### **REVIEW**

# Green Tea Service and Traditional Nursing Practice

### Masahiko KANAMORI, Miho YOSHII, Kaoru HATASHIMA, Yohei MITSUHASHI

配茶と伝統看護の実践

金森昌彦1・吉井美穂2・畑島 郁1,3・三橋陽平1,3

#### Abstract

In 20th century Japan, green tea service was provided as part of nursing practice in many hospitals, however, this service has been gradually disappearing owing to various risks, costs, and changes in tastes and preferences. Cancer prevention and antimicrobial activity are some of the well-known biological characteristics of catechins, the polyphenols that are the main component of green tea leaves. We tested the effects of four major catechins in green tea on cultured osteosarcoma cell growth in vitro. The gallate-group of catechins [epicatechin gallate (ECG)] and epigallocatechin gallate (EGCG)] is a major constituent of the catechins in green tea, induces apoptotic changes in sarcoma cells. In our bacteriological study, moreover, Salmonella enterica mutants lacking the O side chain and with core oligosaccharides of different lengths were more sensitive to catechins than wild-type bacterial strains (i.e., with intact lipopolysaccharide). Although catechins exhibit antibacterial effects, the numbers of living bacteria in the bottled green tea, gradually increase over time at room temperature. This suggests that risks for bacterial contamination of bottled tea increases over the long period of time. On the other hand, bacterial contamination in sports drinks was found to be almost negligible despite long-term storage after opening. Interestingly, to our knowledge, despite the many advantages outlined above, catechins have not been used to treat any disease. Nevertheless, from the perspective of traditional nursing, we recommend the green tea service in nursing care practice because of following three reasons: physical (it warms the body up), psychological (it has a relaxing effect on the mind), and social (it encourages communication between patients and medical staff).

#### 要 旨

20世紀の日本では、看護業務の合間に看護師、看護助手が病棟の配茶(緑茶サービス)を行ってきた。しかし、現在ではこのサービスはリスクやコスト、味覚や嗜好の変化から徐々になくなりつつある。緑茶の茶葉から抽出されたカテキン類(ポリフェノールの一種)には、癌予防や感染予防という生物学的な効能を認めることがよく知られている。我々は4種類の主なカテキン類による骨肉腫細胞の増殖抑制効果をin vitroにて実験した。 ガレート 基 のついたカテキン類(epicatechin gallate [ECG]、and epigallocatechin gallate [EGCG])にその効果が高い結果が得られた。それらは細胞内にアポトーシス変化を誘導した。さらに細菌学的実験ではO鎖を欠損し異なる長さの糖鎖を持つSalmonella enterica変異株で、カテキン類に対する感受性が高いことを見出した。カテキン類は感染予防に対して効果はあるものの、室温に置いたペットボトル内のお茶では細菌繁殖が認められ、飲み残しによる感染の増大があることも確認した。一方、スポーツ飲料には保存状態にかかわらず、その可能性はほとんどない。実際に何らかの疾病に対してお茶を処方することは行われてないが、伝統的看護という見地において、身体的(体を温める効果)・精神的(心を癒すリラックス効果)・社会的(医療者患者間のコミュニケーションの手段)という3つの効果があり、伝統看護における配茶(緑茶サービス)を推奨したい。

Key words: green tea service, traditional nursing practice, human science

<sup>&</sup>lt;sup>1</sup>Department of Human Science 1, Faculty of Medicine, University of Toyama

<sup>&</sup>lt;sup>2</sup>Department of Fundamental Nursing 1, Faculty of Medicine, University of Toyama

<sup>&</sup>lt;sup>3</sup>Graduate School of Medicine and Pharmacetutical Sciences for Education, University of Toyama

#### **HUMAN SCIENCE AND GREEN TEA SERVICE**

Giorgi A<sup>1)</sup> was the first to use the term of "Human Science" in nursing science in 1970. However, as a nursing theory, connecting the "Human Science" and "Nursing Practice" was achieved by Watson J2, who wrote the book "Nursing: Human Science and Human Care", which contains the "Ten Caritas Processes". Caritas No. 8 is "Assist with basic physical, emotional, and spiritual human needs", whereas No. 9 is "Open to mystery and allow miracles to enter". We believe in following these processes while caring for patients. The purpose of this study was to investigate methods of traditional nursing that support human health, particularly the efficacy of the green tea service in traditional nursing practice in Japan. We aimed to connect of the results from laboratory experiments to the "Human Science" and "Nursing Theory".

In Japan, the green tea ceremony was established in the 16th century as a popular and traditional ritual that comprises the preparation and consumption of tea<sup>3)</sup>. While this tea ceremony may sound simple, there are many important details in the serving and drinking of the tea. The architecture of the tea room and display of traditional flower arrangements are also important aspect of the tea ceremony. The tea ceremony is not only a cultural practice but green tea consumption also promotes health. Furthermore, it is traditional to serve hot green tea for inpatients as part of nursing care in Japan. This does not merely quench thirst, but also relaxes the mind and promotes strong relationships and interactive communication between patients and medical staffs. From perspective of traditional nursing, medical care must be considered in terms of three factors, physical, psychological, and social. Thus, "Nursing Theory" is based on fundamentals of "Human Science".

# BENEFITS AND RISKS OF A GREEN TEA SERVICE IN MEDICAL WARDS

Asian patients may habitually or subconsciously associate hot green tea with kind-hearted nursing care. In 20th century Japan, green tea service was provided in many hospitals, however, this service has been gradually disappearing. Previously, green tea was dispensed to patients from a big kettle by each nursing staff, however, recently, patients have been able to select various tea services by themselves from the hospital vending machines (Figure 1). There are several reasons for this change, including safety, cost, and changes in tastes and preferences. Moreover, nurses and nursing assistants

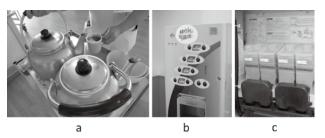


Figure 1 Green tea service.

Formerly, patients could get green tea service using by big kettles from nurses (a), but recently patients can select various tea services from 4-kinds of tasty by themselves from a vending machine at ward in our hospital (b, c).

are too busy to perform this additional task. Consequently, vending machines in many hospitals are stocked with many kinds of tea in plastic bottles.

The health benefits of green tea have been known for many years, and tea-extracts have been used as bioactive substances (e.g. major catechins) for over one-fourth century. Therefore, the green tea service may still be of value if its benefits are supported by scientific evidences because it represents a traditional nursing practice in Asian countries including Japan. Small-plastic-bottled beverages (SPBB) are convenient and useful for preventing dehydration in patients. On the other hand, SPBB appears to hold no emotional value for the Asian people, partly because the tea is not hot and there is no social interaction.

Furthermore, the health benefits from the major catechins of represent an important advantage of the green tea service. Laboratory studies have shown that catechins exhibit antioxidant4, antitumor5-10, and anti-infection effects11-16). However, many physicians do not consider the important roles of catechins in disease therapy, because they are not powerful. On the other hand, how about the new strategy in view point of the preventive disease or nursing care? The latest trend is supplements for the healthy, and is booming. Supplements claiming to prevent various chronic diseases, such as cardiovascular disease, allergies, diabetes, and cancer, comprise the majority of health supplements. In particular, traditional Asian medicine, foods and food-derived supplements have now become popular worldwide. Currently, we would like to support traditional Asian practices, measures and tools in nursing care.

### EXPERIMENTAL STUDY FOR TUMOR GROWTH PREVENTION

Some evidences<sup>11-17)</sup> have suggested that catechins, which are polyphenols found in green tea and other

foods, exhibit cancer-preventive effects by inhibiting of mutagenesis and tumorigenesis (Table 1). Catechins are the major antioxidants in green tea, and include epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (EGC), and epigallocatechin gallate (EGCG). The structures of these compounds are very similar (Figure 2), but the gallate structure has been suggested to be important for the activities of catechins, including antiproliferative effects on some types of cancer cells. However, to date, few studies have been conducted on the effects of catechins on sarcomas. The purpose of our study was, therefore, to examine the antiproliferative and apoptotic action of major catechins in sarcoma cells.

We tested the effects of these four major catechins on cultured MG-63 human osteosarcoma cells *in vitro*. We

Table 1 The articles overview about the effects of catechins on each tumor.

	N 1 6 1 1:	NT 1 C + 1:	
	Number of studies	Number of studies	
	showing inhibitory	showing no	
	effects	inhibitory effects	
Lung	20	2	
Oral cavity	6	0	
Esophagus	4	0	
Stomach	9	0	
Small intestine	8	1	
Colon	11	6	
Skin	27	0	
Prostate	4	0	
Breast	10	0	
Liver	7	1	
Bladder	3	0	
Pancreas	2	0	
Thyroid	1	0	

The data were obtained by a literature search of Pubmed from 1965 to 2008 of animal carcinogenesis models<sup>17)</sup>.

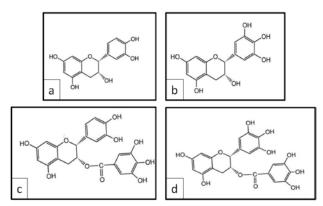


Figure 2 Structures of major catechins.

- a: (-) Epicatechin (EC), b: (-) Epigallocatechin (EGC)
- c: (-) Epicatechingallate (ECG),
- d: Epigallocatechin gallate (EGCG)

chose osteosarcoma cells because they are one of the high-grade sarcoma. Recently, the 5-year survival rate has increased up to 60-70%, due to advancements in high-dose chemotherapy regimens<sup>18</sup>). However, a number of children are diagnosed with osteosarcoma every year, and some of them died from the lung metastasis. Experimentally, MG-63 cells were cultured in Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum, L-glutamine, and antibiotics in a humidified incubator at 5% CO<sub>2</sub> and 95% air at 37°C. The cells were seeded at 5 × 10 $^5$  cells per a flask. Exponential cell growth was observed in the pre-culture. Cells were treated with EC [ $C_{15}H_{14}O_{6}$ ], EGC [ $C_{15}H_{14}O_{7}$ ], ECG [ $C_{22}H_{18}O_{10}$ ], or EGCG [ $C_{22}H_{18}O_{11}$ ] (Funakoshi, Tokyo, Japan) for 3 days.

Treatment with the three major catechins (EGC, ECG and EGCG) decreased the cell numbers in a dose-dependent manner. After the treatment, the cells became elongated and cell processes were extended initially. EGCG exhibited the strongest antiproliferative properties; in addition, the antiproliferative action of ECG (50- $75\mu\mathrm{M}$ ) and EGCG (50- $75\mu\mathrm{M}$ ) appeared to be linked to apoptosis showing by the morphological changes (Figure 3). Moreover, an increase in the cell number during the sub-G1 phase of the cell cycle indicated that apoptosis was induced, as suggested by the flow cytometry (FACS Calibur) data. Treatment with EGCG activated caspase-3, an established inducer of apoptosis, as detected by western blot analysis. Caspase-3 activation is crucial for the induction of apoptosis, and fragments of the cleaved caspase-3 (19, and 17 kDa) were detected in the

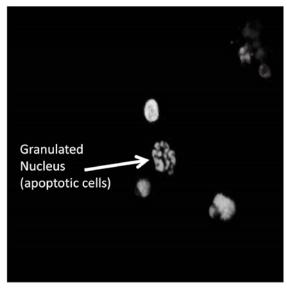


Figure 3 The finding of fluorescence microscope. Many apoptotic nucleoli are seen in response to ECCG.

Table 2 Apoptotic effects of catechins in our study.

	EC	EGC	ECG	EGCG
Growth inhibition	×	0	0	0
Nucleus atrophy	×	×	0	0
Increase of Sub-G1	×	×	0	0
Phosphatydyl Serine	×	×	0	0
Cleaved Caspase-3	×	×	0	0

O: positive findings in apoptosis, ×: negative findings in apoptosis

EC: epicatechin, EGC: epigallocatechin, ECG: epicatechin gallate, EGCG: epigallocatechin gallate

cells treated with EGCG (unpublished data).

A summary of our results is shown in Table 2. These data clearly indicate the induction of apoptosis in osteosarcoma cells by ECG and EGCG. Thus, we can conclude that the gallate-group of catechins is a major contributor to these effects, and thus, may prevent the progression of some sarcomas. Why is this gallate-substrate important? Hou, et al.<sup>19)</sup> has illustrated a mechanism for EGCG. This mechanism shows that superoxide is produced, when EGCG binds to oxygen. Moreover, the production of superoxide and H<sub>2</sub>O<sub>2</sub> increases after continued exposure of EGCG to oxygen. H<sub>2</sub>O<sub>2</sub> production may indicate the induction of apoptosis, and may also stimulate the checkpoints of apoptosis. Cells are induced apoptosis via the mitochondria or caspase-3. The identification of specific kinases activated by catechin treatment would shed some lights on the properties of each catechin related to apoptosis.

## EXPERIMENTAL STUDY FOR BACTERIAL INFECTION

Catechins are well-known for their antimicrobial activities<sup>11-16</sup>). It is considered that they are transported into the bacterial cell membrane and damage the lipid bilayer. In our department, Matsubara et al.<sup>20</sup>) previously investigated the anti-infection effects of Japanese green tea (middle grade) in terms of catechin-concentration using several bacteria (*Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*) to lower the risks of infection in patients (Figure 4).

Consequently, Yoshii et al. <sup>21)</sup> reported that lipopoly-saccharide-deficient mutants (lack the O side chain and have core oligosaccharides of different lengths) of *Salmonella enterica* have increased sensitivity to catechins. These rough mutants were more sensitive to catechins than the bacterial strains with intact lipopolysaccharides.

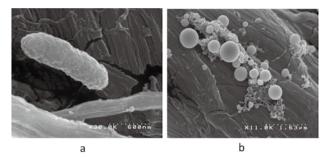


Figure 4 Scanning electron micrographs of bacterial cell membrane.

Normal bacterial Cells (Escherichia coli C600) (a). Cells after incubation with EGCG for 4 hours (b).

### EXPERIMENTAL STUDY FOR THE VIRUS INFECTION

Matsubara et al.<sup>20)</sup> performed a study in which standard green tea extracts (SGTE) with catechin concentrations ranging 1.2 mg/ml to 2.7 mg/ml were incubated with influenza A/Aichi/2/68 virus (Hong Kong subtype) at 37°C for at least 30 min. The SGTE completely inhibited the viral hemagglutination (HA) activity essential for viral attachment to the cell surface during the first steps of viral growth cycle. On the other hand, catechin-deficient SGTE, which was prepared by treatment with FeCl<sub>3</sub>, showed neither bactericidal nor HA inhibitory activities, confirming that catechins were mainly responsible for these activities. Green tea is a beneficial herbal medicine that prevents infection in patients. However, application of green tea as a method of preventing infections via effects of catechins requires long-term intake of green tea. Moreover, the concentrations of catechins (need to be high enough for any effects to occur; concentrations of at least 1 mg/ml) are required for efficacy against the influenza virus.

### INFECTION RISKS OF PLASTIC-BOTTLED TEA

Catechins exhibit antimicrobial activities. However, the method of cathecin-deliver into the body needs to be considered. Some patients obtain green tea from the automatic tea dispenser, while others drink green tea packaged in plastic-bottles. Bedridden patients can obtain green tea directly from the ward nurses or assistants. We know that the antibacterial properties of catechins are not powerful enough to prevent the bacterial growth. However, the effects and the risks of catechins as a prophylaxis for infection control need to be considered.

SPBB are becoming increasingly popular among inpatients, and some buy many bottles and store them in their rooms. Others drink green tea out of the same plastic-bottle, for long periods of time. While it is important to prevent dehydration in patients, particularly in the hot weather during summer, bacterial contamination in bottles containing unfinished tea, may increase the risk of infection. Our first question was the safety of the SPBB. Most patients drink directly from plastic bottles. Bacterial contamination is inevitable for direct drinking (DD), and bacterial infection is always a risk, particularly in immunocompromised hosts. Yoshii, et al.<sup>22)</sup> administrated a questionnaire to 40 inpatients, and the results showed that 26.7% of the patients consumed SPBB, especially green tea. Other beverages such as sports-drinks and mineral water were also popular. The results also showed that approximately half of the patients stored SPBB at room temperature, while the rest stored it in the refrigerator. Based on these data we calculated the DD-mediated bacterial contamination rate in three kinds of SPBB (green tea, sports drinks, and water) according to the storage method. Bacterial contamination in sports drinks was almost negligible regardless of the storage method. In green tea and mineral water, however, the numbers of living bacteria gradually increased overtime when stored at room temperature. Conversely, bacterial growth was suppressed when these SPBB was stored in the refrigerator<sup>22)</sup>.

These data suggest that inpatients should pay close attention to the hygienic considerations of DD-mediated bacterial contamination in SPBB. Sports drinks are the most recommended SPBB solely from the perspective of bacterial contamination. Green tea and mineral water should be stored in the refrigerator to lower the risk of contamination. However, unlike the catechins in green tea, there is no evidence of infection prophylaxis by the components of the sports drinks. Thus, from a traditional nursing point of view, we recommend the consumption of fresh, hot green tea. The value of green tea as a part of traditional nursing in Japan should be reconsidered.

### FUTURE DIRECTIONS FOR TRADITIONAL NURS-ING PRACTICE IN ASIA

Antimicrobial activity is well-known biological characteristic of catechins. Studies have shown that the major catechins with a gallate-group, such as ECG and EGCG, induce apoptosis, which is in agreement with our data. We presented our results at the 6<sup>th</sup> Asia- Pacific Traditional Nursing Conference in Seoul (South Korea) in 2014. We hope that our findings will bring the bene-

fits of the green tea service to the attention of Asian people based on the above scientific evidences.

The green tea service is an important tradition in nursing in Asian countries owing to the following factors; physical (it warms the body up), psychological (it has a relaxing effect on the mind), and social (it encourages communication between patients and medical staffs). In summary, we recommend that the green tea service is reinstated in hospital wards as part of traditional nursing practices.

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### **REFERENCES**

- Giorgi A.: An application of phenomenological method in psychology. In: Duquesne studies in phenomenological psychology (Vol. 2), Giorgi A., Fisher C. & Murray E., (eds), Pittsburgh, Pa., Duquesne University Press, 1975.
- 2) Watson J.: Nursing: Human science and human care. A theory of nursing. Appleton-Century-Crofts, 1985.
- Okakura K.: The book of tea. G.P. Putnam's sons. London & New York, 1906.
- 4) Luczaj W., Skrzudlewska E.: Antioxidative propertries of black tea. Prev. Med. 40: 910-918, 2005.
- 5) Thompson L., Wang S., Tawfik O., et al: Effect of 25-hydroxyvitamin D3 and 1  $\alpha$ , 25 dihydroxyvitmin D3 on differentiation and apoptosis of human osteosarcoma cell lines. J Orthop Res. 30: 831-834, 2012.
- Philips B.J., coyle C.H., Morrisroe S.N., et al: Induction of apoptosis in human bladder cancer cells by green tea catechins. Biomed Res. 30: 207-215, 2009.
- 7) Babich H., Krupka M.E., Nissim H.A., et al: Differential in vitro cytotoxicity of (-)-epicatechin gallate ECG to cancer and normal cells from the human oral cavity. Toxicology in vitro. 19: 231-242, 2005.
- 8) Okada N., Tanabe H., Tazoe H., et al: Differentiation associated alteration in sensitivity to apoptosis induced by EGCG in HL-60 cells. Biomed Res. 30: 201-206, 2009.
- 9) Ji S.J., Han D.H., Kim J.H.: Inhibition of proliferation and

- induction of apoptosis by EGCG in human osteogenic sarcoma (HOS) cells. Arch Pharm Res. 29: 363-368, 2006.
- 10) Yang W-H., Fong Y-C., Lee C-Y., et al: Epigallocatechin gallate induces cell apoptosis of human chondrosarcoma cells through apoptosis signal regulating kinase 1 pathway. J Cell Biochem. 112: 1601-1611, 2011.
- 11) Toda M., Okubo S., Ohnishi R., et al: Antibacterial and bactericidal activities of Japanese green tea. Jpn J Bacteriol. 44: 669-672, 1989 (in Japanese with English abstract).
- 12) Ito I., Okubo S., Fukuchi K., et al.: Antibacterial and bactericidal activities of EGCg on *Streptococcus pneumoniae*. Chemotherapy. 50: 118-125, 2002 (in Japanese with English abstract).
- 13) Shiraishi T.: Effect of the mouth-spraying with green tea on the reduction of MRSA. Nara Pref Hosp Nursing J. 19: 49-52, 2003 (in Japanese).
- 14) Nakayama M., Toda M., Okubo S., et al: Inhibition of influenza virus infection by tea. Lett Appl Microbiol. 11: 38-40, 1990.
- 15) Imanishi N., Tsuji Y., Katada Y., et al: Additional inhibitory effect of tea extract on the growth of influenza A and B viruses in MDCK cells. Microbiol Immunol. 46: 491-494, 2002
- 16) Mantani N., Andoh T., Kawamata H., et al: Inhibitory

- effect of Ephedrae herba, an oriental traditional medicine, on the growth of influenza A/PR/8 virus in MDCK cells. Antiviral Res. 44: 193-200, 1999.
- 17) Yang C.S., Wang X, Lu G, et al: Cancer prevention by tea: animal studies, molecular mechanisms and human relevance. Nature Rev. 9: 429-439, 2009.
- 18) Patterson F.R.: Osteosarcoma. In: Oncology and basic science, Damron T.A. (ed), pp177-187, Philadelphia, Wolters Kluwer-LWW, 2008.
- 19) Hou Z., Sang S., You H., et al: Mechanism of action of (-)-epigallocatechin -3-gallate: auto-oxidation-dependent inactivation of epidermal growth factor receptor and direct effects on growth inhibition in human esophageal cancer KYSE 150 cells. Cancer Res. 65: 8050-8056, 2005.
- 20) Matsubara H., Yoshii M., Miyahara T., et al: Study on the infection-preventive characteristics of Japanese green tea. J Nursing Soc Univ Toyama. 7: 23-31, 2007.
- 21) Yoshii. M., Okamoto A., Ohta M.: Lipopolysaccharide-deficient mutations of *Salmonella enterica* have increased sensitivity to catechins. Adv in Microbiol. 3: 399-402, 2013.
- 22) Yoshii M., Yatsuzuka M., Yasuda T.: Bacteriological study on the safety of small-plastic-bottled beverages. Jpn J Nursing Res. 32: 125-129, 2009 (in Japanese).