

## Quercetin and Indole 3-carbinol downregulate extracellular matrix expression in human primary uterine leiomyoma cells

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Uterine leiomyomas (fibroids or myomas) are the most common benign tumors of female reproductive tract, originating from myometrial smooth muscle cells of the uterus. They affect about 77% of women of reproductive-age and approximately 25% of reproductive-age women bear clinically apparent tumors. The incidence and severity of symptoms typically depend on the size, number, and location of the fibroids. The common symptoms are irregular and excessive menstrual bleeding, pelvic pain, pressure on the bladder, miscarriage, and infertility. They are the leading indication for hysterectomy. Unfortunately, no long-term medical treatments are available. The cause of uterine leiomyomas remains unknown, but the current understanding is that stem cells, genetic and epigenetic factors, sex steroids, growth factors, cytokines, chemokines, and extracellular matrix (ECM) components are known factors involved in the development and growth of leiomyomas. The ECM components, mainly collagen1A1, fibronectin and versican are over-expressed in leiomyoma, and their upregulation is induced by activin A. ECM proteins transmit mechanical signals from the outside of the cell to the cell interior through transmembrane integrin proteins. In modern pharmaceutical industries, dietary phytochemicals are used as source of new potential drugs for many kinds of tumors. Dietary phytochemicals may exert therapeutic effects by interfering with key cellular events of the tumorigenesis. Quercetin (3,3',4',5,7-pentahydroxyflavone) is a plant bioflavonoid, found in most edible fruits and vegetables. Indole-3-carbinol (I3C; 1H-indol-3-ylmethanol) is produced from naturally occurring glucosinolates contained in a wide variety of plants, including members of the family Cruciferae and particularly members of the genus Brassica [2,3]. In the present study, we aimed to investigate if quercetin and indole-3-carbinol can regulate ECM in human myometrium and leiomyoma cells. In the previous time we investigated about the purity of cells was assessed by immunocytochemical staining with a specific smooth muscle cell marker. All cells were strongly positive for alpha-sma. Leiomyoma and myometrial cells, were treated with Quercetin and I3C (10 µg/ml; 50 µg/ml; 100 µg/ml; 250 µg/ml) for 48 h to measure mRNA and proteins expressions of ECM. Quercetin and I3C significantly decreased collagen1A1 and fibronectin mRNA and protein expression in leiomyoma cells. Immunocytochemical stained showed the decreased expression of fibronectin in primary leiomyoma and myometrial cells after treatments of quercetin and indole-3-carbinol. This study suggests that quercetin and indole-3-carbinol extracts can be developed as therapeutic and/or preventive agent for uterine leiomyomas.

### References

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### Key words

Quercetin, indole-3-carbinol, uterine fibroid, antifibrotic, dietary phytochemicals, extracellular matrix.