

## Review

Systematics and health effects of chemically distinct  
tannins in medicinal plants ☆Takuo Okuda <sup>\*,1</sup>*Okayama University, Tsushima, Okayama 700-8530, Japan*

Received 23 August 2004; received in revised form 20 December 2004

Available online 27 June 2005

## Abstract

The research began with an investigation of tannins from traditional medicinal plants and resulted in isolation and structure determination of hundreds of ellagitannins and dehydroellagitannins, as well as their oligomers and oxidized derivatives with various structures specific to each plant species. These polyphenols have been classified according to the stage of oxidative structural transformation and oligomerization, into types I–IV and I+ to IV+, etc. Parallels were found between their oxidative transformations and plant evolution. They were also classified by the linkage units between the monomers, into DOG, GOD, GOG and DOGOD types (D = Diphenoyl, G = Galloyl, O = Oxygen), etc. Besides their fundamental activities, e.g., reduction and anti-peroxidation properties, remarkable biological and pharmacological activities of various potencies have also been found, including, amongst others, inhibition of lipid-peroxidation, mutagenicity of carcinogens and tumor promotion, host-mediated antitumor effects specific to particular tannin structures, antiviral activity and potentiation of antibacterial activity.

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**Keywords:** Hydrolyzable tannins; Polyphenols; Classification of hydrolyzable tannins; Hydrolyzable tannin oligomers; Oxidized polyphenols; Plant evolution; Inhibition of peroxidation, Radical scavenger; Antimutagenicity; Anti-tumor promotion; Host-mediated antitumor activity; Antiviral activity

*Abbreviations:* ACTH, adrenocorticotrophic hormone; ADP, adenine 5'-diphosphate; AIBN, 2,2'-azobisisobutyronitrile; B[a]p diol epoxide,  $\pm 7\beta$  8 $\alpha$ -dihydroxy-9 $\alpha$ ,10 $\alpha$ -epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene; DHHDP, dehydrohexahydroxydiphenoyl; DMBA, 7,12-dimethylbenz[a]anthracene; D-MPO, 5,5-dimethyl-1-pyrrolidone-N-oxide; DPPH, 1,1-diphenyl-2-picrylhydrazyl; EVB-EA, Epstein-Barr virus early antigen; ECG, (–)-epicatechin gallate; EGCG, (–)-epigallocatechin gallate; ENNG, N-ethyl-N'-nitro-N-nitrosoguanidine; ESR, electron spin resonance; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; HHDP, hexahydroxydiphenoyl; 5-HETE, 5-hydroxy-6,8,11,14-eicosatetraenoic acid; 5-HPETE, 5-hydroperoxy-6,8,11,14-eicosatetraenoic acid; MM2, mouse mammary cancer 2; MNNG, N-methyl-N'-nitroso[4,3-b]indole; NADPH, nicotinamide adenine dinucleotide phosphate; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; N-OH-Trp-P-2, 3-hydroxyamino-1-methyl-5H-pyrido[4,3-b]indole; RA, relative astringency; RAG, astringency relative to that of geraniin; RMB, relative affinity to methylene blue; RMBG, affinity to methylene blue relative to that of geraniin; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; TPA, 12-O-tetradecanoylphorbol 13-acetate; XOD, xanthine oxidase.

☆ The Tannin Conference Award Address at the 4th Tannin Conference, of the Fall Meeting of the American Chemical Society, Philadelphia, PA, USA, 22–26 August 2004.

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## 1. Introduction

Many tannin-rich medicinal and food plants have been appreciated for their beneficial effects without being troubled by any obvious toxicity (Okuda et al., 1992a). Research on the tannins in traditional medicinal plants, presented here, started (Okuda et al., 1975, 1991, 1992a,b, 1995, 1999a; Yoshida et al., 2000) when the chemical, biological and pharmacological properties of

tannins in most medicinal plants were not yet subjected to modern analyses.

## 2. Dehydroellagitannins and their oxidized congeners in *Geranium thunbergii*

A crystalline tannin named geraniin (**1**), the main component accounting for over 10% of the dry leaf

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