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「The tea type Brazilian herb prevent lung cancer induced by 4-nitroquinoline 1-oxide and glycerol in mice」

4NQOとグリセロールで誘発される肺がんに対する飲料用茶形態のブラジル産薬用植物による抑制

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Lung cancer incidence is higher in Japanese peoples compared to other organ cancer and it is acute problems in our life style.

Since herbal tea have been known to prevent against the several organ cancer through so many examinations and published papers, herbal tea may be useful in chemoprevention, which have strong potential activity by contained active constituents. *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 and Japan as a healthy purpose herb tea. Previously, we reported that extract essence of TA (known is common herbal tea as Taheebo)(TA ess.) and including naphthoquinones type compounds, NQ801, inhibited TPA-induced *in vitro* assay for chemopreventive potency and also inhibited TPA-induced *in vivo* assay on two-stage mouse skin test. We have now extended these investigations to lung adenoma tumorigenesis model in which we initiated the tumors with 4-nitroquinoline 1-oxide(4NQO) and promoted with glycerol in SENCAR mice. Female SENCAR mice were injected s.c. with 4NQO dissolved in olive oil, 1 week a part, and then randomized into the different group of each 15 mice. After waiting 5 weeks following injection, mice were maintained either on 8 % glycerol oral drinking group and supplemented 0.0025 % TA ess. for 25 weeks. At necropsy, lungs were removed and grossly visible lesions on the surface of all lobes of the lung were counted and one tumor from each mouse was observed for histopathological analysis. Mice treated with 8 % glycerol and fed conventional diet had 45 adenoma and incidences were 86.6 %. Compared to mice treated with 8 % glycerol and 0.0025 % TA ess. had a lower tumor multiplicity, 9 adenoma and incidences were 33.3 %, corresponding to a reduction by 80 %, multiplicity and 62 %, incidence, respectively. These tumors showed the typical adenoma by microscopic observation. These findings established an inhibitory effects of TA ess. in lung tumor model, an effect that is modulated through inhibition of MAPK signaling pathway, using western blotting analysis. Importantly, consumption of the TA ess. in the drinking water for a period 30 weeks did not appear to induce any over toxicity. Based on the fact, these results suggested that oral tea type herb have the potential as preventive reagents against cancer through pathway of MAPK signaling.

■日本語要約

日本では他の臓器に比べて肺がんの割合が高く、我々の生活において早急に治療法を確立することが熱望されている。その中で健康茶が種々の臓器に対して抑制することが、多くの論文や実験結果より知られている。このことから、健康茶には有用ながん予防の物質が含有し、それががん予防として有用であると示されてきた。タバコ・アベラネダエ(TA)それは南米ブラジルから北部アルゼンチンまで植生する500年以上前より種々の疾患に有用である、伝承薬として知られている。このブラジルで産生する植物の内部樹皮は、日本を含むアジアにおいて健康志向を目指して使用されている。先に我々は、TAの抽出エキス(通常タヒボと呼ばれている)とそこに含まれるナフトキノンタイプでNQ801はがん予防活性を評価する細胞実験、TPAを用いたマウス皮膚二段階発がん試験で有意な活性を示した。今回さらに詳細な試験として、4NQOを発がんイニシエーション、グリセロールを発がんプロモーターとするマウス肺二段階モデルを用いて評価した。雌SENCARマウスに4NQOを接種した後、その5週間目より、8%グリセロールを自由接種する発がん系で、発がんプロモーション段階で0.0025%TAを同時に自由接種させた。25週目に実験個体より肺を採取して、誘発された肺腺腫の数を計測するとともに病理学的な検討も行った。その結果、腫瘍の発生率で62%、腫瘍数において80%の抑制を示した。これらの所見はタンパク質レベルでの解析も併せて、MAPK経路においてこのTAは抑制を示すとともに、重要事項として7か月間TAを連続的に摂取しても異常が認められなかったことで、その有用性が示唆される。