

Ekstrak *Trigonella Foenum-Graecum* (Klabet) sebagai Fitoestrogen Topikal untuk Terapi Penuaan Kulit Wajah Pascamenopause: Kajian terhadap COL1A1, COL3A1, Kerutan Kulit dan Ketebalan Dermis = Fenugreek as Topical Phytoestrogen for Facial Skin Aging Therapy in Postmenopausal Women: Study on COL1A1, COL3A1, Dermal Thickness, and Skin Wrinkles

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Abstrak

Menopause menyebabkan hipoestrogenisme dan mengakibatkan penuaan kulit. Fitoestrogen dari biji *T. foenum-graecum* (klabet) diharapkan dapat mengatasi penuaan kulit pascamenopause. Penelitian ini bertujuan untuk mengetahui konsentrasi optimal ekstrak klabet dalam menstimulasi sekresi COL1A1 dan COL3A1, cara kerjanya melalui jalur reseptor estrogen $RE\hat{1}\pm$ ($RE\hat{1}\pm$) atau $RE\hat{1}^2$, dan peran klabet dalam mengurangi kerutan serta meningkatkan ketebalan kulit wajah.

Studi *in vitro* menggunakan *human dermal fibroblast* (HDF) tua yang diperoleh dari kultur sel fibroblas kulit perempuan pascamenopause dan HDF muda dari prepusium, dilakukan di Laboratorium Universitas YARSI. Sekresi COL1A1 dan COL3A1 diperiksa dengan ELISA lalu ditambah antagonis REa dan b. Penelitian *in vivo* merupakan uji klinis acak tersamar ganda berdurasi 12 minggu, di RSCM, Januari–November 2019. Subjek 50 perempuan pascamenopause yang dibagi dua: kelompok perlakuan mendapat krim klabet 5% dan kelompok plasebo mendapat krim dasar. Skor kerutan dahi, *crow's feet*, dan nasolabial diukur dengan skoring atlas *skin aging* Bazin dan tebal dermis dengan *high resolution ultrasound* (HRU) 18 MHz.

Ekstrak klabet 2 μ g/mL merupakan konsentrasi optimal dalam meningkatkan sekresi COL1A1 dan COL3A1 pada HDF tua dan muda dibandingkan tanpa perlakuan dan 5 nM estradiol. Uji inhibisi menunjukkan hambatan $RE\hat{1}\pm$ 50%; $RE\hat{1}^2$ dan $RE\hat{1}\pm, \hat{1}^2$ sampai 75%. Penurunan skor kerutan dahi, *crow's feet*, dan nasolabial berbeda bermakna pada kedua kelompok minggu ke-4, ke-8, dan ke-12. Peningkatan selisih skor kerutan dahi, *crow's feet*, dan nasolabial tidak bermakna pada kedua kelompok antara *baseline*, minggu ke-4, ke-8, dan ke-12. Ketebalan dermis meningkat bermakna pada minggu ke-4 dibandingkan *baseline*. Pada minggu ke-8 dibandingkan minggu ke-4 dan pada minggu ke-12 dibandingkan minggu ke-8, ketebalan dermis menurun bermakna pada kedua kelompok. Peningkatan selisih ketebalan dermis pada minggu ke-4 dan ke-8 tidak bermakna.

Simpulan: Ekstrak klabet 2 μ g/mL meningkatkan COL1A1 dan COL3A1 lebih banyak dibandingkan kelompok tanpa perlakuan dan estradiol 5 nM. Klabet bekerja terutama melalui $RE\hat{1}^2$. Penurunan skor kerutan kulit dan peningkatan ketebalan kulit wajah tidak bermakna dibandingkan plasebo. Diduga, krim klabet konsentrasi 5% tidak tepat untuk mengurangi kerutan dan menambah ketebalan kulit. Perlu penelitian lebih lanjut untuk mengetahui konsentrasi optimal klabet sebagai terapi penuaan kulit wajah pascamenopause.

Kata kunci: COL1A1, COL3A1, kerutan kulit, ketebalan dermis, klabet, pascamenopause, penuaan kulit wajah, *Trigonella foenum-graecum*.

Hypoestrogenism in menopause leads to skin aging, for which phytoestrogen originated from the seeds of *T. foenum-graecum*

(fenugreek) is expected to be a solution. This study aims to show the effect of phytoestrogen from fenugreek extract in stimulating COL1A1 and COL3A1 through its mechanism of action on estrogen receptor (ER) ERa or ERb and its role in diminishing facial wrinkles and increasing dermal thickness.

The *in vitro* study was carried out in YARSI University Laboratory throughout March 2017–March 2018. This study looks into the effect of fenugreek extract on collagen level secretion in old and young human dermal fibroblast (HDF) compared to control. The *in vivo* study was a randomized, double-blind, 12-week trial conducted in RSCM from January–November 2019. Fifty postmenopausal women divided into two groups: the intervention group was given 5% fenugreek cream while the placebo group was given base cream.

The *in vitro* study showed that a concentration of 2 mg/mL was the optimal dose to stimulate COL1A1 and COL3A1 secretion in both old and young HDF compared to control (no treatment) and 5 nM estradiol. The inhibition test demonstrated suppression of ERa by 50%; ERb and ERa,b by up to 75%, indicating that the fenugreek activates both receptors, especially ERb. However, the success of the *in vitro* study did not translate into the *in vivo* study. Both the intervention group and the placebo group were able to achieve statistically significant in facial wrinkle scores from all focus areas without any significant disparity between both groups at all timepoints. Dermal thickness of facial skin showed similar results for both groups with significant improvements in the 8th week compared to baseline and significant decrease by the 12th week.

Conclusion: Fenugreek extract with a concentration of 2 mg/mL increased COL1A1 and COL3A1 secretion more potently compared to control and estradiol 5 nM. However, the decrease in facial skin wrinkles scores and the increase in dermal thickness were not significant compared to placebo. We suspect that a concentration of 5% was not adequate for the expected antiaging effects. Further studies are necessary to determine a more appropriate fenugreek concentration to permit clinical use as a postmenopausal antiaging therapy.

Keywords: COL1A1, COL3A1, dermal thickness, fenugreek, postmenopausal women, facial skin aging, skin wrinkles, *Trigonella foenum-graecum*.