Advances in Pharmacoepidemiology & Drug Safety

Szomor, Adv Pharmacoepidem Drug Safety 2012, 1:6
DOI: 10.4172/2167-1052.1000121

Research Article Open Access

Inhibition of Interaction between CagA and Shp-2 Domain by Using Medicinal Plant Products

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Abstract

Aim: Inhibition of CagA tyrosine phosphorylation or disruption of the CagA–SHP-2 complex, to prevent the bacteria function which may leads to the peptic ulcers and gastric Adeno carcinoma, by using medicinal plants.

The CagA–SHP-2 interaction is dependent on CagA tyrosine phosphorylation and, through the complex formation. SHP2 plays a pivotal role in growth factor and cytokine signaling.

By inhibiting this CagA-SHP-2 domain complex, we can prevent the survival of the bacteria in the host.

This inhibition of CagA-SHP-2 complex can be done by using various chemical compounds like NSC87877, Salicylic acid etc. These compounds have the ability to inhibit the CagA-SHP-2 domain. The functional compounds of these compounds can inhibit the CagA-SHP-2.

In our study here we targeting the CagA-SHP2 complex inhibition by using some medicinal plants like quinoline compounds, black tea, turmeric, nutmeg, ginger [1]. Previous studies proven that, these medicinal plants products have the bactericidal effect on *H. pylori* culture, that these plants have nearly 95-100% of *H. Pylori* growth inhibition, it predict that these plant products can be inhibit the growth the *H. Pylori* culture, so here we focusing on that these plants can able to inhibit the CagA-SHP-2 domain complex.

Keywords: CagA; SHP-2; CagA-SHP-2 domain complex

Introduction

Helicobacter pylori, a spiral-shaped bacterium that colonizes the human gastric mucosa, is estimated to inhabit at least half of the world's human population. Since its first report in 1984 by Marshall and Warren, *H. pylori* has been recognized as the etiological agent of gastric diseases such as chronic atrophic gastritis and peptic ulcers, with each strain showing differences in their genome sequence by more than 20% [2]. Epidemiological studies have revealed the importance of several genetic elements, such as *CagA* pathogenicity island (PAI), in the development of gastro duodenal disorders.

H. pylori also play a critical role in the development of both intestinal and diffuse types of gastric adenocarcinoma [3–5].

A number of genes, including *CagA, VacA, BabA*, and *IceA*, have been implicated in enhancement of virulence of *H. pylori* bacteria.

Helicobacter pylori strains produce a 120–145 kDa immunodominant protein called Ctotoxin associated gene A (CagA) antigen. The *CagA* gene that encodes CagA protein by a process of horizontal transfer, through the type IV secretion system, through which macromolecules are delivered into the host.

SHP-2, a cellular target of tyrosine phosphorylated CagA. Upon tyrosine phosphorylation by SFK, CagA acquires the ability to bind specifically to SHP-2, the injected CagA binds and deregulates SHP-2 and other intracellular signaling molecules in both tyrosine phosphorylation-dependent and –independent manners, generating deregulated signals for cell growth and cell movement CagA also disrupts the cell-cell junctions, destroying normal epithelial architecture.

Rationale of The Proposal

Helico bacter pylori induce gastric inflammations in virtually all colonized individuals and such gastritis increase the risk for peptic ulcer diseases and distal gastric adenocarcinoma [6-8].

The Src homology -2 domain containing protein tyrosine phosphatase-2 (SHP-2) plays a pivotal role in growth factor and cytokine signaling.

In this studies our aim and objective is to inhibit the complex formation of Cag A-SHP-2, which plays a major responsible in the peptic ulcers and gastric adenocarcinomas, by using medicinal plants, which already used in the inhibition of the growth of helicon bacter cultures.

Methodology

Here our main target is on the CagA-SHP-2 domain complex. For the inhibition of this complex we perform the following tests.

Cell culture, immunoprecipitation and immunoblotting

Cell culture will be treated with the plant products as described in Chen L et al. [9].

In this tests the cell culture will be treated with plant compounds as described in Chen L et al. 2001 Erk1/2 kinase assay will be done as described in Cunnick et al. [10].

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Received June 29, 2012; **Accepted** October 27, 2012; **Published** October 29, 2012

Citation: Szomor Z (2012) Inhibition of Interaction between Caga and Shp-2 Domain by Using Medicinal Plant Products. Adv Pharmacoepidem Drug Safety 1:121. doi:10.4172/2167-1052.1000121

Immune complex PTP (Protein tyrosine phosphatase) assay

Cell culture is treated with plant compounds and EGF as described in Chen L et al. 2001.

Immunoprecipitation complex signal is measured by DiFMUP (6,8-difluoro-4-methylumbelliferyl phosphate) [a fluorescent dye].

The culture growth in Cell culture assay can be observed with the comparison of control and test.

In test wells there is a presence of all compounds like cells, inhibitor (plant compounds), and growth factors of like EGF were to be added, whereas in control wells everything were to be added except the inhibitor.

Cytotoxicity or cell viability assay

Here viable cells can be identified with the help of fluorescent dyes here also we use both controls and tests. It resemble with MTT assay.

In control wells there is no inhibitor and in the test wells there is an inhibitor.

Discussion

1. It is proved that *H. pylori* growth can be inhibited by using medicinal plants.

2. The Cag A-SHP-2 domain complex can be inhibited with the chemicals like NSC87877, salicylic acid, etc.

Based on these criteria, here we aimed to inhibit CagA-SHP-2 complex by using medicinal plants.

Conclusion

By performing these studies, with the help of medicinal plant products to inhibit the CagA-SHP2 domain complex, there will be a less chance for occurrence of side effects and it will be low in costs also.

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