# 4-クロロフェノールのラットにおける
# 28 日間反復投与毒性試験

－最終報告書－

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# 要 約

OECD 既存化学物質安全性点検に係わる毒性調査の一環として，4-クロロフェノールを 0 (対照)，20，100 及び 500 mg/kg の用量で 1 群雌雄各 6 匹の Crj:CD(SD)IGS ラットに 28 日間反復経口投与する毒性試験を実施し，以下の結果を得た．なお，対照群及び 500 mg/kg 群にはそれぞれ雌雄各 6 匹の 14 日間回復群も設けた．

死亡はいずれの群にもみられなかった．一般状態の観察では，500 mg/kg 群の雌雄で振戦，頻呼吸，流涎が認められた．本症状は投与後約 5 分から発現し，発現後 20 ないし 30 分以内に消失する変化であった．

体重及び摂餌量では，被験物質投与に関連すると考えられる変化は認められなかった．

尿検査では，100 mg/kg 群の雄及び 500 mg/kg 群の雌雄で尿量の増加又は増加傾向が認められ，更に 100 mg/kg 群の雄で尿浸透圧及び比重の低下，500 mg/kg 群の雄で尿浸透圧の低下傾向が認められた．また，500 mg/kg 群の雄(1 例のみ)で重度の尿潜血陽性及び尿沈渣における軽度の赤血球陽性が認められた．

血液学的検査では，500 mg/kg 群の雄で白血球数の増加が認められた．

血液生化学的検査，剖検，器官重量及び病理組織学的検査では，被験物質投与に関連すると考えられる変化は認められなかった．

回復試験では，投与期間中にみられた変化に回復性が認められた．

以上のように，本試験では 100 mg/kg 群の雄で尿量の増加が認められ，500 mg/kg 群の雌雄で振戦，頻呼吸，流涎及び尿量の増加又は増加傾向，雄で白血球数の増加が認められたことから，無影響量は雄で 20 mg/kg，雌で 100 mg/kg と考えられた．

# 緒 言

4-クロロフェノールの安全性に関する毒性試験の一環として，本被験物質を雌雄ラットに 28 日間反復経口投与するとともに，投与期間終了後に 14 日間の休薬期間を設けて，その毒性及び回復性について検討したので報告する．

# 試 験 材 料 及 び 方 法

## 1. 被験物質

より提供された 4-クロロフェノール(Lot No.　　)を試験に使用した．本被験物質は純度 99.29%，分子量 128.56 の白色～淡褐色の結晶である(添付資料 1-1)．試験期間中の被験物質の安定性については，投与期間終了後に残余の被験物質を上記の供給源にて分析することにより確認した(添付資料 1-2)．媒体にはコーンオイル(ナカライテスク株式会社，Lot No. V9F1519)を使用した．なお，被験物質は室温，遮光下で，コーンオイルは室温でそれぞれ被験物質室の保管庫に保存した．

## 2. 使用動物及び飼育条件

5 週齢の Crj:CD(SD)IGS ラット(日本チャールス・リバー株式会社)を雌雄各 45 匹購入し，雄は 6 日間，雌は 7 日間の検疫馴化を行った．この間に，全例について一般状態の観察及び体重測定を実施するとともに，雌雄各 3 匹を抜粋して剖検し，異常がないことを確認したのち，雌雄各 36 匹を選んで 6 週齢で試験に使用した．投与開始時の体重は，雄が 187.0～214.0 g，雌が 145.3～171.5 g であった．動物は，温度 24±2°C(許容範囲 21～27°C)，湿度 55±10%(許容範囲 35～75%)，照明 12 時間(午前 7 時～午後 7 時)及び換気回数 13～15 回/時に設定したバリアーシステム飼育室(04 番)でステンレススチール製ハンガーケージ(W260×H200×D380 mm)に個別に収容して飼育した．なお，試験期間中の温度の実測値は最高 26°C，最低 22°C，湿度の実測値は最高 63%，最低 53%であった．飼料は高圧蒸気滅菌処理した固型飼料(MF，オリエンタル酵母工業株式会社)を，飲水は次亜塩素酸ナトリウムを添加(約 2 ppm)した井戸水を自動給水装置によりそれぞれ自由に摂取させた．飼料については財団法人 日本食品分析センターにて，また，飲水については株式会社鶴城 南九科研センターにて分析を行い，いずれも許容基準に適合していることを確認した．飼育器材は高圧蒸気滅菌したものを使用し，ケージは 2 週間に 1

回以上，受皿は週 3 回以上，ラックは 4 週間に 1 回以上交換するとともに，飼育室は毎日清掃し，消毒薬を浸したモップで清拭した．

3. 試験群構成，投与量設定の根拠及び群分け

試験群構成を下表に示した．

| 試験群 | 投与量 (mg/kg) | 性別 | 使用動物数 | 動物番号 |
|---|---|---|---|---|
| 対照群 | 0 | ♂ | 6 + 6* | 901~906, 907*~912* |
| | | ♀ | 6 + 6* | 951~956, 957*~962* |
| 低用量群 | 20 | ♂ | 6 | 913~918 |
| | | ♀ | 6 | 963~968 |
| 中間用量群 | 100 | ♂ | 6 | 919~924 |
| | | ♀ | 6 | 969~974 |
| 高用量群 | 500 | ♂ | 6 + 6* | 925~930, 931*~936* |
| | | ♀ | 6 + 6* | 975~980, 981*~986* |

*：回復試験に使用した動物

投与量は，先に当研究所で実施した 2 週間反復投与毒性予備試験[試験番号 29843(GLP 非適用)，投与量：0，20，100 及び 500 mg/kg]の結果を基に設定した．すなわち，予備試験においては，500 mg/kg 群の雌雄で呼吸促迫，振戦，自発運動の低下及び流涎が認められた．したがって，本試験では，予備試験と同様に 500 mg/kg を高用量とし，以下公比 5 をもって，100 及び 20 mg/kg を設定した．

試験群は，上記 3 用量に対照を加え計 4 群とした．1 群当たりの動物数は，投与期間終了時の剖検例として各群とも雌雄各 6 匹とし，更に，対照群及び高用量群については回復期間終了時の剖検例として雌雄各 6 匹を設けた．

群分けは，投与開始前日に当日の体重を基に層別連続無作為化法で行い，群分け後の動物には動物番号を刻印した耳標を取り付けて個体識別した．また，各ケージには試験番号，動物番号，投与量及び性別を表示したラベルを付けて識別した．

4. 投与経路，投与方法，投与期間及び回復期間

投与経路は，化審法ガイドラインで指定されており，また，予想されるヒトへの曝露経路の一つである経口投与とした。投与には胃管を用い，1 日 1 回投与で 28 日間反復投与した．投与容量は 5 mL/kg とし，個体ごとの投与液量は最新の体重を基に算出した．対照群にはコーンオイルを同様に投与した．

回復試験に供した動物は，投与期間終了後に 14 日間無処置で飼育した．

5. 被験物質と媒体との混合物調製法

被験物質を各濃度ごとに必要量秤量し，コーンオイルに溶解させ，0.4，2.0 及び 10.0 w/v% 溶液を調製した．調製は週 1 回以上の頻度で行い，調製した投与液は褐色ガラスバイアルに入れて飼育区域内の検体保管室の保管庫にて室温保存した．また，初回調製時に，各濃度の投与液について被験物質の濃度確認を実施し，設定濃度の許容範囲(±5%以内)にあることを確認した(添付資料 2)．なお，本調製法による 0.2 及び 40 w/v%コーンオイル溶液は，褐色ガラスバイアル中で室温散光下 8 日間の安定性が確認されている(添付資料 3)．

6. 観察，検査，分析及び測定の頻度及び方法

1) 一般状態の観察，体重及び摂餌量の測定

投与期間中は毎日投与前，投与後約 5 分～30 分及び投与後約 1 時間の 3 回，また，回復期間中は毎日午前，午後の 2 回，それぞれ一般状態の観察及び生死の確認を行った．体重及び摂餌量を投与期間及び回復期間を通して週 2 回の頻度で測定し，更に，投与及び回復最終日にも測定した．

2) 尿検査

投与 4 週目及び回復 2 週目に，すべての動物を代謝ケージに個別収容し，絶食，給水下で午前中の時間帯(投与 4 週目は投与前の時間帯)に採取した新鮮尿について，比色試験紙(プレテスト 8a，和光純薬工業株式会社)を用いて pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血及びウロビリノーゲンを検査した．更に，新鮮尿は 1500 回転/分で 5 分間遠心分離し，得られた尿沈渣について鏡検した．また，新鮮尿採取後に給餌，給水下で採取した 24 時間蓄積尿について，尿量，色調，浸透圧(氷点降下法；OSMOMETER OM801，VOGEL 社)及び比重(屈折率法；尿屈折計，株式会社アタゴ)を測定した．

3) 血液学的検査

投与期間終了後及び回復期間終了後に，すべての動物を 18 時間以上絶食させたのち，ペントバルビタール・ナトリウム 30 mg/kg を腹腔内投与して麻酔し，開腹後，後大静脈腹部から採血を行った．採取した血液の一部は EDTA-2K 処理(EDTA-2K 加血液)して多項目自動血球計数装置(Sysmex CC-780，シスメックス株式会社)を用いて，白血球数(電気抵抗検出方式)，赤血球数(電気抵抗検出方式)，ヘモグロビン量(Oxyhemoglobin 法)，ヘマトクリット値(血球 pulse 波高値検出方式)及び血小板数(電気抵抗検出方式)を測定し，赤血球数，ヘモグロビン量及びヘマトクリット値の測定結果を基に Wintrobe の赤血球恒数[平均赤血球容積(MCV)，平均赤血球血色素量(MCH)及び平均赤血球血色素濃度(MCHC)]を算出した．更に，血液の一部は塗抹標本とし，May-Grünwald-Giemsa 染色を施して白血球百分比を算出するとともに，網状赤血球率検査用の New methylene blue 超生体染色標本を作製して保存した．また，3.8%クエン酸ナトリウム加血液を 3000 回転/分で 15 分間遠心分離し，得られた血漿を用いて全自動血液凝固測定装置(Sysmex CA-5000，シスメックス株式会社)により，プロトロンビン時間(散乱光検出方式)及び活性化部分トロンボプラスチン時間(APTT，散乱光検出方式)を測定した．

4) 血液生化学的検査

血液学的検査と同時に採取したすべての動物の血液を室温で約 60 分間放置後，3000 回転/分で 10 分間遠心分離し，得られた血清を用いて自動分析装置(7170，株式会社 日立製作所)により，総蛋白質(T.protein，Biuret 法)，アルブミン(BCG 法)，A/G 比（総蛋白質及びアルブミンより算出)，総ビリルビン(T.bilirubin，Vanadate oxidation 法)，GOT(UV-rate 法)，GPT(UV-rate 法)，γ-グルタミルトランスペプチダーゼ(γ-GTP，L-γ-Glutamyl-3-hydoroxymethyl-4-nitroanilide 基質法)，アルカリ性フォスファターゼ(ALP，p-Nitrophenylphosphate acid 基質法)，コリンエステラーゼ(Butyrylthiocholine-DTNB 法)，アセチルコリンエステラーゼ(Acetylcholine 基質法)，総コレステロール(T.cholesterol，COD-HDAOS 法)，トリグリセライド(GPO-HDAOS 法，glycerol blanking 法)，リン脂質(Choline oxidase-DAOS 法)，グルコース(Hexokinase-G-6-PDH 法)，尿素窒素(BUN，Urease-GLDH 法)，クレアチニン(Jaffé 法)，無機リン(IP，PNP-XOD 法)及びカルシウム(Ca，MXB 法)を測定した．また，電解質分析装置(PVA-αIII，株式会社アナリティカル・インスツルメンツ)によりナトリウム(Na，電極法)，カリウム(K，電極法)及びクロール(Cl，電量滴定法)を測定した．

5) 剖検，器官重量の測定及び病理組織学的検査

投与期間終了後及び回復期間終了後に，すべての動物について採血を行ったのち，放血死させ，解剖してすべての諸器官及び組織について異常の有無を検査した．剖検後，脳，下垂体，甲状腺(上皮小体を含む)，心臓，肺(気管支を含む)，胸腺，肝臓，脾臓，腎臓，副腎，精嚢，精巣上体，精巣及び卵巣を摘出して器官重量(絶対重量)を測定するとともに，剖検日の体重を基に体重比器官重量(相対重量)を算出した．重量測定器官に加え，脊髄(頸部から胸部)，眼球，気管，膵臓，胃，十二指腸，空腸，回腸(パイエル板を含む)，盲腸，結腸，直腸，腸間膜リンパ節，膀胱，子宮，骨髄(大腿骨)，坐骨神経及び肉眼的異常部位を採取して10%中性緩衝ホルマリン溶液に固定した．なお，10%中性緩衝ホルマリン溶液による固定に先だって，眼球は 2.5%グルタールアルデヒド溶液で，精巣及び精巣上体はブアン液でそれぞれ前固定した．投与期間終了時の対照群及び高用量群の眼球を除く上述した器官及び肉眼的異常部位については，常法に従ってパラフィン切片を作製し，ヘマトキシリン・エオジン(HE)染色を施して光学顕微鏡下で観察した．なお，投与期間終了時の検査において被験物質投与に関連する変化がみられなかったことから，回復期間終了時の検査は実施しなかった．

7. 統計学的処理

体重，摂餌量，尿検査(定性反応は除く)，血液学的検査，血液生化学的検査，器官重量及び体重比器官重量について，各群ごとに平均値と標準偏差を求め，Bartlett 法により分散の均一性を検定した．分散が均一な場合は Dunnett の多重比較検定を用いて，分散が不均一な場合は Steel の多重比較検定を用いて対照群との比較を行った．また，病理組織学的検査については，Mann-Whitney の U 検定法を用いて検定を行った．なお，いずれの場合も有意水準を 1 及び 5%とした．

# 試 験 成 績

1. 一般状態

一般状態の観察結果を Table 1, 2 及び Appendix 1~4 に示した．

すべての群に死亡例はなく，20 及び 100 mg/kg 群では観察期間を通して被験物質投与に関連した一般状態の変化は認められなかった．

500 mg/kg 群では，投与期間を通して振戦，頻呼吸及び流涎が認められた．振戦は雄で 2～6 例/日，雌で 1～6 例/日の頻度で認められ，総発現例数は雄で全例，雌で 11 例であった．頻呼吸は雄で 0～3 例/日，雌で 0～2 例/日の頻度で認められ，総発現例数は雄で 11 例，雌で 9 例であった．流涎は雄で 0～6 例/日，雌で 0～4 例/日の頻度で認められ，総発現例数は雄で 9 例，雌で 8 例であった．振戦，頻呼吸及び流涎の発現時間は，投与後約 5 分から認められ，いずれも投与後 20 ないし 30 分以内には消失した．更に，500 mg/kg 群の雄 1 例(No. 934)で投与 1 日(投与開始日)に振戦及び頻呼吸に加え，横臥姿勢が認められ，横臥姿勢の回復後に自発運動の低下及び緩徐呼吸がみられ，投与後 30 分にいずれの症状も回復した．また，500 mg/kg 群の雌 1 例(No. 984)で投与 3 日の投与前から自発運動の低下，腹式呼吸及び喘鳴が認められたが，投与 4 日の投与前には消失し，以降投与期間を通してこれらの症状は認められなかった．回復期間において，500 mg/kg 群の雌雄で変化は認められなかった．

その他，偶発的な変化として，20 mg/kg 群の雄 1 例で頸部に外傷(掻創)が認められた．

2. 体重

体重推移を Fig. 1，2 及び Table 3，4 並びに Appendix 5~8 に示した．

投与期間及び回復期間を通して，4-クロロフェノール各群は対照群とほぼ同様な推移を示した．

3. 摂餌量

摂餌量を Fig.3，4 及び Table 5，6 並びに Appendix 9~12 に示した．

投与期間を通して，4-クロロフェノール各群は対照群とほぼ同様な推移を示した．

回復期間では，500 mg/kg 群の雄で回復 11 日及び 14 日に増加が認められ，500 mg/kg 群の雌で回復 14 日に減少が認められたが，いずれも投与期間中には認められていない変化であることから，被験物質投与と関連のない偶発的な変化と考えられた．

4. 尿検査

投与 4 週目の検査結果を Table 7 及び Appendix 13，14 に，回復 2 週目の検査結果を Table 8 及び Appendix 15，16 に示した．

投与 4 週目の検査では，100 及び 500 mg/kg 群の雄で尿量の増加が認められ，500 mg/kg 群の雌で尿量の増加傾向が認められた．更に 100 mg/kg 群の雄で尿浸透圧及び比重の低下が認め

られ，500 mg/kg 群の雄で尿浸透圧の低下傾向が認められた．また，500 mg/kg 群の雄 1 例(No. 930)で重度の尿潜血陽性及び尿沈渣における軽度の赤血球が認められた．

回復 2 週目の検査では，500 mg/kg 群の雌雄で変化は認められなかった．

5. 血液学的検査

投与期間終了時の検査結果を Table 9 及び Appendix 17，18 に，回復期間終了時の検査結果を Table 10 及び Appendix 19，20 に示した．

投与期間終了時の検査では，500 mg/kg 群の雄で白血球数の増加が認められた．

回復期間終了時の検査では，500 mg/kg 群の雌で MCHC の増加が認められたが，同様の変化は投与期間終了時の検査時には認められていないことから，被験物質投与と関連のない偶発的な変化と考えられた．

6. 血液生化学的検査

投与期間終了時の検査結果を Table 11 及び Appendix 21，22 に，回復期間終了時の検査結果を Table 12 及び Appendix 23，24 に示した．

投与期間終了時の検査では，500 mg/kg 群の雄で GPT 及び K の増加が認められたが，生理的な変動範囲内(下表)の軽度な変化であった．

回復期間終了時の検査では，500 mg/kg 群の雄で BUN の増加が認められ，500 mg/kg 群の雌で GOT の減少，総コレステロール及びリン脂質の増加が認められたが，同様の変化は投与期間終了時の検査時には認められていないことから，被験物質投与と関連のない偶発的な変化と考えられた．

10 週齢 Crj:CD(SD)IGS ラットの背景データ

| 性 | 項目 | 動物数 | 平均値 | 標準偏差 (S.D.) | 最小値 | 最大値 | -2S.D. | +2S.D. |
|---|---|---|---|---|---|---|---|---|
| 雄 | GPT(IU/L) | 120 | 23 | 7 | 13 | 59 | 8 | 37 |
| | K(mEq/L) | 120 | 4.23 | 0.29 | 3.85 | 6.46 | 3.66 | 4.80 |

7. 剖検

投与期間終了時の検査結果を Table 13 及び Appendix 25，26 に，回復期間終了時の検査結果を Table 14 及び Appendix 27，28 に示した．

投与期間終了時の検査では，4-クロロフェノール各群で被験物質投与に関連すると考えられる変化は認められなかった．なお，偶発的な変化として，一般状態で外傷(掻創)がみられた 20mg/kg 群の雄 1 例に頸部皮膚の痂皮形成が認められた．

回復期間終了時の検査では，対照群及び 500 mg/kg 群ともに変化は認められなかった．

8. 器官重量

投与期間終了時の検査結果を Table 15 及び Appendix 29，30 に，回復期間終了時の検査結果を Table 16 及び Appendix 31，32 に示した．

投与期間終了時の検査では，4-クロロフェノール各群で被験物質投与に関連すると考えられる変化は認められなかった．なお，20 mg/kg 群の雄で肝臓の相対重量の減少が認められたが，同様の変化は中間及び高用量群では認められていないことから，偶発的な変化と考えられた．

回復期間終了時の検査では，500 mg/kg 群の雄で肝臓の絶対及び相対重量の増加，精嚢の相対重量の減少が認められ，500 mg/kg 群の雌で下垂体及び副腎の絶対重量の減少が認められたが，同様の変化は投与期間終了時の検査時には認められていないことから，被験物質投与と関連のない偶発的な変化と考えられた．

9. 病理組織学的検査

投与期間終了時の検査結果を Table 17 及び Appendix 33，34 に示した．

投与期間終了時の検査では，4-クロロフェノール各群で被験物質投与に関連すると考えられる変化は認められなかった．なお，偶発的な変化として，20mg/kg 群の雄 1 例で肉眼的に頸部皮膚の痂皮がみられた部位に，扁平上皮細胞の過形成及び真皮から皮下組織にかけてリンパ球を主体とする細胞浸潤が認められ，対照群の雌 1 例に肝臓の門脈周囲性の脂肪変性が認められた．

以上のほか，対照群及び 500 mg/kg 群で検査を行った胃，小腸，大腸，膵臓，気管，肺，胸腺，腸間膜リンパ節，脾臓，骨髄，心臓，腎臓，膀胱，精巣，精巣上体，精嚢，卵巣，子宮，下垂体，甲状腺，副腎，脳，脊髄及び坐骨神経には変化は認められなかった．

# 考 察

4-クロロフェノールの安全性に関する毒性試験の一環として，本被験物質の 0，20，100 及び 500 mg/kg を雌雄ラットに 28 日間反復経口投与し，その毒性及び回復性について検討した．

いずれの群でも死亡例は認められなかった．一般状態観察では，500 mg/kg 群の雌雄で投与後約 5 分から振戦，頻呼吸及び流涎が認められ，いずれも投与後 20 ないし 30 分に消失した．振戦及び頻呼吸については，本被験物質のラットにおける単回投与毒性試験 [1]においても認められており，本被験物質投与による急性中毒による変化と考えられた．流涎については，4-クロロフェノールが皮膚及び眼粘膜に対して刺激性を有することが報告(添付資料 1)されていることから，被験物質の粘膜刺激性に関連した変化であると考えられた．また，500 mg/kg 群で振戦及び頻呼吸に加え，横臥姿勢，自発運動の低下，緩徐呼吸，腹式呼吸あるいは喘鳴が認められ，被験物質投与の影響により，症状が強く発現する例もみられた．

体重及び摂餌量では被験物質投与に関連すると考えられる変化は認められなかった．

尿検査では，100 mg/kg 群の雄及び 500 mg/kg 群の雌雄で尿量の増加又は増加傾向が認められた．また，尿量の増加に伴った変化として，100 mg/kg 群の雄で尿浸透圧及び比重の低下，500 mg/kg 群の雄で尿浸透圧の低下傾向が認められた．また，1 例のみであるが 500 mg/kg 群の雄で重度の尿潜血陽性及び尿沈渣における軽度の赤血球陽性が認められた．これらの尿の変化について，その発生機序は不明であるが，腎機能に関連する血清パラメーターに機能障害を示唆する明らかな変化は認められておらず，腎臓の病理組織学的検査においても器質的な変化は認められていないことから，毒性学的には重篤な変化ではないと考えられた．

血液学的検査では，500 mg/kg 群の雄で白血球数の増加が認められたが，白血球画分の比率に変化は認められておらず，病理組織学的検査においても白血球数の増加を示唆する変化は認められていないことから，毒性学的には重篤な変化ではないと考えられた．

血液生化学的検査では，500 mg/kg 群の雄で GOT 及び K の増加が認められた．GOT は，肝臓，心筋などの細胞内に多く局在する酵素であるが，病理組織学的検査では肝臓，心臓などに器質的な変化はなく，かつ生理的な変動範囲内の軽度な変化であることから，被験物質投与と関連のない変化と考えられた．K の増加については，一般に高 K 血症は腎機能障害や高度の脱水によって生ずることが知られているが，上述のように腎機能及び器質的障害や高度な脱水は認められておらず，かつ生理的な変動範囲内の軽度な変化であることから，被験物質投与と関連のない変化と

考えられた.

剖検，器官重量測定及び病理組織学的検査では，被験物質投与に関連すると考えられる変化は認められなかった.

回復試験では，上述の投与期間中にみられた変化には回復性が認められたことから，被験物質投与で生じた変化は可逆的であると考えられた.

以上のように，本試験では 100 mg/kg 群の雄で尿量の増加が認められ，500 mg/kg 群の雌雄で振戦，頻呼吸，流涎及び尿量の増加又は増加傾向，雄で白血球数の増加が認められたことから，無影響量は雄で 20 mg/kg，雌で 100 mg/kg と考えられた.

# 参 考 文 献

1)　　：4-クロロフェノールのラットにおける単回投与毒性試験，株式会社パナファーム・ラボラトリーズ(PPL 試験番号：19826).

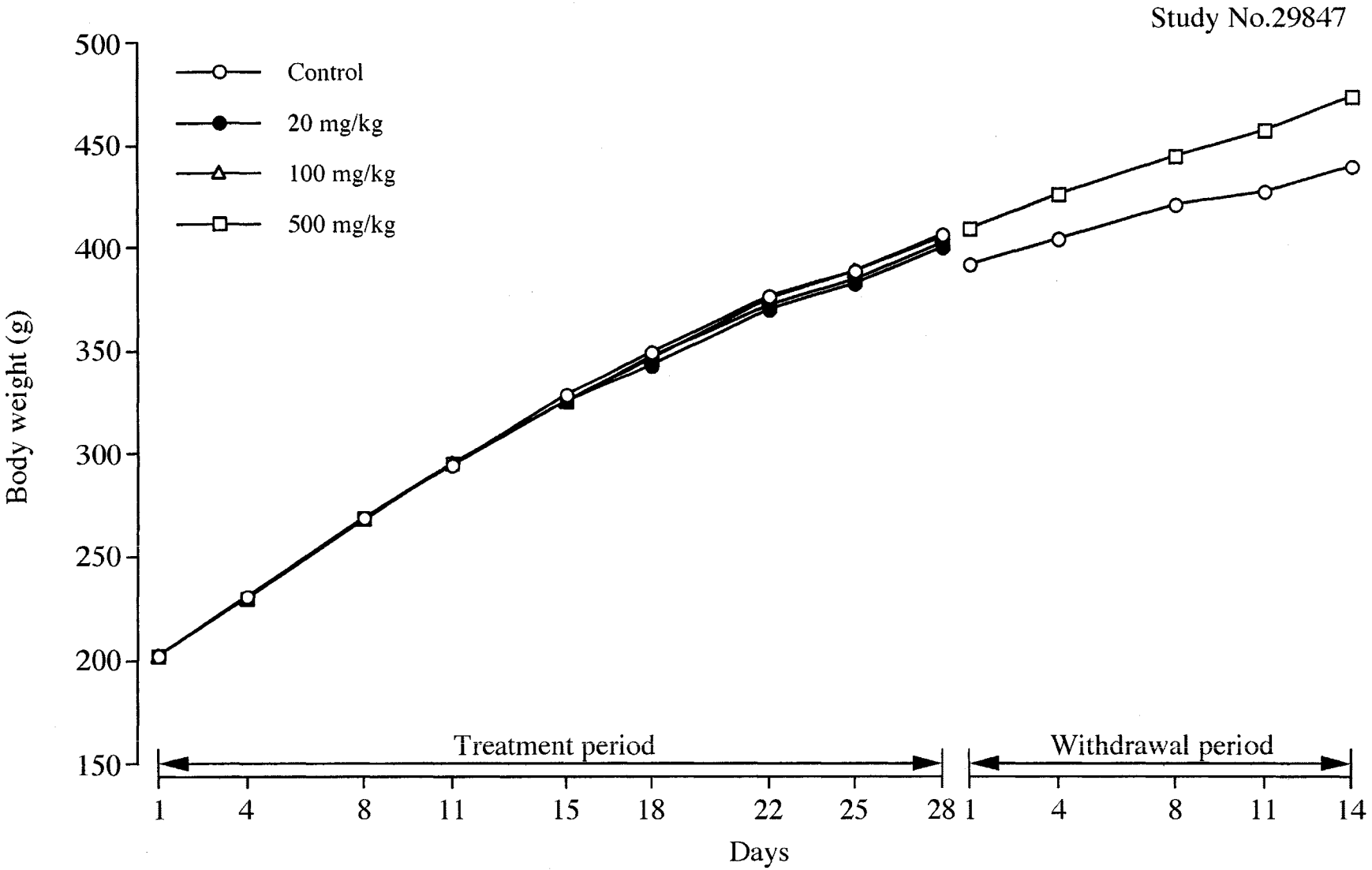


Fig.1 Mean body weight changes in male rats treated orally with 4-chlorophenol for 28 days followed by 14-day withdrawal period.

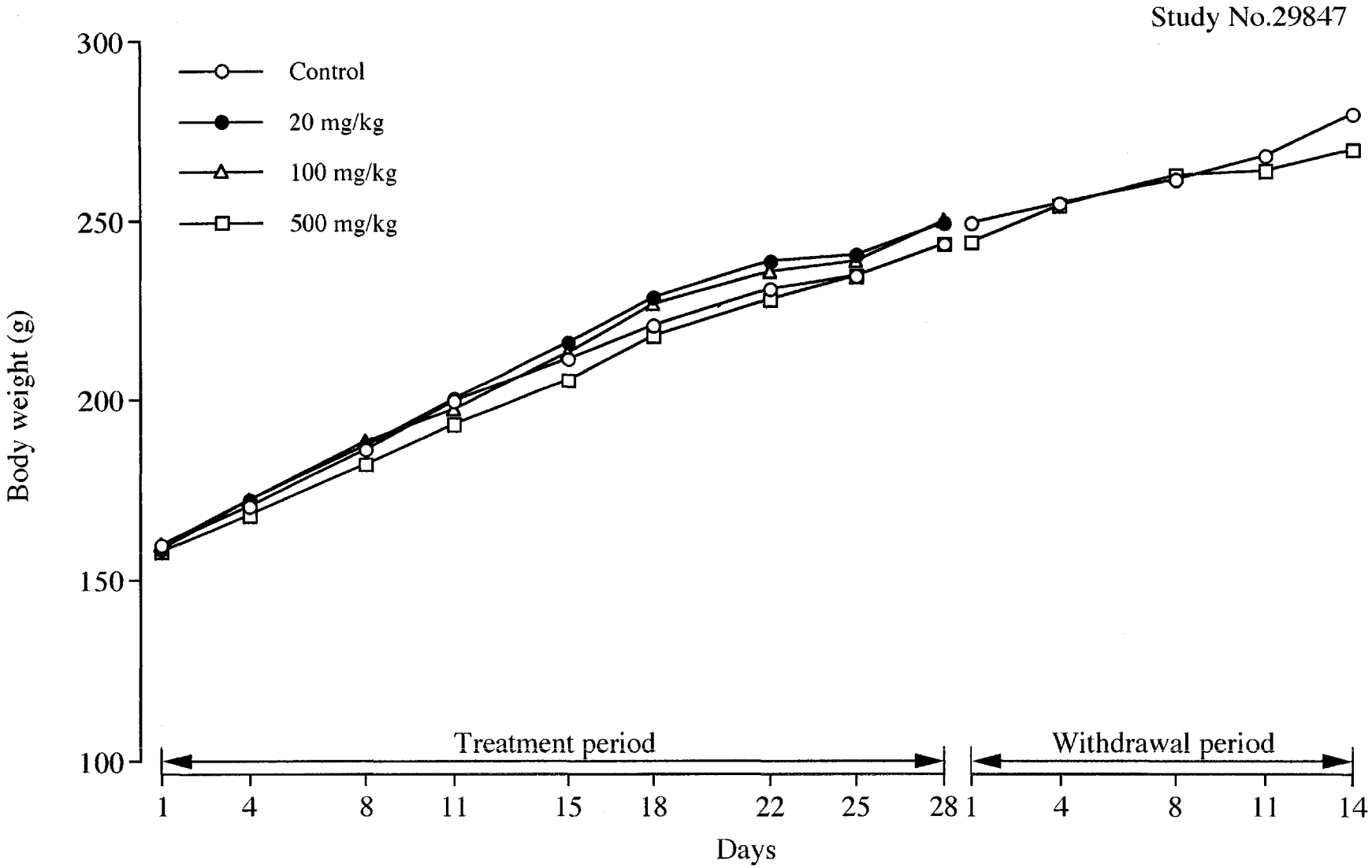


Fig.2 Mean body weight changes in female rats treated orally with 4-chlorophenol for 28 days followed by 14-day withdrawal period.

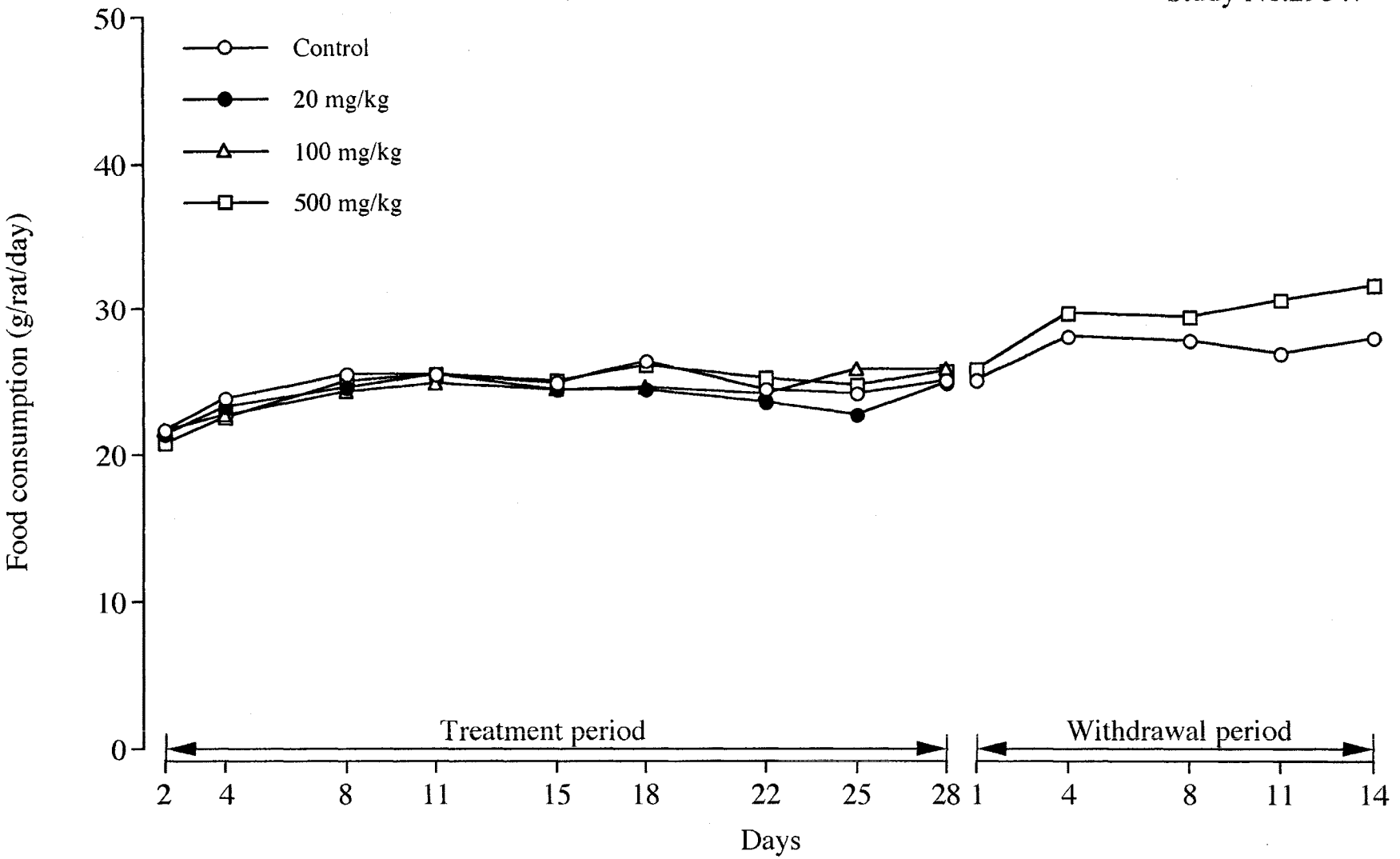


Fig.3 Mean food consumption in male rats treated orally with 4-chlorophenol for 28 days followed by 14-day withdrawal period.

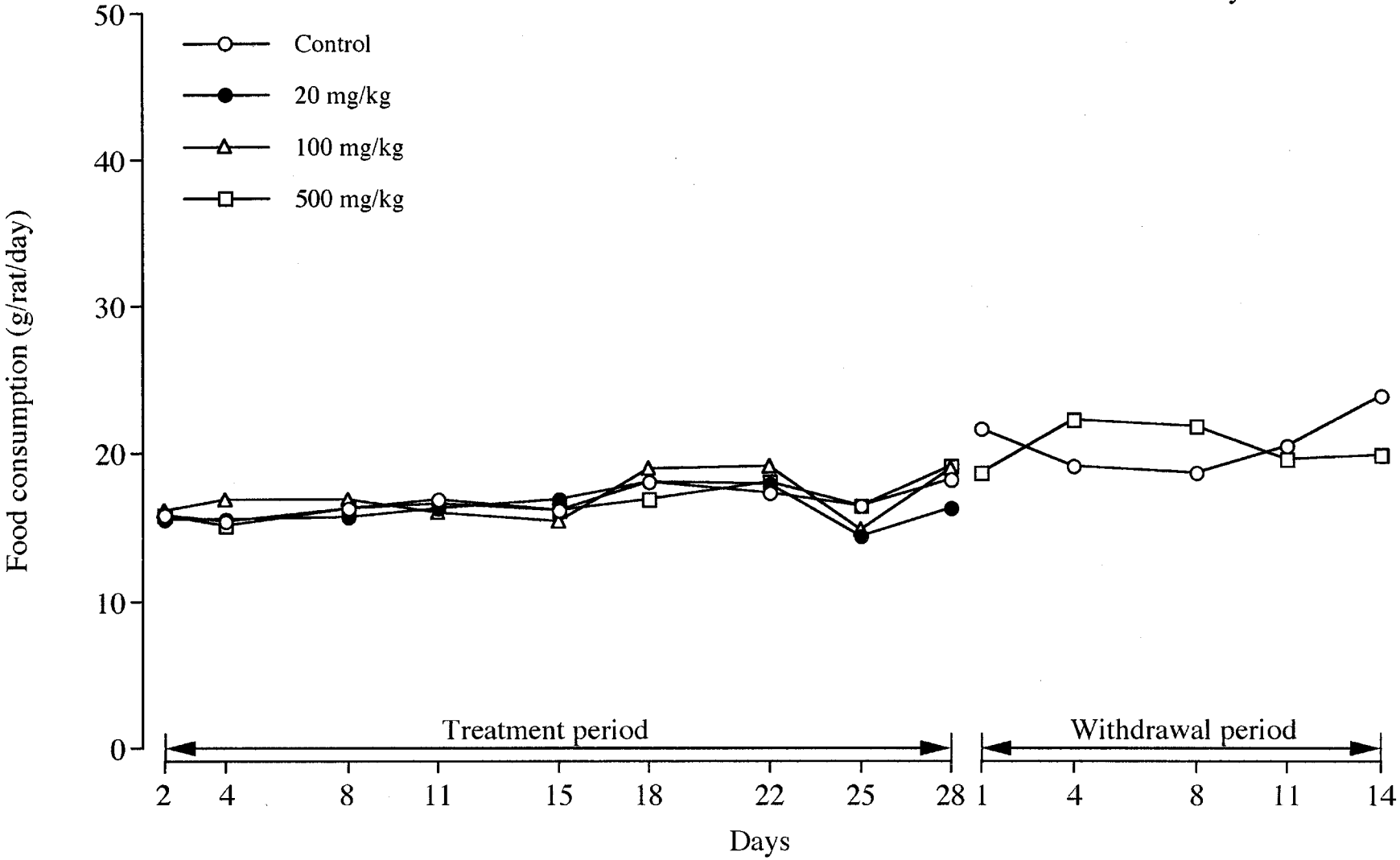


Fig.4 Mean food consumption in female rats treated orally with 4-chlorophenol for 28 days followed by 14-day withdrawal period.

Table 1 Incidence of clinical signs in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | Clinical sign | Days of treatment | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
| Male | Control | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | 20 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 5 | 5 |
| | | Trauma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 100 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 9 | 10 | 6 | 9 | 7 | 6 | 6 | 8 | 7 | 7 | 7 | 6 | 5 | 7 | 8 | 5 | 6 |
| | | Tremor | 3 | 2 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 3 | 3 | 2 | 4 | 2 | 2 | 3 | 4 |
| | | Tachypnea | 2 | 0 | 2 | 1 | 1 | 3 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 3 | 1 |
| | | Salivation | 0 | 0 | 5 | 0 | 1 | 2 | 3 | 1 | 4 | 3 | 3 | 6 | 5 | 4 | 2 | 3 | 2 |
| | | Lateral position | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Hypoactivity | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Bradypnea | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Female | Control | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | 20 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 100 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 7 | 9 | 8 | 8 | 6 | 10 | 8 | 8 | 7 | 6 | 7 | 7 | 10 | 9 | 8 | 7 | 6 |
| | | Tremor | 5 | 1 | 3 | 4 | 3 | 2 | 4 | 2 | 5 | 6 | 2 | 4 | 1 | 2 | 3 | 4 | 4 |
| | | Tachypnea | 1 | 0 | 0 | 1 | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 2 | 0 | 1 | 2 | 1 | 1 |
| | | Salivation | 0 | 2 | 0 | 0 | 1 | 0 | 2 | 3 | 0 | 0 | 4 | 2 | 1 | 1 | 1 | 1 | 3 |
| | | Hypoactivity | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Abdominal respiration | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Wheezing | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Table 1 - continued Incidence of clinical signs in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | Clinical sign | Days of treatment | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
| Male | Control | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | 20 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | | Trauma | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 4 | 6 | 8 | 4 | 6 | 7 | 5 | 7 | 5 | 4 | 5 |
| | | Tremor | 6 | 6 | 3 | 5 | 4 | 3 | 3 | 3 | 3 | 4 | 3 |
| | | Tachypnea | 1 | 1 | 1 | 1 | 1 | 0 | 2 | 1 | 2 | 1 | 1 |
| | | Salivation | 3 | 0 | 3 | 5 | 4 | 4 | 5 | 3 | 3 | 4 | 4 |
| | | Lateral position | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Hypoactivity | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Bradypnea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Female | Control | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | 20 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 100 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | No abnormality | 7 | 8 | 9 | 9 | 7 | 7 | 6 | 9 | 8 | 7 | 7 |
| | | Tremor | 4 | 3 | 2 | 2 | 4 | 5 | 5 | 2 | 3 | 3 | 3 |
| | | Tachypnea | 0 | 2 | 2 | 1 | 1 | 2 | 2 | 1 | 2 | 1 | 0 |
| | | Salivation | 1 | 1 | 1 | 2 | 3 | 2 | 3 | 3 | 2 | 3 | 4 |
| | | Hypoactivity | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Abdominal respiration | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Wheezing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Table 2 Incidence of clinical signs in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | Clinical sign | Days of withdrawal | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| Male | Control | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Female | Control | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 500 mg/kg | Number of examined | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | No abnormality | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

Table 3 Body weights in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Days of treatment 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Body weight (g) | | | | | | | | |
| Male | Control | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 201.5 | 230.4 | 268.8 | 294.6 | 327.7 | 349.2 | 375.2 | 387.5 | 405.4 |
| | | S.D. | ±4.6 | ±6.3 | ±8.2 | ±11.9 | ±18.2 | ±21.3 | ±27.1 | ±28.1 | ±31.1 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 201.3 | 229.9 | 268.7 | 293.7 | 324.8 | 342.5 | 369.7 | 381.3 | 399.4 |
| | | S.D. | ±7.1 | ±9.9 | ±15.2 | ±20.1 | ±24.6 | ±28.3 | ±31.8 | ±34.5 | ±37.7 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 202.0 | 229.4 | 267.0 | 295.3 | 325.3 | 346.1 | 374.0 | 388.2 | 404.5 |
| | | S.D. | ±7.2 | ±9.3 | ±17.0 | ±20.7 | ±25.3 | ±28.5 | ±35.2 | ±37.9 | ±41.2 |
| | 500 mg/kg | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 201.5 | 229.3 | 268.3 | 295.7 | 325.5 | 346.3 | 371.5 | 383.8 | 401.1 |
| | | S.D. | ±7.5 | ±8.8 | ±11.6 | ±14.2 | ±17.3 | ±18.6 | ±20.0 | ±21.7 | ±25.9 |
| Female | Control | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 159.7 | 170.3 | 185.7 | 199.4 | 211.3 | 220.6 | 230.4 | 234.1 | 242.8 |
| | | S.D. | ±7.3 | ±6.7 | ±8.0 | ±11.4 | ±12.1 | ±14.7 | ±15.2 | ±14.7 | ±13.5 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 158.4 | 172.1 | 187.4 | 199.8 | 215.8 | 228.0 | 238.4 | 240.1 | 248.9 |
| | | S.D. | ±9.7 | ±11.2 | ±11.8 | ±13.5 | ±17.2 | ±20.2 | ±21.8 | ±21.4 | ±21.0 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 159.4 | 171.9 | 188.1 | 197.4 | 212.7 | 226.4 | 235.5 | 238.3 | 249.7 |
| | | S.D. | ±5.2 | ±7.4 | ±12.2 | ±14.3 | ±14.7 | ±14.8 | ±17.9 | ±16.7 | ±15.2 |
| | 500 mg/kg | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 157.6 | 168.0 | 182.0 | 192.7 | 205.4 | 217.4 | 227.8 | 234.0 | 242.8 |
| | | S.D. | ±2.8 | ±6.3 | ±10.6 | ±11.6 | ±13.3 | ±12.5 | ±14.3 | ±13.1 | ±12.9 |

Not significantly different from control.

Table 4 Body weights in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Days of withdrawal 1 | 4 | 8 | 11 | 14 |
|---|---|---|---|---|---|---|---|
| | | | Body weight (g) | | | | |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 391.4 | 403.1 | 419.3 | 426.2 | 438.7 |
| | | S.D. | ±30.9 | ±33.8 | ±36.0 | ±34.1 | ±38.9 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 408.3 | 425.0 | 443.6 | 455.3 | 472.1 |
| | | S.D. | ±24.5 | ±28.7 | ±30.3 | ±32.7 | ±33.7 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 248.8 | 254.1 | 260.6 | 266.8 | 279.1 |
| | | S.D. | ±19.2 | ±20.5 | ±20.2 | ±18.0 | ±20.3 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 243.6 | 253.4 | 261.6 | 263.1 | 268.7 |
| | | S.D. | ±14.2 | ±14.7 | ±15.9 | ±17.2 | ±13.8 |

Not significantly different from control.

Table 5 Food consumption in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Days of treatment 2 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Food consumption (g/rat/day) | | | | | | | | |
| Male | Control | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 21.6 | 23.9 | 25.4 | 25.5 | 24.9 | 26.3 | 24.4 | 24.2 | 25.0 |
| | | S.D. | ±1.2 | ±1.6 | ±1.5 | ±2.1 | ±2.7 | ±2.8 | ±3.5 | ±3.3 | ±3.3 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 21.4 | 23.3 | 24.6 | 25.5 | 24.4 | 24.4 | 23.6 | 22.6 | 24.8 |
| | | S.D. | ±2.2 | ±2.3 | ±3.0 | ±4.5 | ±2.6 | ±3.6 | ±3.3 | ±2.9 | ±3.9 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 21.6 | 22.6 | 24.3 | 24.9 | 24.4 | 24.5 | 24.1 | 25.8 | 25.7 |
| | | S.D. | ±1.8 | ±2.0 | ±3.0 | ±2.4 | ±2.3 | ±2.7 | ±2.3 | ±2.8 | ±2.5 |
| | 500 mg/kg | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 20.8 | 22.5 | 25.0 | 25.5 | 25.0 | 26.1 | 25.1 | 24.7 | 25.6 |
| | | S.D. | ±2.1 | ±1.8 | ±1.8 | ±2.0 | ±2.3 | ±1.8 | ±2.0 | ±1.2 | ±2.0 |
| Female | Control | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 15.9 | 15.4 | 16.3 | 16.9 | 16.2 | 18.1 | 17.4 | 16.5 | 18.2 |
| | | S.D. | ±1.6 | ±1.7 | ±2.3 | ±2.4 | ±2.4 | ±2.2 | ±2.2 | ±2.5 | ±4.3 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 15.6 | 15.6 | 15.8 | 16.3 | 16.9 | 18.1 | 18.0 | 14.4 | 16.3 |
| | | S.D. | ±1.7 | ±1.3 | ±1.8 | ±2.0 | ±3.1 | ±3.0 | ±2.5 | ±1.8 | ±2.5 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 16.2 | 16.9 | 16.9 | 16.0 | 15.5 | 19.0 | 19.2 | 14.9 | 19.0 |
| | | S.D. | ±1.0 | ±1.8 | ±2.5 | ±2.2 | ±2.2 | ±0.6 | ±0.9 | ±3.0 | ±1.5 |
| | 500 mg/kg | N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Mean | 15.9 | 15.2 | 16.3 | 16.6 | 16.2 | 17.0 | 18.1 | 16.5 | 19.1 |
| | | S.D. | ±1.2 | ±1.8 | ±1.9 | ±2.0 | ±2.3 | ±2.2 | ±1.7 | ±2.3 | ±2.4 |

Not significantly different from control.

Table 6 Food consumption in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Days of withdrawal 1 | 4 | 8 | 11 | 14 |
|---|---|---|---|---|---|---|---|
| | | | Food consumption (g/rat/day) | | | | |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 25.0 | 28.0 | 27.7 | 26.8 | 27.8 |
| | | S.D. | ±3.5 | ±3.6 | ±3.2 | ±2.6 | ±3.0 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 25.8 | 29.5 | 29.3 | 30.4* | 31.5* |
| | | S.D. | ±1.5 | ±1.0 | ±1.4 | ±0.9 | ±1.9 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 21.6 | 19.2 | 18.7 | 20.4 | 23.8 |
| | | S.D. | ±4.6 | ±4.7 | ±3.7 | ±1.1 | ±2.8 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 18.7 | 22.2 | 21.8 | 19.5 | 19.8* |
| | | S.D. | ±2.2 | ±2.3 | ±2.0 | ±2.9 | ±1.4 |

*: $P<0.05$ (significantly different from control).

Table 7 Urinary findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Urine volume (mL/24hr) | Osmotic pressure (Osm/kg) | Specific gravity |
|---|---|---|---|---|---|
| Male | Control | N | 12 | 12 | 12 |
| | | Mean | 10.7 | 1.642 | 1.056 |
| | | S.D. | ±3.7 | ±0.458 | ±0.015 |
| | 20 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 8.4 | 1.706 | 1.059 |
| | | S.D. | ±1.3 | ±0.220 | ±0.007 |
| | 100 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 18.1** | 0.955* | 1.033** |
| | | S.D. | ±3.8 | ±0.143 | ±0.006 |
| | 500 mg/kg | N | 12 | 12 | 12 |
| | | Mean | 16.1** | 1.293 | 1.052 |
| | | S.D. | ±4.9 | ±0.501 | ±0.018 |
| Female | Control | N | 12 | 12 | 12 |
| | | Mean | 6.4 | 1.629 | 1.055 |
| | | S.D. | ±3.9 | ±0.630 | ±0.022 |
| | 20 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 7.2 | 1.310 | 1.044 |
| | | S.D. | ±3.5 | ±0.424 | ±0.014 |
| | 100 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 6.0 | 1.652 | 1.056 |
| | | S.D. | ±3.1 | ±0.487 | ±0.016 |
| | 500 mg/kg | N | 12 | 12 | 12 |
| | | Mean | 11.5 | 1.320 | 1.051 |
| | | S.D. | ±8.3 | ±0.525 | ±0.020 |

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 7 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | Number of animals | Color | | pH | | | | | | Protein | | | | Glucose | Ketone body |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | PY | Y | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | - | ± | + | ++ | - | - |
| Male | Control | 12 | 0 | 12 | 0 | 0 | 2 | 1 | 9 | 0 | 0 | 1 | 6 | 5 | 12 | 12 |
| | 20 mg/kg | 6 | 0 | 6 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 1 | 5 | 6 | 6 |
| | 100 mg/kg | 6 | 0 | 6 | 0 | 0 | 1 | 0 | 4 | 1 | 0 | 0 | 4 | 2 | 6 | 6 |
| | 500 mg/kg | 12 | 0 | 12 | 0 | 0 | 0 | 0 | 9 | 3 | 0 | 1 | 4 | 7 | 12 | 12 |
| Female | Control | 12 | 0 | 12 | 2 | 1 | 0 | 3 | 5 | 1 | 2 | 2 | 4 | 4 | 12 | 12 |
| | 20 mg/kg | 6 | 0 | 6 | 1 | 0 | 0 | 1 | 4 | 0 | 2 | 1 | 2 | 1 | 6 | 6 |
| | 100 mg/kg | 6 | 0 | 6 | 0 | 0 | 2 | 0 | 4 | 0 | 0 | 4 | 2 | 0 | 6 | 6 |
| | 500 mg/kg | 12 | 1 | 11 | 1 | 0 | 1 | 4 | 6 | 0 | 5 | 4 | 2 | 1 | 12 | 12 |

Abbreviation: PY, pale yellow; Y, yellow.
Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked; ++++, very marked.

Table 7 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | Number of animals | Bilirubin | Occult blood | | | Urobilinogen (mg/dL) |
|---|---|---|---|---|---|---|---|
| | | | - | - | + | +++ | <1 |
| Male | Control | 12 | 12 | 10 | 2 | 0 | 12 |
| | 20 mg/kg | 6 | 6 | 6 | 0 | 0 | 6 |
| | 100 mg/kg | 6 | 6 | 6 | 0 | 0 | 6 |
| | 500 mg/kg | 12 | 12 | 11 | 0 | 1 | 12 |
| Female | Control | 12 | 12 | 10 | 2 | 0 | 12 |
| | 20 mg/kg | 6 | 6 | 6 | 0 | 0 | 6 |
| | 100 mg/kg | 6 | 6 | 6 | 0 | 0 | 6 |
| | 500 mg/kg | 12 | 12 | 11 | 1 | 0 | 12 |

Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked.

Table 7 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | Number of animals | Urinary sediment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Epithelial cells | Erythrocytes | | Leukocytes | Casts | Crystals | | | |
| | | | - | - | + | - | - | - | + | ++ | +++ |
| Male | Control | 12 | 12 | 12 | 0 | 12 | 12 | 9 | 2 | 0 | 1 |
| | 20 mg/kg | 6 | 6 | 6 | 0 | 6 | 6 | 4 | 1 | 0 | 1 |
| | 100 mg/kg | 6 | 6 | 6 | 0 | 6 | 6 | 6 | 0 | 0 | 0 |
| | 500 mg/kg | 12 | 12 | 11 | 1 | 12 | 12 | 11 | 0 | 0 | 1 |
| Female | Control | 12 | 12 | 12 | 0 | 12 | 12 | 9 | 2 | 1 | 0 |
| | 20 mg/kg | 6 | 6 | 6 | 0 | 6 | 6 | 5 | 1 | 0 | 0 |
| | 100 mg/kg | 6 | 6 | 6 | 0 | 6 | 6 | 4 | 2 | 0 | 0 |
| | 500 mg/kg | 12 | 12 | 12 | 0 | 12 | 12 | 8 | 2 | 1 | 1 |

Not significantly different from control.
Grade signs are as follows.
Epithelial cells: -, < 3/field; +, 3/field ≦ and < 10/field; ++, 10/field ≦ and < 20/field; +++, ≧ 20/field.
Erythrocytes : -, < 10/field; +, 10/field ≦ and < 30/field; ++, 30/field ≦ and < 100/field; +++, countless.
Leukocytes : -, < 3/field; +, 3/field ≦ and < 20/field; ++, 20/field ≦ and < 40/field; +++, ≧ 40/field.
Casts : -, none; +, ≧ 1/all field.
Crystals : -, < 10/field; +, 10/field ≦ and < 20/field; ++, 20/field ≦ and < 30/field; +++, countless.

Table 8 Urinary findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Urine volume (mL/24hr) | Osmotic pressure (Osm/kg) | Specific gravity |
|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 |
| | | Mean | 20.6 | 1.284 | 1.041 |
| | | S.D. | ±10.9 | ±0.497 | ±0.015 |
| | 500 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 20.6 | 1.451 | 1.046 |
| | | S.D. | ±8.5 | ±0.729 | ±0.022 |
| Female | Control | N | 6 | 6 | 6 |
| | | Mean | 13.5 | 1.233 | 1.038 |
| | | S.D. | ±7.0 | ±0.293 | ±0.009 |
| | 500 mg/kg | N | 6 | 6 | 6 |
| | | Mean | 11.2 | 1.467 | 1.046 |
| | | S.D. | ±6.2 | ±0.373 | ±0.012 |

Not significantly different from control.

Table 8 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | Number of animals | Color | | pH | | | | Protein | | | | Glucose | Ketone body |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | PY | Y | 7.0 | 7.5 | 8.0 | 8.5 | - | ± | + | ++ | - | - |
| Male | Control | 6 | 2 | 4 | 1 | 1 | 4 | 0 | 0 | 0 | 4 | 2 | 6 | 6 |
| | 500 mg/kg | 6 | 1 | 5 | 0 | 0 | 6 | 0 | 0 | 2 | 2 | 2 | 6 | 6 |
| Female | Control | 6 | 1 | 5 | 0 | 0 | 6 | 0 | 5 | 0 | 1 | 0 | 6 | 6 |
| | 500 mg/kg | 6 | 1 | 5 | 0 | 3 | 2 | 1 | 3 | 0 | 2 | 1 | 6 | 6 |

Abbreviation: PY, pale yellow; Y, yellow.
Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked; ++++, very marked.

Table 8 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | Number of animals | Bilirubin | Occult blood | Urobilinogen (mg/dL) |
|---|---|---|---|---|---|
| | | | - | - | <1 |
| Male | Control | 6 | 6 | 6 | 6 |
| | 500 mg/kg | 6 | 6 | 6 | 6 |
| Female | Control | 6 | 6 | 6 | 6 |
| | 500 mg/kg | 6 | 6 | 6 | 6 |

Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked.

Table 8 - continued Urinary findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | Number of animals | Urinary sediment | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals | | |
| | | | - | - | - | - | - | + | ++ |
| Male | Control | 6 | 6 | 6 | 6 | 6 | 3 | 1 | 2 |
| | 500 mg/kg | 6 | 6 | 6 | 6 | 6 | 5 | 1 | 0 |
| Female | Control | 6 | 6 | 6 | 6 | 6 | 6 | 0 | 0 |
| | 500 mg/kg | 6 | 6 | 6 | 6 | 6 | 6 | 0 | 0 |

Not significantly different from control.
Grade signs are as follows.
Epithelial cells: -, < 3/field; +, 3/field ≦ and < 10/field; ++, 10/field ≦ and < 20/field; +++, ≧ 20/field.
Erythrocytes : -, < 10/field; +, 10/field ≦ and < 30/field; ++, 30/field ≦ and < 100/field; +++, countless.
Leukocytes : -, < 3/field; +, 3/field ≦ and < 20/field; ++, 20/field ≦ and < 40/field; +++, ≧ 40/field.
Casts : -, none; +, ≧ 1/all field.
Crystals : -, < 10/field; +, 10/field ≦ and < 20/field; ++, 20/field ≦ and < 30/field; +++, countless.

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Table 9 Hematological findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Leukocytes ($10^2$ /μL) | Erythrocytes ($10^4$ /μL) | Hemoglobin (g/dL) | Hematocrit (%) | MCV (fL) | MCH (pg) | MCHC (%) | Platelets ($10^4$ /μL) | PT (sec) | APTT (sec) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 84 | 794 | 14.6 | 47.0 | 59 | 18.4 | 31.0 | 96.3 | 14.4 | 22.5 |
| | | S.D. | ±11 | ±19 | ±0.3 | ±0.7 | ±2 | ±0.6 | ±0.5 | ±6.7 | ±2.1 | ±3.2 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 97 | 790 | 14.7 | 47.2 | 60 | 18.7 | 31.2 | 97.1 | 13.8 | 20.4 |
| | | S.D. | ±21 | ±22 | ±0.3 | ±1.2 | ±2 | ±0.4 | ±0.5 | ±10.6 | ±1.6 | ±3.4 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 99 | 781 | 14.5 | 46.8 | 60 | 18.6 | 30.9 | 94.4 | 15.3 | 21.9 |
| | | S.D. | ±16 | ±29 | ±0.4 | ±1.7 | ±4 | ±0.9 | ±0.4 | ±4.8 | ±1.7 | ±1.7 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 114** | 802 | 14.7 | 47.4 | 59 | 18.3 | 30.9 | 95.2 | 14.4 | 22.3 |
| | | S.D. | ±11 | ±19 | ±0.5 | ±1.1 | ±1 | ±0.5 | ±0.6 | ±4.7 | ±1.5 | ±2.5 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 53 | 739 | 13.9 | 44.3 | 60 | 18.8 | 31.4 | 97.7 | 10.7 | 17.8 |
| | | S.D. | ±13 | ±27 | ±0.4 | ±1.8 | ±1 | ±0.3 | ±0.7 | ±6.1 | ±0.5 | ±2.1 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 55 | 758 | 14.3 | 44.9 | 60 | 18.9 | 31.8 | 101.8 | 10.7 | 17.5 |
| | | S.D. | ±22 | ±25 | ±0.2 | ±1.1 | ±2 | ±0.7 | ±0.8 | ±7.0 | ±0.4 | ±2.3 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 50 | 763 | 14.1 | 44.5 | 58 | 18.5 | 31.6 | 104.5 | 10.9 | 17.4 |
| | | S.D. | ±12 | ±29 | ±0.6 | ±1.5 | ±1 | ±0.6 | ±0.4 | ±7.1 | ±0.4 | ±1.0 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 65 | 753 | 13.8 | 44.2 | 59 | 18.3 | 31.2 | 101.1 | 10.9 | 18.2 |
| | | S.D. | ±22 | ±31 | ±0.5 | ±1.3 | ±2 | ±0.5 | ±0.8 | ±8.0 | ±0.6 | ±1.4 |

**: $P<0.01$ (significantly different from control).

Table 9 - continued Hematological findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Differential leukocyte count | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Eosinophil (%) | Stab neutrophil (%) | Segmented neutrophil (%) | Lymphocyte (%) | Basophil (%) | Monocyte (%) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.7 | 0.0 | 11.0 | 87.2 | 0.0 | 1.2 |
| | | S.D. | ±0.5 | ±0.0 | ±5.2 | ±5.6 | ±0.0 | ±0.8 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.3 | 0.0 | 7.8 | 89.8 | 0.0 | 2.0 |
| | | S.D. | ±0.5 | ±0.0 | ±1.9 | ±1.2 | ±0.0 | ±0.9 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.3 | 0.0 | 8.0 | 89.0 | 0.0 | 1.7 |
| | | S.D. | ±1.2 | ±0.0 | ±3.8 | ±3.7 | ±0.0 | ±1.4 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.3 | 0.0 | 10.2 | 88.5 | 0.0 | 1.0 |
| | | S.D. | ±0.5 | ±0.0 | ±4.3 | ±4.4 | ±0.0 | ±0.6 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.7 | 0.0 | 13.2 | 85.2 | 0.0 | 1.0 |
| | | S.D. | ±0.5 | ±0.0 | ±6.6 | ±7.1 | ±0.0 | ±0.9 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.3 | 0.0 | 10.8 | 86.8 | 0.0 | 1.0 |
| | | S.D. | ±1.9 | ±0.0 | ±3.3 | ±5.0 | ±0.0 | ±0.9 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.5 | 0.0 | 10.8 | 86.5 | 0.0 | 1.2 |
| | | S.D. | ±1.2 | ±0.0 | ±4.4 | ±4.1 | ±0.0 | ±1.2 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.0 | 0.0 | 12.7 | 85.0 | 0.0 | 1.3 |
| | | S.D. | ±1.3 | ±0.0 | ±7.1 | ±6.9 | ±0.0 | ±1.2 |

Not significantly different from control.

Table 10 Hematological findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Leukocytes ($10^2$ /μL) | Erythrocytes ($10^4$ /μL) | Hemoglobin (g/dL) | Hematocrit (%) | MCV (fL) | MCH (pg) | MCHC (%) | Platelets ($10^4$ /μL) | PT (sec) | APTT (sec) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 88 | 845 | 14.8 | 47.3 | 56 | 17.5 | 31.2 | 103.2 | 15.0 | 24.6 |
| | | S.D. | ±17 | ±32 | ±0.5 | ±1.5 | ±2 | ±0.7 | ±0.4 | ±10.5 | ±3.3 | ±1.9 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 84 | 807 | 14.4 | 46.3 | 57 | 17.9 | 31.2 | 90.5 | 15.4 | 22.9 |
| | | S.D. | ±11 | ±31 | ±0.6 | ±1.4 | ±1 | ±0.4 | ±0.6 | ±10.6 | ±1.4 | ±1.0 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 53 | 779 | 14.2 | 45.3 | 58 | 18.2 | 31.3 | 92.7 | 11.1 | 18.8 |
| | | S.D. | ±16 | ±35 | ±0.4 | ±1.0 | ±2 | ±0.8 | ±0.6 | ±10.0 | ±0.3 | ±1.4 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 45 | 770 | 14.0 | 43.5 | 57 | 18.1 | 32.1* | 96.6 | 10.8 | 18.3 |
| | | S.D. | ±14 | ±35 | ±0.5 | ±1.9 | ±1 | ±0.3 | ±0.6 | ±8.8 | ±0.2 | ±1.3 |

*: $P<0.05$ (significantly different from control).

Table 10 - continued Hematological findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Differential leukocyte count | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Eosinophil (%) | Stab neutrophil (%) | Segmented neutrophil (%) | Lymphocyte (%) | Basophil (%) | Monocyte (%) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.7 | 0.0 | 12.3 | 85.5 | 0.0 | 1.5 |
| | | S.D. | ±0.8 | ±0.0 | ±4.3 | ±5.0 | ±0.0 | ±1.0 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.8 | 0.0 | 14.8 | 83.5 | 0.0 | 0.8 |
| | | S.D. | ±0.8 | ±0.0 | ±7.8 | ±7.9 | ±0.0 | ±0.8 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.5 | 0.0 | 9.8 | 88.0 | 0.0 | 0.7 |
| | | S.D. | ±0.8 | ±0.0 | ±4.7 | ±5.4 | ±0.0 | ±0.8 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.8 | 0.0 | 10.0 | 87.0 | 0.0 | 1.2 |
| | | S.D. | ±0.8 | ±0.0 | ±4.6 | ±4.1 | ±0.0 | ±1.2 |

Not significantly different from control.

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Table 11 Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | T.Protein (g/dL) | Albumin (g/dL) | A/G ratio | T.Bilirubin (mg/dL) | GOT (IU/L) | GPT (IU/L) | γ-GTP (IU/L) | ALP (IU/L) | Cholinesterase (IU/L) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.2 | 3.7 | 2.36 | 0.0 | 87 | 18 | 0.2 | 348 | 58 |
| | | S.D. | ±0.2 | ±0.1 | ±0.24 | ±0.0 | ±16 | ±2 | ±0.2 | ±34 | ±14 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.2 | 3.6 | 2.33 | 0.0 | 84 | 17 | 0.1 | 344 | 67 |
| | | S.D. | ±0.2 | ±0.2 | ±0.30 | ±0.0 | ±11 | ±2 | ±0.2 | ±63 | ±27 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.1 | 3.6 | 2.38 | 0.0 | 89 | 18 | 0.2 | 350 | 66 |
| | | S.D. | ±0.2 | ±0.1 | ±0.11 | ±0.0 | ±13 | ±1 | ±0.2 | ±100 | ±26 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.2 | 3.7 | 2.51 | 0.0 | 90 | 21* | 0.3 | 425 | 55 |
| | | S.D. | ±0.1 | ±0.1 | ±0.48 | ±0.0 | ±4 | ±1 | ±0.3 | ±77 | ±22 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.2 | 3.8 | 2.85 | 0.0 | 73 | 15 | 0.2 | 217 | 265 |
| | | S.D. | ±0.4 | ±0.3 | ±0.62 | ±0.0 | ±8 | ±3 | ±0.2 | ±40 | ±59 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.1 | 3.8 | 2.97 | 0.0 | 76 | 15 | 0.3 | 222 | 339 |
| | | S.D. | ±0.3 | ±0.3 | ±0.47 | ±0.0 | ±11 | ±3 | ±0.3 | ±37 | ±94 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.4 | 4.0 | 2.81 | 0.0 | 77 | 14 | 0.1 | 196 | 338 |
| | | S.D. | ±0.2 | ±0.2 | ±0.36 | ±0.0 | ±5 | ±2 | ±0.1 | ±49 | ±122 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.6 | 4.0 | 2.59 | 0.0 | 79 | 16 | 0.3 | 236 | 245 |
| | | S.D. | ±0.5 | ±0.5 | ±0.35 | ±0.0 | ±9 | ±3 | ±0.2 | ±37 | ±144 |

*: $P<0.05$ (significantly different from control).

Table 11- continued Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Acetylcholinesterase (⊿pH) | T.Cholesterol (mg/dL) | Triglycerides (mg/dL) | Phospholipids (mg/dL) | Glucose (mg/dL) | BUN (mg/dL) | Creatinine (mg/dL) | IP (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.05 | 57 | 61 | 106 | 137 | 13.3 | 0.4 | 8.0 |
| | | S.D. | ±0.01 | ±5 | ±15 | ±7 | ±24 | ±2.0 | ±0.1 | ±0.4 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.05 | 54 | 64 | 104 | 120 | 13.7 | 0.4 | 7.8 |
| | | S.D. | ±0.02 | ±12 | ±39 | ±22 | ±15 | ±1.1 | ±0.0 | ±0.6 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.05 | 55 | 66 | 108 | 128 | 13.9 | 0.4 | 7.9 |
| | | S.D. | ±0.03 | ±15 | ±39 | ±24 | ±16 | ±1.0 | ±0.1 | ±0.3 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.05 | 54 | 77 | 110 | 131 | 12.7 | 0.4 | 8.2 |
| | | S.D. | ±0.02 | ±6 | ±18 | ±10 | ±21 | ±1.8 | ±0.1 | ±0.8 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.25 | 56 | 14 | 110 | 116 | 16.2 | 0.4 | 6.9 |
| | | S.D. | ±0.05 | ±15 | ±6 | ±29 | ±17 | ±1.4 | ±0.0 | ±0.9 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.32 | 49 | 12 | 97 | 112 | 17.3 | 0.4 | 7.3 |
| | | S.D. | ±0.09 | ±12 | ±5 | ±17 | ±13 | ±2.1 | ±0.0 | ±0.4 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.32 | 55 | 15 | 108 | 117 | 16.8 | 0.4 | 7.0 |
| | | S.D. | ±0.11 | ±12 | ±2 | ±15 | ±14 | ±2.8 | ±0.0 | ±0.6 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.23 | 67 | 19 | 132 | 120 | 16.9 | 0.4 | 6.9 |
| | | S.D. | ±0.13 | ±10 | ±9 | ±18 | ±18 | ±1.8 | ±0.1 | ±0.6 |

Not significantly different from control.

Table 11- continued Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Ca (mg/dL) | Na (mEq/L) | K (mEq/L) | Cl (mEq/L) |
|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 |
| | | Mean | 10.0 | 145.2 | 4.16 | 105.5 |
| | | S.D. | ±0.1 | ±0.8 | ±0.08 | ±1.0 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.9 | 144.5 | 4.18 | 105.1 |
| | | S.D. | ±0.3 | ±0.4 | ±0.13 | ±1.4 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 10.0 | 145.0 | 4.19 | 105.5 |
| | | S.D. | ±0.2 | ±0.8 | ±0.10 | ±2.0 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 10.1 | 144.8 | 4.35* | 104.6 |
| | | S.D. | ±0.2 | ±0.9 | ±0.16 | ±1.4 |
| Female | Control | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.9 | 145.9 | 4.27 | 108.4 |
| | | S.D. | ±0.2 | ±1.3 | ±0.19 | ±1.7 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.7 | 144.7 | 4.25 | 107.2 |
| | | S.D. | ±0.2 | ±0.6 | ±0.25 | ±1.2 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.9 | 145.4 | 4.32 | 108.3 |
| | | S.D. | ±0.2 | ±0.6 | ±0.17 | ±1.5 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.9 | 144.9 | 4.44 | 106.8 |
| | | S.D. | ±0.3 | ±0.6 | ±0.27 | ±1.0 |

*: $P<0.05$ (significantly different from control).

Table 12 Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | T.Protein (g/dL) | Albumin (g/dL) | A/G ratio | T.Bilirubin (mg/dL) | GOT (IU/L) | GPT (IU/L) | γ-GTP (IU/L) | ALP (IU/L) | Cholinesterase (IU/L) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.4 | 3.6 | 2.02 | 0.0 | 80 | 19 | 0.5 | 290 | 38 |
| | | S.D. | ±0.1 | ±0.2 | ±0.28 | ±0.0 | ±10 | ±2 | ±0.2 | ±54 | ±20 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.3 | 3.5 | 1.98 | 0.0 | 87 | 20 | 0.5 | 258 | 50 |
| | | S.D. | ±0.3 | ±0.2 | ±0.22 | ±0.0 | ±9 | ±3 | ±0.2 | ±32 | ±16 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.8 | 4.2 | 2.78 | 0.0 | 89 | 17 | 0.7 | 166 | 392 |
| | | S.D. | ±0.4 | ±0.2 | ±0.28 | ±0.1 | ±11 | ±3 | ±0.3 | ±24 | ±44 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 5.8 | 4.1 | 2.47 | 0.0 | 78* | 18 | 0.8 | 168 | 356 |
| | | S.D. | ±0.4 | ±0.4 | ±0.30 | ±0.0 | ±4 | ±1 | ±0.2 | ±34 | ±124 |

*: $P<0.05$ (significantly different from control).

Table 12- continued Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Acetylcholinesterase (⊿pH) | T.Cholesterol (mg/dL) | Triglycerides (mg/dL) | Phospholipids (mg/dL) | Glucose (mg/dL) | BUN (mg/dL) | Creatinine (mg/dL) | IP (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.05 | 50 | 41 | 92 | 123 | 14.6 | 0.4 | 7.0 |
| | | S.D. | ±0.02 | ±12 | ±23 | ±15 | ±15 | ±1.1 | ±0.1 | ±0.4 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.06 | 55 | 57 | 100 | 125 | 16.4* | 0.4 | 7.1 |
| | | S.D. | ±0.02 | ±10 | ±24 | ±14 | ±8 | ±1.3 | ±0.0 | ±0.4 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.38 | 58 | 22 | 121 | 109 | 18.7 | 0.5 | 6.1 |
| | | S.D. | ±0.05 | ±6 | ±8 | ±12 | ±8 | ±1.6 | ±0.1 | ±0.8 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 0.35 | 73** | 26 | 146* | 114 | 18.8 | 0.5 | 6.0 |
| | | S.D. | ±0.11 | ±6 | ±10 | ±15 | ±13 | ±2.0 | ±0.0 | ±0.9 |

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 12- continued Biochemical findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Ca (mg/dL) | Na (mEq/L) | K (mEq/L) | Cl (mEq/L) |
|---|---|---|---|---|---|---|
| Male | Control | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.7 | 145.0 | 4.22 | 106.0 |
| | | S.D. | ±0.3 | ±0.4 | ±0.11 | ±1.1 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 9.7 | 145.1 | 4.20 | 105.6 |
| | | S.D. | ±0.2 | ±1.1 | ±0.17 | ±2.0 |
| Female | Control | N | 6 | 6 | 6 | 6 |
| | | Mean | 10.0 | 145.0 | 4.10 | 107.7 |
| | | S.D. | ±0.2 | ±1.1 | ±0.20 | ±1.4 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 |
| | | Mean | 10.0 | 144.2 | 4.23 | 107.3 |
| | | S.D. | ±0.2 | ±0.9 | ±0.27 | ±1.4 |

Not significantly different from control.

Table 13 Necropsy findings in rats treated orally with 4-Chlorophenol for 28 days

| Organs and findings \ Sex | Male | | | |
|---|---|---|---|---|
| Group and dose | Control | 20 mg/kg | 100 mg/kg | 500 mg/kg |
| Number of animals | 6 | 6 | 6 | 6 |
| Integumentary system | | | | |
| Integument | | | | |
| Crust | 0 | 1 | 0 | 0 |

No appreciable changes in all other organs and tissues.

Table 13- continued Necropsy findings in rats treated orally with 4-Chlorophenol for 28 days

| Organs and findings \ Sex | Female | | | |
|---|---|---|---|---|
| Group and dose | Control | 20 mg/kg | 100 mg/kg | 500 mg/kg |
| Number of animals | 6 | 6 | 6 | 6 |
| Integumentary system | | | | |
| Integument | | | | |
| Crust | 0 | 0 | 0 | 0 |

No appreciable changes in all other organs and tissues.

Table 14 Necropsy findings in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Organs and findings \ Sex | Male | | Female | |
|---|---|---|---|---|
| Group and dose | Control | 500 mg/kg | Control | 500 mg/kg |
| Number of animals | 6 | 6 | 6 | 6 |
| All organs and tissues | NR | NR | NR | NR |

NR, no remarkable change.

Table 15 Organ weights in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Final body weight | Brain | | Pituitary | | Thyroids | | Heart | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (g) | (g) | (g/100gB.W.) | (mg) | (mg/100gB.W.) | (mg) | (mg/100gB.W.) | (g) | (g/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 394.5 | 2.12 | 0.54 | 12.8 | 3.3 | 24.2 | 6.2 | 1.40 | 0.36 |
| | | S.D. | ±19.0 | ±0.06 | ±0.03 | ±1.6 | ±0.4 | ±4.1 | ±1.2 | ±0.09 | ±0.03 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 375.5 | 2.06 | 0.55 | 12.1 | 3.2 | 23.6 | 6.3 | 1.34 | 0.36 |
| | | S.D. | ±33.6 | ±0.08 | ±0.05 | ±2.1 | ±0.4 | ±2.5 | ±0.7 | ±0.11 | ±0.02 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 378.6 | 2.09 | 0.56 | 12.3 | 3.2 | 24.7 | 6.6 | 1.42 | 0.38 |
| | | S.D. | ±36.4 | ±0.05 | ±0.05 | ±1.2 | ±0.3 | ±3.1 | ±0.9 | ±0.13 | ±0.04 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 367.8 | 2.08 | 0.57 | 12.4 | 3.4 | 23.1 | 6.3 | 1.36 | 0.37 |
| | | S.D. | ±27.6 | ±0.05 | ±0.04 | ±0.6 | ±0.2 | ±3.5 | ±0.6 | ±0.08 | ±0.04 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 226.3 | 1.93 | 0.85 | 14.6 | 6.5 | 16.5 | 7.3 | 0.91 | 0.40 |
| | | S.D. | ±8.5 | ±0.08 | ±0.03 | ±2.8 | ±1.3 | ±3.4 | ±1.4 | ±0.11 | ±0.05 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 235.3 | 1.98 | 0.85 | 16.5 | 7.0 | 18.5 | 7.8 | 0.95 | 0.40 |
| | | S.D. | ±19.6 | ±0.06 | ±0.08 | ±2.5 | ±0.6 | ±4.2 | ±1.5 | ±0.10 | ±0.02 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 233.6 | 1.96 | 0.84 | 14.5 | 6.2 | 16.3 | 7.0 | 0.92 | 0.39 |
| | | S.D. | ±15.4 | ±0.06 | ±0.03 | ±1.4 | ±0.5 | ±2.5 | ±0.7 | ±0.10 | ±0.04 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 226.3 | 1.97 | 0.87 | 14.3 | 6.3 | 17.3 | 7.6 | 0.92 | 0.41 |
| | | S.D. | ±13.8 | ±0.07 | ±0.06 | ±1.4 | ±0.8 | ±3.4 | ±1.2 | ±0.04 | ±0.03 |

Not significantly different from control.

Table 15- continued Organ weights in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Lungs | | Thymus | | Liver | | Spleen | | Kidneys | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.47 | 0.37 | 0.52 | 0.13 | 12.91 | 3.27 | 0.75 | 0.19 | 2.86 | 0.73 |
| | | S.D. | ±0.09 | ±0.03 | ±0.06 | ±0.01 | ±0.87 | ±0.12 | ±0.12 | ±0.02 | ±0.15 | ±0.04 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.41 | 0.38 | 0.60 | 0.16 | 11.11 | 2.95** | 0.73 | 0.20 | 2.65 | 0.71 |
| | | S.D. | ±0.08 | ±0.03 | ±0.10 | ±0.02 | ±1.44 | ±0.15 | ±0.06 | ±0.02 | ±0.27 | ±0.08 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.39 | 0.37 | 0.62 | 0.16 | 11.87 | 3.13 | 0.77 | 0.20 | 2.79 | 0.74 |
| | | S.D. | ±0.11 | ±0.01 | ±0.09 | ±0.01 | ±1.51 | ±0.13 | ±0.10 | ±0.03 | ±0.29 | ±0.08 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.40 | 0.38 | 0.55 | 0.15 | 11.76 | 3.19 | 0.74 | 0.20 | 2.73 | 0.75 |
| | | S.D. | ±0.13 | ±0.02 | ±0.09 | ±0.03 | ±1.44 | ±0.21 | ±0.07 | ±0.01 | ±0.16 | ±0.08 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.07 | 0.47 | 0.45 | 0.20 | 7.00 | 3.10 | 0.52 | 0.23 | 1.75 | 0.77 |
| | | S.D. | ±0.08 | ±0.02 | ±0.07 | ±0.03 | ±0.63 | ±0.28 | ±0.06 | ±0.03 | ±0.11 | ±0.04 |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.14 | 0.48 | 0.55 | 0.23 | 7.07 | 3.01 | 0.56 | 0.24 | 1.78 | 0.76 |
| | | S.D. | ±0.06 | ±0.02 | ±0.09 | ±0.02 | ±0.60 | ±0.13 | ±0.07 | ±0.02 | ±0.10 | ±0.04 |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.10 | 0.47 | 0.48 | 0.20 | 7.08 | 3.03 | 0.58 | 0.25 | 1.78 | 0.77 |
| | | S.D. | ±0.11 | ±0.04 | ±0.12 | ±0.04 | ±0.60 | ±0.13 | ±0.11 | ±0.03 | ±0.14 | ±0.06 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.12 | 0.49 | 0.51 | 0.22 | 7.38 | 3.26 | 0.52 | 0.23 | 1.74 | 0.77 |
| | | S.D. | ±0.05 | ±0.02 | ±0.14 | ±0.06 | ±0.83 | ±0.18 | ±0.06 | ±0.03 | ±0.15 | ±0.05 |

**: $P<0.01$ (significantly different from control).

Table 15- continued Organ weights in rats treated orally with 4-Chlorophenol for 28 days

| Sex | Group and dose | | Adrenals | | Seminal Vesicle | | Epididymides | | Testes | | Ovaries | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (mg) | (mg/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (mg) | (mg/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 55.2 | 14.1 | 1.32 | 0.33 | 0.93 | 0.24 | 3.18 | 0.81 | | |
| | | S.D. | ±5.6 | ±1.9 | ±0.28 | ±0.07 | ±0.07 | ±0.02 | ±0.25 | ±0.10 | | |
| | 20 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 56.2 | 14.9 | 1.49 | 0.40 | 0.92 | 0.25 | 2.94 | 0.78 | | |
| | | S.D. | ±10.0 | ±1.4 | ±0.21 | ±0.08 | ±0.09 | ±0.04 | ±0.31 | ±0.08 | | |
| | 100 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 53.6 | 14.2 | 1.41 | 0.37 | 0.90 | 0.24 | 3.22 | 0.86 | | |
| | | S.D. | ±6.2 | ±1.6 | ±0.19 | ±0.03 | ±0.07 | ±0.03 | ±0.14 | ±0.08 | | |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 54.0 | 14.7 | 1.42 | 0.39 | 0.92 | 0.25 | 3.01 | 0.82 | | |
| | | S.D. | ±5.6 | ±1.3 | ±0.16 | ±0.03 | ±0.05 | ±0.02 | ±0.26 | ±0.06 | | |
| Female | Control | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 66.0 | 29.2 | | | | | | | 78.5 | 34.6 |
| | | S.D. | ±2.0 | ±1.7 | | | | | | | ±14.2 | ±5.5 |
| | 20 mg/kg | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 66.8 | 28.6 | | | | | | | 90.2 | 38.2 |
| | | S.D. | ±4.2 | ±3.5 | | | | | | | ±15.0 | ±4.4 |
| | 100 mg/kg | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 63.5 | 27.3 | | | | | | | 89.6 | 38.2 |
| | | S.D. | ±5.8 | ±2.5 | | | | | | | ±17.8 | ±5.7 |
| | 500 mg/kg | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 59.4 | 26.3 | | | | | | | 83.8 | 37.0 |
| | | S.D. | ±8.0 | ±3.8 | | | | | | | ±11.7 | ±4.3 |

Not significantly different from control.

Table 16 Organ weights in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Final body weight | Brain | | Pituitary | | Thyroids | | Heart | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (g) | (g) | (g/100gB.W.) | (mg) | (mg/100gB.W.) | (mg) | (mg/100gB.W.) | (g) | (g/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 409.6 | 2.16 | 0.53 | 13.7 | 3.4 | 28.2 | 6.9 | 1.50 | 0.37 |
| | | S.D. | ±36.2 | ±0.10 | ±0.04 | ±1.4 | ±0.1 | ±2.3 | ±0.7 | ±0.16 | ±0.03 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 435.1 | 2.19 | 0.51 | 13.9 | 3.2 | 28.5 | 6.6 | 1.44 | 0.33 |
| | | S.D. | ±31.3 | ±0.06 | ±0.05 | ±1.4 | ±0.3 | ±5.5 | ±1.4 | ±0.16 | ±0.04 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 255.5 | 2.02 | 0.80 | 17.8 | 7.0 | 21.1 | 8.4 | 1.02 | 0.40 |
| | | S.D. | ±18.9 | ±0.08 | ±0.06 | ±1.4 | ±0.9 | ±4.3 | ±2.2 | ±0.15 | ±0.04 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 251.6 | 1.97 | 0.78 | 15.5* | 6.2 | 16.7 | 6.7 | 0.94 | 0.37 |
| | | S.D. | ±12.6 | ±0.09 | ±0.06 | ±1.8 | ±0.8 | ±3.1 | ±1.1 | ±0.10 | ±0.03 |

*: $P<0.05$ (significantly different from control).

Table 16- continued Organ weights in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Lungs | | Thymus | | Liver | | Spleen | | Kidneys | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.46 | 0.36 | 0.42 | 0.10 | 11.90 | 2.91 | 0.77 | 0.19 | 3.09 | 0.76 |
| | | S.D. | ±0.14 | ±0.03 | ±0.04 | ±0.01 | ±1.00 | ±0.07 | ±0.16 | ±0.04 | ±0.23 | ±0.04 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.42 | 0.33 | 0.52 | 0.12 | 13.28* | 3.05* | 0.89 | 0.21 | 3.03 | 0.70 |
| | | S.D. | ±0.15 | ±0.02 | ±0.13 | ±0.02 | ±1.00 | ±0.12 | ±0.11 | ±0.03 | ±0.42 | ±0.09 |
| Female | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.14 | 0.45 | 0.45 | 0.18 | 7.38 | 2.89 | 0.57 | 0.22 | 1.89 | 0.74 |
| | | S.D. | ±0.12 | ±0.03 | ±0.08 | ±0.04 | ±0.49 | ±0.11 | ±0.06 | ±0.02 | ±0.19 | ±0.04 |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Mean | 1.11 | 0.44 | 0.39 | 0.15 | 7.16 | 2.85 | 0.52 | 0.21 | 1.83 | 0.73 |
| | | S.D. | ±0.10 | ±0.04 | ±0.07 | ±0.02 | ±0.64 | ±0.19 | ±0.07 | ±0.03 | ±0.29 | ±0.10 |

*: $P<0.05$ (significantly different from control).

Table 16- continued Organ weights in rats treated orally with 4-Chlorophenol for 28 days followed by 14-day withdrawal period

| Sex | Group and dose | | Adrenals | | Seminal Vesicle | | Epididymides | | Testes | | Ovaries | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | (mg) | (mg/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (g) | (g/100gB.W.) | (mg) | (mg/100gB.W.) |
| Male | Control | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 58.0 | 14.3 | 1.81 | 0.44 | 1.22 | 0.30 | 3.26 | 0.80 | | |
| | | S.D. | ±9.4 | ±2.4 | ±0.05 | ±0.03 | ±0.08 | ±0.02 | ±0.30 | ±0.09 | | |
| | 500 mg/kg | N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | | |
| | | Mean | 58.8 | 13.6 | 1.61 | 0.37* | 1.22 | 0.28 | 3.13 | 0.72 | | |
| | | S.D. | ±8.5 | ±1.9 | ±0.21 | ±0.05 | ±0.13 | ±0.04 | ±0.15 | ±0.06 | | |
| Female | Control | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 74.0 | 29.1 | | | | | | | 81.4 | 32.2 |
| | | S.D. | ±8.0 | ±4.0 | | | | | | | ±10.6 | ±5.7 |
| | 500 mg/kg | N | 6 | 6 | | | | | | | 6 | 6 |
| | | Mean | 63.6* | 25.4 | | | | | | | 74.1 | 29.5 |
| | | S.D. | ±6.6 | ±3.2 | | | | | | | ±7.0 | ±2.4 |

*: $P<0.05$ (significantly different from control).

Table 17 Histopathological findings in rats treated orally with 4-Chlorophenol for 28 days

| Organs and findings \ Sex | Male | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group and dose | Control | | | | | 20 mg/kg | | | | | 100 mg/kg | | | | | 500 mg/kg | | | | |
| Number of animals | 6 | | | | | 6 | | | | | 6 | | | | | 6 | | | | |
| | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total |
| Digestive system | | | | | | | | | | | | | | | | | | | | |
| Liver | | | (6) | | | | | (0) | | | | | (0) | | | | | (6) | | |
| Degeneration, hepatocyte, fatty, periportal | 6 | 0 | 0 | 0 | 0 | | | | | | | | | | | 6 | 0 | 0 | 0 | 0 |
| Integumentary system | | | | | | | | | | | | | | | | | | | | |
| Integument | | | (0) | | | | | (1) | | | | | (0) | | | | | (0) | | |
| Crust | | | | | | 0 | 1 | 0 | 0 | 1 | | | | | | | | | | |
| Hyperplasia, squamous cell | | | | | | 0 | 1 | 0 | 0 | 1 | | | | | | | | | | |
| Cellular infiltration, lymphocyte | | | | | | 0 | 1 | 0 | 0 | 1 | | | | | | | | | | |

Not significantly different from control.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the stomach, small intestine, large intestine, pancreas, trachea, lung, thymus, mesenteric lymph node, spleen, bone marrow(femur), heart, kidney, urinary bladder, testis, epididymis, seminal vesicle, pituitary, thyroid, adrenal, brain, spinal cord and sciatic nerve in control and 500 mg/kg groups.

Table 17- continued Histopathological findings in rats treated orally with 4-Chlorophenol for 28 days

| Organs and findings | Sex | Female | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Group and dose | Control | | | | | 20 mg/kg | | | | | 100 mg/kg | | | | | 500 mg/kg | | | | |
| | Number of animals | 6 | | | | | 6 | | | | | 6 | | | | | 6 | | | | |
| | | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total | - | + | ++ | +++ | Total |
| Digestive system | | | | | | | | | | | | | | | | | | | | | |
| Liver | | | | (6) | | | | | (0) | | | | | (0) | | | | | (6) | | |
| Degeneration, hepatocyte, fatty, periportal | | 5 | 1 | 0 | 0 | 1 | | | | | | | | | | | 6 | 0 | 0 | 0 | 0 |
| Integumentary system | | | | | | | | | | | | | | | | | | | | | |
| Integument | | | | (0) | | | | | (0) | | | | | (0) | | | | | (0) | | |
| Crust | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, squamous cell | | | | | | | | | | | | | | | | | | | | | |
| Cellular infiltration, lymphocyte | | | | | | | | | | | | | | | | | | | | | |

Not significantly different from control.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the stomach, small intestine, large intestine, pancreas, trachea, lung, thymus, mesenteric lymph node, spleen, bone marrow(femur), heart, kidney, urinary bladder, ovary, uterus, pituitary, thyroid, adrenal, brain, spinal cord and sciatic nerve in control and 500 mg/kg groups.