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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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URTICA DIOICA EXTRACT DOWNREGULATES THE GENE EXPRESSION OF 5A-RII IN HACAT CELLS: POSSIBLE IMPLICATIONS AGAINST ANDROGENIC SKIN DISEASES

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Abstract.

Background and Aim: Urtica dioica (*Ud*) is a perennial plant of temperate climate regions and has been reported therapeutic activity against benign prostate hyperplasia, mainly due to its 5-alpha-reductase (5α-R) inhibition feature, which has been singly shown only in prostatic tissues until now. Also considering its use in traditional medicine against some dermatological problems and hair loss, we performed an in-vitro study to reveal its 5α-R inhibition activity in skin cells whether this plant may have a therapeutic potential against androgenic skin diseases.

Materials and Methods: After the preparation of *Ud* leaf extract and determination of non-cytotoxic concentration, cultured HaCaT cells were treated with the plant extract. RNA isolations were carried out from both non-treated and treated cell groups. cDNA synthesis was performed using gene specific primers of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as reference gene and 5α-R type II (5α-RII) as study material. Gene expressions were determined by real time reverse transcription quantitative polymerase chain reaction analysis.

Results: Results were represented as 'Target/GAPDH Fold Change'. Results of gene expression analysis showed that plant extract caused statistically significant downregulation of 5α-RII gene expression ($p=0.0021$) in treated cells, compared to untreated control cells, and ended up with 0.5873±0.0586 fold change.

Conclusion: This study is the first one showing the suppression of 5α-RII gene expression on skin cells with unmixed or solitary *Ud* extract. With the currently reported anti-androgenic activity in HaCaT cells, it can be suggested that *Ud* has a solid scientific base and may have a promising future in cosmetic dermatology, and new product development against androgenic skin diseases.

Key words. Urtica dioica, HaCaT cells, 5α-R, androgenic skin diseases.

Introduction.

Urtica dioica (*Ud*), a common perennial plant of temperate climate regions all over the world, belongs to the Urticaceae family [1-3]. It has a potent medicinal value and has been a therapeutic agent in traditional medicine for centuries to treat a vast number of inflammatory conditions [1,3]. Every part of *Ud* plant has been reported to hold antioxidant and anti-microbial potentials. One gram of *Ud* powder has been shown to have a total phenolic coverage as 129 mg gallic acid equivalent. This is approximately twofold of the phenolic content in 100 mL cranberry juice. *Ud* has been reported to consist more polyphenolic molecules than a great number of plants in the nature. Besides its wide-spectrum anti-bacterial features, *Ud* also possesses in-vitro anti-mycotic activity against Candida albicans [2]. *Ud* is a rich source of iron, ascorbic acid, carotenoids, essential amino acids and fatty acids [4]. A more recent and also the most reported use of *Ud* is the treatment of symptomatic benign prostatic hyperplasia (BPH) [1-6]. In addition to its effects on relevant hormones and cytokines, its 5-alpha-reductase (5α-R) inhibition activity has also role in its therapeutic merit [1,2,4,5,7,8]. Inhibition of 5α-R obviates the conversion of testosterone to dihydrotestosterone (DHT), whose high levels are linked with BPH and androgenetic alopecia (AGA) [9-11]. Various *Ud* extracts are also used in cosmetics, and this plant is a common component of shampoos [1]. It has revealed anti-dandruff and astringent activities in preclinical experiments [3]. In traditional medicine *Ud* has been used for various forms of non-scarring alopecia [12], and also there are some promising preclinical studies supporting this beneficial effect. A mixed herbal hair formulation composed of six plants, including *Ud*, was shown to boost viability of human dermal papilla cells significantly [13]. In a telogen effluvium model animal study, application of *Ud* gel on skin dilated the dermal arterial network significantly, and probably due to enhanced perfusion, it was displayed a quantitative increase in anagen hairs [14].

HaCaT cells are immortalized human keratinocyte cell line that has been used for studies of the epidermal homeostasis and its pathophysiology [15]. In this study we investigated the anti-androgenic activity of *Ud* extract in HaCaT cells, regarding these cells a general representative of the integument, for the probable benefits of this plant in androgen associated skin diseases.

Materials and Methods.

Plant material and preparation of the extract: The plant, *Ud*, was collected locally and identified in our laboratory, based on a reference book [16], and a stereo microscope. Dried leaves of the plant were used for extraction. Forty grams of fine-cut leaves were extracted with 500 mL water-alcohol mixture (70-30 v/v) using a Soxhlet extractor at the boiling point of the solvent, completing two full cycles. The extract was filtered through a 0.45 μm filter into a glass vial.

Cell culture: HaCaT cells were maintained in New Brunswick incubator (Eppendorf) at 37°C in a humidified atmosphere at 5% CO_2, in Dulbecco's Modified Eagle's Medium with high glucose, supplemented with 10% heat-inactivated fetal bovine serum and 100 U/ml gentamicin. All supplements and media were purchased from Sigma Aldrich.

Cell proliferation assay and cytotoxicity analysis: Cytotoxicity of the extract was evaluated by XTT assay. HaCaT cells were seeded into 96-well plates at a density of 1×10^4 cells/well. Plant extract was diluted with culture medium and cells were subjected to various concentrations (100%, 10%, 5%, 3%, 1%, 0,5% and 0%) of plant extract. After 72 h incubation period, cells were exposed to XTT and activator reagents (Roche

Diagnostics) for 4 h as described by the manufacturer. The viability of the cells is reflected in the activity of mitochondrial hydrogenases of the cells converting XTT into color-dense formazan compound. The optical density (OD) of soluble formazan compound was measured at 495 nm by microplate reader (Bio-Rad). The cell viability was calculated by using the formula below:

Cell Viability (%) = [Mean OD of test group/Mean OD of control group]×100

Based on cell proliferation ratios of treated cells with respect to the control cells, cytotoxicity levels of the plant extract were determined. Higher concentrations were found to be cytotoxic for HaCaT cells. For the subsequent analysis, the possible highest concentration was determined as 1% and HaCaT cells were incubated with 1% concentration of plant extract (Figure 1).

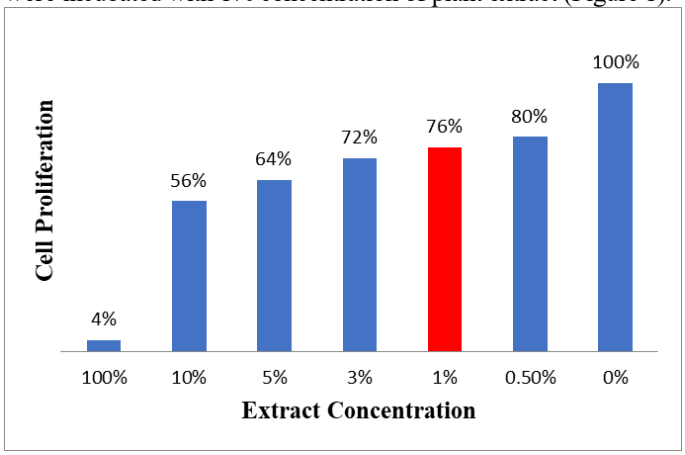

Figure 1. *Cytotoxicity analysis result of Urtica dioica extract. The red bar represents the extract concentration chosen for incubation.*

RNA isolation and reverse transcription: Total RNA was extracted from cells treated with plant extract and from untreated cells by using TRI-reagent according to manufacturer's (Sigma Aldrich) instructions. RNA quantity and purity were determined spectrophotometrically using BioSpec-nano. Transcriptor First Strand cDNA Synthesis Kit (Roche Diagnostics) was used for reverse transcription. cDNA synthesis was carried out using 500 ng total RNA, 2 µM each final concentration of gene specific primers of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as reference gene and 5α-R type II (5α-RII) as study material (Integrated DNA Technologies), 10 U of Transcriptor Reverse Transcriptase, 20 U of Protector RNAse Inhibitor, 1 mM each of dNTP mix, and Transcriptor Reverse Transcription Buffer (5X) according to the manufacturer's (Roche Diagnostics) instructions. Primer sequences (5'-3') are given in Table1.

Table 1. *Primers (5' - 3') of the genes studied.*

Primers	Forward primer	Reverse primer
GAPDH*	ATGGGTGTGAACCAT-GAGAA	GTGCTAAGCAGTTG-GTGGTG
5α-RII**	CGCTCTACCAGTACGC-CAG	AATTAAGCACCGAT-GCCCGT

*Glyceraldehyde-3-phosphate dehydrogenase is the reference gene
**5-alpha-reductase type II

Gene expression analysis.

Real-time reverse transcription quantitative polymerase chain reaction (RT-qPCR) was carried out in Light Cycler 96 (Roche Diagnostics). Amplification of products was detected via Fast Start DNA Green Master Kit (Roche Diagnostics). Each 20 µL reaction contained 10 µL SYBR Green Master Mix (2X), 0.5 µM of forward and reverse primers, 2.5 ng cDNA and appropriate amount of nuclease free water. All samples were run as triplicates in each run including a non-template control and four standards (1:1, 1:10, 1:100 and 1:1000). All reactions subjected to initial denaturation step at 95°C for 10 min and 45 cycle of 3-step amplification. Melting curve analysis was performed to confirm the specificity of the amplified products. The ΔΔCt method of relative quantification was used to determine the fold change in expression. Fold change was calculated by the equation below:

Fold change = $2^{-\Delta\Delta Ct}$

Statistical analysis.

All data are representative of three repeats and expressed as mean and standard error of the means. Statistical evaluation was performed by unpaired *t*-test, using 'Graph Pad Prism 5' software and the results with $p < 0.05$ were accepted as significant.

Results.

Results were represented as 'Target/GAPDH Fold Change'. Results of gene expression analysis via real-time RT-qPCR showed that plant extract caused statistically significant downregulation of 5α-RII gene expression (p=0.0021) in treated cells, compared to untreated control cells, and ended up with 0.5873±0.0586 fold change (Figure 2).

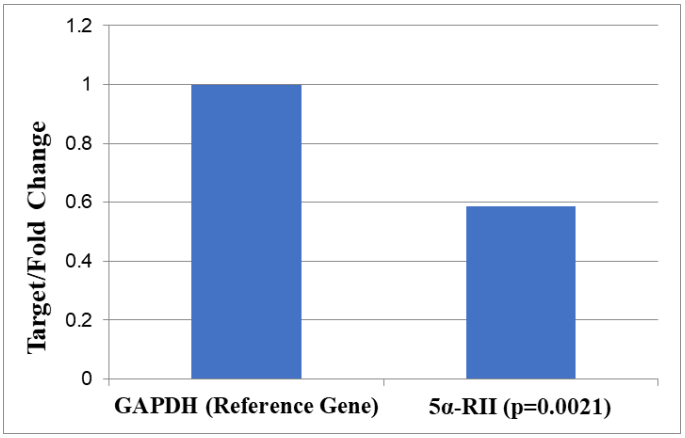

Figure 2. *Gene expression level and p value of 5α-RII in Urtica dioica extract treated cells, compared to untreated control cells.*

Discussion.

The androgen hormones are crucial in modulating hair growth, sebum production and sebaceous gland differentiation. Although DHT is the more active hormone, which is converted from testosterone by the enzyme 5α-R peripherally, both take effect via a unique receptor, the androgen receptor (AR). AR exists in epidermal and follicular keratinocytes, sebaceous gland cells, dermal fibroblasts, sweat gland cells, dermal papilla cells,

endothelial cells, and genital melanocytes [17]. The expression of AR in the epidermis denotes that keratinocytes are among the targets of androgenic hormones in skin. In the dermis, about 10% of the fibroblasts exhibit AR immunostaining [18]. In spite of the fact that the mesenchyme-originated dermal papilla manages the epithelial follicle in various facets, germinative epidermal cells of the lower follicle can also stimulate hair growth, and intrinsic dermo-epidermal relations are vital for the healthy maturation of hair [19,20]. Two steroid 5α-R isoenzymes have been discovered based on their different pH optima and tissue expression patterns. 5α-R type I (5α-RI) is expressed predominantly in epidermis, outer epithelial root sheath of hair follicles, sebaceous glands, and the liver. 5α-RII is expressed primarily in the prostatic tissues, epidermis, sebaceous ducts, inner epithelial root sheath of hair follicles and dermal papilla cells [21,22]. Changes of isoenzyme and/or AR levels in the skin may have important consequences in the precipitation of androgen related skin diseases like seborrhea, acne, hirsutism, and AGA. The essential functions of androgens in the pathophysiology of acne have long been known and validated by scientific experiments [17]. Although indirect effects of excess sebum production stimulated by androgens are the main factors in acne pathogenesis [23], the presence of AR expressing keratinocytes in the pilosebaceous ducts may suggest that androgens can also directly affect keratinization in the course of acne development [18]. It is formed immoderate amounts of DHT in the skin of hirsute women, but it is not apparent if this is due to overactivated hair follicles or the associated hyperplasia of the sebaceous glands [17]. Albeit polygenic heredity is accepted to be the primary cause, androgens have important roles in AGA presumably free from genetic predilection [24]. In AGA, the scalp displays higher expression of AR and higher quantities of DHT as well as 5α-RII. When the levels of androgens and ARs increase, their effects on the expression of genes which regulate follicular cycling increase also [25]. DHT activates AR and reveals the histological features of retarded hair regrowth, shortened anagen stage, early regression, and minimization of hair follicles [26].

It was previously reported the inhibition of 5α-R by *Ud* extracts, but until now this was only shown in prostatic tissues, using biochemical enzyme inhibition methods [5,7,8]. Although it was reported the suppression of 5α-RII gene expression on dermal papilla cells, this study was performed with a mixture of six different plants including *Ud* [13]. The current study is the first one showing the suppression of 5α-RII gene expression on skin cells with *Ud* extract alone. The results of the current study may partially explain the cause of its beneficial activities in traditional use against hair loss. From the point of epithelial keratinocytes in androgenic skin diseases; the effects of androgens may be directly epithelial through keratinocytes and sebocytes as in seborrhea and acne [17,18,23], or both directly and indirectly through epithelial and mesenchymal cell interactions as in hirsutism and AGA [17,19,20,25]. Nevertheless, keratinocytes are one of the target cells for androgen actions in skin and the androgenic interaction is the essential factor in androgen associated skin diseases [17,18]. Considering its abovementioned features like rich polyphenolic content; anti-inflammatory, anti-bacterial, anti-candidial, anti-dandruff properties; rich mineral, vitamin, amino acid and phenolic contents; perfusion increasing characteristics, together with the currently reported anti-androgenic activity in HaCaT cells, it can be suggested that *Ud* has a solid scientific base and a promising future in cosmetic dermatology, and new product development against androgenic skin diseases.

Conclusion.

The androgen hormones are indispensable in modulating hair growth, sebum production and sebaceous gland differentiation, and keratinocytes are one of the target cells for androgen actions in skin. The proven antiandrogenic activity of *Ud* extract on skin cells may further encourage developing new products with this plant and performing relevant clinical trials for various androgenic skin diseases.

Conflict of interest.

The authors declare no conflict of interest.

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