

Effects of allyl sulfur compounds and garlic extract on the expressions of Bcl-2, Bax, and p53 in non small cell lung cancer cell lines

Young-Sook Hong^{1,3}, Yoon-Ae Ham¹,
Ji-Hyung Choi¹ and Jhngook Kim²

¹ Department of Biochemistry, Medical Research Center,
Division of Cancer Research, College of Medicine,
Ewha Womans University, Seoul 158-056, Korea

² Department of Thoracic Surgery, College of Medicine,
Sung Kyun Kwan University, Seoul 135-230, Korea

³ Corresponding author: Tel, +82-2-650-5725; Fax, +82-2-653-8891;
E-mail, yshong@mm.ewha.ac.kr

Accepted 14 September 2000

Abbreviations: DADS, diallyl disulfide; DAS, diallyl sulfide; NSCLC, non small cell lung cancer

Abstract

Allyl sulfur compounds play a major role in the chemoprevention against carcinogenesis. The present study compared the antiproliferative effects of diallyl sulfide (DAS), diallyl disulfide (DADS) and garlic extract on p53-wild type H460 and p53-null type H1299 non small cell lung cancer cells (NSCLC). The DAS and DADS treatment of both H460 and H1299 cells resulted in the highest numbers of cells in apoptotic state as measured by acridine orange staining, however, garlic extract treatment did not induce any significant apoptotic cells by MTT assay. DADS was found to be more effective in inducing apoptosis on NSCLC. The level of p53 protein in H460 cell was increased following DADS treatment. DAS and garlic extract treatment of H460 cells induced a rise in the level of Bax and a fall of Bcl-2 level. These results demonstrate that DAS, DADS and garlic extract are effective in reduction of anti-proliferative gene in NSCLC and suggest that modulation of apoptosis-associated cellular proteins by DAS, DADS and garlic extract may be the mechanism for apoptosis which merit further investigation as potential chemoprevention agents.

Keywords: DAS, DADS, garlic extract, apoptosis, NSCLC

Introduction

Epidemiological investigations provide strong evidence that environmental factors are modifiers in the occurrence of some types of human cancer (Wynder and Gori, 1977; Parmer and Bakshi, 1983). Among these environmental factors, dietary habit is one of the important factors influencing cancer risk (Doll, 1992). Recent studies suggested that garlic and related allium foods might protect human from some types of cancer (Steinmetz *et al.*, 1994), however, the protective effect by these foods was often inconsistent (Dorant *et al.*, 1995). The reason for these inconsistencies remains to be clarified. Nevertheless, laboratory investigations provided some convincing evidence that garlic and associated sulfur compounds reduced experimentally induced colon, esophageal, pulmonary, skin, forestomach and breast cancers (Wargovich *et al.*, 1987; 1988; Sadhana *et al.*, 1988; Hong *et al.*, 1992; Liu *et al.*, 1992; Dorant *et al.*, 1993), suggesting that the protection provided by garlic and related compounds is not limited to a single tissue or to any particular type of carcinogen. Allyl sulfur compounds present in garlic probably account for much of its anticancer effect, and these allyl sulfur compounds have been shown to be effective both in the initiation and promotion phases of the carcinogenic process (Belman, 1983). However, in spite of numerous studies on the garlic oil component, a study on the whole water soluble garlic extract has never been reported.

p53 is involved in the activation of apoptosis by DNA damage induced by such agents as cisplatin. As a transcriptional activator, p53 increases the transcription of a number of genes, and the pattern of transcriptional regulation is critical in determining the cellular response to DNA damage. Indeed, it is known to activate the transcription of death agonist, Bax, but to repress the expression of the death antagonist, Bcl-2 (Miyashita *et al.*, 1994; Perego *et al.*, 1996).

The pharmacological role of allyl sulfide in prevention and treatment of cancer has received increasing attention, but molecular mechanism of action of allyl sulfide compound are poorly defined. The cytotoxicity of most classical antitumor drugs thought to be mediated by their ability to induce apoptosis (Sen and D'Incalci, 1992). Several mechanism have been identified to modulation of apoptosis by induction of p53.

In this study, we examined a possible antiproliferative affect of DAS, DADS and garlic extract on human non