

Inaugural Meeting of the Professional Committee of Biliary Tract Tumors of Chinese Anti-Cancer Association cum the First National Academic Conference on Biliary Tract Tumors

「Investigation on effects of *Tabebuia avellanedae* extract by patients suffering from different forms of cancer in different stages」

がん患者の各種段階と形態でのタベブイア・アベラネダエの効能の検討

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Tabebuia avellanedae (Bignoniaceae) (TA), which is native in South America from Brazil to northern Argentina, is well known in traditional folk medicine used for the treatment of various disease during five hundred years. The inner bark of this plant produced in Brazil is distributed in Asia as a herb tea and healthy purpose, previously, we reported that extract essence of TA (TA ess) and including naphthoquinones type compound, NQ801, inhibited TPA-induced *in vitro* assay for anti-tumor promoting activity, and evaluate for antitumor activity against human origin tumor cells and anti-tumor promoting activity against *in vivo* system, using mouse organ. Our anti-tumor activity assay showed that TA ess. exhibited weaker cytotoxic activity of tumor growth whereas its constituents NQ801 in inner bark of TA treated cytotoxic activity observed stronger than TA ess. and lapachol main constituent of TA. To examine the possible role of anti-tumor promoting activity, we tested the effects of DMBA-TPA in two-stage mouse skin carcinogenesis. SENCAR mice were initiated with single dose of MBA (390 nmol) and promoted with TPA (1.7 nmol) twice a week for 20 weeks. Tumor incidences were 100% with 6 to 7 papillomas per mouse. The present study was carried out to examine the chemopreventive activity of TA and NQ801 activity was also inhibited by 70% in papillomas per mouse at the end of experiment.

To further examine preclinical trials, 2 groups, 12 patients (9 females, 3 males, mean age 54.2 year) suffering from different forms of cancer and 11 healthy subjects (5 females, 6 males, mean age 55.7 years), were given daily *Tabebuia avellanedae* (TA) extract (Taheebo) by oral ingestion during 120 days. Effects on 95 blood parameters were studied on days 0, 30, 120, quality of life was assessed by a standard questionnaire (EORT QLQ-C 30). An immunostimulating and immunosuppressive effect was observed on lymphocyte cell subsets, and a reduction of eosinophil leucocyte cell numbers and IgE levels, which indicate a possible antiallergic property of TA components. A marked rise in reticulocytes (precursor cells of erythrocytes), as well as positive effects on hematocrit and liver parameters were observed. Elevated levels of tumor markers in 2 patients with tumor progression decreased. TA also seems to have an anabolic effect and can raise Serotonin levels, an effect, which should be investigated further. TA extract has the potential to improve quality of life body condition in patients with daily ingestion of 5g and 30g TA extract respectively, No negative side effects were observed. These results clarified the anti-tumor and anti-tumor promoting of TA and its active constituent NQ801, and we tried to arrange a practice of formulate subsequent experimental integrative trial strategies.

■日本語要約

タベブイア・アベラネダエ (ノウゼンカズラ科) (略 TA) は北米アルゼンチンから南部ブラジルに自生し、500年前より伝承薬用植物として、種々の疾患に有用であるとされてきた樹木である。ブラジルにて採取される樹木の内部樹皮はアジアでは主に、健康茶として用いられている。以前に我々はこのTAの抽出物 (TA ess.) と、含有される化合物であるNQ801が抗発がんプロモーターを検索する試験管内発がんプロモーター試験で抑制効果を示し、またヒト由来がん細胞に対して弱いながらも抗腫瘍効果、加えてマウス試験でも評価できる効果を示した。我々の抗腫瘍試験ではTA ess. はNQ801に比較して弱い細胞毒性であり、またNQ801は同様にTAに含有する主な化合物である、ラパコールに比較して強い抑制効果を示した。抗発がんプロモーター試験として、DMBA-TPAのマウス皮膚二段階発がん抑制試験を進め、SENCARにDMBA (390nmol) でイニシエーション後、プロモーション (1.7nmol) を週2回、20週間続けた。この系では100%の割合で腫瘍が発生し、また6から7個の腫瘍が発現する。TA ess. やNQ801を作用させると、それぞれ試験終了時で40から60%の抑制を示した。

これらの知見を基に、前臨床試験を行うと12人のがん患者、2群 (平均年齢54.2歳 9人女性、3人男性) にし、TA essを120日間、経口で摂取する。95の血液パラメーターを投与後、0、30、120日で検査し、またQOLについても調査した。免疫刺激、免疫抑制効果に関しても、リンパ球サブセット好酸球とIgEレベルの減少をTAのアレルギーとの関連で検討した。網状赤血球 (赤血球の前駆体) の増加は、ヘマトクリットと肝臓パラメーターと同様に良好な知見を示した。また2患者でのがんマーカーでの知見は腫瘍の増殖の減衰を示した。TAはまた生体同化作用を有するとともに、セロニンレベルを上昇したがこれらに関してはさらなる調査が必要である。TA抽出物はそれぞれ5gと30gを毎日摂取した患者において、日々の生活状態を改善する事ができ、副作用は認めなかった。これらの結果はTAの抗腫瘍、抗発がんプロモーター作用とその活性成分としてのNQ801に関して評価するとともに、この試料の補完代替医療実験へ試行するための、戦略計画を進めることができた。