第33回 米国生薬学会

■1992年7月26日～30日　米国バージニア州・ウィリアムズバーグ

P-70

「ANTI-TUMOR PROMOTING ACTIVITY OF LAPACHOL.」

ラパコールの抗発がん活性プロモーター

S. Ueda[1], H. Tokuda[2], H, Nis-hino[2] and A. Iwashima[2],

[1]Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606,
[2]Kyoto Prefectural University of Medicine, Kyoto 602, JAPAN

Lapachol, a constituent of bignoniaceous plants is a biosynthetic precursor of various naphthoquinones. On the basis of our preliminary findings on, the inhibitory effect of this compound on tumor promotion, we have examined in detail on the activity. This compound was significantly effective in inhibiting the induction of Epstein-Barr virus(EBV) associated early antigen in EBV genome-carrying human lymphoblastoid cell lines. Furthermore, this compound inhibited the skin carcinogenesis initiated by 7, 12-dimethylbenz(a)anthracene(DMBA) and 12-O-tetradecanoylphorbol-13-acetate(TPA) induced skin carcinogenesis in mice. On treatment of mice with lapachol, the average number of papillomas per mouse in 15 weeks reduced remarkably. Anti-tumor promoting activity and cytotoxicity on pretreatment with lapachol at various dose are to be discussed.

1) S. Ueda and H. Tokuda, Planta Med., 56,669(1990)

■日本語訳

ノウゼンカズラ科植物成分のラパコールは、各種ナフトキノンの生合成前駆体である。ラパコールの発癌プロモーション抑制効果についての予備実験で得た我々の知見に基づき、その作用を更に詳細に検討した。ラパコールはエプスタイン・バールウイルス(EBV)のゲノムを持ったヒトのリンパ芽細胞の早期抗原誘発の阻止に効果的である。更に、ラパコールは7、12-ジメチルベンツ(a)アントラセン(DMBA)や、12-O-テトラデカノイルホルボール-13-アセテート(TPA)によって誘発されるハツカネズミの皮膚での腫瘍発現を抑制した。ラパコールを与えたハツカネズミでは、15週間の実験で、ハツカネズミ固体当たりの乳頭腫の平均数が顕著に減少した。種々の投与量のラパコールで前処置をした場合の発癌プロモーション抑制活性と細胞毒性についても述べる。

第9回 和漢医薬学会

■1992年8月15日～16日　東京都

「Effects of Tabebuia plants of Bignoniaceae from South America on spontaneous autoimmune abnormality in MRL/L mice」

自己免疫異常自然発症MRL／1マウスに対する南米産ノウゼンカズラ科Tabebuia属 植物の効果

Kazuya Okada, Keiji Ajimura, Yoshio Mori, Etsuko Maejima, Youichi Yamada, Masatoshi Sou, Takao Maeda, and Susumu Yukawa
The Third Department of Internal Medicine, Wakayama Medical University

【目的】

難病とされるSLEとRAは、ステロイドが有効であるが、長期の使用では副作用が問題となる。長期に使用できる薬剤が必要とされる。今回、南米産ノウゼンカズラ科Tabebuia属植物(Ta)について検討した。

【方法】

SLEとRAの病変を自然発症するMRL／Lマウス(雄性6週齢)6例にTaの煮沸抽出液を経口投与し(Ta群)、14週後体重、腎、脾、および肝重量、抗核抗体、抗Sm抗体、RA因子の測定と腎組織を無投与の対照群(C群)と比較検討した。

【結果】

C群の平均体重39gに対しTa群は48gとTa群で体重の有意の増加を示した。C群は平均して痩身を呈し毛なみの劣化を認めた。腎重量はC群で平均294mg、Ta群で395mgと有意差を認めた。血清検査では特に有意差を認めなかった。腎組織でも著明な差は認めなかった。

【結論】

SLEとRA病変を示すマウスに対し、Taは血清学的変化を示さなかったが、臨床的所見において有効性を認めた。

■English translation

[Objectives]

Steroids, immunosuppressants, etc. are effective for the treatment of SLE and RA, both being classified as autoimmune diseases, which are regarded as intractable diseases. However, adverse drug reactions may develop in the long-term use of these agents. Therefore, drugs that can be used over a prolonged period of time are in demand. In the present study, the efficacy of a Tabebuia plant (Ta) of Bignoniaceae from South America, which has been used for rheumatism, etc. as a folk remedy in South America, was investigated in MRL/L mice, which spontaneously develop the lesions of SLE and RA.

[Methods]

The extract of Ta, obtained by boiling 8 g of Ta in 1500 mL of water, was orally administered to 6 MRL/L mice (males at 6 weeks of age; Group Ta), which spontaneously develop the lesions of SLE and RA. At 14 weeks after administration, the following measurements and histologic examination on kidneys were conducted, the results were compared with those obtained from the control group (Group C) consisting of untreated mice. The measurement items were body weight; kidney, spleen, and liver weights; antinuclear antibodies; anti-Sm antibodies; and RA-factors. Additionally, the total daily urinary protein at 8 weeks after Ta administration was investigated in 10 animals of each group.

[Results]

The mean body weight in Group Ta was 48 g, which was significantly higher than the value (39 g) obtained in Group C. In Group C, animals were generally slimmer, showing a poor hair condition. The mean kidney weight was 294 mg in Group C and 395 mg in Group Ta, showing a significant difference between these groups. However, no differences were observed in liver and spleen weights. The serum test showed no particular significant differences. The histologic examination on kidneys showed no notable difference. The total daily urinary protein was 28.4 mg in Group C and 9.7 mg in Group Ta, showing a significant decrease in Group Ta.

[Discussion]

Male MRL/L mice have an average life span of 22 weeks and start to develop renal and articular lesions at 4 weeks of age. At the end stage, around 20 weeks of age, prominent development of nephritis and angiitis occur, followed by severe proteinuria and generalized edema, leading to death. In the present study, the animals were compared at 20 weeks of age, and the systemic and urine findings in Group Ta were favorable as compared with Group C. This result suggests that Ta has antiinflammatory action and immunoregulatory action.

[Conclusion]

Ta showed no serologically significant changes in mice exhibiting SLE and RA lesions. However, the efficacy of Ta was observed in the decrease of proteinuria and in the improvement in the physical appearance.