creative commons
COMMONS DEED

저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:

저작자표시. 귀하는 원저작자를 표시하여야 합니다.

비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.

변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 이용허락규약(Legal Code)을 이해하기 쉽게 요약한 것입니다.

Disclaimer

dCollection

연세대학교
YONSEI UNIVERSITY

Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species

Dongu Lee

Department of Medicine

The Graduate School, Yonsei University

연세대학교
YONSEI UNIVERSITY

연세대학교
YONSEI UNIVERSITY

Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species

Dongu Lee

Department of Medicine

The Graduate School, Yonsei University

연세대학교
YONSEI UNIVERSITY

Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species

Directed by Professor Seung Hwan Lee

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Dongu Lee

June 2021

연세대학교
YONSEI UNIVERSITY

This certifies that the Master's Thesis
of Dongu Lee is approved.

Thesis Supervisor : Seung Hwan Lee

Thesis Committee Member#1 : Jong Hun Lee

Thesis Committee Member#2 : Hak Jun Seung

The Graduate School
Yonsei University

June 2021

연세대학교
YONSEI UNIVERSITY

ACKNOWLEDGEMENTS

I would like to express my gratitude to Professor Seung Hwan Lee, my supervisor for helping me with sincerity from designing thesis to the end, Prof. Jong Hoon Lee for continuing kindly corrections, the Department of Food Science and Biotechnology at Gachon University for providing research facilities, and Severance Hospital Department of Urology where I am currently working. And also I conveys my special thanks to my family and loved one who supported me both physically and mentally.

`

연세대학교
YONSEI UNIVERSITY

<TABLE OF CONTENTS>

연세대학교
YONSEI UNIVERSITY

LIST OF FIGURES

연세대학교
YONSEI UNIVERSITY

ABSTRACT

Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species

Dongu Lee

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Seung Hwan Lee)

Benign prostate hyperplasia (BPH) is one of the most common elderly disease, and because of prolonged incubation period and many side effects of medication or surgical interventions, the use of dietary phytochemicals is considered as an effective measure for prevention of BPH. The purpose of this study is to investigate the mechanism of inhibition effect for BPH by flavonoids such as baicalein and kaempferol. BPH cells were collected through biopsy from patients with PSA of 4 or higher, followed by primary culture. In vitro experiments were conducted to evaluate mitochondrial respiration, intracellular reactive oxygen species (ROS) level and expression of inflammatory markers, genes, and anti-oxidants. In conclusion, baicalein and kaempferol have been demonstrated to inhibit BPH through lowering ROS, thereby reducing inflammation triggers, and reduced inflammation. This study is expected to be helpful in the development of flavonoids that have a clinical effect on suppressing BPH.

Key words : flavonoid, bph, mitochondria, ros, inflammation

연세대학교
YONSEI UNIVERSITY

Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species

Dongu Lee

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Seung Hwan Lee)

I. INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common urological diseases in elderly people, characterized by low mortality and high morbidity, and is considered as a public health problem[1]. Symptoms caused by prostatic hyperplasia are various and cause anxiety, sleep disturbances, decreased mobility, and difficulty in sexual intercourse, leading to working and social activities disturbance and negatively affect the quality of life[2, 3]. Because of the high incidence, prolonged incubation period of BPH and many side effects of medication or surgical interventions, the use of dietary phytochemicals is considered as an effective measure for prevent BPH[4, 5].

Various types of plant extracts are commercially available, and representatively, there is saw palmetto (Serenoa repens) bean extract, and the brand names are Saw Palmetto in South Korea and Permixon in Europe. The mechanisms of inhibition of prostatic hypertrophy of Serenoa repens extract (SRE) is known as anti-androgen effects, anti-inflammatory effects, and pro-apoptotic properties, but it has not been clearly defined and did not show a significant difference from placebo in one study [6].

Flavonoids are a type of secondary metabolite of plants or fungi classified as anthoxanthin, flavanone, flavanonol, flavan and anthocyanidin. Kaempferol

연세대학교
YONSEI UNIVERSITY

and baicalein are kinds of flavonoids and are well known for their anti-inflammatory properties [7, 8].

It is generally accepted that intracellular reactive oxygen species (ROS), generated from mitochondrial respiration, is associated with inflammation and increase in cell growth factors, which can lead to prostate cancer or prostatic hyperplasia [9-14]. Inflammatory markers such as inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) are associated with BPH induction [15]. Nuclear factor erythroid-2(NFE2)-related factor 2(Nrf2)-Kelch-like ECH-associated protein 1 (Keap1) pathway is an important regulator in protecting cells against oxidative stress. They bind to the antioxidant response element and activate the transcription of major antioxidant enzymes [16, 17].

The purpose of this study is to determine whether the anti-inflammatory action of flavonoids, kaempferol and baicalein, can inhibit BPH through detection of mitochondrial respiration, intracellular ROS level, inflammatory markers such as iNOS and COX-2, and anti-oxidant regulator Nrf2 and Keap1. Identification of the in vitro mechanism of flavonoids can be used as basic data for future clinical applications.

II. MATERIALS AND METHODS

1. Collection of human prostate specimen

Prostate tissue obtained from prostate biopsy samples performed on patients at Severance hospital, South Korea. Prostate biopsy was performed on patients with a prostate specific antigen (PSA) of 4.0 or higher, and only patients with a pathologic report of benign prostatic hyperplasia were involved. The Institutional Review Board of Severance Hospital approved this study protocol (Approval No: 4-2017-0300). Informed consent was waived by the board.

2. Primary cell culture

Primary hyperplastic prostate cells were obtained by cutting the prostate

연세대학교
YONSEI UNIVERSITY

tissue finely, treating it with collagenase and trypsine, and incubating for 5-10 minutes at 37℃. primary cells were cultured using Dulbecco Modified Eagle Medium (DMEM). A complex medium with 10% (w/v) FBS (Fetal Bovine Serum) and 1% (w/v) penicillin streptomycin added to each medium was prepared and used for cultivation. 37℃, 5% CO_2 incubator (Forma 3546, ThermoScientific, Inc., Massachusetts, USA) was used in the experiment while subculturing at intervals of 4 days.

3. Serenoa repens extract preparation

The stock solution of Serenoa repens extract (SRE) was prepared as an ethanolic (20% solution, wt/vol) extract of Saw Palmetto Berry Powder (PharmaPrint, Irvine, CA, USA) with constant agitation for at least 10 hours at room temperature. The solution was filtered through 3 um filter and centrifuged at 1000g for 10 min to remove debris. The extract then concentrated by passing a stream of nitrogen over it and was stored in the dark at room temperature until use [18].

4. Measurement of the cellular energy consumption through mitochondrial respiration

Kaempferol and baicalein are purchased from Sigma-Aldrich (St. Louis, MO, USA). After treatment with 200 nl of SRE and 10 μM of baicalein or kaempferol, measurement of the mitochondrial respiration of primary prostate cells using Agilent Seahorse Xfp (Agilent Technologies, Santa Clara, CA, USA) was processed. Cells cultured with DMEM were treated with materials and cultured for 24 hours. The SRE group was used as positive control group and the untreated group was used as the control group in this experiment. Recovered cells were transferred to an XFp assay plate. The concentration of the cells was maintained at 1×10^4 cells/well, and cultured for 1 hour in a non-CO_2 incubator with DMEM medium supplemented with 4.5g/L D-glucose,

연세대학교
YONSEI UNIVERSITY

L-glutamine, and sodium pyruvate. At this time, the temperature was set to 37℃, and the medium was maintained at pH 7.4. Cells were sequentially treated with mitochondrial inhibitors oligomycin (1.0 μM), Trifluoromethoxy carbonylcyanide phenylhydrazone (FCCP) (1.0 μM), and rotenone/antimycin A (0.5 μM) according to the manufacturer's protocol. Oxygen consumption rate (OCR) and extracellular acidification rate (ECAR), indexes of oxidative phosphorylation, were calculated with Seahorse™ XFp analyzer and software (Agilent Technologies)

5. Intracellular reactive oxygen species (ROS) level measurement

Intracellular ROS level was evaluated using 2'-7'-dichlorofluorescein diacetate (H_2DCFDA; Invitrogen, USA). H_2DCFDA is deacetylated by intracellular esterase to form H_2DCF, which is oxidized by ROS to strong fluorescent compounds, 2', 7'-dichlorofluorescein (DCF). Dichlorofluorescin diacetate (DCFDA; Sigma, USA) was used as a fluorescent probe to measure the change in the concentration of active oxygen in cells. DCFDA, a non-fluorescent substance, is oxidized by ROS in the presence of peroxides related to hydrogenperoxide in the cell, resulting in green fluorescence. Therefore, the measurement of ROS can be made through DCFDA. 2×10^5 primary hyperplastic prostate cells were inoculated into a 60 mm culture dish and cultured for 24 h. After treatment with the sample and H_2O_2, it was cultured for 2 h. Before harvesting the cells, 10μM DCFDA was treated in the medium and cultured for 30 min. Cultured cells were washed with phosphate-buffered saline (PBS) and treated with 1% trypsin-EDTA solution to harvest the cells, washed again with PBS to resuspend the harvested cells, and in preheated PBS containing 10μM DCFDA for 30 minutes at 37℃. After incubation, it was then transferred to a 5 mL FACS tube (SPL Life Science, Pocheon, Korea). Subsequently, the mean fluorescent intensity (MFI) was determined for the 10,000 cells of each sample using a FACS Calibur flow

연세대학교
YONSEI UNIVERSITY

cytometer (Becton Dickinson, NJ, USA) at an excitation wavelength of 488 nm and an emission wavelength of 530 nm. Data analysis was performed using Cell Quest software (USA).

6. Anti-inflammatory gene and protein expression

Observe the expression of iNOS, COX-2, Nrf2, and Keap1 of primary prostate cell groups treated with flavonoids, SRE (positive control) and control untreated group through Western Blotting[19]. After being incubated for 24 hours treated with flavonoids, primary prostate cells were collected and were lysed in 60 μL of NP40 (Invitrogen, USA) containing protease inhibitors and then incubated on ice for 30 to 40 min. Proteins were measured using bicinchoninic acid (BCA) protein assay kits (Thermo Fisher Scientific, USA) and separated by polyacetylamide gel electrophoresis and transferred to polyvinylidene fluoride (PVDF) membranes (Merck Millipore, Germany). The membranes were blocked with 5% bovine serum albumin (BSA) in Tris-buffered saline containing 0.5% tween-20 (T/TBS) for 1 h at room temperature. After blocking, incubation with 1:1000 dilution of primary antibodies for 24 h at 4℃ occurred, using iNOS antibody (1:5000, Calbiochem, USA), COX-2 antibody (1:1000, BD Biosciences Pharmingen, USA), or β-actin antibody (1:10000, Sigma, USA). The membranes were washed four times in T/TBS for 15 min and incubated with secondary antibodies for 1 h, room temperature. After washing three times with T/TBS, separated protein bands were detected with an ImageQuant LSA4000 (GE Healthcare, USA) using ECL solution (Dyne, Korea).

Real-time polymerase chain reaction (RT-PCR) analysis was done to evaluate Nrf2 mRNA level. Primary prostate cells treated with flavonoids were homogenize and separated by centrifugation for 15 minutes at 4℃. The mRNA was isolated using RNeasy columns (Bio-Rad, Hercules, CA, USA) and the cDNA was synthesized using a high-capacity cDNA reverse

연세대학교
YONSEI UNIVERSITY

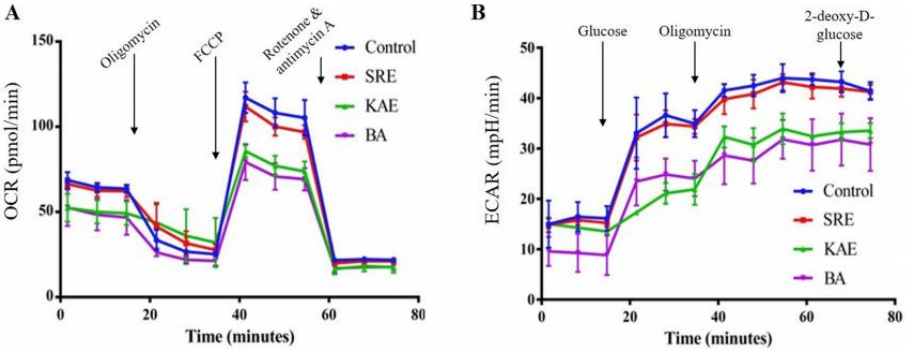
transcriptase kit (Applied Biosystems, Life Technologies, Foster City, CA, USA). RT-PCR was performed using a CFX Real-Time PCR System (Bio-Rad).

III. RESULTS AND DISCUSSION

1. Cellular mitochondrial respiration

OCR and ECAR using oligomycin, FCCP, rotenone and antimycin-A were measured to analyze the change in oxygen consumption more specifically [20]. Oligomycin, ATP synthase inhibitor in the electron transport chain (ETC), is added following the basal measurement to decrease OCR, resulting a reduction in mitochondrial respiration or OCR. Using the difference between basal respiration and oligomycin-stimulated reduced OCR, the oxygen consumption for ATP synthesis can be calculated [21, 22]. Carbonyl cyanide-4 (trifluoromethoxy) phenylhydrazone (FCCP) collapses the proton gradient, making the electron flow unaffected by ETC. Oxygen consumption by complex IV in ETC is maximized [22].

Rotenone and antimycin-A act to shutdown electron transporting systems by inhibiting mitochondrial complexes I and III. Therefore, Using FCCP-stimulated OCRs, the spare respiratory capacity defined as the difference between maximum and basal respiration can be calculated. Spare respiratory capacity refers to the ability of cells to respond to stress or increase their energy demand [22].

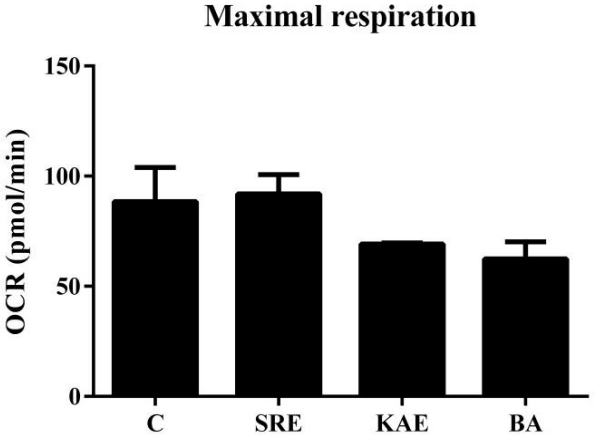


연세대학교
YONSEI UNIVERSITY

Figure 1. Cellular oxygen consumption

(A) Oxygen consumption rate (OCR) and (B) Extracellular acidification rate (ECAR) of hyperplastic prostatic cells treated with flavonoids. Data represent the mean±standard error (n=3).

The OCR and ECAR results are illustrated in Figure 1. The mitochondrial respiration of each sample and control group was measured. In the basal respiration measured before oligomycin was added, it showed that the basal respiration of the sample group was weaker than that of the control and SRE groups. The maximal respiration measured after FCCP addition was also decreased in the sample group compared to the control and SRE groups. In addition, low ECAR after glucose treatment was observed compared to the control and positive control SRE group (Figure 1). In both baicalein and kaempferol treated group, spare respiratory, difference between maximal respiration and basal respiration, were decreased compared with control and SRE groups, since the sample groups showed a remarkable decrease in maximal respiration compared to basal respiration. No significant difference was observed between baicalein and kaempferol (Figure 1, 2). It has been demonstrated that flavonoid treatment caused a decrease in cellular respiration, and it can be inferred that this will lead to a decrease in ROS.



연세대학교
YONSEI UNIVERSITY

Figure 2. Cellular mitochondrial maximal respiration

The maximal mitochondrial respiration was calculated based on OCR. Untreated group was used as control. Data represent the mean±standard error (n = 3).

2. Intracellular ROS level

The generation of intracellular ROS showed through DCF-fluorescence and flow cytometric distribution of DCFDA-stained primary hyperplastic prostate cells were presented in Figure 3.

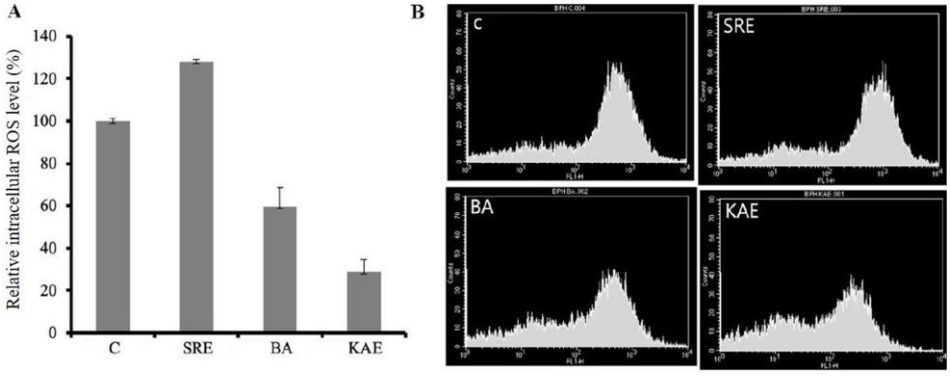


Figure 3. Intracellular reactive oxygen species level

Intracellular ROS level of primary hyperplastic prostate cells treated with flavonoids was measured using H_2DCFDA. (A) Relative intracellular ROS compared to control group. The control group was set to 100 and the MFI values for each group were calculated as relative values. (B) Flow cytometric distribution of DCFDA-stained primary hyperplastic prostate cells. Untreated group was used as control. Data represent the mean±standard error (n=3)

It was determined whether the intracellular ROS level actually decreased in the group treated with baicalein and kaempferol, and the baicalein-treated group showed 40% reduction in ROS concentration compared to the control group without any treatment, and about 60% in kaempferol. These experimental results are consistent with the experimental results in which

연세대학교
YONSEI UNIVERSITY

mitochondrial cell respiration, which is related to the production of active oxygen in cells, decreased (Figure 1~3). Through this, it could be inferred that baicalein and kaempferol would have the effect of preventing BPH through the mechanism of reducing the intracellular ROS level.

3. Anti-inflammatory gene and anti-oxidant expression

In order to elucidate the mechanism of reducing these inflammatory factors, the expression of the inflammatory factors iNOS and COX-2, and the antioxidant enzyme regulator Nrf2 was observed. iNOS and COX-2 are attracting attention as being associated with BPH induction[15].

When the expression level of the untreated control group was set to 1, the expression levels of nuclear factor erythroid-2(NFE2)-related factor 2 (Nrf2), Kelch-like ECH-associated protein 1(Keap1), iNOS, and COX-2 in the positive control SRE group were measured as 0.96, 1.07, 0.98, 1.06, and the baicalein group was 0.87, 0.99, 0.73, 0.91, and the kaempferol group was measured as 0.83, 0.83, 0.53, 0.86, in the same order (Figure 4).

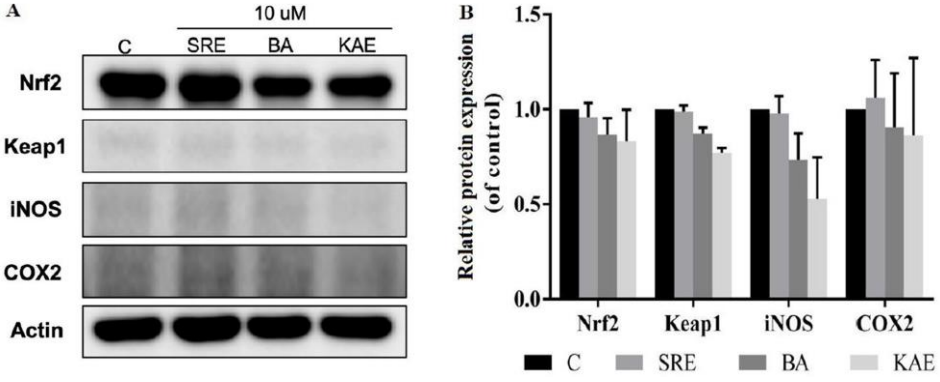


Figure 4. Expressions of anti-oxidants and inflammatory markers

(A) Western blotting analysis for protein expression. (B) Densitometry of repeated western blotting three times. Untreated group was used as control. Data represent the mean±standard error.

연세대학교
YONSEI UNIVERSITY

Nrf2 expression at mRNA level was slightly increased in the group treated with baicalein and SRE, and showed decrease slightly in the group treated with kaempferol (Figure5).

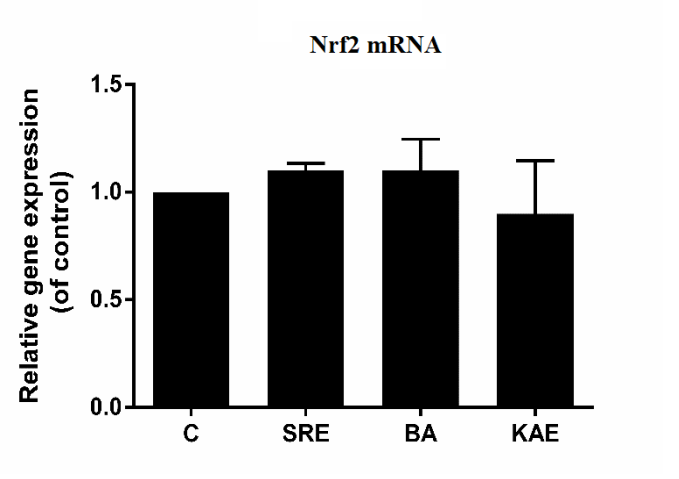


Figure 5. Nrf2 mRNA expression

RT-PCR results for Nrf2 mRNA of hyperplastic prostatic cells treated with flavonoids. Untreated group was used as control. Data represent the mean ± standard error.

Both iNOS and COX-2 decreased in the baicalein and kaempferol groups, and there was no significant difference between the control and SRE groups, especially in the kaempferol-treated group, iNOS decreased by 45% compared to the control group. The expression of Nrf2 was not found to be related to the expression level of Keap1 (Figure 4). Degradation of Keap1 releases Nrf2 bound to keap1 and moves to the nucleus of the cell, resulting in the expression of the downstream antioxidant protein of Nrf2[16]. The increasing in the amount of Nrf2 expression at the mRNA level can be understood as a mechanism to maintain the amount of Nrf2 in the cell due to the decrease in the total amount of Nrf2 (Figure 5).

연세대학교
YONSEI UNIVERSITY

As baicalein and kaempferol showed significant activity against primary prostate cells, the mitochondrial respiration volume, intracellular ROS concentration, and protein level expression of major inflammatory and antioxidant transcription factors were observed. It was confirmed that baicalein and kaempferol induce a decrease in mitochondrial respiration and free radicals in cells, thereby reducing the expression of iNOS and COX-2. This study is considered to be clinically useful because primary culture was performed with cells from patients with BPH rather than normal healthy prostate cells. However, this study has some limitations. At first, overall statistical significance was not secured. Second, this experiment is conducted in vitro, there is a question whether it will be applied equally to the actual human body. Although Prostate cells from BPH patients were used, but further research is needed for actual clinical use. Additional experiments with mice or rats are planned, and according to the results, experiments in humans are being planned.

IV. CONCLUSION

In conclusion, flavonoids such as baicalein and kaempferol have been demonstrated to inhibit BPH through following mechanism: Flavonoids lower ROS, thereby reducing inflammation triggers, and reduced inflammation inhibits BPH. This study is expected to be helpful in the development of flavonoids that have a clinical effect on suppressing BPH.

연세대학교
YONSEI UNIVERSITY

REFERENCES

1. Isaacs JT. Etiology of benign prostatic hyperplasia. Eur Urol. 1994;25 Suppl 1:6-9.
2. Bosch JL, Hop WC, Kirkels WJ, Schroder FH. Natural history of benign prostatic hyperplasia: appropriate case definition and estimation of its prevalence in the community. Urology. 1995 Sep;46(3 Suppl A):34-40.
3. Kirby RS. The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology. 2000 Nov 1;56(5 Suppl 1):3-6.
4. Fourcade RO, Theret N, Taieb C, Group BUS. Profile and management of patients treated for the first time for lower urinary tract symptoms/benign prostatic hyperplasia in four European countries. BJU Int. 2008 May;101(9):1111-8.
5. Dedhia RC, McVary KT. Phytotherapy for lower urinary tract symptoms secondary to benign prostatic hyperplasia. J Urol. 2008 Jun;179(6):2119-25.
6. Keehn A, Lowe FC. Complementary and alternative medications for benign prostatic hyperplasia. Can J Urol. 2015 Oct;22 Suppl 1:18-23.
7. Devi KP, Malar DS, Nabavi SF, Sureda A, Xiao J, Nabavi SM, et al. Kaempferol and inflammation: From chemistry to medicine. Pharmacol Res. 2015 Sep;99:1-10.
8. Lee W, Ku SK, Bae JS. Anti-inflammatory effects of Baicalin, Baicalein, and Wogonin in vitro and in vivo. Inflammation. 2015 Feb;38(1):110-25.
9. Bostanci Y, Kazzazi A, Momtahen S, Laze J, Djavan B. Correlation between benign prostatic hyperplasia and inflammation. Curr Opin Urol. 2013 Jan;23(1):5-10.
10. De Nunzio C, Kramer G, Marberger M, Montironi R, Nelson W, Schroder F, et al. The controversial relationship between benign prostatic hyperplasia and prostate cancer: the role of inflammation. Eur Urol. 2011 Jul;60(1):106-17.
11. Aydin A, Arsova-Sarafinovska Z, Sayal A, Eken A, Erdem O, Erten K, et al. Oxidative stress and antioxidant status in non-metastatic prostate cancer and benign prostatic hyperplasia. Clin Biochem. 2006 Feb;39(2):176-9.
12. Ahmad M, Suhail N, Mansoor T, Banu N, Ahmad S. Evaluation of oxidative stress and DNA damage in benign prostatic hyperplasia patients and comparison with controls. Indian J Clin Biochem. 2012 Oct;27(4):385-8.
13. Kullisaar T, Turk S, Punab M, Mandar R. Oxidative stress--cause or consequence of male genital tract disorders? Prostate. 2012 Jun 15;72(9):977-83.

연세대학교
YONSEI UNIVERSITY

14. Sciarra A, Mariotti G, Salciccia S, Autran Gomez A, Monti S, Toscano V, et al. Prostate growth and inflammation. J Steroid Biochem Mol Biol. 2008 Feb;108(3-5):254-60.
15. Abdel-Aziz AM, Gamal El-Tahawy NF, Salah Abdel Haleem MA, Mohammed MM, Ali AI, Ibrahim YF. Amelioration of testosterone-induced benign prostatic hyperplasia using febuxostat in rats: The role of VEGF/TGFbeta and iNOS/COX-2. Eur J Pharmacol. 2020 Dec 15;889:173631.
16. Lee JH, Khor TO, Shu L, Su Z-Y, Fuentes F, Kong A-NT. Dietary phytochemicals and cancer prevention: Nrf2 signaling, epigenetics, and cell death mechanisms in blocking cancer initiation and progression. Pharmacology & Therapeutics. 2013;137(2):153-71.
17. Kansanen E, Kuosmanen SM, Leinonen H, Levonen AL. The Keap1-Nrf2 pathway: Mechanisms of activation and dysregulation in cancer. Redox Biol. 2013 Jan 18;1:45-9.
18. Goldmann WH, Sharma AL, Currier SJ, Johnston PD, Rana A, Sharma CP. Saw palmetto berry extract inhibits cell growth and Cox-2 expression in prostatic cancer cells. Cell Biol Int. 2001;25(11):1117-24.
19. Mahmood T, Yang PC. Western blot: technique, theory, and trouble shooting. N Am J Med Sci. 2012 Sep;4(9):429-34.
20. Zhang J, Zhang Q. Using Seahorse Machine to Measure OCR and ECAR in Cancer Cells. Methods Mol Biol. 2019;1928:353-63.
21. TeSlaa T, Teitell MA. Techniques to monitor glycolysis. Methods Enzymol. 2014;542:91-114.
22. Lee S, Lee H, Kim KT. Optimization of experimental conditions and measurement of oxygen consumption rate (OCR) in zebrafish embryos exposed to organophosphate flame retardants (OPFRs). Ecotoxicol Environ Saf. 2019 Oct 30;182:109377.

연세대학교
YONSEI UNIVERSITY

APPENDICES

This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Ministry of Science and ICT (No. 2018R1C1B5086106)

This research receives financial support from Handok (No. HANDOK 2017-001)

The authors declare no conflict of interest.

연세대학교
YONSEI UNIVERSITY

ABSTRACT(IN KOREAN)

바이카레인과 카엠페롤과 같은 플라보노이드의 미토콘드리아 호흡 및 새포 내 활성산소 조절을 통한 양성 전립선 비대증 환자 세포내 염증 감소 효과

<지도교수 이승환>

연세대학교 대학원 의학과

이돈구

양성 전립선 증식증은 가장 흔한 노인 질환 중 하나이며, 긴 잠복기와 약물 또는 수술의 부작용으로 인해 식물성 추출물 복용이 예방을 위한 효과적인 방법 중 하나로 간주되고 있습니다. 이 연구의 목적은 바이칼레인과 카엠페롤과 같은 플라보노이드에 의한 전립선 비대증 억제 효과의 메커니즘을 규명하는 것입니다. 전립선 특이 항원 수치가 4 이상인 환자들을 대상으로 생검을 통해 조직을 수집 한 후 1차 배양을 수행하였습니다. 미토콘드리아 호흡, 세포 내 활성 산소 수준 및 염증 인자, 유전자 및 항산화 물질의 발현을 평가하기 위해 시험관 내 실험을 수행했습니다. 결론적으로, 바이칼레인과 카엠페롤은 활성산소 및 염증인자를 낮추어 전립선 비대증을 억제하는 것으로 입증되었습니다. 이 연구는 전립선 비대증 억제에 임상적인 효과가 있는 플라보노이드의 개발에 도움이 될 것으로 기대됩니다.

핵심되는 말 : 플라보노이드, 전립선 비대증, 활성산소

연세대학교
YONSEI UNIVERSITY

PUBLICATION LIST

Lee D, Lee JH, Lee SH. Flavonoids baicalein and kaempferol reduced inflammation in benign prostate hyperplasia patient-derived cells through regulating mitochondrial respiration and intracellular oxygen species. Korean J. Food Sci. Technol. 2021 April; 53-2(16):213-217