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# EFFECT OF GINSENOSIDE-RG1 ON THE PROLIFERATION OF PARAURETHRAL FASCIA FIBROBLASTS DERIVED FROM WOMEN SUFFERING FROM STRESS URINARY INCONTINENCE

Hypothesis / aims of study

The aim of the study was to investigate the effect of ginsenoside-Rg1 on paraurethral fascia fibroblasts proliferation of Stress urinary incontinence (SUI) women in vitro.

Study design, materials and methods

Four women with SUI were recruited at the authors' hospital. The mean age of the patients was 55.3 ± 10.5 years. They did not have concomitant malignant pelvic diseases and did not take any medications containing estrogen in the past 3 months. Paraurethral fascia samples were obtained during TVT or TVT-O procedure. Fibroblasts were cultured in the presence of ginsenoside-Rg1 at different concentrations (0, 5, 10, 20umol/L). The proliferation of paraurethral fascia fibroblasts was measured by MTT assay. Also the expression of proliferation cell nuclear antigen (PCNA), collagen I and III mRNA were evaluated.

Results

Treatment with increasing concentrations of Rg1 (0, 5, 10, 20umol/L) increased the number of fibrablasts in a dose-dependent manner（$P<0.05$）(Figure 1). The stimulating effect of Rg1 peaked at 10umol/L. In addition, the stimulatory effect of Rg1 on fibroblasts production was time-dependent, which was noted at 24 h, became more evident at 48 h, and peaked at 72 h. The results by the immunohistochemical staining of PCNA showed that there was a significant increase of PCNA-positive cells after 48-h treatment with increasing concentrations of Rg1（$P<0.05$）(Figure 2).The expression of collagen I and collagen III mRNA by semiquantitative RT-PCR shown fibroblasts treated with different concentrations of Rg1 for 48 hours exhibited an increase of collagen I and collagen III mRNA expression（$P<0.05$）, which peaked when the concentration of Rg1 was 10umol/L(Figure 3).

Interpretation of results

The weakened pelvic floor support of the low urinary tract plays an important role for SUI. Studies have suggested that the proliferation of paraurethral fascia fibroblasts from women with SUI degraded, which would imply changes in collagen and extracellular matrix (ECM) synthesis and turnover. This decrease in collagen of support tissue from SUI patients may negatively affect tissue strength and elasticity. In addition, some studies have discovered women with SUI had a significant reduction of collagen type I and collagen type III in the support tissue. Many researchers have been exploring a way to raise the collagen content of the weakened support tissue as a main target in the treatment of SUI. These include direct periurethral injection of collagen and fibroblast. Ginsenoside-Rg1, has been proved to promote functional neovascularization in vivo by enhancing the proliferation, chemoinvasion, and tubulogenesis of endothelial cell, which is similar to the effects of basic fibroblast growth factor (bFGF), a potent chemotactic and mitogenic factor for cells of mesodermal, ectodermal, and endodermal origins, including fibroblast. Moreover a previous research has found that ginsenoside-Rg1 has estrogen-like activity. Although it has controversies about estrogen' effect on SUI, a study indicate that, at least in vitro, fibroblasts from pubocervical fascia taken from women suffering from SUI are more capable to proliferate after estrogen treatment, when compared to skin fibroblasts.

The results showed that Rg1 remarkably increased the proliferation of paraurethral fascia fibroblasts. Thus promotion of cell proliferation is validated by its ability to increase PCNA expression, and increase synthesis of collagen type I and collagen type III, which provide the tensile strength and the support to the damaged tissue.

Concluding message

In this study we show for the first time that ginsenoside-Rg1 is a potent stimulator of human paraurethral fascia fibroblasts from patients with SUI in vitro. Ginsenoside-Rg1 promotes fibroblast proliferation in a dose-dependent manner. Most importantly, Rg1 can induce the expression of collagen I and collagen III mRNA. Ginsenoside-Rg1 may be of potential value in the treatment of SUI.

References

Journal articles: Tissue Eng. (2005) 11; 835-46.
Journal articles: Ginekol Pol (2003) 74; 1410-4.
Journal articles: The Journal of Clinical Endocrinology & Metabolism (2002) 87: 3691-3695.

**Figure 1** Rg1 promotes proliferation of fibroblasts

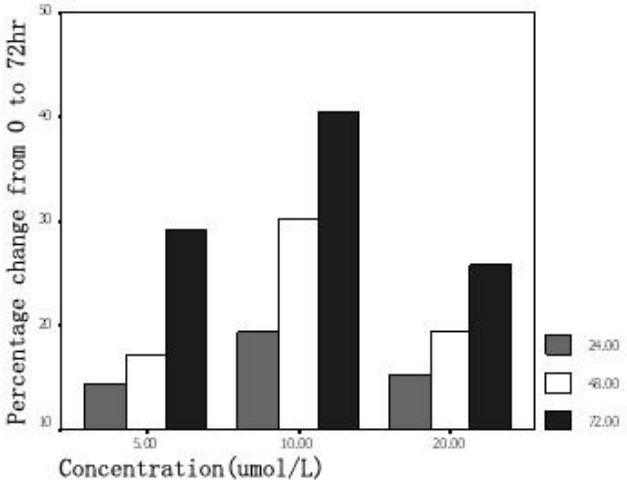



**Figure 2** Proliferation of PCNA expression by Rg1

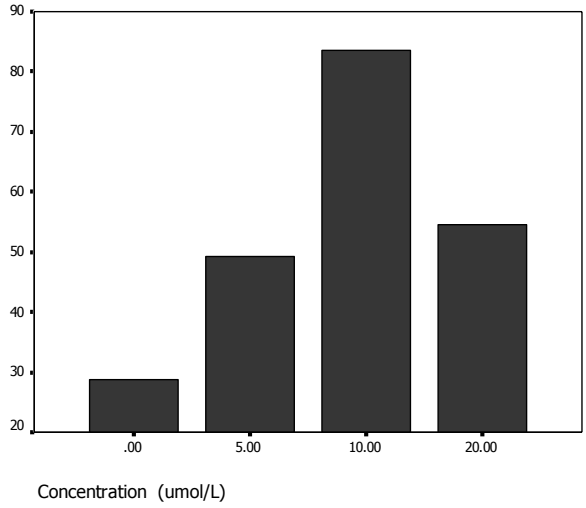
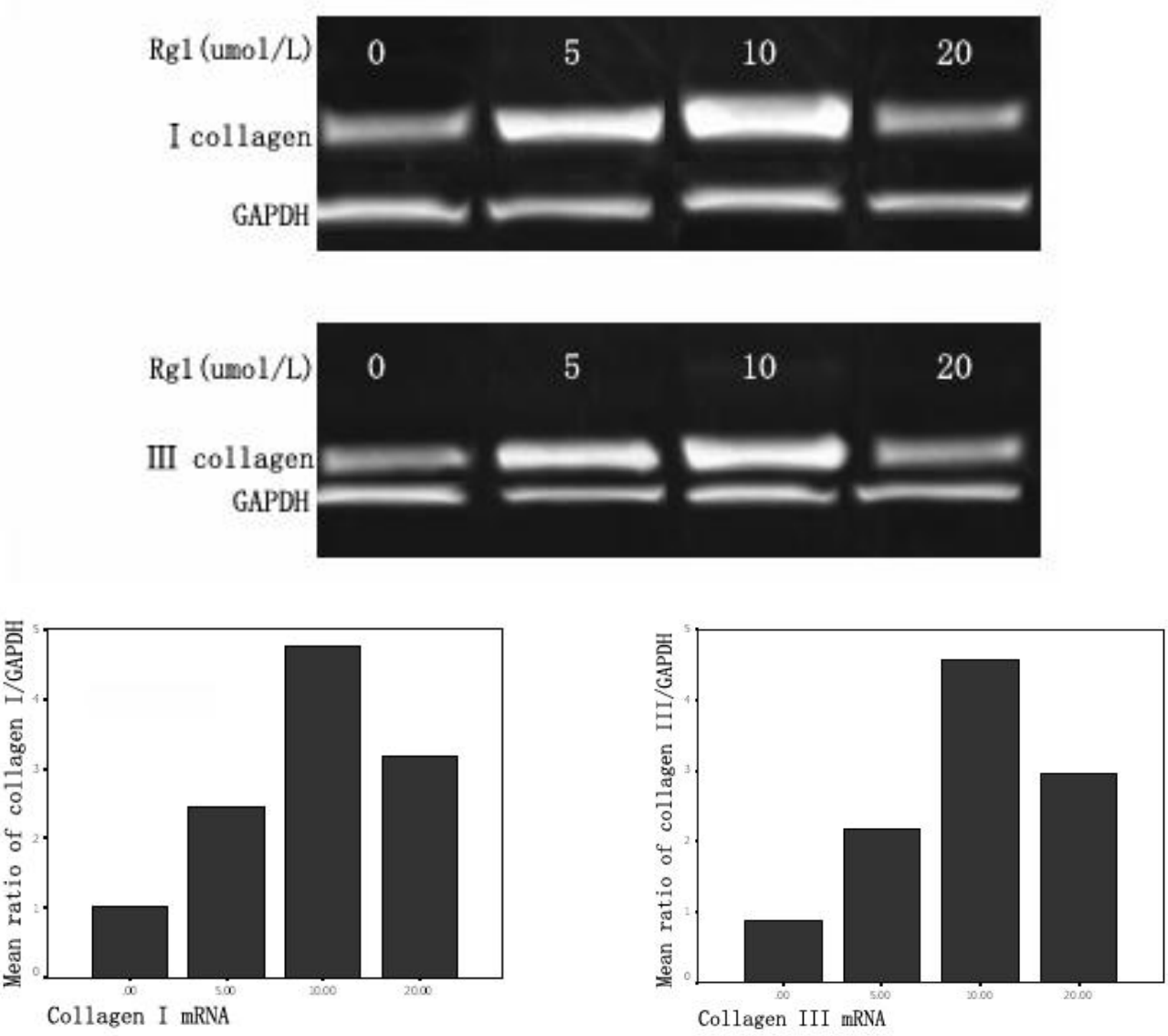



**Figure 3** Effect of Rg1 on collagen mRNA expression of fibroblasts

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|---|---|
| ***Specify source of funding or grant*** | **480** |
| ***Is this a clinical trial?*** | **No** |
| ***What were the subjects in the study?*** | **HUMAN** |
| ***Was this study approved by an ethics committee?*** | **Yes** |
| ***Specify Name of Ethics Committee*** | **Fuzhou Ethics Committee** |
| ***Was the Declaration of Helsinki followed?*** | **Yes** |
| ***Was informed consent obtained from the patients?*** | **Yes** |