

Inhibitory effects of aloe carboxypeptidase fraction on streptozotocin-induced enhancement of vascular permeability in the pancreatic islets

H. Beppu^{a,*}, K. Shimpo^a, T. Chihara^a, I. Tamai^a, S. Nomoto-Yamaji^a,
S. Ozaki^a, S. Ito^b, H. Kuzuya^a

^aFujita Memorial Institute of Pharmacognosy, Fujita Health University, 1865 Isshiki-cho, Hisai, Mie 514-1296, Japan

^bSchool of Health Sciences, Fujita Health University, Toyoake, Aichi 470-1192, Japan

Received 20 April 2004; accepted 25 June 2004

Abstract

The protective actions of components isolated from *Aloe arborescens* Miller var. *natalensis* Berger (Kidachi aloe in Japanese) on streptozotocin (Sz)-induced necrosis of B cells in the pancreatic islets of the mouse were investigated to clarify its action mechanism involved in anti-diabetic effects. In this experiment, phenol low molecular weight components of aloin and aloin A that were anti-oxidants and derived from the leaf skin or pulp extract, an aloe carboxypeptidase fraction that is a inhibitor of enhanced vascular permeability and a glycoprotein component that decreases blood glucose were tested with mice precedently administered with Sz which is known as a cytotoxin specific to B cells. The results showed that the treatment group receiving Sz followed by the aloe carboxypeptidase fraction increased the inhibition of dye leakage by 75.8% ($p < 0.001$) in the extract of whole pancreas in comparison to the control group and the aloe carboxypeptidase fraction group also increased the inhibition effect by 68.4% ($p < 0.001$) in the extract of pancreatic islets as compared to the control group. The carboxypeptidase is an aloe-derived protease known to inhibit the acetic acid-related enhancement of intraperitoneal vascular permeability in mice. Further, the elevation of blood glucose in Sz-induced diabetic mice intraperitoneally given the aloe carboxypeptidase fraction was significantly ($p < 0.01-0.001$) restrained at 3, 7 and 14 days after the injection as compared to the control group given solvent only. The results of this experiment suggested that the inhibitory effect on the enhancement of vascular permeability related to the vascular acute inflammatory response at Sz-induced lesions of pancreatic islets was involved in the action mechanism of this enzyme.

© 2005 Elsevier GmbH. All rights reserved.

Keywords: *Aloe arborescens* Miller; Carboxypeptidase; Anti-diabetes; Streptozotocin; Langerhans islets; Vascular permeability of the pancreatic islets

Introduction

There are plenty of articles related to the anti-diabetic effects of components that are of plant origin (Roman-Ramos et al., 1995; Alarcon-Aguilara et al., 1998; Reynolds and Dweck, 1999; Yeh et al., 2003; Eddouks

*Corresponding author. Tel.: +81 59 252 1010;
fax: +81 59 252 0710.

E-mail address: hbeppu@fujita-hu.ac.jp (H. Beppu).

et al., 2003). Polysaccharides like panaxan A, aconitan A and ganoderan B and C that exhibited hypoglycemic effects were found in Japan from galenicals such as *Panax ginseng*, *Aconitum carmichaeli*, *Ganoderma lucidum* (Takahashi et al., 1985; Konno et al., 1985a, b; Tomoda et al., 1985, 1987, 1990; Hikino et al., 1985, 1989). These active polysaccharides were found to have a structure composed of glucan (Tomoda et al., 1984, 1986a, b), and their actions were reportedly to increase blood concentration of insulin and decrease glycogen in the liver of mice (Hikino et al., 1989).

On the other hand, there are several publications relevant to *Aloe barbadensis* Miller (*Aloe vera* Linne) and Kidachi aloe (Ghannam et al., 1986; Ajabnoor, 1990; Beppu et al., 1993; Chithra et al., 1998; Okyar et al., 2001), and Acemannan, glycoprotein and polysaccharides were cited as active ingredients. We have isolated hypoglycemic components from the mesophyll of Kidachi aloe that is a good source of polysaccharides (Beppu et al., 1990). Meanwhile, it was confirmed that in the leaf skin, there were some components exhibiting inhibitory actions of hyperglycemia as a result of the prevention of necrotic inflammation of pancreatic islet B cells (Beppu et al., 1990).

Streptozotocin (Sz) specifically destroys pancreatic islet B cells (Junod et al., 1967; Like et al., 1978; Agarwal, 1980; Cooperstein and Watkins, 1981). It was detected in the pancreatic islets of mice and rats that dye leakage related to increased vascular permeability reached a peak 4–8 h after Sz injection, when Monastral blue B or Evans blue was serially and intravenously injected (Sandler and Jansson, 1985; Beppu et al., 1987).

Majno et al. (1987) confirmed, using BB rats in Worcester colony (hereinafter referred to as “BB/Wor”) of human insulin-dependent diabetes rat model, that the development of pancreatic vascular leakage (PVL) was intensified by the injection of Monastral blue B of a colloidal pigment into the tail vein of 20–200 days old BB/Wor rats. Nakano (1991) reported that PVL developed before insulinitis manifested in BB/Wor rats. Majno and Doukas group found that intravenous injection of purified immunoglobulins from RT6-depleted diabetes-resistant (DR)-BB rat induced abnormal PVL in mice. The presence of immunoglobulins early in the disease process and their ability to induce PVL would suggest that they might participate in one of diabetes pathogenesis. More specifically, the pathomorphism of PVL would induce insulinitis to be one of pathogenesis of diabetes mellitus (Doukas et al., 1996).

Now therefore, it is expected that the restraint of progressing PVL could retard a chain reaction of insulinitis and the development of diabetes mellitus. The inhibition of vascular permeability in pancreatic islets may reduce the destruction of the pancreatic islets and retard the elevation of blood glucose, thus preventing the development of diabetes.

Previously, we pathologically found that a component of Kidachi aloe leaf skin showed more potent protective actions on B cell necrosis induced by Sz, which is known as a cytotoxin specific to B cells, than a component of Kidachi aloe leaf pulp.

We administered leaf skin and pulp extract components derived from a phenol low molecular weight component, a glycoprotein component and a carboxypeptidase fraction derived from Kidachi aloe to mice to compare the inhibitory effects on the Sz-induced enhancement of vascular permeability so that we can search any component participated in other action mechanisms to protect pancreatic islet B cells than the hypoglycemic action shown by glucans, Acemannan or other polysaccharides.

Materials and methods

Preparation of Kidachi aloe

Fresh aloe leaves (5–6 years old) were harvested from the herb garden of Yurika Co., Ltd. (Hisai, Japan). Leaves weighing over 80 g were selectively collected and processed immediately. Fig. 1 shows the diagram of the separation of aloe materials and yield quantities of samples used in the final experiment.

Preparation of freeze-dried whole leaf, freeze-dried leaf skin and freeze-dried leaf pulp of Kidachi aloe

Fresh whole Kidachi aloe leaves (3 kg) were homogenized in a polytron homogenizer and then freeze-dried (whole leaf FD). Using a knife, 3 kg of the fresh whole Kidachi aloe leaves were separated into the superficial layer of the leaf skin (leaf skin weighing approx. 1 kg) and the succulent layer of the leaf pulp (leaf pulp weighing approx. 2 kg), and prepared by the same method used for the preparation of the whole leaf freeze-dried powder. The leaf skin yielded a freeze-dried Kidachi aloe leaf skin powder (leaf skin FD), while the leaf pulp yielded a freeze-dried leaf pulp powder (leaf pulp FD).

Preparation of acetone-precipitated Kidachi aloe leaf skin juice

Leaf skins were removed from 3 kg of fresh whole Kidachi aloe leaves with a knife, homogenized in a polytron homogenizer and the homogenates were filtered through a Whatman GF/A filter. Approximately 1 l (or 1 kg) of aloe leaf skin juice was treated with a two-fold volume of cold acetone, precipitated and lyophilized. The resulting powder was referred to as

Download English Version:

<https://daneshyari.com/en/article/2497678>

Download Persian Version:

<https://daneshyari.com/article/2497678>

[Daneshyari.com](https://daneshyari.com)