# 「Study on natural products against carcinogenesis induced by an advanced glycation end product, aiming at cancer prevention」

## がん予防を目的としたグリケーション生成物誘発発がんに対する天然物質の検討

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【目的】
病態生理の観点からとくに、糖尿病の慢性合併症、老化現象、神経変性疾患等の分野で注目されているグリケーション生成物（AGE）に関して、われわれはその発がん性を示し、さらに医学的見地からその予防についても検討をすすめてきた。今回はヒト生体内での糖化反応を受けると考えられるたんぱく質から生成したAGEを用い、その発がん性とともに、重要な予防についても日常に用いる素材を試験化合物としてマウスの系で検討した。

【方法・材料】
実際にヒトの疾患、予防としての考えから、ヒトアルブミンをもちいてグルコースとの混合液を、無菌状態で37度で反応しAGEを作製した。そのAGEを発がんイニシエーションとし、その1週間後よりTPAをプロモーションとするマウス皮膚二段階発がんによりその発がん性を検討するとともに、AGEのイニシエーション作用前後1週間、ブラジル産薬用植物であるタベブイア・アベラネダエ（TA）抽出液を飲水し、通常の水道水による系と比較した。

【結果】
5週令、雌、SENCARマウスに作製したAGEを発がんイニシエーター作用で3日連続して塗布後、その1週間目より発がんプロモーターとしてTPAを塗布、20週目でその腫瘍発生率、個数を観察したところ80%以上の発生率、約5個程度の発生を認めた。がん予防を目的としたTA抽出液で処理を行なった群では発生率、腫瘍数で約60%の抑制効果を示し、その素材としての有用性が示唆された。

■English translation
[Objectives]
From the pathophysiological point of view, particularly in the areas of chronic diseases concurrent with diabetes mellitus, aging phenomenon, and neurodegenerative diseases, advanced glycation end products (AGEs) have been attracting attention. We demonstrated the carcinogenicity of AGEs, and investigated prevention of carcinogenicity from the medical point of view. In the present study, using an AGE prepared with a protein that is considered to undergo glycosylation in vivo, its carcinogenicity and cancer prevention, which is an important issue, were investigated in mice using material used in daily life as the test compound.

[Materials and Methods]
From the standpoints of actual diseases in humans and disease prevention, human albumin was used and mixed with glucose. The mixture was incubated at 37℃ in a sterile condition, and an AGE was obtained. A two-stage carcinogenesis test on mouse skin was conducted, using the AGE as an carcinogenic initiator and TPA as a promoter that was applied 1 week after the initiation, in order to assess the carcinogenicity of the AGE. In addition, for 1 week before and after the application of the AGE initiator, the animals received an extract of Tabebuia avellanedae (TA), which is a medicinal plant from Brazil, and they were then compared with animals that received normal tap water.

[Results]
An AGE prepared was applied to female SENCAR mice at 5 weeks of age as a carcinogenic initiator for 3 consecutive days. From 1 week after the initiation, the application of TPA as a carcinogenic promoter started. At the 20th week, the incidence and number of tumors were determined. The incidence was more than 80%, and approximately 5 tumors were detected. In the group treated with the TA extract with the objective of cancer prevention, about 60% inhibition in the incidence and number of tumors was observed. This result suggests the usefulness of the TA extract as a material to prevent cancers.