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Fermented Brown Rice and Rice Bran Inhibits Carcinogenesis in Different Organs of Rodents; A New Promising Agent for Cancer Prevention

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ABSTRACT

Fermented Brown Rice and Rice bran with *Aspergillus* (A) *oryzae* (FBRA) is a food manufactured by fermenting a mixture of brown rice and rice bran with *A. oryzae*. FBRA prevented carcinogen-induced carcinogenesis in 7 animal models. FBRA also acted against spontaneous development of neoplasms in 3 animal models. FBRA could be thus a promising new type of preventive agent for the occurrence of human cancers.

BACKGROUND

It has been recognized that dietary factors play an important role in the prevention of occurrence of cancers. Epidemiological studies have shown that high intake of fruits, vegetables and cereal foods decrease the risk for the occurrence of cancers in different organs. Rice is one of the major cereals, and is the most consumed food worldwide, particularly in Asian countries. Rice seeds and rice bran contain fiber and various types of antioxidants, including phenolic acids, phytic acid and tocopherols. Cellular and preclinical studies have supported that micronutrients in rice bran against the occurrence of several types of cancers. Our group has done a large-scale study to determine possible agents to suppress occurring cancers using animal models and found a number of effective natural or synthetic substances including rice-germ [1].

FBRA is a food manufactured by fermenting a mixture of brown rice and rice bran with *A. oryzae* to improve its digestibility. Composition of FBRA and its manufacturing process were shown previously [2,3]. It is already known that FBRA acts as a potent free radical scavenger [4] and a inducer of apoptosis in human leukemic cells [5]. These evidences of FBRA prompted us to carry out experimental studies to confirm the possible preventive effects on cancer development in different animal models. FBRA was supplied by Genmai Koso Co., Ltd, (Sapporo, Japan). Indeed, FBRA prevented carcinogen-induced tumorigenesis in a number of organs such as colon (azoxymethane-induced rat model) [2], pancreas (N-nitrosobis(2-oxopropyl)amine-induced hamster model) [3], liver (diethylnitrosoamine and phenobarbital-induced rat model) [4], esophagus (N-nitrosomethylbenzylamine-induced rat model) [7], stomach (N-methyl-N'-nitro-N-nitrosoguanidine-induced rat model) [8], urinary bladder (N-butyl-N-(4-hydroxybutyl)-nitrosoamine-induced mouse model) [9], lung (4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone-induced mouse model) [10]. Furthermore, FBRA suppressed spontaneous carcinogenesis of prostate in a transgenic TRAP rat (in this rat, hormonally regulated rat probasin promotor specifically drives the expression driving of SV40 T antigen in the prostatic epithelium) [11] and thymic lymphomatogenesis in a mouse model (AKR/NSlc female mice) [12]. Although FBRA did not indicate preventive effects on the spontaneous development of the colon tumors in *Apc*Min/+ mice, the agent clearly inhibited carcinogenesis in dextran sodium sulfate-exposed *Apc*Min/+ mice [13]. In the studies using chemical carcinogens, exposure of FBRA decreased multiplicity as well as incidence of neoplasms including carcinomas. Through these experiments, effect of FBRA was apparent by exposure during the post-initiation phase (term after the administration of carcinogen). FBRA did not show clear preventing effect by exposure during the initiation phase (term for the administration of carcinogen) suggesting that effect of FBRA is basically not related to metabolic activation or detoxication of carcinogen. Furthermore, FBRA reduced carcinogen-induced cell proliferation in non-neoplastic as well as neoplastic cells of the organs for the carcinogenesis. Present author already stated that control of cell proliferation is quite important for the underlying mechanisms for the cancer chemoprevention [14]. For the case of FBRA against prostate carcinogenesis in TRAP rats, retardation of transition of preneoplastic lesions to neoplasms seemed to be important [11]. As mode of action of FBRA for the inhibition of thymic lymphomatogenesis in the mice, emergence of cellular apoptosis in the preneoplastic and neoplastic cells was suggested to be key issue [12]. Through the all animal experiments for modifying effects of FBRA, FBRA did not exert any toxicity in any organs. Accordingly, FBRA could be a prominent agent for prevention of human cancers and our data emphasize the advantage of unpolished rice as a daily staple food.

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