



Opinion

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Bromelain containing oral nutraceuticals as a potential treatment for ACE inhibitor-induced cough

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Abstract

Hypertension (HTN) has generally been considered as one of the most significant risk factors for cardiovascular diseases; i.e. heart and renal failure, peripheral artery disease, stroke, and death. Moreover, Angiotensin Converting Enzyme (ACE) Inhibitors have also been regarded as one of the most widely prescribed and well-tolerated antihypertensive drugs. However, bradykinin degradation defect and, consequently, chronic/persistent dry cough can be regarded as prevalent side effects of these medications. In this sense, Pineapple (*Ananas comosus*) which includes Bromelain with acceptable oral bioavailability and bradykinase activity (hydrolysis of nonapeptide bradykinin) can be an effective treatment for ACE inhibitor-induced cough.

Keywords: Hypertension, Nutraceuticals, *Ananas comosus*.

INTRODUCTION

A common adverse effect of Angiotensin Converting Enzyme Inhibitors (ACEIs) is the persistent non-productive cough which is not dose-dependent [1,2]. This is often an annoying side effect but, in some cases, results in the discontinuation of the treatment [3,4].

Although the Pathogenesis of the ACEI-induced cough is still a clinical mystery, it has been revealed that the cough mechanism is not related to the inhibition of the renin-angiotensin system because it is not observed in the treatment with either angiotensin receptor blockers or renin inhibitors [5]. Numerous studies have proposed that the cough induced by ACEIs is associated with the accumulation of bradykinin in tissues as a result of inhibition of its metabolic decomposition by ACEIs [6].

Ananas comosus or Pineapple (family Bromeliaceae), as a well-known fruit and folk medicine to cure different diseases, contains Bromelain (a group of proteolytic enzymes) whose oral administration has healing, anti-edematous, anti-inflammatory, anti-cancer, antimicrobial, antithrombotic, antiviral and fibrinolytic effects [7-10]. Interestingly, Bromelain also has bradykinin-degrading activity [8,11].

The Hypothesis/Theory

According to the above-mentioned explanations, the question is "Can Bromelain, containing oral nutraceuticals with bradykinase activity, be an effective cure or treatment for the ACEIs-induced cough that is associated with accumulation of bradykinin in the airways?"

Evaluation of the hypothesis/idea

Ananas comosus which is one of the commonly employed medicinal herbs can play the role of an effective expectorant and antitussive medication for the management of cough [12,13]. In this sense, it is worth mentioning that pharmacologically active Ingredient-Bromelain in combination with honey has been reported to have therapeutic effects against acute irritative cough [13]. Besides, Bromelain has revealed to possess anti-inflammatory and analgesic properties which are thought to be the result of its direct influence on inflammation and pain mediators such as bradykinin [14-17]. Thus, why cannot it be an efficient cure for ACEIs-induced cough which is bradykinin dependent?

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Consequences of the hypothesis and discussion

There is a concern in the prescription of Bromelain-containing nutraceuticals in patients with hypertension which is due to the vasodilatory effect of bradykinin; in the sense that the administration of Bromelain with its bradykinase activity may worsen the HTN of the patients. Thus, extensive studies to confirm the effectiveness of pineapple and nutraceutical products derived from this medicinal plant in ACEIs-induced cough without serious adverse effects, are highly recommended/needed.

Furthermore, Aloe vera (*Aloe barbadensis* Miller) is also a well-known medicinal herb. Aloe vera gel contains at least six different enzymes; i.e. catalase, carboxypeptidase, cellulose, amylase, oxidase, and above all bradykinase [18,19]. Aloe vera has shown an efficient and distinguished bradykinin-degrading activity which is related to analgesic and anti-inflammatory effects of this plant [20,21]. Thus, it is hypothesized that this magic herb can also be considered as an efficient treatment for ACEIs-induced cough in a proper dosage form, just like that of pineapple.

Conflict of interest

None declared.

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