

物の中期多臓器発がん性試験による腎発がんプロモーション作用の検索. 第 24 回日本毒性病理学会, 名古屋, 第 24 回日本毒性病理学会講演要旨集 : p87 (P-79), 2 月, 2008

井上 薫, 渋谷 淳, 吉田 緑, 高橋美和, 富士本仁, 広瀬雅雄, 西川秋佳 : 腎障害性を有するアカネ色素成分あるいは代謝産物の腎発がんプロモーション作用について, 第 145 回日本獣医学会学術総会, 神奈川, 第 145 回日本獣医学会学術総会講演要旨集 : pp176 (BP-27), 3 月, 2008

G. 知的財産権の出願

なし

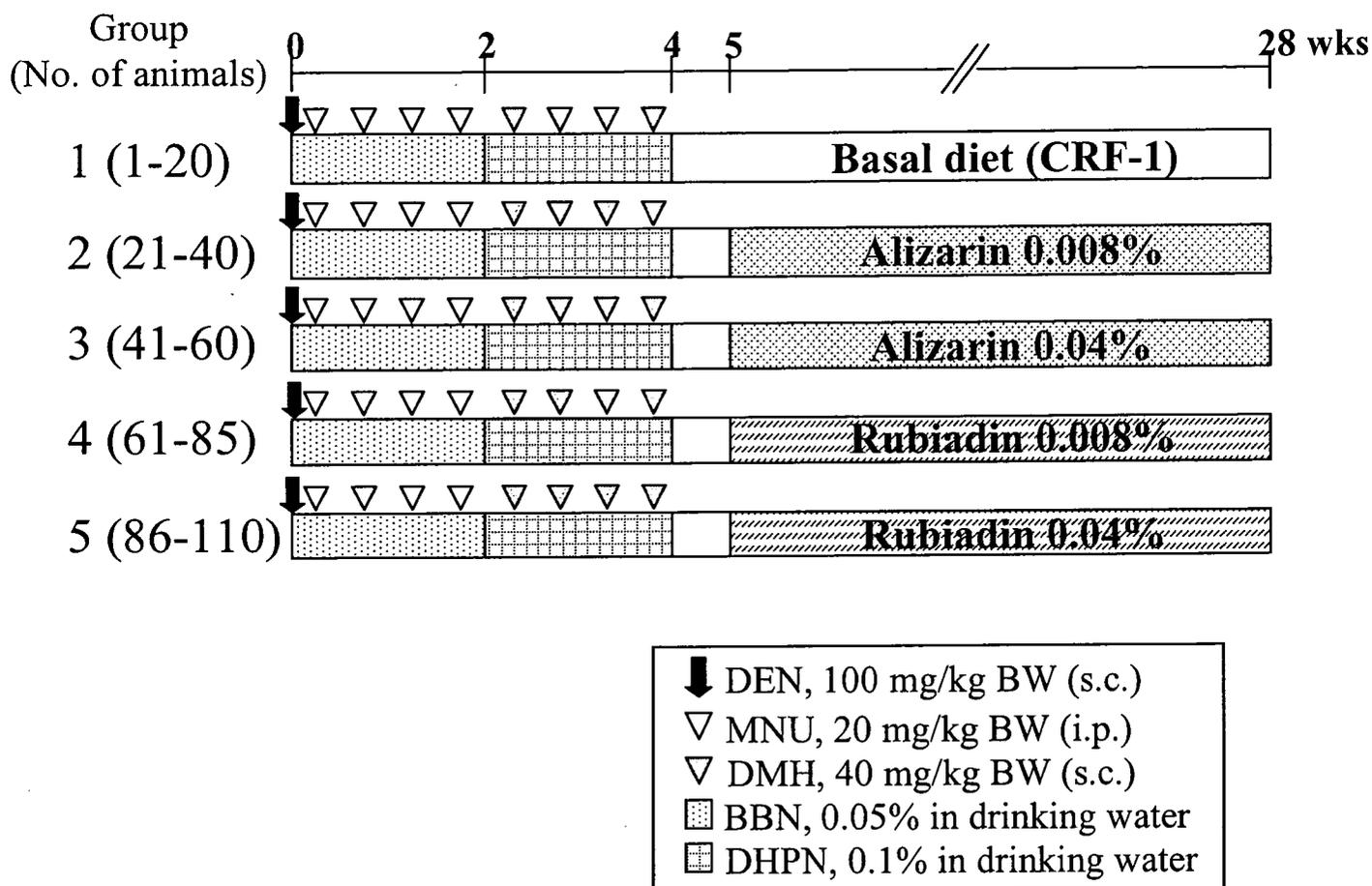


Fig. 1
Experimental design for a rat medium-term multi-organ carcinogenesis bioassay.

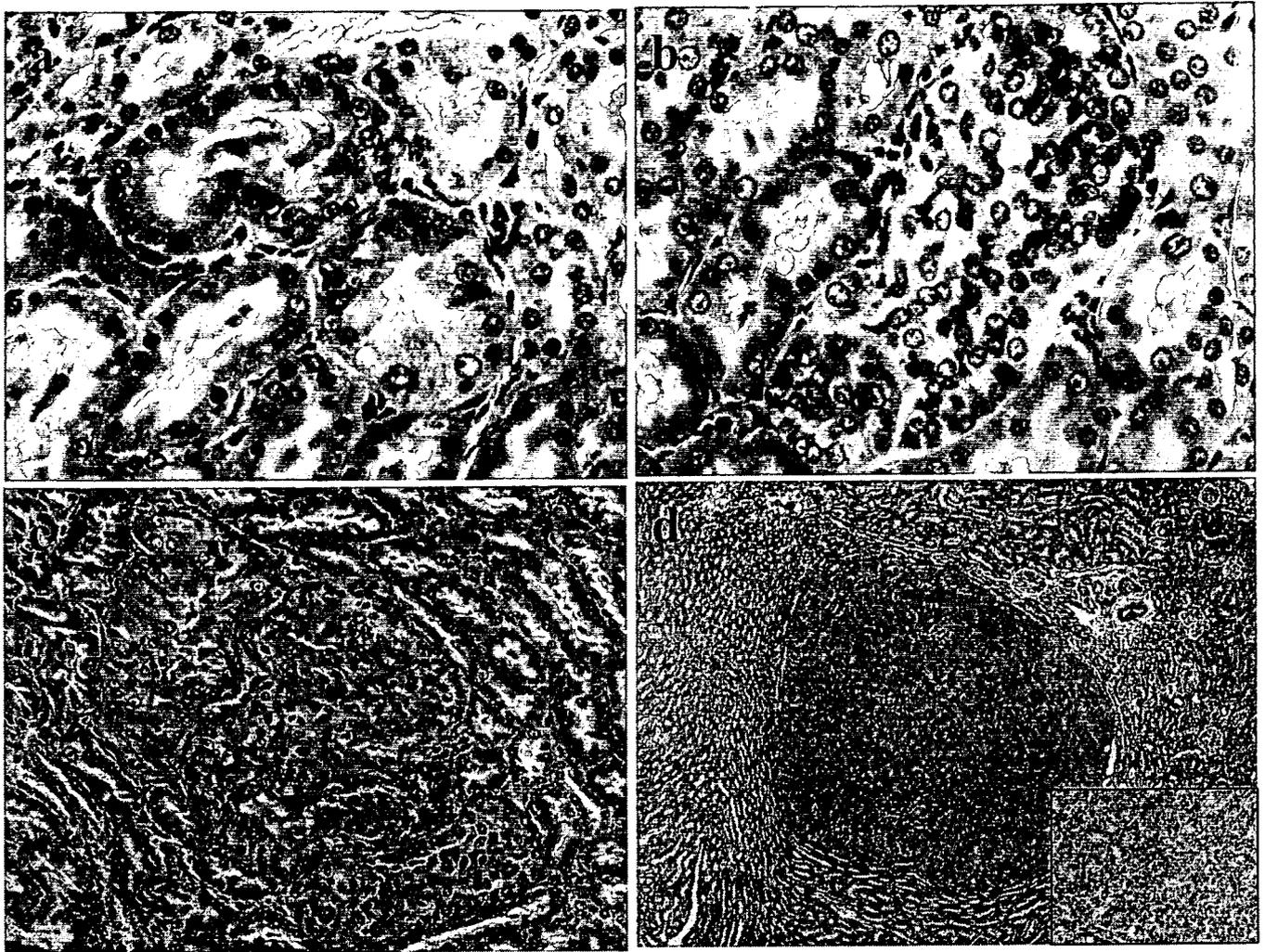


Fig. 2
Representative proliferative lesions in the liver of rats treated with Alz or Rub in a medium-term multi-organ carcinogenesis bioassay. (a) atypical tubule; (b) atypical hyperplasia; (c) adenoma; (d) carcinoma.

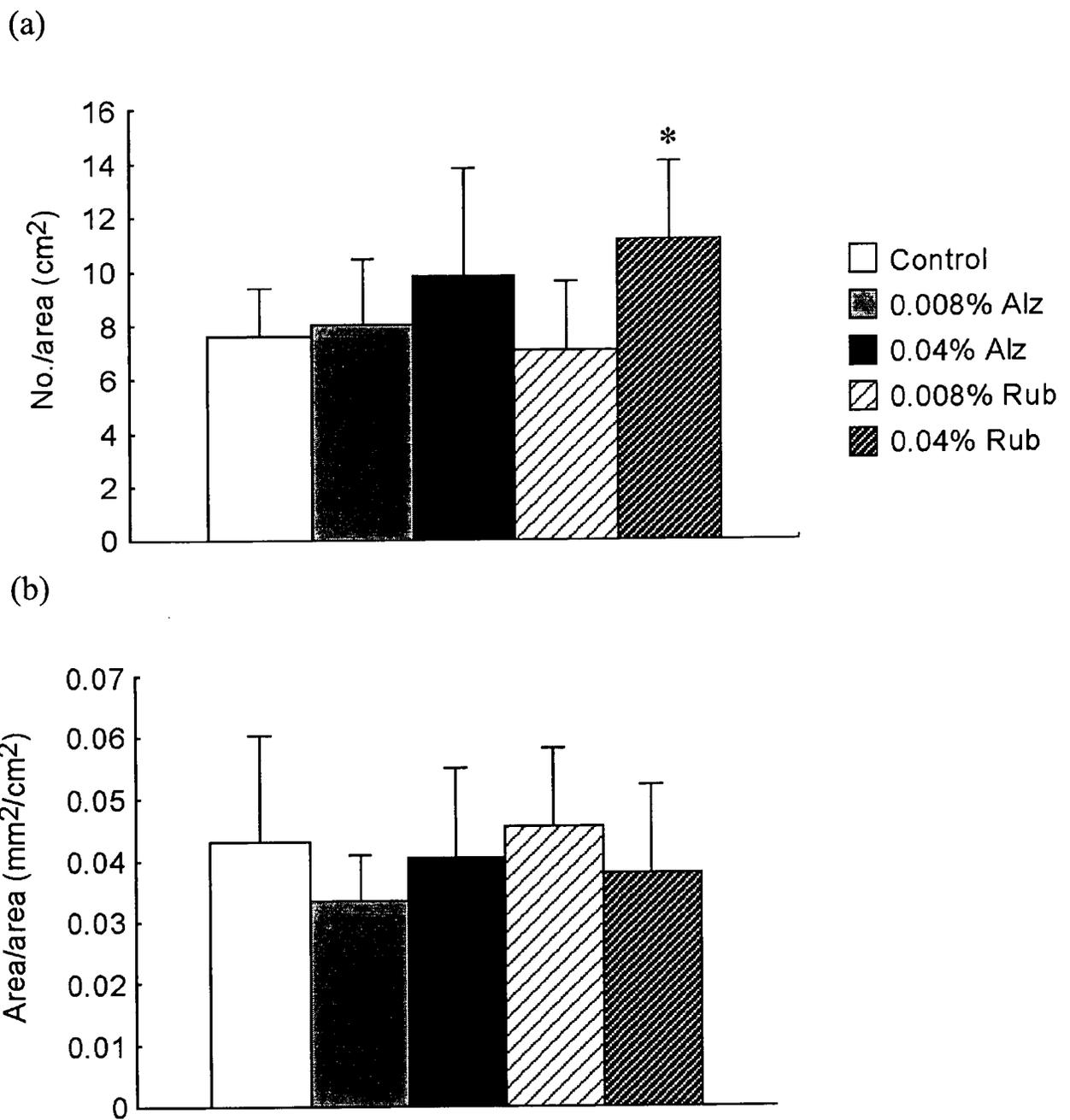


Fig. 3
Number (a) and multiplicity (b) of GST-P-positive foci in the liver of rats treated with Alz or Rub in a medium-term multi-organ carcinogenesis bioassay

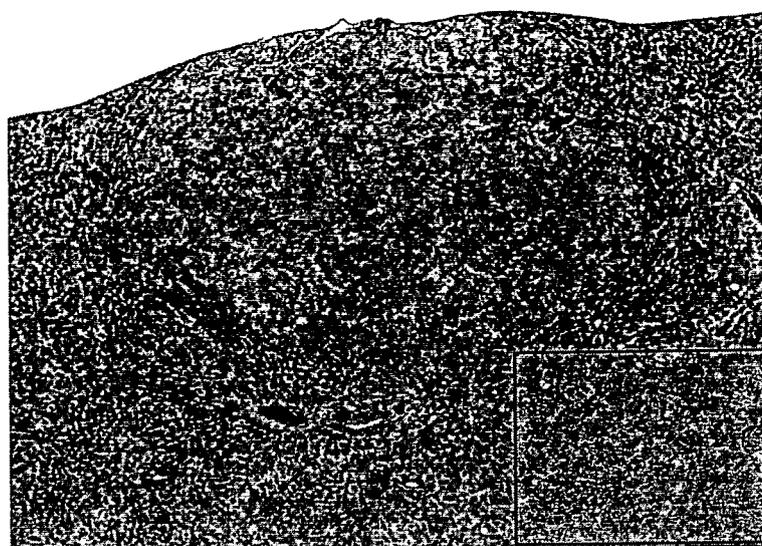


Fig. 4
Hepatocellular adenoma in a rat treated with 0.04% Rub in a medium-term multi-organ carcinogenesis bioassay

Table 1. Final body, kidney and liver weights of F344 rats treated with Alz or Rub in a medium-term multi-organ carcinogenic assay

| Group | No. of animal | Final BW (g) | Kidney (absolute) (g) | Kidney (relative) | Liver (absolute) (g) | Liver (relative) (g/100 g bw) |
|------------|---------------|--------------|-----------------------|-------------------|----------------------|-------------------------------|
| Control | 11 | 287.2 ± 21.4 | 1.91 ± 0.27 | 0.67 ± 0.09 | 7.54 ± 0.91 | 2.62 ± 0.22 |
| 0.008% Alz | 18 | 287.1 ± 18.4 | 1.99 ± 0.30 | 0.69 ± 0.09 | 7.32 ± 0.92 | 2.54 ± 0.25 |
| 0.04% Alz | 17 | 278.0 ± 16.7 | 3.75 ± 6.53 | 1.37 ± 2.42 | 7.01 ± 0.69 | 2.52 ± 0.14 |
| 0.008% Rub | 21 | 279.0 ± 20.6 | 1.98 ± 0.30 | 0.71 ± 0.08 | 7.08 ± 0.69 | 2.54 ± 0.16 |
| 0.04% Rub | 20 | 283.2 ± 17.8 | 2.04 ± 0.32 | 0.72 ± 0.11 | 7.97 ± 0.98 | 2.81 ± 0.23 |

Table 2. Incidence and multiplicity of proliferative lesions in the kidney of rats treated with Alz or Rub in a medium-term, multi-organ carcinogenic assay

| Lesion | Incidence (%) | | | | | Multiplicity (/animal) | | | | |
|-----------------------------|---------------|--------------|-------|--------------|--------|------------------------|--------------|------|--------------|-------|
| | Control | Alizarin (%) | | Rubiadin (%) | | Control | Alizarin (%) | | Rubiadin (%) | |
| | | 0.008 | 0.04 | 0.008 | 0.04 | | 0.008 | 0.04 | 0.008 | 0.04 |
| Cortex | | | | | | | | | | |
| Atypical tubule | 100.0 | 100.0 | 94.1 | 100.0 | 95.0 | 4.5 | 5.4 | 2.9 | 3.4 | 4.7 |
| Atypical hyperplasia | 36.4 | 33.3 | 64.7 | 23.8 | 45.0 | 0.5 | 0.4 | 1.2 | 0.2 | 0.8 |
| Renal cell adenoma | 9.1 | 16.7 | 17.6 | 33.3 | 25.0 | 0.1 | 0.2 | 0.2 | 0.4 | 0.3 |
| Renal cell carcinoma | 0 | 5.6 | 0 | 4.8 | 0 | 0 | 0 | 0 | 0 | 0 |
| Outer medulla | | | | | | | | | | |
| Atypical tubule | 36.4 | 72.2 | 29.4 | 71.4 | 85.0* | 0.6 | 1.2 | 0.5 | 1.2 | 3.5** |
| Atypical hyperplasia | 45.5 | 27.8 | 88.2* | 47.6 | 95.0** | 1.1 | 0 | 2.4 | 0.6 | 3.9** |
| Renal cell adenoma | 0 | 0 | 5.9 | 23.8 | 15.0 | 0 | 0 | 0.1 | 0.2 | 0.2 |
| Renal cell carcinoma | 0 | 0 | 5.9 | 0 | 10.0 | 0 | 0 | 0.1 | 0 | 0.1 |
| Mesenchyme | | | | | | | | | | |
| RMT | 63.6 | 83.3 | 94.1 | 95.2* | 90.0 | 1.6 | 1.8 | 2.4 | 2.0 | 2.1 |
| Pelvis | | | | | | | | | | |
| Transitional cell hyperpl | 18.2 | 0 | 5.9 | 9.5 | 15.0 | 0.2 | 0 | 0.1 | 0.1 | 0.2 |
| Transitional cell carcinoma | 0 | 5.6 | 11.8 | 0 | 0 | 0 | 0.1 | 0.1 | 0 | 0 |

*, **: Significantly different from controls at $p < 0.05$ and $p < 0.01$, respectively (Fisher's exact probably test or Mann-Whitney's U-test)

Table 3. Histopathological findings in the liver of rats treated with Alz or Rub in a medium-term, multi-organ carcinogenicity assay

| Lesions | Group | | | | |
|-----------------------------------------------------------------------|-----------------|-----|--------|-------|--------|
| | Control (n=) | Alz | | Rub | |
| | | 11 | 0.008% | 0.04% | 0.008% |
| Non-proliferative lesions | | | | | |
| Hepatocellular hypertrophy, diffuse | 11 | 18 | 17 | 21 | 20 |
| Nuclear alteration (anisonucleosis, dinucleated cell, vacuolation) | 11 | 18 | 17 | 21 | 20 |
| Proliferative lesions | | | | | |
| Altered hepatocellular foci | 11 | 18 | 17 | 21 | 20 |
| Hepatocellular adenoma | 0 | 0 | 0 | 1 | 1 |
| Hepatocellular hyperplasia | 0 | 0 | 0 | 0 | 2 |
| Hemangiosarcoma | 0 | 0 | 0 | 1 | 0 |
| Cholangiocellular hyperplasia | 1 | 2 | 0 | 0 | 0 |

研究成果の刊行に関する一覧表

書籍

| 著者氏名 | 論文タイトル名 | 書籍全体の 編集者名 | 書 籍 名 | 出版社名 | 出版地 | 出版年 | ページ |
|------|---------|---------------|-------|------|-----|-----|-----|
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雑誌

| 発表者氏名 | 論文タイトル名 | 発表誌名 | 巻号 | ページ | 出版年 |
|------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------|-------|---------|------|
| Inoue, K., <u>Shibutani, M.</u> , Masutomi, N., Toyoda, K., Takagi, H., Uneyama, C., Nishikawa, A. Hirose, M. | A 13-week subchronic toxicity study of madder color in F344 rats | Food Chem. Toxicol. | 46(1) | 241-252 | 2008 |
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