Journal of Functional Foods 26 (2016) 187–195

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jff

Flaxseed lignan secoisolariciresinol diglucoside ameliorates experimental colitis induced by dextran sulphate sodium in mice

Jiqu Xu [a,b], *Guangjing Tian* [a,b], *Congcong Ma* [a,b], *Hui Gao* [c], *Chang Chen* [d,e], *Wei Yang* [c], *Qianchun Deng* [a,b], *Qingde Huang* [a,b], *Zhonghua Ma* [f], *Fenghong Huang* [a,b,*]

[a] *Department of Nutriology, Oil Crops Research Institute, Chinese Academy of Agricultural Sciences, 2 Xudong Second Road, Wuhan 430062, China*

[b] *Hubei Key Laboratory of Lipid Chemistry and Nutrition, Oil Crops Research Institute, Chinese Academy of Agricultural Sciences, 2 Xudong Second Road, Wuhan 430062, China*

[c] *Department of Nutrition and Food Hygiene, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, 13 Hangkong Road, Wuhan 430030, China*

[d] *Department of Gastroenterology, The First People's Hospital of Yichang, The People's Hospital of China Three Gorges University, 2 Jiefang Road, Yichang 443000, China*

[e] *Department of Gastroenterology, The People's Hospital of China Three Gorges University, 2 Jiefang Road, Yichang 443000, China*

[f] *Functional Oil Laboratory Associated by Oil Crops Research Institute, Chinese Academy of Agricultural Sciences and Infinite (China) Co., LTD., 66 Jianzhong Road, Guangzhou 510665, China*

ARTICLE INFO

Article history:
Received 16 March 2016
Received in revised form 1 June 2016
Accepted 12 July 2016
Available online

Keywords:
Secoisolariciresinol diglucoside
Ulcerative colitis
Dextran sulphate sodium
Inflammation
Mucosal permeability

ABSTRACT

The effect of flaxseed lignan secoisolariciresinol diglucoside (SDG) on ulcerative colitis was examined. Experimental colitis was induced in mice by administering 5% dextran sulphate sodium (DSS). SDG in doses of 100 and 200 mg/kg/day and 5-aminosalicylic acid (positive control) were given orally for 3 days before and during DSS administration. Oral SDG treatment significantly decreased the disease activity index and increased colon length. Histological examination revealed that the oral administration of SDG suppressed DSS-induced erosion, ulceration, crypt abscesses and oedema. Furthermore, colonic myeloperoxidase activity and TNF-α expression declined remarkably following treatment with SDG. Additionally, oral SDG treatment significantly increased the expression of several mucoprotection markers, to include zona occludens-1, Tollip and trefoil factor 3, and thus restored intestinal permeability. These results suggested that oral SDG treatment can alleviate DSS-induced colitis and might be a promising supplement for the amelioration of inflammatory bowel disease.

* *Corresponding author.* Oil Crops Research Institute, Chinese Academy of Agricultural Sciences, 2 Xudong Second Road, Wuhan 430062, China. Fax: +86 027 86815916.
E-mail address: fhhuang@foxmail.com (F. Huang).

http://dx.doi.org/10.1016/j.jff.2016.07.013
1756-4646/

1. Introduction

Inflammatory bowel diseases (IBD), principally including Crohn's disease and ulcerative colitis, are chronic recurrent inflammatory disorders primarily affecting the digestive tract. This disease commonly displays classic colitis symptoms, such as rectal bleeding, diarrhoea, abdominal pain and weight loss, thus dramatically interfering with the daily life of a patient with IBD (Conrad, Roggenbuck, & Laass, 2014). Moreover, patients with IBD have a significantly higher risk of colorectal cancer (Tomasello et al., 2014). Furthermore, IBD incidence rates have substantially risen in the past several decades, with IBD now considered a global disease affecting several million people worldwide (Ananthakrishnan, 2015). Because of the increasing IBD incidence rate, the direct and indirect costs are expected to rise exponentially (Kaplan, 2015). While the aetiology of IBD requires further elucidation, evidence suggests that genetic susceptibility, intestinal environment and immune system interactions contribute to an exaggerated or unnecessary inflammatory response to luminal bacteria, thus playing a pivotal role in IBD pathogenesis (Tomasello et al., 2014; Xavier & Podolsky, 2007). Currently, many drugs such as aminosalicylates and immunomodulators are used for IBD treatment (Morrison, Headon, & Gibson, 2009), but the optimal therapy has still not been established. For example, 5-aminosalicylic acid (5-ASA) drugs, which are a common first-line of treatment with a proven efficacy (Feagan & Macdonald, 2012), have a high incidence of side effects (Katsanos, Voulgari, & Tsianos, 2012; Linares, Alonso, & Domingo, 2011) and relatively low compliance rate due to a high pill burden (Kane, 2006; Morrison et al., 2009). Therefore, it is essential to seek alternative and less expensive treatment options to improve IBD outcome.

Lignans are a group of non-caloric, bioactive, polyphenolic compounds found in many food products, but with the highest concentrations found in flaxseed. The principal flaxseed lignan, secoisolariciresinol diglucoside (SDG), has been of particular interest due to its potential health benefits in humans. In the gut, this compound is metabolized by gut microbiota to form the mammalian lignans enterodiol (END) and enterolactone (ENL) (Setchell et al., 2014), which exhibit a weak oestrogenic effect due to a structural similarity to estradiol (Adolphe, Whiting, Juurlink, Thorpe, & Alcorn, 2010). Additionally, SDG and its metabolites have been reported to possess antioxidant, anti-inflammatory, antidiabetic and antitumour properties in addition to serving as a cardiovascular enhancer (Adolphe et al., 2010).

Over the past decades, researchers have reported that SDG has the potential to beneficially modulate colon health and offers protective anti-tumour activity (Kuijsten, Arts, Hollman, van't Veer, & Kampman, 2006). Furthermore, the ability of SDG to act as a colon cancer preventative agent has been partly attributed to its strong antioxidant, anti-proliferative and antiangiogenic activities. However, a recent study showed that flaxseed consumption can exacerbate acute colonic mucosal inflammation and injury in an IBD model induced by dextran sulphate sodium (DSS) (Zarepoor et al., 2014). While SDG is one of major bioactive compounds in flaxseed, the adverse effects seen in DSS-induced colitis were not likely attributed to SDG. This study showed that the flaxseed hull, which contains the highest SDG levels, did not induce colitis aggravation, but rather slightly attenuated DSS-induced body and liver weight loss (Zarepoor et al., 2014). Furthermore, SDG metabolites can pass the enterocyte barrier and modulate intestinal immune cell functions. For example, these enterolignans can prevent I-κB degradation and NF-κB activation, subsequently leading to a decreased TNF-α release in monocytes (Corsini et al., 2010). Moreover, ENL, a phase 2 protein inducer (Wang, Liu, Higuchi, & Chen, 1998), may ameliorate some diseases with a prominent inflammatory component. Based on these observations, we hypothesized that oral SDG consumption would ameliorate IBD *via* its anti-inflammatory activity. Therefore, the goal of the present study was to determine if an ameliorative effect could be achieved following oral SDG treatment in DSS-induced colon injury.

2. Materials and methods

2.1. SDG preparations

SDG was isolated from flaxseed as previously described (Zhang & Xu, 2007). Briefly, flaxseeds were ground to flour, defatted with n-hexane and the flour was extracted with 50% (v/v) aqueous ethanol. The extract was vacuum evaporated and subjected to alkaline hydrolysis for 4 h under constant rotation using 0.25M aqueous sodium hydroxide. After hydrolysis, the samples were acidified to pH 4.0, and crude SDG was collected and filtered through a 0.45 μm cellulose acetate membrane filter. The filtrate was subjected to Sephadex LH-20 (Amersham Pharmacia Biotech AB, Uppsala, Sweden) column chromatography, and pure SDG was obtained by eluting with aqueous ethanol of different concentrations. The isolated SDG had a purity of 96% (by HPLC analysis).

2.2. Animals

Male C57BL/6J mice were purchased at 7 weeks of age from Vital River Laboratory Animal Center (Beijing, China). The animals were housed individually and maintained at a controlled ambient temperature (22 ± 1 °C) under diurnal conditions (light–dark: 08:00–20:00) with access to standard laboratory rodent chow and tap water *ad libitum*. The animals were cared for in accordance with *the Guiding Principles in the Care and Use of Animals*. The experiment was approved by the Oil Crops Research Institute Council on Animal Care Committee of the Chinese Academy of Agricultural Sciences.

2.3. Experimental design

Following the 7 day acclimatization period, mice were randomly divided into five groups (n = 10 per group). The untreated control group received only drinking water without DSS, while the DSS group (DSS) was given 5% (w/v) DSS (MW: 36,000–50,000; MP Biomedicals, Solon, OH, USA) in their drinking water for 7 days to induce ulcerative colitis (Albert, Walker, Thiesen, Churchill, & Madsen, 2010; Cho et al., 2007). For the SDG treatment groups and the 5-ASA positive drug control group, SDG (100 and 200 mg/kg/day, L- and H-SDG groups) and 5-ASA