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*Original article* ■

## Suppressive Effect of Fig (*Ficus carica*) Latex on Esophageal Cancer Cell Proliferation

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### SUMMARY

Fig (*Ficus carica*) tree latex was a source of treatment of different diseases in the Iranian traditional medicine reported by Avicenna in his 10<sup>th</sup> century book Canon of Medicine. The aim of this investigation was to establish the anticancer effect of fig tree latex on human cancer cells.

The *in vitro* effect of different doses of fig tree latex including 2.5 mg/ml, 5 mg/ml, and 10 mg/ml on esophageal cancer cell line was evaluated after 72 hours by MTT assay.

There was a significant change in 10 mg/ml treatment of latex after 72 hours on esophageal cancer line (P; 0.025). Ten mg/ml was the optimum concentration in the inhibition of cell line growth.

Fig (*Ficus carica*) tree latex could be a candidate as a potential agent for the inhibition of cancerous cells production and development.

**Key words:** esophageal cancer, fig, *Ficus carica*, latex

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## INTRODUCTION

According to reports from the Ministry of Health and Medical Education (1,2), cancer is the third cause of death in Iran. The north and northeastern regions of Iran are well-known for high incidence of esophageal malignancy (3,4). Based on the reports by the Iran Cancer Institute, 9% of all malignancies and 27% of gastrointestinal cancers were esophageal carcinoma cases, with a male to female ratio of 1.7:1 (5).

Studies have elucidated that low intake of fresh fruits and vegetables is related to a higher risk of esophageal and digestive organs cancer (6,7). In this regard, plants and herbals as natural products were shown to have anti-cancer effects and even play an important role in the efficacy of chemotherapy (8, 9).

Fig (*Ficus carica*) tree latex is known in the Iranian traditional medicine reported by Avicenna in his 10<sup>th</sup> century book Canon of Medicine (10) for the treatment of warts and papillomatosis (11). It has been revealed that fig tree latex has various therapeutic effects including hypoglycemic induction (12), cancer suppression (13) and anti-helminthic effects (14).

In this study, we have investigated the antiproliferative effect of latex on three-well plates' cultures of human esophageal cancer cells.

## METHODS AND MATERIAL

### Preparation of fig latex

Fig (*Ficus carica*) tree latex was obtained from fig trees in the northern Iran (Sari, harvested in July, 2011) drop-by-drop through cutting young leaves of fig trees and filtered by filter (0.22 $\mu$ m) and then stored at -20<sup>o</sup> C. In the second step, the latex lyophilized and different concentrations of latex were measured and provided, including 2.5 mg/ml, 5 mg/ml and 10 mg/ml.

### Cell line and culture

The esophagus cancer cell line was provided from the National Cell Bank of Iran, NCBI=C-584 (KYSE-30). 3x10<sup>4</sup> cells were cultured in the liquid medium (RMPI 1640) containing 10% fetal calf serum, 100 U/L penicillin and streptomycin. The culture flask's environment was kept at 37<sup>o</sup>C, with a saturated humidity and 5% CO<sub>2</sub>.

### Cell proliferation assay (MTT assay)

The cells from the interphase were washed three times with RPMI (1640 medium, Gibco) and counted and their viability was determined by trypan blue. All samples were run triplicates in 96-well plates. Cultures were incubated at 37<sup>o</sup>C in a humidified 5% CO<sub>2</sub> atmo-

sphere for three days and then pulsed with 200  $\mu$ l 3-[4,5-dimethylthiazolyl]-2,5-diphenyl-tetrazolium bromide (MTT: Sigma) as a color indicator of metabolic activity. The supernatant was harvested for four hours. Later, dimethylsulfoxide (DMSO) was added (200  $\mu$ l) and the color change was read in an ELISA reader at 630 nm wave length (15).

### Statistical analysis

For statistical analysis SPSS software (Chicago, IL, version 15, USA) was used applying a paired t-test. P<0.05 was defined as significant.

## RESULTS

The proliferation level of 2.5 mg/ml and 5mg/ml concentrations of *Ficus carica* latex did not show significant change (P; 0.6, P; 0.06, respectively). There was a significant change in 10 mg/ml treatment of *Ficus carica* latex in comparison to control (P; 0.025) (Table 1).

After 72h incubation in culture media, the 10 mg/ml was the optimum concentration in the inhibition of esophageal cancer line growth.

**Table 1.** The impact of Fig tree latex on esophageal cancer cell line proliferation in comparison with control in culture media, evaluated by MTT assay (optical density of 630 nm)

Latex concentration	Mean $\pm$ SD	P value
2.5(mg/ml)	0.0606 $\pm$ 0.00134	0.6
5(mg/ml)	0.1600 $\pm$ 0.08216	0.06
10(mg/ml)	0.1536 $\pm$ 0.04406	0.025
control	0.1552 $\pm$ 0.13268	

## DISCUSSION

In this research, we examined the antiproliferative effect of fig tree latex in different concentrations including 2.5, 5 and 10 mg/ml on esophageal cancer line.

Experimental studies established that different natural agents, plant crude and extracts act as antioxidants and chemopreventive potential in various animal investigations having relation to human beings (16). Fig tree latex includes high amount of polyphenols, flavonoids, and anthocyanins which are the major components in Mediterranean diet in improving health disorders (17). Fig tree latex has also been reported to have a therapeutic effect on skin tumors and warts both in modern and traditional medicine (10, 18).

In a recent study, Lazreg Aref H et al. (19) have reported that fig tree latex extracts are possible candi-

dates as herbal remedies for herpes virus, echovirus and adenovirus infections. They also showed that extracts had no cytotoxic effect on Vero cells. In this relation, in our former study (20), we revealed that *Ficus carica* latex had no cytotoxicity effects on normal peripheral blood mononuclear cells.

Ali Mostafaie et al. (21) examined the anti-angiogenic and anti-proliferative effects of *Ficus carica* latex extract on human umbilical vein endothelial cells. They elucidated that latex extract can inhibit the proliferation and capillary tube formation of human umbilical vein endothelial cells in a dose-dependent state. They also indicated the extract was not cytotoxic, as shown in our previous research. They concluded that latex extracts of *Ficus carica* consist of strong anti-angiogenic and anti-proliferative impacts.

In our previous investigation, we revealed that *Ficus carica* latex had pharmacological potential in stomach cancer line and inhibit the proliferation of cancer

cells without cytotoxic effects on normal cells. Our current research elucidates that fig tree latex affects the esophageal cancer line in a dose-dependent manner. In this relation, 10 mg/ml was the optimum concentration in culture media in prevention of cancer cells growth.

## CONCLUSION

Based on our previous and present data, we concluded that fig (*Ficus carica*) tree latex could be a candidate as a potential agent for the inhibition of cancerous cells production, development and might have the same effect in clinical studies.

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## SUPRESIVNI EFEKAT LATEKSA SMOKVE (*FICUS CARICA*) NA PROLIFERACIJU KANCEROZNIH ĆELIJA EZOFAGUSA

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### Sažetak

**Lateks smokve (*Ficus carica*) je u iranskoj tradicionalnoj medicini korišćeno za lečenje mnogih bolesti, što je u Kanonu medicine iz 10. veka opisao i Avicena. Cilj ovog ispitivanja bio je da utvrdi antikanцерogeni efekat lateksa smokve na kancerodne ćelije.**

**In vitro efekat različitih doza lateksa smokve, uključujući 2.5 mg/ml, 5 mg/ml i 10 mg/ml na kancerodne ćelije ezofagusa ispitivan je MTT analizom.**

**Utvrđena je značajna promena kod primene doze lateksa od 10 mg/ml na lozu kanceroznih ćelija ezofagusa (P:0.025). Optimalna koncentracija za inhibiciju rasta ove ćelijske loze bila je 10mg/ml.**

**Lateks smokve (*Ficus carica*) bi kao potencijalni agens mogao da se koristi za inhibiciju nastanka i razvoja kanceroznih ćelija.**

**Ključne reči:** kancer ezofagusa, smokva, *Ficus carica*, lateks