Chemopreventive Efficacy of Andrographis paniculata on Azoxymethane-Induced Aberrant Colon Crypt Foci In Vivo

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Abstract

Andrographis paniculata is a grass-shaped medicinal herb, traditionally used in Southeast Asia. The aim of this study was to evaluate the chemoprotective effects of A. paniculata on colorectal cancer. A. paniculata ethanol extract was tested on azoxymethane (AOM)-induced aberrant crypt foci (ACF) in vivo and in vitro. A. paniculata treated groups showed a significant reduction in the number of ACF of the treated rats. Microscopically, ACF showed remarkably elongated and stratified cells, and depletion of the submucosal glands of AOM group compared to the treated groups. Histologically, staining showed slightly elevated masses above the surrounding mucosa with oval or slit-like orifices. Immunohistochemically, expression of proliferating cell nuclear antigen (PCNA) and β-catenin protein were down-regulated in the A. paniculata treated groups compared to the AOM group. When colon tissue was homogenized, malondialdehyde (MDA) and nitric oxide (NO) levels were significantly decreased, whereas superoxide dismutase (SOD) activity was increased in the treated groups compared to the AOM group. A. paniculata ethanol extract showed antioxidant and free radical scavenging activity, as elucidated by the measure of oxidative stress markers. Further, the active fractions were assessed against cell lines of C叔叔841 and HT29 colon cancer cells.

Introduction

Colorectal cancer continues to afflict several thousands of males and females per year, accounting for about 10% of cancer-related deaths and weighed as the third commonest malignancy in Malaysia as reported in 2007 [1]. Therapeutic modalities such as chemotherapy and radical colostomy are considered curative for colorectal cancers [3]. It is the most potent agent that can be used solely for colorectal cancer treatment in an advanced stage [4]. Fluorouracil is one of the chemotherapeutic drugs of choice for the treatment of colon, rectum, stomach, and pancreatic tumours and is also regularly used to alleviate breast benign and malignant lumps. Unfortunately, fluorouracil among other chemotherapies has side effects, which include diarrhoea, heartburn and sores in mouth and on lips. Approximately 20% of the patients develop symptomatic organ failures, manifested as stomach cramps, painful urination, and difficulty in breathing accompanied by fever or chills. The complications of the standard chemotherapies were attributed to their nature as antimetabolites that impair the production of the essential proteins followed by secondary cellular degradation. The strong impact of the fluorouracil on the body tissues increases the risk for delayed unwanted consequences. However, cessation of fluorouracil therapy is not always a choice, because the symptoms of the polyp formation and carcinogenic early/late stage affect the patient’s quality of life even more. Currently, a great number of natural products have been found possessing anti-carcinogenic property by counteracting different etiological factors [5]. Habitual consumption of medicinal plants are known to improve mitochondrial bioenergetics and inhibit various secondary sources of reactive oxygen species (ROS), thus reducing the risk for carcinogenesis [6]. Studying specific natural product molecules selected on the basis of the inhibition of multiple processes responsible for the production of proinflammatory mediators and stimulating the transcriptional machinery necessary for mitochondrial biosynthesis may be a feasible approach for the prevention and treatment of numerous types of cancer.

Andrographis paniculata is a potential cure for several malignancies [7] and treatment of several non-malignant disorders functioning as anti-diabetic [8], anti-ulcerative [9], anti-bacterial and anti-fungal [10], antioxidant [11], anti-HIV [12], antiedema and analgesic [13], anti-inflammatory [14], wound healing [15] renal-protective [8], cardio-protective and hepatoprotective [16] agent. An increase in plasma concentration of andrographolide (AP) and 14-deoxy-11,12-didehydroandrographolide (DIAP) were observed from 30 min