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Surface plasmon resonance applicability study using immobilized recombinant human renin to screen for renin inhibitory activity

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Abstract

Renin is an important target for inhibition to treat high blood pressure. The enzyme catalyzes the first rate-determining step in the renin angiotensin system (RAS), which controls blood pressure in mammals. Renin-inhibitory compounds have been found in several foodstuffs, such as soybeans and cereals, and certain saponins and unsaturated fatty acids have been identified as such. The present study determined the surface plasmon resonance (SPR) responses of various saponins and unsaturated fatty acids using recombinant human (rh)-renin, which was produced with an insect cell-baculovirus expression system and immobilized to sensor chips. We demonstrated that there is a qualitative correlation between SPR responses and half-maximal (50%) renin inhibitory concentration. In addition, the SPR responses of several legume extracts with the immobilized rh-renin agreed for the most part with their reported inhibitory activity. These results indicate that SPR analysis using immobilized rh-renin is applicable to the screening of potential renin-inhibitory compounds in natural foodstuffs.

Keywords : human renin, surface plasmon resonance, renin inhibitory compounds

I Introduction

The renin-angiotensin system (RAS) is the most important physiological regulatory system that controls blood pressure and fluid balance in mammals[1]. The chain of events in the RAS begins with the conversion of inactive angiotensinogen to angiotensin I catalyzed by renin [EC 3.4.23.15], an aspartic proteinase, when arterial blood pressure or sodium levels in the body decrease or potassium levels are high[2]. Angiotensin I is then converted to the hormone angiotensin II by an enzyme known as angiotensin-converting enzyme (ACE), which causes blood vessels to constrict and blood pressure to rise[3]. Angiotensin II also stimulates the release of the hormone aldosterone in the adrenal glands, which acts on the kidneys to retain sodium and water and excrete potassium, together working to increase blood volume and pressure.

Renin and ACE, the key enzymes in the RAS, would be promising targets for repression in the treatment of high blood pressure. Several kinds of ACE inhibitors have already been developed and approved as pharmaceuticals that widen or dilate blood vessels to increase blood flow and lower blood pressure[4]. ACE inhibitors have also been explored in various foodstuffs for daily dietary management. However, no direct inhibitors of renin, the other rate-determining enzyme and a triggering enzyme of the RAS, were available until the relatively recent approval of aliskiren[5]. Hardly any screening for inhibitors in foodstuffs has so far been carried out, largely due to the difficulty in preparing human renin and the complexity of the renin assay. We recently reported on a method for rapid purification of recombinant human (rh)-renin expressed by an insect cell-baculovirus system[6-9]. Using rh-renin and the newly developed internally self-quenched fluorescent (IQF) substrate, we screened for renin inhibitory compounds in soybeans and determined that soyasaponin I has renin-inhibitory activity[10]. In addition, we found that several other saponins in soybeans have renin inhibitory activity[11, 12], as was recently confirmed for legumes[13], rice, cereals[14], and wild vegetables[15]. The renin inhibitors contained in rice were

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