

CYTOTOXICEFFECTS OF CAFFEIC ACID EXTRACTED FROM ECHINACEAPURPUREAON HUMANGASTRIC CANCER CELL LINE

¹F.MORADIAN, ²A. SADEGHI, ³F.SABOUNI, ⁴F.SANJARIAN

^{1,2}Department of Basic Sciences, Sari Agricultural Sciences and Natural Resources University, Mazandaran, Iran

³Department of Molecular medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran

⁴Department of Plant Bioproducts, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran

Email: moradi_f@yahoo.com

Abstract –

Introduction: Echinacea purpurea extract has anticancer and anti-angiogenic properties. The one of component of this plant is caffeic acid is a phenolic compound that has different properties include; antioxidant, anti-inflammatory activity, antiviral, anticancer and immunomodulatory. Gastric cancer is one of the most common malignant diseases throughout the world, that the prevalence rates show considerable diversity of the world.

Objective: In the present study, the toxic effect of caffeic acid extracted from E. purpurea on growth of gastric cancer cell line AGS were investigated.

Methods: Different concentration of caffeic acid 0, 2.0, 2.5 and 3.25 mg/ml and standard caffeic acid with 0, 600, 750 and 850 mM/ml treated on AGS cell line at 24 hours then cell viability determined using MTT assay.

Result: The result obtained from this research showed that the viability percentage after treatment of the plant extract in concentration of 2.0, 2.25 and 3.25 mg/ml and standard caffeic acid in concentration of 600, 750 and 850 mM were 74.3, 52.6 and 25.6% as well as 81, 49, 27%, respectively.

Conclusion: The results showed that the caffeic acid significantly and dose dependent could reduce the growth of gastric cancer cell line AGS.

Keywords - Caffeic acid, Cytotoxic, Echinacea purpurea, Gastric cancer cell line

I. INTRODUCTION

Caffeic acid is an organic compound consists of both phenolic and acrylic functional groups. It is found in all plants because it is a key intermediate in the biosynthesis of lignin [1]. Caffeic acid has a various potential pharmacological effects in vitro and in vivo and its inhibitory effect on cancer cell proliferation has recently been established [2]. Caffeic acid and its derivative, caffeic acid phenethyl ester showed inhibition of invasion, angiogenesis and metastasis in different cancer [3].

Caffeic acid can be found in Echinacea purpurea which in Europe and North America extensively as medicinal plant used in many treatments [4]. In previous study have been reported caffeic acid have antioxidant properties in normal cells and pro-oxidant in cancer cells. Due to its pro-oxidant properties, it is able to cause oxidative damage in DNA and finally induction of apoptosis in cancer cells [5]. Stomach cancer is the second cause of death from cancer and the third most common cancer in the world with the high mortality rate in central, south and east of Asia; east and central of Europe and south America [6], [7].

This disease is diagnosed at advance stage and treatment options are limited therefore still is the medical challenges [8]. Caffeic acid can be used as pharmaceutical agent for treatment of cancer. In this study, the effects of toxicity of caffeic acid extracted from Echinacea purpurea and standard caffeic acid on

growth prevention in gastric cancer cell line (AGS) was evaluated.

II. MATERIALS AND METHODS

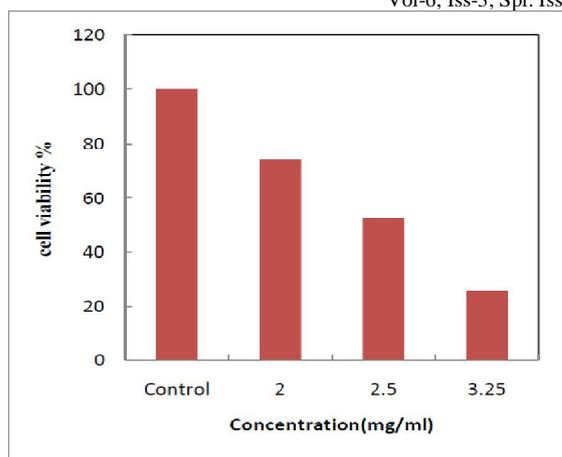
Cell Culture and MTT Assay:

Gastric cancer cell line AGS provided from cell bank of National Institute of Genetic Engineering and Biotechnology. The cells culture in DMEM media with 10% FBS. Incubation was done in 5% CO₂ incubator (Memert, Germany) at 37 °C until they reached to 80% growth confluence then the cells counted and subculture in 96 well plates with 1×10⁴ cells for each well.

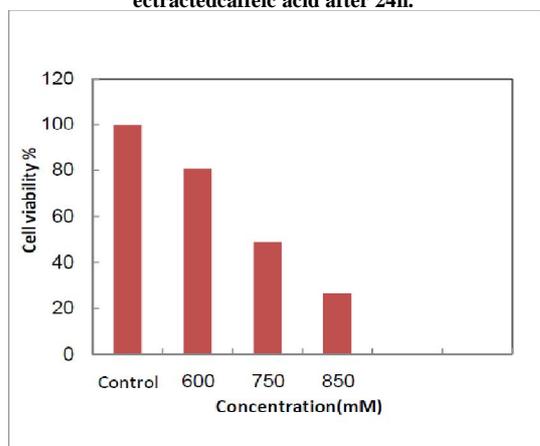
After appropriate cells growth the different concentration of extracted caffeic acid (0, 2.0, 2.5, 3.25 mg/ml) and standard caffeic acid (0, 600, 750, 850 mM/ml) were added to each well in triplicates. Incubation continued for 24 hours. After that MTT assay was done and absorption of purple color formation read at 580 nm using ELISA reader.

III. RESULTS AND DISCUSSION

MTT assay was used to study of the toxicity effect of caffeic acid on gastric cancer cell line AGS. After 24 h of treatment with different concentration of extracted caffeic acid, the cell viability was observed 74.3, 52.6 and 25.6% “fig.” 1. The cell viability percent after treatment of standard caffeic acid was 81, 49, 27% “fig.” 2.



“Fig.”1Graph of the effect of different concentration of extracted caffeic acid after 24h.



“Fig.”2 Graph of the effect of different concentration of standard caffeic acid after 24h.

Gastric cancer is a serious public health problem. According to assessment of cancer incidence, gastric cancer is the third most common cancer in the world[9] therefore, development of new therapeutic drug for stomach cancer is a priority. In this study, cell viability decreased with increase in concentration of both caffeic acids and IC_{50} was 2.5mg/ml and 750 μ M/ml for extracted and standard caffeic acids, respectively. The inhibition of growth in concentrations of 3.25 mg/ml and 850 mM/ml were 74.4% and 73%, respectively. Chang et al.(2010) reported caffeic acid induced apoptosis in human cervical cancer cells[10]. In previous study, the inhibitory effect of caffeic acid on cancer cell proliferation in human HT-1080 fibrosarcoma cell line was shown[2].Growth inhibition by caffeic acid in HCT15 colon cancer cells reported by Jaganathan et al.[11].Echinacea purpurea's extract caused inhibition of angiogenesis induced by kidney and human long cancer cells after interdermal cells injection. Also, the extract had reduced viability in human cancer cells[12].He et al.(2006) have shown that caffeic acid phenethyl ester had inhibitory effect on the growth of SW480 colorectal tumor cells[13]. In other report, caffeic acid phenethyl ester exhibited anti-tumor effects in pre-clinical models of human breast cancer[14].

CONCLUSION

Echinacea spp.'s extract are popularly used as a herbal medicine for enhancing the immune system and many of treatment. Due to the ability of caffeic acid in increased cell death in Gastric cancer cells thus it can be used as a drug to control cancer cells.

ACKNOWLEDGMENT

This original research was performed in National Institute of Genetic Engineering and Biotechnology, Tehran. The authors are thankful for providing facilities and assistance.

REFERENCES

- [1] W. Boerjan, J. Ralph and M. Baucher, "Lignin biosynthesis," *Ann. Rev. Plant Biol.*, vol.54, pp.519-546, 2003.
- [2] N. Prasad, A. Karthikeyan, B.V. Reddy, "Inhibitory effect of caffeic acid on cancer cell proliferation by oxidative mechanism in human HT-1080 fibrosarcoma cell line," *Mol. Cell Biochem.*, vol.349,(1-2, pp.11-19), 2011.
- [3] J.E. Jung, H.S. Kim, C.S. Lee and et al., "Caffeic acid and its synthetic derivative CADPE suppress tumor angiogenesis by blocking STAT3 mediated VEGF expression in human renal carcinoma cells," *Carcinogenesis*, vol.28,(1), pp. 1780-1787, 2007.
- [4] K.M. Kumar and S. Ramaiah, "Pharmacological importance of Echinacea purpurea," *Int. J. Pharma. Bio. Sci.*, vol.2,(4), pp. 304-314, 2011.
- [5] G. Kanimozhi and N.R. Prasad, "Anticancer effect of caffeic acid on human cervical cancer cells," *Cal. Vol.20*, pp.21.
- [6] H. Han, B. Du, X. Pan, J. Zhao and et al., "CADPE inhibits PMA stimulated gastric carcinoma cell invasion and matrix metalloproteinase 9 expression by FAK/MEK/ERK mediated AP1 activation," *Mol. Cancer Res.*, vol.8, pp.1477-1488, 2010.
- [7] T. Takahashi, Y. Saikawa and Y. Kitagawa, "Gastric cancer current status of diagnosis and treatment," *Cancers*, vol.5, pp.45-63, 2013.
- [8] A. Sobero, F. Caprioni, G. Fomanini and et al., "Pemetrexed in gastric cancer," *Oncology*, vol.18, pp.51-55, 2004.
- [9] F. Amiri, F. Moradian and A.R. Rafiei, "Anticancer effect of lactoferrin on gastric cancer cell line," *Res. Mol. Med.*, vol.3,(2), pp.11-16, 2015.
- [10] W.C. Chang, C.H. Hsieh, M.W. Hsiao and et al., "Caffeic acid induces apoptosis in human cervical cancer cells through the mitochondria pathway," *Taiwanese J. Obst. Gynecol.*, vol.49, pp.419-424, 2010.
- [11] S.K. Jaganathan, "Growth inhibition by caffeic acid one of the phenolic constituents of honey in HCT15 colon cancer cells," *The Sci. World J.*, vol.1, pp.1-8, 2012.
- [12] E. Rogala, E. Skopinska, A. Wasitynski and et al., "Echinacea purpurea diminishes neovascular reaction induced in mice skin by human cancer cells and stimulates non specific cellular immunity in humans," *Centr. Eur. J. Immunol.*, vol.33,(3), pp. 127-130, 2008.
- [13] Y.J. He, B.H. Liu, D.B. Xiang and et al., "Inhibitory effect of phenethyl ester on growth of SW480 colorectal tumor cells involves betacatenin associated signaling pathway down regulation," *World J. Gastroent. WJG*, vol.12,(31), pp. 4981-4985, 2006.
- [14] J. Wu, C. Omene, J. Karkoszka and et al., "Caffeic acid phenethyl ester derived from a honey bee product propolis exhibits a diversity of anti tumor effects in pre clinical models of human breast cancer," *Cancer Lett.*, vol.308,(1), pp. 43-53, 2011.