Kurozu (or Kurosu) is traditional Japanese black vinegar made by prolonged fermentation of unpolished rice and Kurozu Moromimatsu, its sediment, are both consumed in Japan as health foods or supplements.

Keywords: Kurozu or Kurosu;Kurozu Moromimatsu; Vinegar; Unpolished rice; Antioxidant activity; Anticarcinogenic e ect; Anti-Colitis e ect

## Introduction

Kurozu (or Kurosu) is traditional Japanese black vinegar made by prolonged fermentation of unpolished rice that contains rice germ and rice bran [1]. While there are several preparation methods, one native to Kagoshima prefecture involves drying the fermented product in the sun for more than a year in earthenware jars. e liquid concentrate a er drying is called Kurozu and the sediment at the bottom is called Kurozu Moromimatsu (Kurozu-M). Kurozu and Kurozu-M contain acetic acid as well as abundant organic materials, minerals, and amino acids not found in other vinegars. Kurozu-M is also rich in metabolites generated by lactobacillus and koji bacillus among other microbes. Kurozu has been reported to alleviate hyperlipidemia and hypertension [2,3]. Both Kurozu and Kurozu-M are widely consumed in Japan as health foods and supplements.

Oxidative stress is widely accepted as an important factor in the progression of in ammation and carcinogenesis. Kurozu has established antioxidant activity that may confer the anti-in ammatory and anticarcinogenic e ects reported in animal models [4-6]; however, the active ingredients are unclear at present. In this report, we summarized the studies demonstrating the anticarcinogenic and anti-colitis e ects of Kurozu and Kurozu-M.

## Kurozu and Kurozu-M as Antioxidants

An ethyl acetate extract of Kurozu (EK) reportedly exhibits strong free radical-scavenging activity in both 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging system and linoleic acid autoxidation system [4-6]. In addition, EK suppressed lipid peroxidation in mouse skin more e ectively than other vinegars and prevented dimethylbenzanthracene-induced skin carcinogenesis in mice [6]. ese results suggest that the antitumor e ects are partially due to the antioxidant properties of EK. Kurozu and Kurozu-M reduce nitrotyrosine levels, which is a marker of oxidative and nitrative stress [7,8]. Nitrotyrosine is produced through at least two pathways: reaction with peroxynitrite formed from superoxide ($O_2^-$) and nitric oxide (NO) and reaction of tyrosine with nitrite catalyzed by myeloperoxidase [9]. Black vinegar produced in Kagoshima prefecture, Izumi, has recently been reported to have potential antioxidant activity [10].

## Anti-Colitis E ects of Kurozu on Experimental Animal Model

We demonstrated the protective e ects of Kurozu in a rodent model of dextran sulfate sodium (DSS)-induced colitis [8]. Oral administration of Kurozu signi cantly attenuated DSS-induced colitis and decreased nitrotyrosine levels in colonic epithelium, possibly by antioxidant activity. Acetic acid, the main component of Kurozu, has been reported to improve hyperlipidemia in humans and animal models [3]. However, our study indicated that acetic acid did not ameliorate DSS-induced colitis [8]. In another study, we chromatographically separated Kurozu into 4 molecular weight fractions and found active ingredients against DSS-induced colitis in rats within the 800-4,000 dalton fractions [11]. However, the speci c anti-colitis factors remain to be identi ed.

## Anticancer E ects of Kurozu in vitro

Nanda et al. [12] reported that EK inhibited the proliferation of several human cancer cell lines, including those derived from colon adenocarcinoma (Caco-2), lung carcinoma (A549), breast adenocarcinoma (MCF-7), bladder carcinoma (5637), and prostate carcinoma (LNCaP) [12]. Possible anticarcinogenic mechanisms in Caco-2 cells include induction of cell cycle arrest and apoptosis. is study also suggested that phenolic compounds in Kurozu are the active ingredients. In addition, Izumi reportedly inhibited the proliferation of the human squamous cell carcinoma cell line (HSC-5) in vitro, possibly by activating programmed necrosis (necroptosis) rather than apoptosis [13].

erefore, apoptosis induction of Kurozu has not been uni ed among published studies; a possible reason being the di erences in the manufacturing methods of the vinegar.

## Anticancer E ect of Kurozu against Colon Cancer In Animal Models

Shimoji et al. [14] reported that EK inhibited the development of aberrant crypt foci-precursor lesions for colonic adenocarcinoma-in

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the azoxymethane (AOM)-induced animal model. In this paper, EK inhibited the production of prostaglandin E2 (PGE2)-which induces hyper-proliferation-in colonic mucosa, and elevated glutathione S-transferase (GST) and quinone reductase activities in the liver [14]. These mechanisms may explain the anticarcinogenic effect of EK. Furthermore, they reported that oral administration of EK significantly inhibited the incidence and multiplicity of colon adenocarcinoma in the AOM-induced animal model [1]; thus, EK may effectively inhibit colon carcinogenesis possibly by suppressing cyclooxygenase (COX)-2.

The activation of certain matrix metalloproteinases (MMPs), particularly MMP-2 and -9, results in enhanced release of angiogenic factors into the extracellular matrix, which may promote and sustain angiogenesis and tumor growth [15]. We reported that oral administration of Kurozu-M inhibited the proliferation of the human colon adenocarcinoma cell line LoVo after subcutaneous implantation in nude mice and decreased both activated MMP-2 and -9 and nitrotyrosine levels in colonic epithelium; however, apoptosis was not induced [7]. Unlike Kurozu-M, Kurozu did not inhibit tumor growth in this study; this suggests that the antiangiogenic ingredient is contained in the sediment.

## Kurozu-M Inhibition of Hepatocellular Carcinoma (HCC) In an Animal Model

We reported that oral administration of Kurozu-M significantly decreased the sizes of GST placental form-positive foci and prolonged survival in a diethylnitrosamine-induced HCC animal model [16]. HCC is typically hypervascular, and angiogenesis is considered to play an important role in its growth and progression. Therefore, one possible anti-HCC mechanism of Kurozu-M is reduced hepatic MMP-2 and -9 activities [16].

## Conclusions

The anticarcinogenic and anti-colitis effects of Kurozu and Kurozu-M are demonstrated in several experimental animal models and in vitro studies. However, the active ingredients in the vinegar and sediment remain to be identified. At present, there is no clear evidence for anticancer or anti-colitis effects of Kurozu in humans, but clinical studies of this widely-used dietary supplement are warranted.

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1. Shimoji Y, Kohno H, Nanda K, Nishikawa Y, Ohigashi H, et al. (2004) Extract of Kurosu, a vinegar from unpolished rice, inhibits azoxymethane-induced colon carcinogenesis in male F344 rats. Nutr Cancer 49: 170-173.

2. Nishikawa Y, Takata Y, Nagai Y, Mori T, Kawada T, et al. (2001) Antihypertensive effect of Kurosu extract, a traditional vinegar produced from unpolished rice, in