 ]						[ 5 ]					
Fatty change, periportal	3	2	0	0	0	2		3	2	0	0	2

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

## Histological findings in females at the end of the recovery period

Dose	0 mg/kg						60 mg/kg					
	-	±	+	++	+++	Pos.	-	±	+	++	+++	Pos.
(Liver)	[ 5 ]						[ 5 ]					
Fatty change, periportal	3	2	0	0	0	2		4	1	0	0	1

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe; Pos., total of positive grade.

[ ], number of animals examined.

検査成績表

秦野研究部 試験部  
化学物質管理室  
三枝 克彦 様

2003年11月17日

山本化成株式会社  
大牟田品質保証課

品名 2-AAQ			
Lot No.	01-13001-50		
製品量 (kg)	2		
検査項目	分析値	分析法	
2-アミルアントラキノン (%)	98.6	QW-22-02 3.3	
アントラキノン (%)	0.5	QW-22-02 3.3	
他ピーク合計* (%)	0.9	QW-22-02 3.3	
* 10ピーク以上			
備考		確認印	
			

QZ-12-01



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FAX 0729-49-5479

検査成績表

2005年 3月25日

食品薬品安全センター様

山本化成株式会社  
大牟田品質保証課

品名 2-AAQ			
Lot No.	01-13001-50		
製品量 (kg)			
検査項目	分析値		分析法
2-アミルアントラキノン (%)	98.6		QW-22-02 3.3
アントラキノン (%)	0.5		QW-22-02 3.3
他ピーク合計* (%)	0.9		QW-22-02 3.3
* 10ピーク以上			
備考	確認印		
経時変化確認のための再検査 ('04年11月4日)			

QZ-12-01

## Appendix B

#### **Stability of the test article in the prepared sample**

Test article : 2-Pentylanthraquinone Date of preparation : Mar.18,2004  
 Lot No. : 01-13001-50 Date of determination A : Mar.18,2004 (0 day)  
 Carrier : Corn oil B : Mar.26,2004 (8 day)  
 Condition for storage : Cooling

Indicated (mg/mL)	A			B		
	Sample No.	Found-1 (mg/mL)	Content <sup>a)</sup> (%)	Sample No.	Found-2 (mg/mL)	Content <sup>b)</sup> (%)
0.500	1	0.5045	101	7	0.5077	100
	2	0.5095	102	8	0.4987	98.6
	3	0.5037	101	9	0.5030	99.4
	mean	0.5059	101	mean	—	99.3
50.0	4	51.37	103	10	51.55	99.0
	5	51.27	103	11	50.52	97.0
	6	53.55	107	12	51.50	98.9
	mean	52.06	104	mean	—	98.3

a) Found-1 / Indicated × 100

b) Found-2 / Found-1 mean × 100

**Investigator**

**Director, Chemical Analysis**

Toyohiko Ohyaghi  
Takako Ony

Appendix C

Content of the test article in the prepared sample

Test article : 2-Pentylanthraquinone Date of preparation : Mar. 29, 2004

Lot No. : 01-13001-50 Date of determination : Mar. 29, 2004

Carrier : Corn oil

Sample No.	Indicated (A) (mg/mL)	Found (B) (mg/mL)	Mean (C) (mg/mL)	Content B/A×100 (%)	Mean (%)	B/C×100 (%)
13	0.750	0.7080	0.6960	94.4	92.8	102
14		0.6892		91.9		99.0
15		0.6910		92.1		99.3
16	3.00	2.884	2.880	96.1	96.0	100
17		2.892		96.4		100
18		2.866		95.5		99.5
19	12.0	11.96	11.82	99.7	98.5	101
20		11.75		97.9		99.4
21		11.76		98.0		99.5

investigator

Toyohiko Ohyagi

Director, Chemical Analysis

Takao Araki

## Appendix D

白血球分類での各自血球の絶対数

Compound Dose (mg/kg)	2-Pentylanthraquinone			
	0 a)	3.75	15	60
<u>End of the dosing period</u>				
Males				
WBC (x10 <sup>2</sup> /μL)	84.2 ± 18.6 (5)	86.0 ± 15.6 (5)	90.2 ± 22.0 (5)	82.9 ± 31.0 (5)
Neutrophil (x10 <sup>2</sup> /μL)	13.00 ± 2.83 (5)	9.80 ± 2.01 (5)	7.95 ± 2.78 (5)	12.15 ± 5.56 (5)
Eosinophil (x10 <sup>2</sup> /μL)	0.84 ± 0.19 (5)	0.64 ± 0.36 (5)	0.69 ± 0.43 (5)	0.83 ± 0.31 (5)
Basophil (x10 <sup>2</sup> /μL)	0.00 ± 0.00 (5)	0.00 ± 0.00 (5)	0.00 ± 0.00 (5)	0.00 ± 0.00 (5)
Monocyte (x10 <sup>2</sup> /μL)	3.67 ± 2.44 (5)	3.19 ± 1.05 (5)	1.95 ± 0.41 (5)	2.25 ± 0.65 (5)
Lymphocyte (x10 <sup>2</sup> /μL)	66.46 ± 16.70 (5)	72.31 ± 16.28 (5)	79.84 ± 20.00 (5)	67.50 ± 26.04 (5)
Females				
WBC (x10 <sup>2</sup> /μL)	59.9 ± 27.9 (5)	61.2 ± 9.6 (5)	60.9 ± 21.2 (4)	64.0 ± 11.1 (5)
Neutrophil (x10 <sup>2</sup> /μL)	6.35 ± 3.06 (5)	10.64 ± 6.69 (5)	13.10 ± 4.57 (4)	5.92 ± 2.54 (5)
Eosinophil (x10 <sup>2</sup> /μL)	0.68 ± 0.26 (5)	0.72 ± 0.24 (5)	0.88 ± 0.32 (4)	0.75 ± 0.25 (5)
Basophil (x10 <sup>2</sup> /μL)	0.00 ± 0.00 (5)	0.00 ± 0.00 (5)	0.00 ± 0.00 (4)	0.00 ± 0.00 (5)
Monocyte (x10 <sup>2</sup> /μL)	1.91 ± 1.03 (5)	1.87 ± 0.66 (5)	3.93 ± 2.59 (4)	1.35 ± 0.78 (5)
Lymphocyte (x10 <sup>2</sup> /μL)	51.33 ± 25.23 (5)	47.93 ± 14.59 (5)	43.17 ± 21.14 (4)	56.15 ± 9.57 (5)
<u>End of the recovery period</u>				
Males				
WBC (x10 <sup>2</sup> /μL)	118.8 ± 18.5 (5)		124.9 ± 31.1 (5)	
Neutrophil (x10 <sup>2</sup> /μL)	10.87 ± 4.59 (5)		13.22 ± 3.40 (5)	
Eosinophil (x10 <sup>2</sup> /μL)	1.19 ± 0.18 (5)		1.25 ± 0.31 (5)	
Basophil (x10 <sup>2</sup> /μL)	0.00 ± 0.00 (5)		0.00 ± 0.00 (5)	
Monocyte (x10 <sup>2</sup> /μL)	4.27 ± 1.11 (5)		5.20 ± 2.61 (5)	
Lymphocyte (x10 <sup>2</sup> /μL)	101.92 ± 18.20 (5)		105.99 ± 30.78 (5)	
Females				
WBC (x10 <sup>2</sup> /μL)	68.6 ± 13.7 (5)		70.8 ± 12.5 (5)	
Neutrophil (x10 <sup>2</sup> /μL)	6.25 ± 2.46 (5)		7.61 ± 4.15 (5)	
Eosinophil (x10 <sup>2</sup> /μL)	0.83 ± 0.35 (5)		0.71 ± 0.13 (5)	
Basophil (x10 <sup>2</sup> /μL)	0.00 ± 0.00 (5)		0.00 ± 0.00 (5)	
Monocyte (x10 <sup>2</sup> /μL)	2.56 ± 1.38 (5)		2.10 ± 1.37 (5)	
Lymphocyte (x10 <sup>2</sup> /μL)	58.99 ± 15.30 (5)		60.50 ± 8.32 (5)	

a), vehicle control (corn oil, 5 mL/kg)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

Appendix E  
甲状腺重量の背景データ

Species: Rat

Strain: Crj:CD(SD)IGS

Sex: Male

Study no.	Animal age (week)	Absolute weight (mg)		Relative weight (mg/g)	
1	9	23.6 ± 3.0	(5)	0.072 ± 0.008	(5)
2	9	15.0 ± 2.2	(10)	0.047 ± 0.005	(10)
3	9	15.0 ± 3.0	(10)	0.051 ± 0.012	(10)
4	11	22.6 ± 3.6	(5)	0.054 ± 0.010	(5)
5	11	19.4 ± 4.7	(10)	0.045 ± 0.010	(10)

Values represent at mean ± S.D.

Parentheses indicate the number of animals

## Appendix 1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Clinical signs in individual males; dosage of 0 mg/kg (vehicle control)

Animal No.	Clinical signs	Day of the dosing period																												Day of the recovery period		Total frequency		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14			
1 (R)	No abnormality in general condition																																	
2 (R)	No abnormality in general condition																																	
3 (R)	No abnormality in general condition																																	
4 (R)	No abnormality in general condition																																	
5 (R)	No abnormality in general condition																																	
6 (D)	No abnormality in general condition																																	
7 (D)	No abnormality in general condition																																	
8 (D)	No abnormality in general condition																																	
9 (D)	No abnormality in general condition																																	
10 (D)	No abnormality in general condition																																	

Clinical signs in individual males; dosage of 3.75 mg/kg

Animal No.	Clinical signs	Day of the dosing period																														Total frequency		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28					
11 (D)	No abnormality in general condition																																	
12 (D)	No abnormality in general condition																																	
13 (D)	No abnormality in general condition																																	
14 (D)	No abnormality in general condition																																	
15 (D)	No abnormality in general condition																																	

+, observed; -, not observed; D, scheduled sacrifice at the end of the dosing period; R, scheduled sacrifice at the end of the recovery period

## Appendix 1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Clinical signs in individual males; dosage of 15 mg/kg

Animal No.	Clinical signs	Day of the dosing period																												Total frequency	
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28		
16 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
17 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
18 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
19 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Clinical signs in individual males; dosage of 60 mg/kg

Animal No.	Clinical signs	Day of the dosing period																													Total frequency
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14
21 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	+	-	-	3
22 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
23 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
24 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
25 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
26 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
27 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
28 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	+	-	-	-	3	
29 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	1	
30 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	

+, observed; -, not observed; D, scheduled sacrifice at the end of the dosing period; R, scheduled sacrifice at the end of the recovery period

## Appendix 1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Clinical signs in individual females; dosage of 0 mg/kg (vehicle control)

Animal No.	Clinical signs	Day of the dosing period														Day of the recovery period				Total frequency											
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14
31 (R)	No abnormality in general condition																														
32 (R)	No abnormality in general condition																														
33 (R)	No abnormality in general condition																														
34 (R)	No abnormality in general condition																														
35 (R)	No abnormality in general condition																														
36 (D)	No abnormality in general condition																														
37 (D)	No abnormality in general condition																														
38 (D)	No abnormality in general condition																														
39 (D)	No abnormality in general condition																														
40 (D)	No abnormality in general condition																														

Clinical signs in individual females; dosage of 3.75 mg/kg

Animal No.	Clinical signs	Day of the dosing period														Day of the recovery period				Total frequency											
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14
41 (D)	No abnormality in general condition																														
42 (D)	No abnormality in general condition																														
43 (D)	No abnormality in general condition																														
44 (D)	No abnormality in general condition																														
45 (D)	No abnormality in general condition																														

+, observed; -, not observed; D, scheduled sacrifice at the end of the dosing period; R, scheduled sacrifice at the end of the recovery period

## Appendix 1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Clinical signs in individual females; dosage of 15 mg/kg

Animal No.	Clinical signs	Day of the dosing period																											Total frequency	
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
46 (D) a)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
47 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
48 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
49 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
50 (D)	No abnormality in general condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0

Clinical signs in individual females; dosage of 60 mg/kg

Animal No.	Clinical signs	Day of the dosing period																												Day of the recovery period		Total frequency
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1-7	8-14	
51 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	
52 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0		
53 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		
54 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6		
55 (R)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		
56 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		
57 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0		
58 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0		
59 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0		
60 (D)	Salivation immediately after administration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0		

+, observed; -, not observed; D, scheduled sacrifice at the end of the dosing period; R, scheduled sacrifice at the end of the recovery period

a) This animal was observed bleeding from claw on day of necropsy.

## Appendix 2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males during the acclimatizing period

Observations	Score/code	Dose Animal No.	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
<b>Home cage observations</b>																																
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	R	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O		
Locomotor	- 4		4	-	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	-	4		
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
<b>Responses to handling</b>																																
Behavior while removing from cage	0 2 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	0	
Handling behavior	0 2 4		4	4	4	4	0	4	4	4	4	4	4	4	4	4	4	0	4	4	4	4	4	4	4	0	0	0	4	4	0	
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Observed at the outside of home cage</b>																																
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	
Urination	(frequency/30sec)		0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	1	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Detailed clinical observations in individual females during the acclimatizing period

Observations	Score/code	Dose Animal No.	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
			31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
<b>Home cage observations</b>																																
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	R	O	O	O	O	O	O	O	O	O	O	O	O	O	O	R		
Locomotor	- 4		-	4	4	4	-	4	4	-	4	-	4	4	4	4	-	4	4	4	4	4	4	4	4	4	4	4	4	4		
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
<b>Responses to handling</b>																																
Behavior while removing from cage	0 2 4		0	2	0	4	4	4	2	4	4	4	4	4	4	4	4	4	4	4	4	0	4	4	4	4	4	4	4	4	4	
Handling behavior	0 2 4		4	4	0	4	4	4	4	4	0	4	4	4	4	4	4	4	4	0	4	4	4	4	4	4	4	2	4	4	4	
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Observed at the outside of home cage</b>																																
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	
Urination	(frequency/30sec)		1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	1	0	0	0
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex  
The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 1st week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg																		
			Animal No.										1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
<b>Home cage observations</b>																																									
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O						
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4							
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							
<b>Responses to handling</b>																																									
Behavior while removing from cage	0 2 4		0	0	0	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0						
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	4	2	0	0	0	2	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0	0						
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							
<b>Observed at the outside of home cage</b>																																									
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O						
Urination	(frequency/30sec)		0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0						
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	2	0	0	1	0	2	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0						
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-						

Detailed clinical observations in individual females in the 1st week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg																		
			Animal No.										31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
<b>Home cage observations</b>																																									
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O						
Locomotor	- 4		-	4	-	4	-	4	-	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4							
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
<b>Responses to handling</b>																																									
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0					
Handling behavior	0 2 4		0	0	0	4	4	4	2	0	0	0	0	4	4	0	4	0	4	0	0	0	0	4	0	0	0	2	0	0	0	0	0	0	4						
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
<b>Observed at the outside of home cage</b>																																									
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O					
Urination	(frequency/30sec)		0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0						
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0						
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-3

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 2nd week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
			Animal No.										11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
<b>Home cage observations</b>																																
Posture	O R		O	O	O	O	O	O	R	R	O	O	O	O	R	R	O	O	R	O	O	R	O	O	O	O	O	O	O	O	O	
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Responses to handling</b>																																
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Observed at the outside of home cage</b>																																
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Detailed clinical observations in individual females in the 2nd week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg																		
			Animal No.										31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
<b>Home cage observations</b>																																									
Posture	O R		O	O	O	O	O	O	R	O	O	O	O	R	O	R	O	O	R	O	O	R	O	O	O	R	O	O	O	O	O	O	O								
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4									
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
<b>Responses to handling</b>																																									
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	2	0	0	0	0	0	0	2	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0									
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	2	0	0	0	0	0	0	0	0	0									
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
<b>Observed at the outside of home cage</b>																																									
Posture	O R		O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O								
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0									
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-4

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 3rd week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
			Animal No.										11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
<b>Home cage observations</b>																																
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Responses to handling</b>																																
Behavior while removing from cage	<u>0</u> 2 4		0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Handling behavior	<u>0</u> 2 4		0	0	0	0	0	0	0	0	0	0	4	4	0	0	0	0	4	0	0	0	0	0	0	0	0	0	4	0	0	
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Observed at the outside of home cage</b>																																
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Urination	(frequency/30sec)		0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Detailed clinical observations in individual females in the 3rd week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg																		
			Animal No.										31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
<b>Home cage observations</b>																																									
Posture	O R		0	0	0	0	0	0	R	0	R	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	R	0									
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4									
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-								
<b>Responses to handling</b>																																									
Behavior while removing from cage	<u>0</u> 2 4		0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Handling behavior	<u>0</u> 2 4		0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-								
<b>Observed at the outside of home cage</b>																																									
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-5

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 4th week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg										
			Animal No.										11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
<b>Home cage observations</b>																																	
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	R	0	0	0	0	0	0	0	0	0	0		
Locomotor	- 4		-	4	-	-	-	-	-	-	-	4	4	4	-	4	-	4	-	4	4	4	4	4	-	-	-	-	-	-	-		
Others <sup>a)</sup>	(none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Responses to handling</b>																																	
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Handling behavior	0 2 4		0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Others <sup>b)</sup>	(normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>Observed at the outside of home cage</b>																																	
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Urination	(frequency/30sec)		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Others <sup>c)</sup>	(normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Detailed clinical observations in individual females in the 4th week of the dosing period

Observations	Score/code	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg																		
			Animal No.										31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
<b>Home cage observations</b>																																									
Posture	O R		0	0	0	R	R	O	R	O	O	O	0	0	0	0	0	R	R	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O						
Locomotor	- 4		-	4	-	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4								
Others <sup>a)</sup>	(none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							
<b>Responses to handling</b>																																									
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Others <sup>b)</sup>	(normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							
<b>Observed at the outside of home cage</b>																																									
Posture	O R		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Others <sup>c)</sup>	(normal/none)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-6

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 1st week of the recovery period

Observations	Score/code	Dose Animal No.	0 mg/kg					60 mg/kg				
			1	2	3	4	5	21	22	23	24	25
<b>Home cage observations</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Locomotor	- 4		-	-	-	4	4	-	-	-	-	4
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-
<b>Responses to handling</b>												
Behavior while removing from cage	0 2 4		0	0	0	2	0	0	0	0	0	0
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	0	0
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-
<b>Observed at the outside of home cage</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Urination	(frequency/30sec)		0	0	0	1	0	0	0	0	0	1
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-

Detailed clinical observations in individual females in the 1st week of the recovery period

Observations	Score/code	Dose Animal No.	0 mg/kg					60 mg/kg				
			31	32	33	34	35	51	52	53	54	55
<b>Home cage observations</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Locomotor	- 4		-	4	-	-	4	-	4	-	-	-
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-
<b>Responses to handling</b>												
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0
Handling behavior	0 2 4		0	0	0	0	0	0	4	0	0	0
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-
<b>Observed at the outside of home cage</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 2-7

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Detailed clinical observations in individual males in the 2nd week of the recovery period

Observations	Score/code	Dose Animal No.	0 mg/kg					60 mg/kg				
			1	2	3	4	5	21	22	23	24	25
<b>Home cage observations</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-
<b>Responses to handling</b>												
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0
Handling behavior	0 2 4		0	0	0	0	0	0	0	0	0	0
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-
<b>Observed at the outside of home cage</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Urination	(frequency/30sec)		0	0	0	1	0	0	0	1	1	2
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-

Detailed clinical observations in individual females in the 2nd week of the recovery period

Observations	Score/code	Dose Animal No.	0 mg/kg					60 mg/kg				
			31	32	33	34	35	51	52	53	54	55
<b>Home cage observations</b>												
Posture	O R		0	0	0	0	R	0	0	0	0	0
Locomotor	- 4		4	4	4	4	4	4	4	4	4	4
Others <sup>a)</sup>	- (none)		-	-	-	-	-	-	-	-	-	-
<b>Responses to handling</b>												
Behavior while removing from cage	0 2 4		0	0	0	0	0	0	0	0	0	0
Handling behavior	0 2 4		0	0	2	0	0	0	0	2	0	0
Others <sup>b)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-
<b>Observed at the outside of home cage</b>												
Posture	O R		0	0	0	0	0	0	0	0	0	0
Urination	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Defecation	(frequency/30sec)		0	0	0	0	0	0	0	0	0	0
Others <sup>c)</sup>	- (normal/none)		-	-	-	-	-	-	-	-	-	-

a) vocalization, tremor, convulsion

b) heart beats, body temperature, fur, skin color/mucous membranes, lacrimation, exophthalmos, pupil size, salivation

c) exploration, grooming, vocalization, straub tail, gait, stereotypy, bizarre behavior, tremor, convulsion, respiratory rate, piloerection, palpebral opening, touch response, withdrawal reflex, pinna reflex

The score with under line, normal score (normal behavior or no observation)

Posture: O, sitting or standing position; R, rearing

Locomotor: -, not determined due to the usual sleep; 4, normal

Behavior while removing form cage: 0, very easy; 2, easy (vocalization without resisting being picked up); 4, rat flinched

Handling behavior: 0, very low (no resistance, rat was easy to handle); 2, low (vocalizes but dose not resist handling); 4, moderately low (slight resistance to being handled)

## Appendix 3-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Functional observations in individual males in the 4th week of the dosing period (sensory reactivity to stimuli)

Score	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
		Animal No. 1 2 3 4 5 6 7 8 9 10										11 12 13 14 15					16 17 18 19 20					21 22 23 24 25 26 27 28 29 30									
<b>Auditory</b>																															
Startle response	0 2 <u>4</u> 6 8	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
<b>Visual</b>																															
Visual placing	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
Pupillary reflex	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
<b>Proprioceptive stimuli</b>																															
Righting reflex	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	

Functional observations in individual females in the 4th week of the dosing period (sensory reactivity to stimuli)

Score	Dose	0 mg/kg										3.75 mg/kg					15 mg/kg					60 mg/kg									
		Animal No. 31 32 33 34 35 36 37 38 39 40										41 42 43 44 45					46 47 48 49 50					51 52 53 54 55 56 57 58 59 60									
<b>Auditory</b>																															
Startle response	0 2 <u>4</u> 6 8	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
<b>Visual</b>																															
Visual placing	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
Pupillary reflex	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	
<b>Proprioceptive stimuli</b>																															
Righting reflex	0 2 <u>4</u>	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	

The score with under line, normal score

Score 4, normal score

## Appendix 3-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Functional observations in individual males in the 2nd week of the recovery period (sensory reactivity to stimuli)

Score	Dose	Animal No.	0 mg/kg					60 mg/kg				
			1	2	3	4	5	21	22	23	24	25
Auditory												
Startle response	0 2 <u>4</u> 6 8		4	4	4	4	4		4	4	4	4
Visual												
Visual placing	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4
Pupillary reflex	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4
Proprioceptive stimuli												
Righting reflex	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4

Functional observations in individual females in the 2nd week of the recovery period (sensory reactivity to stimuli)

Score	Dose	Animal No.	0 mg/kg					60 mg/kg				
			31	32	33	34	35	51	52	53	54	55
Auditory												
Startle response	0 2 <u>4</u> 6 8		4	4	4	4	4		4	4	4	4
Visual												
Visual placing	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4
Pupillary reflex	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4
Proprioceptive stimuli												
Righting reflex	0 2 <u>4</u>		4	4	4	4	4		4	4	4	4

The score with under line, normal score

Score 4, normal score

Appendix 4-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Body weight changes in individual males; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period										Day of the recovery period				
	1	2	4	8	11	15	18	22	25	28	1	4	8	11	14
1 (R)	162.4	171.2	187.6	221.8	247.3	285.6	313.3	341.9	363.7	384.0	389.6	411.8	427.0	441.1	453.0
2 (R)	160.5	168.1	181.7	209.9	235.2	260.4	278.0	295.4	310.0	323.5	328.8	346.2	371.2	384.4	398.8
3 (R)	171.1	178.7	197.5	223.2	248.3	278.7	296.9	329.8	351.4	370.0	381.2	396.7	420.3	436.0	452.9
4 (R)	161.9	169.1	189.5	219.1	242.9	276.3	300.1	328.2	347.9	362.0	367.2	380.3	399.0	414.7	422.6
5 (R)	156.0	166.2	184.6	219.8	243.2	275.4	303.0	331.6	349.1	364.3	371.1	383.2	390.3	398.4	405.1
6 (D)	169.1	178.3	193.8	229.9	255.3	301.1	332.2	368.3	387.9	403.7					
7 (D)	163.9	173.7	189.6	225.8	248.5	278.1	296.2	325.7	339.5	353.7					
8 (D)	161.6	171.7	186.5	221.5	240.8	269.7	293.0	316.3	331.6	352.3					
9 (D)	167.0	175.0	187.6	218.6	242.7	282.7	312.7	349.6	374.5	401.4					
10 (D)	165.5	170.4	186.7	210.4	231.4	260.5	282.3	307.4	318.2	337.6					
N	10	10	10	10	10	10	10	10	10	10	5	5	5	5	5
Mean	163.9	172.2	188.5	220.0	243.6	276.9	300.8	329.4	347.4	365.3	367.6	383.6	401.6	414.9	426.5
S.D.	4.4	4.2	4.5	6.2	6.9	12.0	15.8	20.8	24.1	25.8	23.4	24.4	22.7	24.2	25.7
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	F→S	F→S	F→S	F→S	F→S

Body weight changes in individual males; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period									
	1	2	4	8	11	15	18	22	25	28
11 (D)	160.7	167.6	186.7	225.3	252.0	290.0	305.7	339.6	357.1	374.2
12 (D)	176.2	182.3	204.1	245.2	272.0	307.6	334.1	367.0	379.4	408.3
13 (D)	167.2	177.1	194.3	232.4	254.2	285.7	308.2	338.8	353.1	373.3
14 (D)	161.2	170.1	184.9	221.4	246.4	284.6	307.6	340.4	358.2	375.6
15 (D)	163.6	173.8	191.1	220.3	246.1	273.6	296.2	321.1	337.0	347.3
N	5	5	5	5	5	5	5	5	5	5
Mean	165.8	174.2	192.2	228.9	254.1	288.3	310.4	341.4	357.0	375.7
S.D.	6.4	5.8	7.6	10.3	10.6	12.4	14.1	16.4	15.2	21.7
S.A.	...	...	...	...	...	...	...	...	...	...

Parameter, body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 4-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Body weight changes in individual males; dosage of 15 mg/kg

Animal No.	Day of the dosing period									
	1	2	4	8	11	15	18	22	25	28
16 (D)	166.9	176.5	192.7	227.8	252.9	277.6	302.6	323.9	341.1	359.3
17 (D)	157.1	164.1	180.1	211.5	235.1	265.1	280.5	309.5	321.8	342.4
18 (D)	173.3	179.9	195.7	231.1	253.3	283.6	302.1	335.0	353.3	366.5
19 (D)	167.2	175.5	191.6	223.1	246.5	282.5	308.8	335.5	350.4	363.1
20 (D)	158.6	164.2	176.2	199.0	222.0	251.6	273.3	300.7	315.7	331.9
N	5	5	5	5	5	5	5	5	5	5
Mean	164.6	172.0	187.3	218.5	242.0	272.1	293.5	320.9	336.5	352.6
S.D.	6.7	7.4	8.6	13.2	13.4	13.6	15.6	15.5	16.9	14.8
S.A.	...	...	...	...	...	...	...	...	...	...

Body weight changes in individual males; dosage of 60 mg/kg

Animal No.	Day of the dosing period										Day of the recovery period				
	1	2	4	8	11	15	18	22	25	28	1	4	8	11	14
21 (R)	167.9	176.7	196.6	228.6	257.1	285.5	310.4	343.2	356.5	371.9	376.3	387.3	405.6	412.6	424.8
22 (R)	164.1	172.6	192.2	225.7	250.4	280.1	303.1	332.8	351.4	365.4	371.5	377.3	394.5	409.9	421.6
23 (R)	156.4	162.7	177.9	216.3	242.3	275.6	297.0	333.3	349.3	366.9	371.5	388.8	409.7	420.4	435.2
24 (R)	174.5	183.1	205.0	238.9	262.6	297.0	315.3	346.2	364.6	381.5	386.6	399.1	421.2	428.0	447.6
25 (R)	162.4	169.9	186.2	217.1	237.7	268.6	284.9	312.1	327.9	343.6	349.4	360.5	372.3	378.2	390.4
26 (D)	161.5	168.9	184.8	211.6	233.3	263.3	281.4	309.3	323.6	336.8					
27 (D)	171.3	180.2	197.5	237.9	264.5	302.9	326.8	354.8	379.0	396.2					
28 (D)	168.3	176.3	190.5	226.1	252.6	296.5	323.2	358.4	373.7	392.8					
29 (D)	159.8	168.8	183.1	221.7	249.4	290.3	319.5	355.2	375.5	393.5					
30 (D)	167.4	175.5	192.4	230.8	257.9	294.6	316.9	353.0	368.3	384.0					
N	10	10	10	10	10	10	10	10	10	10	5	5	5	5	5
Mean	165.4	173.5	190.6	225.5	250.8	285.4	307.9	339.8	357.0	373.3	371.1	382.6	400.7	409.8	423.9
S.D.	5.5	6.1	7.9	9.0	10.4	13.2	15.8	17.7	19.3	20.6	13.6	14.6	18.5	19.0	21.3
S.A.	...	...	...	...	...	...	...	...	...	...	0.29	0.08	0.07	0.37	0.17

Parameter, body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 4-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Body weight changes in individual females; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period										Day of the recovery period				
	1	2	4	8	11	15	18	22	25	28	1	4	8	11	14
31 (R)	138.3	146.8	156.9	174.6	189.7	203.1	215.2	233.5	240.6	247.2	255.2	258.2	265.9	278.7	283.9
32 (R)	132.0	137.9	149.9	169.8	179.3	194.6	202.7	213.7	219.6	232.4	229.9	240.7	240.7	249.5	251.0
33 (R)	148.9	155.8	170.4	184.3	198.8	213.2	224.0	239.1	246.5	262.9	258.6	272.3	281.0	286.5	298.4
34 (R)	144.7	149.1	160.8	182.2	193.8	211.8	231.7	247.1	261.8	277.2	281.1	290.7	302.7	299.8	308.8
35 (R)	135.7	139.5	146.5	161.2	166.9	175.4	184.5	198.4	204.2	210.1	210.5	215.2	221.0	224.7	229.4
36 (D)	142.3	145.0	155.8	171.2	175.6	187.8	193.9	202.5	209.7	212.3					
37 (D)	138.8	145.8	154.2	167.0	170.9	178.3	181.3	188.3	188.1	196.6					
38 (D)	131.2	136.6	146.4	164.6	174.1	183.9	191.5	201.8	210.2	223.4					
39 (D)	141.7	146.6	156.7	178.9	193.4	204.9	219.3	231.8	244.1	255.6					
40 (D)	133.1	143.4	155.0	165.2	178.4	189.7	197.1	210.9	215.8	231.0					
N	10	10	10	10	10	10	10	10	10	10	5	5	5	5	5
Mean	138.7	144.7	155.3	171.9	182.1	194.3	204.1	216.7	224.1	234.9	247.1	255.4	262.3	267.8	274.3
S.D.	5.8	5.7	7.1	7.9	11.0	13.5	17.4	19.8	23.0	25.6	27.3	29.0	32.3	30.4	33.2
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	F→S	F→S	F→S	F→S	F→S

Body weight changes in individual females; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period									
	1	2	4	8	11	15	18	22	25	28
41 (D)	128.9	135.0	144.8	156.6	163.7	175.2	175.1	186.4	193.2	204.7
42 (D)	140.4	148.6	163.6	185.3	191.8	204.7	218.9	240.8	243.3	252.2
43 (D)	135.5	141.9	154.6	165.9	179.8	187.0	190.9	204.0	215.0	229.5
44 (D)	128.5	133.6	140.5	157.1	157.6	169.7	175.7	184.2	190.7	193.5
45 (D)	144.8	152.7	163.5	179.5	192.1	201.0	207.9	216.6	218.6	228.4
N	5	5	5	5	5	5	5	5	5	5
Mean	135.6	142.4	153.4	168.9	177.0	187.5	193.7	206.4	212.2	221.7
S.D.	7.1	8.3	10.6	13.0	15.9	15.4	19.5	23.4	21.4	23.0
S.A.	...	...	...	...	...	...	...	...	...	...

Parameter, body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 4-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Body weight changes in individual females; dosage of 15 mg/kg

Animal No.	Day of the dosing period									
	1	2	4	8	11	15	18	22	25	28
46 (D)	133.2	139.3	150.3	168.9	177.9	190.4	200.6	215.1	221.4	237.3
47 (D)	135.0	141.1	149.3	177.6	180.8	193.8	205.0	219.2	222.1	240.6
48 (D)	146.2	150.2	164.2	193.6	203.4	222.6	237.0	260.9	278.2	289.6
49 (D)	142.8	146.7	156.8	180.2	190.6	211.1	225.6	246.9	255.8	268.6
50 (D)	135.6	140.5	142.9	158.5	166.8	176.8	183.2	194.7	204.1	208.5
N	5	5	5	5	5	5	5	5	5	5
Mean	138.6	143.6	152.7	175.8	183.9	198.9	210.3	227.4	236.3	248.9
S.D.	5.6	4.7	8.1	13.1	13.8	18.0	21.2	26.4	30.0	31.1
S.A.	...	...	...	...	...	...	...	...	...	...

Body weight changes in individual females; dosage of 60 mg/kg

Animal No.	Day of the dosing period										Day of the recovery period				
	1	2	4	8	11	15	18	22	25	28	1	4	8	11	14
51 (R)	150.4	158.5	169.5	197.0	209.1	225.9	235.0	255.2	262.4	273.1	275.3	270.7	282.6	294.0	303.0
52 (R)	140.3	147.1	157.6	178.6	192.4	211.0	217.1	234.0	240.4	261.4	255.9	271.1	281.3	289.9	302.9
53 (R)	130.5	136.4	145.9	160.5	168.7	186.4	195.1	206.6	213.2	222.1	224.8	232.1	239.7	249.1	251.9
54 (R)	145.0	145.2	154.8	167.5	171.8	182.9	198.6	210.3	214.9	227.5	225.3	236.9	241.7	242.6	258.3
55 (R)	133.8	140.2	148.9	162.0	178.7	194.7	188.3	207.7	222.9	230.5	232.7	236.9	247.8	248.3	265.8
56 (D)	132.4	137.2	149.0	167.7	171.5	185.0	194.1	209.4	214.6	223.0					
57 (D)	148.0	150.4	163.3	182.5	190.9	204.5	220.9	237.8	246.6	252.2					
58 (D)	140.7	145.5	152.8	170.1	174.5	182.7	197.2	206.1	210.8	213.4					
59 (D)	128.8	135.2	145.1	157.3	171.3	182.4	189.2	199.9	202.1	218.1					
60 (D)	146.5	149.2	161.1	184.7	197.1	213.4	218.3	236.4	239.8	244.0					
N	10	10	10	10	10	10	10	10	10	10	5	5	5	5	5
Mean	139.6	144.5	154.8	172.8	182.6	196.9	205.4	220.3	226.8	236.5	242.8	249.5	258.6	264.8	276.4
S.D.	7.8	7.3	8.0	12.6	13.8	15.8	16.1	18.7	19.4	20.1	22.1	19.6	21.5	25.0	24.7
S.A.	...	...	...	...	...	...	...	...	...	...	0.27	0.38	0.21	0.17	0.11

Parameter, body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

Appendix 5-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in individual males; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period									Day of the recovery period			
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28	1- 4	4- 8	8-11	11-14
1 (R)	8.8	16.4	34.2	25.5	38.3	27.7	28.6	21.8	20.3	22.2	15.2	14.1	11.9
2 (R)	7.6	13.6	28.2	25.3	25.2	17.6	17.4	14.6	13.5	17.4	25.0	13.2	14.4
3 (R)	7.6	18.8	25.7	25.1	30.4	18.2	32.9	21.6	18.6	15.5	23.6	15.7	16.9
4 (R)	7.2	20.4	29.6	23.8	33.4	23.8	28.1	19.7	14.1	13.1	18.7	15.7	7.9
5 (R)	10.2	18.4	35.2	23.4	32.2	27.6	28.6	17.5	15.2	12.1	7.1	8.1	6.7
6 (D)	9.2	15.5	36.1	25.4	45.8	31.1	36.1	19.6	15.8				
7 (D)	9.8	15.9	36.2	22.7	29.6	18.1	29.5	13.8	14.2				
8 (D)	10.1	14.8	35.0	19.3	28.9	23.3	23.3	15.3	20.7				
9 (D)	8.0	12.6	31.0	24.1	40.0	30.0	36.9	24.9	26.9				
10 (D)	4.9	16.3	23.7	21.0	29.1	21.8	25.1	10.8	19.4				
N	10	10	10	10	10	10	10	10	10	5	5	5	5
Mean	8.3	16.3	31.5	23.6	33.3	23.9	28.7	18.0	17.9	16.1	17.9	13.4	11.6
S.D.	1.6	2.4	4.5	2.1	6.3	5.0	5.9	4.3	4.2	4.0	7.2	3.1	4.3
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→K	F→S	F→S	F→S	F→S

Gain in body weight in individual males; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period								
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28
11 (D)	6.9	19.1	38.6	26.7	38.0	15.7	33.9	17.5	17.1
12 (D)	6.1	21.8	41.1	26.8	35.6	26.5	32.9	12.4	28.9
13 (D)	9.9	17.2	38.1	21.8	31.5	22.5	30.6	14.3	20.2
14 (D)	8.9	14.8	36.5	25.0	38.2	23.0	32.8	17.8	17.4
15 (D)	10.2	17.3	29.2	25.8	27.5	22.6	24.9	15.9	10.3
N	5	5	5	5	5	5	5	5	5
Mean	8.4	18.0	36.7	25.2	34.2	22.1	31.0	15.6	18.8
S.D.	1.8	2.6	4.5	2.0	4.6	3.9	3.6	2.3	6.7
S.A.	...	...	...	...	...	...	...	...	...

Parameter, gain in body weight (g)

(D), scheduled sacrifice at the end of the dosing period  
(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 5-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in individual males; dosage of 15 mg/kg

Animal No.	Day of the dosing period								
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28
16 (D)	9.6	16.2	35.1	25.1	24.7	25.0	21.3	17.2	18.2
17 (D)	7.0	16.0	31.4	23.6	30.0	15.4	29.0	12.3	20.6
18 (D)	6.6	15.8	35.4	22.2	30.3	18.5	32.9	18.3	13.2
19 (D)	8.3	16.1	31.5	23.4	36.0	26.3	26.7	14.9	12.7
20 (D)	5.6	12.0	22.8	23.0	29.6	21.7	27.4	15.0	16.2
N	5	5	5	5	5	5	5	5	5
Mean	7.4	15.2	31.2	23.5	30.1	21.4	27.5	15.5	16.2
S.D.	1.6	1.8	5.1	1.1	4.0	4.5	4.2	2.3	3.3
S.A.	...	...	...	...	...	...	...	...	...

Gain in body weight in individual males; dosage of 60 mg/kg

Animal No.	Day of the dosing period								Day of the recovery period				
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28	1- 4	4- 8	8-11	11-14
21 (R)	8.8	19.9	32.0	28.5	28.4	24.9	32.8	13.3	15.4	11.0	18.3	7.0	12.2
22 (R)	8.5	19.6	33.5	24.7	29.7	23.0	29.7	18.6	14.0	5.8	17.2	15.4	11.7
23 (R)	6.3	15.2	38.4	26.0	33.3	21.4	36.3	16.0	17.6	17.3	20.9	10.7	14.8
24 (R)	8.6	21.9	33.9	23.7	34.4	18.3	30.9	18.4	16.9	12.5	22.1	6.8	19.6
25 (R)	7.5	16.3	30.9	20.6	30.9	16.3	27.2	15.8	15.7	11.1	11.8	5.9	12.2
26 (D)	7.4	15.9	26.8	21.7	30.0	18.1	27.9	14.3	13.2				
27 (D)	8.9	17.3	40.4	26.6	38.4	23.9	28.0	24.2	17.2				
28 (D)	8.0	14.2	35.6	26.5	43.9	26.7	35.2	15.3	19.1				
29 (D)	9.0	14.3	38.6	27.7	40.9	29.2	35.7	20.3	18.0				
30 (D)	8.1	16.9	38.4	27.1	36.7	22.3	36.1	15.3	15.7				
N	10	10	10	10	10	10	10	10	10	5	5	5	5
Mean	8.1	17.2	34.9	25.3	34.7	22.4	32.0	17.2	16.3	11.5	18.1	9.2	14.1
S.D.	0.8	2.6	4.2	2.6	5.2	4.0	3.7	3.3	1.8	4.1	4.0	3.9	3.3
S.A.	...	...	...	...	...	...	...	...	...	1.76	0.04	1.87	1.05

Parameter, gain in body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

Appendix 5-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in individual females; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period									Day of the recovery period			
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28	1- 4	4- 8	8-11	11-14
31 (R)	8.5	10.1	17.7	15.1	13.4	12.1	18.3	7.1	6.6	3.0	7.7	12.8	5.2
32 (R)	5.9	12.0	19.9	9.5	15.3	8.1	11.0	5.9	12.8	10.8	0.0	8.8	1.5
33 (R)	6.9	14.6	13.9	14.5	14.4	10.8	15.1	7.4	16.4	13.7	8.7	5.5	11.9
34 (R)	4.4	11.7	21.4	11.6	18.0	19.9	15.4	14.7	15.4	9.6	12.0	-2.9	9.0
35 (R)	3.8	7.0	14.7	5.7	8.5	9.1	13.9	5.8	5.9	4.7	5.8	3.7	4.7
36 (D)	2.7	10.8	15.4	4.4	12.2	6.1	8.6	7.2	2.6				
37 (D)	7.0	8.4	12.8	3.9	7.4	3.0	7.0	-0.2	8.5				
38 (D)	5.4	9.8	18.2	9.5	9.8	7.6	10.3	8.4	13.2				
39 (D)	4.9	10.1	22.2	14.5	11.5	14.4	12.5	12.3	11.5				
40 (D)	10.3	11.6	10.2	13.2	11.3	7.4	13.8	4.9	15.2				
N	10	10	10	10	10	10	10	10	10	5	5	5	5
Mean	6.0	10.6	16.6	10.2	12.2	9.9	12.6	7.4	10.8	8.4	6.8	5.6	6.5
S.D.	2.3	2.1	3.9	4.3	3.2	4.8	3.4	4.0	4.7	4.4	4.4	5.9	4.0
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	F→S	F→S	F→S	F→S

Gain in body weight in individual females; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period								
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28
41 (D)	6.1	9.8	11.8	7.1	11.5	-0.1	11.3	6.8	11.5
42 (D)	8.2	15.0	21.7	6.5	12.9	14.2	21.9	2.5	8.9
43 (D)	6.4	12.7	11.3	13.9	7.2	3.9	13.1	11.0	14.5
44 (D)	5.1	6.9	16.6	0.5	12.1	6.0	8.5	6.5	2.8
45 (D)	7.9	10.8	16.0	12.6	8.9	6.9	8.7	2.0	9.8
N	5	5	5	5	5	5	5	5	5
Mean	6.7	11.0	15.5	8.1	10.5	6.2	12.7	5.8	9.5
S.D.	1.3	3.0	4.2	5.4	2.4	5.2	5.5	3.7	4.3
S.A.	...	...	...	...	...	...	...	...	...

Parameter, gain in body weight (g)

(D), scheduled sacrifice at the end of the dosing period  
(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 5-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Gain in body weight in individual females; dosage of 15 mg/kg

Animal No.	Day of the dosing period								
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28
46 (D)	6.1	11.0	18.6	9.0	12.5	10.2	14.5	6.3	15.9
47 (D)	6.1	8.2	28.3	3.2	13.0	11.2	14.2	2.9	18.5
48 (D)	4.0	14.0	29.4	9.8	19.2	14.4	23.9	17.3	11.4
49 (D)	3.9	10.1	23.4	10.4	20.5	14.5	21.3	8.9	12.8
50 (D)	4.9	2.4	15.6	8.3	10.0	6.4	11.5	9.4	4.4
N	5	5	5	5	5	5	5	5	5
Mean	5.0	9.1	23.1	8.1	15.0	11.3	17.1	9.0	12.6
S.D.	1.1	4.3	6.0	2.9	4.6	3.4	5.3	5.3	5.3
S.A.	...	...	...	...	...	...	...	...	...

Gain in body weight in individual females; dosage of 60 mg/kg

Animal No.	Day of the dosing period								Day of the recovery period				
	1- 2	2- 4	4- 8	8-11	11-15	15-18	18-22	22-25	25-28	1- 4	4- 8	8-11	11-14
51 (R)	8.1	11.0	27.5	12.1	16.8	9.1	20.2	7.2	10.7	-4.6	11.9	11.4	9.0
52 (R)	6.8	10.5	21.0	13.8	18.6	6.1	16.9	6.4	21.0	15.2	10.2	8.6	13.0
53 (R)	5.9	9.5	14.6	8.2	17.7	8.7	11.5	6.6	8.9	7.3	7.6	9.4	2.8
54 (R)	0.2	9.6	12.7	4.3	11.1	15.7	11.7	4.6	12.6	11.6	4.8	0.9	15.7
55 (R)	6.4	8.7	13.1	16.7	16.0	-6.4	19.4	15.2	7.6	4.2	10.9	0.5	17.5
56 (D)	4.8	11.8	18.7	3.8	13.5	9.1	15.3	5.2	8.4				
57 (D)	2.4	12.9	19.2	8.4	13.6	16.4	16.9	8.8	5.6				
58 (D)	4.8	7.3	17.3	4.4	8.2	14.5	8.9	4.7	2.6				
59 (D)	6.4	9.9	12.2	14.0	11.1	6.8	10.7	2.2	16.0				
60 (D)	2.7	11.9	23.6	12.4	16.3	4.9	18.1	3.4	4.2				
N	10	10	10	10	10	10	10	10	10	5	5	5	5
Mean	4.9	10.3	18.0	9.8	14.3	8.5	15.0	6.4	9.8	6.7	9.1	6.2	11.6
S.D.	2.4	1.7	5.1	4.6	3.4	6.6	4.0	3.6	5.6	7.6	2.9	5.1	5.9
S.A.	...	...	...	...	...	...	...	...	...	0.41	0.95	0.17	1.61

Parameter, gain in body weight (g)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 6-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Food consumption in individual males; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period				Day of the recovery period	
	1- 2	8- 9	15-16	22-23	1- 2	8- 9
1 (R)	21.3	21.4	24.5	26.3	28.3	28.1
2 (R)	21.8	23.3	24.7	22.7	25.2	27.3
3 (R)	24.4	23.4	24.2	28.8	29.1	33.1
4 (R)	19.5	20.8	21.0	24.4	24.5	28.3
5 (R)	18.8	19.8	23.4	25.7	26.9	26.3
6 (D)	21.4	23.2	29.0	30.0		
7 (D)	22.4	24.1	22.4	23.9		
8 (D)	22.6	20.5	22.3	24.6		
9 (D)	20.4	22.5	26.3	28.4		
10 (D)	21.5	20.7	21.9	25.4		
N	10	10	10	10	5	5
Mean	21.4	22.0	24.0	26.0	26.8	28.6
S.D.	1.6	1.5	2.4	2.4	2.0	2.6
S.A.	B→O	B→O	B→O	B→K	F→S	F→S

Food consumption in individual males; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period			
	1- 2	8- 9	15-16	22-23
11 (D)	18.2	23.3	25.4	25.8
12 (D)	23.2	26.0	25.5	30.0
13 (D)	20.5	23.4	22.9	23.4
14 (D)	19.8	20.3	21.0	24.0
15 (D)	20.4	21.1	20.7	18.7
N	5	5	5	5
Mean	20.4	22.8	23.1	24.4
S.D.	1.8	2.2	2.3	4.1
S.A.	...	...	...	...

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 6-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Food consumption in individual males; dosage of 15 mg/kg

Animal No.	Day of the dosing period			
	1- 2	8- 9	15-16	22-23
16 (D)	23.4	22.9	21.3	22.8
17 (D)	21.6	22.2	21.9	21.5
18 (D)	20.5	23.1	22.0	21.2
19 (D)	20.4	20.9	27.0	22.1
20 (D)	19.0	20.0	20.2	22.0
N	5	5	5	5
Mean	21.0	21.8	22.5	21.9
S.D.	1.6	1.3	2.6	0.6
S.A.	...	...	...	...

Food consumption in individual males; dosage of 60 mg/kg

Animal No.	Day of the dosing period				Day of the recovery period	
	1- 2	8- 9	15-16	22-23	1- 2	8- 9
21 (R)	22.2	23.4	25.6	22.5	31.0	27.6
22 (R)	22.7	23.6	27.5	24.7	26.9	30.0
23 (R)	18.7	20.8	21.1	21.1	27.0	27.7
24 (R)	21.9	23.1	22.3	28.8	27.8	29.7
25 (R)	21.1	22.6	23.2	22.4	25.2	27.9
26 (D)	20.0	21.5	20.4	21.2		
27 (D)	22.9	25.6	23.7	28.4		
28 (D)	18.6	22.2	24.9	28.5		
29 (D)	17.2	21.9	25.0	25.4		
30 (D)	21.6	23.4	24.2	25.5		
N	10	10	10	10	5	5
Mean	20.7	22.8	23.8	24.9	27.6	28.6
S.D.	2.0	1.3	2.1	3.0	2.1	1.2
S.A.	...	...	...	...	0.60	0.03

Parameter, food consumption (g/day)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 6-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Food consumption in individual females; dosage of 0 mg/kg (vehicle control)

Animal No.	Day of the dosing period				Day of the recovery period	
	1- 2	8- 9	15-16	22-23	1- 2	8- 9
31 (R)	17.5	17.5	17.0	19.6	21.8	23.6
32 (R)	17.1	17.6	16.4	17.7	18.6	16.8
33 (R)	19.4	15.4	19.0	21.2	22.6	19.7
34 (R)	19.1	20.3	22.3	24.6	25.6	26.8
35 (R)	19.6	18.7	16.7	16.5	20.1	21.3
36 (D)	16.8	17.3	16.6	13.8		
37 (D)	18.9	11.8	14.3	14.9		
38 (D)	17.9	15.3	17.6	18.3		
39 (D)	17.3	18.8	20.6	18.7		
40 (D)	18.9	17.4	18.3	21.0		
N	10	10	10	10	5	5
Mean	18.3	17.0	17.9	18.6	21.7	21.6
S.D.	1.0	2.4	2.3	3.2	2.7	3.8
S.A.	B→O	B→O	B→O	B→O	F→S	F→A

Food consumption in individual females; dosage of 3.75 mg/kg

Animal No.	Day of the dosing period			
	1- 2	8- 9	15-16	22-23
41 (D)	15.2	16.6	14.6	13.5
42 (D)	18.8	19.2	19.1	14.4
43 (D)	17.0	19.6	16.2	15.3
44 (D)	17.3	16.0	14.3	14.4
45 (D)	19.9	15.5	17.7	16.5
N	5	5	5	5
Mean	17.6	17.4	16.4	14.8
S.D.	1.8	1.9	2.0	1.1
S.A.	...	...	...	...

Parameter, food consumption (g/day)

(D), scheduled sacrifice at the end of the dosing period  
(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

..., D was not performed

Value in S.A., statistic of D, S or A

## Appendix 6-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Food consumption in individual females; dosage of 15 mg/kg

Animal No.	Day of the dosing period			
	1- 2	8- 9	15-16	22-23
46 (D)	16.9	15.6	18.5	16.8
47 (D)	16.8	14.7	18.1	20.2
48 (D)	18.9	21.3	21.9	21.4
49 (D)	17.9	19.7	19.6	17.8
50 (D)	17.7	14.0	17.4	13.5
N	5	5	5	5
Mean	17.6	17.1	19.1	17.9
S.D.	0.9	3.2	1.8	3.1
S.A.	...	...	...	...

Food consumption in individual females; dosage of 60 mg/kg

Animal No.	Day of the dosing period				Day of the recovery period	
	1- 2	8- 9	15-16	22-23	1- 2	8- 9
51 (R)	18.4	18.6	18.0	16.6	21.5	22.4
52 (R)	17.9	15.7	17.9	18.9	22.0	23.1
53 (R)	16.9	17.6	14.0	19.8	21.2	21.5
54 (R)	16.3	16.3	16.5	15.2	19.8	21.7
55 (R)	19.4	20.0	17.4	17.9	22.9	25.2
56 (D)	16.0	17.1	13.5	16.5		
57 (D)	17.5	18.5	19.9	16.5		
58 (D)	17.7	16.8	16.9	12.8		
59 (D)	15.8	17.2	15.2	16.2		
60 (D)	16.7	19.2	15.8	19.2		
N	10	10	10	10	5	5
Mean	17.3	17.7	16.5	17.0	21.5	22.8
S.D.	1.1	1.3	1.9	2.1	1.1	1.5
S.A.	...	...	...	...	0.20	0.62

Parameter, food consumption (g/day)

(D), scheduled sacrifice at the end of the dosing period

(R), scheduled sacrifice at the end of the recovery period

S.A., statistical analysis for significantly different

..., D was not performed

Value in S.A., statistic of D, S or A

Appendix 7-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 23 of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
1	ly	-	8.0	++	-	++	-	-	+
2	ly	-	7.0	++	-	±	-	-	+
3	ly	-	6.5	++	-	+	-	-	+
4	ly	-	7.5	+	-	+	-	-	±
5	ly	-	8.5	++	-	±	-	-	+
6	ly	-	7.0	++	-	±	-	-	+
7	ly	-	8.5	+	-	±	-	-	±
8	ly	-	8.0	++	-	+	-	-	±
9	ly	-	8.5	+	-	-	-	-	±
10	ly	-	≥9.0	+	-	±	-	-	±
N	10	10	10	10	10	10	10	10	10
S.A.	C	—	D	D	—	C	C	—	C

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
1	-	±	-	-	-
2	-	±	-	-	-
3	-	-	-	-	-
4	-	±	-	-	-
5	-	±	-	-	-
6	-	±	-	-	-
7	-	±	-	-	-
8	-	±	-	-	-
9	-	±	-	-	-
10	-	±	-	-	-
N	10	10	10	10	10
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

D, Dunnett type mean rank test

C, Chi-square

## Appendix 7-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 23 of the dosing period; dosage of 3.75 mg/kg

Animal No.	Color	Turbidity	pH	Quality					
				Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
11	ly	-	7.5	+	-	±	-	-	±
12	y	-	7.0	++	-	+	+	-	+
13	ly	-	≥9.0	+	-	±	-	-	±
14	ly	-	8.5	++	-	±	-	-	±
15	ly	-	8.5	+	-	-	-	-	±
N	5	5	5	5	5	5	5	5	5
S.A.	...	—	0.59	0.72	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
11	-	±	-	-	-
12	-	±	-	-	-
13	-	±	-	-	-
14	-	±	-	-	-
15	-	±	-	-	-
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

Appendix 7-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 23 of the dosing period; dosage of 15 mg/kg

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
16	ly	-	7.0	++	-	+	-	-	+
17	ly	-	7.0	+	-	±	-	-	±
18	ly	-	7.0	++	-	+	-	-	+
19	ly	-	7.0	++	-	+	-	-	±
20	ly	-	7.5	+	-	-	-	-	±
N	5	5	5	5	5	5	5	5	5
S.A.	...	—	1.97	0.00	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
16	-	±	-	-	-
17	-	±	-	-	-
18	-	±	-	-	-
19	-	±	-	-	-
20	-	±	-	-	-
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

## Appendix 7-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 23 of the dosing period; dosage of 60 mg/kg

Animal No.	Color	Turbidity	pH	Quality					
				Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
21	ly	-	7.5	++	-	±	-	-	±
22	ly	-	7.0	++	-	+	+	-	+
23	ly	-	7.5	++	-	±	-	-	+
24	y	-	7.0	++	-	±	-	-	+
25	y	-	7.5	++	-	±	-	-	±
26	y	-	7.0	++	-	+	+	-	+
27	ly	-	8.5	+	-	±	-	-	±
28	ly	-	7.0	+	-	-	-	-	±
29	ly	-	7.5	+	-	+	-	-	±
30	ly	-	7.5	+	-	-	-	-	±
N	10	10	10	10	10	10	10	10	10
S.A.	...	—	1.18	0.00	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
21	-	±	-	-	-
22	-	±	-	-	-
23	-	±	-	-	-
24	-	±	-	-	-
25	-	±	-	-	-
26	-	±	-	-	-
27	-	±	-	-	-
28	-	±	-	-	-
29	-	±	-	-	-
30	-	±	-	-	-
N	10	10	10	10	10
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

## Appendix 7-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 23 of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
31	ly	-	8.0	-	-	-	-	-	±
32	ly	-	8.5	-	-	-	-	-	±
33	ly	-	7.5	+	-	-	-	-	±
34	ly	-	7.5	+	-	±	-	-	+
35	ly	-	5.5	+	-	-	-	-	+
36	ly	-	7.0	+	-	±	-	-	+
37	ly	-	7.0	-	-	-	-	-	±
38	ly	-	7.0	+	-	±	-	-	+
39	ly	-	6.5	-	-	-	-	-	±
40	ly	-	7.0	+	-	-	-	-	+
N	10	10	10	10	10	10	10	10	10
S.A.	C	—	D	C	—	C	C	—	C

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
31	-	-	-	-	-
32	-	-	-	-	-
33	-	±	-	-	-
34	-	±	-	-	-
35	-	±	-	-	-
36	-	±	-	-	-
37	-	±	-	-	-
38	-	±	-	-	-
39	-	±	-	-	-
40	-	±	-	-	-
N	10	10	10	10	10
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

D, Dunnett type mean rank test

C, Chi-square

## Appendix 7-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 23 of the dosing period; dosage of 3.75 mg/kg

Animal No.	Color	Turbidity	pH	Quality					Urobilinogen
				Protein	Glucose	Ketone	Bilirubin	Occult blood	
41	ly	-	7.0	-	-	-	-	-	±
42	ly	-	5.5	++	-	±	-	-	+
43	ly	-	6.5	+	-	±	-	-	+
44	ly	-	7.0	+	-	±	-	-	+
45	ly	-	7.5	±	-	-	-	-	±
N	5	5	5	5	5	5	5	5	5
S.A.	...	—	0.98	...	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
41	-	±	-	-	-
42	-	-	-	-	-
43	-	±	-	-	-
44	-	±	-	-	-
45	-	±	-	-	-
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

## Appendix 7-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 23 of the dosing period; dosage of 15 mg/kg

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
46	ly	-	8.5	±	-	-	-	-	±
47	ly	-	8.0	++	-	±	-	-	+
48	ly	-	7.0	±	-	-	-	-	±
49	ly	-	7.5	++	-	±	-	-	+
50	ly	-	6.5	+	-	±	-	-	+
N	5	5	5	5	5	5	5	5	5
S.A.	...	—	0.71	...	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
46	-	±	-	-	-
47	-	±	-	-	-
48	-	-	-	-	-
49	-	±	-	-	-
50	-	±	-	-	-
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

## Appendix 7-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 23 of the dosing period; dosage of 60 mg/kg

Animal No.	Color	Turbidity	pH	Quality					
				Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
51	ly	-	≥9.0	+	-	-	-	-	+
52	y	-	7.0	++	-	±	+	-	+
53	ly	-	7.5	+	-	-	-	-	±
54	y	-	6.0	++	-	±	+	-	+
55	ly	-	6.5	+	-	-	-	-	±
56	ly	-	7.5	-	-	-	-	-	±
57	ly	-	6.5	+	-	±	+	-	+
58	ly	-	6.0	++	-	±	-	-	+
59	ly	-	7.5	-	-	-	-	-	±
60	ly	-	7.5	+	-	-	-	-	±
N	10	10	10	10	10	10	10	10	10
S.A.	...	—	0.26	...	—	...	...	—	...

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
51	-	±	-	-	-
52	-	±	-	-	-
53	-	±	-	-	-
54	-	±	-	-	-
55	-	±	-	-	-
56	-	±	-	-	-
57	-	±	-	-	-
58	-	-	-	-	-
59	-	±	-	-	-
60	-	±	-	-	-
N	10	10	10	10	10
S.A.	—	—	—	—	—

Color: ly, light yellow; y, yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., Dunnett type mean rank test was not performed

## Appendix 7-2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 11 of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
1	ly	-	7.0	+	-	+	-	-	±
2	ly	-	7.0	+	-	+	-	-	±
3	ly	-	7.0	+	-	-	-	-	±
4	ly	-	7.0	++	-	+	-	-	+
5	ly	-	7.0	++	-	+	-	-	+
N	5	5	5	5	5	5	5	5	5
S.A.	—	—	W	W	—	W	—	—	W

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
1	-	±	-	-	-
2	-	±	-	-	-
3	-	±	-	-	-
4	-	±	-	-	-
5	-	±	-	-	±
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

W, Wilcoxon rank sum test

## Appendix 7-2-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual males on day 11 of the recovery period; dosage of 60 mg/kg

Animal No.	Color	Turbidity	pH	Quality					
				Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
21	ly	-	8.5	+	-	-	-	-	±
22	ly	-	7.0	++	-	±	-	-	+
23	ly	-	7.0	++	-	+	-	-	+
24	ly	-	7.5	+	-	+	-	-	+
25	ly	-	7.0	+	-	±	-	-	+
N	5	5	5	5	5	5	5	5	5
S.A.	—	—	1.34	-0.12	—	0.83	—	—	1.10

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
21	-	±	-	-	-
22	-	±	-	-	-
23	-	±	-	-	-
24	-	±	-	-	-
25	-	±	-	-	±
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

## Appendix 7-2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 11 of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Color	Turbidity	pH	Protein	Quality				
					Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
31	ly	-	8.0	-	-	-	-	-	±
32	ly	-	8.5	-	-	-	-	-	±
33	ly	-	7.5	-	-	-	-	-	±
34	ly	-	7.5	-	-	-	-	-	±
35	ly	-	6.5	-	-	-	-	-	±
N	5	5	5	5	5	5	5	5	5
S.A.	—	—	W	W	—	—	—	—	W

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
31	-	±	-	-	-
32	-	-	-	-	-
33	-	±	-	-	-
34	-	±	-	-	-
35	-	-	-	-	-
N	5	10	10	10	10
S.A.	—	—	—	—	—

Color: ly, light yellow

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

S.A., statistical analysis for significantly different

—, S.A. was not performed

W, Wilcoxon rank sum test

## Appendix 7-2-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Urinalysis in individual females on day 11 of the recovery period; dosage of 60 mg/kg

Animal No.	Quality								
	Color	Turbidity	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen
51	ly	-	7.5	-	-	-	-	-	±
52	ly	-	7.5	-	-	-	-	-	±
53	ly	-	8.0	±	-	-	-	-	+
54	ly	-	7.5	+	-	-	-	-	+
55	ly	-	7.0	-	-	-	-	-	±
N	5	5	5	5	5	5	5	5	5
S.A.	—	—	0.33	1.34	—	—	—	—	1.35

Animal No.	Microscopic examination of urinary sediment				
	Red blood cells	Crystal	Cast	White blood cells	Epithelial cells
51	-	±	-	-	-
52	-	±	-	-	-
53	-	±	-	-	-
54	-	±	-	-	-
55	-	±	-	-	-
N	5	5	5	5	5
S.A.	—	—	—	—	—

Color: ly, light yellow

S.A., statistical analysis for significantly different

Turbidity, ketone, bilirubin and occult blood: -, negative; ±, trace; +, slight; ++, moderate; +++, marked

—, S.A. was not performed

Protein: -, negative; ±, trace; +, 30 mg/dL; ++, 100 mg/dL

Glucose: -, negative

Urobilinogen: ±, 0.1 EU/dL; +, 1.0 EU/dL

Crystal and epithelial cells: -, not observed; ±, a few

Red blood cells, white blood cells and Cast (count/3 visual field): -, not observed; ±, 1-10; +, 10-100

Appendix 8-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal	RBC	Hemoglobin	Hematocrit	MCV	MCH	MCHC	Reticulocyte	Platelet	PT	APTT
No.	(x10 <sup>4</sup> /µL)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(%)	(x10 <sup>4</sup> /µL)	(sec)	(sec)
6	745	15.1	45.7	61.3	20.3	33.0	2.0	114.2	21.4	25.7
7	754	14.8	44.1	58.5	19.6	33.5	1.5	120.0	14.6	21.3
8	717	14.1	42.4	59.2	19.7	33.4	1.6	103.6	22.1	26.5
9	660	13.8	41.1	62.2	20.9	33.5	1.7	94.6	14.3	21.1
10	768	15.6	46.5	60.5	20.3	33.5	2.4	121.1	17.2	21.6
N	5	5	5	5	5	5	5	5	5	5
Mean	729	14.7	44.0	60.3	20.2	33.4	1.8	110.7	17.9	23.2
S.D.	43	0.7	2.2	1.5	0.5	0.2	0.4	11.4	3.7	2.6
S.A.	B→O	B→O→D	B→O	B→O	B→O	B→O	B→O	B→O	B→O→D	B→O

Animal	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte
No.	(x100/µL)	(%)	(%)	(%)	(%)	(%)
6	86.7	11	1	0	9	79
7	102.0	15	1	0	2	81
8	75.8	14	1	0	3	82
9	99.6	16	1	0	4	79
10	56.8	24	1	0	4	71
N	5	5	5	5	5	5
Mean	84.2	16	1	0	4	78
S.D.	18.6	5	0	0	3	4
S.A.	B→O	B→O→D	B→K	—	B→K	B→O→D

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 8-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
11	774	15.6	45.6	58.9	20.1	34.2	2.6	107.1	17.5	23.5
12	741	15.4	45.6	61.6	20.8	33.9	2.7	107.0	17.9	21.8
13	791	15.9	47.6	60.1	20.1	33.5	1.6	114.5	25.2	27.9
14	694	14.5	43.5	62.6	20.9	33.4	3.5	120.1	19.8	26.3
15	718	14.3	43.0	59.9	20.0	33.3	2.1	99.0	20.9	26.2
N	5	5	5	5	5	5	5	5	5	5
Mean	744	15.1	45.1	60.6	20.4	33.7	2.5	109.5	20.3	25.1
S.D.	40	0.7	1.9	1.5	0.4	0.4	0.7	8.1	3.1	2.4
S.A.	...	1.21	...	...	...	...	...	...	1.14	...

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
11	111.0	8	0	0	2	89
12	86.0	14	1	0	5	80
13	76.3	13	1	0	3	83
14	86.6	8	1	0	5	86
15	70.2	16	1	0	4	80
N	5	5	5	5	5	5
Mean	86.0	12	1	0	4	84
S.D.	15.6	4	0	0	1	4
S.A.	...	1.92	...	—	...	2.32

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 8-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the dosing period; dosage of 15 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
16	722	14.4	42.8	59.3	19.9	33.6	2.2	113.7	24.5	23.8
17	713	14.0	41.7	58.5	19.6	33.5	2.0	121.9	20.4	24.8
18	668	13.3	39.6	59.4	19.9	33.5	3.2	124.8	22.9	24.7
19	756	14.3	43.4	57.4	18.9	32.9	1.7	101.9	23.5	24.8
20	692	14.6	43.5	62.9	21.1	33.5	2.6	108.6	27.2	28.8
N	5	5	5	5	5	5	5	5	5	5
Mean	710	14.1	42.2	59.5	19.9	33.4	2.3	114.2	23.7	25.4
S.D.	33	0.5	1.6	2.1	0.8	0.3	0.6	9.4	2.5	2.0
S.A.	...	1.48	...	...	...	...	...	...	2.82 *	...

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
16	107.0	7	1	0	2	90
17	61.1	9	1	0	2	88
18	108.0	8	0	0	2	90
19	72.0	8	1	0	3	88
20	103.0	12	1	0	2	86
N	5	5	5	5	5	5
Mean	90.2	9	1	0	2	88
S.D.	22.0	2	0	0	0	2
S.A.	...	3.30 *	...	—	...	4.45 **

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

## Appendix 8-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the dosing period; dosage of 60 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
26	679	13.9	41.6	61.3	20.5	33.4	2.4	116.2	25.1	24.4
27	717	14.5	43.3	60.4	20.2	33.4	2.4	118.1	22.9	28.6
28	639	13.6	40.1	62.8	21.3	33.9	2.3	122.0	30.5	27.5
29	713	14.2	42.9	60.1	19.9	33.2	1.6	126.2	26.0	27.8
30	708	14.5	42.9	60.6	20.5	33.9	3.8	104.2	21.0	23.1
N	5	5	5	5	5	5	5	5	5	5
Mean	691	14.1	42.2	61.0	20.5	33.6	2.5	117.3	25.1	26.3
S.D.	33	0.4	1.3	1.1	0.5	0.3	0.8	8.3	3.6	2.4
S.A.	...	1.42	...	...	...	...	...	...	3.50 **	...

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
26	116.0	13	1	0	2	84
27	64.2	15	1	0	3	81
28	73.9	11	1	0	2	85
29	46.3	16 §	1 §	0 §	7 §	76 §
30	114.0	18	1	0	2	79
N	5	5	5	5	5	5
Mean	82.9	15	1	0	3	81
S.D.	31.0	3	0	0	2	4
S.A.	...	0.64	...	—	...	1.16

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

§: the re-measurement was carried out and the re-measurement value was employed.

Appendix 8-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
36	698	14.3	42.7	61.1	20.5	33.6	1.4	109.4	13.0	24.6
37	732	14.1	41.7	57.0	19.3	33.8	0.8	111.3	12.2	19.2
38	691	13.7	40.8	59.0	19.9	33.7	1.8	111.6	12.6	18.3
39	735	14.5	43.3	58.8	19.8	33.6	1.2	100.5	13.0	21.3
40	695	14.2	41.8	60.2	20.4	33.9	2.1	126.1	12.2	22.5
N	5	5	5	5	5	5	5	5	5	5
Mean	710	14.2	42.1	59.2	20.0	33.7	1.5	111.8	12.6	21.2
S.D.	21	0.3	1.0	1.6	0.5	0.1	0.5	9.2	0.4	2.5
S.A.	B→O	B→O	B→O	B→O	B→K	B→K	B→K	B→O	B→O	B→O

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
36	38.8	21	2	0	3	74
37	42.3	8	1	0	3	88
38	54.5	8	1	0	2	90
39	56.1	9	1	0	5	85
40	108.0	10	1	0	3	87
N	5	5	5	5	5	5
Mean	59.9	11	1	0	3	85
S.D.	27.9	6	0	0	1	6
S.A.	B→O	B→O	B→O	—	B→O→D	B→O→D

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 8-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the dosing period; dosage of 3.75 mg/kg

Animal	RBC	Hemoglobin	Hematocrit	MCV	MCH	MCHC	Reticulocyte	Platelet	PT	APTT
No.	(x10 <sup>4</sup> /µL)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(%)	(x10 <sup>4</sup> /µL)	(sec)	(sec)
41	755	14.3	43.0	57.0	18.9	33.1	1.4	122.5	15.3	23.1
42	713	14.8	43.7	61.3	20.8	33.9	0.7	100.5	12.4	20.4
43	638	13.4	38.2	59.9	21.0	35.1	3.1	117.8	12.3	20.0
44	692	14.5	42.9	62.0	20.9	33.8	0.7	123.8	12.6	25.1
45	703	13.8	41.5	59.1	19.6	33.1	1.0	107.5	10.8	17.8
N	5	5	5	5	5	5	5	5	5	5
Mean	700	14.2	41.9	59.9	20.2	33.8	1.4	114.4	12.7	21.3
S.D.	42	0.6	2.2	2.0	0.9	0.8	1.0	10.1	1.6	2.8
S.A.	...	...	...	...	...	...	...	...	...	...

Animal	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte
No.	(x100/µL)	(%)	(%)	(%)	(%)	(%)
41	57.1	20	1	0	3	77
42	53.8	10	1	0	4	85
43	56.2	38	2	0	4	56
44	60.9	17	1	0	4	77
45	77.8	6	1	0	1	92
N	5	5	5	5	5	5
Mean	61.2	18	1	0	3	77
S.D.	9.6	12	0	0	1	14
S.A.	...	...	...	—	0.00	1.28

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 8-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the dosing period; dosage of 15 mg/kg

Animal		RBC	Hemoglobin	Hematocrit	MCV	MCH	MCHC	Reticulocyte	Platelet	PT	APTT
No.		(x10 <sup>4</sup> /µL)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(%)	(x10 <sup>4</sup> /µL)	(sec)	(sec)
46	a)	(279)	(5.7)	(16.5)	(59.3)	(20.4)	(34.4)	(6.9)	(80.9)	(10.2)	(18.9)
47		684	13.8	41.0	59.9	20.1	33.6	1.6	101.8	11.8	20.6
48		706	14.3	42.9	60.7	20.2	33.3	0.8	123.4	12.9	20.6
49		723	14.4	43.0	59.5	20.0	33.6	0.9	113.4	12.0	21.9
50		722	14.5	43.3	60.0	20.1	33.6	1.3	114.4	12.6	21.3
N		4	4	4	4	4	4	4	4	4	4
Mean		709	14.3	42.6	60.0	20.1	33.5	1.2	113.3	12.3	21.1
S.D.		18	0.3	1.0	0.5	0.1	0.2	0.4	8.9	0.5	0.6
S.A.		...	...	...	...	...	...	...	...	...	...

Animal		WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte
No.		(x100/µL)	(%)	(%)	(%)	(%)	(%)
46	a)	(47.9)	(35)	(1)	(0)	(3)	(62)
47		42.0	23	1	0	3	73
48		91.2	10	1	0	8	82
49		55.1	27	2	0	8	63
50		55.1	34	2	0	5	59
N		4	4	4	4	4	4
Mean		60.9	24	2	0	6	69
S.D.		21.2	10	1	0	2	10
S.A.		...	...	...	—	2.79 *	2.54

a), values in parenthesis were excepted from statistical analysis because this animal was observed bleeding from claw on day of necropsy

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

## Appendix 8-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the dosing period; dosage of 60 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
56	709	14.2	42.4	59.8	20.0	33.4	1.6	106.5	13.0	22.6
57	645	13.6	40.8	63.3	21.1	33.3	1.6	104.4	11.7	22.3
58	646	13.1	39.0	60.3	20.2	33.5	1.1	97.7	12.9	23.7
59	689	14.4	42.6	61.8	20.9	33.9	1.4	96.2	14.0	25.5
60	780	15.1	45.3	58.0	19.4	33.4	1.3	128.0	14.3	26.4
N	5	5	5	5	5	5	5	5	5	5
Mean	694	14.1	42.0	60.6	20.3	33.5	1.4	106.6	13.2	24.1
S.D.	56	0.8	2.3	2.0	0.7	0.2	0.2	12.7	1.0	1.8
S.A.	...	...	...	...	...	...	...	...	...	...

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
56	57.8	10	2	0	1	87
57	72.4	5	1	0	3	91
58	48.3	7	1	0	1	91
59	66.4	14	1	0	3	83
60	75.3	10	1	0	2	87
N	5	5	5	5	5	5
Mean	64.0	9	1	0	2	88
S.D.	11.1	3	0	0	1	3
S.A.	...	...	...	—	1.27	0.52

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 8-2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
1	823	15.5	46.3	56.3	18.8	33.4	2.5	107.1	39.1	30.2 ◇
2	810	15.5	46.1	56.9	19.2	33.7	3.8	118.0	19.0	24.0
3	807	14.9	45.3	56.2	18.4	32.8	2.4	135.9	13.6	20.8
4	803	15.5	44.7	55.7	19.2	34.5	2.8	122.7	13.3	21.7
5	789	14.9	44.1	55.9	18.8	33.7	2.4	120.1	32.1	27.1
N	5	5	5	5	5	5	5	5	5	5
Mean	806	15.3	45.3	56.2	18.9	33.6	2.8	120.8	23.4	24.8
S.D.	12	0.3	0.9	0.5	0.3	0.6	0.6	10.3	11.6	3.9
S.A.	F→S	F→S	F→S	F→A	F→S	F→S	F→S	F→S	F→S	F→A

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
1	138.0	6	1	0	3	89
2	126.0	15	1	0	3	81
3	116.0	9	1	0	3	86
4	88.8	9	1	0	7	83
5	125.0	7	1	0	3	89
N	5	5	5	5	5	5
Mean	118.8	9	1	0	4	86
S.D.	18.5	3	0	0	2	4
S.A.	F→S	F→S	—	—	F→S	F→S

◇: the re-measurement was carried out and the mean value in three measurements was employed.

S.A., statistical analysis for significantly different

F, F-test

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

## Appendix 8-2-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual males at the end of the recovery period; dosage of 60 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
21	812	14.9	44.9	55.3	18.3	33.2	3.4	126.6	32.8	27.4
22	735	13.9	41.0	55.8	18.9	33.8	2.7	104.7	18.3	23.6
23	763	15.2	46.1	60.3	19.9	33.0	1.6	81.9	17.9	24.7
24	740	14.7	43.7	59.0	19.8	33.5	4.8	103.2	22.2	25.4
25	775 §	14.1 §	42.8 §	55.2 §	18.2 §	33.0 §	4.1	110.0 §	22.7	24.5
N	5	5	5	5	5	5	5	5	5	5
Mean	765	14.6	43.7	57.1	19.0	33.3	3.3	105.3	22.8	25.1
S.D.	31	0.5	2.0	2.4	0.8	0.3	1.2	16.0	6.0	1.4
S.A.	2.78 *	2.46 *	1.65	0.85	0.36	1.01	0.88	1.81	0.11	0.19

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
21	114.0	10	1	0	8	81
22	149.0	12	1	0	3	84
23	126.0	8	1	0	3	89
24	157.0	7	1	0	4	89
25	78.7 §	20 §	1 §	0 §	3 §	77 §
N	5	5	5	5	5	5
Mean	124.9	11	1	0	4	84
S.D.	31.1	5	0	0	2	5
S.A.	0.38	0.79	—	—	0.32	0.57

§: the re-measurement was carried out and the re-measurement value was employed.

S.A., statistical analysis for significantly different

—, S.A. was not performed

\*, significant difference from control, p&lt;0.05

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

## Appendix 8-2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	RBC (x10 <sup>4</sup> /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /μL)	PT (sec)	APTT (sec)
31	739	13.9	41.7	56.5	18.9	33.4	1.3	109.0	12.4	19.9
32	756	14.9	43.8	58.0	19.8	34.1	1.2	124.1	12.7	19.4
33	730 §	14.2 §	41.9 §	57.4 §	19.4 §	33.8 §	0.9	103.2 §	12.5	20.1
34	738	14.4	43.1	58.4	19.5	33.5	1.5	97.8	11.9	20.9
35	763	14.5	43.7	57.3	19.1	33.2	1.9	104.0	11.9	18.1
	5	5	5	5	5	5	5	5	5	5
Mean	745	14.4	42.8	57.5	19.3	33.6	1.4	107.6	12.3	19.7
S.D.	14	0.4	1.0	0.7	0.4	0.4	0.4	10.0	0.4	1.0
S.A.	F→S	F→S	F→S	F→A	F→S	F→S	F→S	F→S	F→S	F→S

Animal No.	WBC (x100/μL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
31	51.6	9	1	0	5	85
32	78.2	6	1	0	1	91
33	84.6 §	6 §	1 §	0 §	2 §	91 §
34	58.2	18	1	0	6	75
35	70.6	9	2	0	6	84
	5	5	5	5	5	5
Mean	68.6	10	1	0	4	85
S.D.	13.7	5	0	0	2	7
S.A.	F→S	F→S	—	—	F→S	F→S

§: the re-measurement was carried out and the re-measurement value was employed.

S.A., statistical analysis for significantly different

—, S.A. was not performed

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

## Appendix 8-2-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Hematological findings in individual females at the end of the recovery period; dosage of 60 mg/kg

Animal No.	RBC (x10 <sup>4</sup> /µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Reticulocyte (%)	Platelet (x10 <sup>4</sup> /µL)	PT (sec)	APTT (sec)
51	689	13.2	38.6	56.0	19.1	34.2	2.1	116.3	11.9	19.9
52	686	14.0	41.2	60.1	20.4	33.9	2.3	103.2	13.0	18.1
53	727	14.2	41.9	57.7	19.5	33.9	1.0	124.4	11.9	18.5
54	742	14.6	44.0	59.4	19.7	33.2	2.0	107.3	12.6	18.6
55	732	13.5	39.6	54.2	18.5	34.1	2.3	110.2	12.0	21.0
N	5	5	5	5	5	5	5	5	5	5
Mean	715	13.9	41.1	57.5	19.4	33.9	1.9	112.3	12.3	19.2
S.D.	26	0.6	2.1	2.4	0.7	0.4	0.5	8.3	0.5	1.2
S.A.	2.29	1.61	1.72	0.04	0.28	1.10	1.98	0.80	0.00	0.65

Animal No.	WBC (x100/µL)	Neutrophil (%)	Eosinophil (%)	Basophil (%)	Monocyte (%)	Lymphocyte (%)
51	56.4	5	1	0	2	93
52	69.1	11	1	0	2	86
53	62.5	13	1	0	2	84
54	87.7	16	1	0	5	78
55	78.3	7	1	0	3	89
N	5	5	5	5	5	5
Mean	70.8	10	1	0	3	86
S.D.	12.5	4	0	0	1	6
S.A.	0.26	0.27	—	—	1.00	0.21

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

## Appendix 9-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
6	5.6	3.7	1.95	13	0.7	182	32	19	0.02
7	5.5	3.5	1.75	15	0.5	147	50	15	0.02
8	5.5	3.6	1.89	18	0.7	150	56	35	0.03
9	5.4	3.7	2.18	15	0.6	154	48	22	0.02
10	5.7	3.6	1.71	21	0.7	164	36	25	0.00
N	5	5	5	5	5	5	5	5	5
Mean	5.5	3.6	1.90	16	0.6	159	44	23	0.02
S.D.	0.1	0.1	0.19	3	0.1	14	10	8	0.01
S.A.	B→O→D	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→K

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
6	7.1	9.6	142.5	3.95	104.9	416	21	59	0
7	6.7	9.3	144.1	3.86	106.7	267	28	51	1
8	7.8	9.5	142.5	4.08	106.3	316	18	46	1
9	7.0	9.3	142.8	3.57	105.3	344	32	64	0
10	6.6	9.2	142.6	3.87	106.4	427	22	59	3
N	5	5	5	5	5	5	5	5	5
Mean	7.0	9.4	142.9	3.87	105.9	354	24	56	1
S.D.	0.5	0.2	0.7	0.19	0.8	68	6	7	1
S.A.	B→O	B→O	B→O	B→O	B→O	B→O→D	B→O	B→O	B→O

S.A., statistical analysis for significantly different

B, Bartlett's test

—, S.A. was not performed

O, one-way layout analysis of variance

..., D was not performed

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 9-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
11	5.8	3.8	1.90	15	0.7	164	51	49	0.02
12	5.5	3.4	1.62	14	0.6	159	42	17	0.01
13	5.7	4.1	2.56	15	0.7	174	50	25	0.02
14	5.3	3.5	1.94	10	0.6	163	46	25	0.02
15	5.4	3.6	2.00	15	0.5	150	39	25	0.02
N	5	5	5	5	5	5	5	5	5
Mean	5.5	3.7	2.00	14	0.6	162	46	28	0.02
S.D.	0.2	0.3	0.34	2	0.1	9	5	12	0.00
S.A.	0.00	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	$\gamma$ -GTP (U/L)
11	7.1	9.6	140.6	4.11	102.8	191	18	55	0
12	7.2	9.5	141.9	3.77	106.1	278	39	81	1
13	7.2	9.9	142.0	4.21	104.7	305	24	43	0
14	6.8	9.2	142.1	3.92	106.4	293	26	54	2
15	6.4	9.3	143.1	3.37	107.0	363	26	69	1
N	5	5	5	5	5	5	5	5	5
Mean	6.9	9.5	141.9	3.88	105.4	286	27	60	1
S.D.	0.3	0.3	0.9	0.33	1.7	62	8	15	1
S.A.	...	...	...	...	...	2.06	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 9-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
16	5.3	3.4	1.79	16	0.7	143	47	44	0.02
17	5.1	3.5	2.19	12	0.6	154	28	17	0.02
18	5.1	3.4	2.00	13	0.6	142	34	18	0.02
19	5.5	3.9	2.44	10	0.6	155	52	31	0.02
20	5.3	3.7	2.31	13	0.6	151	39	17	0.02
N	5	5	5	5	5	5	5	5	5
Mean	5.3	3.6	2.15	13	0.6	149	40	25	0.02
S.D.	0.2	0.2	0.26	2	0.0	6	10	12	0.00
S.A.	2.94 *	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
16	7.9	9.2	143.1	4.02	107.0	407	20	53	1
17	6.6	9.0	142.9	3.58	106.5	440	23	55	1
18	7.4	9.4	141.5	3.86	104.9	416	22	58	1
19	7.0	9.2	142.8	3.74	106.2	381	23	68	2
20	7.3	9.2	141.7	3.92	106.9	419	28	61	0
N	5	5	5	5	5	5	5	5	5
Mean	7.2	9.2	142.4	3.82	106.3	413	23	59	1
S.D.	0.5	0.1	0.7	0.17	0.8	21	3	6	1
S.A.	...	...	...	...	...	1.78	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

## Appendix 9-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
26	5.4	3.4	1.70	17	0.7	154	44	18	0.02
27	5.3	3.6	2.12	18	0.7	164	34	10	0.00
28	5.3	3.5	1.94	14	0.7	164	42	16	0.01
29	5.2	3.6	2.25	14	0.7	158	60	27	0.02
30	5.4	3.4	1.70	12	0.6	166	38	15	0.03
N	5	5	5	5	5	5	5	5	5
Mean	5.3	3.5	1.94	15	0.7	161	44	17	0.02
S.D.	0.1	0.1	0.25	2	0.0	5	10	6	0.01
S.A.	2.31	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	$\gamma$ -GTP (U/L)
26	8.5	9.4	141.3	4.32	104.4	269	26	62	1
27	6.7	8.8	141.3	3.90	104.4	300	20	57	2
28	7.4	9.6	142.3	4.10	104.9	301	28	57	0
29	6.9	9.4	143.7	3.64	105.5	192	23	49	0
30	6.0	9.3	143.1	3.52	106.6	278	22	54	1
N	5	5	5	5	5	5	5	5	5
Mean	7.1	9.3	142.3	3.90	105.2	268	24	56	1
S.D.	0.9	0.3	1.1	0.33	0.9	45	3	5	1
S.A.	...	...	...	...	...	2.61 *	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

Appendix 9-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
36	6.1	3.8	1.65	18	0.7	132	38	12	0.03
37	5.6	3.8	2.11	22	0.7	121	44	7	0.05
38	5.5	3.9	2.44	25	0.7	124	46	10	0.07
39	5.7	3.9	2.17	17	0.6	141	72	23	0.03
40	6.1	4.3	2.39	21	0.6	134	58	41	0.05
N	5	5	5	5	5	5	5	5	5
Mean	5.8	3.9	2.15	21	0.7	130	52	19	0.05
S.D.	0.3	0.2	0.31	3	0.1	8	14	14	0.02
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→K	B→O

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
36	5.8	9.1	140.7	3.38	108.0	145	23	58	1
37	6.4	8.6	140.9	4.26	107.9	202	20	67	1
38	7.2	9.2	141.4	3.74	107.7	310	22	53	1
39	5.6	9.2	140.0	3.93	105.2	225	19	55	1
40	6.6	9.9	142.1	3.49	106.8	230	21	66	3
N	5	5	5	5	5	5	5	5	5
Mean	6.3	9.2	141.0	3.76	107.1	222	21	60	1
S.D.	0.6	0.5	0.8	0.35	1.2	59	2	6	1
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 9-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
41	5.2	3.4	1.89	16	0.7	137	38	7	0.03
42	5.5	3.9	2.44	19	0.7	121	55	18	0.06
43	5.4	3.8	2.38	21	0.7	166	45	13	0.08
44	5.8	3.7	1.76	23	0.7	106	37	6	0.03
45	5.8	4.0	2.22	18	0.6	148	55	13	0.03
N	5	5	5	5	5	5	5	5	5
Mean	5.5	3.8	2.14	19	0.7	136	46	11	0.05
S.D.	0.3	0.2	0.30	3	0.0	23	9	5	0.02
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
41	6.9	9.1	144.0	3.31	109.6	244	22	70	1
42	6.2	9.5	140.0	4.06	105.1	212	16	53	1
43	6.1	9.0	141.7	4.06	108.7	270	26	61	1
44	6.4	9.2	141.7	3.67	108.5	140	17	55	2
45	6.9	9.6	141.3	3.62	107.5	167	23	53	2
N	5	5	5	5	5	5	5	5	5
Mean	6.5	9.3	141.7	3.74	107.9	207	21	58	1
S.D.	0.4	0.3	1.4	0.32	1.7	54	4	7	1
S.A.	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 9-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
46 a)	(5.5)	(3.8)	(2.24)	(23)	(0.6)	(222)	(67)	(197)	(0.01)
47	6.0	4.1	2.16	22	0.7	128	75	20	0.03
48	5.9	3.8	1.81	17	0.6	163	52	45	0.05
49	5.5	3.4	1.62	20	0.6	106	54	12	0.03
50	6.0	3.5	1.40	20	0.7	129	43	9	0.03
N	4	4	4	4	4	4	4	4	4
Mean	5.9	3.7	1.75	20	0.7	132	56	22	0.04
S.D.	0.2	0.3	0.32	2	0.1	24	14	16	0.01
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
46 a)	(6.8)	(9.5)	(138.2)	(3.98)	(104.8)	(298)	(22)	(40)	(1)
47	6.2	9.5	139.0	3.69	106.0	187	26	63	2
48	6.3	9.8	141.9	3.33	105.3	199	21	52	1
49	5.8	9.6	140.2	3.58	106.3	220	22	54	1
50	7.7	9.3	141.4	3.85	107.9	221	24	55	1
N	4	4	4	4	4	4	4	4	4
Mean	6.5	9.6	140.6	3.61	106.4	207	23	56	1
S.D.	0.8	0.2	1.3	0.22	1.1	17	2	5	1
S.A.	...	...	...	...	...	...	...	...	...

a), values in parenthesis were excepted from statistical analysis because this animal was observed bleeding from claw on day of necropsy

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 9-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
56	5.7	3.8	2.00	17	0.7	140	53	11	0.03
57	6.1	4.2	2.21	20	0.7	114	60	18	0.05
58	5.8	3.7	1.76	18	0.6	123	38	9	0.04
59	5.9	3.8	1.81	18	0.6	134	58	12	0.03
60	5.7	4.0	2.35	22	0.7	133	54	10	0.03
N	5	5	5	5	5	5	5	5	5
Mean	5.8	3.9	2.03	19	0.7	129	53	12	0.04
S.D.	0.2	0.2	0.25	2	0.1	10	9	4	0.01
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	$\gamma$ -GTP (U/L)
56	6.6	9.1	140.9	4.09	107.3	148	22	55	2
57	6.5	9.6	140.2	3.88	105.3	193	21	52	2
58	7.0	9.6	141.0	3.74	106.8	181	32	73	1
59	6.3	9.4	141.2	3.45	108.2	254	22	58	1
60	7.5	9.6	142.7	3.52	108.1	148	25	58	1
N	5	5	5	5	5	5	5	5	5
Mean	6.8	9.5	141.2	3.74	107.1	185	24	59	1
S.D.	0.5	0.2	0.9	0.26	1.2	44	5	8	1
S.A.	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

Appendix 9-2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
1	5.9	3.7	1.68	16	0.8	178	44	24	0.05
2	5.7	3.4	1.48	14	0.6	165	46	31	0.08
3	5.8	3.6	1.64	17	0.7	142	48	24	0.04
4	5.8	3.9	2.05	17	0.6	171	65	39	0.04
5	5.7	3.7	1.85	16	0.6	145	57	27	0.05
N	5	5	5	5	5	5	5	5	5
Mean	5.8	3.7	1.74	16	0.7	160	52	29	0.05
S.D.	0.1	0.2	0.22	1	0.1	16	9	6	0.02
S.A.	F→A	F→S	F→S	F→S	F→S	F→S	F→A	F→S	F→S

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
1	7.7	8.7 #	141.3	3.88	104.3	228	33	72	1
2	7.3	9.2	143.5	3.90	106.6	284	24	54	1
3	7.0	9.2	143.3	3.89	105.5	273	21	59	1
4	6.8	9.5	143.5	4.52	105.5	188	20	56	2
5	6.5	9.0	143.8	3.92	106.8	250	30	69	4
N	5	5	5	5	5	5	5	5	5
Mean	7.1	9.1	143.1	4.02	105.7	245	26	62	2
S.D.	0.5	0.3	1.0	0.28	1.0	38	6	8	1
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	—

#: the first measured value was either higher than the upper control limit, or lower than the lower control limit stated in the standard operating procedures.

One re-measurement was carried out, and the difference between the values in two measurements was not more than 10% of the lower value. The first measured value was employed as the measured value for the specimen.

S.A., statistical analysis for significantly different

—, S.A. was not performed

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

## Appendix 9-2-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual males at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
21	5.9	3.6	1.57	17	0.7	172	49	41	0.05
22	5.2	3.4	1.89	15	0.6	145	49	35	0.05
23	5.3	3.3	1.65	21	0.7	148	46	21	0.05
24	6.0	3.8	1.73	16	0.8	193	46	49	0.06
25	5.8	3.5	1.52	16	0.8	158	41	12	0.04
N	5	5	5	5	5	5	5	5	5
Mean	5.6	3.5	1.67	17	0.7	163	46	32	0.05
S.D.	0.4	0.2	0.15	2	0.1	20	3	15	0.01
S.A.	0.84	1.18	0.58	0.85	1.10	0.26	1.38	0.36	0.25

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	$\gamma$ -GTP (U/L)
21	6.7	9.1	141.0	3.88	102.9	273	25	57	1
22	7.0	8.7 #	142.4	3.97	104.8	229	27	53	1
23	7.1	9.0	142.1	3.97	105.8	206	15	45	1
24	7.6	9.1	142.5	4.02	103.9	316	30	64	1
25	8.4	9.0	143.4	4.40	105.6	236	26	69	1
N	5	5	5	5	5	5	5	5	5
Mean	7.4	9.0	142.3	4.05	104.6	252	25	58	1
S.D.	0.7	0.2	0.9	0.20	1.2	43	6	9	0
S.A.	0.83	0.93	1.34	0.17	1.62	0.29	0.28	0.80	—

#: the first measured value was either higher than the upper control limit, or lower than the lower control limit stated in the standard operating procedures.

One re-measurement was carried out, and the difference between the values in two measurements was not more than 10% of the lower value. The first measured value was employed as the measured value for the specimen.

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

Appendix 9-2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
31	6.3	4.6	2.71	18	0.7	182	74	33	0.09
32	5.7	3.7	1.85	17	0.8	145	52	15	0.04
33	6.1	4.3	2.39	25	0.7	163	66	37	0.07
34	6.1	4.0	1.90	23	0.8 †	159	87	57	0.07
35	5.9	3.8	1.81	21	0.7	165	66	12	0.04
N	5	5	5	5	5	5	5	5	5
Mean	6.0	4.1	2.13	21	0.7	163	69	31	0.06
S.D.	0.2	0.4	0.40	3	0.1	13	13	18	0.02
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→A	F→S

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	γ-GTP (U/L)
31	4.6	9.3	143.6	4.20	108.1	135 #	16	51	1
32	4.7	8.6 #	142.8	3.86	108.1	103 #	16	52	1
33	6.1	9.5	140.6	4.18	105.8	108 #	11	44	1
34	4.9	9.1	141.4	3.51	105.6	111 #	13	56	3
35	6.7	9.2	142.5	3.91	107.6	147 #	20	79	2
N	5	5	5	5	5	5	5	5	5
Mean	5.4	9.1	142.2	3.93	107.0	121	15	56	2
S.D.	0.9	0.3	1.2	0.28	1.2	19	3	13	1
S.A.	F→S	F→S	F→A	F→S	F→S	F→S	F→S	F→S	F→S

†: the first measured value was either higher than the upper control limit, or lower than the lower control limit stated in the standard operating procedures.

Two re-measurements were carried out, and two sets of data were obtained, showing the same differences between the values from three measurements. The middle value was therefore employed as the measured value for the specimen.

#: the first measured value was either higher than the upper control limit, or lower than the lower control limit stated in the standard operating procedures.

One re-measurement was carried out, and the difference between the values in two measurements was not more than 10% of the lower value. The first measured value was employed as the measured value for the specimen.

S.A., statistical analysis for significantly different

—, S.A. was not performed

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

Appendix 9-2-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Biochemical findings in individual females at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Total protein (g/dL)	Albumin (g/dL)	A/G	BUN (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total cholesterol (mg/dL)	Tri-glyceride (mg/dL)	Total bilirubin (mg/dL)
51	6.1	4.1	2.05	19	0.7	144	60	20	0.09
52	5.9	3.8	1.81	21	0.7	140	55	17	0.06
53	5.5	3.6	1.89	20	0.7	150	71	29	0.07
54	6.2	3.9	1.70	17	0.8	123 #	61	16	0.06
55	6.2	4.2	2.10	19	0.7	152	51	25	0.06
N	5	5	5	5	5	5	5	5	5
Mean	6.0	3.9	1.91	19	0.7	142	60	21	0.07
S.D.	0.3	0.2	0.17	1	0.0	12	8	6	0.01
S.A.	0.24	0.81	1.15	0.98	0.63	2.67 *	1.41	1.10	0.53

Animal No.	Inorganic phosphorus (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	$\gamma$ -GTP (U/L)
51	5.3	9.4	141.3	3.99	105.8	143 #	14	50	1
52	7.2	9.6	141.5	4.66	106.4	153 #	15	55	1
53	6.4	9.0	141.8	4.09	107.1	131 #	15	46	2
54	5.8	9.2	142.0	4.18	106.2	163 #	18	63	2
55	5.9	9.2	141.9	3.60	108.2	113 #	13	50	2
N	5	5	5	5	5	5	5	5	5
Mean	6.1	9.3	141.7	4.10	106.7	141	15	53	2
S.D.	0.7	0.2	0.3	0.38	0.9	19	2	7	1
S.A.	1.36	0.77	0.88	0.81	0.43	1.62	0.11	0.54	0.00

#: the first measured value was either higher than the upper control limit, or lower than the lower control limit stated in the standard operating procedures.

One re-measurement was carried out, and the difference between the values in two measurements was not more than 10% of the lower value. The first measured value was employed as the measured value for the specimen.

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

\*: significant difference from control, p<0.05

## Appendix 10-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
6	374.6	1854.1	500.3	1315.4	12014.6	3018.6	1545.0	1473.6	700.5
7	326.8	1896.2	521.6	1080.0	12049.0	2752.1	1365.3	1386.8	698.3
8	323.7	1878.8	659.8	1099.7	10238.5	2333.6	1187.7	1145.9	710.5
9	370.1	1865.4	491.5	1279.6	13710.6	2628.0	1258.5	1369.5	857.7
10	306.2	1853.8	352.1	1077.3	10616.9	2359.4	1189.4	1170.0	639.9
N	5	5	5	5	5	5	5	5	5
Mean	340.3	1869.7	505.1	1170.4	11725.9	2618.3	1309.2	1309.2	721.4
S.D.	30.4	18.0	109.3	117.0	1375.6	285.6	150.4	143.8	81.1
S.A.	B→O	B→K	B→O	B→O	B→O→D	B→O	B→O	B→O	B→O

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
6	13.5	51.8	25.1	26.7	3375.6	1701.4	1674.2	756.7	381.6	375.1
7	12.4	65.4	31.9	33.5	2692.2	1323.5	1368.7	659.1	330.7	328.4
8	10.2	45.5	22.0	23.5	2984.8	1505.3	1479.5	730.3	374.0	356.3
9	17.3	51.7	25.4	26.3	2880.5	1459.1	1421.4	829.4	414.2	415.2
10	12.9	46.0	22.5	23.5	2764.6	1374.7	1389.9	714.3	368.3	346.0
N	5	5	5	5	5	5	5	5	5	5
Mean	13.3	52.1	25.4	26.7	2939.5	1472.8	1466.7	738.0	373.8	364.2
S.D.	2.6	8.0	3.9	4.1	268.1	146.1	123.3	62.3	29.9	33.1
S.A.	B→K→D	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 10-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
11	344.1	1944.3	732.8	1321.0	12284.3	2611.7	1321.3	1290.4	792.4
12	375.9	1944.7	496.8	1314.3	11913.4	3487.6	1735.3	1752.3	870.6
13	339.7	1936.7	463.9	1234.3	12714.6	2736.9	1356.7	1380.2	719.8
14	347.2	2007.8	448.0	1126.0	12266.4	2683.3	1360.7	1322.6	801.8
15	324.5	1945.3	423.6	1014.4	10904.6	2534.3	1273.0	1261.3	614.4
N	5	5	5	5	5	5	5	5	5
Mean	346.3	1955.8	513.0	1202.0	12016.7	2810.8	1409.4	1401.4	759.8
S.D.	18.7	29.3	125.7	131.1	683.5	386.0	185.6	201.1	97.3
S.A.	...	...	...	...	0.46	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
11	27.9	66.6	32.3	34.3	2951.4	1501.2	1450.2	771.8	375.0	396.8
12	19.2	43.3	21.5	21.8	3845.9	1946.7	1899.2	855.3	431.0	424.3
13	17.4	51.8	25.3	26.5	3242.4	1647.5	1594.9	735.6	374.8	360.8
14	14.5	57.3	27.0	30.3	3225.7	1605.1	1620.6	707.5	350.3	357.2
15	15.6	58.7	27.4	31.3	2709.3	1334.1	1375.2	614.6	317.0	297.6
N	5	5	5	5	5	5	5	5	5	5
Mean	18.9	55.5	26.7	28.8	3194.9	1606.9	1588.0	737.0	369.6	367.3
S.D.	5.3	8.6	3.9	4.8	424.9	225.1	201.4	88.1	41.7	47.8
S.A.	2.19	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 10-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
16	330.5	1941.5	532.3	1327.5	10578.8	2710.4	1367.3	1343.1	624.8
17	316.4	1927.2	509.1	1117.5	10540.2	2667.2	1345.8	1321.4	790.8
18	342.6	1712.4	482.5	986.0	11412.9	2596.7	1280.9	1315.8	694.0
19	339.4	2141.0	623.4	1256.8	11704.2	2831.0	1349.1	1481.9	759.8
20	311.7	2015.6	449.8	1004.8	10890.1	2534.6	1262.9	1271.7	946.2
N	5	5	5	5	5	5	5	5	5
Mean	328.1	1947.5	519.4	1138.5	11025.2	2668.0	1321.2	1346.8	763.1
S.D.	13.7	156.4	65.8	151.1	515.8	113.2	46.2	79.9	120.6
S.A.	...	...	...	...	1.11	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
16	18.6	48.6	23.6	25.0	3070.3	1572.2	1498.1	729.4	362.1	367.3
17	16.6	52.5	25.9	26.6	2945.0	1448.3	1496.7	743.5	374.5	369.0
18	18.3	35.3	16.8	18.5	2576.2	1293.9	1282.3	646.6	319.6	327.0
19	18.7	52.9	25.8	27.1	3222.2	1598.0	1624.2	718.2	352.4	365.8
20	17.9	41.1	19.7	21.4	2786.6	1407.4	1379.2	724.0	362.2	361.8
N	5	5	5	5	5	5	5	5	5	5
Mean	18.0	46.1	22.4	23.7	2920.1	1464.0	1456.1	712.3	354.2	358.2
S.D.	0.9	7.7	4.0	3.7	250.3	124.5	130.2	37.9	20.9	17.6
S.A.	2.33	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 10-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
26	313.6	1919.9	630.5	1031.5	11634.3	2678.4	1334.3	1344.1	793.5
27	367.4	1898.3	673.6	1282.3	14425.8	2874.3	1477.9	1396.4	919.9
28	357.6	2063.1	443.0	1081.2	13985.1	3087.8	1472.7	1615.1	713.2
29	358.2	1903.1	445.3	1058.7	14233.8	2739.6	1337.9	1401.7	751.1
30	356.1	1792.5	487.5	1273.0	14156.9	2819.6	1420.9	1398.7	1231.2
N	5	5	5	5	5	5	5	5	5
Mean	350.6	1915.4	536.0	1145.3	13687.2	2839.9	1408.7	1431.2	881.8
S.D.	21.1	96.7	108.5	122.1	1158.5	157.5	70.0	105.5	210.3
S.A.	...	...	...	...	3.11 *	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
26	17.0	39.5	19.1	20.4	3033.1	1490.4	1542.7	702.8	336.0	366.8
27	19.1	50.3	23.8	26.5	3177.6	1594.6	1583.0	787.5	397.9	389.6
28	18.6	50.6	24.9	25.7	2878.3	1438.2	1440.1	662.1	330.5	331.6
29	14.9	58.7	27.3	31.4	2924.3	1546.4	1377.9	705.8	358.8	347.0
30	19.6	54.8	27.0	27.8	3257.1	1619.2	1637.9	780.9	392.6	388.3
N	5	5	5	5	5	5	5	5	5	5
Mean	17.8	50.8	24.4	26.4	3054.1	1537.8	1516.3	727.8	363.2	364.7
S.D.	1.9	7.2	3.3	4.0	161.8	74.3	105.9	54.3	31.2	25.4
S.A.	2.43 *	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different  
D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

## Appendix 10-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
36	194.6	1629.6	443.4	744.1	5910.1	1559.7	786.3	773.4	381.2
37	184.9	1742.1	394.3	638.0	5926.6	1668.1	822.7	845.4	447.1
38	202.1	1807.9	462.4	721.7	6415.7	1729.4	887.6	841.8	466.8
39	236.0	1795.4	414.4	855.2	7483.7	1732.2	879.4	852.8	450.7
40	209.2	1821.1	490.9	825.1	7819.4	1729.3	870.0	859.3	520.5
N	5	5	5	5	5	5	5	5	5
Mean	205.4	1759.2	441.1	756.8	6711.1	1683.7	849.2	834.5	453.3
S.D.	19.4	78.4	38.2	86.4	890.2	74.4	43.2	34.8	49.9
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
36	10.4	52.7	25.3	27.4	93.8	46.5	47.3
37	18.4	80.8	39.9	40.9	72.0	40.8	31.2
38	10.5	66.6	31.0	35.6	78.0	41.6	36.4
39	14.9	65.7	32.4	33.3	77.2	39.0	38.2
40	12.1	68.0	34.6	33.4	83.9	44.9	39.0
N	5	5	5	5	5	5	5
Mean	13.3	66.8	32.6	34.1	81.0	42.6	38.4
S.D.	3.4	10.0	5.3	4.9	8.3	3.1	5.8
S.A.	B→K	B→O	B→O	B→O	B→O	B→O→D	B→O

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 10-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
41	186.0	1737.1	387.1	626.5	6170.1	1568.2	814.8	753.4	471.1
42	234.9	1818.7	566.5	876.4	7882.8	2006.9	1016.4	990.5	566.2
43	207.6	1686.1	340.1	750.5	6341.2	1582.4	779.2	803.2	645.5
44	180.5	1812.8	452.9	708.5	5440.4	1512.5	733.3	779.2	443.4
45	215.6	1799.4	313.2	722.3	7644.9	1864.2	934.8	929.4	496.5
N	5	5	5	5	5	5	5	5	5
Mean	204.9	1770.8	412.0	736.8	6695.9	1706.8	855.7	851.1	524.5
S.D.	22.2	57.4	101.4	90.6	1035.4	216.4	116.8	103.2	81.5
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
41	15.1	63.3	30.2	33.1	78.2	41.9	36.3
42	15.6	66.2	33.1	33.1	76.9	41.0	35.9
43	14.5	55.7	26.6	29.1	82.3	40.4	41.9
44	15.8	52.3	26.0	26.3	94.4	47.2	47.2
45	14.9	68.6	34.5	34.1	90.2	50.1	40.1
N	5	5	5	5	5	5	5
Mean	15.2	61.2	30.1	31.1	84.4	44.1	40.3
S.D.	0.5	7.0	3.8	3.3	7.6	4.3	4.6
S.A.	...	...	...	...	...	0.61	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 10-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
46	213.6	1803.6	319.8	903.6	9040.7	1760.9	880.2	880.7	450.0
47	221.4	1877.7	403.9	649.7	7965.4	1780.9	924.0	856.9	473.1
48	266.9	1816.3	532.9	1001.2	9591.4	2184.9	1094.2	1090.7	737.1
49	246.8	1923.2	481.8	900.7	8058.7	2026.0	1006.1	1019.9	497.9
50	188.4	1655.1	403.9	694.5	5830.1	1749.0	866.8	882.2	344.4
N	5	5	5	5	5	5	5	5	5
Mean	227.4	1815.2	428.5	829.9	8097.3	1900.3	954.3	946.1	500.5
S.D.	30.3	101.7	81.8	150.5	1438.9	195.8	95.3	103.3	144.6
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
46	16.7	81.1	38.4	42.7	82.7	41.6	41.1
47	13.0	61.1	29.9	31.2	62.8	33.7	29.1
48	8.9	81.4	40.1	41.3	90.2	40.2	50.0
49	17.9	63.2	30.8	32.4	79.1	39.8	39.3
50	12.6	61.6	28.9	32.7	82.8	42.0	40.8
N	5	5	5	5	5	5	5
Mean	13.8	69.7	33.6	36.1	79.5	39.5	40.1
S.D.	3.6	10.6	5.2	5.5	10.2	3.3	7.4
S.A.	...	...	...	...	...	1.22	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 10-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
56	204.0	1813.5	565.3	731.2	7529.4	1802.9	887.3	915.6	498.1
57	230.8	1749.6	488.4	828.5	8785.0	1910.2	952.4	957.8	571.0
58	200.6	1699.2	435.8	678.9	6786.3	1790.9	874.1	916.8	443.8
59	197.7	1748.8	587.5	741.4	6716.2	1741.0	864.3	876.7	411.2
60	226.2	1716.3	605.5	759.1	7911.4	1638.1	835.6	802.5	502.3
N	5	5	5	5	5	5	5	5	5
Mean	211.9	1745.5	536.5	747.8	7545.7	1776.6	882.7	893.9	485.3
S.D.	15.4	43.7	71.8	54.1	856.5	99.0	43.3	58.6	61.3
S.A.	...	...	...	...	...	...	...	...	...

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
56	15.0	49.6	22.5	27.1	97.5	51.3	46.2
57	18.6	64.0	29.6	34.4	95.1	53.1	42.0
58	10.6	64.3	31.0	33.3	87.4	46.3	41.1
59	16.8	50.2	23.9	26.3	77.9	40.1	37.8
60	12.1	59.4	29.2	30.2	91.3	46.4	44.9
N	5	5	5	5	5	5	5
Mean	14.6	57.5	27.2	30.3	89.8	47.4	42.4
S.D.	3.3	7.2	3.8	3.6	7.7	5.1	3.3
S.A.	...	...	...	...	...	1.92	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 10-2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
1	415.5	2006.5	280.1	1322.7	12009.3	2962.6	1499.2	1463.4	755.9
2	364.5	1802.8	436.0	1317.8	10360.7	2862.3	1465.0	1397.3	826.5
3	413.5	1960.5	312.5	1269.5	13161.8	2958.2	1517.2	1441.0	694.1
4	387.2	2026.3	475.9	1212.3	12790.3	2841.0	1455.1	1385.9	690.1
5	376.5	1852.8	339.6	1033.8	12351.9	2983.0	1508.8	1474.2	754.0
N	5	5	5	5	5	5	5	5	5
Mean	391.4	1929.8	368.8	1231.2	12134.8	2921.4	1489.1	1432.4	744.1
S.D.	22.5	97.7	83.5	119.0	1083.4	64.8	27.5	39.3	55.8
S.A.	F→S	F→S	F→S	F→S	F→S	F→A	F→A	F→A	F→S

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
1	11.7	51.5	25.0	26.5	2843.6	1416.4	1427.2	970.3	486.9	483.4
2	19.7	51.4	25.1	26.3	3201.6	1557.4	1644.2	938.8	461.0	477.8
3	14.2	52.1	26.1	26.0	2797.7	1393.6	1404.1	958.5	476.5	482.0
4	12.2	61.8	29.9	31.9	3015.9	1506.8	1509.1	922.1	461.0	461.1
5	17.9	55.1	27.1	28.0	3090.0	1554.1	1535.9	1016.8	495.1	521.7
N	5	5	5	5	5	5	5	5	5	5
Mean	15.1	54.4	26.6	27.7	2989.8	1485.7	1504.1	961.3	476.1	485.2
S.D.	3.5	4.4	2.0	2.5	168.7	76.7	95.6	36.1	15.3	22.3
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S

S.A., statistical analysis for significantly different

—, S.A. was not performed

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

## Appendix 10-2-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual males at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
21	394.1	2009.1	386.4	1243.8	12162.7	2974.9	1501.6	1473.3	722.3
22	396.7	1873.7	398.0	1257.6	12865.2	3419.0	1670.3	1748.7	868.6
23	399.3	1880.5	452.8	1250.7	12048.7	2971.6	1498.6	1473.0	802.4
24	407.3	1954.7	587.7	1435.5	13129.4	2989.4	1455.6	1533.8	887.0
25	359.6	1884.2	257.5	1181.4	10843.1	3113.2	1571.4	1541.8	896.0
N	5	5	5	5	5	5	5	5	5
Mean	391.4	1920.4	416.5	1273.8	12209.8	3093.6	1539.5	1554.1	835.3
S.D.	18.5	59.4	119.5	95.4	890.4	191.1	84.1	113.5	73.0
S.A.	0.00	0.18	0.73	0.62	0.12	1.91	1.28	2.27	2.22

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Testes (mg)	Testis(R) (mg)	Testis(L) (mg)	Epididymides (mg)	Epididymis (R) (mg)	Epididymis (L) (mg)
21	22.2	48.3	24.5	23.8	3460.8	1739.8	1721.0	919.2	468.5	450.7
22	16.9	57.4	28.3	29.1	2766.3	1359.3	1407.0	885.9	429.4	456.5
23	18.2	54.9	26.5	28.4	3304.9	1675.2	1629.7	916.7	456.3	460.4
24	20.3	55.7	27.7	28.0	3233.9	1606.1	1627.8	872.3	437.8	434.5
25	15.0	63.2	32.6	30.6	3159.8	1562.6	1597.2	865.4	421.7	443.7
N	5	5	5	5	5	5	5	5	5	5
Mean	18.5	55.9	27.9	28.0	3185.1	1588.6	1596.5	891.9	442.7	449.2
S.D.	2.8	5.3	3.0	2.5	259.2	144.8	115.6	24.9	19.3	10.3
S.A.	1.67	0.49	0.79	0.15	1.41	1.40	1.38	3.54 **	3.03 *	3.28 *

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

## Appendix 10-2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
31	261.6	1788.6	396.2	864.2	7518.0	1741.8	874.4	867.4	373.4
32	231.4	1802.2	451.2	663.0	6626.7	1706.9	868.5	838.4	470.9
33	272.8	1919.4	544.9	918.4	8974.3	2000.3	977.1	1023.2	744.9
34	284.4	1854.1	406.6	934.3	9990.4	2001.6	1044.1	957.5	607.9
35	210.4	1780.7	388.7	811.9	6909.6	1886.1	953.8	932.3	422.3
N	5	5	5	5	5	5	5	5	5
Mean	252.1	1829.0	437.5	838.4	8003.8	1867.3	943.6	923.8	523.9
S.D.	30.5	58.1	64.7	109.2	1433.4	139.2	73.7	73.4	151.4
S.A.	F→S	F→S	F→A	F→S	F→S	F→S	F→S	F→S	F→A

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
31	16.0	54.6	27.9	26.7	88.4	49.5	38.9
32	17.0	62.8	31.0	31.8	67.7	35.8	31.9
33	16.5	76.9	37.6	39.3	90.5	41.2	49.3
34	18.2	88.3	42.8	45.5	102.6	57.9	44.7
35	12.8	64.8	31.2	33.6	62.2	23.8	38.4
N	5	5	5	5	5	5	5
Mean	16.1	69.5	34.1	35.4	82.3	41.6	40.6
S.D.	2.0	13.2	6.0	7.2	16.8	13.0	6.6
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S

S.A., statistical analysis for significantly different  
—, S.A. was not performed

F, F-test  
S, Student's t-test  
A, Aspin-Welch's t-test

## Appendix 10-2-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Absolute organ weights in individual females at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg)	Thymus (mg)	Heart (mg)	Liver (mg)	Kidneys (mg)	Kidney(R) (mg)	Kidney(L) (mg)	Spleen (mg)
51	275.7	1875.7	730.4	885.2	9171.3	2218.4	1107.1	1111.3	624.9
52	272.5	1907.6	424.3	875.2	8272.6	2283.9	1152.0	1131.9	630.7
53	231.9	1754.9	508.5	803.4	6893.1	1711.5	871.6	839.9	541.3
54	235.5	1847.1	334.0	782.8	7239.5	1867.4	922.0	945.4	612.2
55	236.1	1824.5	291.6	948.5	8568.7	2191.4	1099.3	1092.1	542.6
N	5	5	5	5	5	5	5	5	5
Mean	250.3	1842.0	457.8	859.0	8029.0	2054.5	1030.4	1024.1	590.3
S.D.	21.8	57.8	173.9	66.8	944.6	250.4	124.9	126.5	44.7
S.A.	0.11	0.35	0.24	0.36	0.03	1.46	1.34	1.53	0.94

Animal No.	Thyroid gland (mg)	Adrenal glands (mg)	Adrenal gland(R) (mg)	Adrenal gland(L) (mg)	Ovaries (mg)	Ovary(R) (mg)	Ovary(L) (mg)
51	20.8	66.5	31.4	35.1	97.9	53.0	44.9
52	15.3	78.4	39.4	39.0	124.3	67.7	56.6
53	11.5	58.2	29.7	28.5	74.0	34.5	39.5
54	15.1	68.2	33.5	34.7	92.8	44.4	48.4
55	18.2	74.3	37.1	37.2	90.3	48.6	41.7
N	5	5	5	5	5	5	5
Mean	16.2	69.1	34.2	34.9	95.9	49.6	46.2
S.D.	3.5	7.7	4.0	4.0	18.2	12.2	6.7
S.A.	0.04	0.05	0.04	0.13	1.22	1.00	1.32

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

## Appendix 11-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
6	374.6	4.950	1.336	3.511	32.073	8.058	4.124	3.934	1.870
7	326.8	5.802	1.596	3.305	36.870	8.421	4.178	4.244	2.137
8	323.7	5.804	2.038	3.397	31.630	7.209	3.669	3.540	2.195
9	370.1	5.040	1.328	3.457	37.046	7.101	3.400	3.700	2.317
10	306.2	6.054	1.150	3.518	34.673	7.705	3.884	3.821	2.090
N	5	5	5	5	5	5	5	5	5
Mean	340.3	5.530	1.490	3.438	34.458	7.699	3.851	3.848	2.122
S.D.	30.4	0.500	0.345	0.089	2.562	0.559	0.324	0.265	0.164
S.A.	B→O	B→O	B→O	B→O	B→O→D	B→O	B→O	B→O	B→O

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
6	0.036	0.138	0.067	0.071	9.011	4.542	4.469	2.020	1.019	1.001
7	0.038	0.200	0.098	0.103	8.238	4.050	4.188	2.017	1.012	1.005
8	0.032	0.141	0.068	0.073	9.221	4.650	4.571	2.256	1.155	1.101
9	0.047	0.140	0.069	0.071	7.783	3.942	3.841	2.241	1.119	1.122
10	0.042	0.150	0.073	0.077	9.029	4.490	4.539	2.333	1.203	1.130
N	5	5	5	5	5	5	5	5	5	5
Mean	0.039	0.154	0.075	0.079	8.656	4.335	4.322	2.173	1.102	1.072
S.D.	0.006	0.026	0.013	0.014	0.617	0.317	0.308	0.146	0.084	0.064
S.A.	B→K→D	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O	B→O

S.A., statistical analysis for significantly different

—, S.A. was not performed

..., D was not performed

B, Bartlett's test

O, one-way layout analysis of variance

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 11-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
11	344.1	5.650	2.130	3.839	35.700	7.590	3.840	3.750	2.303
12	375.9	5.173	1.322	3.496	31.693	9.278	4.616	4.662	2.316
13	339.7	5.701	1.366	3.634	37.429	8.057	3.994	4.063	2.119
14	347.2	5.783	1.290	3.243	35.329	7.728	3.919	3.809	2.309
15	324.5	5.995	1.305	3.126	33.604	7.810	3.923	3.887	1.893
N	5	5	5	5	5	5	5	5	5
Mean	346.3	5.660	1.483	3.468	34.751	8.093	4.058	4.034	2.188
S.D.	18.7	0.303	0.363	0.289	2.184	0.684	0.316	0.370	0.184
S.A.	...	...	...	...	0.25	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
11	0.081	0.194	0.094	0.100	8.577	4.363	4.214	2.243	1.090	1.153
12	0.051	0.115	0.057	0.058	10.231	5.179	5.052	2.275	1.147	1.129
13	0.051	0.152	0.074	0.078	9.545	4.850	4.695	2.165	1.103	1.062
14	0.042	0.165	0.078	0.087	9.291	4.623	4.668	2.038	1.009	1.029
15	0.048	0.181	0.084	0.096	8.349	4.111	4.238	1.894	0.977	0.917
N	5	5	5	5	5	5	5	5	5	5
Mean	0.055	0.161	0.077	0.084	9.199	4.625	4.573	2.123	1.065	1.058
S.D.	0.015	0.030	0.014	0.017	0.759	0.415	0.352	0.157	0.070	0.093
S.A.	1.82	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 11-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
16	330.5	5.874	1.611	4.017	32.008	8.201	4.137	4.064	1.890
17	316.4	6.091	1.609	3.532	33.313	8.430	4.253	4.176	2.499
18	342.6	4.998	1.408	2.878	33.313	7.579	3.739	3.841	2.026
19	339.4	6.308	1.837	3.703	34.485	8.341	3.975	4.366	2.239
20	311.7	6.466	1.443	3.224	34.938	8.132	4.052	4.080	3.036
N	5	5	5	5	5	5	5	5	5
Mean	328.1	5.947	1.582	3.471	33.611	8.137	4.031	4.105	2.338
S.D.	13.7	0.576	0.170	0.438	1.148	0.333	0.193	0.191	0.453
S.A.	...	...	...	...	0.72	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
16	0.056	0.147	0.071	0.076	9.290	4.757	4.533	2.207	1.096	1.111
17	0.052	0.166	0.082	0.084	9.308	4.577	4.730	2.350	1.184	1.166
18	0.053	0.103	0.049	0.054	7.520	3.777	3.743	1.887	0.933	0.954
19	0.055	0.156	0.076	0.080	9.494	4.708	4.786	2.116	1.038	1.078
20	0.057	0.132	0.063	0.069	8.940	4.515	4.425	2.323	1.162	1.161
N	5	5	5	5	5	5	5	5	5	5
Mean	0.055	0.141	0.068	0.073	8.910	4.467	4.443	2.177	1.083	1.094
S.D.	0.002	0.025	0.013	0.012	0.803	0.398	0.418	0.187	0.101	0.086
S.A.	3.30 **	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different  
D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p<0.05

\*\*, significant difference from control, p<0.01

## Appendix 11-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
26	313.6	6.122	2.011	3.289	37.099	8.541	4.255	4.286	2.530
27	367.4	5.167	1.833	3.490	39.265	7.823	4.023	3.801	2.504
28	357.6	5.769	1.239	3.023	39.108	8.635	4.118	4.516	1.994
29	358.2	5.313	1.243	2.956	39.737	7.648	3.735	3.913	2.097
30	356.1	5.034	1.369	3.575	39.755	7.918	3.990	3.928	3.457
N	5	5	5	5	5	5	5	5	5
Mean	350.6	5.481	1.539	3.267	38.993	8.113	4.024	4.089	2.516
S.D.	21.1	0.453	0.359	0.274	1.096	0.446	0.192	0.300	0.577
S.A.	...	...	...	...	3.85 **	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
26	0.054	0.126	0.061	0.065	9.672	4.753	4.919	2.241	1.071	1.170
27	0.052	0.137	0.065	0.072	8.649	4.340	4.309	2.143	1.083	1.060
28	0.052	0.141	0.070	0.072	8.049	4.022	4.027	1.852	0.924	0.927
29	0.042	0.164	0.076	0.088	8.164	4.317	3.847	1.970	1.002	0.969
30	0.055	0.154	0.076	0.078	9.147	4.547	4.600	2.193	1.102	1.090
N	5	5	5	5	5	5	5	5	5	5
Mean	0.051	0.144	0.070	0.075	8.736	4.396	4.340	2.080	1.036	1.043
S.D.	0.005	0.015	0.007	0.009	0.680	0.274	0.432	0.163	0.073	0.097
S.A.	2.28	...	...	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

\*, significant difference from control, p&lt;0.05

\*\*, significant difference from control, p&lt;0.01

## Appendix 11-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the dosing period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
36	194.6	8.374	2.279	3.824	30.371	8.015	4.041	3.974	1.959
37	184.9	9.422	2.133	3.451	32.053	9.022	4.449	4.572	2.418
38	202.1	8.946	2.288	3.571	31.745	8.557	4.392	4.165	2.310
39	236.0	7.608	1.756	3.624	31.711	7.340	3.726	3.614	1.910
40	209.2	8.705	2.347	3.944	37.378	8.266	4.159	4.108	2.488
N	5	5	5	5	5	5	5	5	5
Mean	205.4	8.611	2.161	3.683	32.652	8.240	4.153	4.087	2.217
S.D.	19.4	0.678	0.240	0.199	2.721	0.627	0.291	0.346	0.266
S.A.	B→O	B→O	B→O→D	B→O	B→O	B→O	B→O	B→O	B→O

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
36	0.053	0.271	0.130	0.141	0.482	0.239	0.243
37	0.100	0.437	0.216	0.221	0.389	0.221	0.169
38	0.052	0.330	0.153	0.176	0.386	0.206	0.180
39	0.063	0.278	0.137	0.141	0.327	0.165	0.162
40	0.058	0.325	0.165	0.160	0.401	0.215	0.186
N	5	5	5	5	5	5	5
Mean	0.065	0.328	0.160	0.168	0.397	0.209	0.188
S.D.	0.020	0.066	0.034	0.033	0.056	0.027	0.032
S.A.	B→O	B→O	B→O	B→O	B→O	B→O	B→O

S.A., statistical analysis for significantly different

B, Bartlett's test

—, S.A. was not performed

O, one-way layout analysis of variance

..., D was not performed

K, Kruskal-Wallis' h test

D, Dunnett's d test or Dunnett type mean rank test

## Appendix 11-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the dosing period; dosage of 3.75 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
41	186.0	9.339	2.081	3.368	33.173	8.431	4.381	4.051	2.533
42	234.9	7.742	2.412	3.731	33.558	8.544	4.327	4.217	2.410
43	207.6	8.122	1.638	3.615	30.545	7.622	3.753	3.869	3.109
44	180.5	10.043	2.509	3.925	30.141	8.380	4.063	4.317	2.457
45	215.6	8.346	1.453	3.350	35.459	8.647	4.336	4.311	2.303
N	5	5	5	5	5	5	5	5	5
Mean	204.9	8.718	2.019	3.598	32.575	8.325	4.172	4.153	2.562
S.D.	22.2	0.947	0.465	0.245	2.218	0.406	0.266	0.192	0.317
S.A.	...	...	0.65	...	...	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
41	0.081	0.340	0.162	0.178	0.420	0.225	0.195
42	0.066	0.282	0.141	0.141	0.327	0.175	0.153
43	0.070	0.268	0.128	0.140	0.396	0.195	0.202
44	0.088	0.290	0.144	0.146	0.523	0.261	0.261
45	0.069	0.318	0.160	0.158	0.418	0.232	0.186
N	5	5	5	5	5	5	5
Mean	0.075	0.300	0.147	0.153	0.417	0.218	0.199
S.D.	0.009	0.029	0.014	0.016	0.070	0.033	0.039
S.A.	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 11-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the dosing period; dosage of 15 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
46	213.6	8.444	1.497	4.230	42.325	8.244	4.121	4.123	2.107
47	221.4	8.481	1.824	2.935	35.977	8.044	4.173	3.870	2.137
48	266.9	6.805	1.997	3.751	35.936	8.186	4.100	4.087	2.762
49	246.8	7.793	1.952	3.650	32.653	8.209	4.077	4.132	2.017
50	188.4	8.785	2.144	3.686	30.945	9.283	4.601	4.683	1.828
N	5	5	5	5	5	5	5	5	5
Mean	227.4	8.062	1.883	3.650	35.567	8.393	4.214	4.179	2.170
S.D.	30.3	0.790	0.244	0.463	4.354	0.503	0.219	0.301	0.352
S.A.	...	...	1.27	...	...	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
46	0.078	0.380	0.180	0.200	0.387	0.195	0.192
47	0.059	0.276	0.135	0.141	0.284	0.152	0.131
48	0.033	0.305	0.150	0.155	0.338	0.151	0.187
49	0.073	0.256	0.125	0.131	0.321	0.161	0.159
50	0.067	0.327	0.153	0.174	0.439	0.223	0.217
N	5	5	5	5	5	5	5
Mean	0.062	0.309	0.149	0.160	0.354	0.176	0.177
S.D.	0.018	0.048	0.021	0.027	0.060	0.032	0.033
S.A.	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 11-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the dosing period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
56	204.0	8.890	2.771	3.584	36.909	8.838	4.350	4.488	2.442
57	230.8	7.581	2.116	3.590	38.063	8.276	4.127	4.150	2.474
58	200.6	8.471	2.172	3.384	33.830	8.928	4.357	4.570	2.212
59	197.7	8.846	2.972	3.750	33.972	8.806	4.372	4.434	2.080
60	226.2	7.588	2.677	3.356	34.975	7.242	3.694	3.548	2.221
N	5	5	5	5	5	5	5	5	5
Mean	211.9	8.275	2.542	3.533	35.550	8.418	4.180	4.238	2.286
S.D.	15.4	0.651	0.379	0.163	1.867	0.705	0.290	0.417	0.167
S.A.	...	...	1.75	...	...	...	...	...	...

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
56	0.074	0.243	0.110	0.133	0.478	0.251	0.226
57	0.081	0.277	0.128	0.149	0.412	0.230	0.182
58	0.053	0.321	0.155	0.166	0.436	0.231	0.205
59	0.085	0.254	0.121	0.133	0.394	0.203	0.191
60	0.053	0.263	0.129	0.134	0.404	0.205	0.198
N	5	5	5	5	5	5	5
Mean	0.069	0.272	0.129	0.143	0.425	0.224	0.200
S.D.	0.015	0.030	0.017	0.015	0.034	0.020	0.017
S.A.	...	...	...	...	...	...	...

S.A., statistical analysis for significantly different

D, Dunnett's d test or Dunnett type mean rank test

—, S.A. was not performed

..., D was not performed

Value in S.A., statistic of D

## Appendix 11-2-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
1	415.5	4.829	0.674	3.183	28.903	7.130	3.608	3.522	1.819
2	364.5	4.946	1.196	3.615	28.424	7.853	4.019	3.833	2.267
3	413.5	4.741	0.756	3.070	31.830	7.154	3.669	3.485	1.679
4	387.2	5.233	1.229	3.131	33.033	7.337	3.758	3.579	1.782
5	376.5	4.921	0.902	2.746	32.807	7.923	4.007	3.916	2.003
N	5	5	5	5	5	5	5	5	5
Mean	391.4	4.934	0.951	3.149	30.999	7.479	3.812	3.667	1.910
S.D.	22.5	0.186	0.252	0.311	2.186	0.382	0.191	0.195	0.231
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
1	0.028	0.124	0.060	0.064	6.844	3.409	3.435	2.335	1.172	1.163
2	0.054	0.141	0.069	0.072	8.784	4.273	4.511	2.576	1.265	1.311
3	0.034	0.126	0.063	0.063	6.766	3.370	3.396	2.318	1.152	1.166
4	0.032	0.160	0.077	0.082	7.789	3.892	3.897	2.381	1.191	1.191
5	0.048	0.146	0.072	0.074	8.207	4.128	4.079	2.701	1.315	1.386
N	5	5	5	5	5	5	5	5	5	5
Mean	0.039	0.139	0.068	0.071	7.678	3.814	3.864	2.462	1.219	1.243
S.D.	0.011	0.015	0.007	0.008	0.872	0.411	0.466	0.168	0.069	0.100
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S

S.A., statistical analysis for significantly different

F, F-test

—, S.A. was not performed

S, Student's t-test

..., D was not performed

A, Aspin-Welch's t-test

## Appendix 11-2-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual males at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
21	394.1	5.098	0.980	3.156	30.862	7.549	3.810	3.738	1.833
22	396.7	4.723	1.003	3.170	32.431	8.619	4.210	4.408	2.190
23	399.3	4.709	1.134	3.132	30.175	7.442	3.753	3.689	2.010
24	407.3	4.799	1.443	3.524	32.235	7.340	3.574	3.766	2.178
25	359.6	5.240	0.716	3.285	30.153	8.657	4.370	4.288	2.492
N	5	5	5	5	5	5	5	5	5
Mean	391.4	4.914	1.055	3.253	31.171	7.921	3.943	3.978	2.141
S.D.	18.5	0.241	0.265	0.162	1.100	0.658	0.333	0.342	0.244
S.A.	0.00	0.15	0.63	0.67	0.16	1.30	0.76	1.77	1.53

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Testes (mg/g)	Testis(R) (mg/g)	Testis(L) (mg/g)	Epididymides (mg/g)	Epididymis (R) (mg/g)	Epididymis (L) (mg/g)
21	0.056	0.123	0.062	0.060	8.782	4.415	4.367	2.332	1.189	1.144
22	0.043	0.145	0.071	0.073	6.973	3.427	3.547	2.233	1.082	1.151
23	0.046	0.137	0.066	0.071	8.277	4.195	4.081	2.296	1.143	1.153
24	0.050	0.137	0.068	0.069	7.940	3.943	3.997	2.142	1.075	1.067
25	0.042	0.176	0.091	0.085	8.787	4.345	4.442	2.407	1.173	1.234
N	5	5	5	5	5	5	5	5	5	5
Mean	0.047	0.144	0.072	0.072	8.152	4.065	4.087	2.282	1.132	1.150
S.D.	0.006	0.020	0.011	0.009	0.750	0.400	0.355	0.100	0.052	0.059
S.A.	1.46	0.38	0.57	0.11	0.92	0.98	0.85	2.05	2.25	1.80

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

## Appendix 11-2-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the recovery period; dosage of 0 mg/kg (vehicle control)

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
31	261.6	6.837	1.515	3.304	28.739	6.658	3.343	3.316	1.427
32	231.4	7.788	1.950	2.865	28.637	7.376	3.753	3.623	2.035
33	272.8	7.036	1.997	3.367	32.897	7.332	3.582	3.751	2.731
34	284.4	6.519	1.430	3.285	35.128	7.038	3.671	3.367	2.137
35	210.4	8.463	1.847	3.859	32.840	8.964	4.533	4.431	2.007
N	5	5	5	5	5	5	5	5	5
Mean	252.1	7.329	1.748	3.336	31.648	7.474	3.776	3.698	2.067
S.D.	30.5	0.788	0.259	0.354	2.856	0.881	0.450	0.448	0.464
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→S	F→A

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
31	0.061	0.209	0.107	0.102	0.338	0.189	0.149
32	0.073	0.271	0.134	0.137	0.293	0.155	0.138
33	0.060	0.282	0.138	0.144	0.332	0.151	0.181
34	0.064	0.310	0.150	0.160	0.361	0.204	0.157
35	0.061	0.308	0.148	0.160	0.296	0.113	0.183
N	5	5	5	5	5	5	5
Mean	0.064	0.276	0.135	0.141	0.324	0.162	0.162
S.D.	0.005	0.041	0.017	0.024	0.029	0.036	0.020
S.A.	F→S	F→S	F→S	F→S	F→S	F→S	F→S

S.A., statistical analysis for significantly different

—, S.A. was not performed

F, F-test

S, Student's t-test

A, Aspin-Welch's t-test

## Appendix 11-2-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

Relative organ weights in individual females at the end of the recovery period; dosage of 60 mg/kg

Animal No.	Terminal body weight (g)	Brain (mg/g)	Thymus (mg/g)	Heart (mg/g)	Liver (mg/g)	Kidneys (mg/g)	Kidney(R) (mg/g)	Kidney(L) (mg/g)	Spleen (mg/g)
51	275.7	6.803	2.649	3.211	33.266	8.046	4.016	4.031	2.267
52	272.5	7.000	1.557	3.212	30.358	8.381	4.228	4.154	2.314
53	231.9	7.567	2.193	3.464	29.724	7.380	3.759	3.622	2.334
54	235.5	7.843	1.418	3.324	30.741	7.930	3.915	4.014	2.600
55	236.1	7.728	1.235	4.017	36.293	9.282	4.656	4.626	2.298
N	5	5	5	5	5	5	5	5	5
Mean	250.3	7.388	1.810	3.446	32.076	8.204	4.115	4.089	2.363
S.D.	21.8	0.460	0.591	0.336	2.714	0.702	0.347	0.360	0.135
S.A.	0.11	0.15	0.22	0.50	0.24	1.45	1.33	1.52	1.37

Animal No.	Thyroid gland (mg/g)	Adrenal glands (mg/g)	Adrenal gland(R) (mg/g)	Adrenal gland(L) (mg/g)	Ovaries (mg/g)	Ovary(R) (mg/g)	Ovary(L) (mg/g)
51	0.075	0.241	0.114	0.127	0.355	0.192	0.163
52	0.056	0.288	0.145	0.143	0.456	0.248	0.208
53	0.050	0.251	0.128	0.123	0.319	0.149	0.170
54	0.064	0.290	0.142	0.147	0.394	0.189	0.206
55	0.077	0.315	0.157	0.158	0.382	0.206	0.177
N	5	5	5	5	5	5	5
Mean	0.064	0.277	0.137	0.140	0.381	0.197	0.185
S.D.	0.012	0.030	0.017	0.014	0.051	0.036	0.021
S.A.	0.10	0.04	0.17	0.08	2.19	1.53	1.80

S.A., statistical analysis for significantly different

—, S.A. was not performed

S, Student's t-test

A, Aspin-Welch's t-test

Value in S.A., statistic of S or A

## Appendix 12-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Macroscopical findings in individual males at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
Animal No.	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	26	27	28	29	30
(Forestomach)																				

Increase thickness, mucosa

-, negative; +, positive.

No significant changes were observed in organs unless otherwise described above.

## Macroscopical findings in individual females at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
Animal No.	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	56	57	58	59	60
(All organs)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-, negative; +, positive.

## Appendix 12-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Macroscopical findings in individual males at the end of the recovery period

Dose	0 mg/kg					60 mg/kg				
	1	2	3	4	5	21	22	23	24	25
(All organs)										
Abnormality										

-, negative; +, positive.

## Macroscopical findings in individual females at the end of the recovery period

Dose	0 mg/kg					60 mg/kg				
	31	32	33	34	35	51	52	53	54	55
(All organs)										
Abnormality										

-, negative; +, positive.

## Appendix 13-1-1

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in individual males at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	26	27	28	29	30
Animal No.																				
(Liver)																				
Hypertrophy, hepatocyte, centrilobular	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	±	±	±	±	±
Single cell necrosis	-	-	-	-	-	-	±	-	-	-	-	-	-	-	-	-	-	±	-	-
Fatty change, periportal	±	±	-	-	±	+	-	-	±	-	-	±	-	±	-	-	-	-	±	-
(Kidney)																				
Basophilic tubule	±	±	-	-	-											-	±	±	-	-
Hyaline droplet	±	±	±	±	±											±	+	±	±	-
Cellular infiltration, lymphocyte	-	-	±	-	-											-	-	±	-	-
(Spleen)																				
Hematopoiesis, extramedullary	±	++	+	+	+											+	+	+	+	++
(Heart)																				
Myocardial degeneration/fibrosis	-	-	-	-	±											-	-	-	-	-
(Prostate)																				
Cellular infiltration, lymphocyte	-	-	+	-	-											-	-	++	-	-
(Thymus)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Stomach)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Brain)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Spinal cord)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Ileum)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Colon)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Adrenal gland)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Thyroid gland)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Trachea)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Lung & Bronchus)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.

## Appendix 13-1-1 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in individual males at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	26	27	28	29	30
Animal No.																				
(Testis)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Epididymis)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Urinary bladder)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Submandibular lymphnode)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Mesenteric lymphnode)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Sciatic nerve & Gastrocnemial muscle)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Bone marrow of femur)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Pancreas)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Submandibular & sublingual gland)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Pituitary gland)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(Eye)																				
Abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.

## Appendix 13-1-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in individual females at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
Animal No.	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	56	57	58	59	60
(Liver)																				
Fatty change, periportal	-	±	-	±	±	+	+	±	±	+	-	-	±	+	±	±	+	±	-	+
(Kidney)																				
Basophilic tubule	-	-	-	-	±											-	±	±	-	±
Cellular infiltration, lymphocyte	-	-	-	±	±											-	-	±	-	±
(Spleen)																				
Hematopoiesis, extramedullary	±	±	±	±	±											±	±	±	±	±
(Brain)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Spinal cord)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Stomach)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Ileum)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Colon)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Adrenal gland)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Heart)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Thymus)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Thyroid gland)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Trachea)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Lung & Bronchus)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.

## Appendix 13-1-2 (continued)

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in individual females at the end of the dosing period

Dose	0 mg/kg					3.75 mg/kg					15 mg/kg					60 mg/kg				
	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	56	57	58	59	60
(Ovary)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Uterus)																-	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Urinary bladder)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Submandibular lymphnode)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Mesenteric lymphnode)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Sciatic nerve & Gastrocnemial muscle)																				
Abnormality	-	-	-	-	-											-	-	-	-	-
(Bone marrow of femur)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Pancreas)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Submandibular & sublingual gland)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Pituitary gland)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-
(Eye)																	-	-	-	-
Abnormality	-	-	-	-	-											-	-	-	-	-

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.

## Appendix 13-2

Twenty-eight-day repeat dose oral toxicity study with subsequent 14-day recovery test of 2-pentylanthraquinone in rats

## Histological findings in individual males at the end of the recovery period

Dose	0 mg/kg					60 mg/kg				
	1	2	3	4	5	21	22	23	24	25
Animal No.										
(Liver)										

## Fatty change, periportal

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.

## Histological findings in individual females at the end of the recovery period

Dose	0 mg/kg					60 mg/kg				
	31	32	33	34	35	51	52	53	54	55
Animal No.										
(Liver)										

## Fatty change, periportal

-, negative; ±, very slight; +, slight; ++, moderate; +++, severe.